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Lewis Acid Mediated Tandem Reaction of Propargylic Alcohols with Hydroxylamine Hydrochloride To Give α,β-Unsaturated Amides and Alkenyl Nitriles

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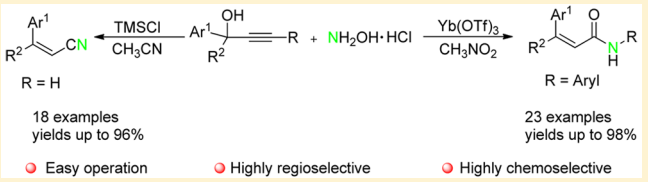
Supporting Information

ABSTRACT: We have developed a highly selective method for the synthesis of α,β-unsaturated amides and alkenyl nitriles from readily available propargylic alcohols. The reaction proceeded smoothly under the neutral conditions with hydroxylamine hydrochloride ($NH_2OH·HCl$) as the nitrogen source. The development of these new strategies has significantly extended the application of hydroxylamine hydrochloride to the chemistry of propargylic alcohols. Moreover, both secondary and tertiary alcohols have been highly regioselectively transformed to the desired products with good functional group compatibility.



INTRODUCTION

The nitrogen-containing compounds, as an important class of biological organic products, have been studied to exist in many biological medicine such as anticancer drugs, antioxidants, and antimitotic agents.[1] Such compounds are also useful structural skeletons in a wide variety of pharmaceuticals and functional materials.[2] Therefore, the development of atom-economical and versatile approaches to synthesize the nitrogen-containing compounds, especially amides and nitriles, has attracted considerable attention.[3−6] The classical method for the nitrogenation of alkynol and alkynes relies on the use of trimethylsilyl azide via a nucleophilic substitution reaction. Recently, the Zhan and Jiao groups have reported the transformation of alkynols to alkenyl nitriles, respectively (Scheme 1a).[7] The transformation of alkynes to amides has also been developed by the Jiao group by using the Au−Ag−TFA cocatalytic system (Scheme 1b).[8] The high cost of nitrogen sources and catalysts, however, reduce the potential for further application. Very recently, Chiba and co-workers disclosed a $BF_3·OEt_2$ promoted transformation of vinyl azides to amides (Scheme 1c).[9] Nevertheless, the difficulty in unstable substrate synthesis imposes restrictions on application in synthetic chemistry. Whereas the addition of trimethylsilyl azide to alkynol and alkynes is widely studied for the synthesis of amides and nitriles, the reaction of related hydroxylamine hydrochloride as the nitrogen source is to be disclosed.

Hydroxylamine hydrochloride has been extensively used as an important nucleophilic reagent in organic synthesis due to its lower cost and high stability. The employment of hydroxylamine hydrochloride as the nitrogenation reagents for the construction of nitrogen-containing compounds, such as pyrazoles,[10a] isoquinolines,[10b] pyridine *N*-oxides,[10c] and isoxazoles,[10d] has been widely investigated. Illuminated by these intriguing studies and our recent success on the transformation of propargylic alcohols,[11] we paid attention to the amidation and cyanation reactions of alkynols. Herein, we demonstrated a new method for the synthesis of α,β-unsaturated amides and alkenylnitrile derivatives by the reaction of propargylic alcohols and hydroxylamine hydrochloride.

RESULTS AND DISCUSSION

The initial exploration began by employing compound **1a** (0.1 mmol) as the model substrate to optimize the reaction conditions. To our delight, the expected product **2a** was obtained in 33% yield in the presence of $NH_2OH·HCl$ (3.0 equiv), $Yb(OTf)_3$ (20 mol %), and H_2O (6.0 equiv) in CH_3NO_2/CH_3OH (1.5 mL, 2:1) at 80 °C for 14 h (Table 1, entry 1). A subsequent investigation on the effect of temperature showed that the reaction gave the best result at 100 °C (Table 1, entries 2−4). Further studies revealed that the $Yb(OTf)_3$ was the most effective catalyst among various Lewis acids (Table 1, entries 5−7). No better result was obtained by adjusting the amount of water (Table 1, entries 8−10). Reactions in other solvents did not result in any improvement in the yield (Table 1, entries 11−14). After a series of detailed investigations mentioned above, the optimal reaction conditions were eventually finalized with the use of **1a** (0.1 mmol), $NH_2OH·HCl$ (3.0 equiv), and H_2O (6.0 equiv) in the presence of $Yb(OTf)_3$ (20 mol %) in CH_3NO_2/CH_3OH (1.5 mL, 2:1) at 100 °C for 14 h.

With the optimized reaction conditions in hand, the scope of propargylic alcohols for this transformation was subsequently examined. The results are summarized in Scheme 2. A variety of

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Scheme 1. Summary of the Present Studies and Our New Anticipation toward the Nitrogen-Containing Compounds

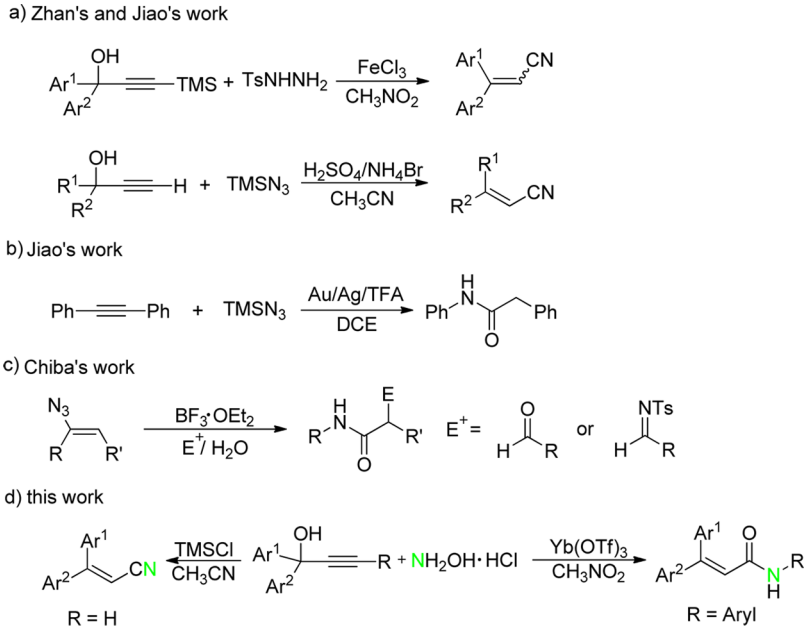
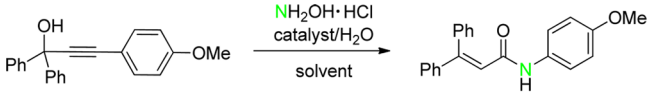


Table 1. Optimization Reaction Conditions of 1a with Hydroxylamine Hydrochloride[a]



1a **2a**

entry	catalyst (mol %)	solvent (2:1)	T (°C)	yield[b]
1	$Yb(OTf)_3$ (20)	CH_3NO_2/MeOH	80	33
2	**$Yb(OTf)_3$ (20)**	**CH_3NO_2/MeOH**	**100**	**71**
3	$Yb(OTf)_3$ (20)	CH_3NO_2/MeOH	120	66
4	$Yb(OTf)_3$ (20)	CH_3NO_2/MeOH	130	69
5	$Cu(OTf)_2$ (20)	CH_3NO_2/MeOH	100	32
6	LiOTf (20)	CH_3NO_2/MeOH	100	41
7	*p*-TsOH (20)	CH_3NO_2/MeOH	100	0
8[c]	$Yb(OTf)_3$ (20)	CH_3NO_2/MeOH	100	47
9[d]	$Yb(OTf)_3$ (20)	CH_3NO_2/MeOH	100	53
10[e]	$Yb(OTf)_3$ (20)	CH_3NO_2/MeOH	100	62
11	$Yb(OTf)_3$ (20)	CH_3CN/MeOH	100	64
12	$Yb(OTf)_3$ (20)	DCE/MeOH	100	44
13	$Yb(OTf)_3$ (20)	1,4-dioxane/MeOH	100	49
14	$Yb(OTf)_3$ (20)	$PhCH_3$/ MeOH	100	32

[a]Unless otherwise noted, all reactions were performed with **1a** (0.1 mmol), NH_2OH·HCl (3.0 equiv), and H_2O (6.0 equiv) in the presence of a Lewis acid in solvent (1.5 mL) under an air atmosphere for 14 h. [b]Yields are given for isolated products. [c]This reaction was performed in the absence of water. [d]H_2O (2.0 equiv) was used. [e]H_2O (4.0 equiv) was used. TMS: trimethylsilyl. *p*-TsOH: *p*-toluenesulfonic acid.

tertiary propargylic alcohols were found to be compatible with this protocol and were easily converted to the corresponding acrylamides in moderate to excellent yields (up to 98%). Both electron-donating (OMe, Me, Et; **2a**−**2g**) and electron-withdrawing substituents (F, Cl, Br; **2i**−**2m**) on the aromatic rings (R^3) were tolerated. It is noteworthy that halo-substituted propargylic alcohols worked smoothly and furnished the corresponding halo-substituted amides, which are readily applied in various cross-coupling coupling reactions (**2k**−**2m**). Additionally, the substrates bearing electron-donating and/or electron-withdrawing groups on the aromatic rings (R^1, R^2) were also employed, and the desired products were obtained in moderate to good yields (**2n**−**2q**). However, when alkyl-substituted (R^3) tertiary propargylic alcohols (**1r, 1s**) were used, no acrylamide products were detected. This might be attributed to the fact that the alkyl group is difficult to migrate (see Scheme 5). In the meantime, the reactions of various secondary propargylic alcohols proceed smoothly to give the corresponding *α,β*-unsaturated amides in high regioselectivity (**2u**−**2w**).

The nitrile product was obtained when terminal alkynol was used. Nitriles are important structural moieties found in many natural products, biological compounds, interesting materials, and versatile building blocks in organic synthesis.[12−15] Herein, we also demonstrated an efficient and direct metal-free transformation of terminal alkynols to corresponding alkenyl nitriles.

1-(2-Methoxyphenyl) prop-2-yn-1-ol (**4a**) was chosen as the model substrate to investigate the exploration. Initially, the reaction was performed in the presence of NH_2OH·HCl (3.0 equiv), TFA (3.0 equiv), and NH_4Cl (0.1 equiv) in CH_3CN (2.0 mL) at 100 °C, and the desired product 3-(2-ethoxyphenyl) acrylonitrile (**5a**) was obtained in 39% yield after 6.0 h (Table 2, entry 1). The acid promoters were then investigated, and a 70% yield of **5a** was obtained when trimethylchlorosilane (TMSCl) was used (Table 2, entries 2−5). Subsequent investigation of the effect of temperature revealed that 120 °C is the most suitable for this transformation (Table 2, entries 5−7). Various representative solvents such as DCM, DMF, CH_3NO_2, and $PhCH_3$ proved to be less effective (Table 2, entries 8−11). The use of 3.0 equiv of TMSCl proved to be suitable and gave the desired product in 86% yield (Table 2, entries 12−14). Other additives including TBAB gave unsatisfactory yields of the desired product (Table 2, entry 16). Ultimately, the optimal conditions for the generation of **5a** were settled as **4a** (0.2 mmol), NH_2OH·HCl (3.0 equiv), TMSCl (3.0 equiv), and additive NH_4Cl (0.1 equiv) in CH_3CN (2.0 mL) under an air atmosphere at 120 °C for 6.0 h.

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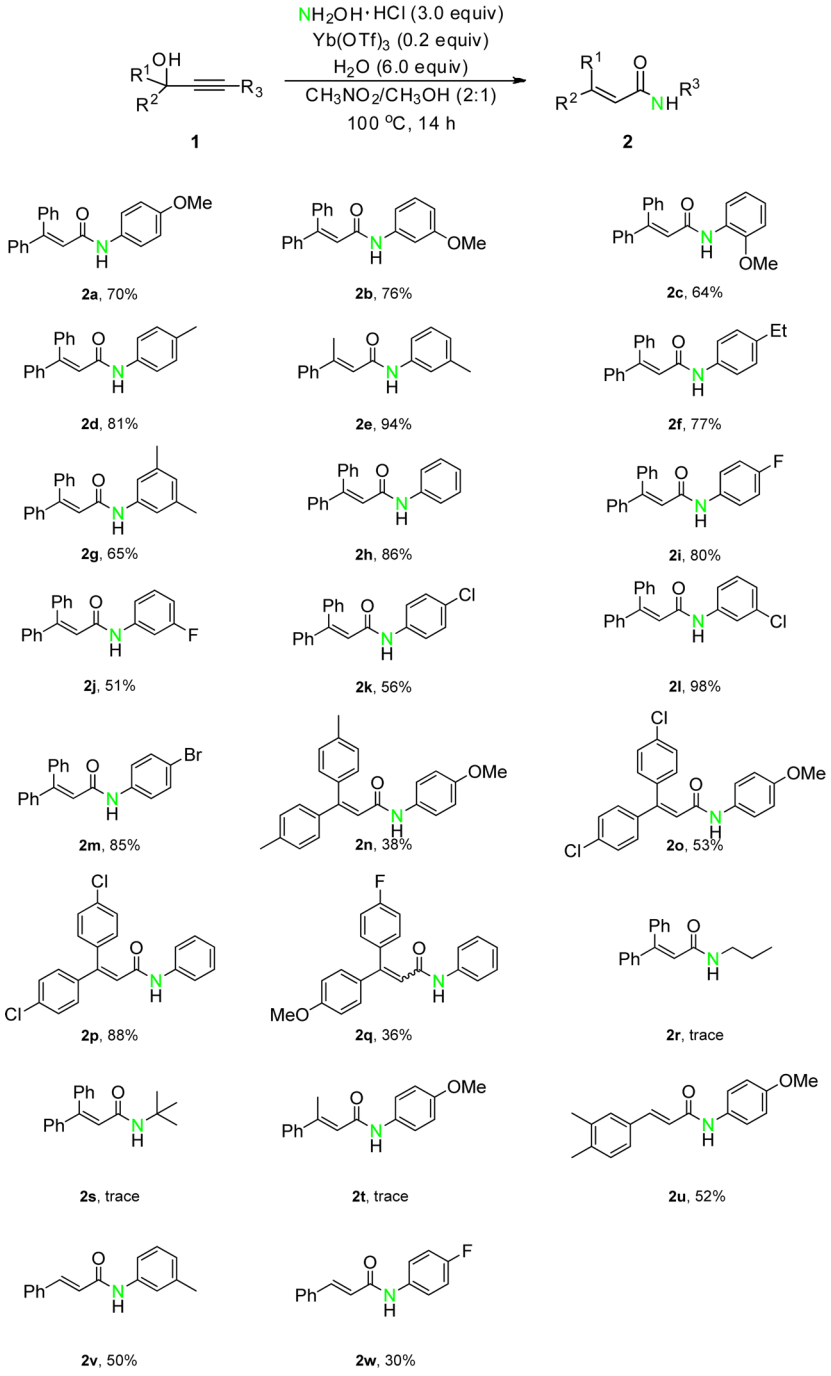
Scheme 2. Transformation of Propargylic Alcohols to α,β-Unsaturated Amides[a,b]



[a]Unless otherwise noted, all reactions were performed with substrate **1** (0.1 mmol), $NH_2OH·HCl$ (3.0 equiv), $Yb(OTf)_3$ (0.2 equiv), and H_2O (6.0 equiv) in CH_3NO_2/CH_3OH (1.5 mL, 2:1) at 100 °C for 14 h. [b]Yields are given for isolated products.

The scope of the transformation was then investigated under the standard conditions outlined in Scheme 3. Various secondary and tertiary alkynols were easily converted to the corresponding alkenyl nitriles in moderate to excellent yields. The structure of **5h** was further identified by the X-ray crystal structure analysis (see the Supporting Information). When secondary alkynols were employed, the (*E*)-acrylonitriles were selectively obtained (**5a**−**5k**). Despite the fact that an electron-donating substituent (OMe) was attached on the *ortho*-, *meta*-, or *para*-positions of the aryl group (Ar^1), the reactions performed well and gave the desired products in good to excellent yields (**5a**−**5c**). Satisfactorily, the reaction of cinnamyl alkynol **4i** gave conjugated diene nitrile **5i** in 83% yield. In particular, products with multiple rings, naphthyl **5j** and **5k**, were obtained in moderate yields as well. Notably, the reactions of various tertiary propargylic alcohols proceed smoothly to give the corresponding alkenyl nitriles (**5o**−**5r**). It is worth noting that the asymmetric tertiary alkynol was compatible with this transformation as well (**5p**), and the substrate with two methyl substituents gave a satisfactory yield of 96% (**5r**). However, the electronic effect was very distinct in this transformation; the substrates with electron-withdrawing F

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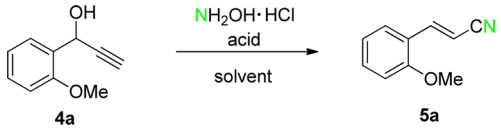
Table 2. Screening of the Reaction Conditions[a]



4a 5a

entry	acid (equiv)	T (°C)	solvent	yield[b]
1	TFA (3.0)	100	CH_3CN	39
2	TsOH (3.0)	100	CH_3CN	57
3	CH_3COOH (3.0)	100	CH_3CN	60
4	HCOOH (3.0)	100	CH_3CN	49
5	TMSCl (3.0)	100	CH_3CN	70
6	TMSCl (3.0)	80	CH_3CN	60
7	**TMSCl (3.0)**	**120**	**CH_3CN**	**86**
8	TMSCl (3.0)	120	DCE	0
9	TMSCl (3.0)	120	DMF	42
10	TMSCl (3.0)	120	CH_3NO_2	61
11	TMSCl (3.0)	120	$PhCH_3$	0
12	TMSCl (2.0)	120	CH_3CN	73
13	TMSCl (4.0)	120	CH_3CN	72
14	TMSCl (5.0)	120	CH_3CN	82
15[c]	TMSCl (3.0)	120	CH_3CN	62
16[d]	TMSCl (3.0)	120	CH_3CN	73

[a]Unless otherwise noted, all reactions were performed with **4a** (0.2 mmol), $NH_2OH·HCl$ (3.0 equiv), and additive (0.1 equiv) in solvent (2.0 mL) at 120 °C for 6.0 h. [b]Yields are given for isolated products. [c]$NH_2OH·HCl$ (2.0 equiv) was used. [d]TBAB instead of NH_4Cl was employed. TMS: trimethylsilyl. TBAB: tetrabutylammomium bromide. TfOH: trifluoromethanesulfonic acid.

failed to give the desired product under the optimized conditions (**5e**, **5q**).

To probe the mechanism of this novel transformation, additional mechanistic studies with possible key intermediates have been conducted (Scheme 4). One possible pathway for this transformation is likely to generate an α,β-unsaturated ketone through Lewis acid mediated Meyer−Schuster rearrangement of propargylic alcohol, followed by a subsequent Beckmann rearrangement to form an amide.[7b] Thereby, the reaction of 1-(4-methoxyphenyl)-3,3-diphenylprop-2-en-1-one (**3**) was carried out under the standard conditions. Only a 49% yield of the desired product **2a** was obtained. This indicated that this reaction pathway may partially contribute to the formation of the desired product.

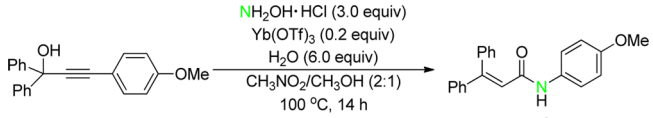
A plausible mechanism is then proposed on the basis of literature[11,16,17] (Scheme 5). The dehydration of alkynol **1** generates propargyl cation **A** in the presence of a Lewis acid, which may involve in two paths to the subsequent transformation. In path **a**, the attack of $NH_2OH·HCl$ onto allenyl cation **B** generates intermediate **C**, which will be captured by a proton to afford intermediate **D**. The tautomerization of **D** forms intermediate **E**, which could eliminate a molecule of water through Schimidt-type rearrangement to afford the intermediate **F**. The subsequent nucleophilic attack of H_2O leads to **G**, which could undergo a keto−enol tautomerization to give the desired α,β-unsaturated amide **2**. In path **b**, the substitution reaction of the allenyl cation **B** attack of H_2O leads to the intermediate **H**. Then the rapid tautomerization of **H** would lead to the α,β-unsaturated ketone **I**, which could react with $NH_2OH·HCl$ to generate ketoxime **J** by eliminating a molecule of water, and the desired product **2** could be obtained through Beckmann rearrangement in the presence of the acid as well. Based on the above consequence, the mechanism of this transformation may involve two paths at the same time. Terminal alkynols proceed through path **a** until formation of the intermediate **F**. Subsequently, the desired alkenyl nitriles **5** could be afforded through elimination of the proton in intermediate **F**.

CONCLUSIONS

In summary, we have reported a novel and efficient Lewis acid mediated tandem reaction of propargylic alcohols with hydroxylamine hydrochloride as the nitrogen source to give α,β-unsaturated amides and alkenylnitrile derivatives; the products were formed through a C−H or C−C bond cleavage and a C−N bond formation. The value of this reaction has been reflected by its applicability to a wide range of alkynol substrates.

EXPERIMENTAL SECTION

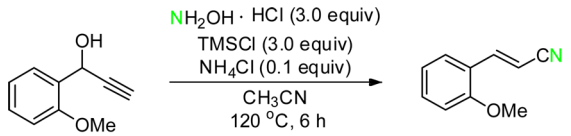
General Procedure for the Synthesis of 2a. The reaction of propargylic acohol **1a** (31.4 mg, 0.1 mmol), $NH_2OH·HCl$ (3.0 equiv),



1a 2a

$Yb(OTf)_3$ (0.2 equiv), and H_2O (6.0 equiv) in CH_3NO_2/CH_3OH (1.5 mL, 2:1) was conducted at 100 °C under an air atmosphere. The reaction was complete within 14.0 h by TLC monitoring. The resulting mixture was cooled down to room temperature. The reaction mixture was then diluted with ethyl acetate (2 × 15 mL), washed with a saturated aqueous solution of brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was further purified by chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) to afford **2a** (23.4 mg). Compounds **2a**−**2w**[11a] are known compounds.

General Procedure for the Synthesis of 5a. The reaction of propargylic acohol **4a** (32.4 mg, 0.2 mmol), $NH_2OH·HCl$ (3.0 equiv),



4a 5a

and TMSCl (3.0 equiv) in CH_3CN (2.0 mL) was conducted at 120 °C under an air atmosphere. The reaction was complete within 6.0 h by TLC monitoring. The resulting mixture was cooled down to room temperature. The reaction mixture was then diluted with ethyl acetate (2 × 15 mL), washed with a saturated aqueous solution of brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was further purified by chromatography on silica gel (petroleum ether/ethyl acetate, 10:1) to afford **5a** (27.4 mg). The crystal of **5h** is a very small colorless block; the WR_2 value to date is 0.359 because of the poor quality and disorder of the crystal. Compounds **5a**−**5d**, **5h**, **5k**−**5o**,[7a,13d,18] **5f**,[19a] **5g**, **5i**,[19b] **5j**,[19c] and **5p**−**5r**[19d] are known compounds.

General Remarks. Column chromatography was carried out on silica gel. ^1H NMR spectra were recorded on a 400 MHz instrument in $CDCl_3$, and ^{13}C NMR spectra were recorded on a 100 MHz instrument in $CDCl_3$. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), q (quartet), or m (multiplet). Copies of their ^1H NMR and ^{13}C NMR spectra are provided in the Supporting Information. Solvents were dried under a standard method. Commercially available reagents were used with further purification. THF was distilled immediately before use from Na/benzophenone.

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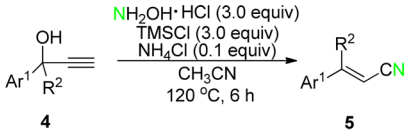
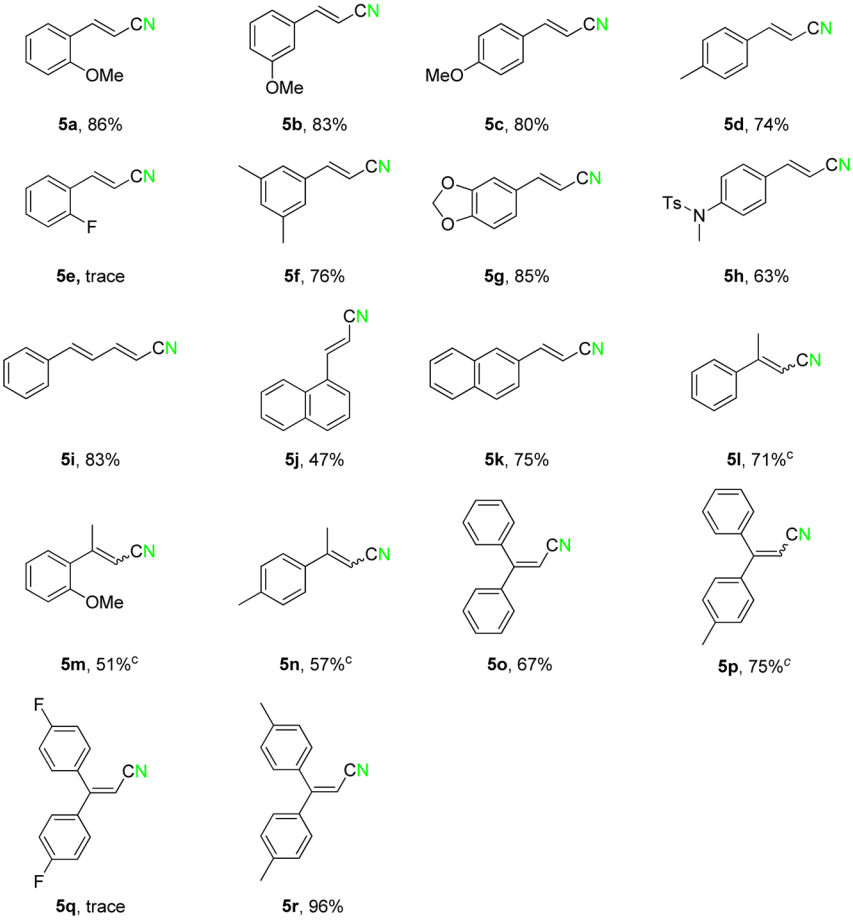
Scheme 3. Transformation of Propargylic Alcohols to Alkenyl Nitriles[a,b]



4 5



5a, 86% **5b**, 83% **5c**, 80% **5d**, 74%

5e, trace **5f**, 76% **5g**, 85% **5h**, 63%

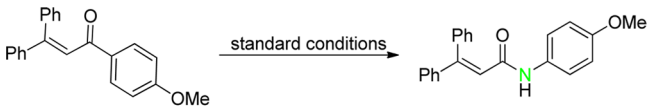
5i, 83% **5j**, 47% **5k**, 75% **5l**, 71%[c]

5m, 51%[c] **5n**, 57%[c] **5o**, 67% **5p**, 75%[c]

5q, trace **5r**, 96%

[a]Unless otherwise noted, all reactions were performed with **4** (0.2 mmol), $NH_2OH{\cdot}HCl$ (3.0 equiv), TMSCl (3.0 equiv), and additive NH_4Cl (0.1 equiv) in CH_3CN (2.0 mL) under an air atmosphere at 120 °C for 6.0 h. [b]Yields are given for isolated products. [c]The olefin isomer *E*/*Z* ratios of **5l**, **5m**, **5n**, and **5p** are 2.03:1, 1.70:1, 1.44:1, and 1.13:1, respectively.

Scheme 4. Investigation of the Possible Key Intermediate



3 **2a** : 49%

Characterization Data of 2a−2u. *N-(4-Methoxyphenyl)-3,3-diphenylacrylamide (**2a**).* The resultant residue was purified by flash silica gel column chromatography to afford **2a** as a white solid (23.4 mg, 71%); mp: 151−153 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.47−7.46 (m, 3H), 7.36−7.30 (m, 7H), 7.03 (d, *J* = 8.8 Hz, 2H), 6.85 (s, 1H), 6.75−6.73 (m, 2H), 6.50 (s, 1H), 3.74 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.2, 156.3, 150.1, 140.5, 138.3, 130.8, 129.6, 129.2, 129.0, 129.0, 128.5, 128.1, 123.2, 121.3, 114.0, 55.5.

*N-(3-Methoxyphenyl)-3,3-diphenylacrylamide (**2b**).* The resultant residue was purified by flash silica gel column chromatography to afford **2b** as a white solid (24.9 mg, 76%); mp: 116−118 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.47 (m, 3H), 7.37−7.32 (m, 7H), 7.08 (t, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 1.6 Hz, 2H), 6.59−6.50 (m, 3H), 3.74 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.3, 160.0, 150.5, 140.4, 138.8, 138.1, 129.5, 129.4, 129.2, 129.0, 128.5, 128.0, 123.0, 111.7, 110.0, 105.2, 55.2.

*N-(2-Methoxyphenyl)-3,3-diphenylacrylamide (**2c**).* The resultant residue was purified by flash silica gel column chromatography to afford **2c** as a colorless liquid (21.0 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 7.6 Hz, 1H), 7.70 (s, 1H), 7.41−7.40 (m, 3H), 7.34−7.29 (m, 7H), 6.98−6.87 (m, 2H), 6.72 (dd, *J* = 1.2, 8.0 Hz, 1H), 6.49 (s, 1H), 3.59 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.2, 150.6, 147.7, 141.1, 138.1, 129.7, 129.0, 128.6, 128.4, 128.2, 127.7, 123.4, 123.3, 120.9, 119.6, 109.6, 55.3.

*3,3-Diphenyl-N-(p-tolyl)acrylamide (**2d**).* The resultant residue was purified by flash silica gel column chromatography to afford **2d** as a white solid (25.4 mg, 81%); mp: 154−156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.45 (m, 3H), 7.35−7.30 (m, 7H), 7.00 (s, 4H), 6.90 (s, 1H), 6.50 (s, 1H), 2.25 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.2, 150.2, 140.5, 138.2, 135.0, 133.7, 129.5, 129.3, 129.1, 129.0, 128.9, 128.5, 128.0, 123.2, 119.6, 20.8.

*3,3-Diphenyl-N-(m-tolyl)acrylamide (**2e**).* The resultant residue was purified by flash silica gel column chromatography to afford **2e** as a white solid (29.5 mg, 94%); mp: 141−143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.46 (d, *J* = 2.0 Hz, 3H), 7.35−7.32 (m, 7H), 7.09−7.05 (m, 2H), 6.89 (s, 1H), 6.85−6.80 (m, 2H), 6.50 (s, 1H), 2.26 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.3, 150.4, 140.5, 138.7,

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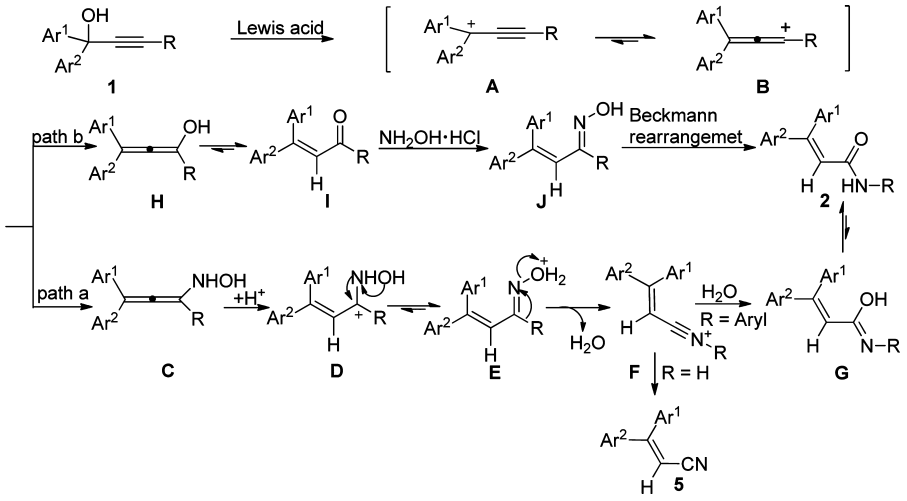
Scheme 5. Proposed Mechanism for the Formation of α,β-Unsaturated Amides and Alkenyl Nitriles



138.2, 137.5, 129.5, 129.2, 129.0, 128.6, 128.5, 128.0, 124.9, 123.1, 120.2, 116.6, 21.4.

*N-(4-Ethylphenyl)-3,3-diphenylacrylamide (**2f**).* The resultant residue was purified by flash silica gel column chromatography to afford **2f** as a white solid (25.2 mg, 77%); mp: 150−152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.45 (m, 3H), 7.35−7.31 (m, 7H), 7.03 (s, 4H), 6.92 (s, 1H), 6.50 (s, 1H), 2.55 (q, *J* = 8.0 Hz, 2H), 1.17 (t, *J* = 7.6 Hz, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.2, 150.2, 140.5, 140.2, 138.2, 135.2, 129.5, 129.1, 129.0, 128.9, 128.5, 128.1, 128.0, 123.1, 119.7, 28.2, 15.6.

*N-(3,5-Dimethylphenyl)-3,3-diphenylacrylamide (**2g**).* The resultant residue was purified by flash silica gel column chromatography to afford **2g** as a white solid (21.2 mg, 65%); mp: 174−176 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.45 (m, 3H), 7.35−7.31 (m, 7H), 6.88 (s, 1H), 6.76 (s, 2H), 6.67 (s, 1H), 6.48 (s, 1H), 2.21 (s, 6 H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.2, 150.4, 140.5, 138.4, 138.2, 137.4, 129.5, 129.1, 128.9, 128.8, 128.4, 128.0, 125.8, 123.0, 117.3, 21.3.

*N,3,3-Triphenylacrylamide (**2h**).* The resultant residue was purified by flash silica gel column chromatography to afford **2h** as a white solid (26.1 mg, 86%); mp: 114−116 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.47 (m, 3H), 7.37−7.31 (m, 7H), 7.22−7.18 (m, 2H), 7.10 (d, *J* = 7.6 Hz, 2H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.92 (s, 1H), 6.51 (s, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.3, 150.4, 140.4, 138.1, 137.6, 129.5, 129.2, 129.1, 129.0, 128.8, 128.5, 128.0, 124.1, 123.1, 119.5.

*N-(4-Fluorophenyl)-3,3-diphenylacrylamide (**2i**).* The resultant residue was purified by flash silica gel column chromatography to afford **2i** as a white solid (25.3 mg, 80%); mp: 134−136 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.48 (m, 3H), 7.37−7.33 (m, 7H), 7.07−7.03 (m, 2H), 6.92−6.87 (m, 2H), 6.84 (s, 1H), 6.50 (s, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.3, 160.4, 160.0, 150.7, 140.3, 138.1, 133.6, 129.5, 129.3, 129.0, 128.5, 128.0, 122.7, 121.3, 121.2, 115.5, 111.3.

*N-(3-Fluorophenyl)-3,3-diphenylacrylamide (**2j**).* The resultant residue was purified by flash silica gel column chromatography to afford **2j** as a white solid (16.1 mg, 51%); mp: 131−133 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51−7.49 (m, 3H), 7.37−7.30 (m, 7H), 7.16−7.09 (m, 2H), 6.95 (s, 1H), 6.74−6.69 (m, 1H), 6.65−6.24 (m, 1H), 6.50 (s, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.3, 164.1, 161.6, 151.1, 140.2, 139.2, 139.1, 138.0, 129.9, 129.8, 129.4, 129.4, 129.1, 129.1, 128.5, 128.0, 122.6, 114.7, 110.8, 110.6, 107.1, 106.8.

*N-(4-Chlorophenyl)-3,3-diphenylacrylamide (**2k**).* The resultant residue was purified by flash silica gel column chromatography to afford **2k** as a white solid (18.7 mg, 56%); mp: 190−192 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.48 (m, 3H), 7.36−7.34 (m, 7H), 7.16 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.87 (s, 1H), 6.50 (s, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.3, 150.9, 140.2, 138.1, 136.2, 129.5, 129.4, 129.1, 128.8, 128.5, 128.0, 122.7, 120.7.

*N-(3-Chlorophenyl)-3,3-diphenylacrylamide (**2l**).* The resultant residue was purified by flash silica gel column chromatography to afford **2l** as a white solid (32.6 mg, 98%); mp: 162−164 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.47(m, 3H), 7.37−7.29 (m, 8H), 7.09 (t, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.49 (s, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.3, 151.2, 140.2, 138.7, 138.0, 134.5, 129.7, 129.4, 129.4, 129.1, 129.1, 128.5, 128.1, 124.1, 122.5, 119.6, 117.4.

*N-(4-Bromophenyl)-3,3-diphenylacrylamide (**2m**).* The resultant residue was purified by flash silica gel column chromatography to afford **2m** as a white solid (32.0 mg, 85%); mp: 190−192 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.48 (m, 3H), 7.37−7.29 (m, 9H), 6.99 (d, *J* = 8.8 Hz, 2H), 6.86 (s, 1H), 6.49 (s, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.3, 150.9, 140.2, 138.0, 136.7, 131.8, 129.5, 129.1, 128.5, 128.0, 122.7, 121.0.

*N-(4-Methoxyphenyl)-3,3-di-p-tolylacrylamide (**2n**).* The resultant residue was purified by flash silica gel column chromatography to afford **2n** as a faint yellow solid (13.3 mg, 37%); mp: 153−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (s, 1H), 7.26−7.19 (m, 5H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 2H), 6.82 (s, 1H), 6.75 (d, *J* = 8.8 Hz, 2H), 6.44 (s, 1H), 3.75 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.5, 156.2, 150.2, 139.2, 138.8, 137.9, 135.3, 131.0, 129.6, 129.5, 129.1, 128.0, 122.0, 121.3, 114.0, 55.4, 21.3, 21.2.

*3,3-Bis(4-chlorophenyl)-N-(4-methoxyphenyl)acrylamide (**2o**).* The resultant residue was purified by flash silica gel column chromatography to afford **2o** as a faint yellow solid (20.9 mg, 53%); mp: 200−202 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 9.6 Hz, 2H), 7.21−7.15 (m, 4H), 6.95 (s, 1H), 6.79 (d, *J* = 8.8 Hz, 2H), 6.42 (s, 1H), 3.76 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 163.6, 156.6, 148.7, 139.0, 136.3, 135.5, 135.1, 130.9, 129.4, 129.0, 128.8, 123.1, 121.5, 114.2, 55.5.

*3,3-Bis(4-chlorophenyl)-N-phenylacrylamide (**2p**).* The resultant residue was purified by flash silica gel column chromatography to afford **2p** as a white solid (32.3 mg, 88%); mp: 180−182 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.33−7.29 (m, 4H), 7.24 (d, *J* = 5.6 Hz, 4H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.08−7.05 (m, 2H), 6.42 (s, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 163.7, 149.2, 141.9, 138.9, 137.4, 136.2, 135.6, 135.2, 133.6, 130.9, 129.4, 129.1, 129.0, 128.8, 128.7, 127.9, 124.5, 123.0, 119.7.

*(Z)-3-(4-Fluorophenyl)-3-(4-methoxyphenyl)-N-phenylacrylamide (**2q**).* The resultant residue was purified by flash silica gel column chromatography to afford **2q** as a white solid (12.3 mg, 36%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29−7.24 (m, 4H), 7.22 (s,1H), 7.19 (t, *J* = 9.6 Hz, 3H), 7.09 (s, 1H), 7.02 (d, *J* = 8.4 Hz, 3H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.36 (s, 1H), 3.84 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.6, 164.4, 162.1, 160.3, 149.5, 137.7, 137.2, 131.1, 130.1, 130.0, 129.8, 128.8, 124.1, 122.3, 119.6, 115.5, 115.3, 114.4, 55.4.

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*(E)-3-(3,4-Dimethylphenyl)-N-(4-methoxyphenyl)acrylamide (**2u**).* The resultant residue was purified by flash silica gel column chromatography to afford **2s** as a white solid (14.6 mg, 52%); mp: 130−132 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 15.6 Hz, 1H), 7.54−7.49 (m, 3H), 7.27 (s, 1H), 7.24 (s, 1H), 7.11 (d, J = 7.6 Hz, 1H), 6.87 (d, J = 8.8 Hz, 2H), 6.51 (d, J = 15.6 Hz, 1H), 3.79 (s, 3H), 2.27 (s, 3H), 2.25 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.3, 156.4, 142.0, 138.8, 137.0, 132.4, 131.4, 130.1, 129.2, 125.4, 121.8, 119.8, 114.2, 55.4, 19.7, 19.6.

*N-(m-tolyl)cinnamamide (**2v**).* The resultant residue was purified by flash silica gel column chromatography to afford **2t** as a colorless liquid (23.8 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 16.8 Hz, 1H), 7.49 (d, J = 6.8 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.35−7.31 (m, 4H), 7.24 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 16.8 Hz, 1H), 2.42 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 142.3, 139.0, 137.9, 134.7, 129.9, 128.9, 127.9, 125.3, 120.8, 117.1, 21.5.

*N-(4-Fluorophenyl)cinnamamide (**2w**).* The resultant residue was purified by flash silica gel column chromatography to afford **2u** as a white solid (14.5 mg, 35%); mp: 138−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 16.8 Hz, 1H), 7.52−7.49 (m, 4H), 7.35 (d, J = 7.6 Hz, 4H), 7.15−7.11 (m, 2H), 6.76 (d, J = 16.8 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 164.1, 160.7, 158.2, 142.5, 134.5, 134.0, 130.0, 128.9, 127.9, 121.9, 120.6, 115.8, 115.6.

Characterization Data of 5a−5n. *(E)-3-(2-Methoxyphenyl)-acrylonitrile (**5a**).* The resultant residue was purified by flash silica gel column chromatography to afford **5a** (27.4 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 16.8 Hz, 1H), 7.39 (t, J = 8.0 Hz, 2H), 6.99−6.92 (m, 2H), 6.05 (d, J = 16.8 Hz, 1H), 3.89 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 158.2, 146.4, 132.3, 128.9, 122.5, 120.8, 119.0, 111.2, 96.9, 55.5.

*(E)-3-(3-Methoxyphenyl)acrylonitrile (**5b**).* The resultant residue was purified by flash silica gel column chromatography to afford **5b** (26.4 mg, 83%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−7.31 (m, 3H), 6.91 (d, J = 8.8 Hz, 2H), 5.71 (d, J = 16.8 Hz, 1H), 3.85 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 160.0, 150.5, 134.8, 130.1, 119.9, 118.1, 116.8, 112.5, 96.6, 55.4.

*(E)-3-(4-Methoxyphenyl)acrylonitrile (**5c**).* The resultant residue was purified by flash silica gel column chromatography to afford **5c** (25.3 mg, 80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 16.8 Hz, 1H), 6.93−6.90 (m, 2H), 5.71 (d, J = 16.8 Hz, 1H), 3.85 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 162.0, 150.0, 129.0, 126.3, 118.7, 114.5, 93.3, 55.4.

*(E)-3-(p-tolyl)acrylonitrile (**5d**).* The resultant residue was purified by flash silica gel column chromatography to afford **5d** (21.3 mg, 74%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.33 (m, 3H), 7.21 (d, J = 8.0 Hz, 2H), 5.82 (d, J = 16.8 Hz, 1H), 2.38 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 150.5, 141.8, 130.9, 129.8, 127.3, 118.4, 95.0, 21.5.

*(E)-3-(3,4-Dimethylphenyl)acrylonitrile (**5f**).* The resultant residue was purified by flash silica gel column chromatography to afford **5f** (23.7 mg, 76%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, J = 16.4 Hz, 1H), 7.20−7.14 (m, 3H), 5.80 (d, J = 16.8 Hz, 1H), 2.29 (s, 3H), 2.28 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 150.7, 140.5, 137.4, 131.2, 130.3, 128.4, 124.9, 118.5, 94.7, 19.8, 19.7.

*(E)-3-(Benzo[d][1,3]dioxol-5-yl)acrylonitrile (**5g**).* The resultant residue was purified by flash silica gel column chromatography to afford **5g** (29.4 mg, 85%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, J = 14.4 Hz, 1H), 6.94−6.92 (m, 2H), 6.82 (d, J = 8.8 Hz, 1H), 6.03 (s, 2H), 5.67 (d, J = 16.8 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 150.4, 150.0, 148.6, 128.0, 124.1, 118.4, 108.6, 105.5, 101.8, 93.9.

*(E)-N-(4-(2-Cyanovinyl)phenyl)-N,4-dimethylbenzenesulfonamide (**5h**).* The resultant residue was purified by flash silica gel column chromatography to afford **5h** (19.5 mg, 63%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.34 (m, 5H), 7.25 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.4 Hz, 2H), 5.85 (d, J = 16.8 Hz, 1H), 3.17 (s, 3H), 2.42, (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 149.3, 144.0, 143.9, 133.1, 131.9, 129.5, 127.8, 127.6, 126.4, 117.9, 96.7, 37.5, 21.5.

*(2E,4E)-5-Phenylpenta-2,4-dienenitrile (**5i**).* The resultant residue was purified by flash silica gel column chromatography to afford **5i** (26.8 mg, 75%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.45 (m, 2H), 7.40−7.34 (m, 3H), 7.18−7.12 (m, 1H), 6.91−6.79 (m, 2H), 5.44 (d, J = 16.0 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 150.3, 141.4, 135.3, 129.6, 128.9, 127.4, 125.4, 118.3, 98.3.

*(E)-3-(Naphthalen-1-yl)acrylonitrile (**5j**).* The resultant residue was purified by flash silica gel column chromatography to afford **5j** (16.9 mg, 47%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, J = 16.4 Hz, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.95−7.88 (m, 2H), 7.66 (d, J = 7.2 Hz, 1H), 7.62−7.54 (m, 2H), 7.51−7.47 (m, 1H), 5.97 (d, J = 16.4 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 147.9, 133.6, 131.5, 130.9, 130.7, 128.9, 127.4, 126.5, 125.3, 124.6, 122.8, 118.2, 98.8.

*(E)-3-(Naphthalen-2-yl)acrylonitrile (**5k**).* The resultant residue was purified by flash silica gel column chromatography to afford **5k** (26.8 mg, 75%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86−7.83 (m, 4H), 7.55−7.51 (m, 4H), 5.96 (d, J = 16.4 Hz, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 150.6, 134.5, 133.0, 130.9, 129.7, 129.1, 128.7, 127.8, 127.8, 127.1, 122.2, 118.3, 96.3.

*(E)-3-(2-Methoxyphenyl)but-2-enenitrile (**5m**).* The resultant residue was purified by flash silica gel column chromatography to afford **5m** (11.2 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.32 (m, 1H), 7.19−7.17 (m, 1H), 6.98−6.92 (m, 2H), 5.57 (d, J = 1.2 Hz, 1H), 3.85 (s, 3H), 2.43 (d, J = 0.8 Hz, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 160.0, 156.6, 130.6, 128.8, 128.7, 120.7, 117.5, 111.2, 98.7, 55.5, 21.8.

*(Z)-3-(2-Methoxyphenyl)but-2-enenitrile (**5m′**).* The resultant residue was purified by flash silica gel column chromatography to afford **5m** (6.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.33 (m, 1H), 7.23−7.20 (m, 1H), 7.02−6.94 (m, 2H), 5.43 (d, J = 1.6 Hz, 1H), 3.85 (s,3H), 2.24 (d, J = 1.6 Hz, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 161.3, 155.9, 130.5, 128.8, 127.8, 120.7, 117.1, 111.2, 98.0, 55.4, 24.6.

*(E)-3-(p-Tolyl)but-2-enenitrile (**5n**).* The resultant residue was purified by flash silica gel column chromatography to afford **5n** (17.9 mg, 57%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.0 Hz, 1H), 5.37 (d, J = 8.4 Hz, 2H), 7.24−7.20 (m, 4H), 5.60 (s,1H), 5.35 (d, J = 1.2 Hz, 1H), 2.45 (s, 3H), 2.38 (s, 5H), 2.26 (d, J = 1.2 Hz, 2H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 160.8, 159.5, 140.6, 140.1, 135.3, 134.9, 129.5, 129.3, 127.0, 125.7, 117.9, 117.8, 94.6, 94.4, 24.6, 21.3, 21.3, 20.1.

*3,3-Diphenylacrylonitrile (**5o**).* The resultant residue was purified by flash silica gel column chromatography to afford **5l** (27.4 mg, 67%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.41 (m, 6 H), 7.39−7.35 (m, 2H), 7.31−7.28 (m, 2H), 5.74 (s, 1H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 163.1, 138.9, 137.0, 130.4, 130.0, 129.5, 128.6, 128.5, 128.5, 117.9, 94.9.

*3-Phenyl-3-(p-tolyl)acrylonitrile (**5p**).* The resultant residue was purified by flash silica gel column chromatography to afford **5m** (29.8 mg, 75%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.41 (m, 6 H), 7.38−7.29 (m, 6 H), 7.24 (d, J = 4.8 Hz, 2H), 7.18 (s, 4H), 5.69 (d, J = 15.6 Hz, 2H), 2.41 (s, 3H), 2.38 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 163.2, 163.1, 140.9, 140.3, 139.2, 137.2, 136.0, 134.2, 130.3, 129.9, 129.5, 129.3, 129.2, 128.6, 128.5, 128.5, 128.4, 118.1, 94.2, 93.9, 21.4, 21.3.

*3,3-Di-p-tolylacrylonitrile (**5r**).* The resultant residue was purified by flash silica gel column chromatography to afford **5n** (22.3 mg, 96%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.31 (m, 2H), 7.23 (s, 2H), 7.20−7.15 (m, 4H), 5.65 (s, 1H), 2.41 (s, 3H), 2.38 (s, 3H). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 163.1, 140.7, 140.2, 136.3, 134.3, 129.5, 129.3, 129.1, 128.5, 118.3, 93.3, 21.4, 21.3.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01633.

General remarks, crystal preparation and X-ray diffraction analysis, ^{1}H and ^{13}C NMR spectra of the products (PDF)

Crystallographic file of **5h** (CIF)

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Notes

The authors declare no competing financial interest.

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