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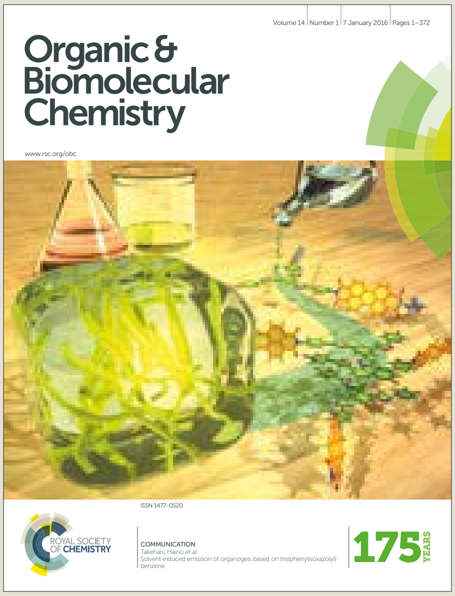

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ARTICLE

Redox reaction between benzyl azides and aryl azides: Concerted synthesis of aryl nitriles and anilines

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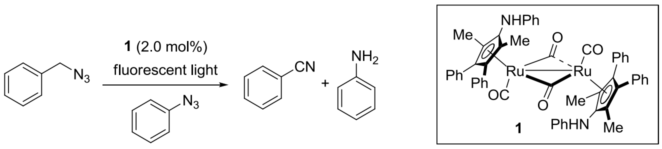
A unique and novel reaction between benzyl azides and aryl azides is described to synthesize aryl nitriles and anilines concurrently, which is catalyzed by a photoactivated diruthenium complex. *N*-Unsubstituted imines (N-H imines) are generated first from benzyl azides, followed by the hydrogen transfer reaction between N-H imines and aryl azides. A wide range of aryl nitriles and anilines were synthesized under neutral and mild reaction conditions.

Introduction

Organic nitriles are important intermediates in organic synthesis for versatile organic compounds such as amides, ketones, amines and heterocyclic compounds[1] and valuable building blocks in natural products, pharmaceuticals, agricultural chemicals, and functional materials.[2]

For these extensive applications, numerous methods for the synthesis of nitriles are reported.[3] Sandmeyer reaction[4] and the cyanation of aryl halides are classic methods for the synthesis of organic nitriles.[5] Although there are considerable advances in the cyanation of aryl halides, these methods suffer from the use of stoichiometric amount of toxic reagents and the generation of large amount of inorganic waste. Alternative methods are reported including the oxidation of benzyl alcohols in the presence of ammonia[6] and the dehydration of aldoximes[7] or primary amides.[8] However, the oxidation requires excess amount of ammonia and oxidants, while the dehydration needs stoichiometric dehydrating reagents or azeotropic conditions. Recently Jiao and co-workers reported the synthesis of nitriles from methyl arenes or benzyl halides with azide source and oxidants such as phenyliodonium diacetate (PIDA) and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ).[9] In these transformations benzylic azides are suggested as the intermediates. Although these transformations are unique and novel, excess amount of strong oxidants are required for the nitrile formation. Some other direct transformations to nitriles from organic azides are also reported such as *tert*-butyl hydroperoxide mediated oxidation of azides,[10] bromine trifluoride mediated transformation of azides[11] and oxidative C-C bond cleavage of α-azido carbonyl compounds.[12] However, these methods are still suffer from the use of stoichiometric or excess amount of oxidant or additives.

Recently, we have reported the transformation of alkyl azides into the corresponding N-H imines, in which a diruthenium complex **1** acts as the catalyst under mild and neutral conditions.[13] In attempts to extend the utility of **1** towards aryl azides, we observed unexpected formation of benzonitrile in the reaction of benzyl azide in the presence of phenyl azide (Scheme 1). Herein, we wish to report a unique and novel redox reaction between benzyl azides and aryl azides to afford a wide range of aryl nitriles and anilines: N-H imines are generated from benzyl azides followed by the dehydrogenation of N-H imines and hydrogenation of aryl azides with the aid of ruthenium catalysis.



Scheme 1. Redox reaction between benzyl azide and phenyl azide.

Results and discussion

To optimize the reaction conditions, the reaction of 1-(azidomethyl)-4-methoxybenzene **2a** with methyl 4-azidobenzoate **4a** was tested under various conditions (Table 1). The transformation of **3a** was not successful in the absence of light (entry 1). Notably, the reaction of **3a** with **4a** was completed at room temperature for 12 h in the presence of 30 W fluorescent light to afford **5a** and **6a** in quantitative yields (entry 2). The use of 12 W blue LED as a light source was also efficient for the transformation to give the products in quantitative yields (entry 3). Interestingly, the reaction was completed within 2 h at 70 °C to afford the products in quantitative yields although the conversion was incomplete in 2 h at 50 °C (entries 4 and 5). As a solvent, acetonitrile was as

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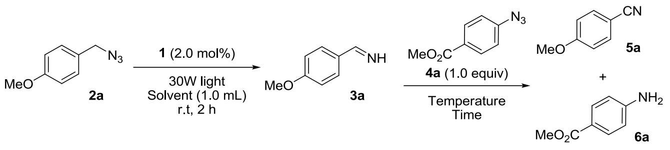
good as THF, while toluene was a little less efficient (entries 6 and 7). One-pot one-step procedure was less efficient than the two-step procedure (entry 8). Products were formed in trace amount without 30 W fluorescent light at 70 °C (entry 9).

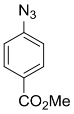
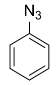
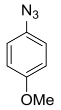
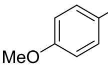
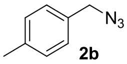
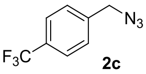
Table 1. Reaction of 1-(azidomethyl)-4-methoxybenzene and methyl 4-azidobenzoate under various conditions.[a]



Entry	Solvent	Temp. (°C)	Time (h)	Yields (**5a**/**6a**) (%)[b]
1	THF	25	12	20/22
2[c]	THF	25	12	97/99
3[d]	THF	35	12	97/99
4	THF	50	2	55/55
5	THF	70	2	99/99
6	Toluene	70	2	90/92
7	Acetonitrile	70	2	98/99
8[e]	THF	70	12	84/89
9[f]	THF	70	12	6/8

[a] Typical reaction conditions: A solution of benzyl azide **2a** (0.25 mmol) and the ruthenium catalyst **1** (2.0 mol%) in a solvent was illuminated with 30W fluorescent light. After the formation of N-H imine, aryl azide **4a** (0.25 mmol) was added and illuminated by light source or heated. [b] Determined by ^{1}H NMR using dibromomethane as an internal standard. [c] Reaction was carried out under 30W fluorescent light. [d] Reaction was carried out under 12 W blue LED. [e] Reaction was carried out by one-pot one-step procedure with 30W fluorescent light. [f] Reaction was carried out by one-pot one-step procedure without fluorescent light.

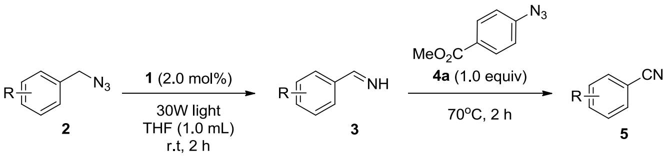
Table 2. Electronic effects on the redox reactions.[a,b]

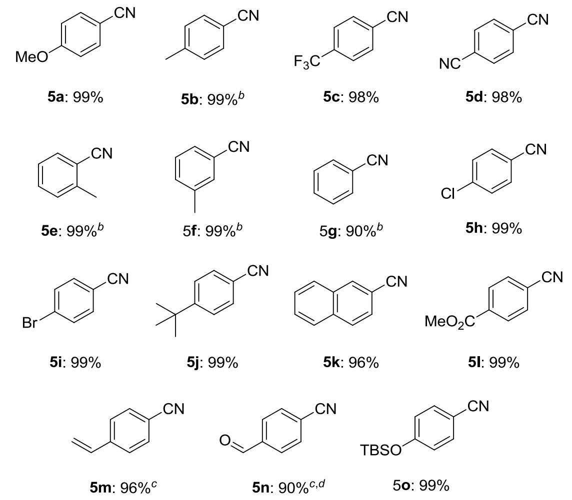
	 **4a**	 **4b**	 **4c**
 **2a**	99%[c]/99%[d]	99%/99%	99%/99%
 **2b**	99%/99%	99%/99%	86%/86%[e]
 **2c**	98%/99%	79%/78%[e]	78%/80%[e]

[a] A solution of benzyl azide **2** (0.25 mmol) and **1** (2.0 mol%) in THF was illuminated with 30 W fluorescent light for 2 h to generate N-H imines. Then aryl azides **4** (0.25 mmol) was added, and the reaction mixture was stirred for 2 h at 70 °C. [b] The yields of aryl nitriles and anilines were determined by ^{1}H NMR using dibromomethane as an internal standard. [c] The yield of aryl nitrile. [d] The yield of aniline. [e] The conversions of **4b** and **4c** were incomplete.

Nine pairs of benzyl azides and aryl azides were reacted under the conditions of entry 5 in Table 1 to investigate electronic effects of *para*-substituents on the redox reaction (Table 2). Generally, the redox reactions were successful to give aryl nitriles and anilines in high yields, but incomplete conversion of azides was observed in some of the reactions. The redox reactions appeared to depend on the stability of N-H imines and the efficiency of the transfer-hydrogenation reaction between N-H imines and aryl azides. The incomplete conversions of azides implicate that the hydrogenation of aryl azides containing electron-donating group was less efficient than that of the aryl azides containing electron-withdrawing group to cause the side reactions of the relatively unstable N-H imines generated from benzyl azides containing electron-withdrawing group. However, it is noticeable that the electron-poor benzyl azide **2c** was converted to the corresponding aryl nitrile almost quantitatively using the electron-poor aryl azide **4a**.

Table 2. Synthesis of various aryl nitriles.[a]





5a: 99% **5b**: 99%[b] **5c**: 98% **5d**: 98%

5e: 99%[b] **5f**: 99%[b] **5g**: 90%[b] **5h**: 99%

5i: 99% **5j**: 99% **5k**: 96% **5l**: 99%

5m: 96%[c] **5n**: 90%[c,d] **5o**: 99%

[a] A solution of benzyl azide **2** (0.25 mmol) and the ruthenium catalyst **1** (2.0 mol%) in THF was illuminated with 30 W fluorescent light. After the formation of N-H imines, aryl azides **4a** (0.25 mmol) was added, and the reaction mixture was stirred for 2 h at 70 °C [b] The yields of aryl nitriles were determined by ^{1}H NMR using dibromomethane as an internal standard due to their volatility, while others were determined after isolation. [c] The reaction was carried out for 4 h. [d] The N-H imine was generated using 4 mol% of **1** for 1 h.

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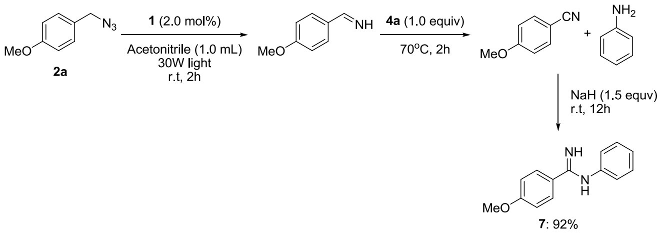
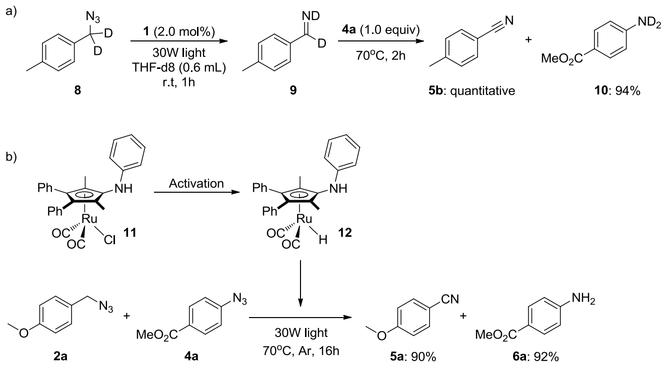
With focusing on the synthesis of aryl nitriles, various benzylic azides were employed in the redox reaction with methyl 4-azidobenzoate (**4a**). In most cases, aryl nitriles were obtained quantitatively. Electronic effect and steric effect were not significant on the formation of aryl nitriles. The redox reaction was compatible with various functional groups such as methoxy, trifluoromethyl, cyano, chloro, bromo, ester, and vinyl group. It is noticeable that formyl group in **5p**, which is labile to oxidation and nucleophilic addition reactions, was also survived. In addition, acid-labile TMS-protected phenolic benzonitrile **5q** was obtained in quantitative yield.

Since both aryl nitrile and aniline are formed in the reaction, we utilized our new finding to the reaction of nitrile and aniline for one-pot synthesis of amidines. In the presence of sodium hydride, amidine **7** was obtained in 92% from the *in situ* generated nitrile and aniline (Scheme 2).



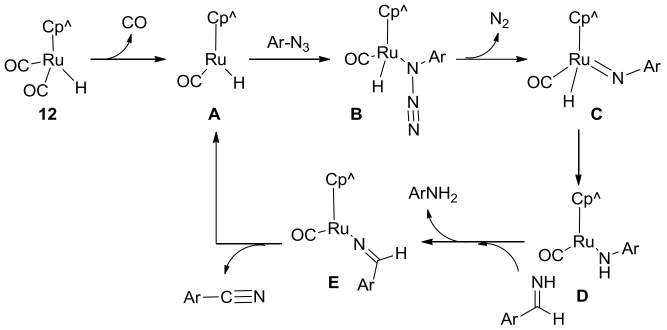
Scheme 2. One-pot synthesis of amidine.

To obtain mechanistic insight on the redox reaction, deuterated benzyl azide **8** was employed to figure out the deuterium transfer from benzyl azide to aryl azide. As a result, nitrile **5b** was obtained in quantitative yield and the deuterated aniline **10** was formed in 94% yield (Scheme 3a). Meanwhile, we investigated the catalytic activity of ruthenium hydride complex **12** for the redox reaction, which is active for the generation of N-H imines from alkyl azides (Scheme 3b).[13] Indeed, the redox reaction between **2a** and **4a** proceeded with the catalytic amount of the ruthenium hydride **12** to give the nitrile **5a** and the aniline **6a** in 90% and 92%, respectively.



Scheme 3. Mechanistic investigation.

Based on the results described above, a reaction pathway for the redox reaction is proposed in Scheme 4. A coordinatively unsaturated ruthenium species **A** is formed from the ruthenium hydride **12** by light or heating.[13] Then the reaction with aryl azide produces a ruthenium azide complex (**B**), followed by the formation of a ruthenium nitrene complex (**C**) with liberation of N_2, which is tautomerized to a ruthenium amido complex (**D**). Proton transfer from N-H imine to the ruthenium amido complex **D** leads to the formation of aniline and a ruthenium imido complex (**E**), from which aryl nitrile is produced through dehydrogenation with regenerating the ruthenium hydride **A**.



Scheme 4. Possible pathway for the formation of nitrile and aniline.

Conclusions

In summary, we found a novel and unique ruthenium catalyzed redox reaction between benzyl azides and aryl azides to produce aryl nitriles and anilines in concerted manner. As far as we know, this is the first observation that aryl azides act as a formal oxidant to transform benzyl azides into aryl nitriles. On the basis of neutral and mild reaction conditions without additives, the substrate scope was wide to give valuable aryl nitriles in high yields, some of which are hard to be afforded by previous synthetic methods.

Experimental section

Air-sensitive manipulations were carried out with standard Schlenk techniques under argon atmosphere. Commercial chemicals used without further purification. Flash column chromatography was carried out on silica gel (230-400 mesh) as the stationary phase. ^1H and ^{13}C NMR spectra were recorded with Bruker AVANCE III 300MHZ FT-NMR spectrometer and chemical shift are given in δ ppm. 1H NMR spectra were referenced to tetramethylsilane (TMS, 0 ppm). 13C NMR spectra were referenced to CDCl3 (77.23 ppm) as an internal standard. Infrared spectra were recorded on a Shimadzu IR-470 spectrometer with NaCl pellet. Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on a Jeol JMS 700 high resolution mass spectrometer. Ruthenium complex **1**[14] and **11**[15] were synthesized according to the literature procedure**.**

General procedure for synthesis of aryl nitriles and anilines.
The ruthenium catalyst **1** (2.0 mol%, 0.005 mmol, 4.9 mg) was added to a flame-dried J-Young flask filled with argon. The dry THF (1.0 mL) and benzyl azide (0.25 mmol) were added under a stream of argon. The reaction mixture was stirred for 2 h at

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room temperature with a household 30W fluorescent light. After the accumulation of N-H aldimine, aryl azide (1.0 equiv, 0.25 mmol) was added then stirred at 70 ^oC for 2 h. After completion of the reaction, solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel to afford corresponding nitrile and aniline.

4-methoxybenzonitrile (5a)[16] Yield: 98%; White solid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.61-7.58 (m, 2H), 6.98-6.94 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.0, 134.2, 119.4, 114.9, 104.2, 55.7.

4-methylbenzonitrile (5b)[17] Yield: 99%; ^1H NMR (300 MHz, $CDCl_3$, in crude mixture with an internal standard (CH_2Br_2)) δ = 7.55-7.52 (m, 2H), 7.28-7.25 (m, 2H), 2.41 (s, 3H).

4-(trifluoromethyl)benzonitrile (5c)[17] Yield: 98%; White solid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.82 (d, J = 8.3 Hz, 2H), 7.77 (d, J = 8.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 135.0, 134.5, 132.9, 126.44, 126.40, 126.34, 126.29, 125.1, 121.4, 117.6, 116.3.

Terephthalonitrile (5d)[17] Yield: 98%; White solid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.80 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 133.0, 117.2, 116.9.

2-methylbenzonitrile (5e)[17] Yield: 99%; ^1H NMR (300 MHz, $CDCl_3$, in crude mixture with an internal standard (CH_2Br_2)) δ = 7.60-7.57 (m, 1H), 7.50-7.44 (m, 1H), 7.32-7.23 (m, 2H), 2.54 (s, 3H).

3-methylbenzonitrile (5f)[17] Yield: 99%; ^1H NMR (300 MHz, $CDCl_3$, in crude mixture with an internal standard (CH_2Br_2)) δ = 7.46-7.31 (m, 4H), 2.38 (s, 3H).

Benzonitrile (5g) Yield: 90%; 1H NMR (300 MHz, THF-d8, in crude mixture with an internal standard (CH_3NO_2)) δ = 7.71-7.68 (m, 2H), 7.65-7.59 (m, 1H), 7.52-7.47 (m, 2H).

4-chlorobenzonitrile (5h)[16] Yield: 99%; White solid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.63-7.59 (m, 2H), 7.49-7.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 139.7, 133.5, 129.8, 118.1, 110.9.

4-bromobenzonitrile (5i)[18] Yield: 99%; White solid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.66-7.62 (m, 2H), 7.55-7.51 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 133.6, 132.8, 128.1, 118.2, 111.4.

4-tert-butylbenzonitrile (5j)[16] Yield: 99%; Colorless liquid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.60-7.57 (m, 2H), 7.50-7.46 (m, 2H), 1.33 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.8, 132.2, 126.4, 119.3, 109.5, 35.5, 31.1.

2-naphthonitrile (5k)[16] Yield: 96%; White solid; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.22 (s, 1H), 7.92-7.87 (m, 3H), 7.67-7.57 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 134.8, 134.3, 132.4, 129.4, 129.2, 128.6, 128.2, 127.8, 126.5, 119.4, 109.6.

Methyl 4-cyanobenzoate (5l)[16] Yield: 99%; White solid; ^1H NMR (300 MHz, $CDCl_3$) δ = 8.16-8.13 (m, 2H), 7.76-7.74 (m, 2H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.6, 134.1, 132.4, 130.3, 118.2, 116.6, 52.9.

4-vinylbenzonitrile (5m)[19] Yield: 96%; Colorless liquid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.61 (d, J = 8.2 Hz, 2H), 7.48 (d, J = 8.2 Hz, 2H), 6.72 (dd, J = 17.6, 10.9 Hz, 1H), 5.87 (d, J = 17.6 Hz, 1H), 5.45 (d, J = 10.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.1, 135.6, 132.6, 126.9, 119.1, 117.9, 111.3.

4-formylbenzonitrile (5n)[17] Yield: 90%; White solid; ^1H NMR (300 MHz, $CDCl_3$) δ = 10.10 (s, 1H), 8.03-7.99 (m, 2H), 7.87-7.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 190.8, 138.9, 133.1, 130.1, 117.9, 117.8.

4-(tert-butyldimethylsilyloxy)benzonitrile (5o)[20] Yield: 99%; Colorless liquid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.56-7.51 (m, 2H), 6.91-6.87 (m, 2H), 0.98 (s, 9H), 0.23 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.9, 134.2, 121.0, 119.4, 104.8, 25.7, 18.4, -4.2.

Synthesis of amidine 7

The ruthenium catalyst **1** was added to a flame-dried J-Young flask filled with argon. The dry THF (1.0 mL) and **2a** (0.25 mmol) were added under a stream of argon. The reaction mixture was stirred for 2 h at room temperature with a household 30W fluorescent light. After the accumulation of **3a**, **4a** (1.0 equiv, 0.25 mmol) was added then stirred at 70 ^oC for 2 h. The reaction mixture was cooled to room temperature then NaH (1.5 equiv, 0.375 mmol) is added at 0 ^oC and stirred at room temperature for 12h. After completion of the reaction, the reaction mixture was quenched with water at 0 ^oC, extracted with diethyl ether (3 x 5 mL). The oragnic layer was washed with H_2O (2 x 30 mL), brine (30 mL), dried over anhydrous sodium sulfate, concentrated under reduced pressure. The residue was recrystallized at -20^{o}C (n-hex:dichloromethane = 2:1) to afford amidine **7**.

4-methoxy-N-phenylbenzimidamide (7)[21] Yield: 92%; White solid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.78 (d, J = 8.5 Hz, 2H), 7.33 (t, J = 7.7 Hz, 2H), 7.06-7.01 (m, 1H), 6.97-6.90 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.7, 154.9, 149.6, 129.6, 128.6, 123.1, 122.0, 113.9, 55.6.

Synthesis of 1-(azidomethyl-d2)-4-methylbenzene 8

To a solution of methyl 4-methylbenzoate (5.0 mmol) in THF (10 mL), lithium aluminum deteride (1.2 equiv, 6.0 mmol) was added at 0 ^oC. The reaction mixture was stirred at room temperature for 3 h. After completion of the reaction, the mixture was quenched with 1 N HCl (10 mL), extracted with ethyl acetate (3 x 10 mL). The oragnic layer was washed with H_2O (30 mL) and brine (30 mL), dried over anhydrous sodium sulfate, concentrated under reduced pressure. The crude residue was directly used for next step without further purification. To a solution of p-tolylmethanol-*d2* and diphenyl phosphoryl azide (DPPA) (2.0 equiv, 10 mmol) in toluene (15 mL), Diazabicyclo[5.4.0]undec-7-ene (DBU) (2.0 equiv, 10 mmol) was added dropwise at 0 ^oC. The reaction mixture was stirred at room temperature for 12 h and quenched with water (30 mL). The solution was extracted with dichloromethane (3 x 20 mL). The organic was washed with H_2O (2 x 30 mL) brine (30 mL), dried over anhydrous sodium sulfate, concentrated under reduced pressure. The residue was purified by flash column chromatography to afford the deuterated azide **8**.

1-(azidomethyl-d2)-4-methylbenzene (8)

Yield: 60% (2 steps); Pale yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ = 7.26-7.18 (m, 4H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 138.3, 132.3, 129.6, 128.4, 54.46, 54.29, 54.11, 53.94, 21.3; IR(NaCl): ν = 3026, 3001, 2924, 2868, 2495, 2106, 1907, 1615, 1516 cm-1; HRMS (EI): m/z calcd. for $C_8H_7D_2N_3$: 149.0922; found: 149.0921.

Synthesis of nitrile and methyl-4-amino-*d2*-benzoate

The ruthenium catalyst **1** (2.0 mol%, 0.0025 mmol) was added to a flame-dried NMR reaction J-young tube and filled with argon. The THF-*d8* (0.6 mL) and **8** (0.125 mmol) were added under a stream of argon. The reaction mixture was stirred for 2 h at room temperature with a household 30W fluorescent light. After the accumulation of N-H aldimine, **4a** (1.0 equiv, 0.125 mmol) was added then stirred at 70 ^{o}C for 2 h.

Methyl 4-amino(*d-2*)benzoate (10)

^{1}H NMR (300 MHz, THF-*d8*, in crude mixture) δ = 7.73-7.68 (m, 2H), 6.55-6.51 (m, 2H), 3.73 (3H).

Synthesis of nitrile and methyl-4-amino-*d2*-benzoate

The ruthenium catalyst **1** (2.0 mol%, 0.0025 mmol) was added to a flame-dried NMR reaction J-young tube and filled with argon. The THF (0.6 mL) and **8** (0.125 mmol) were added under a stream of argon. The reaction mixture was stirred for 2 h at room temperature with a household 30W fluorescent light. After the accumulation of N-H aldimine, aryl azide (1.0 equiv, 0.125 mmol) was added then stirred at 70 ^{o}C for 2 h. The yield of methyl 4-amino-*d2*-benzoate **10** was determined by deuterium NMR using THF-*d8* as an internal standard.

Methyl 4-amino(d-2)benzoate (10)

^{2}D NMR (500 MHz, THF-*d8*, in crude mixture with an internal standard (THF-d8)) δ = 5.16 (s, 2D).

The reaction using Ru-H 12 as a catalyst

To a solution of the ruthenium chloride **11** (0.02 mmol) in THF (1.0 mL), tributyltin hydride (0.02 mmol) was added. The reaction mixture was stirred for 3 h at room temperature with a 12W blue LED to generate the ruthenium hydride **12** (The generation of **12** was checked by ^{1}H and ^{13}C NMR using THF-*d8* as a NMR solvent.[14]). After generation of **12**, **2a** (0.25 mmol) and **4a** (0.25 mmol) were added and stirred at 70 ^{o}C for 16 h under illumination with a household 30 W fluorescent light. After completion of the reaction, solvent was removed under reduced pressure. The yield of **5a** and **6a** was determined by ^{1}H NMR using dibromomethane as an internal standard.

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Notes and references

1 a) Z. Rappoport, *Chemistry of the Cyano Group*, Wiley, London, **1970**; b) R. C. Larock, *Comprehensive Organic Trans-Formations A Guide to Functional Group Preparations*, VCH, New York, **1989**.

2 a) J. Fatiadi in *Preparation and Synthetic Applications of Cyano Compounds* (Eds.: S. Patai, Z. Rappoport), Wiley, New York, **1983**; b) A. Kleemann, J. Engel, B.Kutscher, D. Reichert, *Pharmaceutical Substance: SynthesisPatents, Applications*, 4th ed., Georg Thieme, Stuttgart, **2001**.

3 For recent reports for synthesis of nitriles, see: a) C. B. Kelly, K. M. Lambert, M. A. Mercadante, J. M. Ovian, W. F. Bailey and N. E. Leadbeater, *Angew. Chem. Int. Ed.*, 2015, **54**, 4241-4245; b) B. Xu, Q. Jiang, A. Zhao, J. Jia, Q. Liu, W. Luo and C. Guo, *Chem. Commun.*, 2015, **51**, 11264-11267; c) Y. Zhu, L. Li and Z. Shen, *Chem. Eur. J.*, 2015, **21**, 13246-13252; d) C. A. Malapit, J. T. Reeves, C. A. Busacca, A. R. Howell and C. H. Senanayake, *Angew. Chem. Int. Ed.*, 2016, **55**, 326-330; e) Q. Wu, Y. Luo, A. Lei and J. You, *J. Am. Chem. Soc.*, 2016, **138**, 2885-2888; f) J.-J. Ge, C.-Z. Yao, M.-M. Wang, H.-X. Zheng, Y.-B. Kang and Y. Li, *Org. Lett.*, 2016, **18**, 228-231.

4 a) H. H. Hodgson, *Chem. Rev.*, 1947, **40**, 251-277; b) I. P. Beletskaya, A. S. Sigeev, A. S. Peregudov and P. V. Petrovskii, *J. Organometallic. Chem.*, 2004, **689**, 3810-3812.

5 a) G. P. Ellis and T. M. Romney-Alexander, *Chem. Rev.*, 1987, **87**, 779-794; b) J. Zanon, A. Klapars and S. L. Buchwald, *J. Am. Chem. Soc.*, 2003, **125**, 2890-2891; c) T. Schareina, A. Zapf and M. Beller, *Chem. Commun.*, 2004, 1388-1389; d) H.-J. Cristau, A. Ouali, J.-F. Spindler and M. Taillefer, *Chem. Eur. J.*, 2005, **11**, 2483-2492; e) A. V. Ushkov and V. V. Grushin, *J. Am. Chem. Soc.*, 2011, **133**, 10999-11005; f) D. T. Cohen and S. L. Buchwald, *Org. Lett.*, 2015, **17**, 202-205; g) J. T. Reeves, C. A. Malapit, F. G. Buono, K. P. Sidhu, M. A. Marsini, C. A. Sader, K. R. Fandrick, C. A. Busacca and C. H. Senanayake, *J. Am. Chem. Soc.*, 2015, **137**, 9481-9488; h) B. Mondal, K. Acharyya, P. Howlader and P. S. Mukherjee, *J. Am. Chem. Soc.*, 2016, **138**, 1709-1716.

6 a) S. Iida and H. Togo, *Tetrahedron* 2007, **63**, 8274-8281; b) T. Oishi, K. Yamaguchi and N. Mizuno, *Angew. Chem. Int. Ed.*, 2009, **48**, 6286-6288; c) C. Tao, F. Liu, Y. Zhu, W. Liu and Z. Cao, *Org. Biomol. Chem.*, 2013, **11**, 3349-3354; d) W. Yin, C. Wang and Y. Huang, *Org. Lett.*, 2013, **15**, 1850-1853; e) S. U. Dighe, D. Chowdhury and S. Batra, *Adv. Synth. Catal.*, 2014, **356**, 3892-3896; f) R. V. Jagadeesh, H. Junge and M. Beller, *Nat. Commun.*, 2014, **5**, 4123; g) J.-H. Noh and J. Kim, *J. Org. Chem.*, 2015, **80**, 11624-11628.

7 a) S. H. Yang and S. Chang, *Org. Lett.*, 2001, **3**, 4209-4211; b) Y. F. Kazuaki Ishihara, and H. Yamamoto, *Angew. Chem. Int. Ed.*, 2002, **41**, 2983-2986. c) K. Yamaguchi, H. Fujiwara, Y. Ogasawara, M. Kotani and N. Mizuno, *Angew. Chem. Int. Ed.*, 2007, **46**, 3922-3925; d) L. Yu, H. Li, X. Zhang, J. Ye, J. Liu, Q. Xu and M. Lautens, *Org. Lett.*, 2014, **16**, 1346-1349; e) A. K. Yadav, V. P. Srivastava and L. D. S. Yadav, *RSC Adv.*, 2014, **4**, 4181-4186.

8 a) C.-W. Kuo, J.-L. Zhu, J.-D. Wu, C.-M. Chu, C.-F. Yao and K.-S. Shia, *Chem. Commun.*, 2007, 301-303; b) S. Zhou, K. Junge, D. Addis, S. Das and M. Beller, *Org. Lett.*, 2009, **11**, 2461-2464; c) S. Sueoka, T. Mitsudome, T. Mizugaki, K. Jitsukawa and K. Kaneda, *Chem. Commun.*, 2010, **46**, 8243-8245; d) S. Enthaler, *Chem. Eur. J.*, 2011, **17**, 9316-9319.

9 a) W. Zhou, L. Zhang and N. Jiao, *Angew. Chem. Int. Ed.*, 2009, **48**, 7094-7097; b) W. Zhou, J. Xu, L. Zhang and N. Jiao, *Org. Lett.*, 2010, **12**, 2888-2891.

10 a) M. Lamani and K. R. Prabhu, *Angew. Chem. Int. Ed.*, 2010, **49**, 6622-6625; b) M. Lamani, P. Devadig and K. R. Prabhu, *Org. Biomol. Chem.*, 2012, **10**, 2753-2759; c) Y. Zhao, X. Chew, G. Y. C. Leung and Y.-Y. Yeung, *Tetrahedron Lett.*, 2012, **53**, 4766-4769.

11 R. Sasson and S. Rozen, *Org. Lett.*, 2005, **7**, 2177-2179.

12 S. Chiba, L. Zhang, G. Y. Ang and B. W.-Q. Hui, *Org. Lett.*, 2010, **12**, 2052-2055.

13 J. H. Lee, S. Gupta, W. Jeong, Y. H. Rhee and J. Park, *Angew. Chem. Int. Ed.*, 2012, **51**, 10851-10855.

14 C. P. Casey, T. E. Vos, S. W. Singer and I. A. Guzei, *Organometallics*, 2002, **21**, 5038-5046.

15 J. H. Choi, Y. K. Choi, Y. H. Kim, E. S. Park, E. J. Kim, M.-J. Kim and J. Park, *J. Org. Chem.*, 2004, **69**, 1972-1977.

16 W. Zhou, J. Xu, L. Zhang and N. Jiao, *Org. Lett.*, 2010, **12**, 2888-2891.

17 H.-J. Cristau, A. Ouali, J.-F. Spindler and M. Taillefer, *Chem. Eur. J.*, 2005, **11**, 2483-2492.

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DOI: 10.1039/C6OB02615J

18 S. Chiba, L. Zhang, G. Y. Ang and B. W.-Q. Hui, *Org. Lett.*, 2010, **12**, 2052-2055.

19 J.-z. Zhang and Y. Tang, *Adv. Synth. Catal.*, 2016, **358**, 752-764.

20 B. V. Rokade, S. K. Malekar and K. R. Prabhu, *Chem. Commun.*, 2012, **48**, 5506-5508.

21 Y. Wang, H. Wang, J. Peng and Q. Zhu, *Org. Lett.*, 2011, **13**, 4604-4607.