Halogen-Lithium Exchange of Sensitive (Hetero)Aromatic Halides under Barbier Conditions in a Continuous Flow Set-up

Supporting Information

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General Information

Solvents
THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen and stored over molecular sieves. Solvents for column chromatography were distilled prior to use.

Reagents
All reagents were obtained from commercial sources and used without further purification.

$n$BuLi solution in hexane was purchased from Albermarle and the concentration was determined by titration against $N$-benzylbenzamide.

$t$BuLi solution in hexane was purchased from Albermarle and the concentration was determined by titration against 1,10-phenanthroline in THF using iPrOH.

Chromatography
Flash column chromatography was performed using SiO$_2$ 60 (0.040-0.063 mm, 230-400 mesh ASTM) from Merck. Thin layer chromatography (TLC) was performed using aluminum plates covered with SiO$_2$ (Merck 60, F-254). Spots were visualized under UV light or with KMnO$_4$.

Analytical Data
Yields refer to isolated yields of compounds estimated to be >95% pure as determined by $^1$H-NMR (25 °C) and capillary GC analysis. NMR spectra were recorded on Bruker ARX 200, AC 300, WH 400 or AMX 600 instruments. Chemical shifts are reported as δ-values in ppm relative to the deuterated solvent peak: CDCl$_3$ (δH: 7.26; δC: 77.16) or CD$_2$Cl$_2$ (δH: 5.32; δC: 54.00). For the observation of the observed signal multiplicities, the following abbreviations were used: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet) and m (multiplet). Melting points are uncorrected and were measured on a Büchi B.540 apparatus. Infrared spectra were recorded from 4000-400 cm$^{-1}$ on a Nicolet 510 FT-IR or a Perkin-Elmer 281 IR spectrometer. Samples were measured (Smiths Detection DuraSampl IR II Diamond ATR). The absorption bands are reported in wavenumbers (cm$^{-1}$). Gas chromatography (GC) was performed with instruments of the type Hewlett-Packard 6890 or 5890 Series II, using a column of the type HP 5 (Hewlett-Packard, 5% phenylmethylpolysiloxane; length: 10 m, diameter: 0.25 mm, film thickness: 0.25 μm). The detection was accomplished using a flame ionization detector. Mass spectra (MS) and high resolution mass spectra (HRMS) were recorded on a Finnigan MAT95Q or Finnigan MAT90 instrument for electron impact ionization (EI) and electrospray ionization (ESI). For the
combination of gas chromatography with mass spectroscopic detection, a GC-MS of the type Hewlett-Packard 6890 / MSD 5793 networking was used (column: HP 5-MS, Hewlett-Packard; 5% phenylmethylpolysiloxane; length: 15 m, diameter 0.25 mm; film thickness: 0.25 μm).

**Typical Procedure**

**General remarks on flow and subsequent batch quenching reactions**

Tetradecane ($n$C$_{14}$H$_{30}$), dodecane ($n$C$_{12}$H$_{26}$) or undecane ($n$C$_{11}$H$_{24}$) were used as internal standards for GC-analysis. All flasks were heat gun dried (650 °C) under vacuum and backfilled with argon after cooling. Syringes, which were used to transfer reagents and solvents, were purged with argon three times prior to use. Batch quenching reactions were carried out with magnetic stirring. Flow reactions were performed on commercially available flow systems. A Vapourtec E-series Integrated Flow Chemistry System with 3rd Pump Kit, Organometallic Kit, Collection Valve Kit and Cryogenic Reaction Kit or an Uniqsis FlowSyn system was used. If the Vapourtec System was used, hexane solutions of $n$BuLi or tBuLi and THF solutions of the remaining reactants were kept in flasks with rubber septa under an argon atmosphere during the reactions. If the Uniqsis system was used, carrier solvents as well as reactant solutions were stored under argon and injected to carrier solvent streams. All reactions were performed in coiled tube reactors. Coiled reactors were made from PFA or PTFE Teflon (I.D. = 0.8 mm or 0.25 mm, O.D. = 1.6 mm) tubing and T-pieces (I.D. = 0.5 mm) were used as mixers. Prior to performing reactions, the systems were dried by flushing with dry THF or hexane (flow rate of all pumps: 1.00 mL/min; run-time: 30 min).
Typical procedure 1 (TP1) using an Uniqsis flow setup (Scheme SI 1) for halogen-lithium exchange of (hetero)aryl halides with nBuLi as exchange reagent in the presence of various electrophiles affording functionalized (hetero)arenes:

Scheme SI 1: Uniqsis flow setup for the halogen-lithium exchange of (hetero)arenes with nBuLi in the presence of various electrophiles. See text for abbreviations.

A nBuLi solution in hexane (0.18 M, 0.9 equiv) and a solution of 2-iodopyridine (5a, 41 mg, 0.20 M, 1.0 equiv) and 2-adamantanone (2c, 30 mg, 0.20 M, 1.0 equiv) in THF were prepared. Injection loop A (vol\text{inj} = 1.00 mL) was loaded with nBuLi as exchange reagent and injection loop B (vol\text{inj} = 1.00 mL) was loaded with a solution containing 5a and 2c. The solutions were simultaneously injected into separate streams of THF, respectively (pump A: THF; pump B: THF; flow rates: 6.00 mL/min), which each passed a pre-cooling loop (vol\text{pre} = 1.00 mL, T\text{1} = -78 °C, residence time: 10 s), before they were mixed in a T-mixer (PTFE, I.D. = 0.5 mm). The combined stream passed a PTFE reactor tube (Vol\text{R} = 0.02 mL; residence time: t\text{1} = 0.1 s, T\text{1} = -78 °C) and was subsequently collected flask. The reaction mixture was quenched with a sat. aq. NH₄Cl solution. The aqueous phase was extracted with EtOAc and the organic phases were dried and filtrated. After removal of the solvent in vacuo, flash column chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7ac as white crystals (45 mg, 0.18 mmol, 98%).
Typical procedure 2 (TP2) using a Vapourtec E-series Integrated Flow Chemistry System (Scheme SI 2) for halogen-lithium exchange of (hetero)aryl halides with $t$BuLi as exchange reagent in the presence of various electrophiles affording functionalized (hetero)arenes:

$t$BuLi (0.40 M; 2.0 equiv) in hexane

2-bromopyridine (5a, 0.20 M; 1.0 equiv)

hexamethylacetone (2j, 0.20 M; 1.0 equiv)

in THF

Scheme SI 2: Vapourtec E-series Integrated Flow Chemistry System for the halogen-lithium exchange of (hetero)arenes with $t$BuLi in the presence of various electrophiles. See text for abbreviations.

A $t$BuLi solution in hexane (0.40 M, 2.0 equiv) and a solution of the 2-bromopyridine (5a, 32 mg, 0.20 M, 1.0 equiv) and hexamethylacetone (2j, 28 mg, 0.20 M, 1.0 equiv) in THF were prepared. The solutions were pumped from their flasks through a suction needle with a flowrate of 6.00 mL/min. After passing a PTFE tubing (vol$^{pre}$ = 1.00, $T^1$ = -40 °C, residence time: 10 s) for precooling, the solutions were mixed in a T-mixer (PTFE, I.D. = 0.5 mm). The combined stream passed a PTFE reactor tube (Vol$^R$ = 0.02 mL; residence time: $t^1$ = 0.1 s, $T^1$ = -40 °C) and was subsequently collected in an empty flask. The reaction mixture was quenched with a sat. aq. NH$_4$Cl solution. The aqueous phase was extracted with EtOAc and the organic phases were dried and filtrated. After removal of the solvent in vacuo, flash column chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7aj as yellow solid (41 mg, 0.19 mmol, 93%).
Preparation of the products

(4-Chlorophenyl)(4-methoxyphenyl)methanol (4aa)

According to the TP1, a solution of 1-chloro-4-iodobenzene (1a, 0.20 m, 48 mg, 0.20 mmol) and p-anisaldehyde (2a, 0.20 m, 27 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.20 m in hexane, 0.20 mmol, 1.00 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 100:0 → 95:5 → 7:3) afforded the title compound 4aa as white solid (47 mg, 0.19 mmol, 95%).

¹H-NMR (400 MHz, CD₂Cl₂): δ / ppm = 7.34 – 7.29 (m, 4H), 7.28 – 7.22 (m, 2H), 6.89 – 6.84 (m, 2H), 5.76 (s, 1H), 3.77 (s, 3H), 2.42 (s, 1H).

¹³C-NMR (100 MHz, CD₂Cl₂): δ / ppm = 159.8, 143.6, 136.6, 133.4, 128.9 (2C), 128.3 (4C), 114.4 (2C), 75.5, 55.8.

The spectra match with the literature values.¹

According to the TP1, a solution of 1,3-difluoro-2-iodobenzene (1b, 0.20 M, 50 mg, 0.20 mmol) and p-anisaldehyde (2a, 0.20 M, 27 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.20 M in hexane, 0.20 mmol, 1.0 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (1.3 s, 0 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 100:0 → 95:5 → 8:2) afforded the title compound 4ba as colorless oil (41 mg, 0.16 mmol, 82%).

**1H-NMR (400 MHz, CDCl₃):** δ / ppm = 7.35 – 7.29 (m, 2H), 7.25 (tt, J = 8.4, 6.4 Hz, 1H), 6.95 – 6.83 (m, 4H), 6.19 (d, J = 8.4 Hz, 1H), 3.79 (s, 3H), 2.73 (dt, J = 9.4, 2.4 Hz, 1H).

**13C-NMR (100 MHz, CDCl₃):** δ / ppm = 160.9 (dd, J = 248.2, 8.3 Hz, 2C), 159.2, 134.4, 129.6 (t, J = 10.7 Hz, 1C), 127.1 (2C), 119.6 (t, J = 16.4 Hz, 1C), 113.9 (2C), 112.4 – 111.8 (m, 2C), 67.6 (t, J = 3.5 Hz, 1C), 55.4.

**IR (Diamond-ATR, neat):** υ / cm⁻¹ = 3415, 2936, 2838, 1623, 1612, 1588, 1510, 1468, 1443, 1418, 1303, 1246, 1231, 1199, 1169, 1113, 1064, 1029, 1010, 991, 868, 841, 805, 789, 766, 721, 692.

**MS (EI, 70 eV):** m/z (%) = 250 (45), 233 (27), 189 (13), 141 (98), 137 (34), 135 (15), 109 (100), 108 (29), 94 (22).

**HRMS (EI):** m/z calc. for [C₁₄H₁₂F₂O₂]: 250.0805; found 250.0799.
(4-Methoxyphenyl)(p-tolyl)methanol (4ca)

According to the TP2, a solution of 1-iodo-4-methylbenzene (1c, 0.20 m, 44 mg, 0.20 mmol) and p-anisaldehyde (2a, 0.20 m, 27 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 m in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 8 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (1.9 s, -20 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1) afforded the title compound 4ca as white solid (32 mg, 0.14 mmol, 70%).

$^{1}$H-NMR (400 MHz, CD₂Cl₂): $\delta$/ ppm = 7.31 – 7.19 (m, 4H), 7.19 – 7.10 (m, 2H), 6.89 – 6.81 (m, 2H), 5.75 (d, $J$ = 3.4 Hz, 1H), 3.77 (s, 3H), 2.32 (s, 3H), 2.25 (dd, $J$ = 3.5, 0.6 Hz, 1H).

$^{13}$C-NMR (100 MHz, CD₂Cl₂): $\delta$/ ppm = 159.6, 142.1, 137.7, 137.2, 129.6 (2C), 128.2 (2C), 126.7 (2C), 114.3 (2C), 76.0, 55.8, 21.3.

The spectra match with the literature values.²

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(4-Iodophenyl)(4-methoxyphenyl)methanol (4da)

According to the TP1, a solution of 1,4-diiodobenzene (1d, 0.20 M, 66 mg, 0.20 mmol) and p-anisaldehyde (2a, 0.20 M, 27 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1) afforded the title compound 4da as white solid (53 mg, 0.16 mmol, 87%).

1H-NMR (400 MHz, CDCl₃): δ / ppm = 7.68 – 7.62 (m, 2H), 7.25 – 7.21 (m, 2H), 7.14 – 7.09 (m, 2H), 6.88 – 6.82 (m, 2H), 5.72 (d, J = 2.9 Hz, 1H), 3.79 (s, 3H), 2.30 (d, J = 3.1 Hz, 1H).

13C-NMR (100 MHz, CDCl₃): δ / ppm = 159.4, 143.8, 137.5 (2C), 135.8, 128.5 (2C), 128.0 (2C), 114.1 (2C), 93.0, 75.4, 55.4.

IR (Diamond-ATR, neat): 𝜈 / cm⁻¹ = 3253, 2833, 1741, 1609, 1510, 1481, 1392, 1249, 1217, 1172, 1110, 1031, 1019, 1000, 856, 830, 813, 799, 773.

MS (EI, 70 eV): m/z (%) = 340 (28), 323 (10), 231 (50), 181 (11), 153 (10), 152 (24), 137 (16), 135 (100), 109 (70), 108 (31), 94 (14), 77 (11).

HRMS (EI): m/z calc. for [C₁₄H₁₃IO₂]: 339.9960; found 339.9955.

m.p. (°C): 94.6 – 96.0.
(3-Bromophenyl)(4-methoxyphenyl)methanol (4ea)

According to the TP1, a solution of 1-bromo-3-iodobenzene (1e, 0.20 M, 57 mg, 0.20 mmol) and p-anisaldehyde (2a, 0.20 M, 27 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 6 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (2.5 s, 0 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 100:0 → 95:5 → 9:1) afforded the title compound 4ea as yellow oil (45 mg, 0.15 mmol, 85%).

$$\text{H-NMR (400 MHz, CDCl}_3\) :}$$ δ / ppm = 7.57 (t, $J = 1.8$ Hz, 1H), 7.40 (ddd, $J = 7.9$, 2.1, 1.1 Hz, 1H), 7.32 – 7.25 (m, 3H), 7.21 (t, $J = 7.8$ Hz, 1H), 6.92 – 6.87 (m, 2H), 5.76 (s, 1H), 3.82 (s, 3H), 2.37 (s, 1H).

$$\text{C-NMR (100 MHz, CDCl}_3\) :}$$ δ / ppm = 159.4, 146.4, 135.7, 130.5, 130.1, 129.5, 128.1 (2C), 125.1, 122.7, 114.2 (2C), 75.3, 55.4.

The spectra match with the literature values.³

(2-Methoxyphenyl)(2-(trifluoromethyl)phenyl)methanol (4fb)

According to the TP2, a solution of 1-bromo-2-(trifluoromethyl)benzene (1f, 0.20 M, 45 mg, 0.20 mmol) and o-anisaldehyde (2b, 0.20 M, 27 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 M in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 4 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (3.8 s, -20 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 85:15) afforded the title compound 4fb as pale yellow oil (41 mg, 0.15 mmol, 73%).

$^1$H-NMR (600 MHz, CDCl₃): $\delta$ / ppm = 7.69 (d, $J = 7.9$ Hz, 1H), 7.66 (d, $J = 7.9$ Hz, 1H), 7.56 (t, $J = 7.6$ Hz, 1H), 7.41 (t, $J = 7.6$ Hz, 1H), 7.28 (d, $J = 7.8$ Hz, 1H), 6.99 (d, $J = 1.8$ Hz, 1H), 6.95 (d, $J = 7.7$ Hz, 1H), 6.84 (dd, $J = 8.2$, 2.6 Hz, 1H), 6.31 (d, $J = 3.2$ Hz, 1H), 3.81 (s, 3H), 2.41 (d, $J = 3.7$ Hz, 1H).

$^{13}$C-NMR (150 MHz, CDCl₃): $\delta$ / ppm = 159.8, 144.6, 142.4, 132.5 (d, $J = 1.0$ Hz), 129.7, 129.6, 127.9, 127.8 (q, $J = 30.1$ Hz), 125.7 (q, $J = 5.8$ Hz), 124.5 (q, $J = 274.1$), 118.9, 113.0, 112.3, 70.8 (q, $J = 2.4$ Hz), 55.3.

The spectra match with the literature values.⁴

Adamanton-2-yl(4-chlorophenyl)methanol (4ac)

According to the TP1, a solution of 1-chloro-4-iodobenzene (1a, 0.20 M, 48 mg, 0.20 mmol) and 2-adamantanone (2c, 0.20 M, 30 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.20 M in hexane, 0.20 mmol, 1.0 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 100:0 → 95:5) afforded the title compound 4ac as white solid (45 mg, 0.17 mmol, 86%).

**¹H-NMR (400 MHz, CDCl₃):** δ / ppm = 7.49 – 7.44 (m, 2H), 7.36 – 7.31 (m, 2H), 2.50 (s, 2H), 2.38 (d, J = 12.5 Hz, 2H), 1.90 (t, J = 2.9 Hz, 1H), 1.73 (d, J = 12.9 Hz, 7H), 1.64 (d, J = 13.4 Hz, 2H), 1.55 (s, 1H).

**¹³C-NMR (100 MHz, CDCl₃):** δ / ppm = 144.0, 133.1, 128.9 (2C), 127.2 (2C), 75.4, 37.7, 35.8 (2C), 34.9 (2C), 33.0 (2C), 27.5, 26.9.

**IR (Diamond-ATR, neat):** $\tilde{\nu}$ / cm⁻¹ = 2931, 2905, 2896, 2849, 1493, 1448, 1093, 1044, 1014, 1000, 970, 932, 911, 822, 720.

**MS (EI, 70 eV):** m/z (%) = 253 (21), 251 (11), 165 (10), 153 (12), 152 (14), 141 (33), 139 (100), 125 (15), 115 (15), 93 (12), 91 (25), 81 (20), 80 (19), 79 (45), 78 (12), 77 (18), 67 (12).

**HRMS (EI):** m/z calc. for [C₁₆H₁₉ClO]: 262.1124; found 262.1121.

**m.p. (°C):** 84.2 – 85.7.
Bis(4-chlorophenyl)(cyclopropyl)methanol (4ad)

According to the TP1, a solution of 1-chloro-4-iodobenzene (1a, 0.20 M, 48 mg, 0.20 mmol) and (4-chlorophenyl)(cyclopropyl)methanone (2d, 0.20 M, 36 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.20 M in hexane, 0.20 mmol, 1.0 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 100:0 → 95:5) afforded the title compound 4ad as colorless oil (51 mg, 0.17 mmol, 87%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 7.38 – 7.33 (m, 4H), 7.30 – 7.26 (m, 4H), 1.87 (s, 1H), 1.60 – 1.51 (m, 1H), 0.63 – 0.58 (m, 2H), 0.47 – 0.42 (m, 2H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 145.4 (2C), 133.3 (2C), 128.4 (4C), 128.3 (4C), 76.6, 21.7, 1.9 (2C).

The spectra match with the literature values.⁵

1-(3-Bromophenyl)cyclohexanol (4ee)

According to the TP1, a solution of 1-bromo-3-iodobenzene (1e, 0.20 M, 57 mg, 0.20 mmol) and cyclohexanone (2e, 0.20 M, 20 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 6 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (2.5 s, 0 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH4Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na2SO4 and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 100:0 → 95:5 → 9:1) afforded the title compound 4ee as colorless oil (42 mg, 0.16 mmol, 91%).

1H-NMR (400 MHz, CDCl3): δ / ppm = 7.66 (t, J = 1.9 Hz, 1H), 7.42 (ddd, J = 7.8, 1.8, 1.1 Hz, 1H), 7.37 (ddd, J = 7.9, 2.0, 1.1 Hz, 1H), 7.21 (t, J = 7.9 Hz, 1H), 1.85 – 1.62 (m, 11H).

13C-NMR (100 MHz, CDCl3): δ / ppm = 152.0, 129.9, 129.8, 128.2, 123.4, 122.6, 73.1, 38.9 (2C), 25.5, 22.2 (2C).

The spectra match with the literature values.6

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2-(4-Iodophenyl)bicyclo[2.2.1]heptan-2-ol (4df)

According to the TPI, a solution of 1,4-diiodobenzene (1d, 0.20 m, 66 mg, 0.20 mmol) and norcamphor (2f, 0.20 m, 22 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 m in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1) afforded the title compound 4df as white crystals (43 mg, 0.14 mmol, 76%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 7.68 – 7.63 (m, 2H), 7.29 – 7.24 (m, 2H), 2.54 – 2.51 (m, 1H), 2.31 (td, J = 5.9, 5.3, 2.5 Hz, 1H), 2.23 (ddd, J = 13.2, 4.9, 2.8 Hz, 1H), 2.19 – 2.10 (m, 1H), 1.68 (s, 1H), 1.66 – 1.60 (m, 1H), 1.55 – 1.41 (m, 4H), 1.34 (ddt, J = 10.1, 3.4, 1.7 Hz, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 148.9, 137.4 (2C), 128.2 (2C), 92.5, 80.7, 47.4, 46.9, 38.9, 37.7, 29.1, 22.4.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 3336, 2941, 2865, 1740, 1579, 1481, 1449, 1385, 1309, 1229, 1142, 1075, 1019, 1000, 972, 958, 869, 846, 816, 810, 752, 698.

MS (EI, 70 eV): m/z (%) = 259 (11), 246 (55), 231 (100), 187 (57), 169 (14), 141 (14), 132 (23).

HRMS (EI): m/z calc. for [C₁₃H₁₅IO]: 314.0168; found 314.0163.

m.p. (°C): 92.8 – 94.9.
(4-Chlorophenyl)(cyclopropyl)(4-iodophenyl)methanol (4dd)

According to the TP1, a solution of 1,4-diiodobenzene (1d, 0.20 M, 66 mg, 0.20 mmol) and (4-chlorophenyl)(cyclopropyl)methanone (2d, 0.20 M, 36 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooling solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1) afforded the title compound 4dd as pale yellow oil (58 mg, 0.15 mmol, 84%).

^1H-NMR (400 MHz, CD₂Cl₂): δ / ppm = 7.67 – 7.63 (m, 2H), 7.40 – 7.35 (m, 2H), 7.32 – 7.27 (m, 2H), 7.21 – 7.16 (m, 2H), 2.00 (s, 1H), 1.56 (tt, J = 8.3, 5.5 Hz, 1H), 0.62 – 0.55 (m, 2H), 0.43 (tdd, J = 5.2, 4.2, 1.7 Hz, 2H).

^13C-NMR (100 MHz, CD₂Cl₂): δ / ppm = 147.3, 146.0, 137.6 (2C), 133.5, 129.4 (2C), 128.9 (2C), 128.6 (2C), 93.3, 77.0, 21.8, 2.2, 2.1.

IR (Diamond-ATR, neat): ̃ν / cm⁻¹ = 3575, 3476, 3079, 3005, 1902, 1593, 1583, 1483, 1399, 1390, 1367, 1362, 1316, 1296, 1164, 1144, 1090, 1060, 1026, 1013, 1005, 982, 959, 943, 926, 894, 877, 871, 810, 761, 733, 723, 701, 682, 677.

MS (EI, 70 eV): m/z (%) = 358 (32), 357 (16), 356 (100), 343 (19), 231 (36), 166 (10), 165 (16), 152 (10), 141 (15), 139 (46).

HRMS (EI): m/z calc. for [C₁₆H₁₄ClIO]: 383.9778; found 383.9775.
2-(3,4-Difluorophenyl)adamantan-2-ol (4gc)

According to the TP2, a solution of 4-bromo-1,2-difluorobenzene (1c, 0.20 M, 39 mg, 0.20 mmol) and 2-adamantanone (2g, 0.20 M, 30 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 M in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 8 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (1.9 s, -20 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 4gc as white solid (35 mg, 0.13 mmol, 66%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 7.34 (ddd, J = 12.5, 7.7, 2.3 Hz, 1H), 7.29 – 7.22 (m, 1H), 7.15 (dt, J = 10.1, 8.4 Hz, 1H), 2.46 (t, J = 2.9 Hz, 2H), 2.41 – 2.31 (m, 2H), 1.90 (h, J = 3.1 Hz, 1H), 1.80 – 1.68 (m, 7H), 1.64 (dt, J = 13.6, 2.5 Hz, 2H), 1.53 (s, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 151.3 (dd, J = 120.5, 12.6 Hz), 148.8 (dd, J = 121.6, 12.6 Hz), 142.8 (t, J = 4.2 Hz), 121.8 (dd, J = 6.1, 3.5 Hz), 117.4 (d, J = 16.9 Hz), 115.1 (d, J = 17.8 Hz), 75.3, 37.6, 35.9 (2C), 34.9 (2C), 33.0 (2C), 27.4, 26.8.

IR (Diamond-ATR, neat): ʋ / cm⁻¹ = 3320, 2939, 2906, 2853, 1605, 1520, 1509, 1449, 1423, 1389, 1361, 1276, 1216, 1191, 1148, 1125, 1112, 1102, 1079, 1045, 1010, 999, 984, 945, 929, 889, 868, 816, 779, 768, 713.

MS (EI, 70 eV): m/z (%) = 264 (13), 247 (15), 246 (100), 221 (15), 204 (13), 141 (43), 127 (11), 115 (10), 91 (10), 81 (11), 79 (12).

HRMS (EI): m/z calc. for [C₁₆H₁₈F₂O]: 264.1326; found 264.1313.

m.p. (°C): 89.9 – 90.4.
1-(3,4-Difluorophenyl)1-phenylethan-1-ol (4gg)

According to the TP2, a solution of 4-bromo-1,2-difluorobenzene (1g, 0.20 m, 39 mg, 0.20 mmol) and acetophenone (2g, 0.20 m, 24 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 M in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 8 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (1.9 s, -20 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 4gg as pale yellow oil (30 mg, 0.13 mmol, 64%).

¹H-NMR (400 MHz, CD₂Cl₂): δ / ppm = 7.42 - 7.39 (m, 2H), 7.35 - 7.24 (m, 4H), 7.13 - 7.09 (m, 2H), 2.34 (s, 1H), 1.92 (s, 3H).

¹³C-NMR (100 MHz, CD₂Cl₂): δ / ppm = 150.4 (dd, J = 246.6, 12.7 Hz), 149.6 (dd, J = 246.6, 12.7 Hz), 147.9, 146.3 (dd, J = 4.7, 3.8 Hz), 128.9 (2C), 127.8, 126.2 (2C), 122.5 (dd, J = 6.3, 3.5 Hz), 117.2 (d, J = 16.9 Hz), 115.7 (d, J = 18.3 Hz), 76.0 (d, J = 1.3 Hz), 31.2.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 3417, 3060, 2981, 1608, 1510, 1493, 1446, 1420, 1373, 1326, 1298, 1275, 1205, 1157, 1111, 1101, 1068, 1027, 940, 917, 903, 875, 822, 802, 774, 759, 709, 697, 681.

MS (EI, 70 eV): m/z (%) = 220 (13), 219 (100).

HRMS (EI): m/z calc. for [C₁₄H₁₂F₂O]: 234.0856; found 234.0844.
2-(p-Tolyl)adamantan-2-ol (4cc)

According to the TP2, a solution of 1-iodo-4-methylbenzene (1c, 0.20 m, 44 mg, 0.20 mmol) and 2-adamantanone (2c, 0.20 m, 30 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 M in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 8 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (1.9 s, -20 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1) afforded the title compound 4cc as white solid (37 mg, 0.15 mmol, 76%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 7.44 (d, J = 8.2 Hz, 2H), 7.19 (d, J = 8.2 Hz, 2H), 2.55 (s, 2H), 2.41 (d, J = 12.3 Hz, 2H), 2.35 (s, 3H), 1.91 (s, 1H), 1.76 – 1.70 (m, 9H), 1.48 (s, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 142.6, 137.0, 129.5 (2C), 125.5 (2C), 75.6, 37.8, 35.8 (2C), 35.1 (2C), 33.1 (2C), 27.6, 27.1, 21.1.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 3450, 2930, 2902, 2887, 2850, 1514, 1449, 1349, 1282, 1192, 1101, 1082, 1047, 1020, 999, 971, 934, 912, 815, 794, 724.

MS (EI, 70 eV): m/z (%) = 242 (34), 227 (29), 224 (43), 199 (16), 121 (19), 119 (100), 106 (11), 105 (10), 93 (17), 91 (28).

HRMS (EI): m/z calc. for [C₁₇H₂₂O]: 242.1671; found 242.1659.

m.p. (°C): 73.6 – 75.4.
1-(p-Tolyl)cyclohexan-1-ol (4ce)

According to the TP2, a solution of 1-iodo-4-methylbenzene (1c, 0.20 m, 44 mg, 0.20 mmol) and cyclohexanone (2e, 0.20 m, 20 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 m in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 8 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (1.9 s, -20 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1) afforded the title compound 4ce as white solid (35 mg, 0.18 mmol, 92%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 7.41 (d, J = 8.2 Hz, 2H), 7.17 (d, J = 8.2 Hz, 2H), 2.35 (s, 3H), 1.86 – 1.71 (m, 7H), 1.66 – 1.61 (m, 2H), 1.57 (s, 1H), 1.36 – 1.26 (m, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 146.6, 136.4, 129.0 (2C), 124.6 (2C), 73.1, 39.0 (2C), 25.7, 22.4 (2C), 21.1.

The spectra match with the literature values.⁷

1-Phenyl-1-(2-(trifluoromethyl)phenyl)ethan-1-ol (4fg)

According to the TP2, a solution of 1-bromo-2-(trifluoromethyl)benzene (1f, 0.20 M, 45 mg, 0.20 mmol) and acetophenone (2g, 0.20 M, 24 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 M in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 4 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (3.8 s, -20 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 85:15) afforded the title compound 4fg as pale yellow oil (32 mg, 0.12 mmol, 60%).

**1H-NMR (400 MHz, CD₂Cl₂):** δ / ppm = 7.75 (dd, J = 8.0, 1.2 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.57 (td, J = 7.8, 0.9 Hz, 1H), 7.47 – 7.41 (m, 1H), 7.32 – 7.21 (m, 5H), 2.52 (s, 1H), 1.98 (s, 3H).

**13C-NMR (100 MHz, CD₂Cl₂):** δ / ppm = 148.8 (d, J = 1.3 Hz), 146.5 (d, J = 1.3 Hz), 132.0 (d, J = 1.1 Hz), 129.8, 128.8 (q, J = 6.8 Hz), 128.6 (2C), 128.3 (q, J = 31.2 Hz), 128.1, 127.5, 125.8 (2C), 125.2 (q, J = 273.9 Hz), 77.6, 33.2 (d, J = 1.4 Hz).

**IR (Diamond-ATR, neat):** ν / cm⁻¹ = 3455, 2983, 1601, 1494, 1445, 1374, 1303, 1290, 1270, 1221, 1163, 1121, 1095, 1080, 1070, 1054, 1032, 1001, 959, 927, 909, 764, 754, 697, 652.

**MS (EI, 70 eV):** m/z (%) = 251 (46), 232 (14), 231 (97), 212 (15), 211 (100), 183 (26).

**HRMS (EI):** m/z calc. for [C₁₅H₁₃F₃O]: 266.0918; found 266.0906.
**N-phenyl-2-(trifluoromethyl)benzamide (4fh)**

![Chemical Structure](image)

According to the TP1, a solution of 1-iodo-2-(trifluoromethyl)benzene (1f, 0.20 M, 54 mg, 0.20 mmol) and phenylisocyanate (2h, 0.20 M, 24 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 9:1) afforded the title compound 4fh as white crystals (42 mg, 0.15 mmol, 83%).

**1H-NMR (400 MHz, CDCl₃):** δ / ppm = 7.74 (d, J = 7.6 Hz, 1H), 7.64 (dd, J = 4.2, 1.3 Hz, 2H), 7.61 – 7.56 (m, 4H), 7.37 (dd, J = 8.6, 7.3 Hz, 2H), 7.18 (t, J = 7.5 Hz, 1H).

**13C-NMR (100 MHz, CDCl₃):** δ / ppm = 165.9, 137.5, 135.9 (q, J = 2.0 Hz), 132.3, 130.3, 129.3 (2C), 128.7, 127.5 (q, J = 31.7 Hz), 126.6 (q, J = 4.9 Hz), 125.2, 123.7 (q, J = 273.8 Hz), 120.4 (2C).

The spectra match with the literature values.⁸

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1-Dodecyl-2-(trifluoromethyl)benzene (4fi)

According to the TP2, a solution of 1-iodo-2-(trifluoromethyl)benzene (1f, 0.20 M, 45 mg, 0.20 mmol) and dodecyl iodide (2i, 0.30 M, 89 mg, 0.30 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 M in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 4 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (3.8 s, -20 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with hexane (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane) afforded the title compound 4fi as colorless oil (48 mg, 0.15 mmol, 77%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 7.60 (dd, J = 7.9, 1.3 Hz, 1H), 7.45 (td, J = 7.6, 1.3 Hz, 1H), 7.32 (d, J = 7.7 Hz, 1H), 7.26 (d, J = 15.3 Hz, 1H), 3.19 (t, J = 7.1 Hz, 3H), 1.82 (p, J = 7.1 Hz, 3H), 1.82 – 2.71 (m, 2H), 1.66 – 1.51 (m, 2H), 1.39 (dt, J = 9.1, 4.1 Hz, 7H), 0.88 (t, J = 6.8 Hz, 8H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 141.8 (q, J = 1.6 Hz), 131.6, 130.9, 128.3 (q, J = 29.7 Hz), 125.8 (q, J = 5.8 Hz), 125.6, 124.7 (d, J = 273.9 Hz), 33.6, 32.8, 32.0, 30.5, 29.7, 29.6, 29.5, 29.4, 28.6, 22.7, 14.2, 7.4.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 2955, 2922, 2853, 1466, 1456, 1312, 1167, 1122, 1060, 1035, 766, 721, 654.

MS (EI, 70 eV): m/z (%) = 161 (10), 160 (100), 159 (43), 109 (10), 91 (21).

HRMS (EI): m/z calc. for [C₁₉H₂₉F₃]: 314.2221; found 314.2213.

SI-23
Ethyl 4-(1-hydroxy-1-phenylethyl)benzoate (4hg)

According to the **TP1**, a solution of ethyl 4-iodobenzoate (1h, 0.20 M, 55 mg, 0.20 mmol) and acetophenone (2g, 0.20 M, 24 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.20 M in hexane, 0.20 mmol, 1.0 equiv) were prepared. The precoolied solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 4hg as pale yellow oil (49 mg, 0.18 mmol, 91%).

**1H-NMR (400 MHz, CD₂Cl₂):** δ / ppm = 7.98 – 7.93 (m, 2H), 7.53 – 7.48 (m, 2H), 7.43 – 7.39 (m, 2H), 7.35 – 7.29 (m, 2H), 7.27 – 7.22 (m, 1H), 4.33 (q, J = 7.1 Hz, 2H), 2.40 (s, 1H), 1.96 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H).

**13C-NMR (100 MHz, CD₂Cl₂):** δ / ppm = 166.8, 153.7, 148.1, 129.8 (2C), 129.7, 128.8 (2C), 127.7, 126.3 (2C), 126.3 (2C), 76.5, 61.4, 31.0, 14.7.

The spectra match with the literature values.⁹

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2,2,4,4-Tetramethyl-3-(pyridin-2-yl)pentan-3-ol (7aj)

According to the TP2, a solution of 2-bromopyridine (5a, 0.20 M, 31 mg, 0.20 mmol) and 2,2,4,4-tetramethylpentan-3-one (2j, 0.20 M, 28 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 M in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -40 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7aj as yellow solid (41 mg, 0.19 mmol, 93%).

^1H-NMR (400 MHz, CDCl₃): δ / ppm = 8.50 (ddd, J = 5.0, 1.7, 1.2 Hz, 1H), 7.64 (ddd, J = 8.9, 6.9, 1.8 Hz, 1H), 7.60 (dt, J = 8.2, 1.3 Hz, 1H), 7.20 (ddd, J = 6.9, 5.0, 1.3 Hz, 1H), 1.04 (s, 18H).

^13C-NMR (100 MHz, CDCl₃): δ / ppm = 162.5, 145.9, 135.1, 123.4, 121.9, 82.0, 41.5 (2C), 29.6 (6C).

The spectra match with the literature values.¹⁰

2-(Pyridin-2-yl)adamantan-2-ol (7ac)

According to the TP1, a solution of 2-iodopyridine (5a, 0.20 M, 41 mg, 0.20 mmol) and 2-adamantanone (2c, 0.20 M, 30 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7ac as white crystals (45 mg, 0.18 mmol, 98%).

1H-NMR (400 MHz, CDCl₃): δ / ppm = 8.58 (ddd, J = 4.8, 1.9, 1.0 Hz, 1H), 7.68 (td, J = 7.8, 1.9 Hz, 1H), 7.49 (dt, J = 8.0, 1.1 Hz, 1H), 7.16 (ddd, J = 7.5, 4.8, 1.1 Hz, 1H), 2.67 (q, J = 3.3 Hz, 2H), 2.49 – 2.35 (m, 2H), 2.16 (s, 1H), 1.90 (p, J = 3.1 Hz, 1H), 1.83 – 1.60 (m, 9H).

13C-NMR (100 MHz, CDCl₃): δ / ppm = 164.3, 149.4, 136.7, 122.2, 120.3, 37.9, 35.1 (2C), 35.0 (2C), 33.0 (2C), 27.5, 27.2.

The spectra match with the literature values.¹¹

(4-Chlorophenyl)(cyclopropyl)(pyridin-2-yl)methanol (7ad)

According to the TP1, a solution of 2-iodopyridine (5a, 0.20 M, 41 mg, 0.20 mmol) and (4-chlorophenyl)(cyclopropyl)methanone (2d, 0.20 M, 36 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precoolied solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7ad as colorless oil (50 mg, 0.18 mmol, 99%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.48 (ddd, J = 4.9, 1.7, 1.0 Hz, 1H), 7.63 (td, J = 7.7, 1.7 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.28 – 7.15 (m, 4H), 5.74 (s, 1H), 1.59 (tt, J = 8.2, 5.3 Hz, 1H), 0.67 – 0.54 (m, 2H), 0.45 (dt, J = 9.5, 5.5, 4.3 Hz, 1H), 0.35 (dddd, J = 9.0, 8.1, 6.1, 4.2 Hz, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 163.8, 147.1, 145.3, 137.1, 133.1, 128.7 (2C), 128.3 (2C), 122.4, 121.2, 75.0, 20.5, 1.9, 0.8.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 3339, 3009, 1592, 1571, 1489, 1469, 1433, 1397, 1356, 1302, 1294, 1211, 1192, 1152, 1091, 1048, 1014, 994, 958, 884, 872, 824, 772, 749, 733, 720, 684.

MS (EI, 70 eV): m/z (%) = 258 (14), 244 (10), 240 (16), 230 (16), 225 (20), 218 (23), 207 (19), 204 (14), 167 (16), 154 (10), 148 (13), 141 (25), 139 (78), 134 (58), 132 (20), 125 (17), 124 (12), 115 (13), 106 (28), 96 (54), 93 (21), 79 (37), 78 (100), 75 (28).

HRMS (EI): m/z calc. for [C₁₅H₁₄ClNO]: 259.0764; found 258.0680 (M – H).
Pyridin-2-yl(4-(trifluoromethyl)phenyl)methanone (7ak)

According to the TP1, a solution of 2-iodopyridine (5a, 0.20 M, 41 mg, 0.20 mmol) and N-methoxy-N-methyl-4-(trifluoromethyl)benzamide (2k, 0.20 M, 33 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1) afforded the title compound 7ak as yellow oil (30 mg, 0.11 mmol, 62%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.73 (ddd, J = 4.7, 1.6, 0.9 Hz, 1H), 8.23 – 8.09 (m, 3H), 7.95 (td, J = 7.7, 1.7 Hz, 1H), 7.75 (d, J = 8.2 Hz, 2H), 7.54 (ddd, J = 7.6, 4.8, 1.2 Hz, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 192.9, 154.2, 148.8, 139.4, 137.5, 133.9 (q, J = 32.6 Hz), 131.4 (2C), 126.9, 125.2 (q, J = 3.7 Hz, 2C), 124.9, 123.8 (q, J = 273 Hz).

The spectra match with the literature values.¹²

According to the TPI, a solution of 2-iodopyridine (5a, 0.20 M, 41 mg, 0.20 mmol) and N,1-diphenylmethanimine (2l, 0.20 M, 36 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flow rate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1) afforded the title compound 7al as brown oil (29 mg, 0.12 mmol, 59%).

1H-NMR (400 MHz, CDCl₃): δ / ppm = 8.60 (d, J = 4.3 Hz, 1H), 7.62 (td, J = 7.7, 1.7 Hz, 1H), 7.46 (d, J = 7.3 Hz, 2H), 7.38 (d, J = 7.9 Hz, 1H), 7.33 (t, J = 7.5 Hz, 2H), 7.25 (d, J = 7.0 Hz, 1H), 7.19 – 7.08 (m, 3H), 6.68 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 7.7 Hz, 2H), 5.59 (s, 1H), 5.46 (s, 1H).

13C-NMR (100 MHz, CDCl₃): δ / ppm = 160.9, 149.2, 147.0, 142.5, 136.9, 129.2 (2C), 128.9 (2C), 127.6, 127.4 (2C), 122.3, 121.9, 117.5, 113.6 (2C), 63.3.

The spectra match with the literature values.¹³

2-(Pyridin-3-yl)adamantan-2-ol (7bc)

According to the TP2, a solution of 3-bromopyridine (5b, 0.20 M, 31 mg, 0.20 mmol) and 2-adamantanone (2c, 0.20 M, 30 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of tBuLi (0.40 M in hexane, 0.40 mmol, 2.0 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7bc as white crystals (27 mg, 0.12 mmol, 60%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.63 (d, J = 2.4 Hz, 1H), 8.42 (dd, J = 4.8, 1.6 Hz, 1H), 7.82 (dt, J = 8.1, 2.1 Hz, 1H), 7.27 (dd, J = 8.0, 4.7 Hz, 1H), 2.53 (q, J = 3.1 Hz, 2H), 2.42 (dd, J = 12.8, 3.2 Hz, 2H), 1.91 (t, J = 3.2 Hz, 1H), 1.81 – 1.67 (m, 7H), 1.61 (dt, J = 13.2, 2.7 Hz, 2H), 1.24 (s, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 147.8, 147.5, 141.0, 133.9, 123.7, 74.6, 37.7, 35.4 (2C), 34.7 (2C), 32.8 (2C), 31.53, 2909, 2895, 2851, 1449, 1418, 1104, 1048, 1044, 1028, 1016, 970, 939, 808, 714, 702.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 3153, 2909, 2895, 2851, 1449, 1418, 1104, 1048, 1044, 1028, 1016, 970, 939, 808, 714, 702.

MS (EI, 70 eV): m/z (%) = 228 (22), 211 (100), 186 (16), 168 (21), 156 (16), 151 (56), 134 (28), 132 (16), 130 (19), 122 (18), 118 (19), 117 (25), 109 (21), 108 (47), 106 (79), 93 (25), 91 (43), 81 (57), 80 (63), 79 (86), 78 (76), 77 (40), 67 (22).

HRMS (EI): m/z calc. for [C₁₅H₁₉NO]: 229.1467; found 229.1462.

m.p. (°C): 148.0 – 148.7.

The spectra match with the literature values.¹⁴

2-(5-Bromopyridin-2-yl)adamantan-2-ol (7cc)

According to the TP1, a solution of 5-bromo-2-iodopyridine (5c, 0.20 m, 47 mg, 0.20 mmol) and 2-adamantanone (2c, 0.20 m, 30 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 8 mL/min flowrate in a T-mixer. The combined stream passed a 0.25 mL reactor tube (1.88 s, -20 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7cc as white crystals (37 mg, 0.12 mmol, 64%).

**¹H-NMR (400 MHz, CDCl₃):** δ / ppm = 8.73 (d, J = 2.3 Hz, 1H), 8.59 (d, J = 2.4 Hz, 1H), 7.98 (dd, J = 8.4, 2.2 Hz, 1H), 7.80 (dd, J = 8.5, 2.4 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.28 (dd, J = 8.5, 0.8 Hz, 1H), 2.61 (t, J = 2.9 Hz, 2H), 2.39 (dd, J = 12.7, 3.1 Hz, 2H), 2.19 (s, 1H), 1.93 – 1.86 (m, 1H), 1.81 – 1.66 (m, 6H), 1.60 (dt, J = 13.3, 2.7 Hz, 3H).

**¹³C-NMR (100 MHz, CDCl₃):** δ / ppm = 163.3, 162.9, 155.2, 150.3, 145.0, 139.3, 122.4, 121.9, 119.1, 91.6, 37.7, 35.1, 35.0, 34.9, 32.9, 32.9, 27.4, 27.0.

**IR (Diamond-ATR, neat):** ν / cm⁻¹ = 3367, 2946, 2916, 2892, 2854, 1462, 1451, 1406, 1372, 1354, 1336, 1102, 1092, 1056, 1045, 1004, 975, 942, 916, 841, 832.

**MS (EI, 70 eV):** m/z (%) = 307 (19), 206 (11), 205 (10), 158 (10), 88 (22), 86 (13), 84 (18), 73 (15), 70 (16), 61 (36), 45 (11), 43 (100).

**HRMS (EI):** m/z calc. for [C₁₅H₁₈BrNO]: 307.0572; found 307.0576.

**m.p. (°C):** 115.7 – 117.3.
3-(5-Bromopyridin-2-yl)-2,4-dimethylpentan-3-ol (7cm)

According to the TPI, a solution of 5-bromo-2-iodopyridine (5c, 0.20 m, 47 mg, 0.20 mmol) and 2,4-dimethylpentan-3-one (2m, 0.20 m, 23 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 8 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.15 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7cm as yellow oil (27 mg, 0.11 mmol, 53%).

1H-NMR (400 MHz, CDCl₃): δ / ppm = 8.74 (dd, J = 2.1, 0.8 Hz, 1H), 8.60 (dd, J = 2.3, 0.8 Hz, 1H), 8.45 (dd, J = 2.6, 0.7 Hz, 1H), 7.96 (dd, J = 8.4, 2.1 Hz, 1H), 7.79 (dd, J = 8.5, 2.3 Hz, 1H), 7.60 (dd, J = 8.3, 0.7 Hz, 1H), 7.45 (dd, J = 8.3, 2.6 Hz, 1H), 7.19 (dd, J = 8.5, 0.8 Hz, 1H), 7.09 (dd, J = 8.4, 0.9 Hz, 1H), 4.98 (s, 1H), 2.33 – 2.24 (m, 2H), 0.80 (d, J = 6.7 Hz, 6H), 0.76 (d, J = 6.9 Hz, 6H).

13C-NMR (100 MHz, CDCl₃): δ / ppm = 160.6, 153.2, 152.0, 148.3, 144.2, 140.5, 138.7, 136.2, 122.7, 122.1, 118.9, 91.0, 80.1, 34.4, 17.6, 16.8.

IR (Diamond-ATR, neat): 𝜈 / cm⁻¹ = 3417, 2963, 2933, 2876, 1464, 1440, 1381, 1359, 1318, 1288, 1237, 1209, 1178, 1158, 1136, 1128, 1100, 1092, 1068, 1017, 1001, 957, 926, 918, 874, 865, 827, 762, 738.

MS (EI, 70 eV): m/z (%) = 61 (15), 45 (12), 43 (100).

HRMS (EI): m/z calc. for [C₁₂H₁₈BrNO]: 271.0572; found 229.9995 (M – C₃H₈).
(4-Chlorophenyl)(cyclopropyl)(2-methylpyridin-3-yl)methanol (7dd)

According to the TP1, a solution of 3-iodo-2-methylpyridine (5d, 0.20 M, 44 mg, 0.20 mmol) and (4-chlorophenyl)(cyclopropyl)methanone (2d, 0.20 M, 36 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 6:4) afforded the title compound 7dd as white solid (42 mg, 0.15 mmol, 81%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.40 (dd, J = 4.8, 1.7 Hz, 1H), 8.32 (dd, J = 7.9, 1.7 Hz, 1H), 7.35 – 7.29 (m, 2H), 7.29 – 7.21 (m, 3H), 2.57 (s, 1H), 2.19 (s, 3H), 1.59 (tt, J = 8.0, 5.6 Hz, 1H), 0.73 – 0.58 (m, 3H), 0.49 – 0.40 (m, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 158.3, 147.9, 144.0, 140.1, 134.8, 133.0, 128.3 (2C), 127.7 (2C), 120.6, 76.1, 24.5, 22.1, 2.2, 2.0.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 1576, 1494, 1484, 1456, 1431, 1194, 1178, 1144, 1104, 1092, 1024, 1013, 988, 976, 963, 890, 878, 829, 804, 792, 784, 735, 728, 716.

MS (EI, 70 eV): m/z (%) = 247 (29), 246 (16), 245 (88), 232 (23), 141 (11), 139 (31), 120 (32), 93 (10), 92 (18), 88 (15), 73 (13), 70 (15), 61 (23), 45 (14), 43 (100).

HRMS (EI): m/z calc. for [C₁₆H₁₆ClNO]: 273.0920; found 273.0909.

According to the TP1, a solution of 3-iodo-2-methylpyridine (5d, 0.20 M, 44 mg, 0.20 mmol) and benzophenone (2n, 0.20 M, 36 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, iso/hexane:EtOAc = 6:4) afforded the title compound 7dn as white crystals (49 mg, 0.17 mmol, 92%).

^1H-NMR (400 MHz, CDCl₃): δ / ppm = 8.40 (dt, J = 4.9, 1.6 Hz, 1H), 7.39 – 7.28 (m, 6H), 7.25 – 7.18 (m, 4H), 7.10 – 6.94 (m, 2H), 3.20 (dd, J = 10.0, 3.6 Hz, 1H), 2.36 (s, 3H).

^13C-NMR (100 MHz, CDCl₃): δ / ppm = 159.0, 148.0, 145.8 (2C), 140.3, 136.9 (2C), 128.4 (4C), 127.7 (5C), 120.1, 82.2, 25.5.

IR (Diamond-ATR, neat): \(\tilde{\nu} / \text{cm}^{-1} = 3079, 1588, 1575, 1489, 1434, 1339, 1266, 1186, 1159, 1118, 1047, 1026, 908, 899, 806, 756, 738, 701.

MS (EI, 70 eV): \(m/z\) (%) = 198 (35), 196 (12), 184 (14), 183 (100), 155 (15), 154 (24), 120 (37), 105 (75), 93 (64), 92 (23), 77 (25).

HRMS (EI): \(m/z\) calc. for [C₁₉H₁₇NO]: 275.1310; found 275.1306.

m.p. (°C): 146.1 – 148.1.
Cyclobutyl(phenyl)(pyrimidin-2-yl)methanol (7eo)

According to the TP1, a solution of 2-iodopyrimidine (5e, 0.20 M, 41 mg, 0.20 mmol) and cyclobutyl(phenyl)methanone (2o, 0.20 M, 32 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7eo as white solid (37 mg, 0.14 mmol, 79%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.70 (d, J = 4.8 Hz, 2H), 7.75 – 7.66 (m, 2H), 7.29 (ddd, J = 7.7, 6.9, 1.2 Hz, 2H), 7.22 – 7.17 (m, 1H), 7.15 (t, J = 4.9 Hz, 1H), 5.50 (d, J = 0.7 Hz, 1H), 3.85 – 3.66 (m, 1H), 2.21 – 2.08 (m, 1H), 2.02 – 1.88 (m, 1H), 1.88 – 1.71 (m, 3H), 1.64 – 1.52 (m, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ / ppm = 171.8, 156.8 (2C), 144.3, 128.0 (2C), 127.0, 126.4 (2C), 119.2, 78.7, 44.1, 22.4, 21.7, 17.4.

IR (Diamond-ATR, neat): ʋ / cm⁻¹ = 3441, 2982, 2937, 2856, 1562, 1490, 1446, 1434, 1412, 1369, 1320, 1243, 1214, 1189, 1149, 1092, 1070, 1031, 1010, 996, 968, 920, 899, 891, 826, 810, 788, 756, 733, 702, 684.

MS (EI, 70 eV): m/z (%) = 186 (13), 185 (100), 107 (14), 105 (12), 97 (10), 79 (10), 77 (10).

HRMS (EI): m/z calc. for [C₁₅H₁₆N₂O]: 240.1263; found 240.1256.

m.p. (°C): 84.8 – 85.6.
Diphenyl(pyrimidin-2-yl)methanol (7en)

According to the TP1, a solution of 2-iodopyrimidine (5e, 0.20 M, 41 mg, 0.20 mmol) and benzophenone (2n, 0.20 M, 36 mg, 0.20 mmol) in THF (total volume: 1.00 mL) and a solution of nBuLi (0.18 M in hexane, 0.18 mmol, 0.9 equiv) were prepared. The precooled solutions were mixed with an overall 12 mL/min flowrate in a T-mixer. The combined stream passed a 0.02 mL reactor tube (0.1 s, -78 °C) and was subsequently injected in an empty flask. Stirring was continued for 10 min at 25 °C before sat. aq. NH₄Cl solution was added to quench the reaction. The aqueous phase was extracted three times with EtOAc (3×30 mL) and the combined organic phases were dried over anhydrous Na₂SO₄ and filtrated. After removal of the solvent flash chromatographical purification (silica gel, isohexane:EtOAc = 95:5 → 9:1 → 8:2) afforded the title compound 7en as white solid (51 mg, 0.18 mmol, 99%).

1H-NMR (400 MHz, CDCl₃): δ / ppm = 8.78 (d, J = 4.9 Hz, 2H), 7.48 – 7.43 (m, 4H), 7.34 – 7.26 (m, 6H), 7.24 (d, J = 4.9 Hz, 1H), 6.05 (s, 1H).

13C-NMR (100 MHz, CDCl₃): δ / ppm = 172.1, 156.8 (3C), 145.3, 128.1 (4C), 128.0 (4C), 127.5 (2C), 119.4, 81.2.

IR (Diamond-ATR, neat): ̃ / cm⁻¹ = 3382, 3064, 1597, 1564, 1493, 1483, 1448, 1434, 1418, 1381, 1320, 1251, 1211, 1178, 1166, 1101, 1091, 1077, 1051, 1033, 997, 987, 943, 934, 923, 898, 857, 846, 813, 796, 765, 756, 724, 700, 660.

MS (EI, 70 eV): m/z (%) = 263 (11), 262 (54), 185 (56), 183 (35), 165 (13), 157 (31), 152 (11), 107 (23), 105 (100), 80 (14), 79 (24), 77 (76).

HRMS (EI): m/z calc. for [C₁₇H₁₄N₂O]: 262.1106; found 262.1099.

m.p. (°C): 111.8 – 113.7.

The spectra match with the literature values.¹⁵

NMR data

(4-Chlorophenyl)(4-methoxyphenyl)methanol (4aa)
(2,6-Difluorophenyl)(4-methoxyphenyl)methanol (4ba)
(4-Methoxyphenyl)(p-tolyl)methanol (4ca)
(4-Iodophenyl)(4-methoxyphenyl)methanol (4da)
(3-Bromophenyl)(4-methoxyphenyl)methanol (4ea)
(2-Methoxyphenyl)(2-(trifluoromethyl)phenyl)methanol (4fb)
Adamanton-2-yl(4-chlorophenyl)methanol (4ac)
Bis(4-chlorophenyl)(cyclopropyl)methanol (4ad)
1-(3-Bromophenyl)cyclohexanol (4ee)
2-(4-Iodophenyl)bicyclo[2.2.1]heptan-2-ol (4df)
(4-Chlorophenyl)(cyclopropyl)(4-iodophenyl)methanol (4dd)
2-(3,4-Difluorophenyl)adamantan-2-ol (4gc)
1-(3,4-Difluorophenyl)1-phenylethan-1-ol (4gg)
2-(p-Tolyl)adamantan-2-ol (4cc)
1-(p-Tolyl)cyclohexan-1-ol (4ce)
1-Phenyl-1-(2-(trifluoromethyl)phenyl)ethan-1-ol (4fg)
*N*-phenyl-2-(trifluoromethyl)benzamide (4fh)
1-Dodecyl-2-(trifluoromethyl)benzene (4fi)

\[
\text{CF}_3 \\
\text{C}_{12}\text{H}_{25}
\]
Ethyl 4-(1-hydroxy-1-phenylethyl)benzoate (4hg)
2,2,4,4-Tetramethyl-3-(pyridin-2-yl)pentan-3-ol (7aj)
2-(Pyridin-2-yl)adamantan-2-ol (7ac)
(4-Chlorophenyl)(cyclopropyl)(pyridin-2-yl)methanol (7ad)
(2-Methylpyridin-3-yl)diphenylmethanol (7ak)
$N$-(phenyl(pyridin-2-yl)methyl)aniline (7al)
2-(Pyridin-3-yl)adamantan-2-ol (7bc)
2-(5-Bromopyridin-2-yl)adamantan-2-ol (7cc)
3-(5-Bromopyridin-2-yl)-2,4-dimethylpentan-3-ol (7cm)
(4-Chlorophenyl)(cyclopropyl)(2-methylpyridin-3-yl)methanol (7dd)
(2-Methylpyridin-3-yl)diphenylmethanol (7dn)
Cyclobutyl(phenyl)(pyrimidin-2-yl)methanol (7eo)
Diphenyl(pyrimidin-2-yl)methanol (7en)