A Convenient Method for the Preparation of Benzyl Isocyanides

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Abstract: Treatment of benzyl halides with silver salts ($AgClO_4$, $AgBF_4$, or AgOTf) and trimethylsilyl cyanide (TMSCN) in CH_2Cl_2 followed by cleavage of the carbon–silicon bond with aqueous $NaHCO_3$ or TBAF directly afforded the corresponding isocyanides.

Key words: benzyl isocyanides, benzyl halides, silver salts, trimethylsilyl cyanide, perchlorate

The versatility of isocyanide is well known because it is an important reactant for Passerini[1] and Ugi[2] multi-component reactions[3] and has the ability to function as a bonding partner for metals in complexes.[3a] In addition, it is also noteworthy that various biologically active isocyanides have been isolated[4] and synthesized.[5] Isocyanides are commonly prepared by the dehydration of formamides.[3,6] However, this method is not necessarily convenient, since preparing the formamide, including getting the precursor, is difficult in many cases. Therefore, the development of other simple, efficient methods to prepare isocyanides is very important. Recently, we reported methods for preparing tertiary isocyanides from alcohols[7] and alkenes[8] with Lewis acid and TMSCN. In addition, it is known that 1-isocyanoadamantane was synthesized from 1-haloadamantane with Lewis acid and TMSCN.[7a,9] However, these methods are only limited to the synthesis of tertiary isocyanides. During the course of our investigation on convenient isocyanide synthesis, we found a new method to prepare benzyl isocyanides. We describe herein a direct conversion method for preparing benzyl isocyanides from benzyl halides by using silver salts and TMSCN.

The results for the reaction of 4-*tert*-butylbenzyl bromide (**1a**) with TMSCN and silver salts (AgX) followed by treatment with TBAF or aqueous $NaHCO_3$ are summarized in Scheme 1 and Table 1. The reactions were carried out in CH_2Cl_2 with 1.5 equivalents each of AgX and TMSCN; then, TBAF or aqueous $NaHCO_3$ was added to the reaction mixture as a reagent for the cleavage of the carbon–silicon bond. 4-*tert*-Butylbenzyl isocyanide (**2**) was obtained in excellent yields with $AgClO_4$, $AgBF_4$, or AgOTf as a Lewis acid. This is similar to the case of preparing isocyanide from tertiary alcohol.[7b] Zinc salts, such as ZnI_2, $ZnBr_2$, or $ZnCl_2$ was not used as a Lewis acid here to obtain the desired isocyanide, in contrast to the case of tertiary alcohol.[7a]

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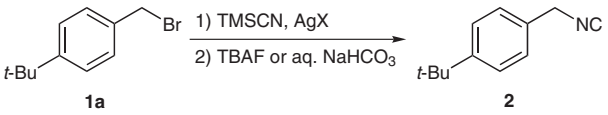


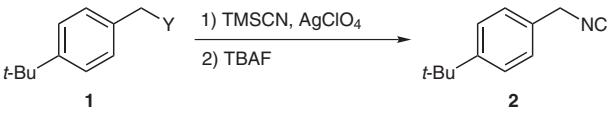
Scheme 1

Table 1 Reactions of 4-*tert*-Butylbenzyl Bromide (**1a**) with TMSCN and AgX

Entry	Reagent	Time (h)	Yield (%)[a]
1	$AgClO_4$	1	99 (92)[b]
2	$AgBF_4$	1	98
3	AgOTf	17	98

[a] Determined by GC analysis.
[b] Isolated yield.

Scheme 2 and Table 2 present the results of the reaction of 4-*tert*-butylbenzyl chloride (**1b**) and 4-*tert*-butylbenzyl alcohol (**1c**) with TMSCN and $AgClO_4$. These results show that **2** was also obtained from the corresponding benzyl chloride **1b** as well as bromide **1a** in good yield, but the reaction time was longer and the yield was lower than in the case of **1a**. On the other hand, benzyl alcohol **1c** was not affected under this condition. It has been reported that benzyl *gem*-difluorides and trifluoride were obtained from the corresponding *gem*-dichlorides and trichloride by halogen exchange with $AgBF_4$[10] and that benzyl nitriles were prepared from the corresponding benzyl chlorides with TMSCN and $TiCl_4$[11] or the corresponding benzyl bromides with TMSCN and TBAF.[12] However, neither of the corresponding benzyl fluoride and benzyl cyanide was observed under the conditions in Schemes 1 and 2 and Tables 1 and 2.



Scheme 2

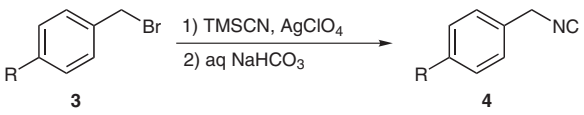
Scheme 3 and Table 3 display the results of the reactions of various benzyl bromides, which have a substituent at the 4-position, with TMSCN and $AgClO_4$. Each gave good yields of the corresponding isocyanides. The desired conversion was not affected by the halogen and acyloxy substituents on the ring (Table 3, entries 1–3). On the other hand, substrates having an alkoxy group as a substitu-

Table 2 Reactions of 4-*tert*-Butylbenzyl Derivatives **1** with TMSCN and $AgClO_4$

Entry[a]	Substrate	Y	Time (h)	Yield (%)[b]
1	**1a**	Br	1	99
2	**1b**	Cl	17	61
3	**1c**	OH	18	–[c]

[a] All reactions were carried out at r.t. with 1.5 equiv each of TMSCN and $AgClO_4$ under argon.
[b] Determined by GC analysis.
[c] Not determined.

ent, like 4-methoxybenzyl or 4-benzyloxybenzyl bromides, afforded messy products (data not shown). Entry 4 shows the result of a substrate which possesses a carboxylic methyl ester through a carbon chain between benzene and the carbonyl group. The corresponding isocyanide was obtained in good yield, and the carboxylic methyl ester substituent was hardly affected under this condition. However, the reaction of the substrate with the carboxyl group directly as a substituent of benzene, which is the (4-bromomethyl)benzoic acid methyl ester, never proceeded under this condition. In addition, the nitrobenzene derivative, which is (4-bromomethyl)nitrobenzene, was never affected under the same condition (data not shown). These results suggest that electron-withdrawing substituents reduce the reactivity of this reaction. In the case of the nitrogen functional group, which includes *N*-alkylamide and imide substituents, the desired benzyl isocyanides were obtained in good yields (Table 3, entries 5 and 6). However, the reaction of benzyl bromides, which have amine and NH-amide as a substituent, afforded messy product mixtures (data not shown). In all entries, the observed main byproduct was the corresponding benzyl alcohol that could be generated by the decomposition of an intermediate.



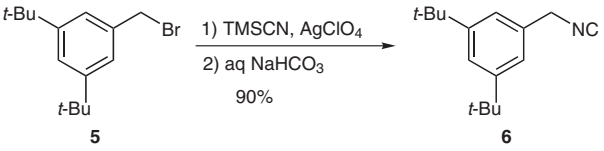
Scheme 3

The results for the reaction of benzyl bromides with two substituents are displayed in Schemes 4 and 5. 3,5-Di-*tert*-butylbenzyl bromide (**5**) afforded the corresponding benzyl isocyanide **6** in high yield. In addition, 4-methoxy-3-nitrobenzyl bromide (**7**) also afforded the corresponding benzyl isocyanide **8** in good yield, although the methoxy and nitro groups were included as substituents. These results suggest that the number and position of substituents do not affect the proceeding of the reaction in the case of the alkyl group and the reactivity depends on and varies according to the combination of substituents when hetero atom functional groups are included.

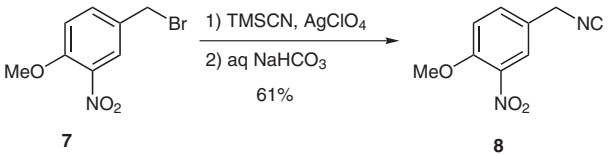
Table 3 Reactions of Benzyl Bromides with TMSCN and $AgClO_4$

Entry[a]	Substrate	R	Product	Yield (%)[b]
1	**3a**	Br	**4a**	63
2	**3b**	Cl	**4b**	55
3	**3c**	BzO	**4c**	71
4	**3d**	MeO_2CCH_2	**4d**	68
5	**3e**	N(Et)Bz	**4e**	52
6	**3f**	succinimide	**4f**	40

[a] All reactions were carried out at r.t. for 1 h with 3.0 equiv each of TMSCN and $AgClO_4$ under argon.
[b] Isolated yield.

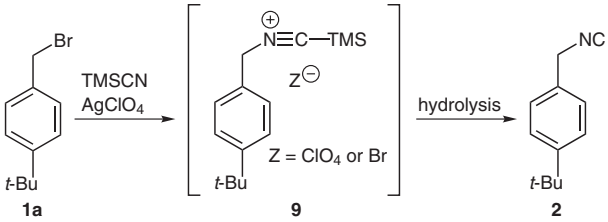


Scheme 4



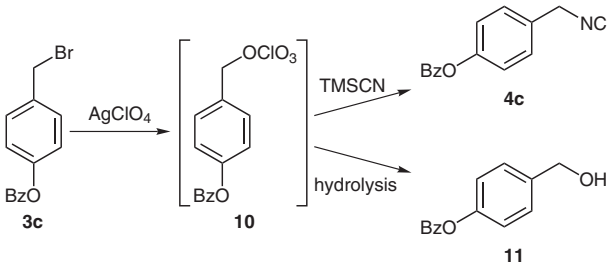
Scheme 5

In order to elucidate an intermediate, a similar reaction of **1a** was carried out in $CDCl_3$, and ^1H NMR was then observed before adding TBAF or aqueous $NaHCO_3$. The ^1H NMR spectrum of the intermediate was evidently different from the simple mixture of **2** and $AgClO_4$. In addition, a singlet signal for 9 H, which does not belong to either TMS or TMSCN, was observed in the ^1H NMR spectrum. This result suggests that an ionic compound **9**, which has the TMS group, exists as the intermediate in the reaction mixture as well as in the case of the synthesis of tertiary isocyanides.[7b] The reaction mechanism including the intermediate **9** is proposed in Scheme 6. The benzyl isocyanide **2** was finally synthesized by the dissociation of the carbon–silicon bond.



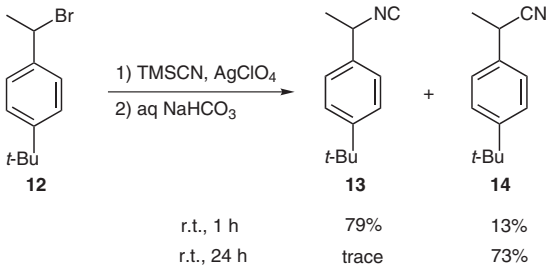
Scheme 6

It has been reported that the reaction of alky iodides with silver perchlorate affords the corresponding alkyl perchlorates.[13] In order to further investigate the reaction mechanism, a reaction of **3c** with only $AgClO_4$ was performed. Although strict isolation was impossible because of the instability, the generation of the corresponding benzyl perchlorate **10** was suggested by ^1H NMR analysis. Then, the addition of TMSCN to the CH_2Cl_2 solution of the perchlorate **10** gave the corresponding isocyanide **4c**. On the other hand, the corresponding alcohol **11** was obtained when aqueous $NaHCO_3$ was added to the CH_2Cl_2 solution of **10**. This could be the reason that the corresponding alcohols were obtained as the main byproduct in this reaction. These results suggest that the desired benzyl isocyanides are obtained via the generation of the corresponding perchlorate, as shown in Scheme 7.



Scheme 7

Scheme 8 shows the result of the reaction for secondary benzyl bromide **12**. The desired benzyl isocyanide **13** was obtained in 79% yield with 13% of the corresponding nitrile **14** when the reaction was carried out for 1 hour. However, as the reaction time became longer, the amount of the isocyanide **13** was reduced. Finally, the total product was nitrile **14** after the reaction had been carried out for 24 hours. The generation of nitrile could be attributed to the rearrangement of the isocyano group due to the stability of the *sec*-benzyl cation. A similar mechanism has been reported in the case of the preparation for benzyl nitrile from the corresponding benzyl halide with TMSCN and $TiCl_4$.[11]



Scheme 8

In conclusion, we have developed a new method for converting benzyl halides to their corresponding isocyanides. We believe this method provides a convenient and useful way to synthesize benzyl isocyanides.

Mps were determined on a Mel-Temp (Laboratory Device) and are uncorrected. NMR spectra were obtained in $CDCl_3$ on a Jeol AL-400 or alpha-600 spectrometer. All ^1H NMR spectra are reported in ppm relative to TMS. All ^{13}C NMR spectra are reported in ppm relative to the central line of the triplet for $CDCl_3$ at 77.03 ppm. IR spectra were recorded on a Jeol Winspec-50 spectrometer. Low- and high-resolution mass spectra were recorded on a JEOL SX-102A spectrometer under the ionization condition (70 eV). GC analyses were carried out on a Hewlett Packard HP 4980A fitted with an HP-5 column (10 m × 0.53 mm i.d.). Chromatographic separations were carried out on a silica gel column (Fuji Silysia Chemical BW-127ZH; 100–270 mesh) unless otherwise stated.

4-Benzoyloxybenzyl Bromide (3c)[14]

Prepared from 4-hydroxybenzaldehyde as follows. First, 4-benzyloxybenzyl alcohol, which was the precursor of **3c**, was synthesized by esterification of phenol with BzCl and in the presence of pyridine followed by reduction of the aldehyde with $NaBH_4$. Then, **3c** was obtained from the precursor by bromination of alcohol with PBr_3 (1.2 equiv); white solid; yield: 78%; mp 108–109 °C.

IR (KBr): 3089, 3070, 2977, 1724, 1592, 1508, 1452, 1313, 1278, 887, 713, 673, 595 cm^{-1}.

^1H NMR (600 MHz): δ = 8.23–8.18 (m, 2 H), 7.67–7.62 (m, 1 H), 7.56–7.49 (m, 2 H), 7.49–7.43 (m, 2 H), 7.22–7.18 (m, 2 H), 4.52 (s, 2 H).

^{13}C NMR (100.4 MHz): δ = 164.77, 150.68, 135.68, 133.23, 130.11, 130.03, 129.17, 128.45, 121.96, 32.81.

LRMS (EI): *m/z* (%) = 290 (M^+, 3), 211 (54), 105 (100), 77 (38).

HRMS (EI): *m/z* calcd for $C_{14}H_{11}BrO_2$ [M^+]: 289.9942; found: 289.9951.

4-(Bromomethyl)phenylacetic Acid Methyl Ester (3d)[15]

Prepared from 4-(Bromomethyl)phenylacetic acid (1.0 g, 4.09 mmol) according to a Mitsunobu reaction in MeOH with Ph_3P (1.2 equiv) and DIAD (1.2 equiv); yield: 71%.

^1H NMR (600 MHz): δ = 7.31–7.28 (2 H, m), 7.18–7.15 (2 H, m), 4.39 (2 H, s), 3.65 (3 H, s), 3.55 (2 H, s).

^{13}C NMR (150.8 MHz): δ = 171.36, 136.43, 134.06, 129.47, 129.04, 51.82, 40.55, 32.99.

***N*-[4-(Bromomethyl)phenyl]-*N*-ethylbenzamide (3e)**

Prepared from 4-aminobenzyl alcohol (300 mg, 2.43 mmol) as follows. First, 4-(ethylamino)benzyl alcohol was prepared by a one-pot reaction via reduction of the corresponding imine with acetaldehyde (excess) and $NaBH_4$ (excess). Then, *N*-ethyl-*N*-[4-(hydroxymethyl)phenyl]benzamide, which was the precursor of **3e**, was synthesized by reacting with BzCl (2.2 equiv) and pyridine (excess) followed by hydrolysis of ester with NaOH (1.5 equiv). Compound **3e** was finally obtained from the precursor by bromination of alcohol with PBr_3 (1.2 equiv); yellow oil; yield: 49%.

IR (neat): 3060, 3033, 2973, 2871, 1645, 1606, 1513, 1392, 1307, 1116, 698, 611 cm^{-1}.

^1H NMR (600 MHz): δ = 7.30–7.21 (m, 5 H), 7.18–7.14 (m, 2 H), 7.01–6.97 (m, 2 H), 4.40 (s, 2 H), 3.97 (q, 2 H, *J* = 7.0 Hz), 1.22 (t, 3 H, *J* = 7.0 Hz).

^{13}C NMR (150.8 MHz): δ = 170.08, 143.23, 136.03, 129.75, 129.59, 128.59, 127.97, 127.73, 45.38, 32.50, 12.95.

LRMS (EI): *m/z* (%) = 317 (M^+, 3), 238 (86), 132 (33), 105 (100), 77 (22).

HRMS (EI): *m/z* calcd for $C_{16}H_{16}BrNO$ [M^+]: 317.0415; found: 317.0403.

1-[4-(Bromomethyl)phenyl]pyrrolidine-2,5-dione (3f)[16]
Prepared from 4-aminobenzyl alcohol (985 mg, 1.0 mmol) as follows. First, *N*-[4-(hydroxymethyl)phenyl]succinamic acid was prepared by a reaction of the corresponding amine with succinic anhydride. Then, 1-[4-(hydroxymethyl)phenyl]pyrrolidine-2,5-dione, which was the precursor of **3f**, was synthesized by refluxing the above succinamic acid in Ac_2O (excess) followed by hydrolysis of the acetate ester with $BF_3{\cdot}OEt_2$ (5.0 equiv) in MeOH. Compound **3f** was finally obtained by bromination of the corresponding benzyl alcohol with PBr_3 (1.2 equiv); yield: 25%.

^{1}H NMR (600 MHz): δ = 7.52–7.49 (m, 2 H), 7.30–7.27 (m, 2 H), 4.49 (s, 2 H), 2.90 (s, 4 H).

^{13}C NMR (150.8 MHz): δ = 175.93, 138.11, 131.78, 129.85, 126.66, 32.29, 28.38.

4-Methoxy-3-nitrobenzyl Bromide (7)
Prepared from 4-hydroxy-3-nitrobenzaldehyde (1.0 g, 5.98 mmol) as follows. First, 4-Methoxy-3-nitrobenzyl alcohol, which was the precursor of **7**, was synthesized by methylation of the phenolic group with MeI (4.0 equiv) and K_2CO_3 (3.0 equiv) followed by reduction of the aldehyde with $NaBH_4$ (2.0 equiv). Then, **7** was obtained by bromination of the alcohol formed with PBr_3 (1.2 equiv); yield: 52%; yellow solid; 95–96 °C.

IR (KBr): 3037, 2985, 1619, 1523, 1355, 1268, 1010, 831, 624 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.89 (d, 1 H, *J* = 2.1 Hz), 7.58 (dd, 1 H, *J* = 8.5, 2.1 Hz), 7.08 (d, 1 H, *J* = 8.5 Hz), 4.47 (2 H, s), 3.97 (3 H, s).

^{13}C NMR (150.8 MHz): δ = 152.60, 139.12, 134.60, 129.99, 126.05, 113.80, 56.70, 31.42.

LRMS (EI): *m*/*z* (%) = 245 (M^+, 2), 197 (21), 166 (100), 150 (2), 135 (4), 120 (2), 91 (65), 69 (7).

HRMS (EI): *m*/*z* calcd for $C_8H_8BrNO_3$ [M^+]: 244.9687; found: 244.9684.

Benzyl Isocyanides 2,4,7; General Procedure
TMSCN (60 mg, 0.6 mmol) and $AgClO_4$ (124 mg, 0.6 mmol) were added to a solution of the appropriate benzyl halide (0.2 mmol) in CH_2Cl_2 (2 mL) under argon. The reaction mixture was adequately stirred at r.t. Then, aq sat. $NaHCO_3$ (2 mL) was added. After stirring for an additional 10 min, the mixture was filtered over Celite and washed with EtOAc. The combined organic extracts were washed with H_2O and brine, and dried ($MgSO_4$). The crude product was purified by silica gel column chromatography (hexane–EtOAc). After removal of the solvent, a 1 M solution of TBAF in THF (1 mL) was added to the residue. After stirring for an additional 10 min, the mixture was filtered over Celite and washed with EtOAc. The combined organic extracts were analyzed by GC. The product was isolated by evaporation of the solvent.

4-*tert*-Butylbenzyl Isocyanide (2)
Yellow oil.

IR (neat): 3031, 2964, 2906, 2148, 1511, 1442, 1365, 1268, 1108, 1020, 821 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.42 (d, 2 H, *J* = 8.4 Hz), 7.28 (d, 2 H, *J* = 8.4 Hz), 4.61 (br t, 2 H, *J* = 1.9 Hz), 1.32 (s, 9 H).

^{13}C NMR (150.8 MHz): δ = 157.25 (t, *J* = 4.9 Hz), 151.64, 129.39, 126.45, 125.92, 45.28 (t, *J* = 7.4 Hz), 34.63, 31.28.

LRMS (EI): *m*/*z* (%) = 173 (M^+, 20), 158 (100), 130 (34), 105 (18), 91 (24).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{15}N$ [M^+]: 173.1206; found: 173.1200.

4-Bromobenzyl Isocyanide (4a)
Yellow oil.

IR (neat): 3086, 2925, 2854, 2144, 1727, 1706, 1592, 1486, 1438, 1409, 1346, 1072, 1012, 948, 794 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.51 (t, 2 H, *J* = 8.3 Hz), 7.21 (t, 2 H, *J* = 8.3 Hz), 4.58 (br s, 1 H).

^{13}C NMR (150.8 MHz): δ = 158.03 (t, *J* = 5.4 Hz), 131.83, 131.06, 128.04, 122.20, 44.95 (t, *J* = 7.5 Hz).

LRMS (EI): *m*/*z* (%) = 195 (M^+, 31), 169 (17), 116 (100), 89 (37).

HRMS (EI): *m*/*z* calcd for C_8H_6BrN [M^+]: 194.9684; found: 194.9689.

4-Chlorobenzyl Isocyanide (4b)
Yellow oil.

IR (neat): 3066, 2954, 2929, 2853, 2150, 1596, 1490, 1442, 1409, 1346, 1091, 952, 798 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.40–7.35 (m, 2 H), 7.31–7.26 (m, 2 H), 4.6 (br t, 2 H, *J* = 1.9 Hz).

^{13}C NMR (150.8 MHz): δ = 158.19 (t, *J* = 5.4 Hz), 134.46, 130.75, 129.20, 128.00, 44.96 (t, *J* = 7.3 Hz).

LRMS (EI): *m*/*z* (%) = 151 (M^+, 40), 125 (32), 116 (100), 89 (21).

HRMS (EI): *m*/*z* calcd for C_8H_6ClN [M^+]: 151.0189; found: 151.0173.

4-Benzoyloxybenzyl Isocyanide (4c)
White solid; mp 92–93 °C.

IR (KBr): 3066, 2923, 2150, 1735, 1602, 1511, 1450, 1263, 1211, 1168, 1966, 869, 703 cm^{-1}.

^{1}H NMR (600 MHz): δ = 8.22–8.19 (m, 2 H), 7.67–7.64 (m, 1 H), 7.54–7.51 (m, 2 H), 7.45–7.41 (m, 2 H, *J* = 8.8, 1.9 Hz), 7.29–7.26 (m, 2 H, *J* = 4.4, 2.2 Hz), 4.68 (br s, 2 H).

^{13}C NMR (150.8 MHz): δ = 165.03, 158.18 (t, *J* = 4.9 Hz), 151.01, 133.79, 130.22, 129.93, 129.28, 128.65, 127.89, 122.41, 45.08 (t, *J* = 7.4 Hz).

LRMS (EI): *m*/*z* (%) = 237 (M^+, 10), 105 (100), 77 (61), 51 (8).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}NO_2$ [M^+]: 237.0790; found: 237.0796.

4-(Isocyanomethyl)phenylacetic Acid Methyl Ester (4d)
Yellow oil.

IR (neat): 3025, 2954, 2917, 2150, 1735, 1517, 1434, 1425, 1257, 1164 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.31 (pseudo s, 4 H), 4.62 (br t, 2 H, *J* = 1.8 Hz), 3.70 (s, 3 H), 3.64 (s, 2 H).

^{13}C NMR (150.8 MHz): δ = 171.83, 158.05 (t, *J* = 4.9 Hz), 134.54, 131.43, 130.09, 127.07, 52.29, 45.42 (t, *J* = 7.4 Hz), 40.89.

LRMS (EI): *m*/*z* (%) = 189 (M^+, 59), 163 (3), 158 (2), 130 (100), 104 (93), 77 (19).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{11}NO_2$ [M^+]: 189.0789; found: 189.0779.

***N*-[4-(Isocyanomethyl)phenyl]-*N*-ethylbenzamide (4e)**
Yellow oil.

IR (neat): 3058, 2971, 2935, 2869, 2150, 1641, 1612, 1513, 1390, 1120, 698 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.31–7.27 (m, 2 H), 7.26–7.15 (m, 5 H), 7.08–7.04 (m, 2 H), 4.57 (br s, 2 H), 3.98 (q, 2 H, *J* = 7.3 Hz), 1.22 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR (150.8 MHz): δ = 170.16, 158.23 (t, *J* = 4.9 Hz), 143.50, 136.06, 130.51, 129.66, 128.59, 128.30, 127.82, 127.35, 45.38, 44.96 (t, *J* = 7.4 Hz), 12.95.

LRMS (EI): *m*/*z* (%) = 264 (M^+, 34), 133 (10), 118 (25), 105 (100), 77 (43).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{16}N_2O$ [M^+]: 264.1263; found: 264.1267.

1-[4-(Isocyanomethyl)phenyl]pyrrolidine-2,5-dione (4f)
White solid; mp 151–153 °C.

IR (KBr): 2991, 2956, 2923, 2854, 2150, 1716, 1517, 1400, 1295, 1187, 806 cm^{-1}.

^{1}H NMR (400 MHz): δ = 7.41–7.39 (m, 2 H), 7.31–7.28 (m, 2 H), 4.62 (br s, 2 H), 2.84 (s, 4 H).

^{13}C NMR (100.5 MHz): δ = 175.46, 158.01 (t, *J* = 5.4 Hz), 132.31, 131.69, 127.08, 126.68, 45.00 (t, *J* = 7.5 Hz), 28.34.

LRMS (EI): *m*/*z* (%) = 214 (M^+, 57), 188 (33), 167 (30), 149 (100), 132 (40), 105 (62), 77 (36).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{10}N_2O_2$ [M^+]: 214.0742; found: 214.0740.

3, 5-Di-*tert*-butylbenzyl Isocyanide (6)
White solid; mp 40–41 °C.

IR (KBr): 3095, 2950, 2900, 2865, 2150, 1600, 1479, 1365, 1251, 867, 711 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.42–7.39 (m, 1 H), 7.18–7.15 (m, 2 H), 4.62 (br s, 2 H), 1.33 (s, 18 H).

^{13}C NMR (150.8 MHz): δ = 157.28 (t, *J* = 4.9 Hz), 151.73, 131.53, 122.44, 120.91, 46.02 (t, *J* = 7.4 Hz), 34.95, 31.40.

LRMS (EI): *m*/*z* (%) = 229 (M^+, 15), 214 (100), 186 (20), 131 (7), 115 (20), 91 (20).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{23}N$ [M^+]: 229.1831; found: 229.1839.

4-(Isocyanomethyl)-1-methoxy-2-nitrobenzene (8)
Yellow solid; 82–83 °C.

IR (KBr): 3031, 2940, 2150, 1623, 1525, 1438, 1348, 1251, 1180, 1016, 933, 821, 665, 549 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.84 (d, 1 H, *J* = 1.8 Hz), 7.57 (dd, 1 H, *J* = 8.8, 1.8 Hz), 7.15 (d, 1 H, *J* = 8.8 Hz), 4.64 (br s, 2 H), 3.99 (s, 3 H).

^{13}C NMR (150.8 MHz): δ = 159.07 (t, *J* = 3.7 Hz), 153.03, 139.62, 132.27, 124.68, 124.25, 114.27, 56.76, 44.29 (t, *J* = 7.4 Hz).

LRMS (EI): *m*/*z* (%) = 192 (M^+, 75), 166 (26), 145 (58), 105 (54), 91 (100), 77 (19).

HRMS (EI): *m*/*z* calcd for $C_9H_8N_2O_3$ [M^+]: 192.0535; found: 192.0541.

Intermediate 9
Not isolated because of instability.

^{1}H NMR (600 MHz): δ = 7.48–7.46 (2 H, m), 7.34–7.32 (2 H, m), 4.86 (2 H, s), 1.32 (9 H, s), 0.07 (9 H, s).

4-Benzyloxybenzyl Perchlorate (10)
Not isolated because of instability.

^{1}H NMR (600 MHz): δ = 8.21–8.19 (2 H, m), 7.67–7.64 (1 H, m), 7.53–7.50 (4 H, m), 7.32–7.30 (2 H, m), 5.52 (2 H, s).

4-Benzoyloxybenzyl Alcohol (11)[17]
^{1}H NMR (600 MHz): δ = 8.21–8.19 (2 H, m), 7.64 (tt, 1 H, *J* = 7.4, 1.8 Hz), 7.53–7.49 (2 H, m), 7.45–7.42 (2 H, m), 7.23–7.19 (2 H, m), 4.73 (d, 2 H, *J* = 3.7 Hz), 1.69 (t, 1 H, *J* = 3.7 Hz).

^{13}C NMR (150.8 MHz): δ = 169.15, 154.33, 142.47, 137.56, 134.12, 133.44, 132.52, 132.08, 125.78.

1-(1-Bromoethyl)-4-*tert*-butylbenzene (12)
Prepared from 4-*tert*-butylbenzaldehyde (1.1 g, 6.78 mmol) by reacting with MeMgBr (1.2 equiv) followed by bromination of the alcohol formed with PBr_3 (1.2 equiv); yellow oil; yield: 94%.

IR (neat): 3095, 3029, 2964, 2863, 1515, 1413, 1365, 1265, 1174, 1108, 833, 599 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.36 (4 H, pseudo s), 5.22 (q, 1 H, *J* = 6.9 Hz), 2.04 (d, 3 H, *J* = 6.9 Hz), 1.31 (9 H, s).

^{13}C NMR (150.8 MHz): δ = 151.13, 140.10, 126.41, 125.41, 49.49, 34.46, 31.20, 26.73.

LR-EIMS: *m*/*z* (%) = 240 (M^+, 1), 161 (100), 146 (33), 131 (21), 91 (7).

HR-EIMS: *m*/*z* calcd for $C_{12}H_{17}Br$ [M^+]: 240.0513; found: 240.0519.

1-*tert*-Butyl-4-[1-(isocyanoethyl)]benzene (13)
Yellow oil.

IR (neat): 3029, 2962, 2138, 1513, 1461, 1365, 1270, 833 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.42–7.39 (m, 2 H), 7.30–7.27 (m, 2 H), 4.80 (tq, 1 H, *J* = 6.9, 1.9 Hz), 1.68 (dt, 3 H, *J* = 6.9, 1.9 Hz), 1.32 (s, 9 H).

^{13}C NMR (150.8 MHz): δ = 156.00 (t, *J* = 4.9 Hz), 151.36, 135.55, 125.82, 125.13, 53.51 (t, *J* = 6.2 Hz), 34.57, 31.28, 24.98.

LRMS (EI): *m*/*z* (%) = 187 (M^+, 20), 172 (100), 144 (17), 105 (59), 77 (18).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{23}N$ [M^+]: 187.1361; found: 187.1365.

2-[4-(*tert*-Butylphenyl)]propionitrile (14)
Colorless oil.

IR (neat): 3039, 2964, 2240, 1679, 1511, 1459, 1365, 1265, 829 cm^{-1}.

^{1}H NMR (600 MHz): δ = 7.42–7.39 (m, 2 H), 7.29–7.26 (m, 2 H), 3.87 (q, 1 H, *J* = 7.3 Hz), 1.64 (d, 3 H, *J* = 7.3 Hz), 1.32 (s, 9 H).

^{13}C NMR (150.8 MHz): δ = 151.11, 133.98, 126.39, 126.04, 121.75, 34.55, 31.26, 30.77, 21.34.

LRMS (EI): *m*/*z* (%) = 187 (M^+, 15), 172 (100), 144 (12), 105 (7), 91 (3).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{23}N$ [M^+]: 187.1361; found: 187.1365.

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