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α-Methylation of 2-Arylacetonitrile by a Trimethylamine-Borane/CO_2 System

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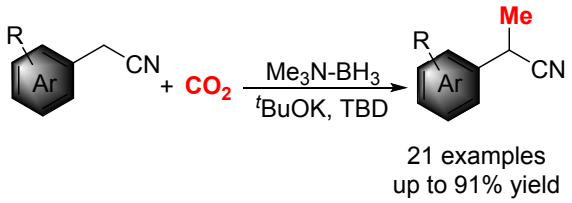
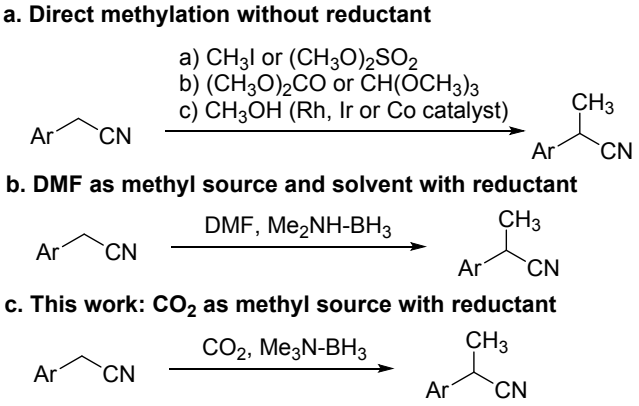


ABSTRACT: A highly selective monomethylation of 2-arylacetonitrile using CO_2 is described. The utilization of trimethylamine-borane facilitates the six-electron reduction of CO_2. This reaction is the first selective six-electron reductive functionalization of CO_2 faciliated by C(sp^3)-H bonds. A variety of 2-arylpropionitrile was obtained in good yields. The reaction could also be applied at gram scale.

INTRODUCTION

Methylation has played a significant role in medicine chemistry for many reasons, such as magic methyl effect.[1] For example, 2-arylpropionitriles, the methylated products of 2-arylacetonitriles, are important precursors in anti-inflammatory products, such as ibuprofen, flurbiprofen, and naproxen[2]. Several methylating reagents have been applied to access the methylated products. (Scheme 1).[1e,2-5] For instance, methyl iodide,[2] dimethyl sulfate[2], dimethyl carbonate,[3a,b] and trimethyl orthoformate[3c] are often used as methylating reagents. However, the methylation reactions using above-mentioned methylating reagents suffered low selectivity and harsh reaction conditions such as high temperature (over 150 °C), which limit their application. Methanol has been widely applied as the methylating reagent[4] in the monomethylation of 2-arylacetonitriles with a transition metal catalyst, such as Ru,[4a-c] Co,[4d] and Ir[4e]. Recently, Wang and co-workers reported Me_2NH-BH_3 assisted α-monomethylation of 2-arylacetonitrile utilizing DMF as the methyl source (Scheme 1b).[5]

Nevertheless, it is still desirable to develop a new methylation reaction using more environmentally-friendly and more efficient methylating reagents. CO_2 has demonstrated great potential as an abundant, renewable, and low-toxic C_1 chemical feedstock.[6] Many reactions in utilization of CO_2 have been reported to generate carboxylic acids and their derivatives.[7,8] However, CO_2 as a methylation reagent[9,10] in the C-C bond formation is rarely reported. Recently, Beller's group first realized a Ru-catalyzed reductive methylation of C(sp^2)-H bond in electron-rich arenes with CO_2 and H_2,[11] which paves a new way for C-C bond formation using CO_2. Selective monomethylation of C(sp^3)-H bond using CO_2 is not achieved up to now, to the best of our knowledge. Herein, we report a transi-



Scheme 1. The Methylation of 2-Arylacetonitriles

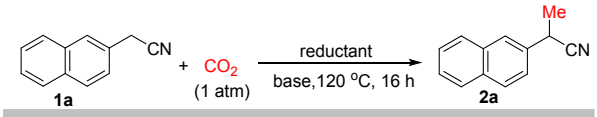
tion-metal-free monomethylation of 2-arylacetonitriles using CO_2 and Me_3N-BH_3 (Scheme

1c). This reaction realized the conversion of CO_2 into methyl group with formation of C(sp^3)-C(sp^3) bond.

RESULTS AND DISCUSSION

The initial optimization studies were conducted using 2-naphthylacetonitrile (**1a**, 0.3 mmol) as a model substrate to test our hypothesis (Table **1**). Learning from our previous studies in the area of reductive functionalization with CO_2[12], we first used $NaBH_4$ as reductant, ^{t}BuOK as base, and DME (1,2-dimethoxyethane) as solvent to realize this methylation reaction (entry 1), no product was observed and **1a** remained. When NH_3-BH_3 served as the reductant, the desired product was obtained in 10% yield (entry 2). TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene) is a powerful organic base, which was frequently employed to activate CO_2. We tried utilization of TBD instead of ^{t}BuOK as the base, there is no improvement in the yield (entry 3). Notably, reaction ran well when TBD and ^{t}BuOK were used together (entry 4). TBD works as a predator of CO_2 and ^{t}BuOK works as a strong base in deprontonation of 2-naphthylacetonitrile **1a**. Other amine-boranes like Me_2HN-BH_3 and Me_3N-BH_3 were also examed as the reductant and the yield of product **2a** improved (entry 5 and 8). After a screening of charge ratio (entries 5-11), we found Me_3N-BH_3 can promote this reaction effectively (entry 9). Notably, an exclusive monomethylated product **2a** was detected on GC-MS and NMR, which revealed high efficiency and selectivity of this reaction. Furthermore, the reaction temperature and time were examined and the yield of **2a** reduced to 80 % and 82 %, respectively (entries 12-13).

Table 1. Optimization of Reaction Conditions[a]



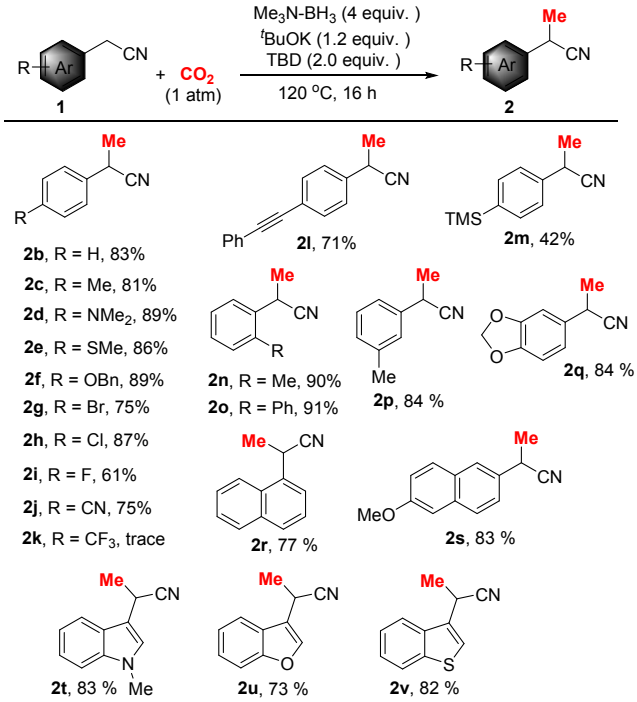
entry	solvent	base (x equiv.)	reductant (x equiv.)	yield [%][b]
1	DME	^{t}BuOK (1)	$NaBH_4$ (3)	0
2	DME	^{t}BuOK (1)	H_3N-BH_3 (3)	10
3	DME	TBD (1)	H_3N-BH_3 (3)	8
4	DME	TBD (1) ^{t}BuOK (1)	H_3N-BH_3 (3)	22
5	DME	TBD (1) ^{t}BuOK (1)	Me_2NH-BH_3 (3)	32
6	DME	TBD (2) ^{t}BuOK (1.2)	Me_2NH-BH_3 (4)	46
7	DME	TBD (1) ^{t}BuOK (1)	Me_2NH-BH_3 (6)	49
8	DME	TBD (1) ^{t}BuOK (1)	Me_3N-BH_3 (3)	34
9	DME	TBD (2) ^{t}BuOK (1.2)	Me_3N-BH_3 (4)	91 (83)
10	DME	TBD (2) ^{t}BuOK (1.2)	Me_3N-BH_3 (5)	90
11	DME	TBD (2) ^{t}BuOK (1.2)	Me_3N-BH_3 (6)	93
12[c]	DME	TBD (2) ^{t}BuOK (1.2)	Me_3N-BH_3 (4)	80
13[d]	DME	TBD (2) ^{t}BuOK (1.2)	Me_3N-BH_3 (4)	82
14	THF	TBD (2) ^{t}BuOK (1.2)	Me_3N-BH_3 (4)	7
15	1,4-dioxane	TBD (2) ^{t}BuOK (1.2)	Me_3N-BH_3 (4)	11
16	Toluene	TBD (2) ^{t}BuOK (1.2)	Me_3N-BH_3 (4)	Trace

[a]The reactions were carried out using 0.3 mmol of **1a** in 0.5 mL solvent. [b]^{1}H NMR yield determined using dibromomethane as an internal standard, isolated yield is given in parenthesis. [c]100 °C. [d]12 h.

In addition, different solvents such as tetrahydrofuran (THF), 1,4-dioxane, and toluene,were screened (entries 14-16), and poor yields were observed.

With the optimized reaction conditions in hand, we investigated the generality of this methylation protocol. A range of arylacetonitriles were treated with Me_3N-BH_3/CO_2 system to gain the methylated products. The representative results are shown in Table 2. First, various *para*-substituted arylacetonitriles were studied. Benzene ring bearing a wide range of functional groups could be converted to methylated products in good to excellent yields. The *para*-substituted arylacetonitriles bearing electron-donating groups, such as -NMe_2 (for **2d**), -SMe (for **2e**), and -OBn (for **2f**) exhibited higher reactivity, respectively. When the substrates with electron-withdrawing groups such as -F and -CN were used and the desired products were obtained in 61% (for **2i**) and 75% (for **2j**) yield, respectively. Notably, the methylation of **1k** failed, which is presumably contributed to the lower nucleophilicity of the corresponding carbon anion. When 2-(4-(phenylethynyl)phenyl)acetonitrile **1l** and 2-(4-(trimethylsilyl)phenyl)acetonitrile **1m** were employed in this reaction and the corresponding methylation product **2l** and **2m** also obtained in good yield. When 2-(*o*-tolyl)propanenitrile **1n** and 2-([1,1'-biphenyl]-2-yl)propanenitrile **1o** were used in this reaction and the desired product **2n** and **2o** were generated in 90% and 91%, respectively, which indicate the reaction is not affected by steric effect. Utilization of 2-(benzo[*d*][1,3]dioxol-5-yl)acetonitrile **1q** in this

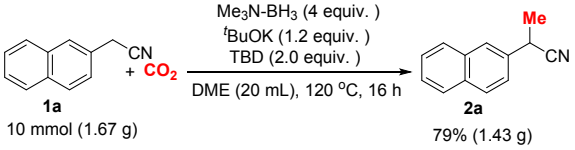
Table 2. Substrate Scope of 2-Arylacetonitriles[a]



[a]Reactions were carried out using 0.3 mmol of **1** in 0.5 mL DME.

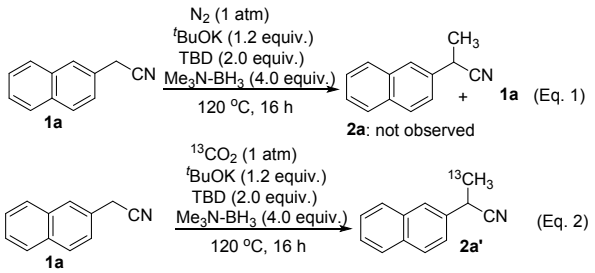
system afforded the corresponding product **2q** in 84% yield. Naphthalenylacetonitriles (**1r** and **1s**) were used and the desired products (**2r** and **2s**) were obtained in 77% and 83% yield, respectively. Remarkably, 2-heteroarylpropanenitriles can also achieve this reaction with desirable yields, including 2-(1-methyl-1H-indol-3-yl)propanenitrile (**2t**), 2-(benzofuran-3-yl)propanenitrile (**2u**), and 2-(benzo[b]thiophen-3-yl)propanenitrile (**2v**). It is noteworthy that in all cases only the monomethylated products were obtained without the detection of any traces of the dimethylated ones. Furthermore, other C(sp^3) nucleophiles such as propanedinitrile, methyl phenylacetate, and dimethyl malonate were employed in this reaction and the reaction led to the formation of complex, inseparable mixture, respectively. Aliphatic nitrile such as pimelic dinitrile can also not achieve this reaction with starting materials remaining.

In order to verify the applicability of the current methodology, the reaction was amplified to 10 mmol scale with a yield of **2a** in 79% (1.43 g) under the standard conditions in 20 mL DME. (Scheme **2**)



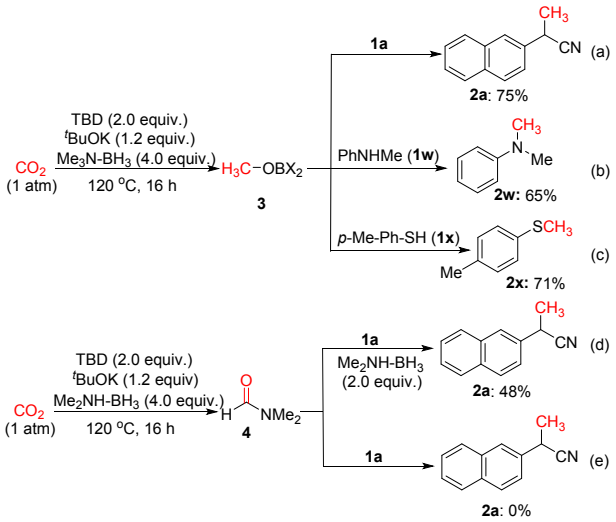
Scheme 2. Gram Scale Reaction

To elucidate the mechanism of the reaction, a series of control experiments were conducted. Initially, the reaction was treated using N_2 instead of CO_2, no product was observed and starting material **1a** remained (Eq. 1). In addition, isotopic labelling $^{13}CO_2$ was also used in the reaction and the corresponding product **2a'** was obtained (Eq. 2) (see Fig. S1 in SI). These results indicate that the methyl group comes from CO_2.



More experiments were conducted to illustrate the key intermediate during the reduction of CO_2 (Scheme 3). CO_2 was treated with TBD, ^{t}BuOK, and Me_3N-BH_3 in DME at 120 °C for 16 hours and methoxyborane **3** was obtained as the major product (see Fig. S2-S3 in SI), which indicates CO_2 undergoes six-electron reduction to form methyl group when using Me_3N-BH_3 as a reductant. Addition of **1a** (1 equiv.) to above mixture under N_2 afforded the corresponding **2a** in 75% yield (Scheme 3, a). Furthermore, the intermediate **3** was captured by other nucleophiles such as thiophenol **1w** and aniline **1x** to give the corresponding methylation product **2w** and **2x** in 65% and 71% yield, respectively (Scheme 3, b and c).

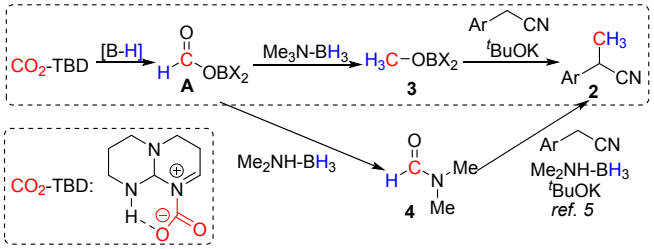
Different kinds of amine-boranes were employed to elucidate the superiority of Me_3N-BH_3 in CO_2 reduction. H_3N-BH_3 can only reduce CO_2 to formyl group according to our previous work.[10a] Furthermore, when CO_2 was treated with TBD and Me_2NH-BH_3 in DME at 120 °C for 16 hours, *N*,*N*-dimethylformamide (DMF) **4** was obtained (see Fig. S4-S5 in SI). Notably, no six-electron reduction product was observed, which indicates CO_2 undergoes two-electron reduction when using Me_2NH-BH_3 as reductant. When compound **1a** (1 equiv.) and Me_2NH-BH_3 (2.0 equiv.) were added into the generated mixture of **4** *in situ* under N_2, the product **2a** was obtained in 48% yield (Scheme 3, d). Remarkably, the desired product **2a** was not observed without addition Me_2NH-BH_3 (Scheme 3, e). These results indicate that Me_2NH-BH_3 is unable to reduce CO_2 to methyl group directly, which is due to side reaction between Me_2NH and the 2-electron intermediate. Me_2NH could cut off the reductive route to the 6-electron intermediate with the formation of amide. As a result, the utilization of Me_3N-BH_3 as reductant avoids the side reaction and facilitate the 6-electron reduction of CO_2.



Scheme 3. Control Experiments

Based on the above results and previous work on CO_2 reduction, a plausible mechanism for the methylation reaction is demonstrated in Scheme 4. First, CO_2-TBD adduct reacts with amine-borane to produce the formatoborohydride intermediate **A**. Then, further reduction of **A** with extra Me_3N-BH_3

affords methyl borate derivative **3**. Finally, 2-arylacetonitrile in the presence of ^{t}BuOK as a nucleophilic reagent attacks the carbon atom of **3** to form the desired C-monomethylated product **2**. In addition, Me_2NH-BH_3 promotes this reaction *via* DMF **4** in the presence of Me_2NH. The reaction of DMF with 2-arylacetonitrile under ^{t}BuOK/Me_2NH-BH_3 led to C-monomethylated product **2**, which has been reported by Wang and co-workers.[5]



Scheme 4. A Plausible Mechanism

CONCLUSION

In summary, the first examples for methylation of C(sp^3)-H bonds using CO_2 and amine-boranes are disclosed. Amine in amine-boranes exhibits competitiveness against boranes in CO_2 reduction and could capture the 2-electron intermediate. The utilization of 3° amine-boranes avoid the side reaction and facilitate the 6-electron reduction of CO_2. 2-Arylacetonitrile could be methylated into the desired 2-arylpropionitrile in good yields. The reaction could also be applied at gram scale. Further detailed studies on this selective reductive mechanism and expansion of CO_2 utilization are in progress in our group.

EXPERIMENTAL SECTION

General Information: Toluene, THF (tetrahydrofuran), 1,4-dioxane were purified by solvent purification system. Arylacetonitriles **1d**,[13] **1h**,[13] **1j**[14], **1t**[14], **2l**[15] were known compounds and prepared according to the literature procedures. Unless otherwise mentioned, reagents were commercially available and used without further purification. HRMS were recorded with ESI in positive ion mode on IT-TOF instrument. ^{1}H NMR, ^{13}C{^{1}H} NMR, ^{19}F NMR spectra were recorded with 600 MHz, 400 MHz spectrometer. $CDCl_3$ was selected as the solvent and residual proton resonance of $CDCl_3$ was referenced using the 7.26 ppm in ^{1}H NMR and 77.16 ppm in ^{13}C{^{1}H} NMR. Coupling constants (*J*) were obtained in Hertz (Hz). The abbreviation of s, d, t, q and m means singlet, doublet, triplet, quartet and multiplet, respectively. Flash column chromatography was performed using silica gel with distilled solvents. CO_2 comes from tank directly.

***General procedure*:** 25 mL Sealed tube was evacuated and backfilled will CO_2 for 3 times, 2-arylacetonitriles (**1**) (0.3 mmol), Me_3N-BH_3 (87.7 mg, 1.2 mmol), ^{t}BuOK (40.3 mg, 0.36 mmol), TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene) (83.5 mg, 0.6 mmol) and 0.5 mL DME were added. The reaction mixture was stirred at 120 °C (heating mantle temperature) for 16 h. The reaction was then quenched with H_2O (10 mL) and extracted with ethyl acetate (20 mL x 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Then, it was isolated by silica gel flash chromatography (petroleum ether/ EtOAc: 20/1). The product was charactered by NMR.

A gram scale reaction: 250 mL Sealed tube was evacuated and backfilled will CO_2 for 3 times, 2-(naphthalen-2-yl)acetonitrile (**1a**) (1.67 g, 10 mmol), Me_3N-BH_3 (2.9 g, 40 mmol), ^{t}BuOK (1.34 g, 12 mmol), TBD (2.78 mg, 20 mmol) and 25 mL DME were added. The reaction mixture was stirred at 120 °C (heating mantle temperature) for 16 h. The reaction was then quenched with H_2O (50 mL) and extracted with ethyl acetate (80 mL x 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated as well as isolated by silica gel flash chromatography (petroleum ether/ EtOAc).

*2-(Naphthalen-2-yl)propanenitrile (**2a**):* white solid, yield: 83%, 54.3 mg; mp: 61-64 °C; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.95 – 7.83 (m, 3H), 7.70 (d, *J* = 6.9 Hz, 1H), 7.61 – 7.46 (m, 3H), 4.62 (q, *J* = 7.2 Hz, 1H), 1.78 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 134.1, 132.7, 129.9, 129.4, 129.0, 127.0, 126.2, 125.7, 124.8, 122.2, 121.9, 28.4, 20.7. The spectral data for this compound match that reported in the literature.[5] GC-MS:181

*2-Phenylpropanenitrile (**2b**):* colorless oil, yield: 83%, 32.6 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.46 – 7.29 (m, 5H), 3.90 (q, *J* = 7.3 Hz, 1H), 1.65 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 137.2, 129.2, 128.1, 126.8, 121.7, 31.3, 21.6. The spectral data for this compound match that reported in the literature.[5] GC-MS:131

*2-(p-Tolyl)propanenitrile (**2c**):* colorless oil, yield: 81%, 35.2 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.23 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 3.85 (q, *J* = 7.3 Hz, 1H), 2.34 (s, 3H), 1.61 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 137.9, 134.2, 129.9, 126.7, 121.9, 31.0, 21.6, 21.1. The spectral data for this compound match that reported in the literature.[5] GC-MS:145

*2-(4-(Dimethylamino)phenyl)propanenitrile (**2d**):* colorless oil, yield: 89%, 46.5 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.19 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 8.7 Hz, 2H), 3.80 (q, *J* = 7.3 Hz, 1H), 2.94 (s, 6H), 1.59 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 150.3, 127.5, 124.6, 122.3, 112.8, 40.6, 30.4, 21.6. The spectral data for this compound match that reported in the literature.[5] GC-MS:174

*2-(4-(Methylthio)phenyl)propanenitrile (**2e**):* colorless oil, yield: 86%, 45.7 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.24 – 7.26 (m, 4H), 3.85 (q, *J* = 7.3 Hz, 1H), 2.47 (s, 3H), 1.60 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 138.8, 133.8, 127.2, 127.1, 121.6, 30.8, 21.5, 15.8. The spectral data for this compound match that reported in the literature.[5] GC-MS:177

*2-(4-(Benzyloxy)phenyl)propanenitrile (**2f**):* white solid, yield: 89%, 63.2 mg; mp: 70-72 °C ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.44 – 7.28 (m, 5H), 7.29 – 7.22 (m, 2H), 7.00 – 6.95 (m, 2H), 5.06 (s, 2H), 3.84 (q, *J* = 7.3 Hz, 1H), 1.61 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 158.6, 136.8, 129.4, 128.7, 128.2, 128.1, 127.5, 121.9, 115.5, 70.2, 30.6, 21.6. The spectral data for this compound match that reported in the literature.[16] GC-MS:237

*2-(4-Bromophenyl)propanenitrile (**2g**):* colorless oil, yield: 75%, 47.0 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.55 – 7.49 (m, 2H), 7.26 – 7.21 (m, 2H), 3.87 (q, *J* = 7.3 Hz, 1H), 1.63 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 136.1, 132.4, 128.5, 122.2, 121.1, 30.9, 21.4. The spectral data for this compound match that reported in the literature.[5] GC-MS: 208, 210

*2-(4-Chlorophenyl)propanenitrile (**2h**):* colorless oil, yield: 87%, 43.1 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.37 (d, *J* = 8.6 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 3.88 (q, *J* = 7.3 Hz, 1H), 1.63 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 135.6, 134.2, 129.4, 128.2, 121.2, 30.8, 21.5. The spectral data for this compound match that reported in the literature.[5] GC-MS:165

*2-(4-Fluorophenyl)propanenitrile (**2i**):* colorless oil, yield: 61%, 27.3 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.35 – 7.28 (m, 2H), 7.06 (t, *J* = 8.6 Hz, 2H), 3.88 (q, *J* = 7.3 Hz, 1H), 1.62 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 162.4 (d, *J* = 247.2 Hz), 132.9 (d, *J* = 3.3 Hz), 128.5 (d, *J* = 8.4 Hz), 121.6, 116.2 (d, *J* = 21.7 Hz), 30.7, 21.6; ^{19}F NMR (565 MHz, CHLOROFORM-D) δ -113.81 (s). The spectral data for this compound match that reported in the literature.[5] GC-MS:149

*4-(1-Cyanoethyl)benzonitrile (**2j**):* colorless oil, yield: 75%, 35.3 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.68 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 3.96 (q, *J* = 7.3 Hz, 1H), 1.65 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 142.2, 133.1, 127.8, 120.4, 118.2, 112.4, 31.4, 21.3. HRMS (ESI) calcd for $C_{10}H_9N_2^+$[M+H]: 157.0760, found: 157.0761.

*2-(4-(Phenylethynyl)phenyl)propanenitrile (**2l**):* white solid, yield: 71%, 49.2 mg; mp: 105-106 °C ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.55 – 7.51 (m, 4H), 7.35 – 7.32 (m, 5H), 3.91 (q, *J* = 7.3 Hz, 1H), 1.64 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 137.0, 132.4, 131.7, 128.6, 128.5, 126.9, 123.4, 123.0, 121.3, 90.2, 88.6, 31.2, 21.4. The spectral data for this compound match that reported in the literature.[5] GC-MS:231

*2-(4-(Trimethylsilyl)phenyl)propanenitrile (**2m**):* colorless oil, yield: 48%, 29.2 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.54 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 3.89 (q, *J* = 7.3 Hz, 1H), 1.64 (d, *J* = 7.3 Hz, 3H), 0.27 (s, 9H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 140.7, 137.6, 134.2, 126.1, 100.0, 31.3, 21.4, -1.1. The spectral data for this compound match that reported in the literature.[5] GC-MS:203

*2-(o-Tolyl)propanenitrile (**2n**):* colorless oil, yield: 90%, 39.2 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.51 – 7.42 (m, 1H), 7.30 – 7.19 (m, 3H), 4.06 (q, *J* = 7.2 Hz, 1H), 2.38 (s, 3H), 1.63 (d, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 135.3, 134.8, 131.1, 128.2, 127.1, 126.8, 121.9, 28.2, 20.1, 19.1. The spectral data for this compound match that reported in the literature.[5] GC-MS:145

*2-([1,1'-Biphenyl]-2-yl)propanenitrile (**2o**):* colorless oil, yield: 91%, 56.6 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.69 – 7.61 (m, 1H), 7.49 – 7.34 (m, 5H), 7.31 – 7.23 (m, 3H), 4.03 (q, *J* = 7.2 Hz, 1H), 1.49 (d, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 141.1, 140.1, 135.2, 130.6, 129.1, 128.8, 128.6, 128.0, 127.8, 127.2, 122.4, 28.0, 21.5. HRMS (ESI) calcd for $C_{15}H_{14}N^+$[M+H]: 208.1121, found: 208.1120. GC-MS:174

*2-(m-Tolyl)propanenitrile (**2p**):* colorless oil, yield: 84%, 36.54 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.27 – 7.22 (m, 1H), 7.18 – 7.08 (m, 3H), 3.85 (q, *J* = 7.3 Hz, 1H), 2.36 (s, 3H), 1.62 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 139.1, 137.1, 129.1, 128.8, 127.5, 123.8, 121.8, 31.3, 21.6, 21.5. HRMS (ESI) calcd for $C_{10}H_{12}N^+$[M+H]: 146.0964, found: 146.0964

*2-(Benzo[d][1,3]dioxol-5-yl)propanenitrile (**2q**):* colorless oil, yield: 84%, 44.1 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 6.87 – 6.74 (m, 3H), 5.98 (s, 2H), 3.81 (q, *J* = 7.3 Hz, 1H), 1.61 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 148.4, 147.5, 130.8, 121.7, 120.2, 108.7, 107.3, 101.5, 31.0, 21.6. The spectral data for this compound match that reported in the literature.[5] GC-MS:175

*2-(Naphthalen-1-yl)propanenitril (**2r**):* colorless oil, yield: 77%, 41.8 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.91 – 7.79 (m, 4H), 7.55 – 7.47 (m, 2H), 7.46 – 7.39 (m, 1H), 4.05 (q, *J* = 7.3 Hz, 1H), 1.72 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 134.4, 133.4, 132.9, 129.2, 128.0, 127.8, 126.8, 126.6, 125.7, 124.5, 121.7, 31.5, 21.5. The spectral data for this compound match that reported in the literature.[5] GC-MS:181

*2-(6-Methoxynaphthalen-2-yl)propanenitrile (**2s**):* white solid, yield: 83%, 52.5 mg; mp: 71-73 °C; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.85 – 7.74 (m, 2H), 7.71 – 7.60 (m, 1H), 7.41 – 7.31 (m, 1H), 7.24 – 7.13 (m, 2H), 4.53 (q, *J* = 7.2 Hz, 1H), 3.96 (s, 3H), 1.80 (d, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 158.5, 131.2, 130.9, 129.5, 128.8, 125.4, 123.4, 121.8, 118.5, 101.3, 100.0, 55.5, 28.5, 20.1. The spectral data for this compound match that reported in the literature.[5] GC-MS:211

*2-(1-Methyl-1H-indol-3-yl)propanenitrile (**2t**):* white solid, yield: 83%, 45.9 mg; mp: 62-63 °C; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.67 – 7.60 (m, 1H), 7.35 – 7.25 (m, 2H), 7.19 – 7.14 (m, 1H), 7.09 – 7.04 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 1H), 3.77 (s, 3H), 1.74 (d, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 137.4, 126.3, 125.7, 122.4, 122.0, 119.7, 118.6, 110.5, 109.8, 32.9, 22.9, 20.1. The spectral data for this compound match that reported in the literature.[5] GC-MS:184

*2-(Benzofuran-3-yl)propanenitrile (**2u**):* colorless oil, yield: 73%, 37.5 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.70 – 7.63 (m, 2H), 7.57 – 7.47 (m, 1H), 7.42 – 7.27 (m, 2H), 4.09 (q, *J* = 7.2 Hz, 1H), 1.77 (d, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 155.8, 141.8, 125.4, 125.3, 123.2, 120.5, 119.4, 117.0, 112.1, 21.8, 18.9. The spectral data for this compound match that reported in the literature.[5] GC-MS:171

*2-(Benzo[b]thiophen-3-yl)propanenitrile (**2v**):* white solid, yield: 82%, 46.0 mg; mp: 108-109 °C; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.99 – 7.84 (m, 1H), 7.84 – 7.73 (m, 1H), 7.53 – 7.32 (m, 3H), 4.24 (q, *J* = 7.2 Hz, 1H), 1.78 (d, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 140.9, 136.4, 130.9, 125.0, 124.7, 123.8, 123.4, 121.2, 120.9, 25.6, 19.2. The spectral data for this compound match that reported in the literature.[5] GC-MS:187

*N, N-Dimethylaniline (**2w**):* colorless oil, yield: 65%, 23.6 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.41 – 7.31 (m, 2H), 6.80 – 6.88 (m, 3H), 3.03 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 150.8, 129.3, 116.8, 112.8, 40.8. The spectral data for this compound match that reported in the literature.[10b] GC-MS:121

*Methyl(p-tolyl)sulfane (**2x**):* colorless oil, yield: 71%, 29.3 mg; ^{1}H NMR (400 MHz, CHLOROFORM-D) δ 7.17 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 2.45 (s, 3H), 2.30 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, CHLOROFORM-D) δ 137.7, 135.9, 129.9, 126.6, 124.7, 20.1, 15.4. The spectral data for this compound match that reported in the literature.[17] GC-MS:138

ASSOCIATED CONTENT

Supporting Information.

These materials are available free of charge via the Internet at http://pubs.acs.org.

NMR spectrum for mechanistic study as shown in Figure S1-S5, and NMR spectra for all products

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Notes

The authors declare no competing financial interest.

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