

Supporting Information

Preparation of Tertiary Amines from Tris-(2-cyanoethyl)amine Using Three Successive Cobalt-Catalyzed Electrophilic Aminations with Organozinc Halides

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General Information

All reactions were carried out under an argon atmosphere in flame-dried glassware. Syringes, which were used to transfer anhydrous solvents or reagents, were purged with argon prior to use. THF was continuously refluxed and freshly distilled from sodium benzophenone under nitrogen and stored over molecular sieves (4 Å). EtOAc was purchased from Sigma-Aldrich with a purity of 99 % and used without distillation or drying prior to use. Yields refer to isolated yields of compounds estimated to be >95% purity as determined by ¹H-NMR (25 °C) and capillary gas-chromatographical analyses. Column chromatographical purifications were performed using SiO₂ (0.040-0.063 mm, 230–400 mesh ASTM) from Merck.

Melting points were measured using a Büchi B-540 apparatus and are uncorrected. NMR spectra were recorded in CDCl₃ and chemical shifts are reported in parts per million (ppm); CDCl₃ ¹H: 7.26 ppm; ¹³C: 77.16 ppm. Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; p = quintet; hep = sextet, m, multiplet. Mass spectra and high resolution mass spectra (HRMS) were recorded using electron ionization (EI) except otherwise noted. Gas-chromatographical analyses were performed on machines of the types hewlett-Packard 6890 or 5890 Series II (Hewlett Packard, 5 % phenylmethylpolysiloxane; length: 10 m, diameter: 0.25 mm; film thickness: 0.25 μm). All reagents not listed in the Supporting Information (SI) were obtained from commercial sources.

Titration of Organozinc Reagents Using Iodine¹

Accurately weighted aliquots of the iodine (50 mg, 0.20 mmol) were dissolved in dry THF (2 mL). To the resulting solution the organozinc reagent was added till complete disappearance of the dark brown colour of iodine. Thus, the concentration of the active species (in mmol/mL) is determined and thereof the yield of the zinc reagent.²

¹ A. Krasovskiy, P. Knochel, *Synthesis* **2006**, 2006, 890-891.

² A. Krasovskiy, P. Knochel *Synthesis* **2006**, 5, 890-891.

Typical Procedures

TP1: Typical Procedure for the Preparation of the Organozinc Chlorides by Halogen-Magnesium Exchange and Subsequent Transmetalation with ZnCl₂³

A dry and argon flushed Schlenk-flask equipped with a magnetic stirring bar and a septum was charged with the aryl halide (5.00 mmol, 1.00 equiv) and dissolved in dry THF (15 mL). The reaction mixture was set to the appropriate temperature, before *i*PrMgCl·LiCl (4.30 mL, 1.28 M, 5.50 mmol, 1.10 equiv) was added dropwise. The progress of the halogen-magnesium exchange was monitored by GC-analysis of reaction aliquots quenched with aq. sat. NH₄Cl solution and/or I₂. Upon completion of the exchange, ZnCl₂ (1 M in THF, 6.00 mL, 6.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C and the mixture was allowed to slowly warm up to 25 °C. After stirring at ambient temperature for 15 min, the mixture was titrated using iodine in order to determine its actual content in zinc species and the yield of the reaction.

TP2: Typical Procedure for the Preparation of the Organozinc Chlorides by Magnesium Insertion and Subsequent Transmetalation with ZnCl₂⁴

A dry and argon flushed Schlenk-flask equipped with a magnetic stirring bar and a septum was charged with anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv), magnesium turnings (122 mg, 5.00 mmol, 2.00 equiv) and suspended in dry THF (5 mL). The alkyl or aryl halide (2.50 mmol, 1.00 equiv) was added in one portion and the magnesium activated by gentle heating. After the exothermic reaction started, the reaction mixture was cooled to rt and stirred for the indicated time. Upon completion of the insertion, ZnCl₂ (1 M in THF, 3.00 mL, 3.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C and the mixture was allowed to slowly warm up to 25 °C. After stirring at ambient temperature for 15 min, the mixture was titrated using iodine in order to determine its actual content in zinc species and the yield of the reaction.

TP3: Typical Procedure for the Preparation of the Organozinc halides by Zinc Insertion⁵

³ A. Krasovskiy, P. Knochel *Angew. Chem. Int. Ed.* **2004**, *43*, 3333-3336.

⁴ F. M. Piller, P. Appukkuttan, A. Gavryushin, M. Helm, P. Knochel *Angew. Chem. Int. Ed.* **2008**, *47*, 6802-6806.

⁵ A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel *Angew. Chem. Int. Ed.* **2006**, *45*, 6040-6044.

A dry and argon flushed Schlenk-flask equipped with a magnetic stirring bar and a septum was charged with anhydrous LiCl (127 mg, 3.00 mmol, 1.20 equiv) and zinc dust (245 mg, 3.75 mmol, 1.50 equiv) and suspended in dry THF (5 mL). Zinc was activated with 1,2-dibromoethane (5 drops) and TMSCl (5 drops). Then, the alkyl or aryl halide (2.50 mmol, 1.00 equiv) was added in one portion and the reaction mixture was stirred at the appropriate temperature for the indicated time. Upon completion of the insertion the mixture was filtered through a syringe filter and titrated using iodine in order to determine its actual content in zinc species and the yield of the reaction.

TP4: Typical Procedure for the Preparation of N-Hydroxylamine Derivatives of⁶

A dry and argon flushed flask equipped with a magnetic stirring bar and a septum was charged with 1,4-addition product **6** (1.00 mmol, 1.00 equiv) and dissolved in dry CH₂Cl₂ (2 mL). The solution was cooled to -78 °C and *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was added slowly as a solution in dry CH₂Cl₂ (2 mL). The mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography to afford the desired product.

TP5: Typical Procedure for the Electrophilic Amination of Organozinc Chlorides with N-Hydroxylamine Derivatives

A dry and argon flushed flask equipped with a magnetic stirring bar and a septum was charged with *N*-hydroxylamine derivative **2** (0.50 mmol, 1.00 equiv) and THF (2 mL). To the mixture

⁶ I. A. O'Neil, E. Cleator, D. J. Tapolczay *Tetrahedron Lett.* **2001**, *42*, 8247-8249.

pre-dried CoCl_2 (3-6 mg, 5.0-10 mol%) was added. Then, organozinc chloride **1** (0.75 mmol, 1.50 equiv) in THF was added dropwise. The solution was stirred for 2 h at rt and the reaction progress checked by thin layer chromatography. Upon completion of starting material (approximately less than 2 h) the reaction was quenched with sat. aqueous NH_4Cl solution (1 mL). The mixture was extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with sat. aqueous NaHCO_3 solution (15 mL), brine (15 mL) and subsequent dried over MgSO_4 . Evaporation of the solvents *in vacuo* and purification by flash column chromatography afforded the expected products.

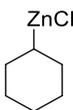
Preparation of Organozinc Chlorides

Cyclopentylzinc chloride (2a)



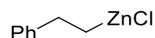
According to **TP2**, bromocyclopentan (373 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and magnesium turnings (122 mg, 5.00 mmol, 2.00 equiv) in dry THF (5 mL). The mixture was stirred at rt overnight and then ZnCl₂ (1 M in THF, 3.0 mL, 3.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C. Titration with iodine gave a concentration of 0.29 mmol/mL active zinc species, corresponding to 98% yield.

Cyclohexylzinc chloride (2b)



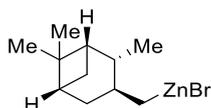
According to **TP2**, bromocyclohexyl (408 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and magnesium turnings (122 mg, 5.00 mmol, 2.00 equiv) in dry THF (5 mL). The mixture was stirred at rt overnight and then ZnCl₂ (1 M in THF, 3.0 mL, 3.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C. Titration with iodine gave a concentration of 0.27 mmol/mL active zinc species, corresponding to 88% yield.

Phenethylzinc chloride (2c)



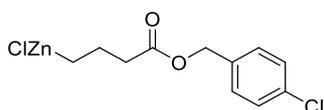
According to **TP2**, (2-bromoethyl)benzene (463 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and magnesium turnings (122 mg, 5.00 mmol, 2.00 equiv) in dry THF (5 mL). The mixture was stirred at rt overnight and then ZnCl₂ (1 M in THF, 3.0 mL, 3.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C. Titration with iodine gave a concentration of 0.28 mmol/mL active zinc species, corresponding to 92% yield.

(((1*S*,2*S*,3*S*,5*R*)-2,6,6-Trimethylbicyclo[3.1.1]heptan-3-yl)methyl)zinc chloride (2e)



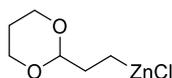
According to **TP3**, (1*S*,2*S*,3*S*,5*R*)-3-(bromomethyl)-2,6,6-trimethylbicyclo[3.1.1]heptane (578 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and activated zinc dust (245 mg, 3.75 mmol, 1.50 equiv) in dry THF (5 mL). The mixture was stirred at 50 °C overnight. Titration with iodine gave a concentration of 0.32 mmol/mL active zinc species, corresponding to 67% yield.

(4-((4-Chlorobenzyl)oxy)-4-oxobutyl)zinc chloride (2f)



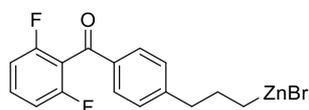
According to **TP3**, 4-chlorobenzyl 4-bromobutanoate (738 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and activated zinc dust (245 mg, 3.75 mmol, 1.50 equiv) in dry THF (5 mL). The mixture was stirred at 50 °C overnight. Titration with iodine gave a concentration of 0.40 mmol/mL active zinc species, corresponding to 84% yield.

(2-(1,3-Dioxan-2-yl)ethyl) (2g)



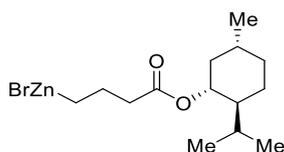
According to **TP3**, 2-(2-bromoethyl)-1,3-dioxane (488 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and activated zinc dust (245 mg, 3.75 mmol, 1.50 equiv) in dry THF (5 mL). The mixture was stirred at 50 °C overnight. Titration with iodine gave a concentration of 0.45 mmol/mL active zinc species, corresponding to 95% yield.

(3-(4-(2,6-Difluorobenzoyl)phenyl)propyl)zinc chloride (2h)



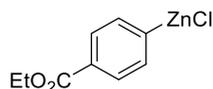
According to **TP3**, (4-(3-bromopropyl)phenyl)(2,6-difluorophenyl)methanone (848 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and activated zinc dust (245 mg, 3.75 mmol, 1.50 equiv) in dry THF (5 mL). The mixture was stirred at 50 °C overnight. Titration with iodine gave a concentration of 0.41 mmol/mL active zinc species, corresponding to 86% yield.

(4-(((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl)oxy)-4-oxobutyl)zinc chloride (2j)



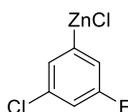
According to **TP3**, (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-bromobutanoate (763 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and activated zinc dust (245 mg, 3.75 mmol, 1.50 equiv) in dry THF (5 mL). The mixture was stirred at 50 °C overnight. Titration with iodine gave a concentration of 0.43 mmol/mL active zinc species, corresponding to 90% yield.

(4-(Ethoxycarbonyl)phenyl)zinc chloride (2k)



According to **TP1** ethyl 4-iodobenzoate (1.38 g, 5.00 mmol, 1.00 equiv) was dissolved in dry THF (5 mL) and *i*PrMgCl·LiCl (4.30 mL, 1.28 M, 5.50 mmol, 1.10 equiv) was added. After stirring for 30 min at -30 °C ZnCl₂ (1 M in THF, 6.0 mL, 6.00 mmol) was added. Titration with iodine gave a concentration of 0.30 mmol/mL active zinc species, corresponding to 95% yield.

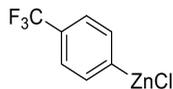
(3-Chloro-5-fluorophenyl)zinc chloride (2l)



According to **TP2**, 1-bromo-3-chloro-5-fluorobenzene (524 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and magnesium turnings (122 mg, 5.00 mmol, 2.00 equiv) in dry THF (5 mL). The mixture was stirred at rt

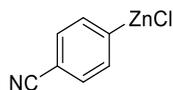
overnight and then ZnCl_2 (1 M in THF, 3.0 mL, 3.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C. Titration with iodine gave a concentration of 0.27 mmol/mL active zinc species, corresponding to 92% yield.

(4-(Trifluoromethyl)phenyl)zinc chloride (2m)



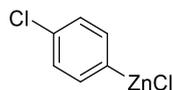
According to **TP1** 1-bromo-4-(trifluoromethyl)benzene (563 mg, 2.50 mmol) was dissolved in dry THF (7.5 mL) and *i*PrMgCl·LiCl (2.15 mL, 1.28 M, 2.75 mmol) was added. After stirring for 4 h at 25 °C ZnCl_2 (1 M in THF, 3.0 mL, 3.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C. Titration with iodine gave a concentration of 0.29 mmol/mL active zinc species, corresponding to 96% yield.

(4-Cyanophenyl)zinc chloride (2n)



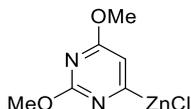
According to **TP1**, 4-iodobenzonitrile (1.15 g, 5.00 mmol, 1.00 equiv) was dissolved in dry THF (5 mL) and *i*PrMgCl·LiCl (4.30 mL, 1.28 M, 5.50 mmol, 1.10 equiv) was added. After stirring for 2 h at 0 °C ZnCl_2 (1 M in THF, 6.0 mL, 6.00 mmol) was added. Titration with iodine gave a concentration of 0.25 mmol/mL active zinc species, corresponding to 81% yield.

(4-(Trifluoromethyl)phenyl)zinc chloride (2o)



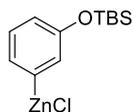
According to **TP1** 1-bromo-4-chlorobenzene (479 mg, 2.50 mmol) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and magnesium turnings (122 mg, 5.00 mmol, 2.00 equiv) in dry THF (5 mL). The mixture was stirred at rt overnight and then ZnCl_2 (1 M in THF, 3.0 mL, 3.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C. Titration with iodine gave a concentration of 0.27 mmol/mL active zinc species, corresponding to 92% yield.

(2,6-Dimethoxypyrimidin-4-yl)zinc chloride (2p)



According to **TP2**, 4-bromo-2,6-dimethoxypyrimidine (549 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and magnesium turnings (122 mg, 5.00 mmol, 2.00 equiv) in dry THF (5 mL). The mixture was stirred at rt overnight and then ZnCl₂ (1 M in THF, 3.0 mL, 3.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C. Titration with iodine gave a concentration of 0.28 mmol/mL active zinc species, corresponding to 96% yield.

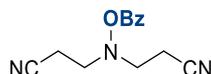
(3-((*tert*-Butyldimethylsilyl)oxy)phenyl)zinc chloride (2q)



According to **TP2**, (3-bromophenoxy)(*tert*-butyl)dimethylsilane (718 mg, 2.50 mmol, 1.00 equiv) was added to a suspension of anhydrous LiCl (159 mg, 3.75 mmol, 1.50 equiv) and magnesium turnings (122 mg, 5.00 mmol, 2.00 equiv) in dry THF (5 mL). The mixture was stirred at rt overnight and then ZnCl₂ (1 M in THF, 3.0 mL, 3.00 mmol, 1.20 equiv) was added as a solution in THF at 0 °C. Titration with iodine gave a concentration of 0.26 mmol/mL active zinc species, corresponding to 88% yield.

Preparation of *N*-Hydroxylamine Derivatives

3,3'-((Benzoyloxy)azanediyl)dipropanenitrile (**8**)



According to **TP5** 3,3',3''-nitrilotripropanenitrile (**1**, 217 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 2:1) to afford the desired product a pale white solid (139 mg, 0.57 mmol, 57%).

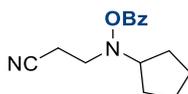
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 7.99 – 7.83 (m, 2H), 7.58 – 7.48 (m, 1H), 7.39 (dt, *J* = 20.7, 7.9 Hz, 2H), 3.32 (t, *J* = 6.7 Hz, 4H), 2.62 (td, *J* = 6.8, 1.9 Hz, 4H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 164.1, 134.0, 129.8 (2C), 128.8 (2C), 128.0, 117.6 (2C), 54.6 (2C), 16.1 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 1771, 1600, 1493, 1454, 1316, 1294, 1229, 1204, 1151, 1075, 1038, 1016, 1002, 977, 933, 914, 797, 781, 767, 700, 691.

HRMS (EI): *m/z* calc. for [C₁₃H₁₅N₃O₂]: 243.1008; found 243.1001.

3-((Benzoyloxy)(cyclopentyl)amino)propanenitrile (**9a**)



According to **TP4** 3,3'-(cyclopentylazanediyl)dipropanenitrile (**3a**, 191 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 3:1) to afford the desired product a pale white solid (189 mg, 0.73 mmol, 73%).

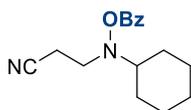
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.06 – 7.86 (m, 2H), 7.67 – 7.52 (m, 1H), 7.50 – 7.35 (m, 2H), 3.48 (p, *J* = 7.3 Hz, 1H), 3.30 (t, *J* = 7.2 Hz, 2H), 2.65 (td, *J* = 7.2, 4.1 Hz, 2H), 1.85 (tdd, *J* = 9.3, 4.2, 2.5 Hz, 2H), 1.79 – 1.51 (m, 3H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 165.8, 133.5, 129.7 (2C), 128.6 (2C), 127.8, 118.1, 69.1, 53.4, 29.9 (2C), 24.5 (2C), 16.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 2961, 2871, 2251, 1742, 1601, 1575, 1473, 1451, 1423, 1358, 1315, 1282, 1276, 1238, 1177, 1103, 1080, 1061, 1024, 1002, 903, 885, 862, 804, 744, 709, 687, 674.

HRMS (EI): *m/z* calc. for [C₁₅H₁₆N₂O₂]: 258.1368; found 258.1362.

3-((Benzoyloxy)(cyclohexyl)amino)propanenitrile (**9b**)



According to **TP4** 3,3'-(cyclohexylazanediyl)dipropanenitrile (**3b**, 205 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 3:1) to afford the desired product a pale white solid (193 mg, 0.71 mmol, 71%).

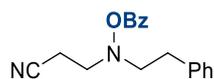
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.05 – 7.89 (m, 2H), 7.59 (dddd, *J* = 14.2, 8.0, 2.5, 1.2 Hz, 1H), 7.50 – 7.38 (m, 2H), 3.36 (t, *J* = 7.2 Hz, 2H), 2.94 (tt, *J* = 10.8, 3.6 Hz, 1H), 2.64 (td, *J* = 7.2, 4.5 Hz, 2H), 2.03 – 1.92 (m, 2H), 1.86 – 1.77 (m, 2H), 1.70 – 1.59 (m, 1H), 1.42 – 1.06 (m, 5H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 164.6, 133.5, 129.7 (2C), 128.6 (2C), 127.8, 118.1, 66.0, 50.6, 29.0, 25.7 (2C), 25.0 (2C), 16.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 2934, 2857, 2251, 1742, 1601, 1451, 1422, 1372, 1349, 1315, 1238, 1194, 1177, 1159, 1079, 1063, 1022, 1002, 913, 895, 866, 852, 826, 802, 780, 731, 707, 687, 674.

HRMS (EI): *m/z* calc. for [C₁₆H₂₀N₂O₂]: 272.1525; found 272.1529.

3-((Benzoyloxy)(phenethyl)amino)propanenitrile (**9c**)



According to **TP4** 3,3'-(phenethylazanediyl)dipropanenitrile (**3c**, 227 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 3:1) to afford the desired product a pale white solid (185 mg, 0.63 mmol, 63%).

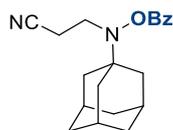
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.05 – 7.86 (m, 2H), 7.64 – 7.55 (m, 1H), 7.52 – 7.38 (m, 2H), 7.30 – 7.24 (m, 2H), 7.23 – 7.15 (m, 3H), 3.43 – 3.23 (m, 4H), 3.01 – 2.87 (m, 2H), 2.69 (td, *J* = 7.1, 5.7 Hz, 2H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 164.4, 138.4, 134.8, 133.7 (2C), 129.9 (2C), 129.7 (2C), 128.6 (2C), 127.8, 126.6, 117.8, 61.0, 54.6, 33.4, 16.0

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 3028, 2923, 2851, 1742, 1602, 1575, 1496, 1452, 1424, 1362, 1315, 1283, 1238, 1178, 1117, 1100, 1088, 1079, 1060, 1044, 1022, 1002, 883, 802, 743, 708, 699, 673.

HRMS (EI): *m/z* calc. for [C₁₈H₁₈N₂O₂]: 294.1368; found 294.1363.

3-(((3*s*,5*s*,7*s*)-adamantan-1-yl)(benzoyloxy)amino)propanenitrile (**9d**)



According to **TP4**, 3,3'-(((3*s*,5*s*,7*s*)-adamantan-1-yl)azanediyl)dipropanenitrile (**3d**, 257 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 3:1) to afford the desired product a pale white solid (172 mg, 0.53 mmol, 53%).

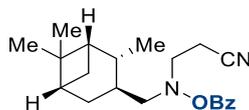
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.11 – 8.01 (m, 2H), 7.66 – 7.55 (m, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 3.35 (t, *J* = 7.3 Hz, 2H), 2.61 (t, *J* = 7.3 Hz, 2H), 2.19 – 2.08 (m, 3H), 1.84 (d, *J* = 3.0 Hz, 6H), 1.76 – 1.57 (m, 6H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 166.1, 133.5, 129.7 (2C), 128.7 (2C), 128.5, 118.4, 61.2, 46.3, 38.2 (3C), 36.4 (3C), 29.2 (3C), 17.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 3018, 1642, 1622, 1595, 1482, 1476, 1434, 1395, 1301, 1261, 1221, 1189, 1135, 1122, 1050, 1060, 1021, 1001, 879, 812, 734, 718, 694, 667.

HRMS (EI): *m/z* calc. for [C₂₀H₂₄N₂O₂]: 324.1838; found 324.1830.

3-((Benzoyloxy)(((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)propanenitrile (9e)



According to **TP4** 3,3'-((((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)azanediyl)dipropanenitrile (**3e**, 273 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (pure EtOAc 2:1) to afford the desired product a pale white solid (238 mg, 0.670 mmol, 70%).

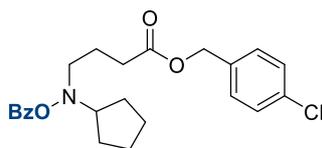
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.04 – 7.88 (m, 2H), 7.62 – 7.54 (m, 1H), 7.49 – 7.40 (m, 2H), 3.41 – 3.27 (m, 2H), 3.10 (dd, *J* = 12.4, 4.8 Hz, 1H), 2.87 (dd, *J* = 12.4, 9.7 Hz, 1H), 2.73 – 2.65 (m, 2H), 2.30 (dtd, *J* = 9.8, 6.2, 2.1 Hz, 1H), 2.19 (dddd, *J* = 12.1, 10.0, 3.6, 1.9 Hz, 1H), 1.94 – 1.82 (m, 2H), 1.81 – 1.67 (m, 3H), 1.16 (s, 3H), 1.04 (d, *J* = 7.1 Hz, 3H), 0.91 (s, 3H), 0.72 (d, *J* = 9.7 Hz, 1H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 165.2, 133.5, 129.6 (2C), 128.6 (2C), 127.7, 118.1, 69.1, 54.6, 47.8, 41.5, 41.4, 38.8, 34.4, 33.9, 33.5, 27.9, 23.0, 21.7, 15.9.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 2903, 2870, 1744, 1472, 1451, 1423, 1385, 1374, 1367, 1315, 1239, 1177, 1101, 1084, 1056, 1024, 1002, 906, 862, 801, 735, 707, 687, 673, 657.

HRMS (EI): *m/z* calc. for [C₂₁H₂₈N₂O₂]: 340.2151; found 340.2155.

4-Chlorobenzyl 4-((benzyloxy)(cyclopentyl)amino)butanoate (10a)



According to **TP4** 4-chlorobenzyl 4-((2-cyanoethyl)(cyclopentyl)amino)butanoate (**4a**, 349 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH_2Cl_2 (2 mL) and cooled to -78°C . Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH_2Cl_2 (2 mL) and the resulting mixture was stirred at -78°C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH_2Cl_2 (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0°C . The resulting solution was stirred at 0°C for 1 h and quenched with sat. aqueous NH_4Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO_3 solution (2 mL), brine (2 mL), and dried over Na_2SO_4 . The crude mixture was purified with flash column chromatography (hexane:EtOAc 4:1) to afford the desired product a pale white solid (345 mg, 0.83 mmol, 83%).

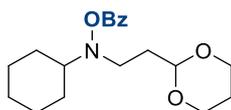
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 8.05 – 7.88 (m, 2H), 7.61 – 7.52 (m, 1H), 7.48 – 7.37 (m, 2H), 7.32 – 7.24 (m, 4H), 5.06 (d, $J = 2.0$ Hz, 2H), 3.82 – 3.71 (m, 1H), 3.41 (td, $J = 7.4, 2.4$ Hz, 1H), 3.01 (t, $J = 7.0$ Hz, 2H), 2.55 (t, $J = 7.2$ Hz, 2H), 1.94 – 1.76 (m, 5H), 1.74 – 1.52 (m, 4H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 173.2, 165.9, 133.1, 129.8, 129.6, 129.6, 129.2, 128.7, 128.5, 127.7, 69.2, 68.0, 65.3, 57.0, 31.6, 29.9, 25.6, 24.5, 22.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2959, 2869, 1740, 1682, 1601, 1574, 1450, 1425, 1412, 1355, 1314, 1282, 1239, 1176, 1116, 1101, 1080, 1061, 1023, 1002, 861, 850, 833, 775, 744, 708, 686, 674.

HRMS (EI): m/z calc. for $[\text{C}_{23}\text{H}_{26}\text{ClNO}_4]$: 415.1550; found 415.1559.

***N*-(2-(1,3-dioxan-2-yl)ethyl)-*O*-benzoyl-*N*-cyclohexylhydroxylamine (10b)**



According to **TP4** 3-((2-(1,3-dioxan-2-yl)ethyl)(cyclohexyl)amino)propanenitrile (**4b**, 266 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 3:1) to afford the desired product a pale white solid (263 mg, 0.79 mmol, 79%).

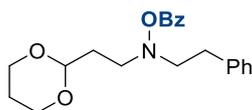
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.02 – 7.86 (m, 2H), 7.56 – 7.48 (m, 1H), 7.44 – 7.30 (m, 2H), 4.67 (t, *J* = 5.1 Hz, 1H), 4.05 – 3.98 (m, 2H), 3.70 (ddt, *J* = 12.3, 10.3, 2.4 Hz, 2H), 3.13 (dd, *J* = 8.5, 6.4 Hz, 2H), 2.85 (tt, *J* = 11.0, 3.5 Hz, 1H), 2.08 – 1.88 (m, 3H), 1.84 (ddd, *J* = 9.9, 7.9, 4.0 Hz, 2H), 1.75 (dt, *J* = 12.6, 3.2 Hz, 2H), 1.65 – 1.53 (m, 1H), 1.42 – 1.05 (m, 6H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 165.9, 133.1, 129.6 (2C), 129.2, 128.5 (2C), 100.7, 66.9 (2C), 65.8, 50.0, 32.5, 29.1 (2C), 25.9, 25.8, 25.2 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 2933, 2854, 1742, 1602, 1575, 1469, 1451, 1428, 1407, 1377, 1315, 1284, 1239, 1195, 1177, 1140, 1081, 1059, 1024, 998, 974, 967, 938, 927, 907, 893, 856, 824, 745, 734, 709, 688, 674.

HRMS (EI): *m/z* calc. for [C₁₉H₂₇NO₄]: 333.1940; found 333.1947.

N-(2-(1,3-Dioxan-2-yl)ethyl)-*O*-benzoyl-*N*-phenethylhydroxylamine (10c)



According to **TP4** 3-((2-(1,3-dioxan-2-yl)ethyl)(phenethyl)amino)propanenitrile (**4c**, 288 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 3:1) to afford the desired product a pale white solid (263 mg, 0.74 mmol, 74%).

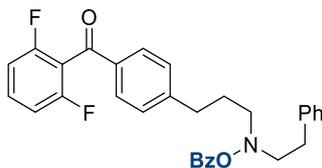
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.04 – 7.98 (m, 2H), 7.60 – 7.54 (m, 1H), 7.47 – 7.41 (m, 2H), 7.25 – 7.14 (m, 5H), 4.71 (t, *J* = 5.1 Hz, 1H), 4.11 – 4.02 (m, 2H), 3.81 – 3.70 (m, 2H), 3.30 – 3.22 (m, 2H), 3.16 (dd, *J* = 8.2, 6.6 Hz, 2H), 2.96 – 2.88 (m, 2H), 2.10 – 1.97 (m, 2H), 1.91 (ddd, *J* = 10.2, 7.9, 4.1 Hz, 2H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 165.6, 139.3, 133.1, 129.6 (2C), 128.7 (2C), 128.5 (2C), 128.4 (2C), 126.2, 100.4, 66.9 (2C), 61.2, 54.4, 33.4, 32.4, 25.8, 14.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 3062, 3028, 2961, 2854, 1740, 1602, 1584, 1496, 1470, 1451, 1429, 1409, 1378, 1315, 1241, 1176, 1139, 1092, 1080, 1058, 1024, 1001, 972, 940, 926, 893, 854, 747, 709, 700, 673.

HRMS (EI): *m/z* calc. for [C₂₁H₂₅NO₄]: 355.1784; found 355.1795.

**(4-(3-((Benzoyloxy)(phenethyl)amino)propyl)phenyl)(2,6-difluorophenyl)methanone
(10d)**



According to **TP4** 3-((3-(4-(2,6-difluorobenzoyl)phenyl)propyl)(phenethyl)amino)propanenitrile (**4d**, 433 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 4:1) to afford the desired product a pale white solid (435 mg, 0.87 mmol, 87%).

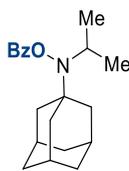
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.04 – 8.00 (m, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.61 – 7.56 (m, 1H), 7.49 – 7.39 (m, 3H), 7.29 – 7.23 (m, 4H), 7.23 – 7.14 (m, 3H), 7.03 – 6.95 (m, 2H), 3.28 – 3.19 (m, 2H), 3.03 (t, *J* = 7.1 Hz, 2H), 2.97 – 2.89 (m, 2H), 2.82 (t, *J* = 7.7 Hz, 2H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 188.6, 165.8, 159.8 (dd, *J* = 251.5, 7.7 Hz), 149.1, 139.3, 134.9, 133.3, 131.9 (t, *J* = 9.8 Hz), 130.1, 129.7, 129.1, 129.0, 128.8, 128.6, 128.6, 126.4, 117.27 (t, *J* = 22.0 Hz), 112.2 – 111.8 (m), 61.5, 59.0, 33.7, 28.3, 21.2.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 3063, 3030, 2955, 2866, 1739, 1713, 1672, 1622, 1604, 1589, 1496, 1464, 1452, 1416, 1361, 1312, 1277, 1243, 1235, 1222, 1177, 1146, 1090, 1063, 1024, 1005, 930, 911, 853, 791, 750, 729, 708, 700, 670.

HRMS (EI): *m/z* calc. for [C₃₁H₂₇FNO₃]: 499.1959; found 499.1967.

***N*-((3*s*,5*s*,7*s*)-adamantan-1-yl)-*O*-benzoyl-*N*-isopropylhydroxylamine (10e)**



According to **TP4** 3-(((3*s*,5*s*,7*s*)-adamantan-1-yl)(isopropyl)amino)propanenitrile (**4e**, 246 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 4:1) to afford the desired product a pale white solid (210 mg, 0.67 mmol, 67%).

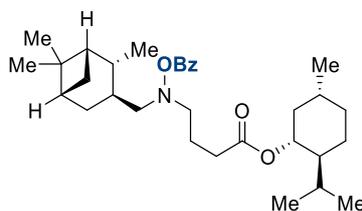
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.11 – 8.06 (m, 2H), 7.67 – 7.53 (m, 1H), 7.50 – 7.44 (m, 2H), 3.67 (p, *J* = 6.5 Hz, 1H), 2.15 – 2.06 (m, 3H), 1.96 – 1.83 (m, 6H), 1.70 – 1.59 (m, 6H), 1.26 – 1.14 (m, 6H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 166.6, 132.9, 129.6, 129.6 (2C), 128.5 (2C), 61.2, 50.7, 39.7 (3C), 36.6 (3C), 29.5 (3C), 24.2, 19.0.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 2980, 2906, 2846, 1739, 1699, 1600, 1583, 1448, 1381, 1361, 1344, 1311, 1274, 1259, 1240, 1190, 1177, 1130, 1120, 1081, 1061, 1044, 1020, 977, 970, 939, 906, 876, 860, 819, 801, 707, 686, 672.

HRMS (EI): *m/z* calc. for [C₂₀H₂₇NO₂]: 313.2042; found 313.2050.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 4-((benzyloxy)((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (10f)



According to **TP4** (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-((2-cyanoethyl)((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (**4f**, 445 mg, 1.00 mmol, 1.00 equiv) was dissolved in dry CH₂Cl₂ (2 mL) and cooled to -78 °C. Then, *m*CPBA (190 mg, 1.10 mmol, 1.10 equiv) was slowly added as a solution in dry CH₂Cl₂ (2 mL) and the resulting mixture was stirred at -78 °C for 1 h. Following, the cooling bath was removed and the mixture stirred at rt overnight. The solvent was removed and the acid by-product removed by filtration through a silica plug. After solvent removal, the resulting *N*-hydroxylamine was dissolved in CH₂Cl₂ (4 mL) followed by the addition of triethylamine (0.21 mL, 1.50 mmol, 1.50 equiv), DMAP (1 mg, 0.01 mmol, 1.00 mol%) and benzoyl chloride (168 mg, 1.20 mmol, 1.20 equiv) at 0 °C. The resulting solution was stirred at 0 °C for 1 h and quenched with sat. aqueous NH₄Cl solution (2 mL). The mixture was extracted with EtOAc (3 x 5 mL) and the combined organic phases were washed with saturated NaHCO₃ solution (2 mL), brine (2 mL), and dried over Na₂SO₄. The crude mixture was purified with flash column chromatography (hexane:EtOAc 4:1) to afford the desired product a pale white solid (363 mg, 0.71 mmol, 71%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 8.05 – 7.86 (m, 2H), 7.61 – 7.50 (m, 1H), 7.49 – 7.35 (m, 2H), 4.66 (td, *J* = 10.9, 4.3 Hz, 1H), 3.12 – 2.95 (m, 4H), 2.81 (t, *J* = 11.3 Hz, 1H), 2.53 – 2.43 (m, 2H), 2.34 – 2.14 (m, 2H), 2.00 – 1.80 (m, 8H), 1.79 – 1.70 (m, 2H), 1.65 (ddd, *J* = 13.0, 6.1, 2.3 Hz, 4H), 1.54 – 1.39 (m, 1H), 1.33 (ddt, *J* = 12.2, 10.7, 3.1 Hz, 1H), 1.16 (s, 3H), 1.04 (d, *J* = 7.1 Hz, 3H), 0.92 (s, 3H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.72 (d, *J* = 7.0 Hz, 3H).

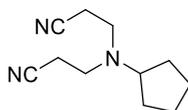
¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 173.1, 165.3, 133.0, 129.4 (2C), 128.5 (2C), 127.6, 74.1, 69.3, 58.4, 47.9, 46.9, 41.6, 41.5, 40.9, 38.9, 34.4, 34.2, 33.9, 33.5, 31.9, 31.4, 28.0, 26.2, 23.4, 23.1, 22.2, 22.0, 21.7, 20.8, 16.3.

IR (Diamond-ATR, neat): $\tilde{\nu} / \text{cm}^{-1} = 2951, 2926, 2869, 1744, 1727, 1602, 1576, 1469, 1451, 1385, 1370, 1345, 1314, 1239, 1176, 1152, 1134, 1099, 1083, 1057, 1039, 1024, 1010, 985, 966, 935, 912, 843, 824, 802, 744, 707, 687, 673.$

HRMS (EI): m/z calc. for $[\text{C}_{32}\text{H}_{49}\text{NO}_4]$: 511.3662; found 511.3669.

Preparation of Amination Products

3,3'-(Cyclopentylazanediyl)dipropanenitrile (**3a**)



According to **TP5** 3,3'-((benzyloxy)azanediyl)dipropanenitrile (**8**, 122 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot (3 \text{ mg}, 25 \mu\text{mol}, 5.00 \text{ mol}\%)$ was added and subsequent cyclopentylzinc chloride (**2a**, 2.6 mL, 0.29 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:3) afforded the title compound as a colourless oil (62 mg, 0.33 mmol, 65%).

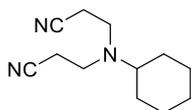
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 3.06 (p, $J = 8.6, 8.1 \text{ Hz}$, 1H), 2.89 (t, $J = 6.9 \text{ Hz}$, 4H), 2.46 (t, $J = 6.9 \text{ Hz}$, 3H), 1.87 – 1.76 (m, 2H), 1.74 – 1.62 (m, 1H), 1.61 – 1.48 (m, 1H), 1.44 – 1.30 (m, 2H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 118.9 (2C), 63.4, 47.9 (2C), 29.9 (2C), 23.8 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2955, 2868, 2247, 1463, 1453, 1421, 1362, 1338, 1312, 1265, 1238, 1130, 1085, 1040, 1023, 966, 945, 757.

HRMS (EI): m/z calc. for $[\text{C}_{11}\text{H}_{17}\text{N}_3]$: 191.1422; found 191.1425.

3,3'-(Cyclohexylazanediyl)dipropanenitrile (**3b**)



According to **TP5** 3,3'-((benzyloxy)azanediyl)dipropanenitrile (**8**, 122 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent cyclohexylzinc chloride (**2b**, 2.8 mL, 0.27 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:3) afforded the title compound as a colourless oil (75 mg, 0.37 mmol, 73%).

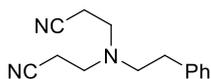
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 2.81 (t, J = 6.8 Hz, 4H), 2.42 (t, J = 6.8 Hz, 4H), 2.40 – 2.35 (m, 1H), 1.76 (ddt, J = 10.7, 8.1, 4.9 Hz, 4H), 1.64 – 1.57 (m, 1H), 1.27 – 0.98 (m, 5H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 118.9 (2C), 60.4, 46.8 (2C), 29.4 (2C), 26.0, 25.9 (2C), 19.2 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2995, 2247, 1432, 1442, 2, 1355, 1321, 1305, 1287, 1230, 1070, 1065, 955, 760.

HRMS (EI): m/z calc. for $[\text{C}_{12}\text{H}_{19}\text{N}_3]$: 205.1579; found 205.1586.

3,3'-(Phenethylazanediyldipropanenitrile (3c))



According to **TP5** 3,3'-((benzyloxy)azanediyldipropanenitrile (**8**, 122 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried CoCl_2 (3 mg, 25 μmol , 5.00 mol%) was added and subsequent phenethylzinc chloride (**2c**, 2.7 mL, 0.28 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:3) afforded the title compound as a colourless oil (69 mg, 0.31 mmol, 61%).

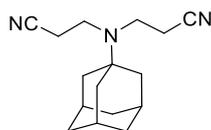
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 7.33 – 7.27 (m, 2H), 7.25 – 7.18 (m, 3H), 2.90 (t, J = 6.8 Hz, 4H), 2.85 – 2.73 (m, 4H), 2.41 (t, J = 6.8 Hz, 4H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 139.4, 128.8 (2C), 128.6 (2C), 126.5, 118.7 (2C), 55.7, 49.9 (2C), 34.3, 17.2 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 3062, 3028, 2930, 2849, 2248, 1626, 1602, 1584, 1495, 1465, 1454, 1420, 1362, 1336, 1242, 1180, 1128, 1080, 1030, 966, 910, 825, 748, 700.

HRMS (EI): m/z calc. for $[\text{C}_{14}\text{H}_{17}\text{N}_3]$: 227.1422; found 227.1415.

3,3'-(((3*s*,5*s*,7*s*)-adamantan-1-yl)azanediyl)dipropanenitrile (**3d**)



According to **TP5** 3,3'-((benzyloxy)azanediyl)dipropanenitrile (**8**, 122 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent ((3*s*,5*s*,7*s*)-adamantan-1-yl)zinc chloride (**2d**, 2.7 mL, 0.28 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:3) afforded the title compound as a white solid (66 mg, 0.26 mmol, 51%).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 2.88 (t, $J = 7.1$ Hz, 4H), 2.39 (t, $J = 7.1$ Hz, 4H), 2.07 – 2.00 (m, 3H), 1.59 (t, $J = 3.7$ Hz, 9H), 1.57 – 1.48 (m, 3H).

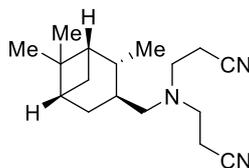
$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 118.9 (2C), 55.7, 45.4 (2C), 40.0 (3C), 36.4 (3C), 29.4 (3C), 20.8 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2980, 2906, 2847, 1740, 1600, 1583, 1448, 1381, 1361, 1344, 1311, 1273, 1257, 1240, 1190, 1176, 1130, 1120, 1081, 1061, 1044, 1020, 977, 954, 939, 907, 876, 860, 818, 801, 771, 747, 707, 686, 672.

HRMS (EI): m/z calc. for $[\text{C}_{16}\text{H}_{23}\text{N}_3]$: 257.1892; found 257.1899.

m.p.: 45.2–46.0 °C

3,3'-((((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)azanediyl)dipropanenitrile (3e)



According to **TP5** 3,3'-((benzyloxy)azanediyl)dipropanenitrile (**8**, 122 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent (((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)zinc chloride (**2e**, 2.3 mL, 0.32 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:3) afforded the title compound as a colourless oil (90 mg, 0.33 mmol, 66%).

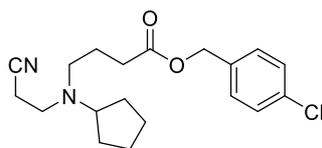
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 2.89 – 2.75 (m, 4H), 2.51 – 2.35 (m, 5H), 2.29 – 2.19 (m, 2H), 2.14 – 2.04 (m, 1H), 1.92 – 1.84 (m, 1H), 1.78 – 1.66 (m, 2H), 1.54 – 1.39 (m, 2H), 1.13 (s, 3H), 0.99 (d, $J = 7.2$ Hz, 3H), 0.94 (s, 3H), 0.62 (d, $J = 9.7$ Hz, 1H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 118.6 (2C), 64.1, 49.7 (2C), 47.9, 41.6, 41.6, 38.9, 34.3, 33.8, 33.2, 27.9, 23.1, 22.0, 16.7 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2932, 2856, 2249, 2197, 1742, 1621, 1601, 1584, 1464, 1450, 1421, 1372, 1350, 1315, 1239, 1194, 1177, 1162, 1137, 1080, 1063, 1023, 1002, 894, 866, 825, 802, 780, 746, 709, 687, 674.

HRMS (EI): m/z calc. for $[\text{C}_{17}\text{H}_{27}\text{N}_3]$: 273.2205; found 273.2212.

4-Chlorobenzyl 4-((2-cyanoethyl)(cyclopentyl)amino)butanoate (**4a**)



According to **TP5** 3-((benzyloxy)(cyclopentyl)amino)propanenitrile (**9a**, 129 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent 4-((4-chlorobenzyl)oxy)-4-oxobutylzinc bromide (**2f**, 1.9 mL, 0.40 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 2:1) afforded the title compound as a colourless oil (152 mg, 0.44 mmol, 81%).

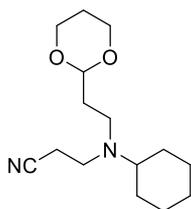
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 7.35 – 7.27 (m, 4H), 5.07 (s, 2H), 3.04 – 2.93 (m, 1H), 2.82 (t, $J = 7.1$ Hz, 2H), 2.50 (dd, $J = 7.9, 6.4$ Hz, 2H), 2.39 (td, $J = 7.1, 3.6$ Hz, 4H), 1.79 – 1.70 (m, 2H), 1.69 – 1.58 (m, 2H), 1.56 – 1.45 (m, 2H), 1.37 – 1.24 (m, 2H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 173.3, 134.5, 134.2, 129.8 (2C), 128.8 (2C), 119.2, 65.4, 63.1, 50.5, 47.3, 31.6, 29.7 (2C), 23.9 (2C), 22.6, 16.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953, 2868, 2247, 1732, 1695, 1621, 1600, 1493, 1463, 1452, 1417, 1412, 1378, 1355, 1316, 1255, 1212, 1161, 1122, 1091, 1015, 971, 944, 838, 805.

HRMS (EI): m/z calc. for $[\text{C}_{19}\text{H}_{25}\text{ClN}_2\text{O}_2]$: 348.1605; found 348.1613.

3-((2-(1,3-Dioxan-2-yl)ethyl)(cyclohexyl)amino)propanenitrile (**4b**)



According to **TP5** 3-((benzoyloxy)(cyclohexyl)amino)propanenitrile (**9b**, 136 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent (2-(1,3-dioxan-2-yl)ethyl)zinc chloride (**2g**, 1.7 mL, 0.45 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:1) afforded the title compound as a colourless oil (125 mg, 0.47 mmol, 94%).

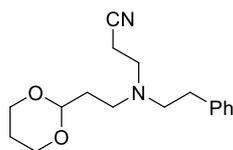
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 4.66 (t, J = 5.3 Hz, 1H), 4.03 (ddt, J = 10.5, 5.0, 1.4 Hz, 2H), 3.78 – 3.70 (m, 2H), 2.66 (t, J = 6.7 Hz, 2H), 2.52 (t, J = 6.9 Hz, 2H), 2.35 (t, J = 6.7 Hz, 2H), 2.01 (dtt, J = 15.8, 12.5, 5.0 Hz, 1H), 1.79 – 1.68 (m, 4H), 1.63 (td, J = 6.9, 5.3 Hz, 2H), 1.59 – 1.50 (m, 1H), 1.37 – 1.25 (m, 2H), 1.20 – 1.09 (m, 4H), 1.08 – 0.93 (m, 1H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 119.4, 100.4, 66.8, 59.4, 46.2, 44.8, 34.3, 29.0, 26.2, 26.1, 25.9, 18.6.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2963, 2926, 2850, 1469, 1458, 1451, 1432, 1405, 1380, 1336, 1290, 1283, 1273, 1251, 1240, 1222, 1169, 1155, 1132, 1108, 1090, 1073, 1046, 1025, 1007, 994, 973, 958, 925, 902, 894, 888, 859, 845, 826, 752.

HRMS (EI): m/z calc. for $[\text{C}_{15}\text{H}_{26}\text{N}_2\text{O}_2]$: 266.1994; found 266.1999.

3-((2-(1,3-Dioxan-2-yl)ethyl)(phenethyl)amino)propanenitrile (**4c**)



According to **TP5** 3-((benzoyloxy)(phenethyl)amino)propanenitrile (**9c**, 147 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent (2-(1,3-dioxan-2-yl)ethyl)zinc bromide (**2g**, 1.7 mL, 0.45 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:1) afforded the title compound as a colourless oil (108 mg, 0.38 mmol, 75%).

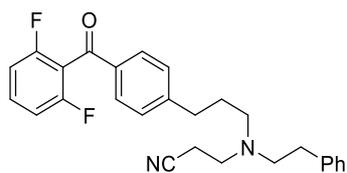
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 7.31 – 7.26 (m, 2H), 7.23 – 7.17 (m, 3H), 4.56 (t, J = 5.3 Hz, 1H), 4.07 (ddt, J = 10.5, 5.1, 1.4 Hz, 2H), 3.74 (ddt, J = 12.3, 10.3, 2.0 Hz, 2H), 2.79 (t, J = 6.9 Hz, 2H), 2.76 – 2.67 (m, 4H), 2.61 (t, J = 7.0 Hz, 2H), 2.40 (t, J = 6.8 Hz, 2H), 2.12 – 1.98 (m, 1H), 1.70 (td, J = 7.0, 5.3 Hz, 2H), 1.36 – 1.24 (m, 1H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 140.2, 128.9 (2C), 128.4 (2C), 126.1, 119.2, 100.4, 66.9 (2C), 55.8, 49.9, 48.1, 34.0, 32.9, 25.9, 16.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2957, 2851, 2247, 1624, 1604, 1496, 1462, 1454, 1429, 1407, 1379, 1286, 1238, 1218, 1202, 1135, 1088, 1048, 1031, 1006, 974, 961, 930, 892, 853, 748, 700.

HRMS (EI): m/z calc. for $[\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_2]$: 288.1838; found 288.1842.

3-((3-(4-(2,6-Difluorobenzoyl)phenyl)propyl)(phenethyl)amino)propanenitrile (4d)



According to **TP5** 3-((benzyloxy)(phenethyl)amino)propanenitrile (**9c**, 147 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 3\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and 3-((3-(4-(2,6-difluorobenzoyl)phenyl)propyl)zinc bromide (**2h**, 1.8 mL, 0.41 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 2:1) afforded the title compound as a yellowish oil (160 mg, 0.37 mmol, 74%).

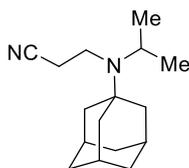
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 7.71 (d, J = 8.1 Hz, 2H), 7.36 (tt, J = 8.5, 6.4 Hz, 1H), 7.24 – 7.16 (m, 4H), 7.15 – 7.08 (m, 3H), 6.96 – 6.89 (m, 2H), 2.75 (t, J = 6.8 Hz, 2H), 2.65 (s, 4H), 2.61 (dd, J = 8.6, 6.8 Hz, 2H), 2.46 (t, J = 7.0 Hz, 2H), 2.29 (t, J = 6.8 Hz, 2H), 1.76 – 1.66 (m, 2H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 188.6, 159.8 (dd, J = 251.4, 7.7 Hz, 2C), 149.5, 140.1, 134.8, 131.8 (t, J = 9.8 Hz), 130.0 (2C), 128.9 (2C), 128.8 (2C), 128.5 (2C), 126.2, 119.1, 117.2 (t, J = 22.0 Hz), 112.3 – 111.5 (m, 2C), 55.6, 53.0, 49.6, 33.9, 33.4, 28.7, 16.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2938, 1712, 1670, 1622, 1604, 1589, 1496, 1464, 1416, 1362, 1311, 1277, 1234, 1183, 1145, 1080, 1030, 1004, 930, 852, 790, 748, 724, 699.

HRMS (EI): m/z calc. for $[\text{C}_{27}\text{H}_{26}\text{F}_2\text{N}_2\text{O}]$: 432.2013; found 432.2018.

3-(((3*s*,5*s*,7*s*)-adamantan-1-yl)(isopropyl)amino)propanenitrile (**4e**)



According to **TP5** 3-(((3*s*,5*s*,7*s*)-adamantan-1-yl)(benzoyloxy)amino)propanenitrile (**9d**, 162 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried CoCl₂·(3 mg, 25 μmol, 5.00 mol%) was added and subsequent isopropylzinc chloride (**2i**, 1.4 mL, 0.52 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:1) afforded the title compound as a colourless oil (89 mg, 0.36 mmol, 72%).

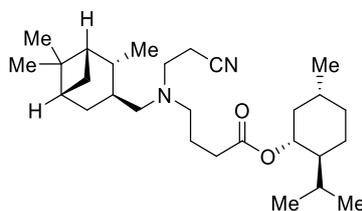
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 3.44 – 3.33 (m, 1H), 2.91 – 2.83 (m, 2H), 2.31 – 2.24 (m, 2H), 2.00 (s, 3H), 1.64 – 1.48 (m, 12H), 0.94 (d, *J* = 6.6 Hz, 6H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 119.3, 55.7, 44.7, 41.5 (3C), 37.4, 36.6 (3C), 29.7 (3C), 23.2 (2C), 22.9.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 2951, 2924, 2869, 1729, 1596, 1557, 1466, 1456, 1402, 1384, 1370, 1333, 1314, 1284, 1265, 1241, 1175, 1153, 1134, 1123, 1107, 1097, 1076, 1039, 1013, 984, 964, 938, 919, 801, 710.

HRMS (EI): *m/z* calc. for [C₁₆H₂₆N₂]: 246.2096; found 246.2101.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 4-((2-cyanoethyl)((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (4f)



According to **TP5** 3-((benzoyloxy)((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)propanenitrile (**9e**, 170 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 3\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent (4-(((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)-4-oxobutyl)zinc bromide (**2j**, 1.7 mL, 0.43 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 2:1) afforded the title compound as a colourless oil (171 mg, 0.39 mmol, 77%).

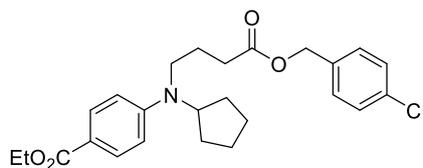
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 4.58 (qt, $J = 7.0, 2.6$ Hz, 1H), 2.90 – 2.75 (m, 2H), 2.73 – 2.65 (m, 4H), 2.53 – 2.42 (m, 2H), 2.39 (t, $J = 7.1$ Hz, 2H), 2.08 – 1.73 (m, 8H), 1.72 – 1.38 (m, 9H), 1.38 – 1.26 (m, 2H), 1.00 (d, $J = 6.8$ Hz, 6H), 0.94 (s, 3H), 0.91 (dd, $J = 6.8, 1.5$ Hz, 3H), 0.89 – 0.85 (m, 6H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 173.7, 118.0, 76.2, 57.0, 53.7, 52.3, 47.0, 45.1, 40.3, 40.0, 39.5, 39.4, 38.3, 34.3, 33.0, 31.3, 31.3, 30.4, 26.3, 24.7, 24.6, 24.4, 24.3, 22.0, 19.1, 19.0, 17.6, 15.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2953, 2870, 1727, 1456, 1420, 1385, 1370, 1345, 1328, 1298, 1252, 1178, 1151, 1133, 1119, 1097, 1081, 1059, 1039, 1010, 984, 966, 939, 914, 844.

HRMS (EI): m/z calc. for $[\text{C}_{28}\text{H}_{48}\text{N}_2\text{O}_2]$: 444.3716; found 444.3722.

Ethyl 4-((4-((4-chlorobenzyl)oxy)-4-oxobutyl)(cyclopentyl)amino)benzoate (5a)



According to **TP5** 4-chlorobenzyl 4-((benzoyloxy)(cyclopentyl)amino)butanoate (**10a**, 208 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot (3 \text{ mg}, 25 \mu\text{mol}, 5.00 \text{ mol}\%)$ was added and subsequent (4-(ethoxycarbonyl)phenyl)zinc chloride (**2**, 2.5 mL, 0.30 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:1) afforded the title compound as a colourless oil (195 mg, 0.44 mmol, 88%).

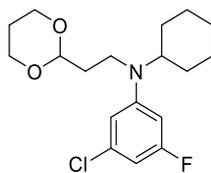
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 7.87 (d, $J = 9.1$ Hz, 2H), 7.39 – 7.24 (m, 4H), 6.71 (d, $J = 9.2$ Hz, 2H), 5.10 (s, 2H), 4.31 (q, $J = 7.1$ Hz, 2H), 4.11 (p, $J = 9.0, 8.5$ Hz, 1H), 3.29 – 3.19 (m, 2H), 2.42 (t, $J = 7.0$ Hz, 2H), 2.02 – 1.85 (m, 4H), 1.78 – 1.65 (m, 2H), 1.65 – 1.56 (m, 2H), 1.36 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 172.8, 166.9, 152.4, 134.3, 131.3, 129.8 (2C), 128.8 (2C), 127.2 (2C), 117.3, 111.6 (2C), 65.6, 60.1, 59.7, 44.8, 31.4, 29.2 (2C), 23.8, 23.4 (2C), 14.5.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2926, 2854, 1736, 1688, 1667, 1462, 1453, 1417, 1371, 1347, 1317, 1241, 1219, 1165, 1145, 1095, 1072, 1046, 1020, 987, 906, 892, 869, 844, 825, 725, 681.

HRMS (EI): m/z calc. for $[\text{C}_{25}\text{H}_{30}\text{ClNO}_4]$: 443.1863; found 443.1869.

***N*-(2-(1,3-Dioxan-2-yl)ethyl)-3-chloro-*N*-cyclohexyl-5-fluoroaniline (5b)**



According to **TP5** *N*-(2-(1,3-dioxan-2-yl)ethyl)-*O*-benzoyl-*N*-cyclohexylhydroxylamine (**10b**, 167 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried CoCl₂·(3 mg, 25 μmol, 5.00 mol%) was added and subsequent (3-chloro-5-fluorophenyl)zinc chloride (**2l**, 2.8 mL, 0.27 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 1:1) afforded the title compound as a white solid (179 mg, 0.43 mmol, 86%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 6.49 (t, *J* = 2.2 Hz, 1H), 6.38 – 6.26 (m, 2H), 4.59 (t, *J* = 4.8 Hz, 1H), 4.12 (ddd, *J* = 12.0, 5.0, 1.4 Hz, 2H), 3.76 (ddt, *J* = 12.3, 10.4, 2.4 Hz, 2H), 3.44 (tt, *J* = 11.4, 3.4 Hz, 1H), 3.38 – 3.24 (m, 2H), 2.22 – 2.02 (m, 1H), 1.93 – 1.78 (m, 6H), 1.78 – 1.60 (m, 1H), 1.54 – 1.25 (m, 5H), 1.21 – 1.07 (m, 1H).

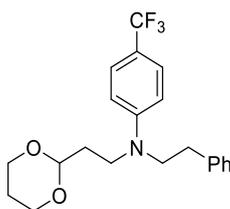
¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 164.1 (d, *J* = 243.1 Hz), 150.6 (d, *J* = 12.0 Hz), 135.5 (d, *J* = 14.4 Hz), 108.2 (d, *J* = 2.3 Hz), 102.9 (d, *J* = 25.8 Hz), 100.5, 97.7 (d, *J* = 26.3 Hz), 67.0 (2C), 57.8, 39.6, 34.6, 30.6 (2C), 26.2(2C), 25.8, 25.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 2967, 2927, 2860, 2843, 1611, 1594, 1574, 1564, 1486, 1474, 1455, 1448, 1434, 1406, 1364, 1340, 1274, 1257, 1240, 1200, 1172, 1142, 1131, 1100, 1033, 1003, 995, 978, 951, 922, 888, 861, 848, 834, 813, 778, 760, 734, 677.

HRMS (EI): *m/z* calc. for [C₁₈H₂₅ClFNO₂]: 341.1558; found 341.1563.

m.p.: 60.9–62.5 °C

***N*-(2-(1,3-Dioxan-2-yl)ethyl)-*N*-phenethyl-4-(trifluoromethyl)aniline (5c)**



According to **TP5** *N*-(2-(1,3-dioxan-2-yl)ethyl)-*O*-benzoyl-*N*-phenethylhydroxylamine (**10c**, 178 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent (4-(trifluoromethyl)phenyl)zinc chloride (**2m**, 2.6 mL, 0.29 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 2:1) afforded the title compound as a colourless oil (154 mg, 0.41 mmol, 81%).

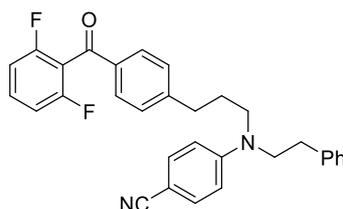
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 7.37 (d, J = 8.8 Hz, 2H), 7.27 – 7.20 (m, 2H), 7.18 – 7.10 (m, 3H), 6.69 – 6.62 (m, 2H), 4.46 (t, J = 4.9 Hz, 1H), 4.03 (ddt, J = 10.5, 5.0, 1.4 Hz, 2H), 3.65 (ddt, J = 12.3, 10.5, 2.4 Hz, 2H), 3.50 – 3.41 (m, 2H), 3.34 (t, J = 7.4 Hz, 2H), 2.78 (dd, J = 9.0, 6.7 Hz, 2H), 2.09 – 1.93 (m, 1H), 1.82 – 1.74 (m, 2H), 1.26 (dt, J = 13.5, 2.7, 1.4 Hz, 1H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 149.7, 139.1, 129.3, 128.8, 128.7, 126.7 (d, J = 3.7 Hz), 126.5, 125.2 (d, J = 270.1 Hz), 117.1 (q, J = 32.7 Hz), 110.8, 100.2, 66.9, 52.5, 45.7, 33.2, 32.6, 25.7.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2956, 2872, 1733, 1697, 1601, 1519, 1493, 1479, 1462, 1452, 1432, 1403, 1386, 1365, 1314, 1271, 1170, 1104, 1016, 958, 829, 805, 769, 746, 700, 674, 653.

HRMS (EI): m/z calc. for $[\text{C}_{21}\text{H}_{24}\text{F}_3\text{NO}_2]$: 379.1759; found 379.1768.

4-((3-(4-(2,6-Difluorobenzoyl)phenyl)propyl)(phenethyl)amino)benzonitrile (**5d**)



According to **TP5** (4-(3-((benzoyloxy)(phenethyl)amino)propyl)phenyl)(2,6-difluorophenyl)methanone (**10d**, 250 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 3\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent (4-cyanophenyl)zinc chloride (**2n**, 3.0 mL, 0.25 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 3:1) afforded the title compound as a colourless oil (190 mg, 0.40 mmol, 79%).

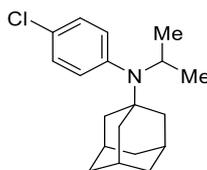
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 7.90 (d, $J = 8.2$ Hz, 2H), 7.59 – 7.51 (m, 3H), 7.37 (ddt, $J = 11.5, 8.8, 7.0$ Hz, 5H), 7.26 – 7.21 (m, 2H), 7.15 – 7.07 (m, 2H), 6.70 – 6.65 (m, 2H), 3.72 – 3.54 (m, 2H), 3.41 – 3.25 (m, 2H), 2.94 (t, $J = 7.5$ Hz, 2H), 2.78 (t, $J = 7.6$ Hz, 2H), 2.04 – 1.88 (m, 2H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 188.5, 159.8 (dd, $J = 251.5, 7.6$ Hz, 2C), 150.1, 148.2, 138.6, 135.1, 133.8 (2C), 132.9, 131.9 (t, $J = 9.9$ Hz), 130.1 (2C), 128.8 (2C), 128.7 (2C), 128.7 (2C), 126.7, 117.1 (t, $J = 21.9$ Hz), 112.1 – 111.8 (m, 2C), 111.2 (2C), 97.2, 52.7, 50.4, 33.3, 33.2, 27.9.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2932, 2211, 1670, 1622, 1602, 1519, 1496, 1463, 1405, 1360, 1311, 1294, 1277, 1234, 1202, 1174, 1145, 1117, 1004, 967, 930, 815, 790, 748, 724, 699.

HRMS (EI): m/z calc. for $[\text{C}_{31}\text{H}_{26}\text{F}_2\text{N}_2\text{O}]$: 480.2013; found 480.2023.

(3*s*,5*s*,7*s*)-*N*-(4-chlorophenyl)-*N*-isopropyladamantan-1-amine (5e)



According to **TP5** *N*-((3*s*,5*s*,7*s*)-adamantan-1-yl)-*O*-benzoyl-*N*-isopropylhydroxylamine (**10e**, 157 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried CoCl₂·(3 mg, 25 μmol, 5.00 mol%) was added and subsequent naphthalen-1-ylzinc chloride (**2o**, 2.8 mL, 0.27 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 9:1) afforded the title compound as a colourless oil (94 mg, 0.31 mmol, 62%).

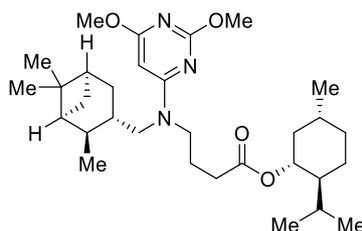
¹H-NMR (400 MHz, CDCl₃): δ / ppm = 7.33 – 7.17 (m, 2H), 6.90 – 6.79 (m, 2H), 3.84 (p, *J* = 6.8 Hz, 1H), 2.17 – 1.97 (m, 9H), 1.73 – 1.62 (m, 6H), 1.24 (d, *J* = 6.8 Hz, 6H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 142.9, 129.4 (2C), 127.6, 119.3 (2C), 60.5, 47.3, 40.7 (3C), 36.3 (3C), 29.7 (3C), 22.4 (2C).

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 2950, 1738, 1657, 1598, 1493, 1435, 1357, 1337, 1213, 1175, 1157, 1124, 1095, 1031, 977, 907, 809, 729, 699.

HRMS (EI): *m/z* calc. for [C₁₉H₂₆ClN]: 303.1754; found 303.1749.

(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 4-((2,6-dimethoxypyrimidin-4-yl)((1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (5f)



According to **TP5** (1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-((benzoyloxy) (((1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (**10f**, 256 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried $\text{CoCl}_2 \cdot 3\text{H}_2\text{O}$ (3 mg, 25 μmol , 5.00 mol%) was added and subsequent (2,6-dimethoxypyrimidin-4-yl)zinc chloride (**2p**, 2.7 mL, 0.28 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 4:1) afforded the title compound as a colourless oil (215 mg, 0.41 mmol, 81%).

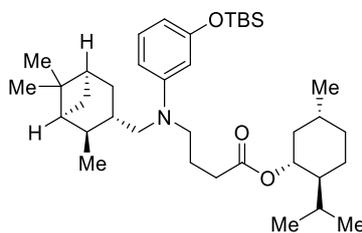
$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ / ppm = 7.89 (s, 1H), 4.64 (td, $J = 10.8, 4.3$ Hz, 1H), 3.98 (s, 3H), 3.94 (s, 3H), 3.10 (dd, $J = 12.5, 5.3$ Hz, 1H), 2.96 (dd, $J = 7.9, 6.4$ Hz, 2H), 2.66 (dd, $J = 12.5, 9.6$ Hz, 1H), 2.32 (t, $J = 7.4$ Hz, 2H), 2.28 – 2.20 (m, 1H), 2.01 – 1.89 (m, 2H), 1.89 – 1.76 (m, 2H), 1.74 – 1.57 (m, 7H), 1.58 – 1.40 (m, 2H), 1.37 – 1.28 (m, 1H), 1.14 (s, 3H), 0.93 (d, $J = 7.0$ Hz, 3H), 0.89 – 0.84 (m, 12H), 0.72 (d, $J = 6.8$ Hz, 3H).

$^{13}\text{C-NMR}$ (101 MHz, CDCl_3): δ / ppm = 173.1, 167.1, 161.2, 152.7, 126.1, 74.0, 62.9, 54.7, 53.8, 53.0, 48.0, 47.0, 41.6, 41.4, 40.9, 38.9, 34.2, 34.1, 33.6, 32.9, 31.9, 31.4, 27.9, 26.3, 23.4, 23.1, 23.0, 22.0, 21.8, 20.8, 16.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm^{-1} = 2951, 2924, 2869, 1729, 1596, 1557, 1466, 1456, 1402, 1384, 1370, 1333, 1314, 1284, 1265, 1241, 1175, 1153, 1134, 1123, 1107, 1097, 1076, 1039, 1013, 984, 964, 938, 919, 844, 801, 764, 733, 710.

HRMS (EI): m/z calc. for $[\text{C}_{31}\text{H}_{51}\text{N}_3\text{O}_4]$: 529.3880; found 529.3888.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 4-((3-((*tert*-butyldimethylsilyl)oxy)phenyl)((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (5g)



According to **TP5** (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-((benzoyloxy)((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (**10f**, 256 mg, 0.50 mmol, 1.00 equiv) was dissolved in dry THF (2 mL). Predried CoCl₂·(3 mg, 25 μmol, 5.00 mol%) was added and subsequent (3-((*tert*-butyldimethylsilyl)oxy)phenyl)zinc chloride (**2q**, 2.9 mL, 0.26 M, 0.75 mmol, 1.50 equiv) was added dropwise and the resulting mixture was stirred for 2 h at rt. Purification of the crude product by flash chromatography (hexane:EtOAc 4:1) afforded the title compound as a colourless oil (257 mg, 0.43 mmol, 86%).

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 6.84 (t, *J* = 8.1 Hz, 1H), 6.03 (t, *J* = 2.3 Hz, 1H), 5.97 (ddd, *J* = 7.9, 2.2, 0.7 Hz, 1H), 4.51 (d, *J* = 4.4 Hz, 1H), 3.27 – 3.13 (m, 2H), 3.08 (dd, *J* = 14.3, 6.8 Hz, 1H), 2.94 (dt, *J* = 14.2, 7.2 Hz, 1H), 2.17 – 2.07 (m, 4H), 2.06 – 1.95 (m, 1H), 1.87 (dddd, *J* = 13.1, 9.7, 3.3, 1.9 Hz, 1H), 1.79 (dtd, *J* = 11.9, 3.8, 1.7 Hz, 1H), 1.75 – 1.43 (m, 10H), 1.29 (dddd, *J* = 11.8, 9.2, 6.2, 3.8 Hz, 3H), 1.18 (ddt, *J* = 12.5, 10.9, 3.2 Hz, 1H), 0.98 (s, 3H), 0.89 – 0.81 (m, 1H), 0.83 (d, *J* = 7.1 Hz, 3H), 0.78 (s, 9H), 0.77 (s, 3H), 0.70 (dd, *J* = 6.8, 3.6 Hz, 6H), 0.56 (d, *J* = 7.0 Hz, 3H), -0.00 (d, *J* = 1.7 Hz, 6H).

¹³C-NMR (101 MHz, CDCl₃): δ / ppm = 172.8, 156.7, 149.4, 129.7, 107.9, 106.3, 104.8, 74.2, 61.0, 51.5, 48.3, 47.0, 41.7, 41.6, 41.0, 38.8, 34.3, 34.0, 33.9, 32.4, 32.0, 31.4, 28.0, 26.3, 25.8 (3C), 23.4, 23.0, 22.1, 22.1, 22.0, 20.8, 18.3, 16.3, -4.3, -4.3.

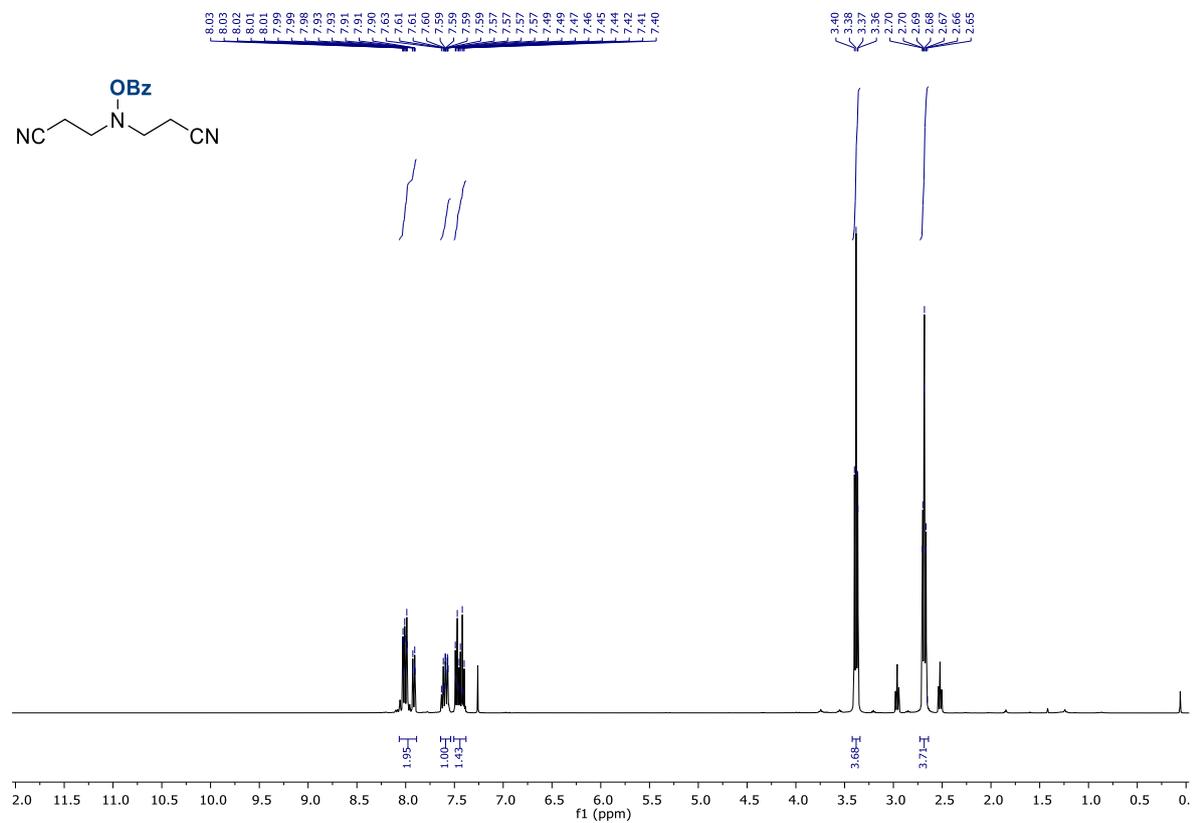
IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm⁻¹ = 2953, 2928, 2859, 1729, 1601, 1573, 1496, 1471, 1462, 1456, 1386, 1368, 1252, 1231, 1193, 1172, 1159, 1126, 1096, 1081, 1037, 1004, 984, 963, 953, 909, 834, 780, 757, 732, 690, 664.

HRMS (EI): *m/z* calc. for [C₃₇H₆₃NO₃Si]: 597.4577; found 597.4588.

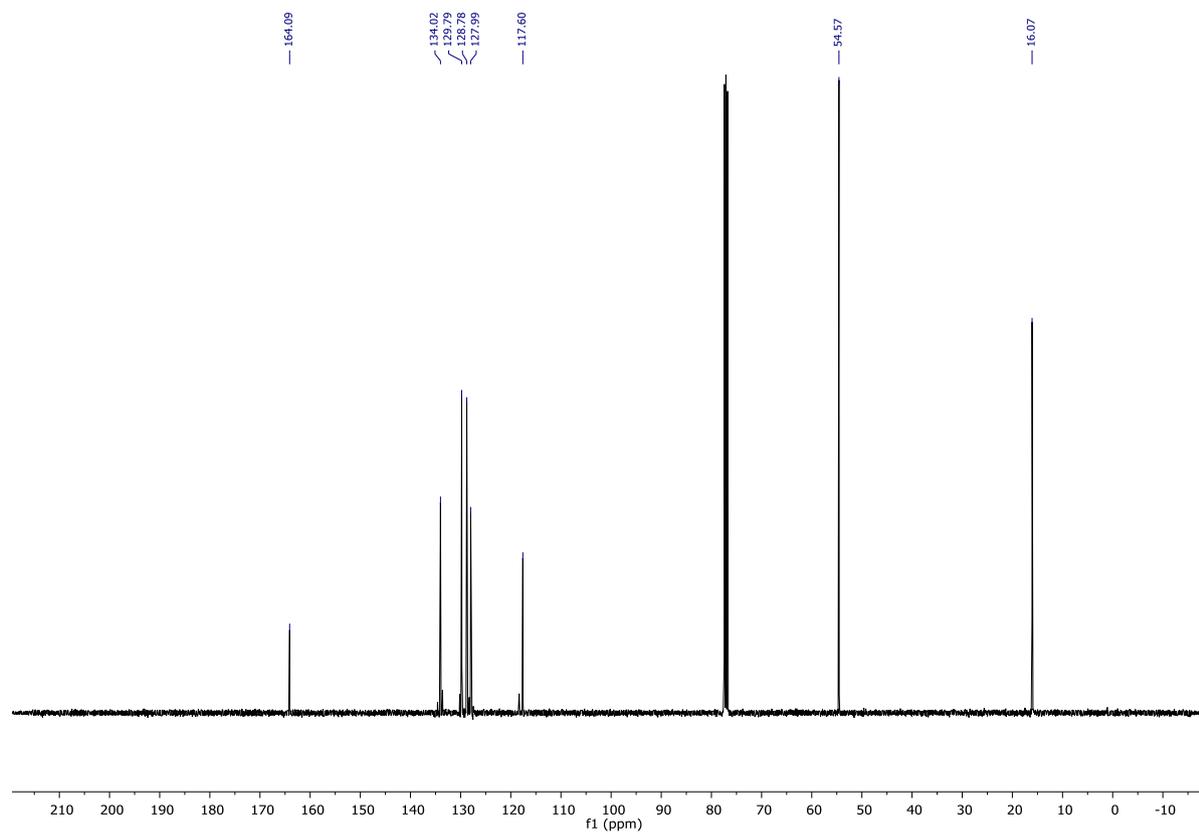
NMR Spectra

3,3'-((Benzoyloxy)azanediyldipropanenitrile (8)

¹H-NMR (400 MHz, CDCl₃)

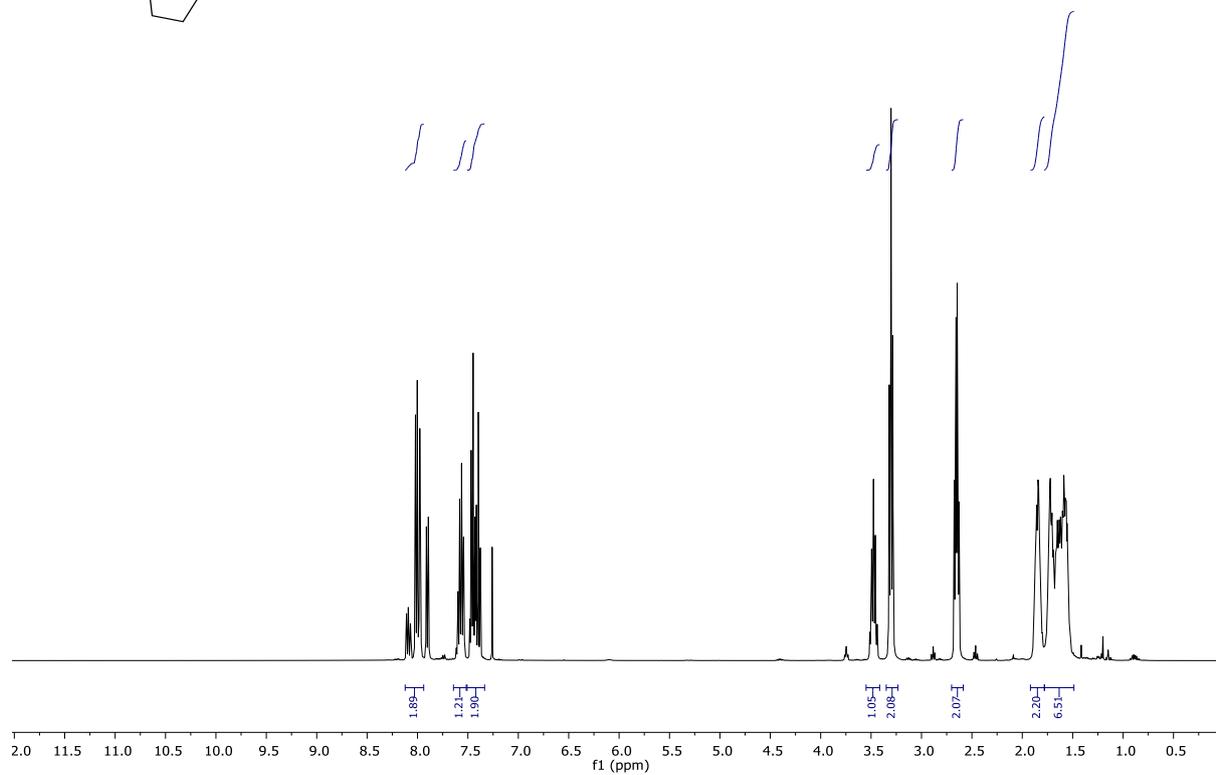
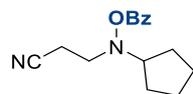


¹³C-NMR (101 MHz, CDCl₃)

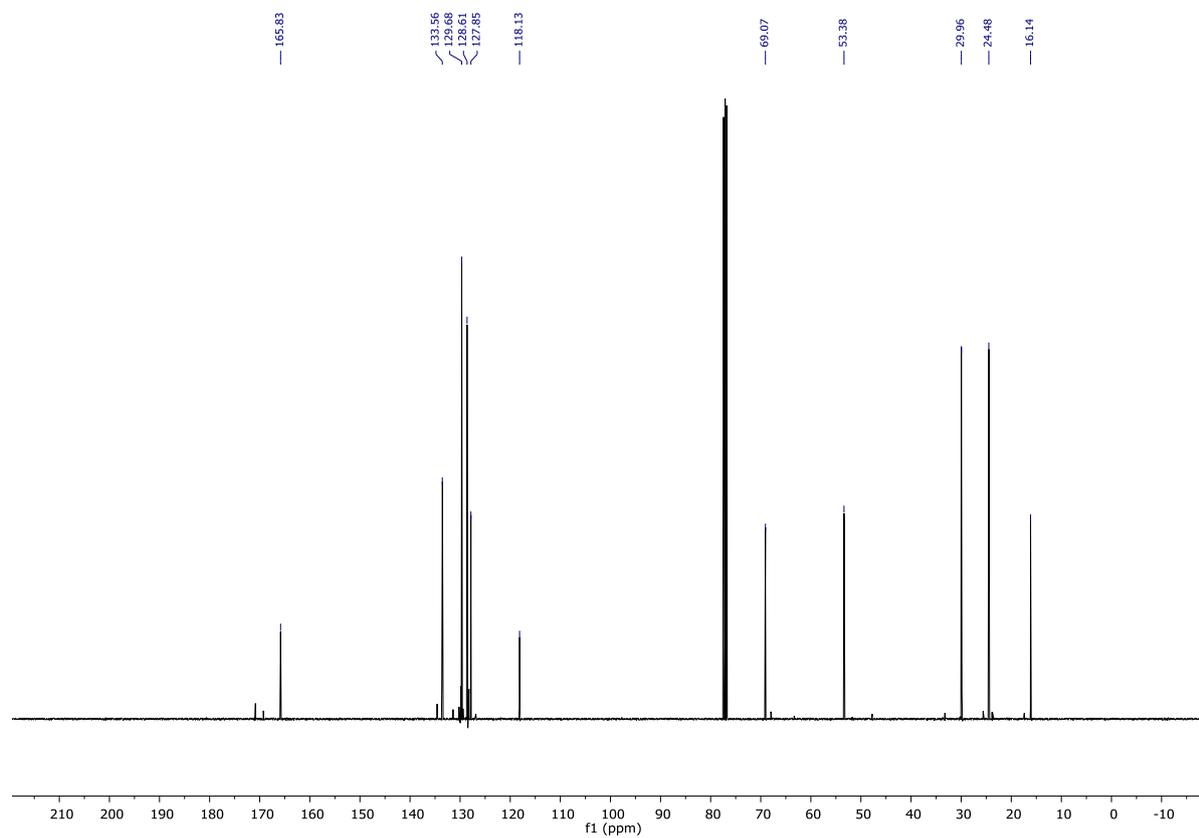


3-((Benzoyloxy)(cyclopentyl)amino)propanenitrile (9a)

¹H-NMR (400 MHz, CDCl₃)

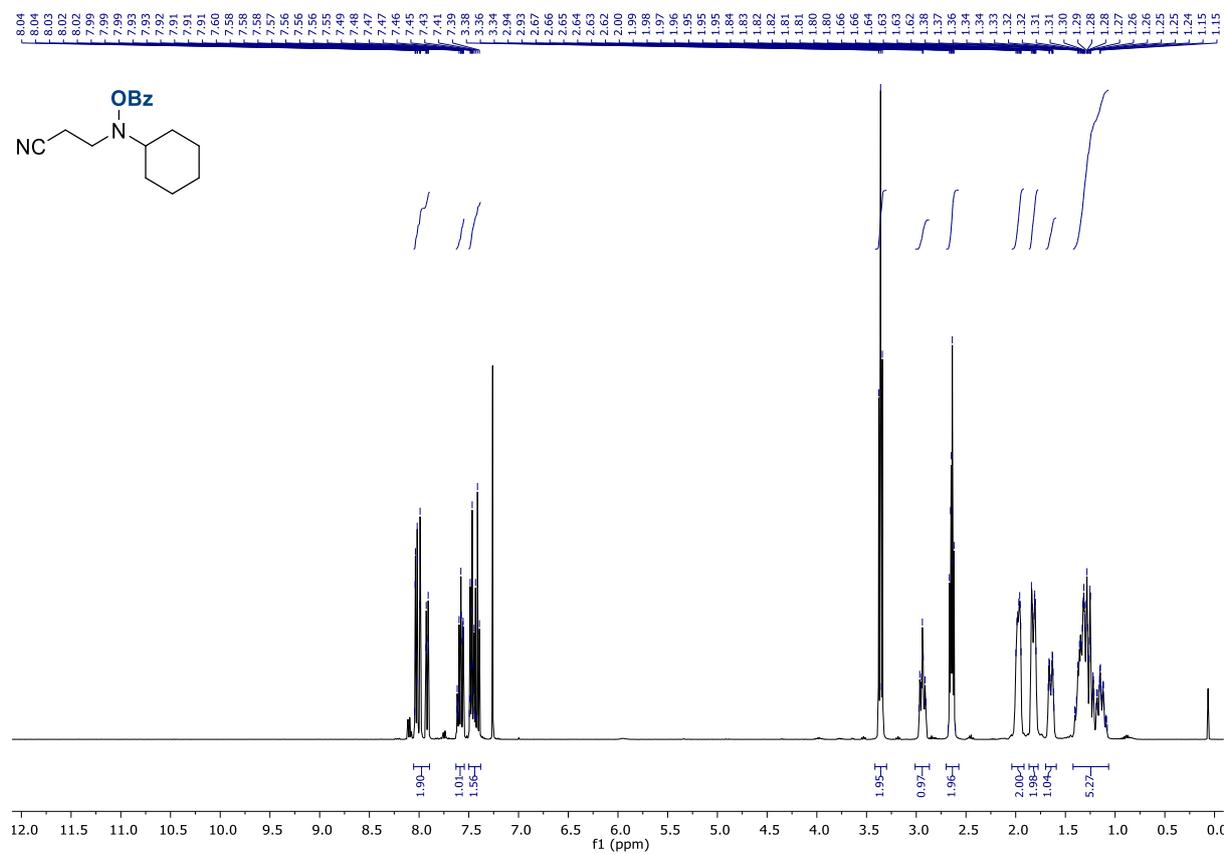


¹³C-NMR (101 MHz, CDCl₃)

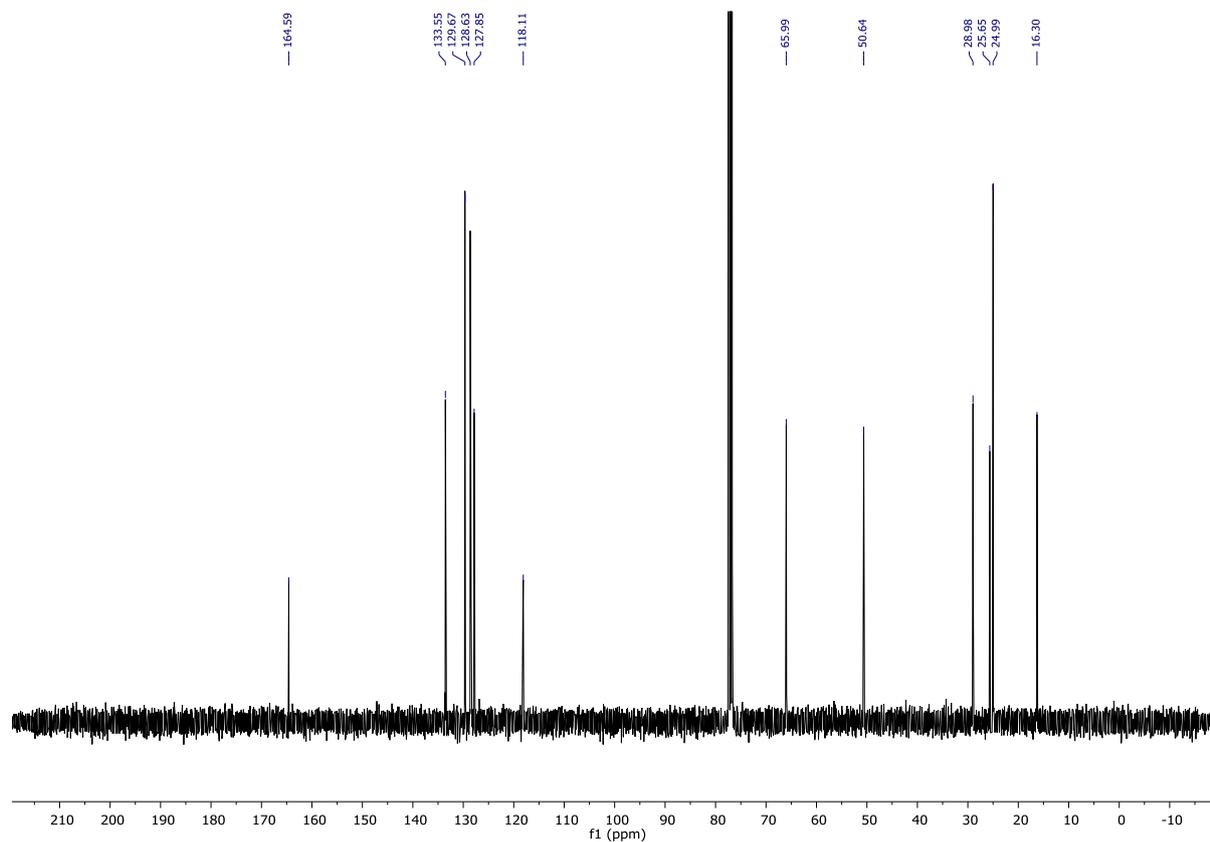


3-((Benzoyloxy)(cyclohexyl)amino)propanenitrile (9b)

¹H-NMR (400 MHz, CDCl₃)

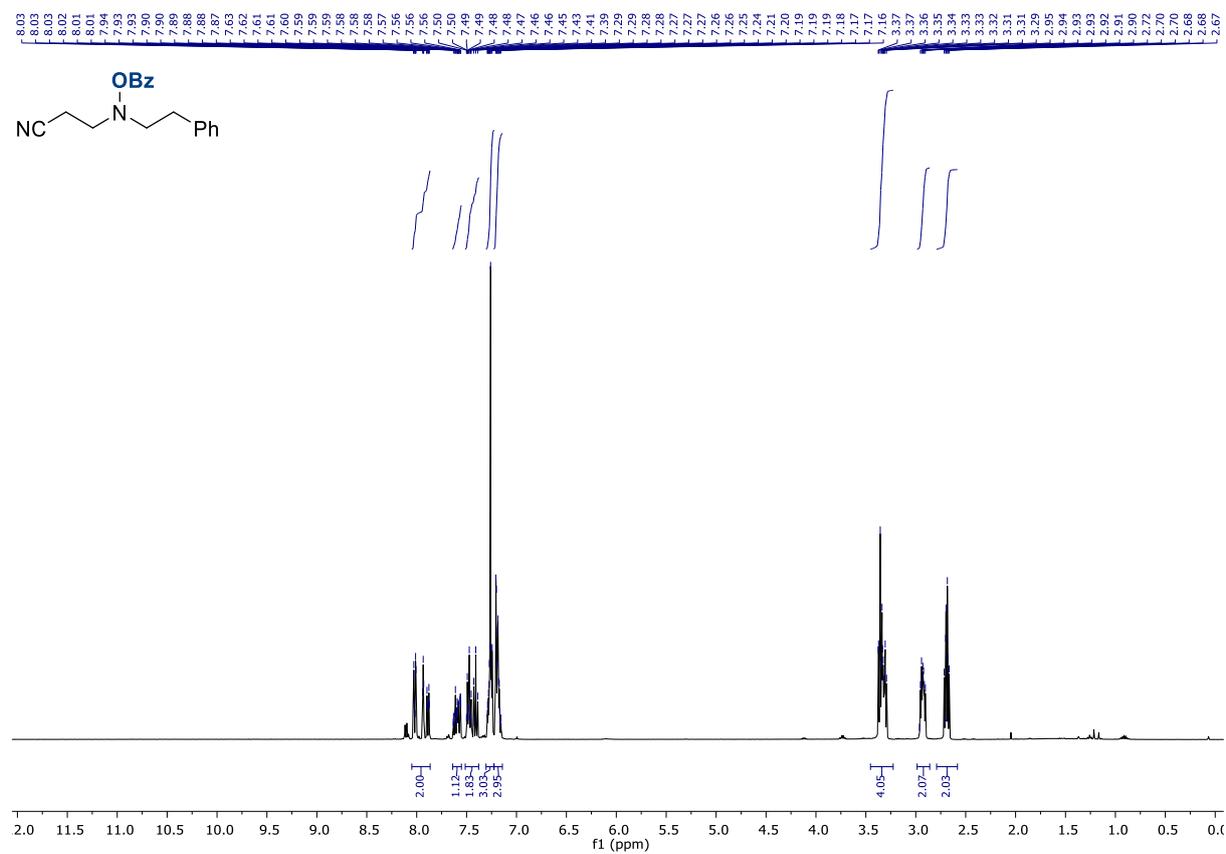


¹³C-NMR (101 MHz, CDCl₃)

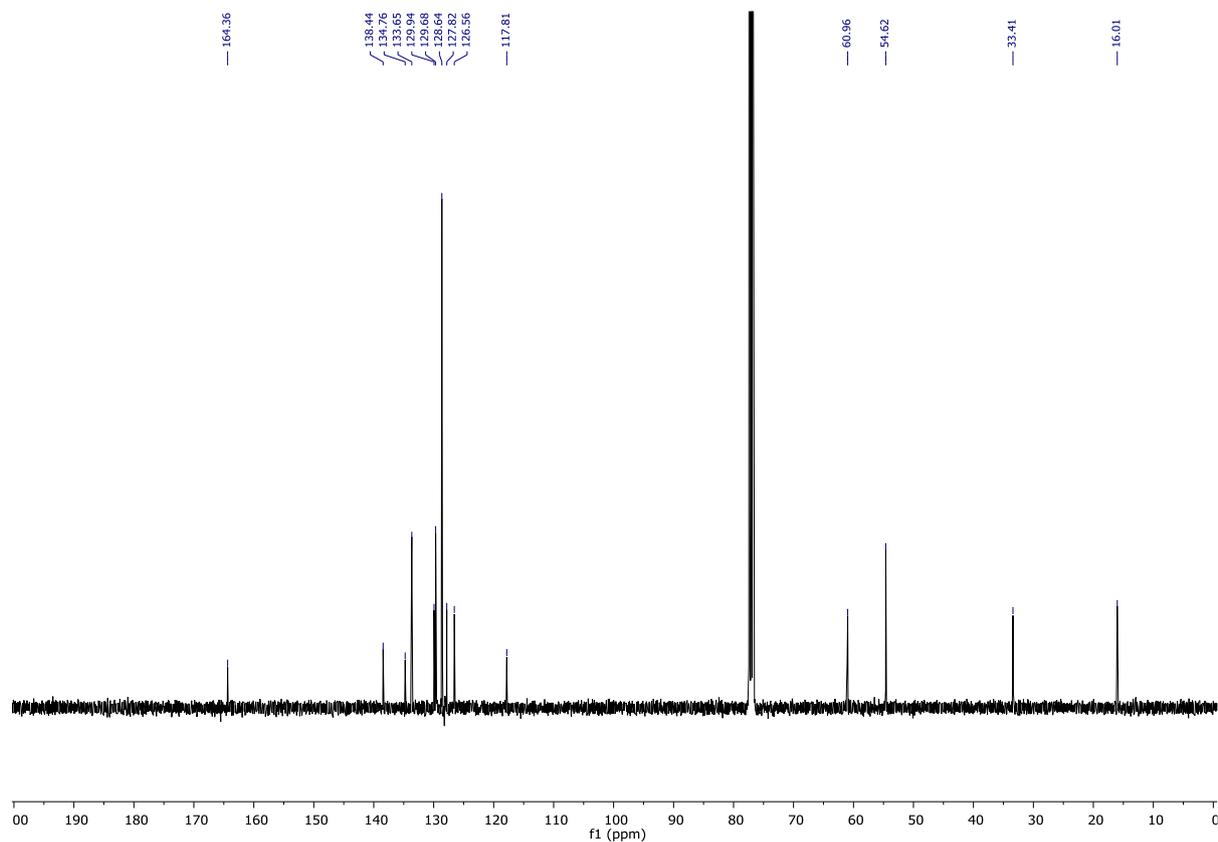


3-((Benzoyloxy)(phenethyl)amino)propanenitrile (9c)

¹H-NMR (400 MHz, CDCl₃)

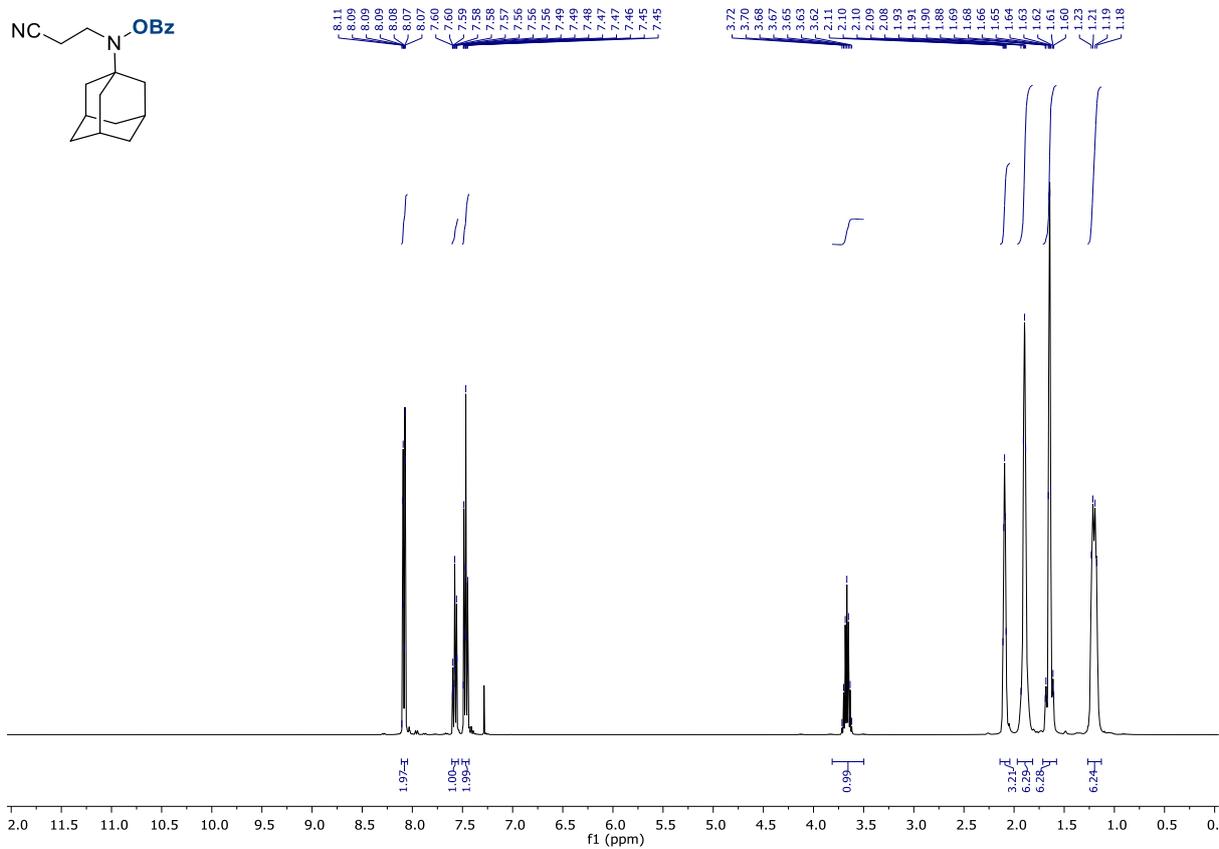


¹³C-NMR (101 MHz, CDCl₃)

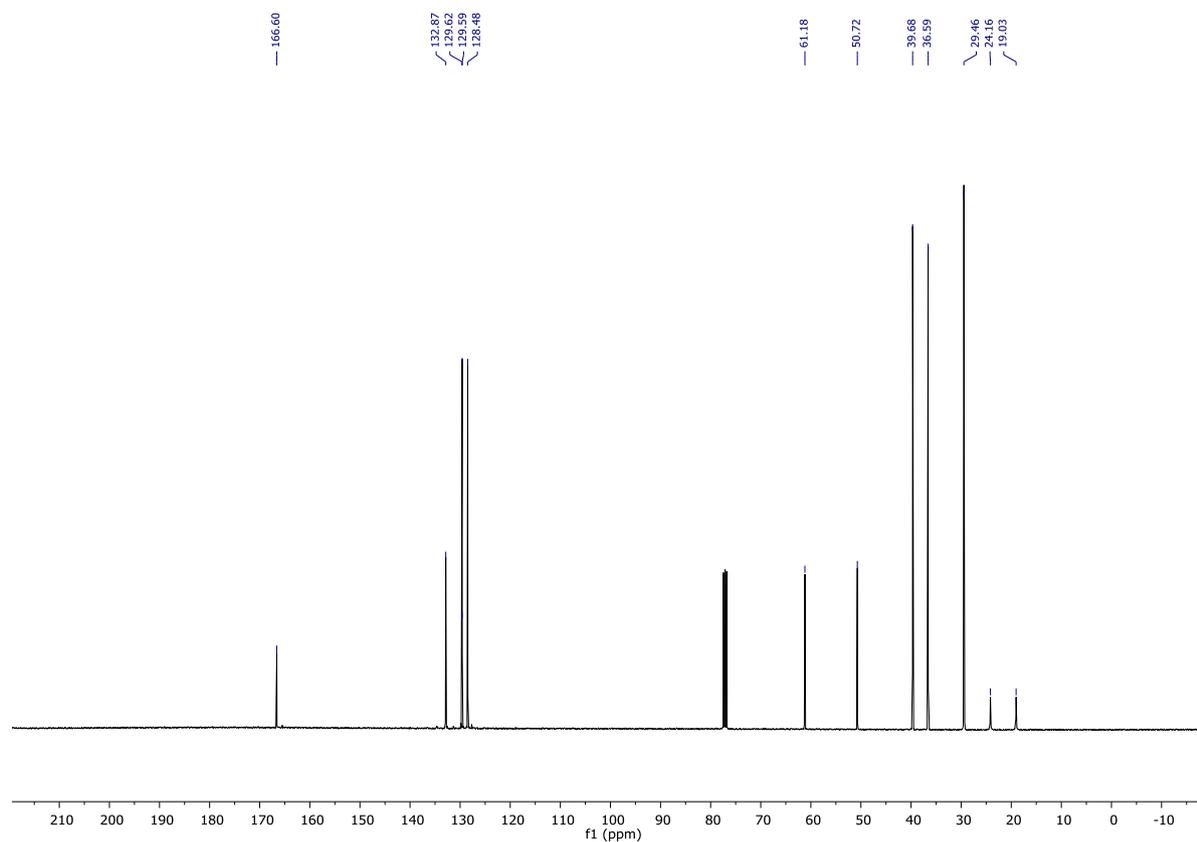


3-(((3*s*,5*s*,7*s*)-Adamantan-1-yl)(benzoyloxy)amino)propanenitrile (9d)

¹H-NMR (400 MHz, CDCl₃)

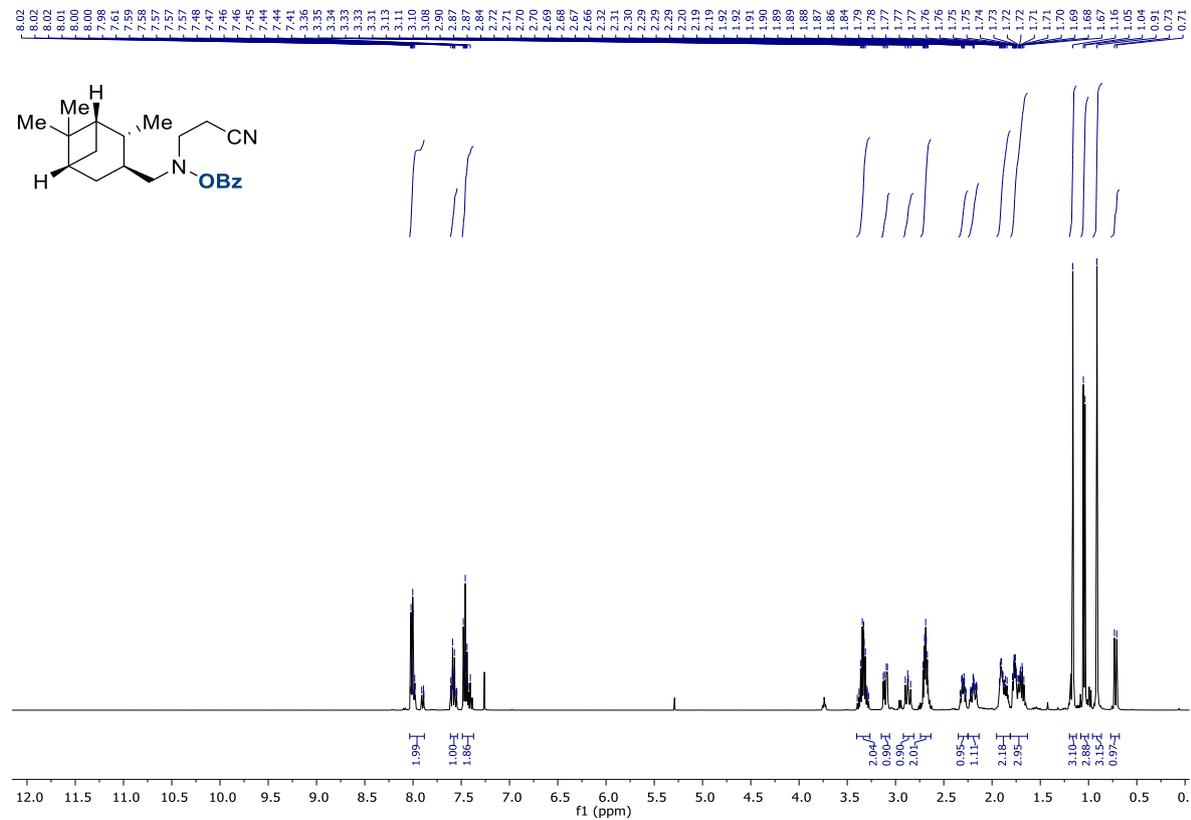


¹³C-NMR (101 MHz, CDCl₃)

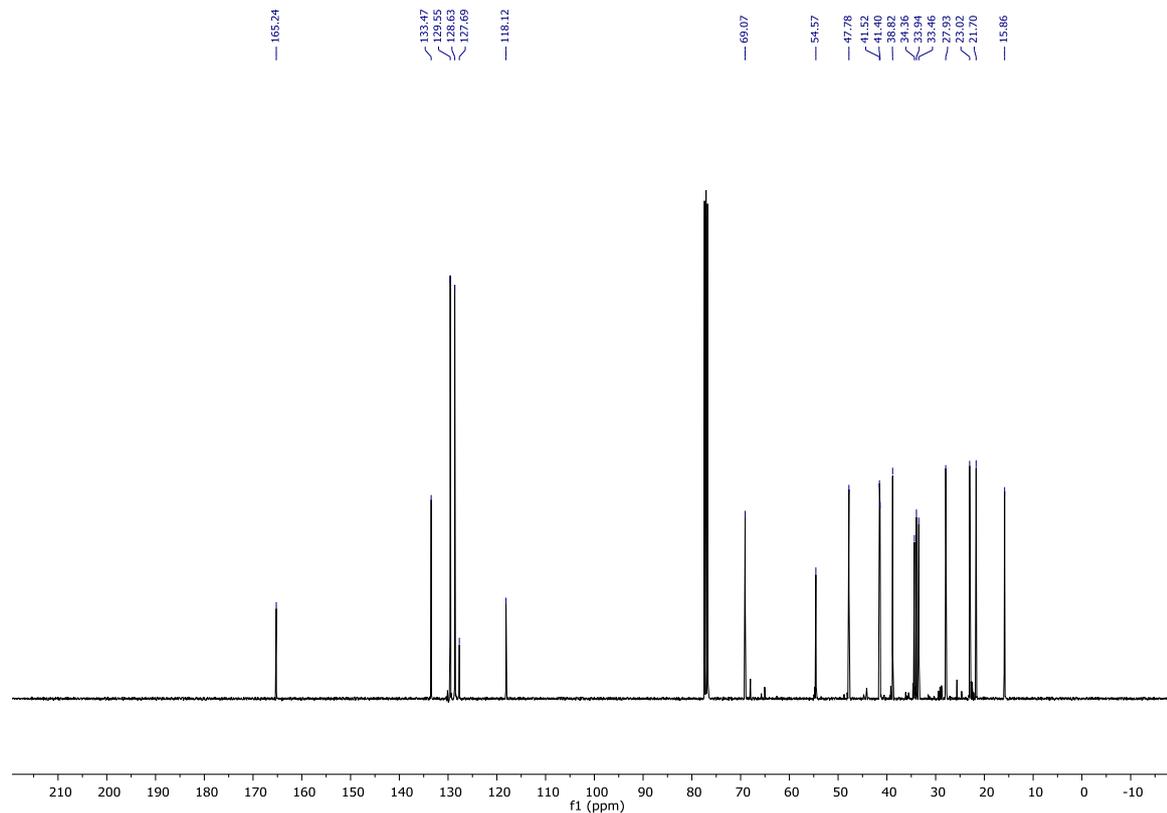


3-((Benzoyloxy)(((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)propanenitrile (9e)

¹H-NMR (400 MHz, CDCl₃)

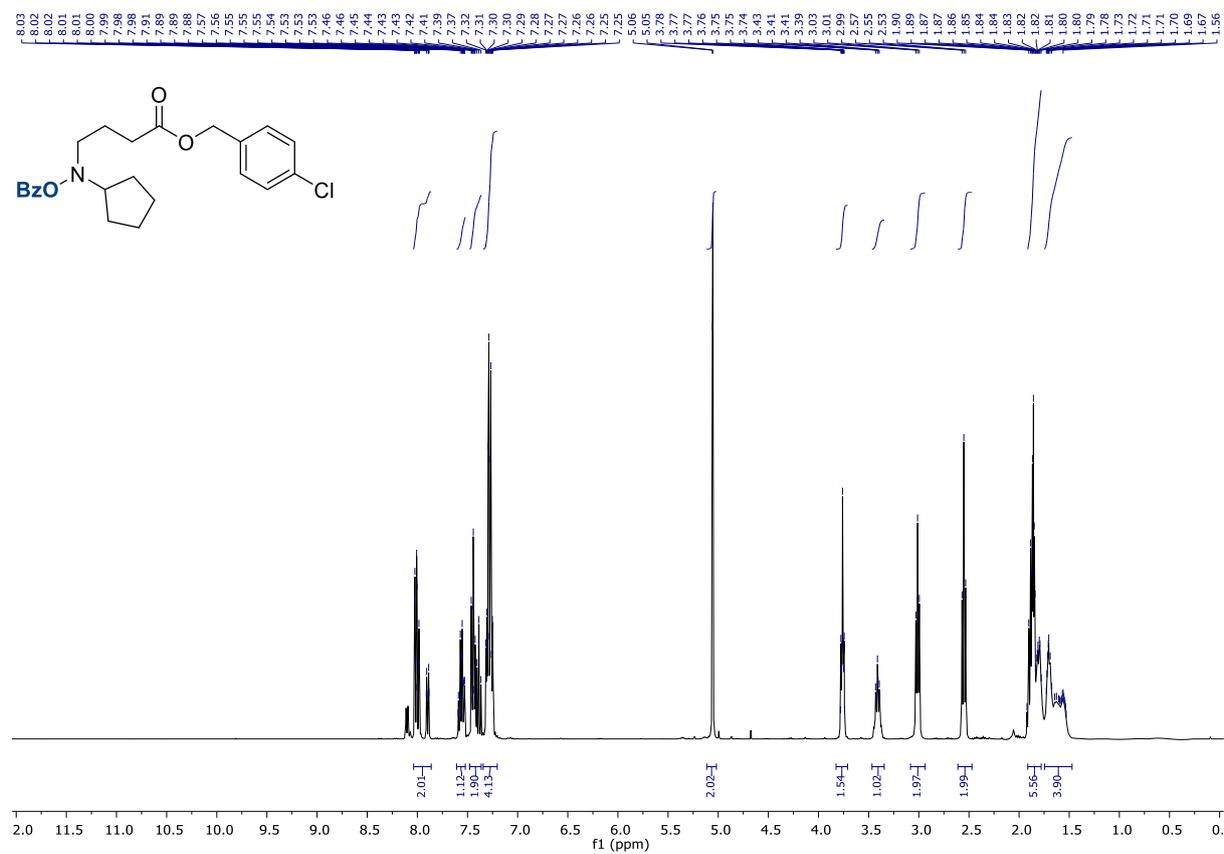


¹³C-NMR (101 MHz, CDCl₃)

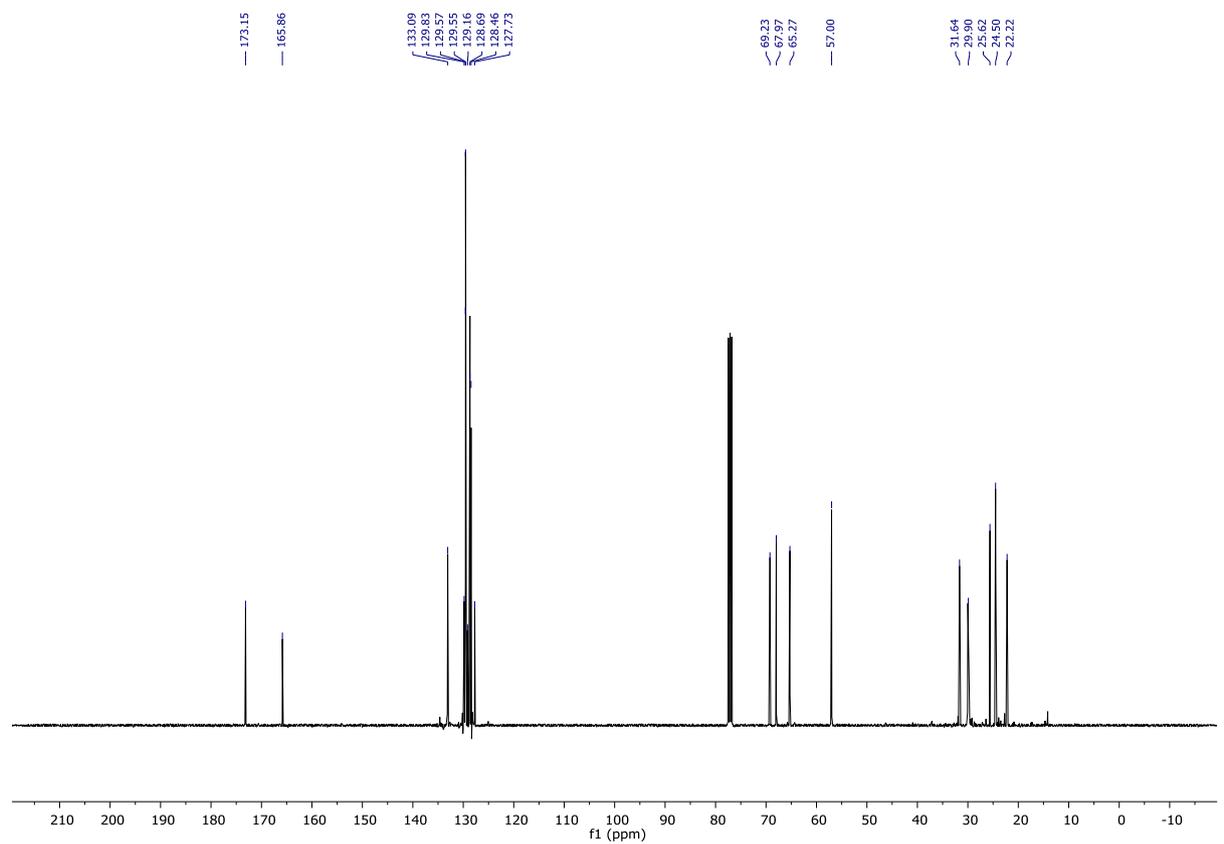


4-Chlorobenzyl 4-((benzyloxy)(cyclopentyl)amino)butanoate (10a)

¹H-NMR (400 MHz, CDCl₃)

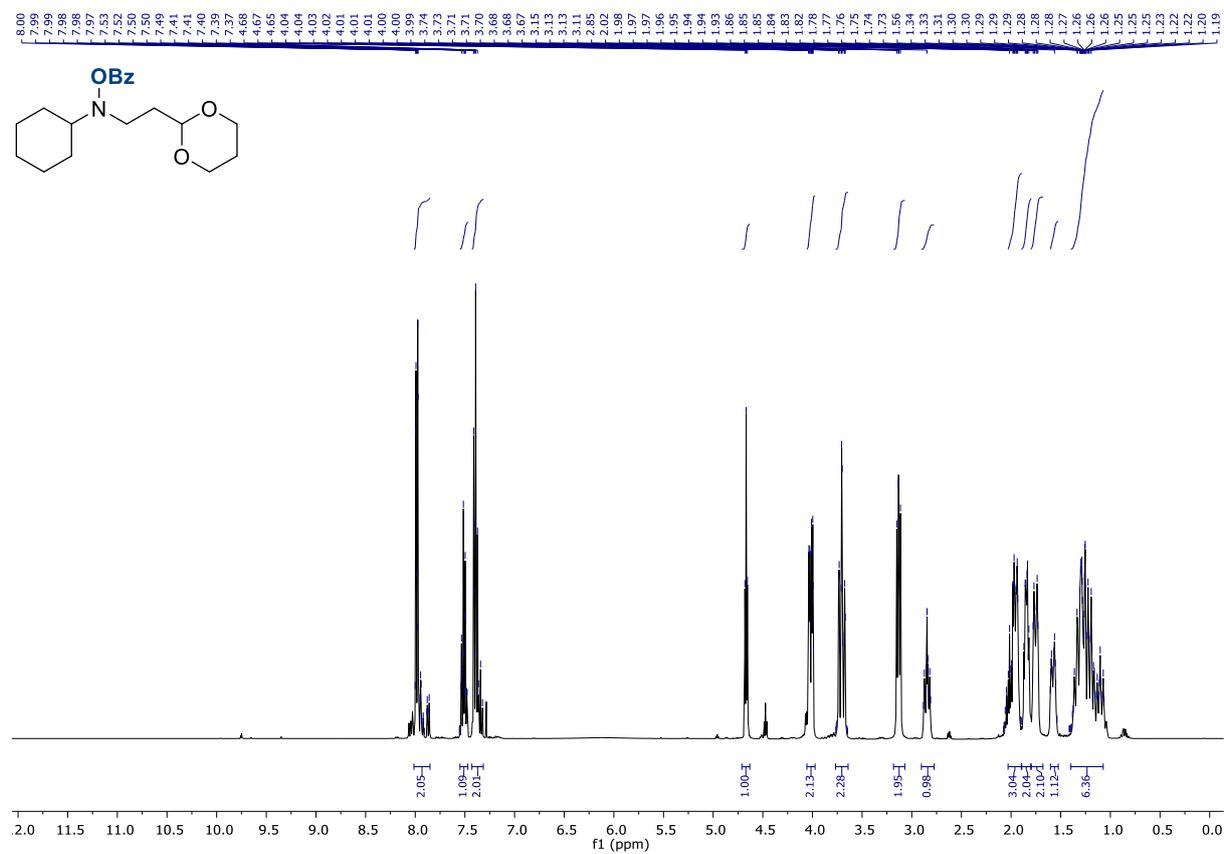


¹³C-NMR (101 MHz, CDCl₃)

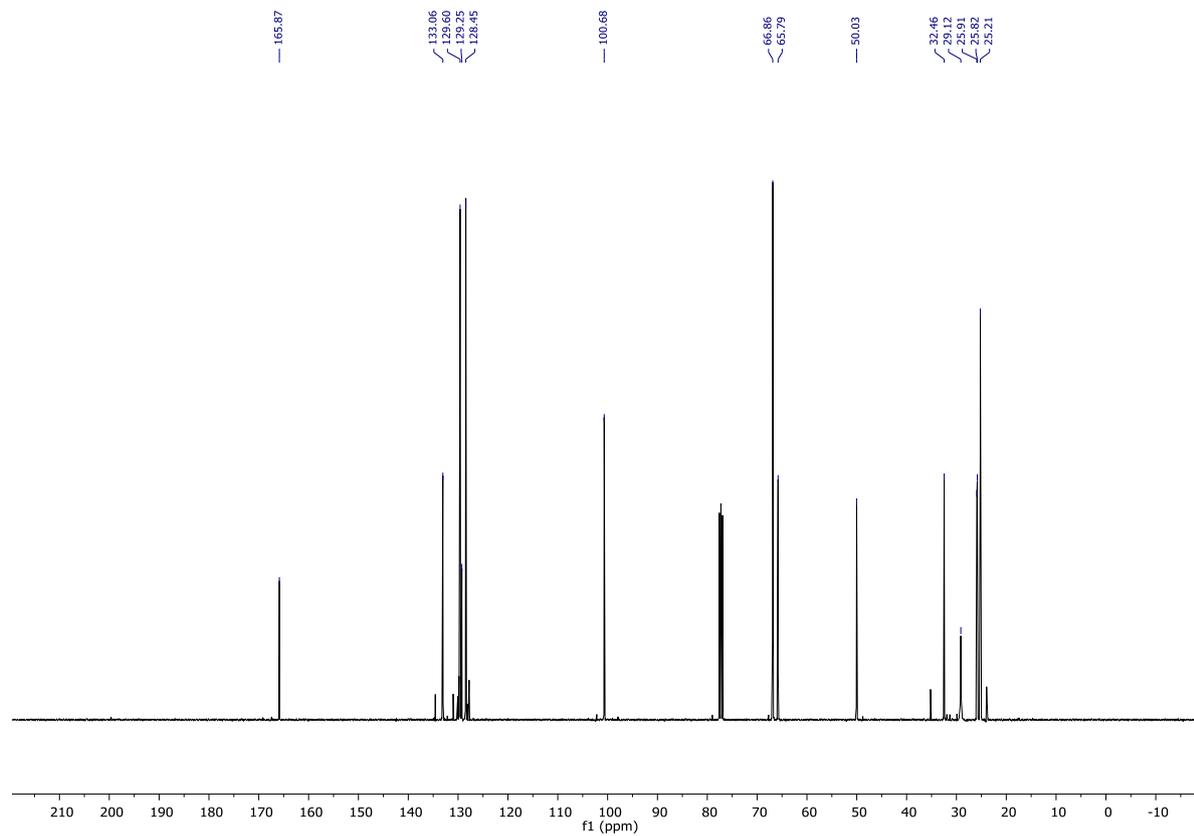


N-(2-(1,3-dioxan-2-yl)ethyl)-*O*-benzoyl-*N*-cyclohexylhydroxylamine (10b)

¹H-NMR (400 MHz, CDCl₃)

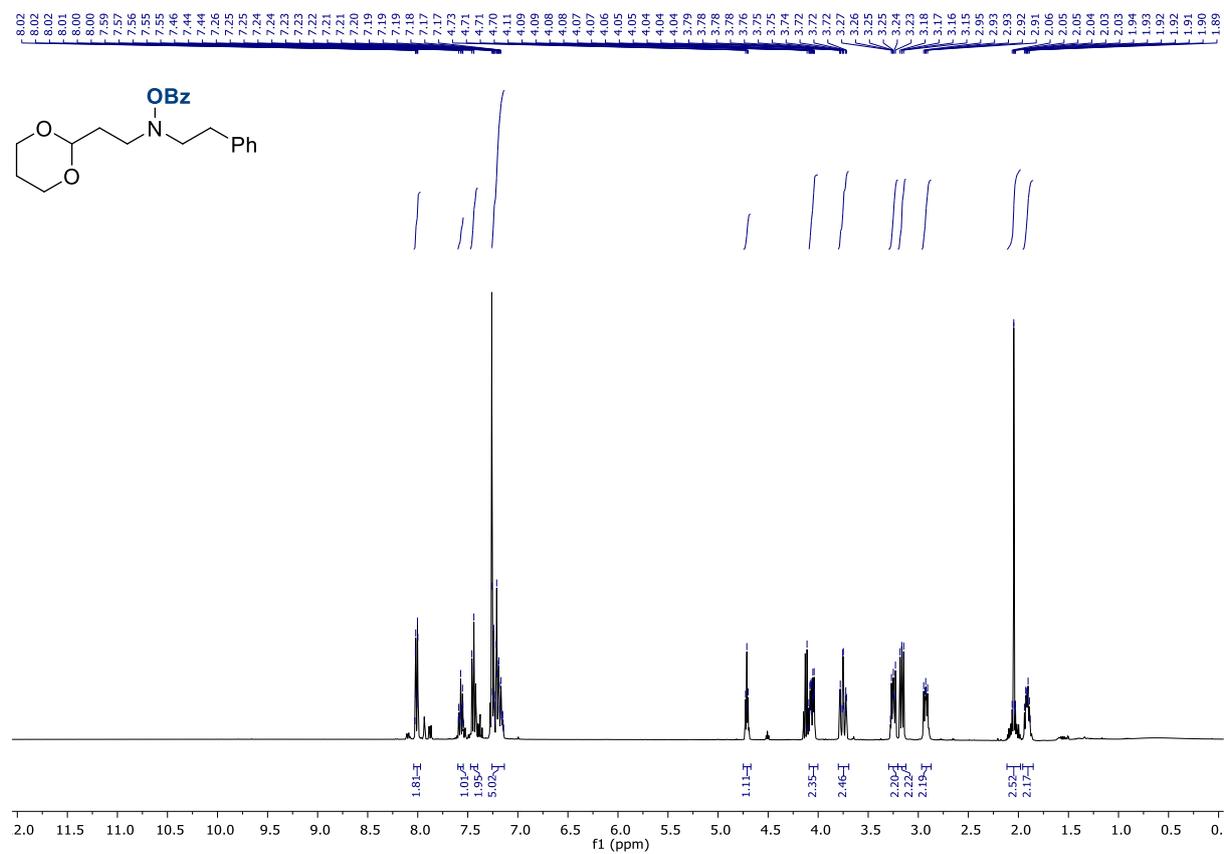


¹³C-NMR (101 MHz, CDCl₃)

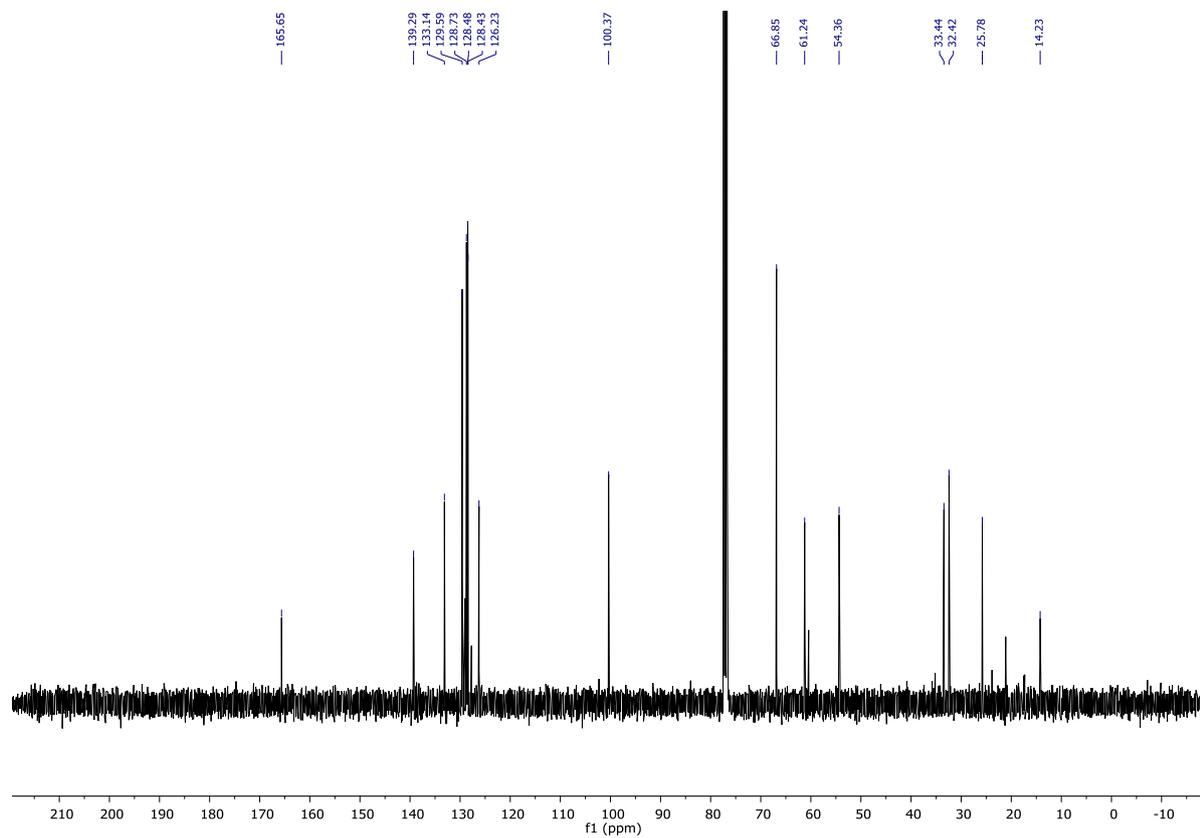


N-(2-(1,3-Dioxan-2-yl)ethyl)-*O*-benzoyl-*N*-phenethylhydroxylamine (10c)

¹H-NMR (400 MHz, CDCl₃)

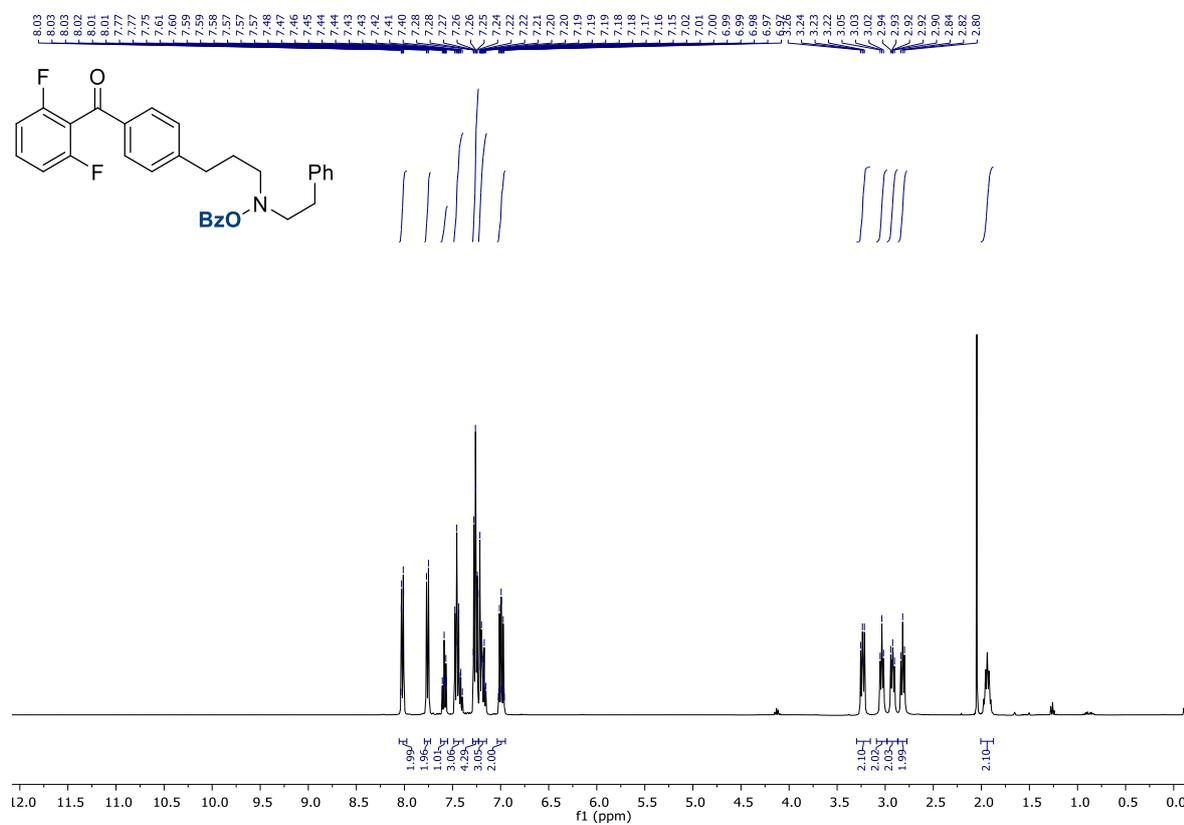


¹³C-NMR (101 MHz, CDCl₃)

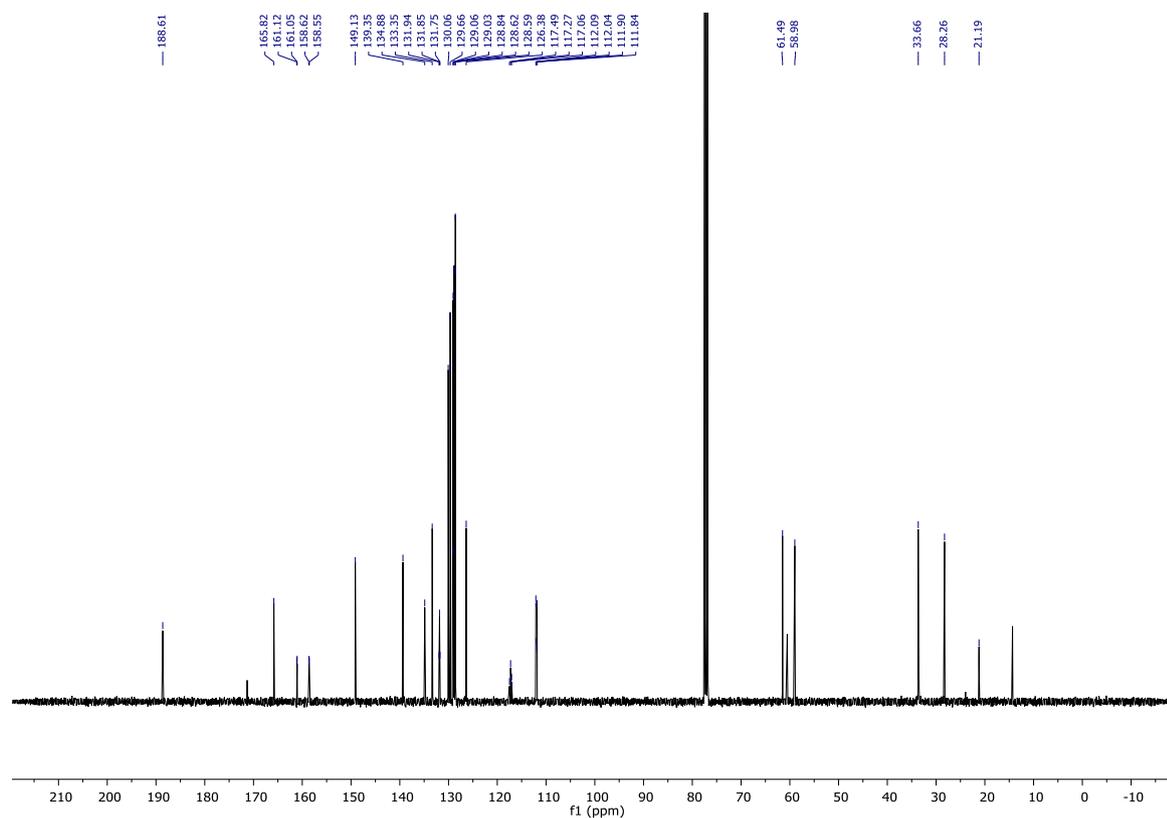


**(4-(3-((Benzoyloxy)(phenethyl)amino)propyl)phenyl)(2,6-difluorophenyl)methanone
(10d)**

¹H-NMR (400 MHz, CDCl₃)

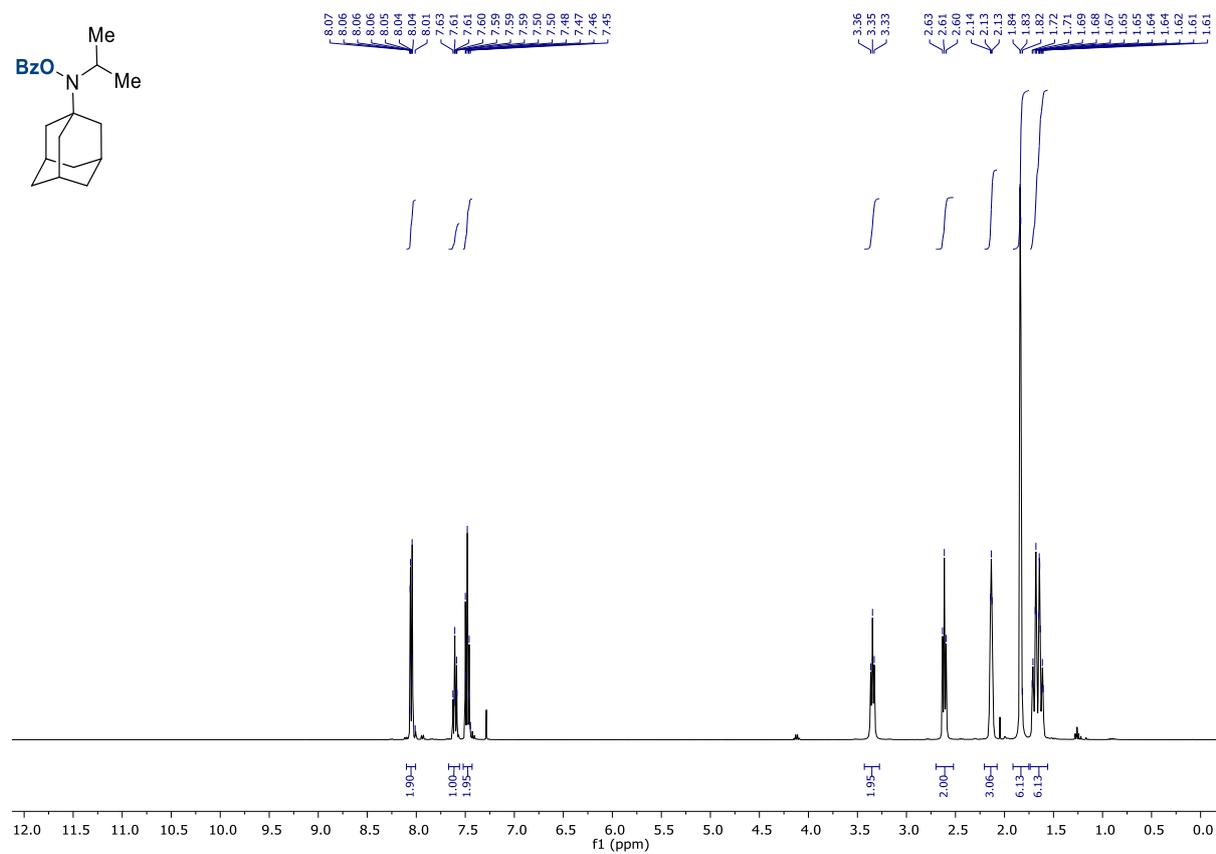
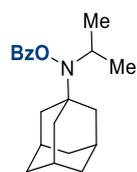


¹³C-NMR (101 MHz, CDCl₃)

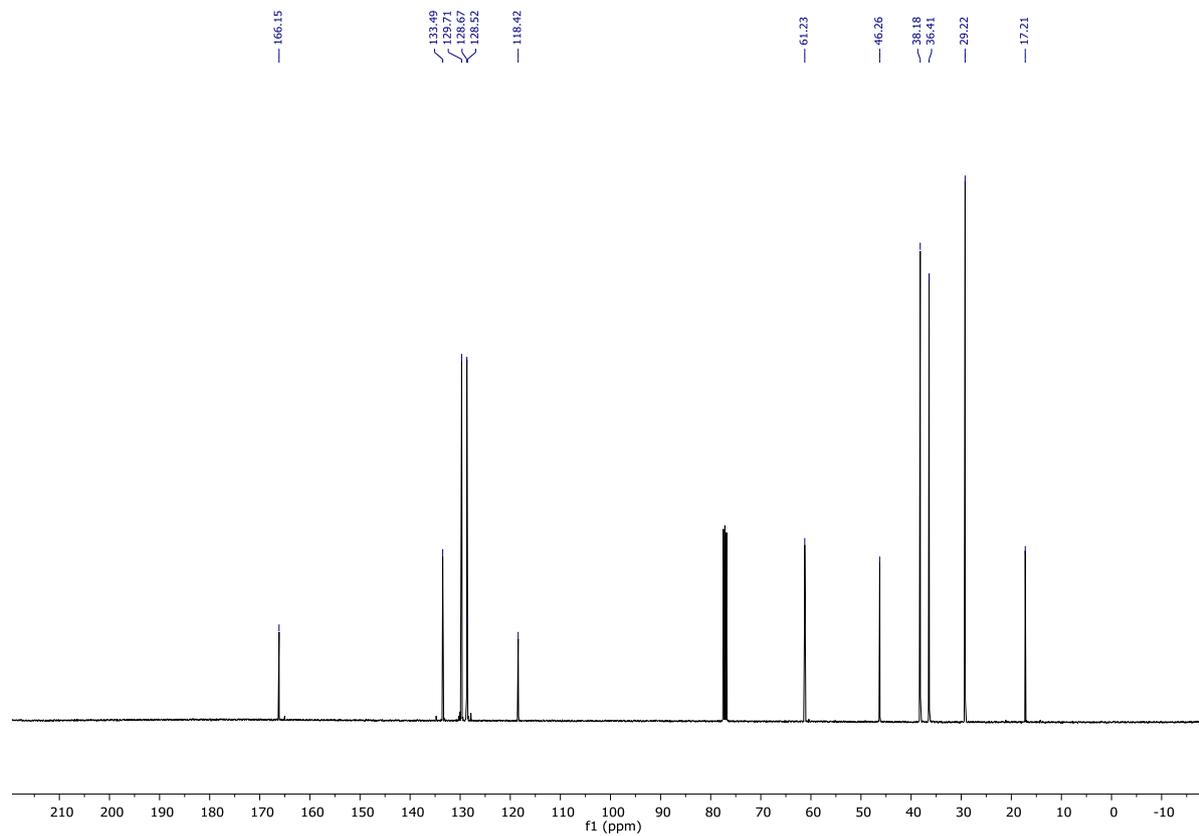


***N*-((3*s*,5*s*,7*s*)-adamantan-1-yl)-*O*-benzoyl-*N*-isopropylhydroxylamine (10e)**

¹H-NMR (400 MHz, CDCl₃)

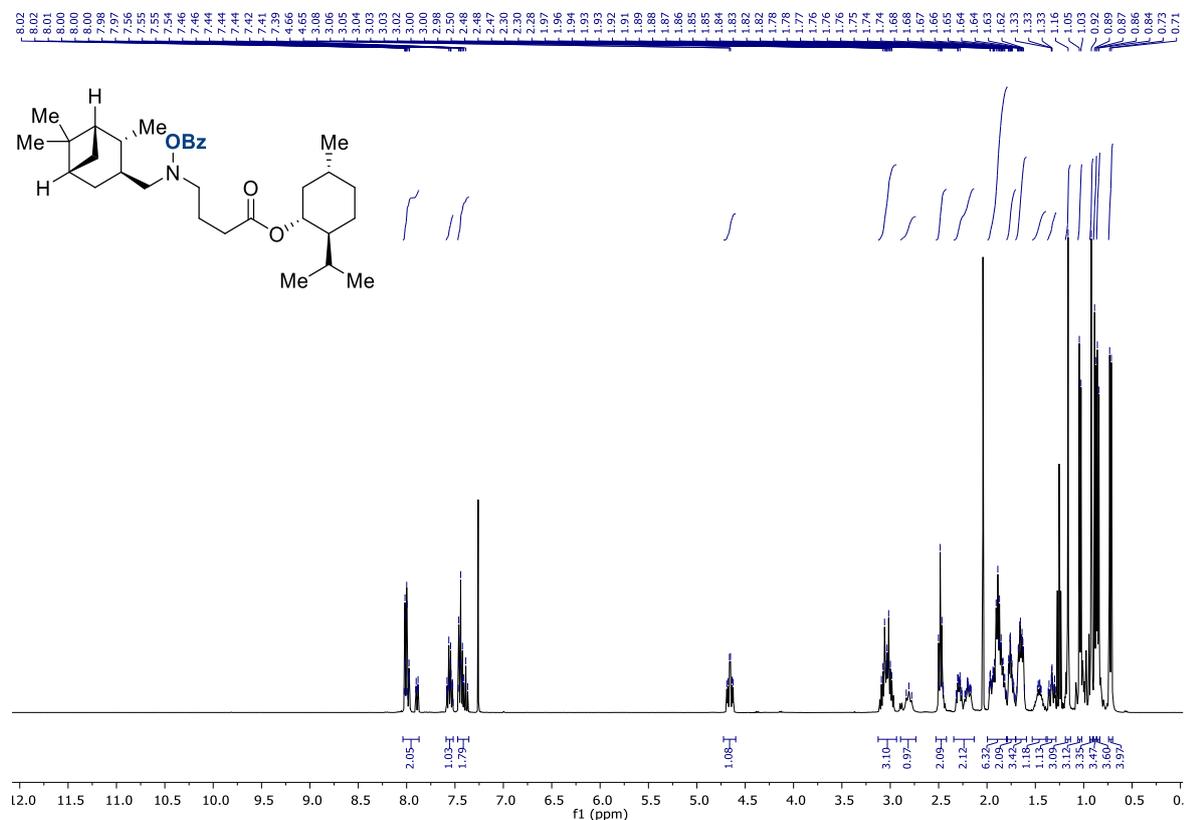


¹³C-NMR (101 MHz, CDCl₃)

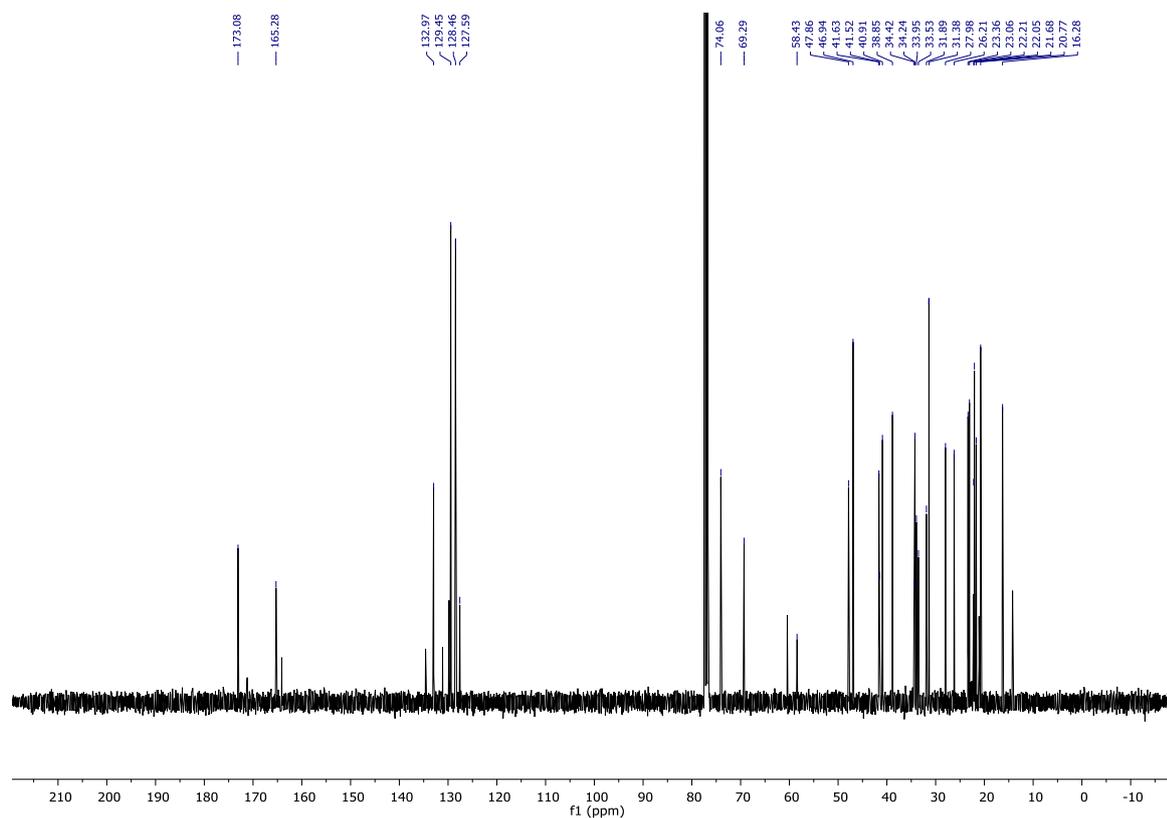


(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 4-((benzyloxy)((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (10f)

¹H-NMR (400 MHz, CDCl₃)

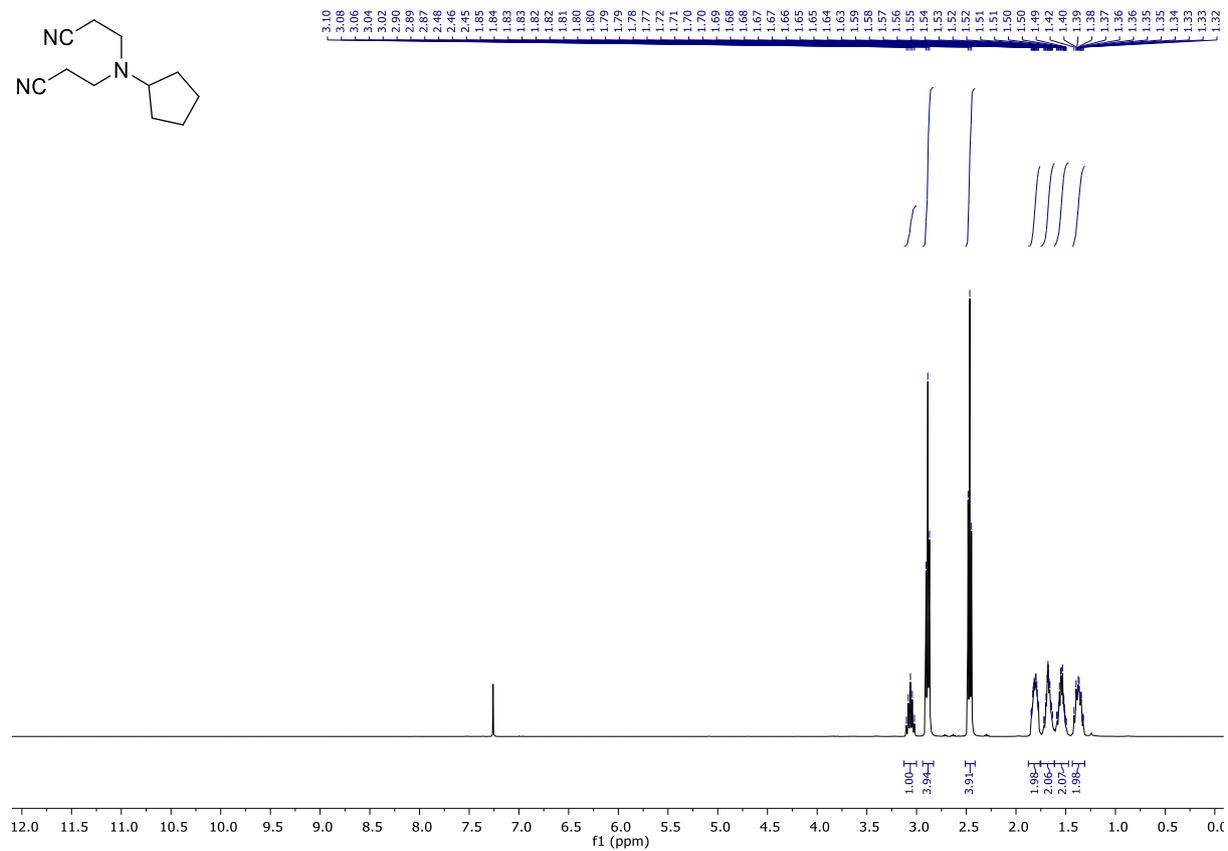
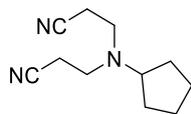


¹³C-NMR (101 MHz, CDCl₃)

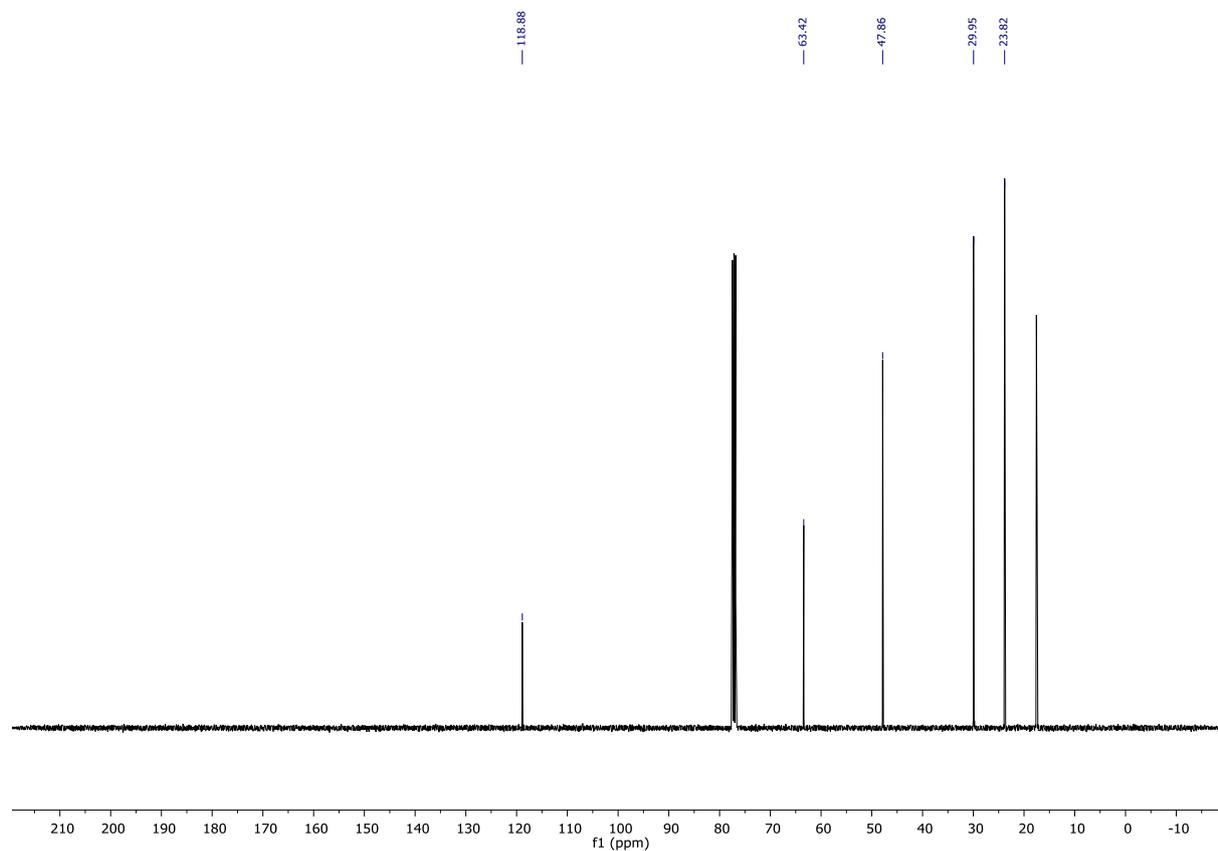


3,3'-(Cyclopentylazanediy) dipropanenitrile (3a)

¹H-NMR (400 MHz, CDCl₃)

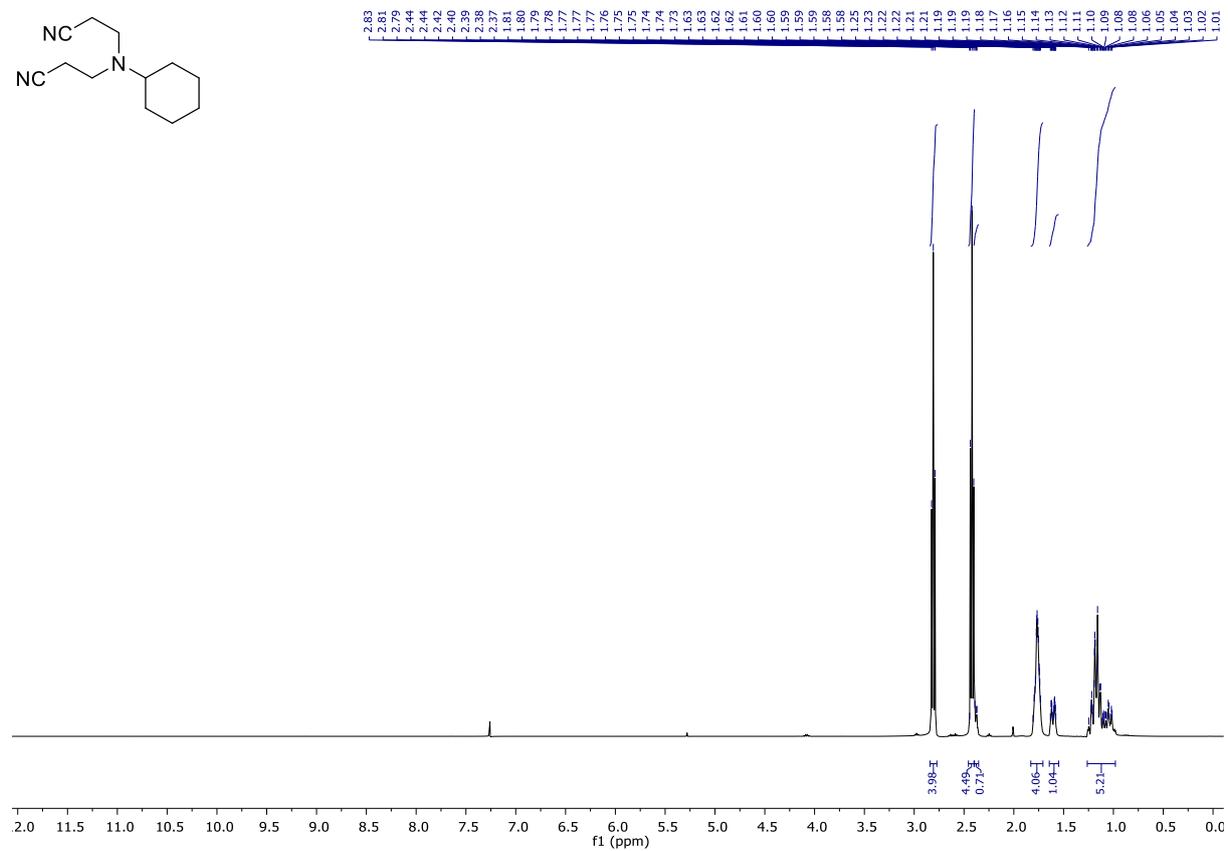
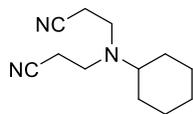


¹³C-NMR (101 MHz, CDCl₃)

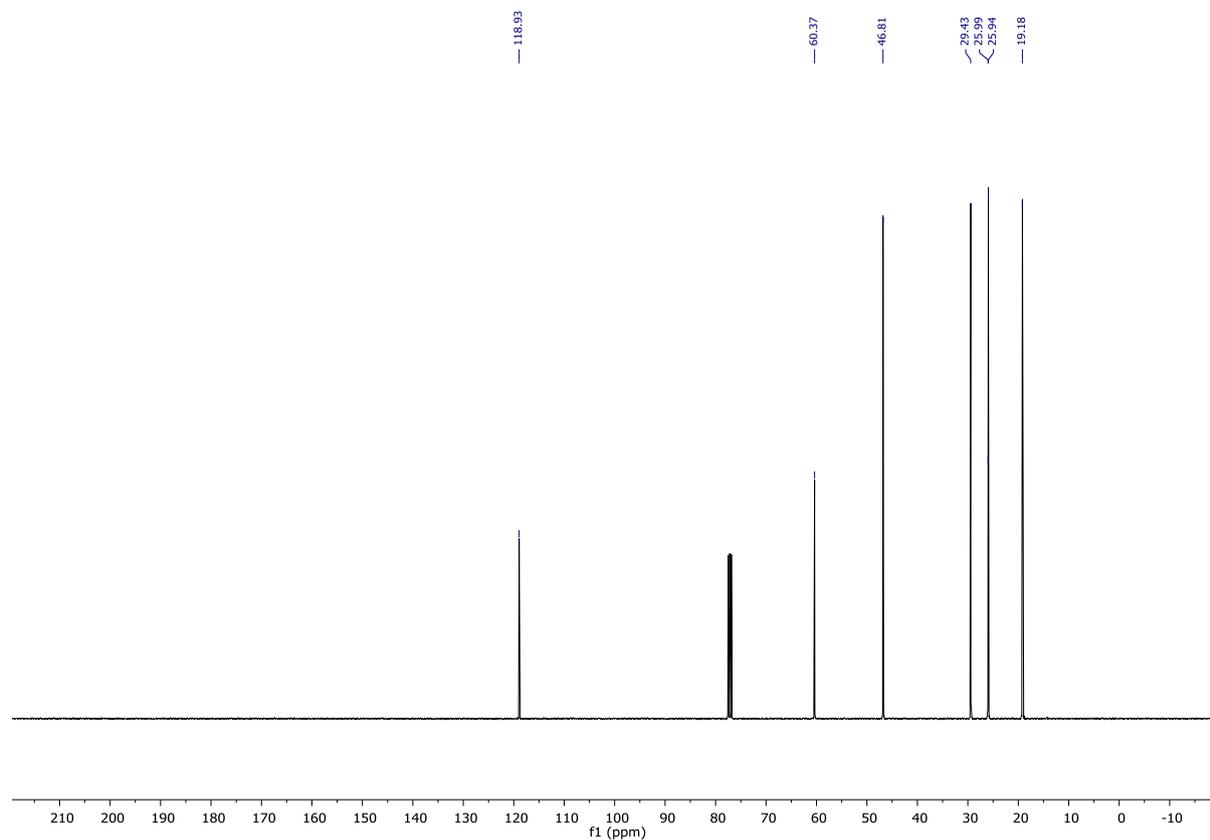


3,3'-(Cyclohexylazanediyl)dipropanenitrile (3b)

¹H-NMR (400 MHz, CDCl₃)

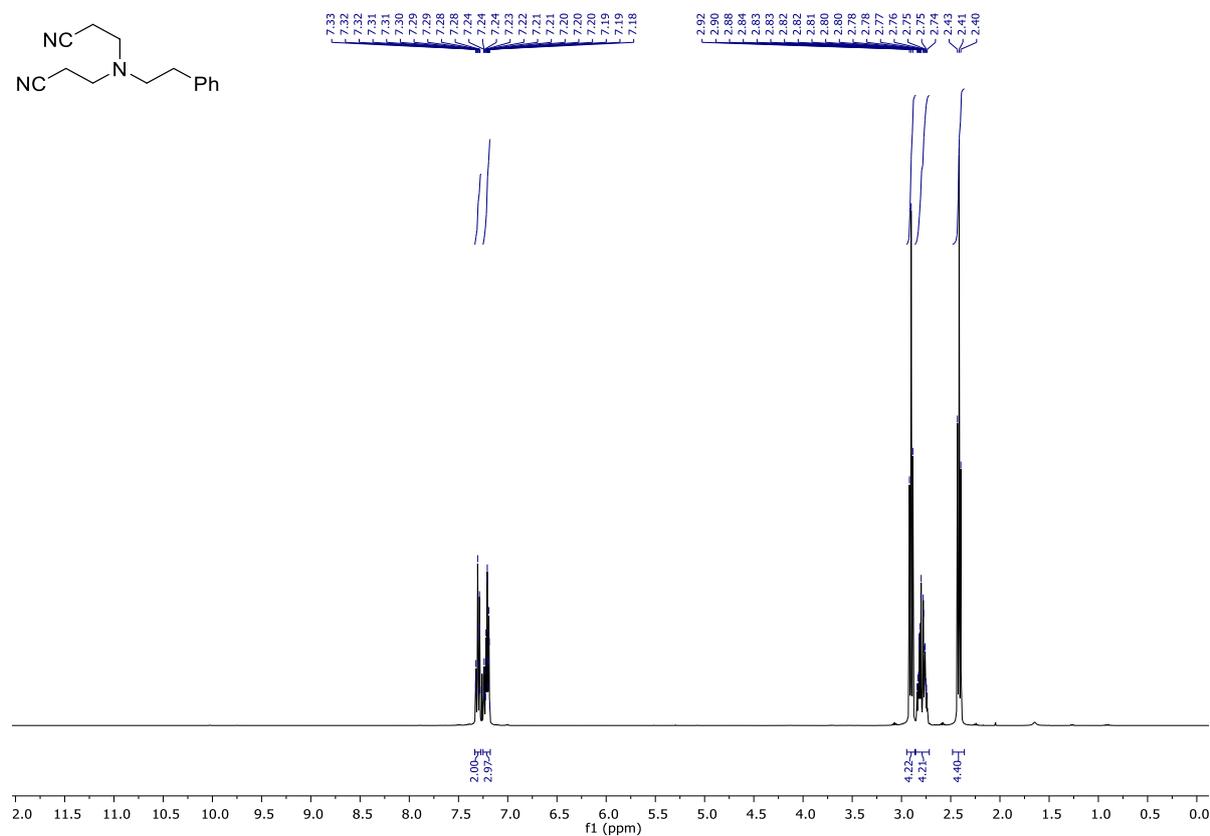
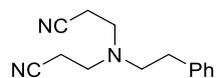


¹³C-NMR (101 MHz, CDCl₃)

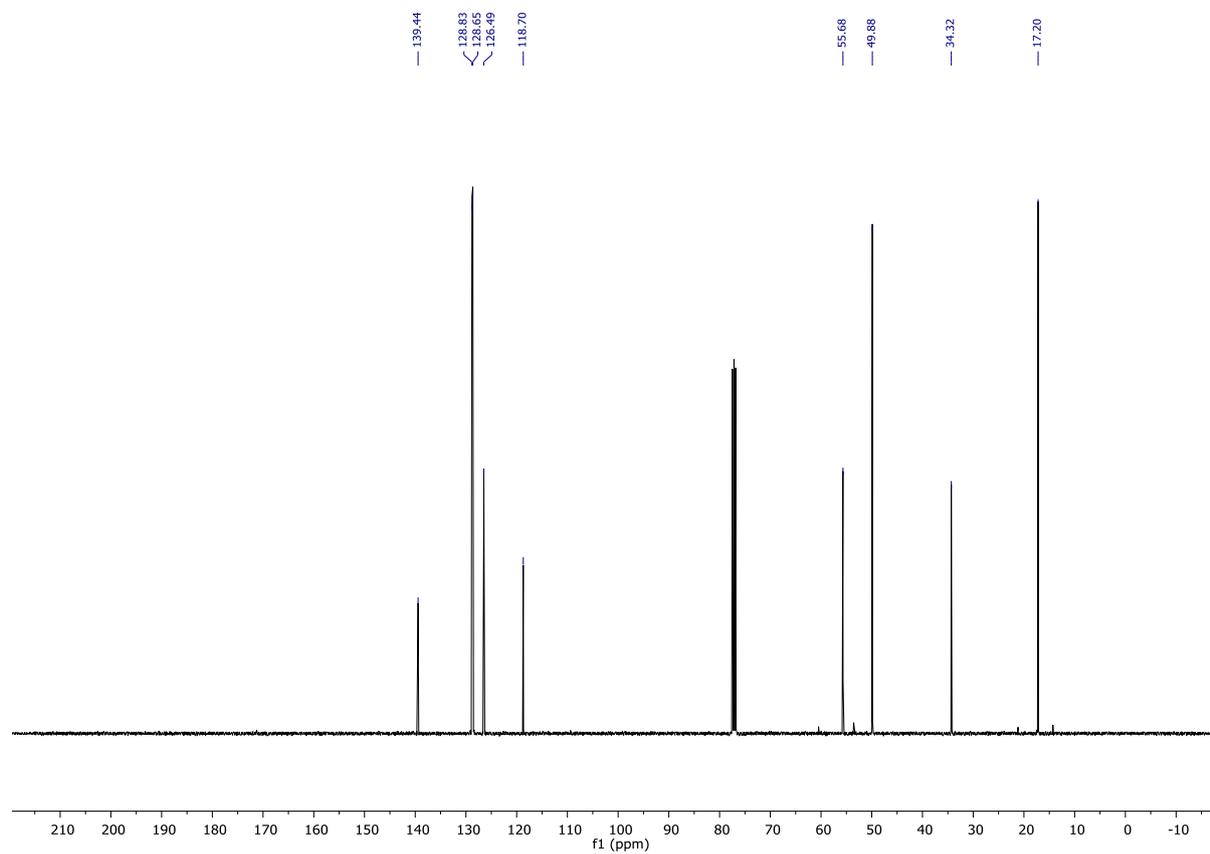


3,3'-(Phenethylazanediyldipropanenitrile (3c)

¹H-NMR (400 MHz, CDCl₃)

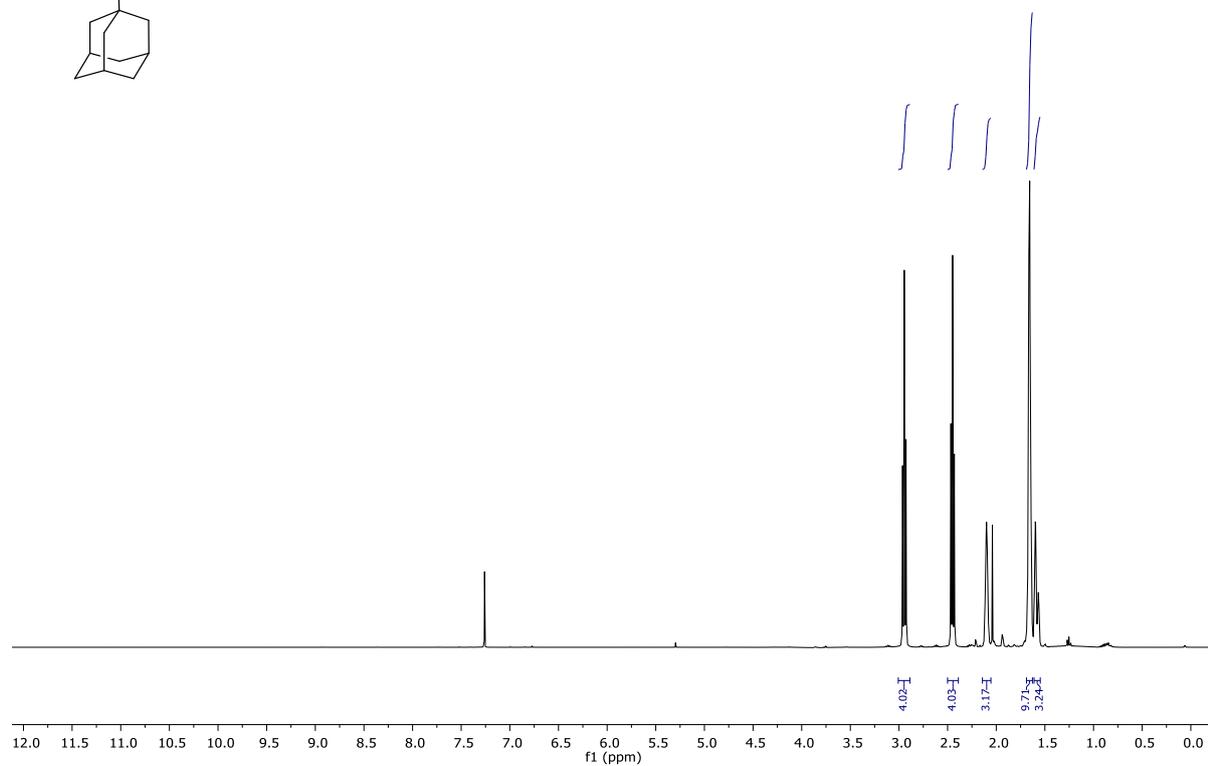
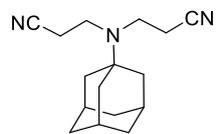


¹³C-NMR (101 MHz, CDCl₃)

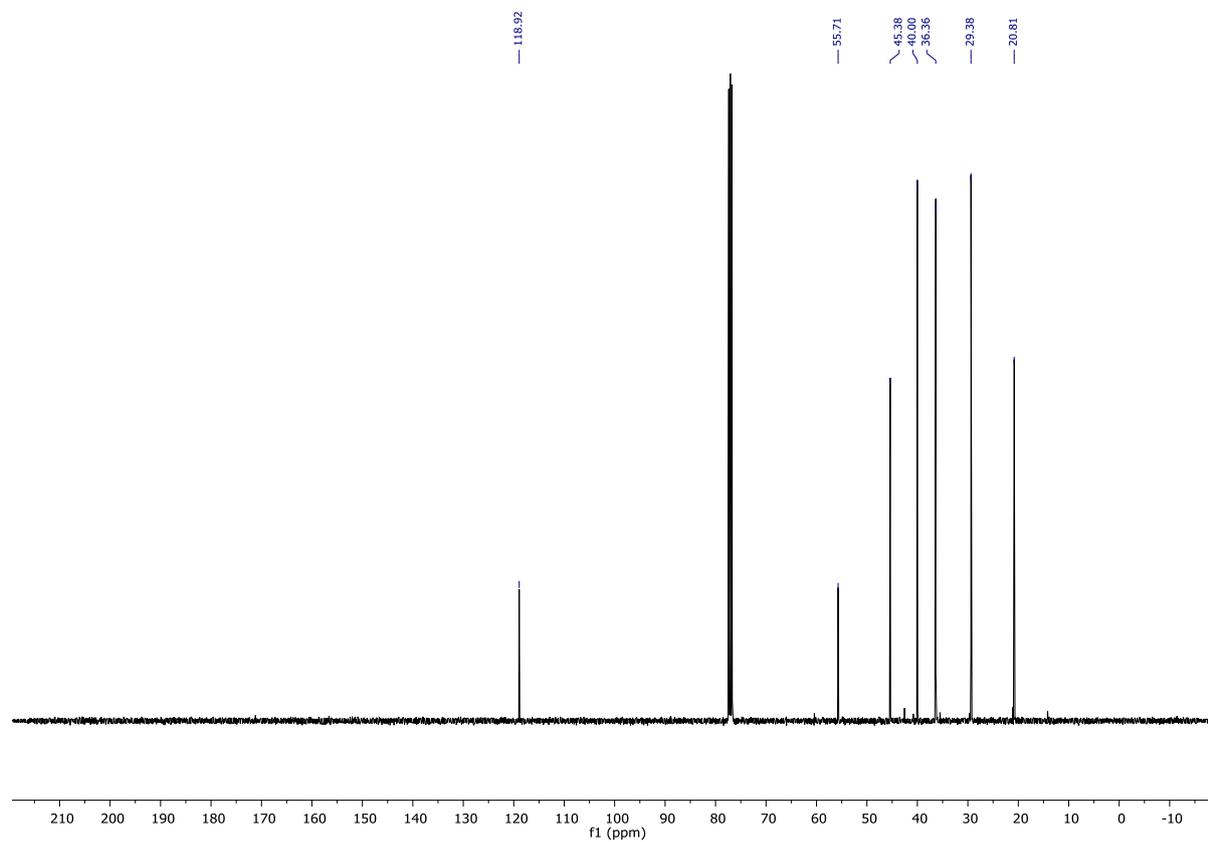


3,3'-(((3*s*,5*s*,7*s*)-adamantan-1-yl)azanediyl)dipropanenitrile (3d)

¹H-NMR (400 MHz, CDCl₃)

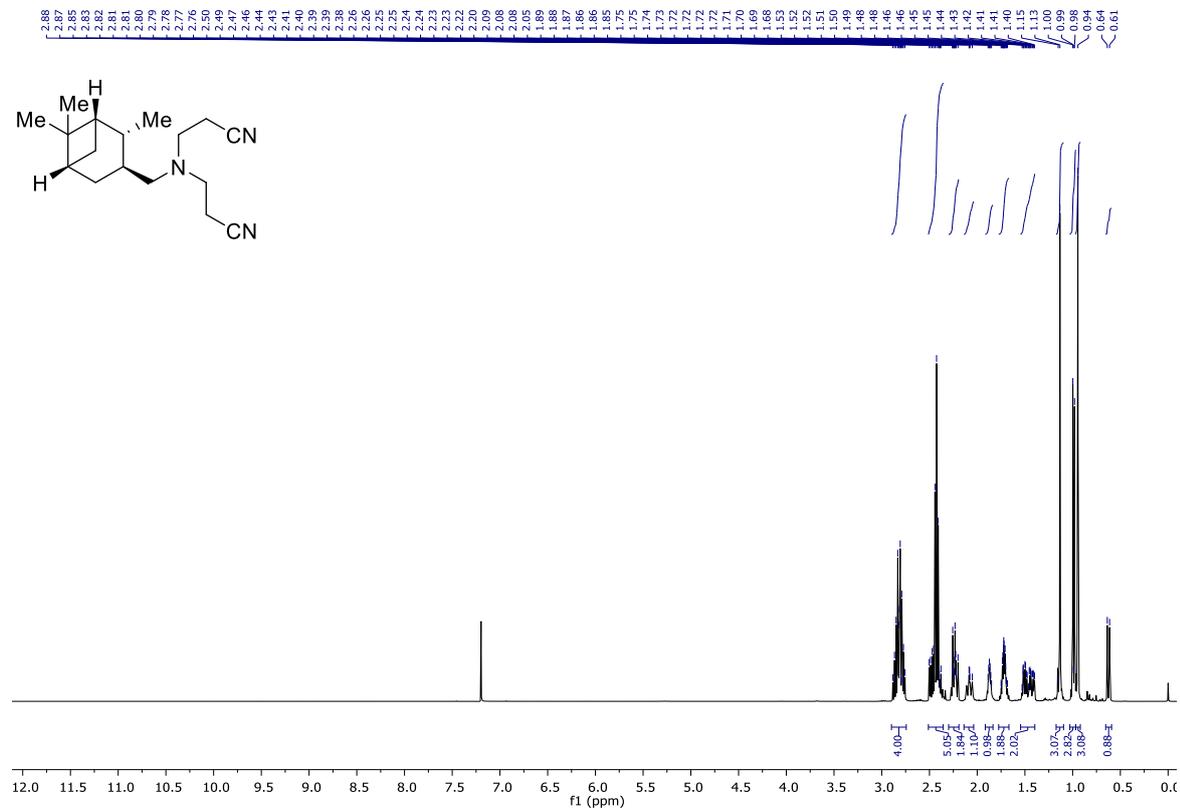


¹³C-NMR (101 MHz, CDCl₃)

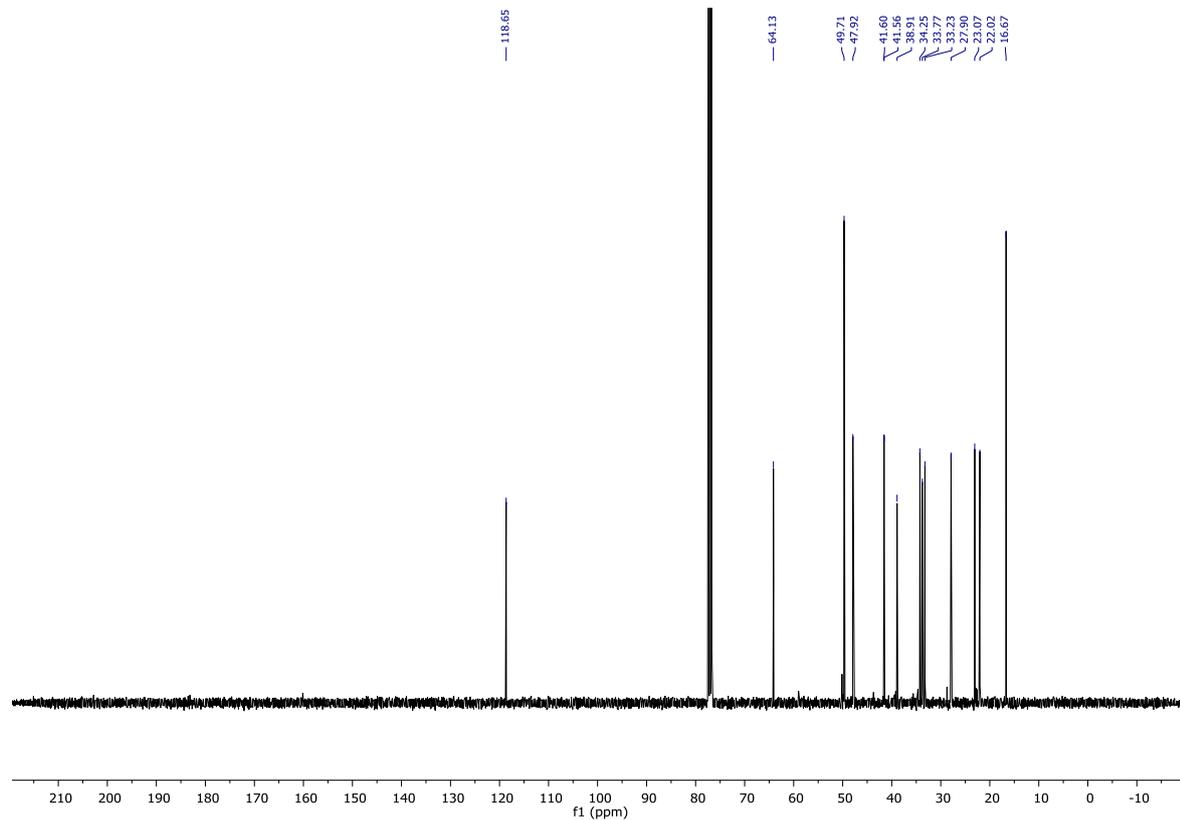


3,3'-((((1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)azanediyl)dipropanenitrile (3e)

¹H-NMR (400 MHz, CDCl₃)

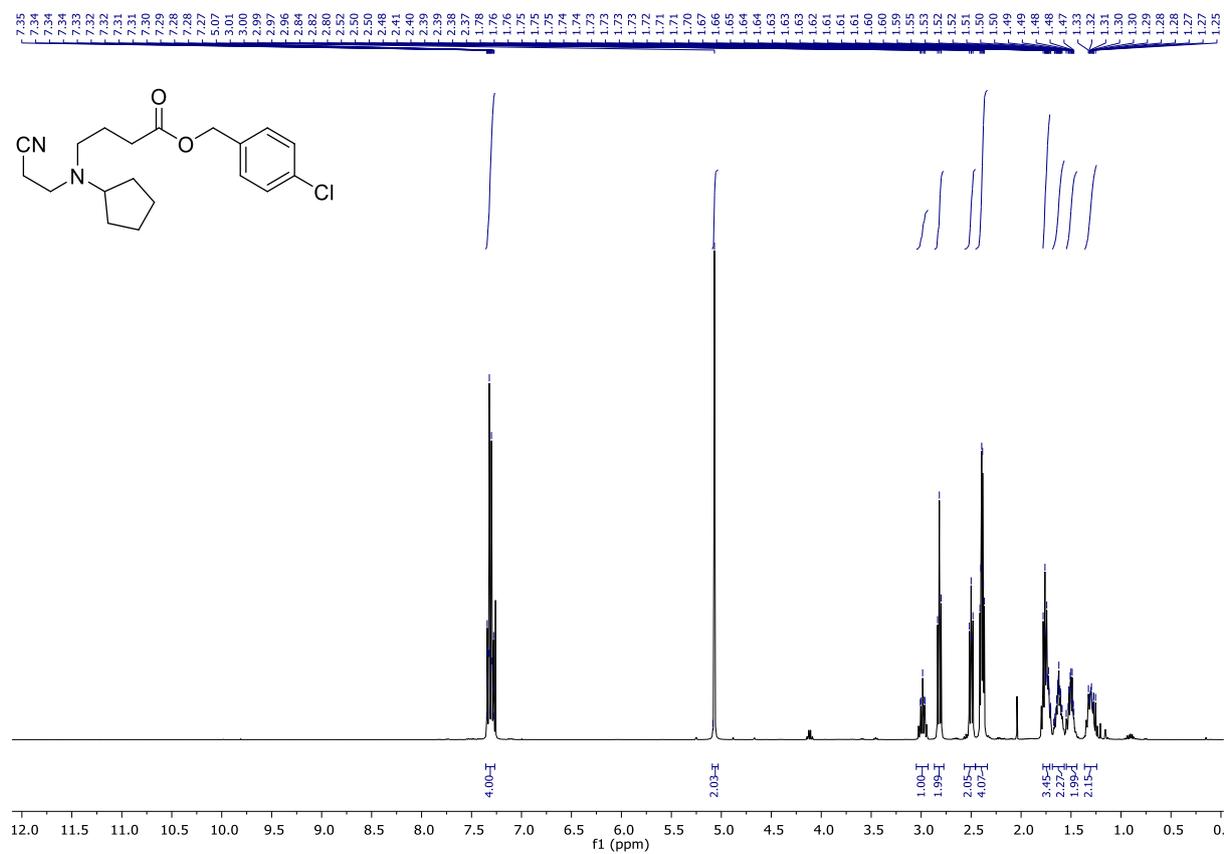


¹³C-NMR (101 MHz, CDCl₃)

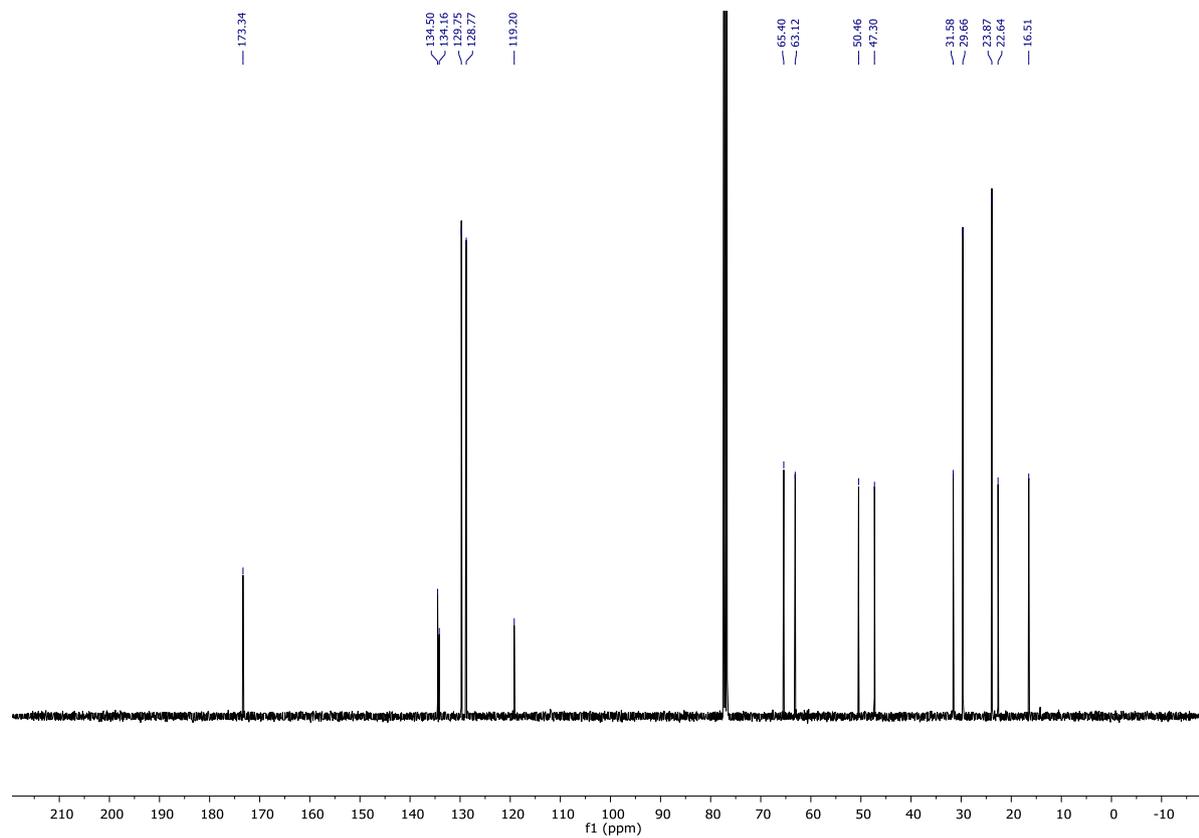


4-Chlorobenzyl 4-((2-cyanoethyl)(cyclopentyl)amino)butanoate (4a)

¹H-NMR (400 MHz, CDCl₃)

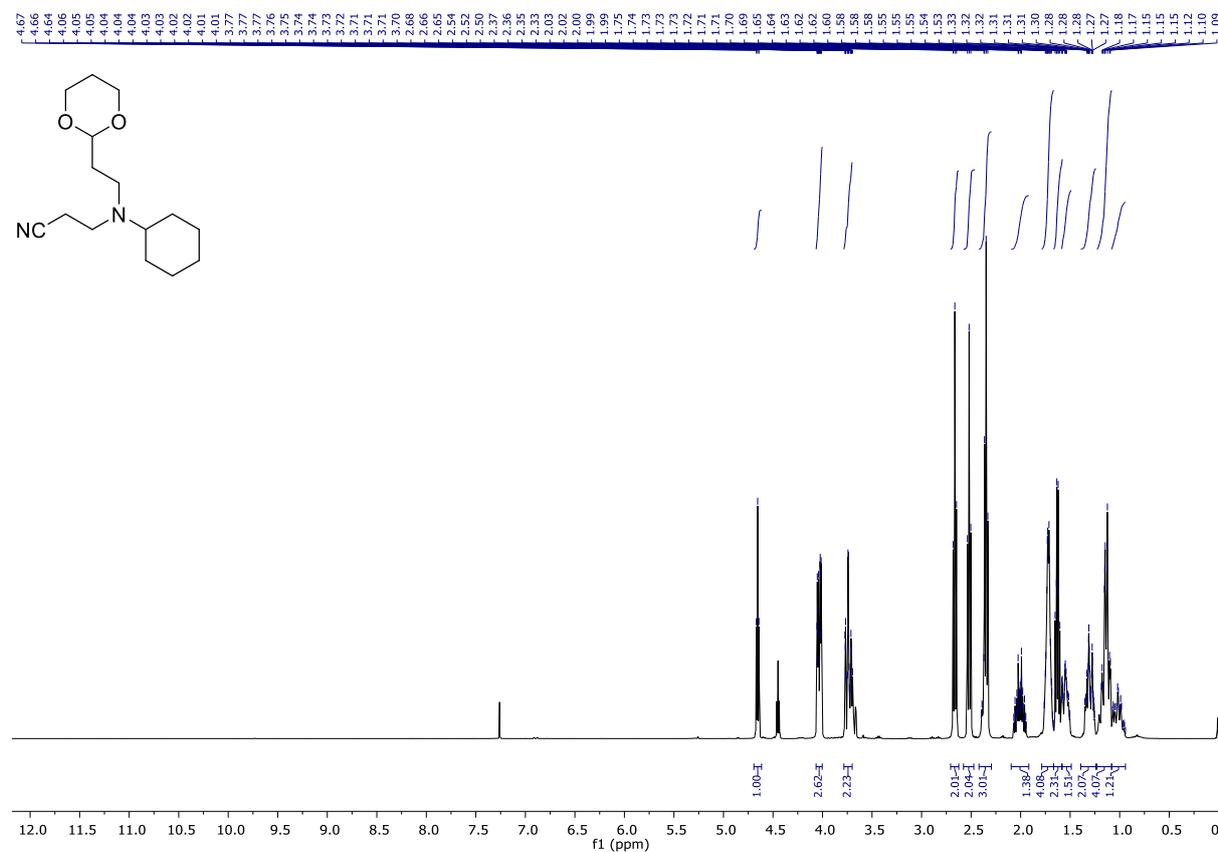


¹³C-NMR (101 MHz, CDCl₃)

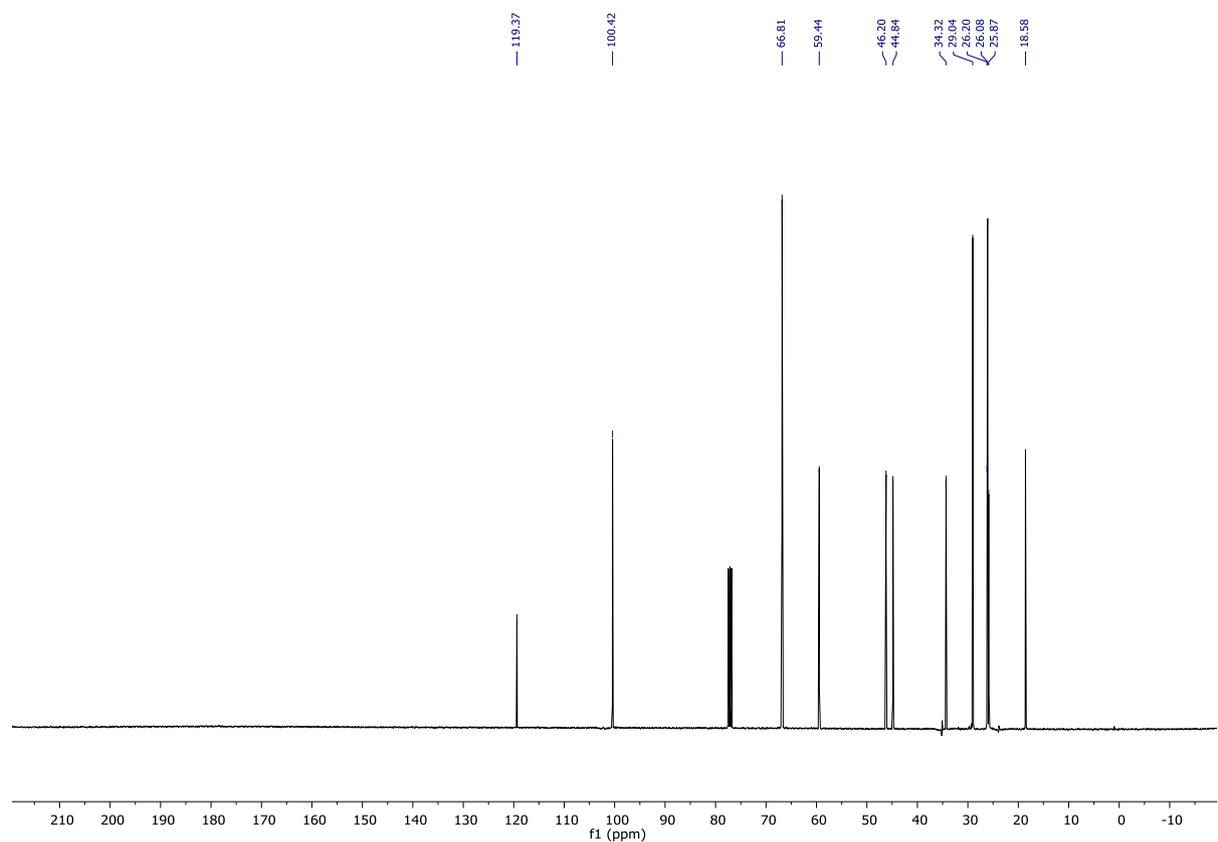


3-((2-(1,3-Dioxan-2-yl)ethyl)(cyclohexyl)amino)propanenitrile (4b)

¹H-NMR (400 MHz, CDCl₃)

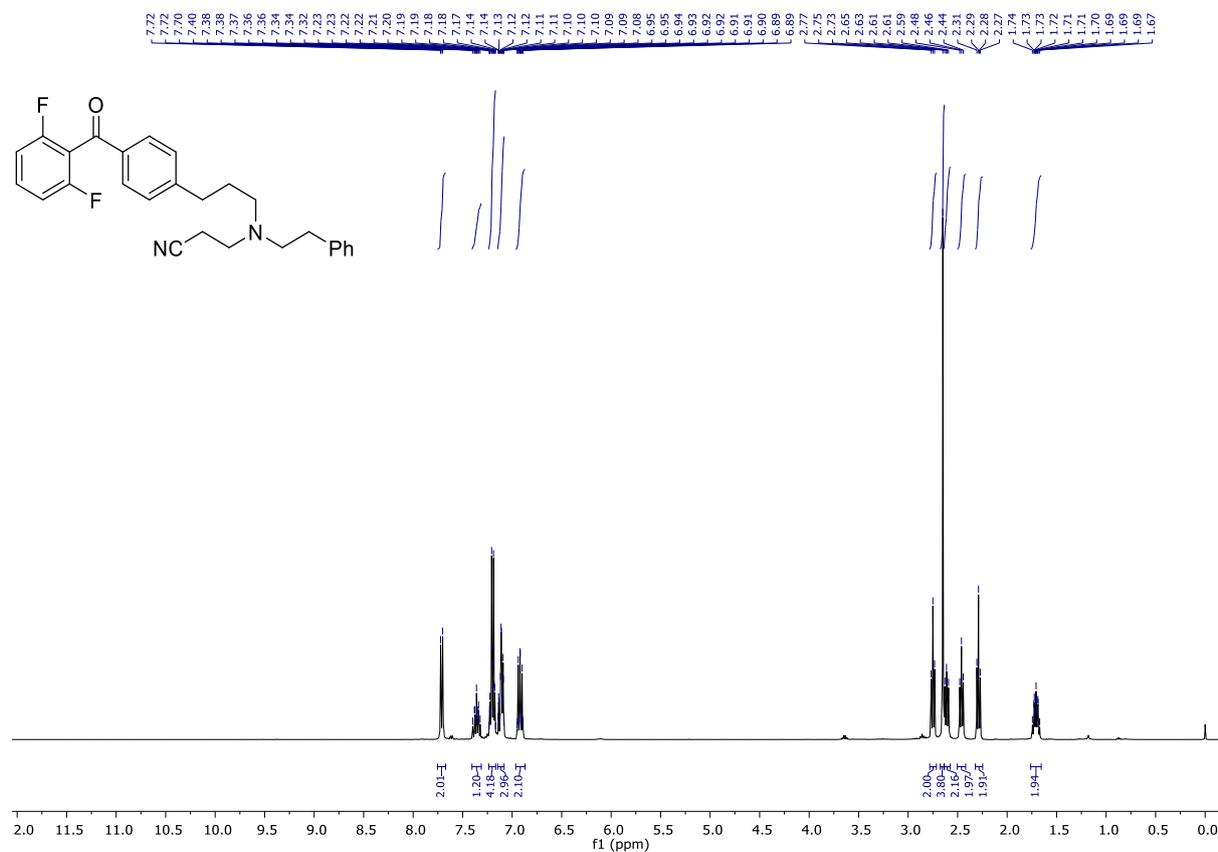


¹³C-NMR (101 MHz, CDCl₃)

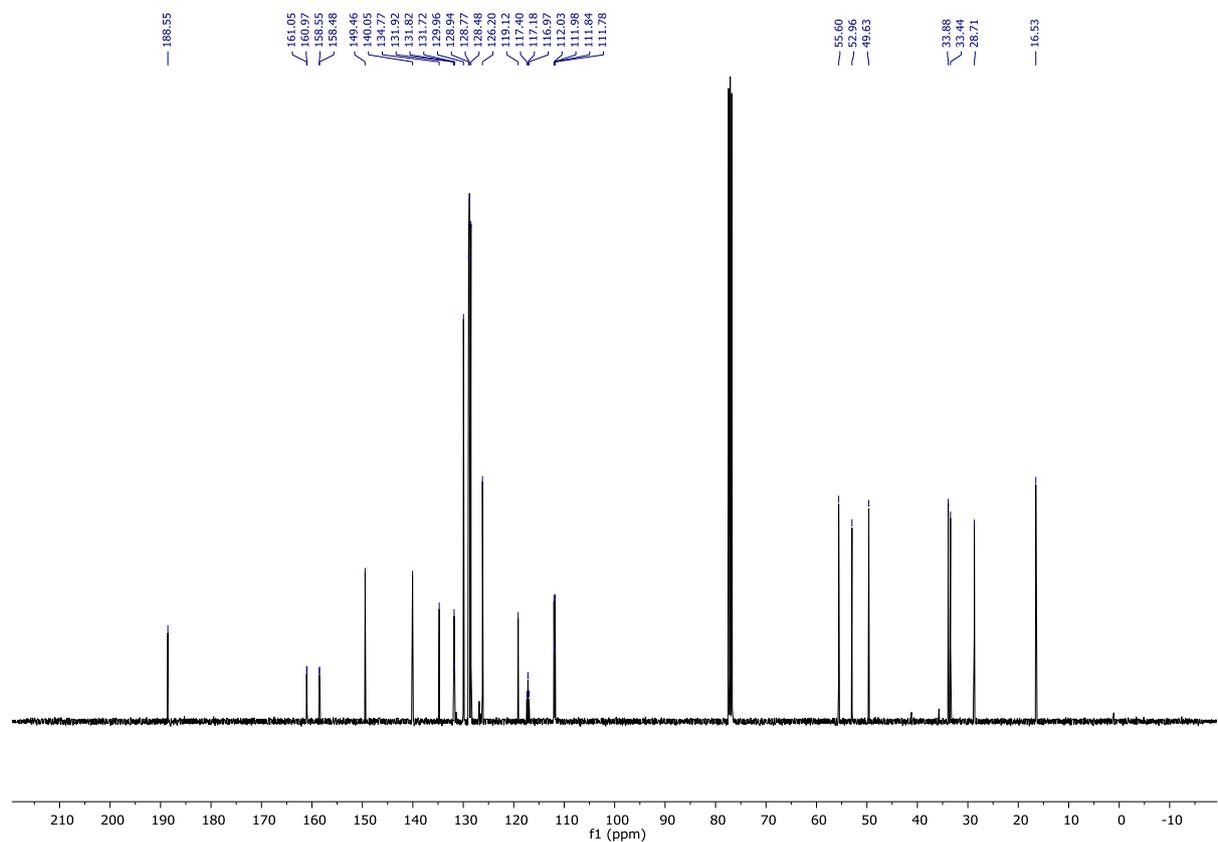


3-((3-(4-(2,6-Difluorobenzoyl)phenyl)propyl)(phenethyl)amino)propanenitrile (4d)

¹H-NMR (400 MHz, CDCl₃)

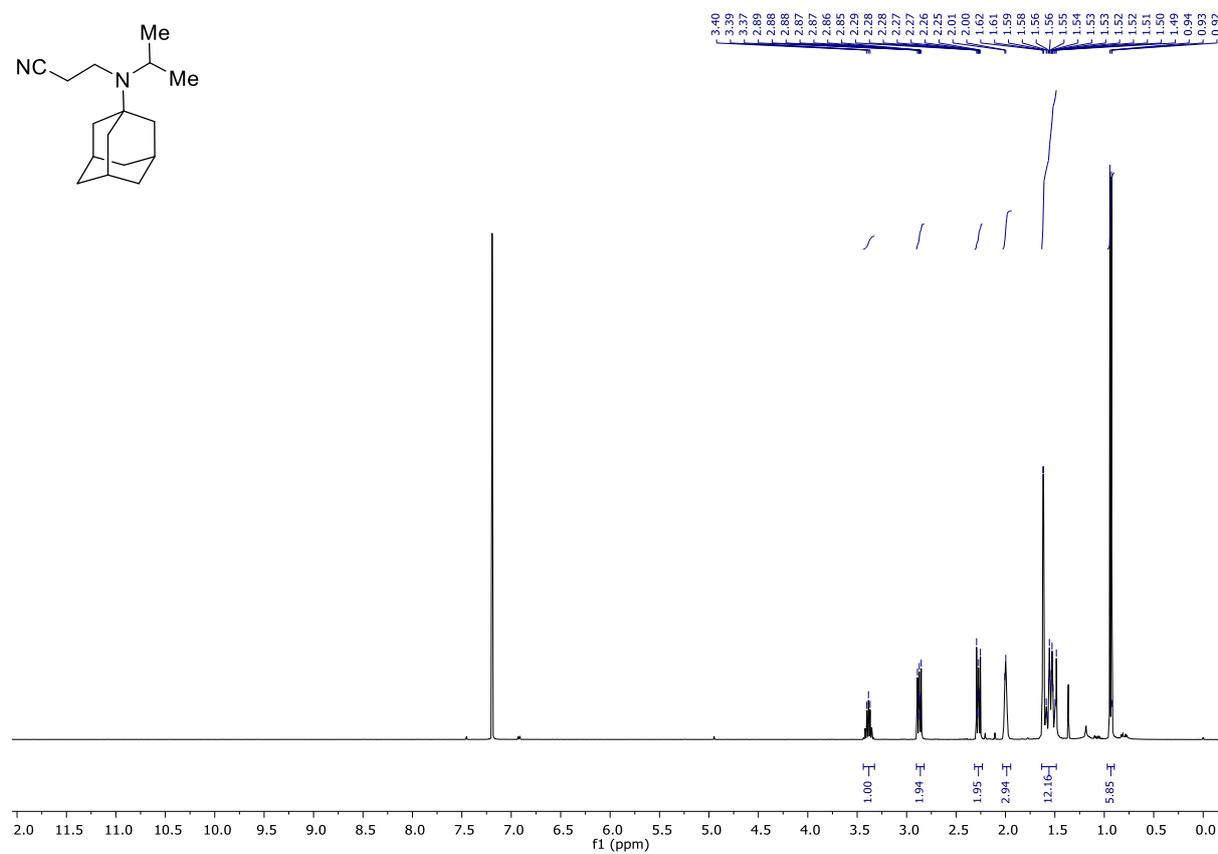
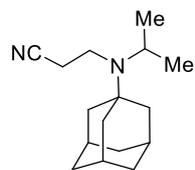


¹³C-NMR (101 MHz, CDCl₃)

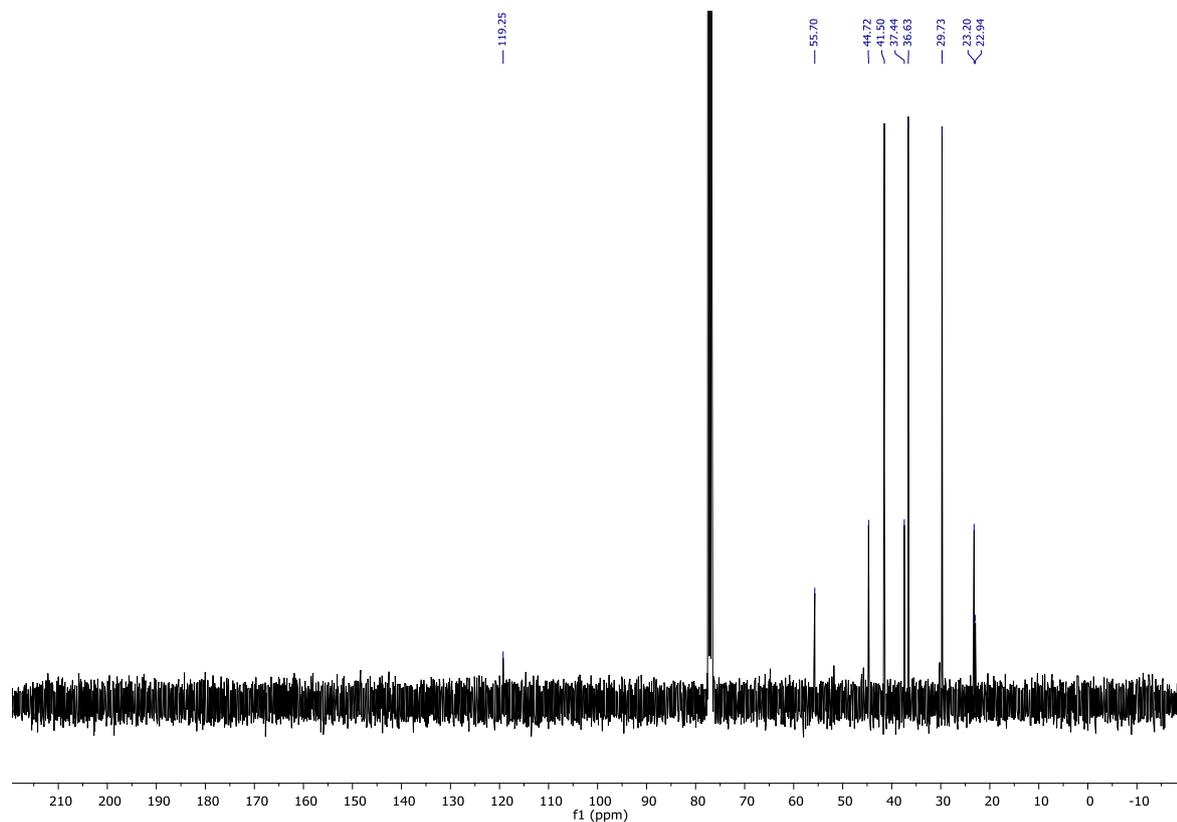


3-(((3*s*,5*s*,7*s*)-adamantan-1-yl)(isopropyl)amino)propanenitrile (4e)

¹H-NMR (400 MHz, CDCl₃)

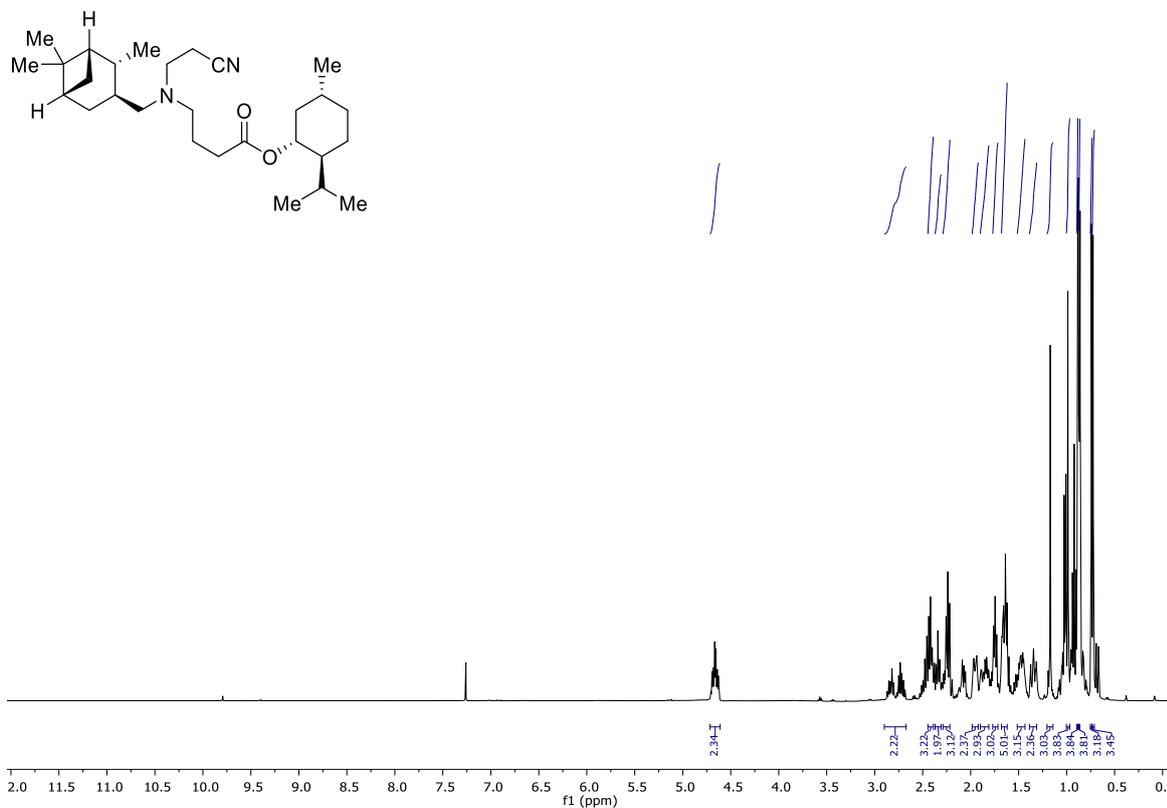


¹³C-NMR (101 MHz, CDCl₃)

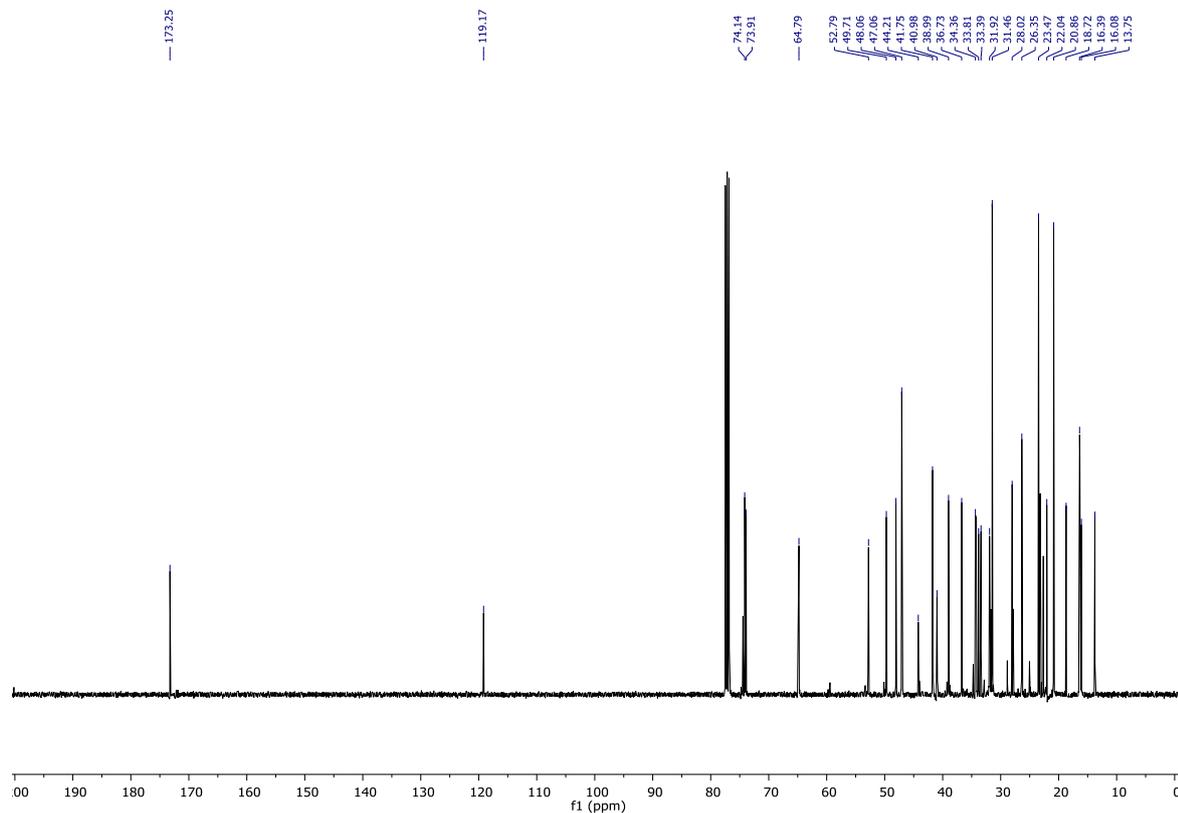


(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 4-((2-cyanoethyl)((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (4f)

¹H-NMR (400 MHz, CDCl₃)

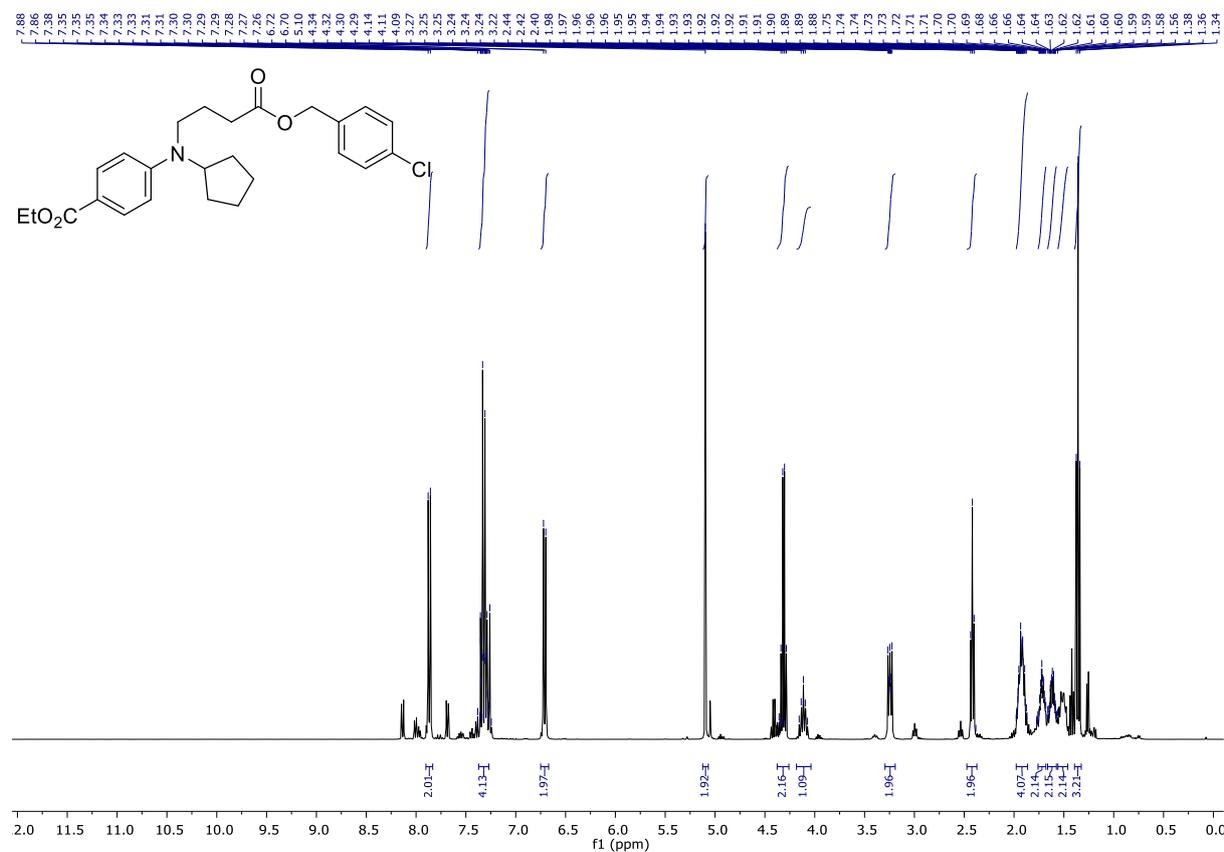


¹³C-NMR (101 MHz, CDCl₃)

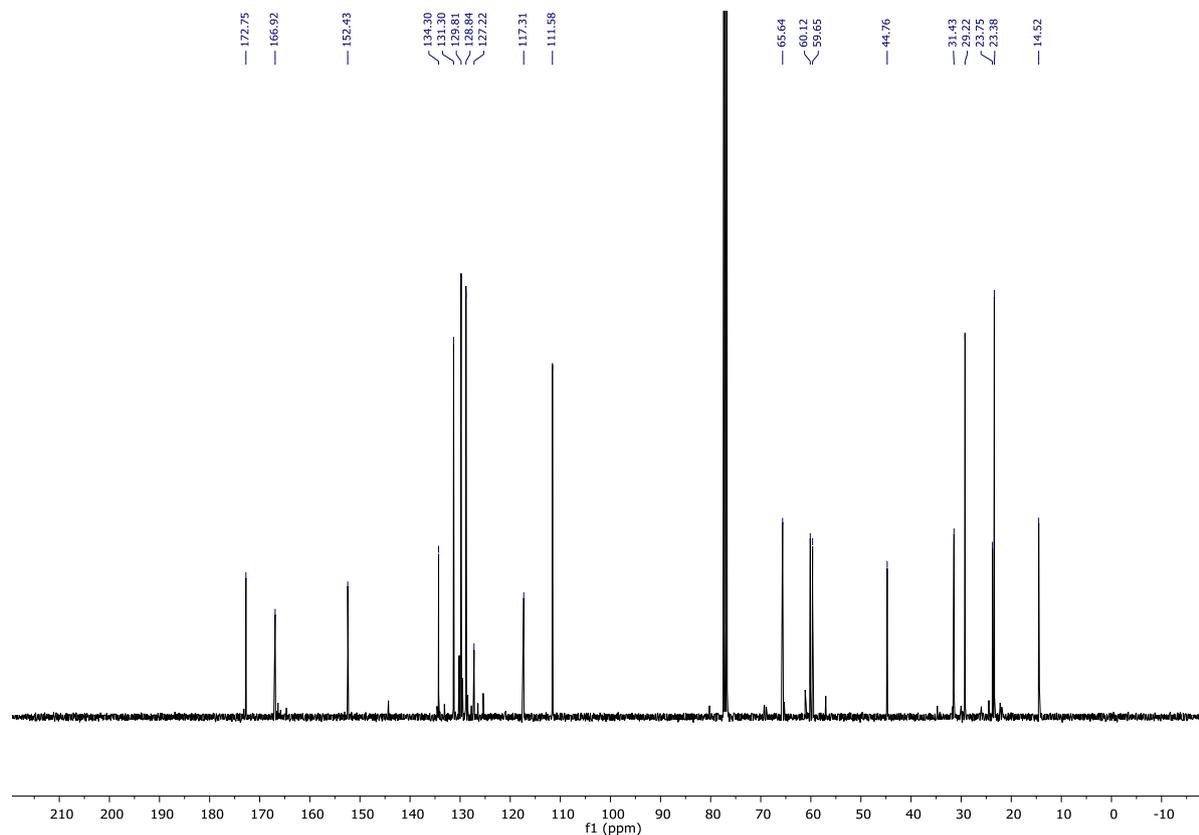


Ethyl 4-((4-((4-chlorobenzyl)oxy)-4-oxobutyl)(cyclopentyl)amino)benzoate (5a)

¹H-NMR (400 MHz, CDCl₃)

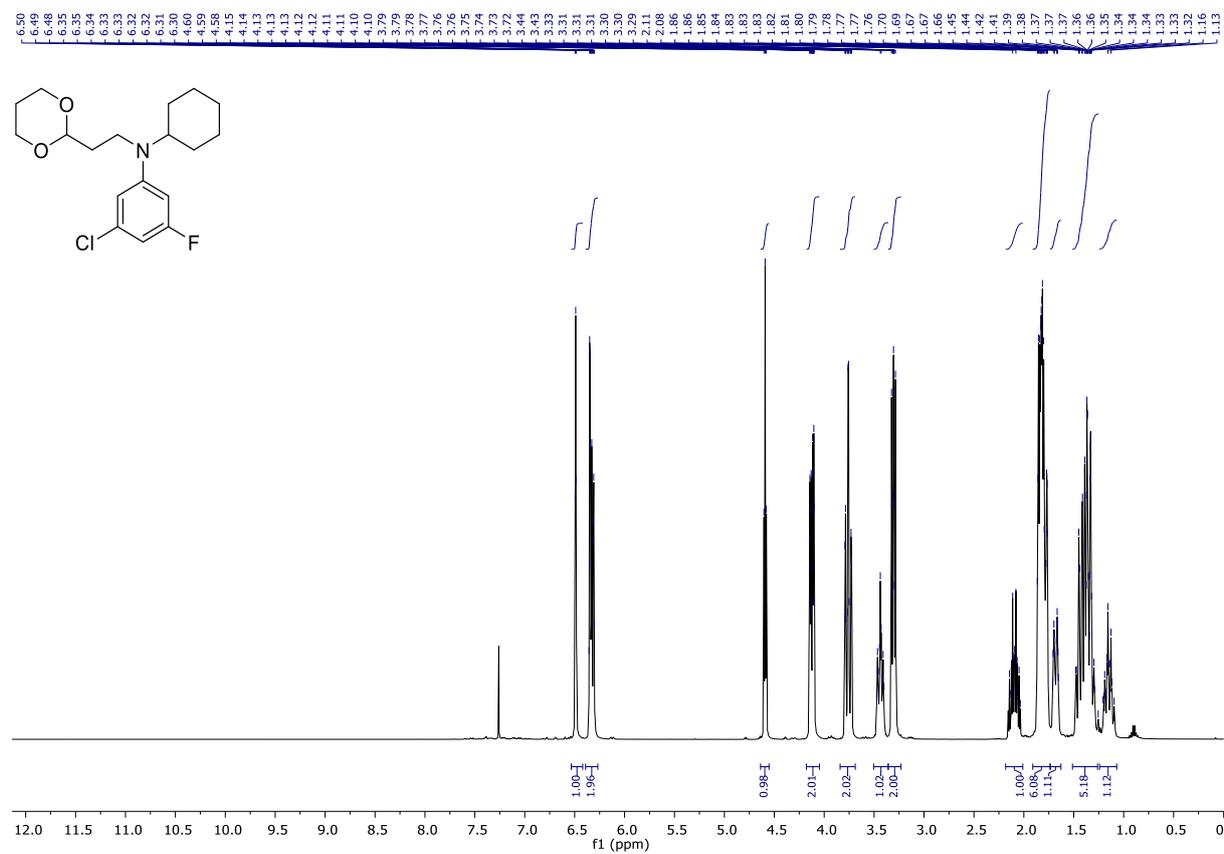


¹³C-NMR (101 MHz, CDCl₃)

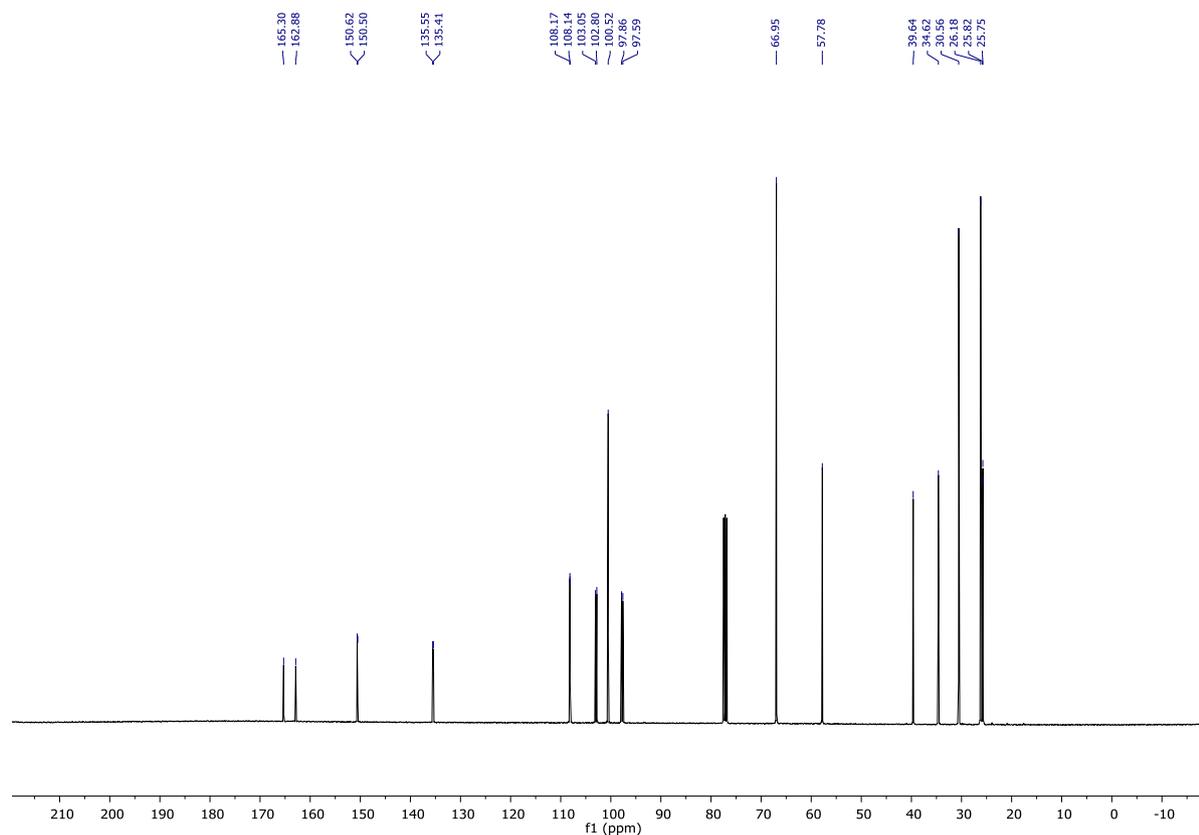


N-(2-(1,3-Dioxan-2-yl)ethyl)-3-chloro-*N*-cyclohexyl-5-fluoroaniline (5b)

¹H-NMR (400 MHz, CDCl₃)

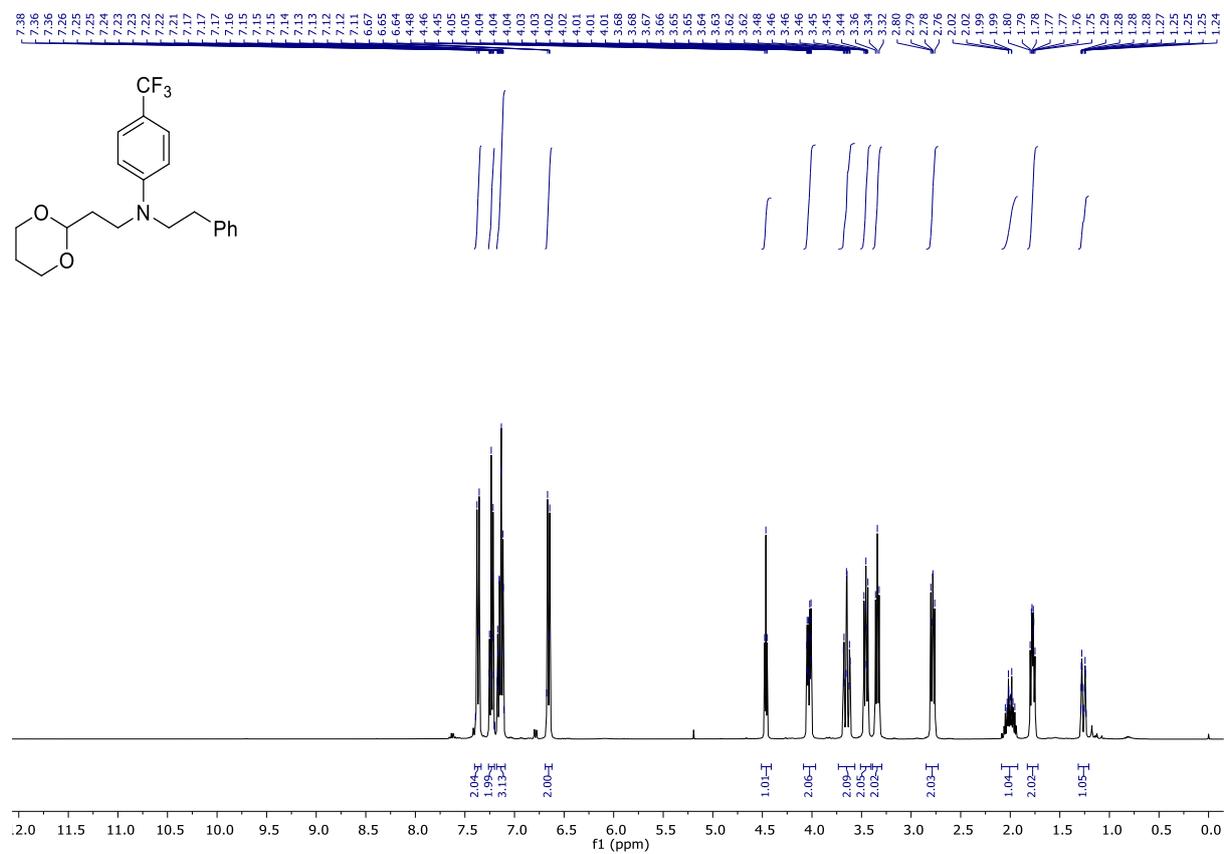


¹³C-NMR (101 MHz, CDCl₃)

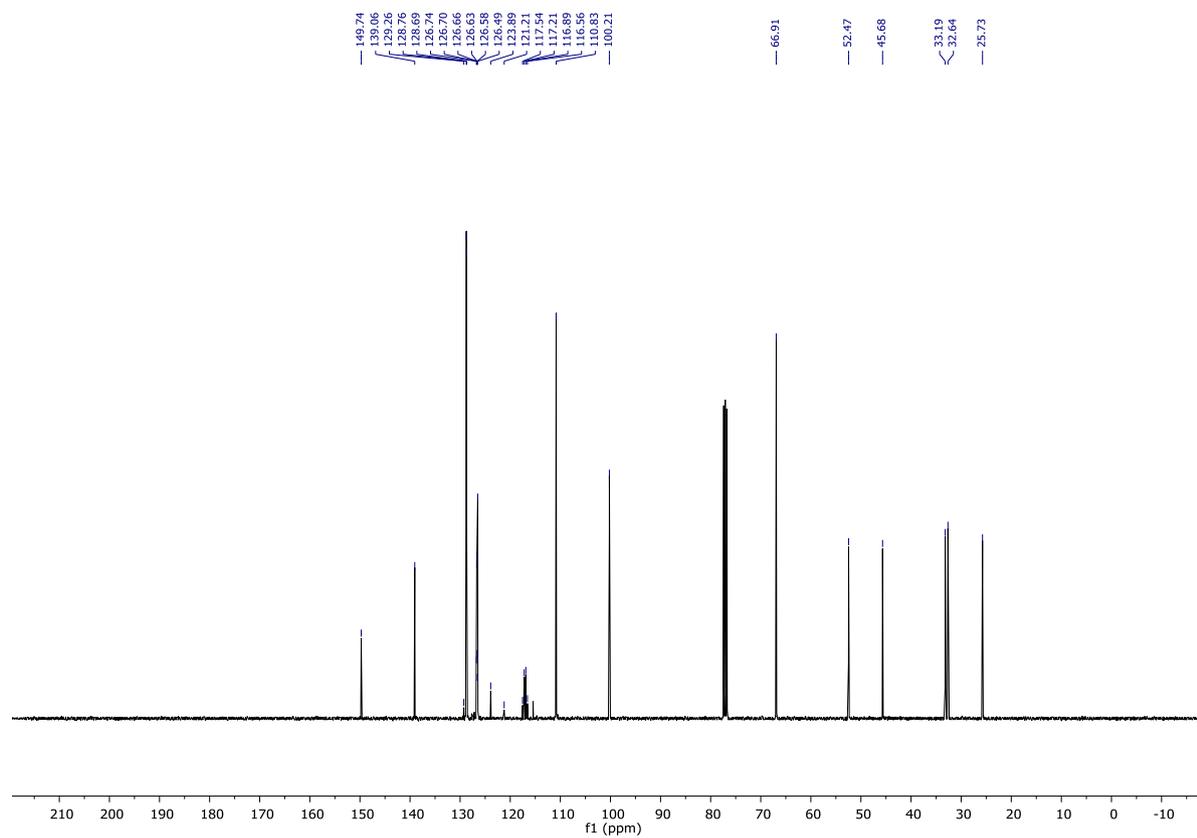


N-(2-(1,3-Dioxan-2-yl)ethyl)-*N*-phenethyl-4-(trifluoromethyl)aniline (5c)

¹H-NMR (400 MHz, CDCl₃)

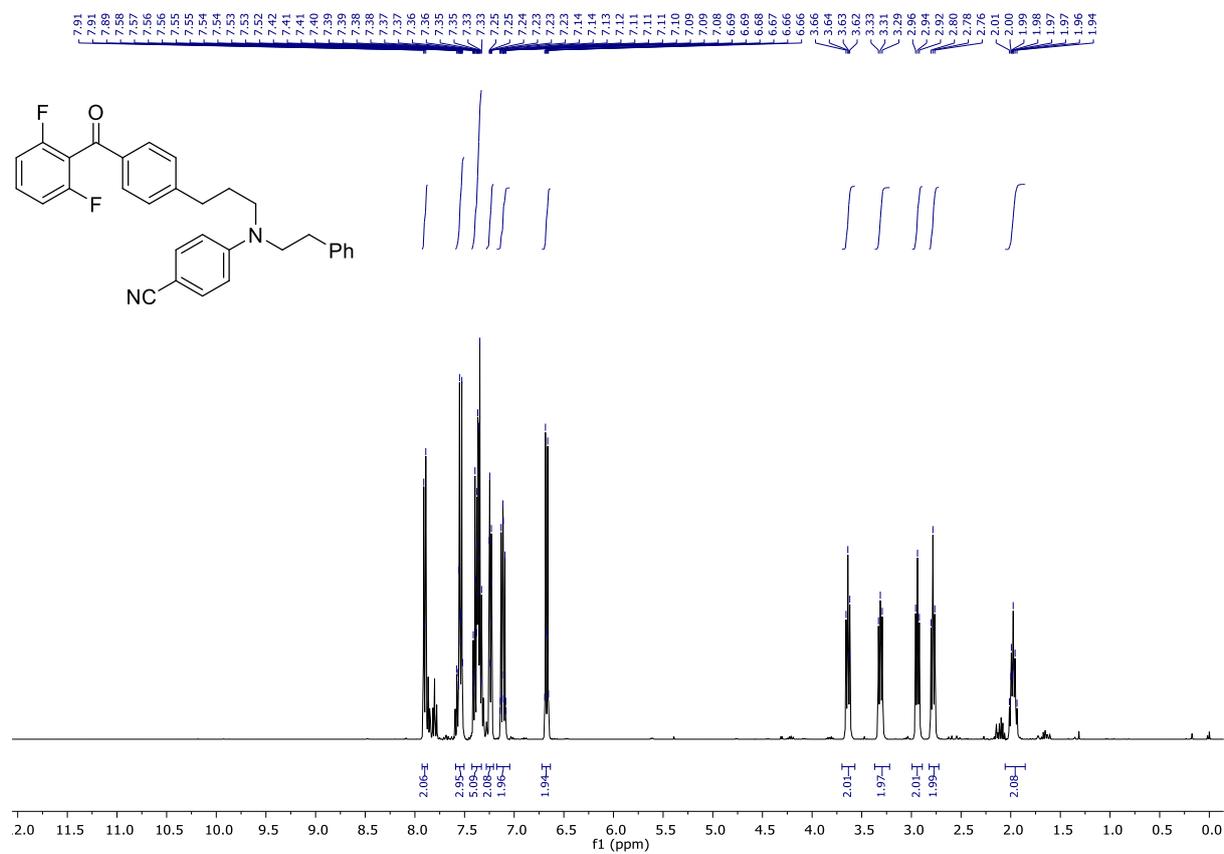


¹³C-NMR (101 MHz, CDCl₃)

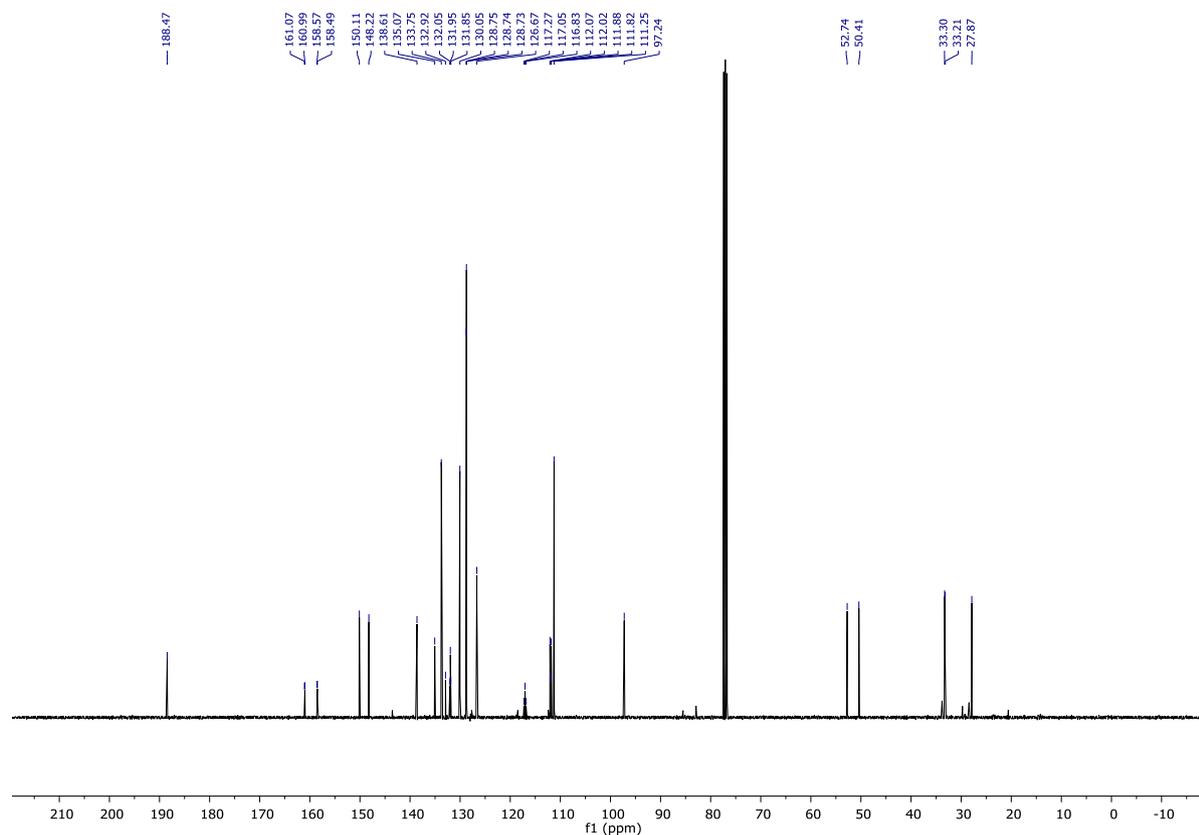


4-((3-(4-(2,6-Difluorobenzoyl)phenyl)propyl)(phenethyl)amino)benzonitrile (5d)

¹H-NMR (400 MHz, CDCl₃)

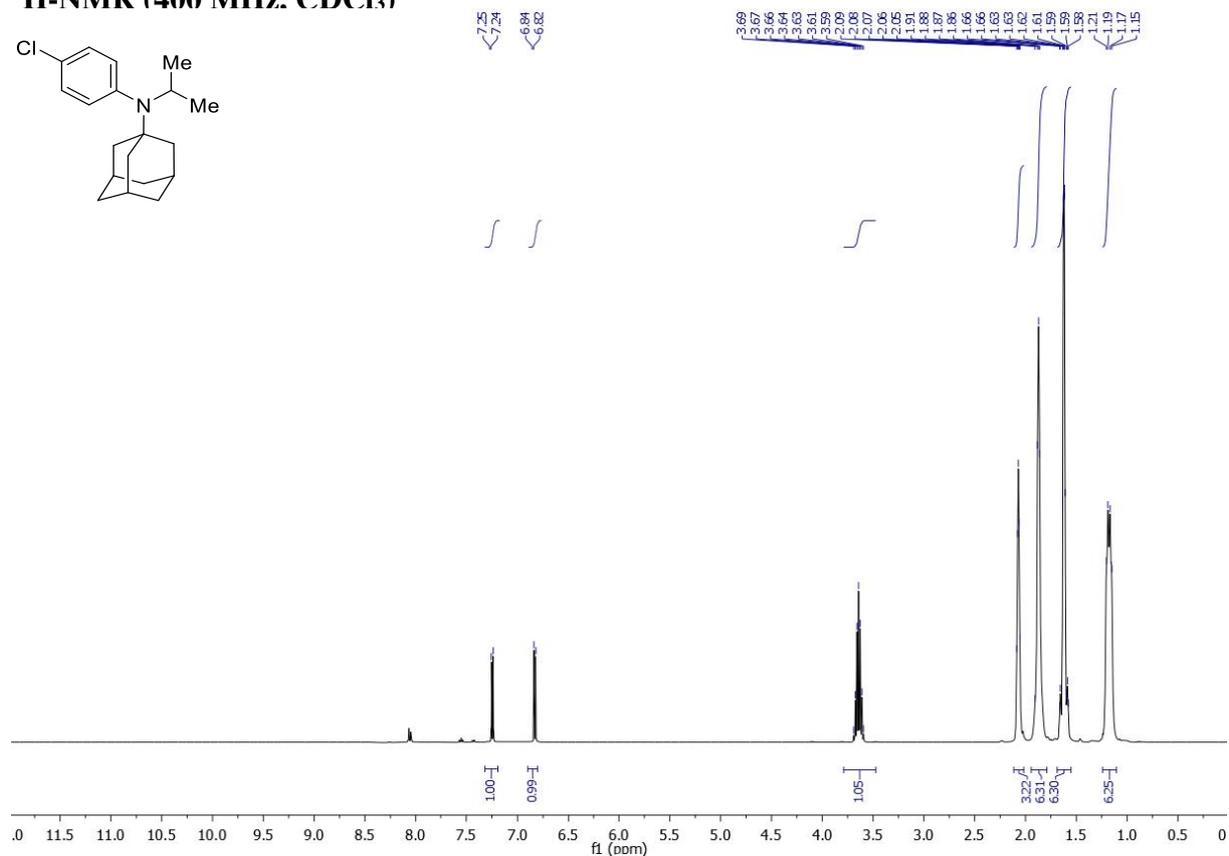


¹³C-NMR (101 MHz, CDCl₃)

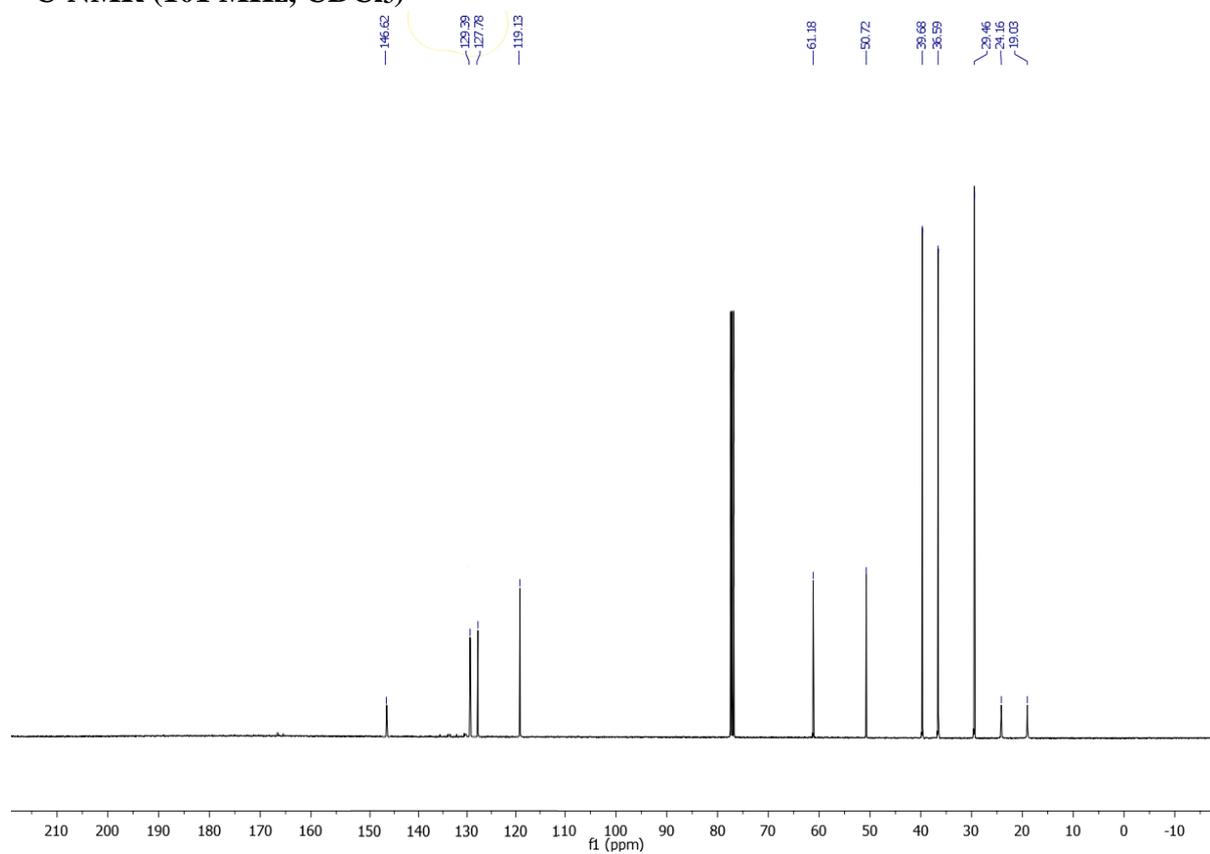


(3*s*,5*s*,7*s*)-*N*-(4-chlorophenyl)-*N*-isopropyladamantan-1-amine (5e)

¹H-NMR (400 MHz, CDCl₃)

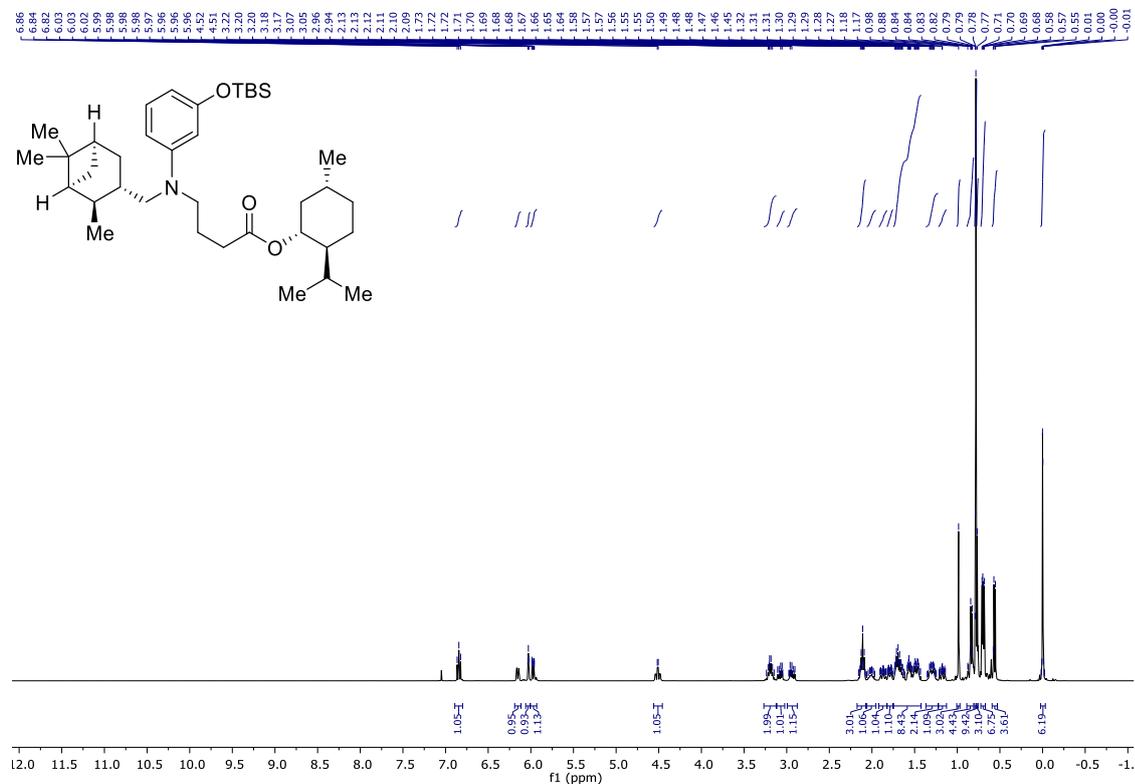


¹³C-NMR (101 MHz, CDCl₃)



(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 4-((3-((*tert*-butyldimethylsilyl)oxy)phenyl)((1*S*,2*S*,3*S*,5*R*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)methyl)amino)butanoate (5g)

¹H-NMR (400 MHz, CDCl₃)



¹³C-NMR (101 MHz, CDCl₃)

