Photoinduced, Copper-Catalyzed Carbon–Carbon Bond Formation with Alkyl Electrophiles: Cyanation of Unactivated Secondary Alkyl Chlorides at Room Temperature

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Supporting Information

Table of Contents

I. General Information

The following reagents were purchased and used as received: CuI (Aldrich; 99.999%), TBACN (Aldrich; 95%), 4-chlorotetrahydro-*2H*-pyran (Acros), (1-chloro-2-methylpropan-2-yl)benzene (Aldrich), and *tert*-butyl 4-bromopiperidine-1-carboxylate (Aldrich). CH_3CN was deoxygenated and dried by sparging with nitrogen followed by passage through a column of activated alumina.

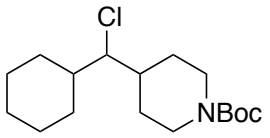
^{1}H and ^{13}C spectroscopic data were collected on a Varian 500 MHz spectrometer, a Varian 400 MHz spectrometer, or a Bruker 400 MHz spectrometer at ambient temperature. GC analyses were carried out on an Agilent 6890 Series system with an HP-5 column (length 30 m, I.D. 0.25 mm). All cyanations were conducted in oven-dried quartz test tubes or a quartz flask, under an inert atmosphere, with the use of 15W, 120V, UV Germicidal CFL Lamps (Norman Lamps, Inc.) and a Fantec 172 x 150 x 51 mm Dual Ball Bearing AC High Speed Fan (240 CFM).

II. Preparation of Electrophiles

These procedures have not been optimized.

General procedure for the chlorination of secondary alcohols. To an oven-dried 500-mL round-bottom flask containing a stir bar was added dry CH_2Cl_2 (0.2 M) and the alcohol (1.00 equiv). The mixture was cooled to 0 °C in an ice bath, and PPh_3 (1.00 equiv) and NCS (1.00 equiv) were slowly added in turn. The round-bottom flask was then capped with a rubber septum and placed under a nitrogen atmosphere (through a needle attached to a vacuum manifold). The reaction mixture was allowed to warm to r.t. in the water bath. After 5–8 h, the reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl. The organic phase was separated, dried over anhydrous Na_2SO_4, and then concentrated carefully on a rotary

evaporator (careful evaporation was important for volatile products). The product was purified by column chromatography (hexanes or Et_2O/hexanes).



***tert*-Butyl 4-(chloro(cyclohexyl)methyl)piperidine-1-carboxylate.** Cyclohexylmagnesium chloride (2.0 M in Et_2O; 23.5 mL, 46.9 mmol) was added dropwise to a solution of *tert*-butyl 4-formylpiperidine-1-carboxylate (10.0 g, 46.9 mmol) in THF (230 mL) at −78 °C (dry ice/acetone bath). The resulting solution was allowed to warm to r.t. (while remaining in the acetone bath) and stirred for 6 h. Next, the reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (100 mL), and the resulting mixture was extracted with Et_2O. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The residue was passed through a plug of silica gel (60% Et_2O/hexanes), and the resulting filtrate was concentrated on a rotary evaporator and used in the next step without further purification.

The title compound was prepared according to the general procedure for the chlorination of secondary alcohols, using the unpurified *tert*-butyl 4-(cyclohexyl(hydroxy)methyl)piperidine-1-carboxylate. The product was purified by flash chromatography (5%→30% Et_2O/hexanes), which furnished an off-white solid (1.05 g, 7% over two steps).

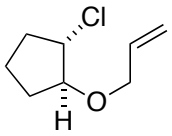
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.21–4.12 (m, 2H), 3.58 (dd, 1H, J = 6.8, 5.5 Hz), 2.73–2.62 (m, 2H), 1.96–1.75 (m, 5H), 1.73–1.65 (m, 2H), 1.65–1.57 (m, 2H), 1.47 (s, 9H), 1.45–1.17 (m, 7H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.1, 79.8, 74.7, 40.8, 39.9, 31.5, 30.3, 28.8, 26.61, 26.60, 26.2.

ATR-IR (neat) 2928, 2848, 1682, 1445, 1417, 1368, 1284, 1265, 1246, 1163, 1121, 773 cm^{-1}.

HRMS (ESI) *m*/*z* $[M–(isobutylene)–(CO_2)+H]^+$ calcd for $C_{12}H_{23}ClN$: 216.1519, found: 216.1504.

Mp: 88.0–89.5 °C.



***(1S,2S)*-1-(Allyloxy)-2-chlorocyclopentane.** This procedure was adapted from a literature procedure.[2] Cyclopentene (5.00 mL, 56.6 mmol) was added dropwise over 30 min to a suspension of *N*-chlorosuccinimide (7.60 g, 56.6 mmol) in dry CH_2Cl_2 (100 mL). The resulting suspension was stirred at r.t. for 2 h, and then allyl alcohol (7.70 mL, 113.2 mmol) was added dropwise by syringe pump over 2 h. The reaction mixture was stirred at r.t. for 6 h. The solvent was then removed on a rotary evaporator, and the crude residue was poured into a separatory funnel containing H_2O (100 mL). The mixture was extracted with Et_2O (3 x 50 mL), and the combined organic phases were washed with water (50 mL), dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. The product was purified by column chromatography (100% hexanes). Clear oil (695 mg, 4% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 (ddt, 1H, *J* = 17.2, 10.4, 5.6 Hz), 5.28 (dq, 1H, *J* = 17.2, 1.7 Hz), 5.21–5.16 (m, 1H), 4.22–4.17 (m, 1H), 4.08–4.01 (m, 2H), 4.00–3.95 (m, 1H), 2.27–2.06 (m, 2H), 1.93–1.72 (m, 3H), 1.70–1.60 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6, 117.0, 87.2, 70.5, 63.1, 34.2, 29.9, 21.4.

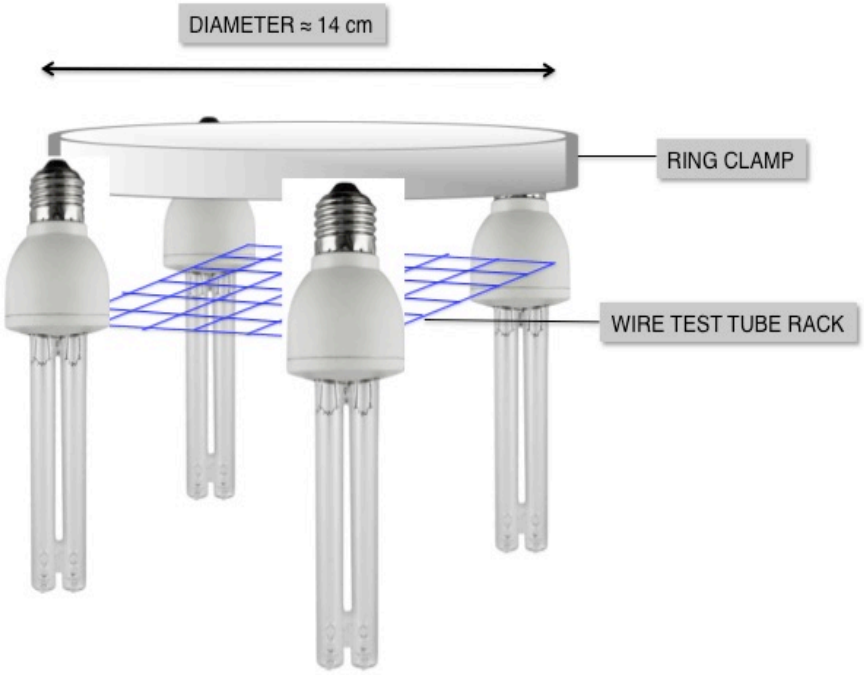
ATR-IR (neat) 3100, 2960, 2861, 1651, 1463, 1433, 1341, 1256, 1082, 1013, 922, 793, 702, 655, 560 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_8H_{13}ClO$: 160.1, found: 160.1.

III. Photoinduced, Copper-Catalyzed Cyanation Reactions

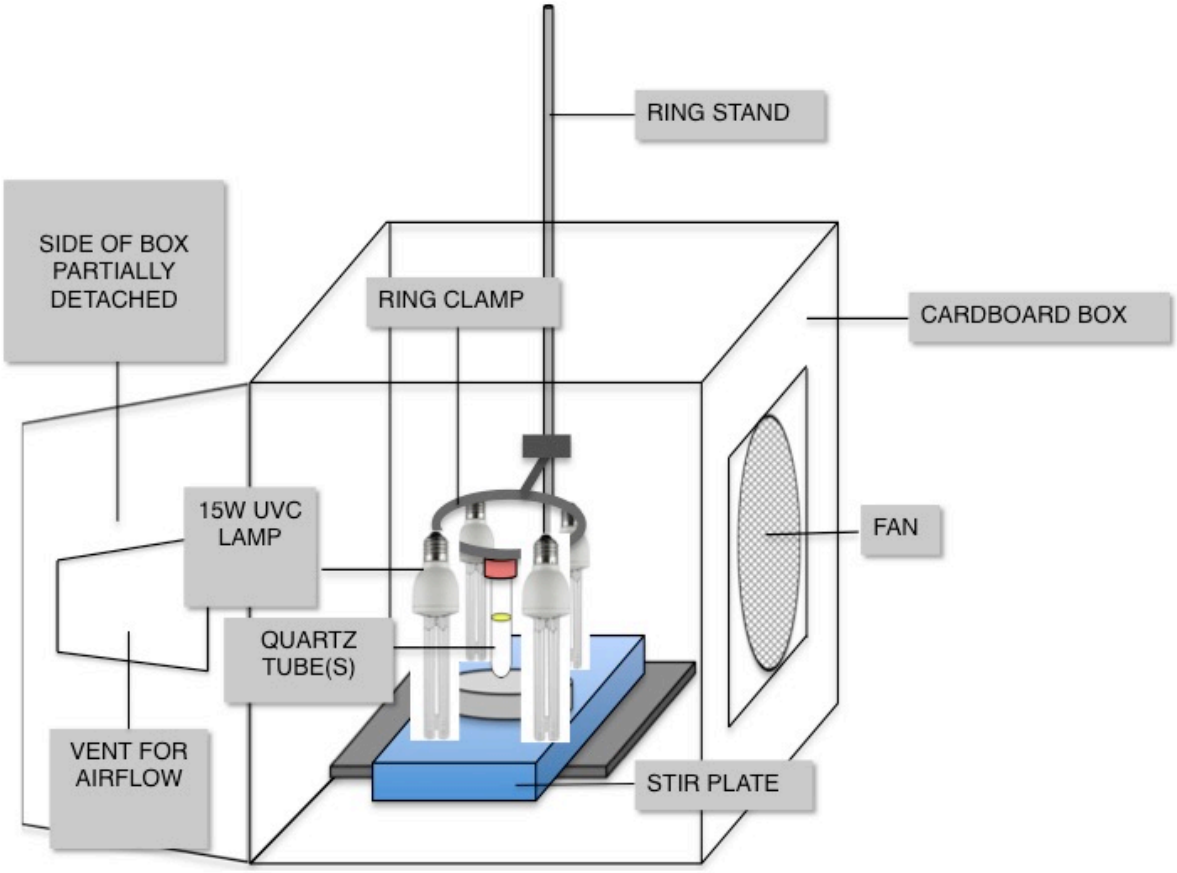
Four 15W, 120V, UV germicidal CFL lamps were suspended from a ring clamp on a ring stand (Figure S1). The lamps were spaced approximately evenly around the circumference of the ring clamp with a diameter of ≈14 cm. In a second clamp below the ring clamp, the top of a wire test tube rack was placed interior to the lamps.

Figure S1. Placement of CFL lamps around a ring clamp.

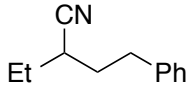


A stir plate covered in aluminum foil was placed underneath the lamps (Figure S2). A cardboard box lined with aluminum foil was placed over the ring stand, lamps, and stir plate. In one side of the cardboard box, part of the side was cut out, and a 172 x 150 x 51 mm high-speed (240 CFM) fan was fitted into this side of the box. In the side of the box directly opposite the fan, a vent was cut out. Photoreactions were carried out in quartz tubes or a quartz flask placed approximately in the center of the wire test tube rack, ensuring that the reaction vessels were within the line of airflow from the fan and did not touch the lamps.

Figure S2. **Placement of cardboard box and fan relative to the CFL lamps.**



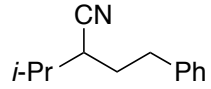
General Procedure. Inside a glovebox, an oven-dried 20-mL vial equipped with a stir bar was charged with TBACN (***Caution: Highly toxic!***; 601 mg, 2.24 mmol, 1.60 equiv), and then it was capped with a PTFE-lined septum cap and sealed with electrical tape. The vial was then removed from the glovebox, and CH_3CN (18.0 mL) was added via syringe. The mixture was vigorously stirred for 5 min, resulting in a colorless solution. An oven-dried 20-mL quartz tube containing a stir bar was then charged with CuI (20.0 mg, 0.105 mmol, 0.0750 equiv), capped with a rubber septum, and sealed with electrical tape. The tube was evacuated and backfilled with nitrogen three times (through a needle attached to a vacuum manifold), and the solution of TBACN was added via syringe, followed by the electrophile (1.40 mmol, 1.00 equiv; via microsyringe (if the electrophile is a solid, then it was added immediately after the addition of CuI)). The reaction mixture was stirred vigorously for 1 min. The quartz tube was then removed from the manifold, and the resulting mixture was next stirred vigorously and irradiated in the center of four 15W, 120V, UV germicidal CFL lamps at r.t. for 24 h. Then, the reaction mixture was transferred to a 100-mL round-bottom flask and concentrated using a rotary evaporator in a well-ventilated fume hood. The residue was purified by column chromatography.



2-Ethyl-4-phenylbutanenitrile (Table 2, Entry 1) [1126479-77-3]. The title compound was prepared according to the General Procedure from (3-chloropentyl)benzene (258 μL, 256 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (5→10% EtOAc/hexanes). Tan oil. First run: 223 mg (92% yield). Second run: 227 mg (94% yield).

Gram-scale reaction. In a glovebox, a 200-mL quartz flask was charged with TBACN (3.44 g, 12.8 mmol, 1.60 equiv), and a stir bar was added. The flask was capped with a rubber septum and sealed with electrical tape, and then it was removed from the glovebox. A separate 250-mL flask (borosilicate glass) was charged with CuI (114 mg, 0.600 mmol, 0.0750 equiv), CH_3CN (110 mL), and a stir bar. The CuI/CH_3CN solution was vigorously stirred for 1 min under a nitrogen atmosphere, after which the homogeneous solution was transferred via cannula to the quartz flask that contained the TBACN. Then, the alkyl chloride (1.50 mL, 8.00 mmol, 1.00 equiv) was added via syringe. The reaction mixture was irradiated for 24 h using the irradiation set-up described above, except that the wire test tube rack was removed, and the quartz flask was placed in the center of the four lamps. Then, the stir bar was removed, and the reaction mixture was concentrated using a rotary evaporator in a well-ventilated fume hood. The product was purified by column chromatography on silica gel (10→20% Et_2O/hexanes). Tan oil. 1.30 g, 94% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.30 (m, 2H), 7.26–7.19 (m, 3H), 2.91 (ddd, 1H, *J* = 14.2, 9.1, 5.2 Hz), 2.75 (ddd, 1H, *J* = 13.8, 8.9, 7.6 Hz), 2.49–2.43 (m, 1H), 2.01–1.92 (m, 1H), 1.90–1.82 (m, 1H), 1.70–1.63 (m, 2H), 1.09 (t, 3H, *J* = 7.4 Hz).



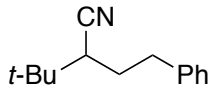
2-Isopropyl-4-phenylbutanenitrile (Table 2, Entry 2). The title compound was prepared according to the General Procedure from (3-chloro-4-methylpentyl)benzene (280 μL, 275 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (5→10% EtOAc/hexanes). Tan oil. First run: 220 mg (84% yield). Second run: 222 mg (85% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.29 (m, 2H), 7.25–7.19 (m, 3H), 2.92 (ddd, 1H, *J* = 14.1, 9.2, 5.0 Hz), 2.71 (ddd, 1H, *J* = 13.8, 9.0, 7.6 Hz), 2.40 (dt, 1H, *J* = 10.4, 5.0 Hz), 1.96 (dddd, 1H, *J* = 13.9, 10.7, 9.0, 5.0 Hz), 1.89–1.78 (m, 2H), 1.08–1.02 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.6, 129.0, 128.8, 126.7, 121.3, 38.8, 33.9, 32.2, 30.4, 21.3, 19.0.

ATR-IR (neat) 3028, 2964, 2932, 2900, 2874, 2236, 1603, 1497, 1455, 1391, 1373, 751, 701 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{13}H_{17}N$: 187.1, found 187.2.



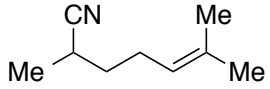
3,3-Dimethyl-2-phenethylbutanenitrile (Table 2, Entry 3). The title compound was prepared according to the General Procedure from (3-chloro-4,4-dimethylpentyl)benzene (95.0 μL, 92.8 mg, 0.440 mmol) as the electrophile. The product was purified by column chromatography on silica gel (hexanes→10% Et_2O/hexanes). Yellow oil. First run: 75.0 mg (85% yield). Second run: 74.1 mg (84% yield).

^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.29 (m, 2H), 7.25–7.20 (m, 3H), 3.01 (ddd, 1H, *J* = 13.8, 8.9, 4.9 Hz), 2.67 (dt, 1H, *J* = 13.8, 8.5 Hz), 2.25 (dd, 1H, *J* = 11.6, 4.3 Hz), 1.92–1.79 (m, 2H), 1.03 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.7, 129.0, 128.8, 126.7, 121.6, 43.8, 34.5, 33.3, 29.5, 27.8.

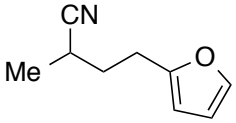
ATR-IR (neat) 3028, 2963, 2938, 2875, 2233, 1602, 1498, 1488, 1472, 1463, 1456, 1399, 1375, 1368, 1317, 1233, 1030, 770, 757, 701 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{14}H_{19}N$: 201.2, found 201.2.



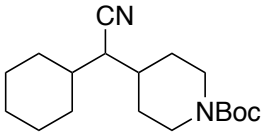
2,6-Dimethylhept-5-enenitrile (Table 2, Entry 4) [54088-65-2]. The title compound was prepared according to the General Procedure from 6-chloro-2-methylhept-2-ene (205 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (4% Et_2O/hexanes). Clear oil. First run: 161 mg (84% yield). Second run: 164 mg (85% yield).

^1H NMR (400 MHz, $CDCl_3$) δ 5.09–5.02 (m, 1H), 2.67–2.55 (m, 1H), 2.23–2.11 (m, 2H), 1.72–1.62 (m, 7H), 1.59–1.49 (m, 1H), 1.33–1.29 (m, 3H).



4-(Furan-2-yl)-2-methylbutanenitrile (Table 2, Entry 5) [71649-14-4]. The title compound was prepared according to the General Procedure from 2-(3-chlorobutyl)furan (221 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (10% Et_2O/hexanes). Yellow oil. First run: 160 mg (77% yield). Second run: 148 mg (71% yield).

^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.30 (m, 1H), 6.31–6.27 (m, 1H), 6.08–6.04 (m, 1H), 2.92–2.75 (m, 2H), 2.67–2.56 (m, 1H), 2.01–1.85 (m, 2H), 1.36–1.31 (m, 3H).



***t*-Butyl 4-(cyano(cyclohexyl)methyl)piperidine-1-carboxylate (Table 2, Entry 6)**. The title compound was prepared according to the General Procedure from tert-butyl 4-(chloro(cyclohexyl)methyl)piperidine-1-carboxylate (442 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (20→60% Et_2O/hexanes). Off-white solid. First run: 392 mg (91% yield). Second run: 406 mg (95% yield).

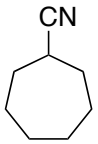
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.28–4.06 (m, 2H), 2.74–2.61 (m, 2H), 2.22 (t, 1H, *J* = 7.0 Hz), 1.91–1.84 (m, 2H), 1.83–1.72 (m, 3H), 1.72–1.56 (m, 4H), 1.45 (s, 9H), 1.36–1.10 (m, 7H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0, 120.3, 80.0, 44.9, 36.0, 35.0, 32.0, 30.7, 29.8, 26.4, 26.3, 26.1.

ATR-IR (neat) 2930, 2923, 2855, 2236, 1692, 1452, 1431, 1365, 1285, 1235, 1179, 1135 cm^{-1}.

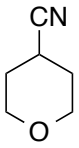
HRMS (ESI) *m*/*z* [M–(isobutylene)–(CO_2)+H]$^+$ calcd for $C_{13}H_{23}N_2$: 207.1861, found: 207.1848.

Mp: 96.5–99.0 °C.



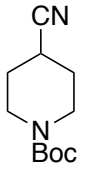
Cycloheptanecarbonitrile (Table 2, Entry 7) [32730-85-1]. The title compound was prepared according to the General Procedure from chlorocycloheptane (193 μL, 186 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (10→20% EtOAc/hexanes; fractions were analyzed by GC). Clear oil. First run: 138 mg (80% yield). Second run: 135 mg (78% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.79 (tt, 1H, *J* = 7.9, 4.6 Hz), 1.96–1.82 (m, 4H), 1.80–1.70 (m, 2H), 1.67–1.53 (m, 6H).



Tetrahydro-2*H*-pyran-4-carbonitrile (Table 2, Entry 8) [4295-99-2]. The title compound was prepared according to the General Procedure from 4-chlorotetrahydro-2*H*-pyran (152 μL, 169 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (10→50% EtOAc/hexanes; fractions were analyzed by GC). Tan oil. First run: 103 mg (66% yield). Second run: 111 mg (71% yield).

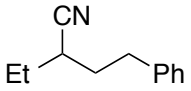
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.91–3.85 (m, 2H), 3.62–3.56 (m, 2H), 2.86 (tt, 1H, *J* = 8.2, 4.3 Hz), 1.96–1.90 (m, 2H), 1.89–1.82 (m, 2H).



***t*-Butyl 4-cyanopiperidine-1-carboxylate (Table 2, Entry 9) [91419-52-2]**. The title compound was prepared according to the General Procedure from *tert*-butyl 4-chloropiperidine-1-carboxylate (277 μL, 308 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (40→70% Et_2O/hexanes). Off-white solid. First run: 262 mg (89% yield). Second run: 248 mg (84% yield).

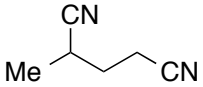
^1H NMR (500 MHz, $CDCl_3$) δ 3.69–3.60 (m, 2H), 3.37–3.29 (m, 2H), 2.83–2.76 (m, 1H), 1.91–1.83 (m, 2H), 1.82–1.74 (m, 2H), 1.47–1.43 (m, 9H).

Mp: 59.0–60.0 °C.



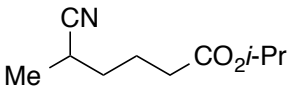
2-Ethyl-4-phenylbutanenitrile (Table 3, Entry 1) [1126479-77-3]. The title compound was prepared according to the General Procedure from (3-bromopentyl)benzene (259 μL, 318 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (10→20% Et_2O/hexanes). Tan oil. First run: 202 mg (83% yield). Second run: 205 mg (84% yield).

The ^1H NMR spectrum of the product was identical to that of Table 2, Entry 1.



2-Methylpentanedinitrile (Table 3, Entry 2) [4553-62-2]. The title compound was prepared according to the General Procedure from 4-bromopentanenitrile (162 μL, 227 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (40→80% Et_2O/hexanes). Yellow oil. First run: 124 mg (82% yield). Second run: 122 mg (81% yield).

^1H NMR (500 MHz, $CDCl_3$) δ 2.87–2.79 (m, 1H), 2.65–2.51 (m, 2H), 2.02–1.91 (m, 2H), 1.42–1.39 (m, 3H).



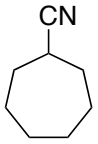
Isopropyl 5-cyanohexanoate (Table 3, Entry 3). The title compound was prepared according to the General Procedure from isopropyl 5-bromohexanoate (237 μL, 332 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (20→60% Et_2O/hexanes). Yellow oil. First run: 211 mg (82% yield). Second run: 208 mg (81% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.05–4.96 (m, 1H), 2.66–2.58 (m, 1H), 2.32 (t, 2H, J = 7.2 Hz), 1.89–1.70 (m, 2H), 1.69–1.55 (m, 2H), 1.34–1.31 (m, 3H), 1.23 (d, 6H, J = 6.3 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 122.8, 68.0, 34.0, 33.4, 25.5, 22.5, 22.0, 18.0.

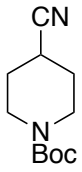
ATR-IR (neat) 2982, 2940, 2878, 2239, 1729, 1457, 1420, 1375, 1340, 1294, 1274, 1253, 1181, 1146, 1110 cm^{-1}.

MS (EI) m/z $[M - (C_3H_7O)]^+$ calcd for $C_7H_{10}NO$: 124.1, found: 124.1.



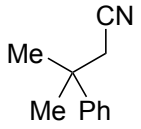
Cycloheptanecarbonitrile (Table 3, Entry 4) [32730-85-1]. The title compound was prepared according to the General Procedure from bromocycloheptane (208 μL, 248 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (20→40% Et_2O/hexanes; fractions were analyzed by GC). Yellow oil. First run: 157 mg (91% yield). Second run: 160 mg (93% yield).

The ^{1}H NMR spectrum of the product was identical to that of Table 2, Entry 7.



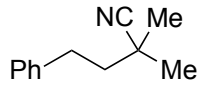
***t*-Butyl 4-cyanopiperidine-1-carboxylate (Table 3, Entry 5) [91419-52-2]**. The title compound was prepared according to the General Procedure from *tert*-butyl 4-bromopiperidine-1-carboxylate (276 μL, 370 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (40→80% Et_2O/hexanes). Off-white solid. First run: 242 mg (82% yield). Second run: 250 mg (85% yield).

The ^{1}H NMR spectrum of the product was identical to that of Table 2, Entry 9.



3-Methyl-3-phenylbutanenitrile (eq 2) [17684-33-2]. The title compound was prepared according to the General Procedure from (1-chloro-2-methylpropan-2-yl)benzene (226 μL, 236 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (10→20% EtOAc/hexanes). Tan oil. First run: 184 mg (83% yield). Second run: 174 mg (78% yield).

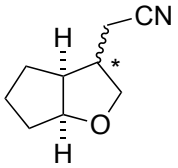
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.34 (m, 4H), 7.28–7.24 (m, 1H), 2.62 (s, 2H), 1.52 (s, 6H).



2,2-Dimethyl-4-phenylbutanenitrile (eq 3) [75490-38-9]. The title compound was prepared according to the General Procedure from (3-chloro-3-methylbutyl)benzene (256 mg, 1.40 mmol) as the electrophile. The product was purified by column chromatography on silica gel (hexanes→10% Et_2O/hexanes). Clear oil. First run: 149 mg (61% yield). Second run: 153 mg (63% yield).

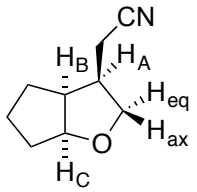
^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.27 (m, 2H), 7.25–7.18 (m, 3H), 2.85–2.76 (m, 2H), 1.88–1.78 (m, 2H), 1.42 (s, 6H).

Electrophile Competition Experiments (eq 4 and eq 5). Inside a glovebox, TBACN (26.8 mg, 0.10 mmol, 1.0 equiv) was added to an oven-dried 10-mL quartz test tube. Then, CH_3CN (0.60 mL) and each alkyl halide (0.50 mmol, 5.0 equiv) were added in turn, along with a stir bar. The reaction mixture was stirred for 2 min, and then a solution of CuI in CH_3CN (0.011 M, 0.70 mL) was added. The quartz test tube was capped with a rubber septum and wrapped with electrical tape, and the reaction mixture was stirred for 1 min. The quartz tube was removed from the glovebox, and the resulting mixture was then stirred vigorously and irradiated at r.t. for 24 h (see General Procedure). The ratio of products was determined by GC analysis.



2-((3a*S*,6a*S*)-Hexahydro-2*H*-cyclopenta[*b*]furan-3-yl)acetonitrile (eq 7). In a glovebox, a 20-mL vial was charged with TBACN (266 mg, 0.991 mmol, 1.6 equiv), a stir bar, and CH_3CN (8.3 mL). The resulting solution was stirred vigorously for 5 min. Next, CuCl (9.23 mg, 0.093 mmol, 0.15 equiv) was weighed into an oven-dried 20-mL quartz test tube, and the solution of TBACN was added to the tube. To this suspension was added (1*S*,2*S*)-1-(allyloxy)-2-chlorocyclopentane (100 mg, 0.622 mmol, 1.0 equiv), and the tube was capped with a rubber septum and sealed with electrical tape. The solution was stirred for another 3 min, and then the tube was removed from the glovebox and irradiated at r.t. for 24 h (see General Procedure). The ratio of diastereomers was determined by GC analysis of the unpurified reaction mixture. The product was isolated as a mixture of diastereomers by column chromatography (5% Et_2O/hexanes→Et_2O). Clear liquid. First run: 25 mg (27%, 2.3:1). Second run: 28 mg (30%, 2.1:1).

Major diastereomer. The major diastereomer could be purified by preparative HPLC (ZORBAX RX-SIL column, 9.4 x 250 mm, 20% EtOAc/hexanes).



^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56 (td, 1H, *J* = 5.8, 2.5 Hz), 3.97—3.89 (m, 1H), 3.48 (t, 1H, *J* = 8.3 Hz), 2.75—2.62 (m, 2H), 2.46—2.33 (m, 2H), 1.87—1.58 (m, 5H), 1.53—1.41 (m, 1H).

2D NOESY (400 MHz, $CDCl_3$) δ [4.55 (H_C), 3.91 (H_{eq})], [4.55 (H_C), 2.68 (H_A/H_B)], [3.91 (H_{eq}), 4.55 (H_C)], [3.91 (H_{eq}), 2.68 (H_A/H_B)], [2.68 (H_A/H_B), 3.91 (H_{eq})], [2.68 (H_A/H_B), 4.55 (H_C)].

^{13}C NMR (100 MHz, $CDCl_3$) δ 118.9, 86.5, 71.5, 46.1, 39.6, 34.2, 26.2, 25.7, 16.7.

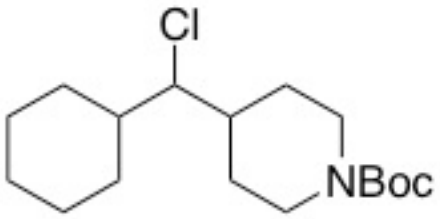
ATR-IR (neat) 2955, 2869, 2246, 1483, 1468, 1451, 1426, 1339, 1307, 1261, 1205, 1154, 1080, 1043, 960, 950, 922, 901, 806, 649 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_9H_{13}NO$: 151.1, found: 151.1.

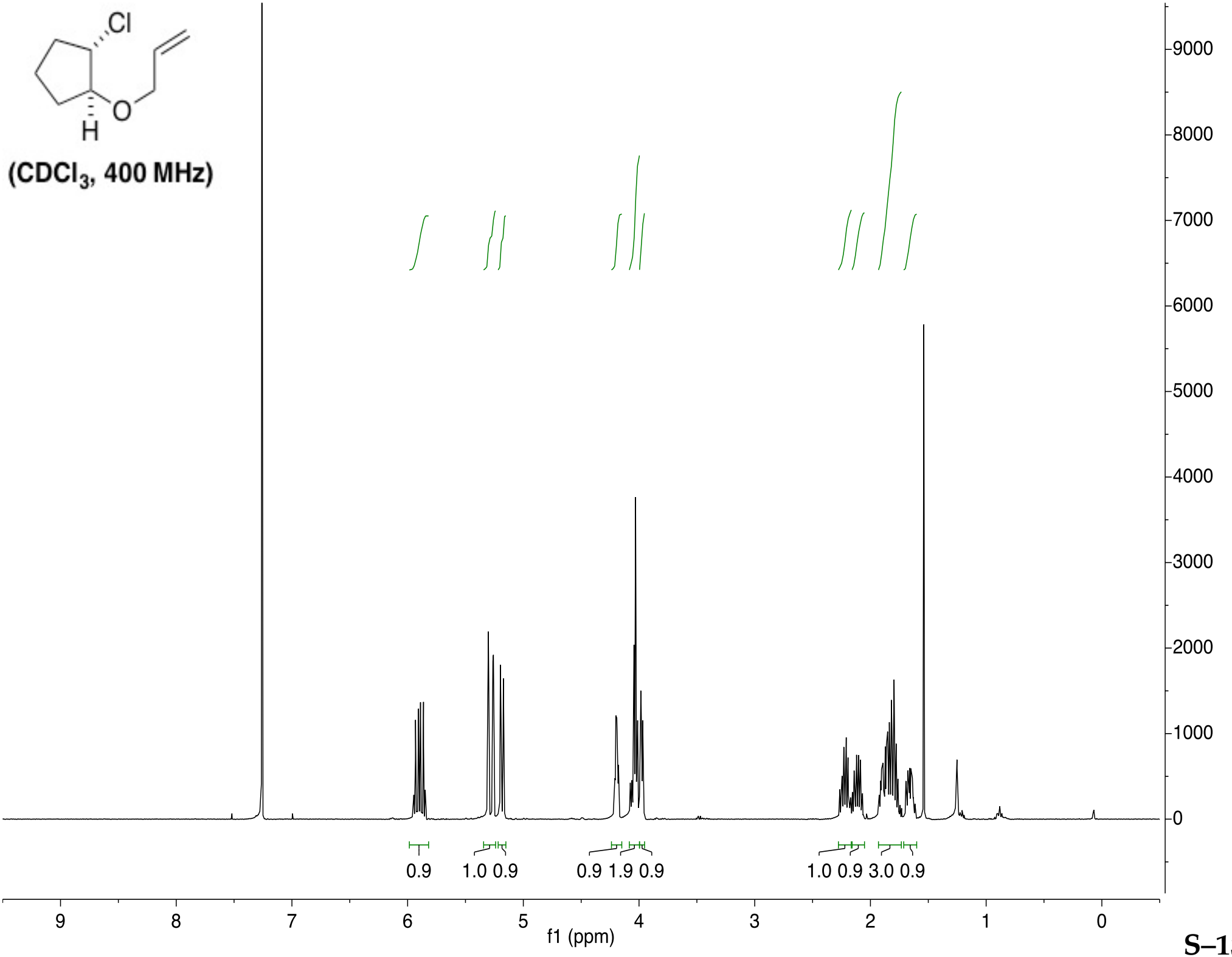
References

(1) Contributed equally.
(2) Powell, D. A.; Maki, T.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 510–511.

IV. ^{1}H NMR Spectra



($CDCl_3$, 500 MHz)


Cl
O
H
(CDCl3, 400 MHz)
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
0.9
1.0 0.9
0.9 1.9 0.9
1.0 0.9 3.0 0.9
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

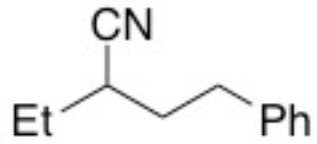


Table 2, Entry 1
($CDCl_3$, 500 MHz)

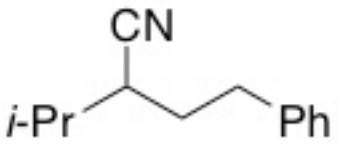


Table 2, Entry 2
($CDCl_3$, 500 MHz)

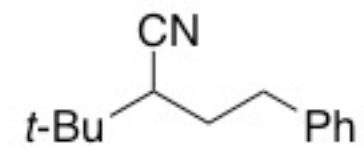


Table 2, Entry 3
($CDCl_3$, 500 MHz)

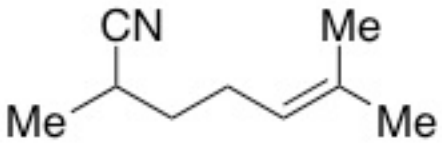


Table 2, Entry 4
($CDCl_3$, 400 MHz)

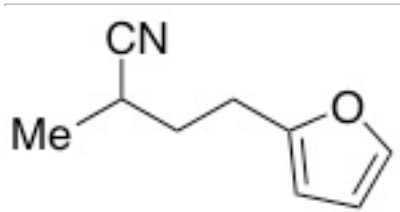


Table 2, Entry 5
($CDCl_3$, 400 MHz)

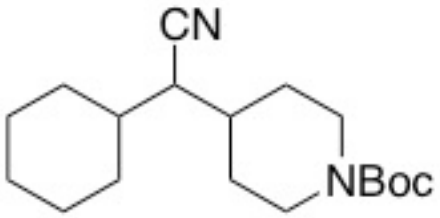


Table 2, Entry 6
($CDCl_3$, 500 MHz)

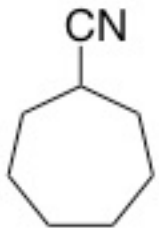


Table 2, Entry 7
($CDCl_3$, 500 MHz)

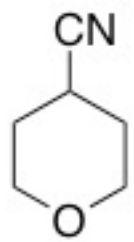


Table 2, Entry 8
($CDCl_3$, 500 MHz)

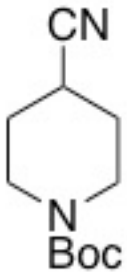


Table 2, Entry 9
($CDCl_3$, 500 MHz)

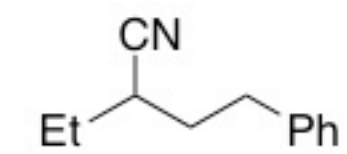


Table 3, Entry 1
($CDCl_3$, 500 MHz)

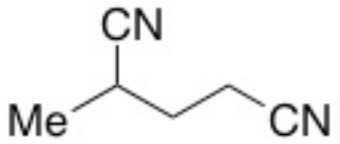


Table 3, Entry 2
($CDCl_3$, 500 MHz)

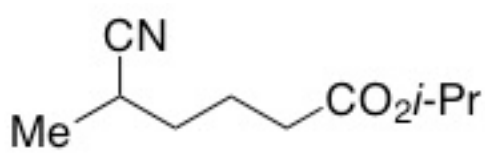


Table 3, Entry 3
($CDCl_3$, 500 MHz)

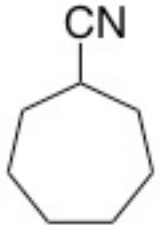


Table 3, Entry 4
($CDCl_3$, 500 MHz)

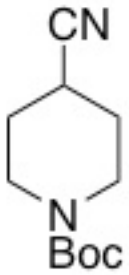
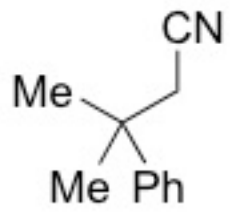
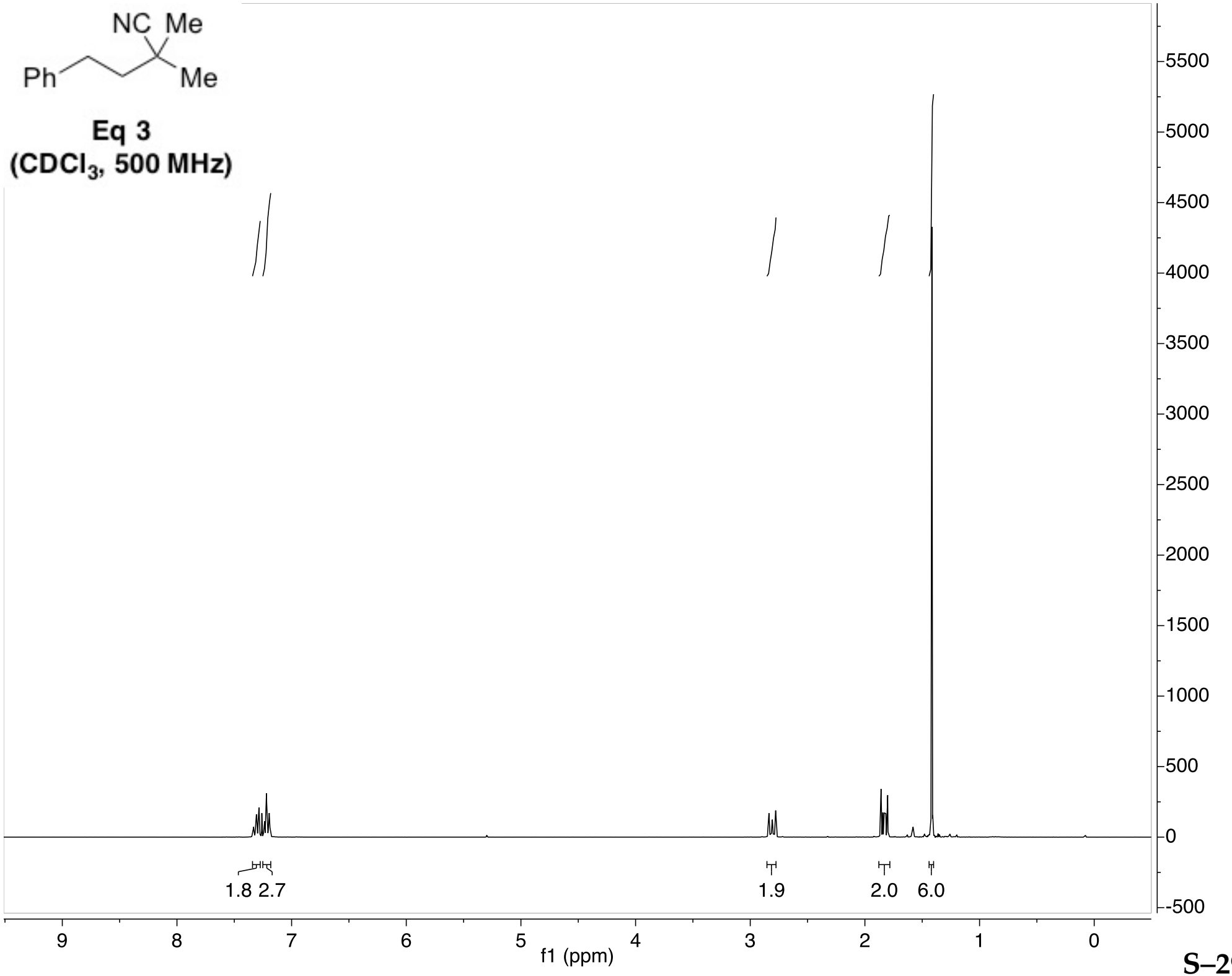
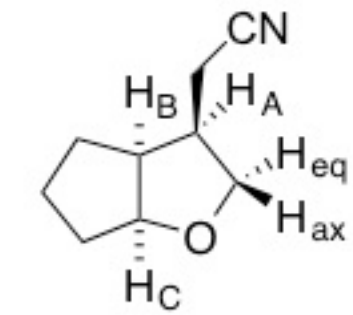


Table 3, Entry 5
($CDCl_3$, 500 MHz)



Eq 2
($CDCl_3$, 500 MHz)


NC Me
Ph
Me
Eq 3
(CDCl3, 500 MHz)
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
1.8 2.7
1.9
2.0
6.0
9
8
7
6
5
4
3
2
1
0
f1 (ppm)



Eq 7
($CDCl_3$, 400 MHz)