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Nickel-Catalyzed Arylcyanation of Alkynes

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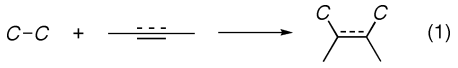
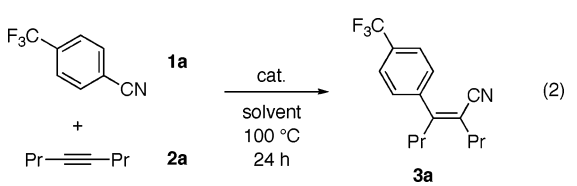
Increasing demand for "green chemistry" urges development of novel carbon−carbon bond-forming reactions with defined chemo- and stereoselectivity and high atom economy.[1] In this regard, transition metal-catalyzed cleavage and direct addition of C−C single bonds, namely, simultaneous formation of two C−C bonds without forming byproducts should be of great synthetic potential as depicted in eq 1. Nevertheless, reported examples of such reactions rely totally on the release of strain energy to cleave the C−C bonds and thus lack generality.[2]



(1)

Whereas C−CN bonds that are very common and abundant in many organic molecules are shown to be cleavable upon treatment with certain transition metal complexes,[3] catalytic reactions utilizing these elemental reactions are limited to decarbonylation of acyl cyanides[4] and cross-coupling reaction of aryl cyanides;[5] the addition reaction of acyl cyanides across arylacetylenes is suggested to proceed through acylation of terminal alkynes followed by hydrocyanation of the resulting alkynyl ketones via conjugate addition.[6] Herein, we report that cleavage and addition reaction of aryl-CN bonds across alkynes takes place effectively to give various β-aryl-substituted alkenenitriles.

We first screened effective conditions for an equimolar reaction of 4-trifluoromethylbenzonitrile (**1a**) with 4-octyne (**2a**) in toluene at 100 °C (eq 2 and Table 1). Of many catalysts examined, we found that a combination of $Ni(cod)_2$ with PMe_3 was optimum to give expected (*Z*)-3-(4-trifluoromethylphenyl)-2-propyl-2-hexenenitrile (**3a**) in 80% yield (entry 1). A similar catalyst prepared in situ from air-stable $(Me_3P)_2NiCl_2$ and DIBAL-H also effected the reaction (entry 2). Yields were lower when methyl groups in PMe_3 were substituted by phenyls (entries 3−5); use of other trialkylphosphines such as PBu_3, PCy_3, and $P(t\text{-}Bu)_3$ (entries 6−8) and use of polar solvents, 1,4-dioxane and DMF (entries 9 and 10) also gave inferior results. Bidentate ligands, $Me_2P(CH_2)_2PMe_2$ and 2,2′-bipyridyl, or other metal complexes such as $Cp(\eta^3\text{-allyl})Pd$, $Pt(cod)_2$, $[RhCl(cod)]_2$, and $[IrCl(cod)]_2$ along with PMe_3 completely retarded the catalytic reaction.



(2)

With the optimized conditions in hand, we next studied the scope of the reaction (Table 2). Benzonitriles having an electron-withdrawing substituent at the 4-position reacted effectively with 4-octyne (**2a**) in good to excellent yields. A wide variety of functional groups including fluoro, keto, ester, and formyl were tolerated to give the corresponding arylcyanation products (entries 1−4). The reaction of 1,4-dicyanobenzene proceeded at one C−CN bond exclusively with an equimolar amount of **2a** (entry 5), whereas use of 2.0 mol equiv of **2a** gave a double addition product (entry 18). Electron-neutral and -donating substituents at the 4-position also allowed the reaction to proceed successfully, but at slower rate (entries 6−9), suggesting that oxidative addition of the C−CN bonds to Ni(0) might be a rate-determining step. It is worth noting that a boryl group that is convertible to various organic groups by the Suzuki−Miyaura coupling survived the present conditions (entry 10). Meta- and ortho-substituents did not affect the reaction (entries 11−16). Pyridine could be introduced (entry 17). Alkenyl cyanides such as acrylonitrile and fumaronitrile did not afford any adducts under the present reaction conditions.

Table 1. Arylcyanation of 4-Octyne

entry	catalyst	solvent	yield of **3a** (%)[a]
1	$Ni(cod)_2$/2 PMe_3	toluene	84 (80)[b]
2	$(Me_3P)_2NiCl_2$/2 DIBAL-H	toluene	80
3	$Ni(cod)_2$/2 PMe_2Ph	toluene	76
4	$Ni(cod)_2$/2 $PMePh_2$	toluene	44
5	$Ni(cod)_2$/2 PPh_3	toluene	31
6	$Ni(cod)_2$/2 PBu_3	toluene	30
7	$Ni(cod)_2$/2 PCy_3	toluene	35
8	$Ni(cod)_2$/2 $P(t\text{-}Bu)_3$	toluene	13
9	$Ni(cod)_2$/2 PMe_3	1,4-dioxane	60
10	$Ni(cod)_2$/2 PMe_3	DMF	47

[a] Determined by ^{19}F NMR using 4-F_3C−C_6H_4−I as an internal standard. [b] Isolated yield.

We further examined the scope of alkynes using methyl 4-cycanobenzoate. 2-Butyne reacted similarly (entry 19); an unsymmetrical alkyne 4-methyl-2-pentyne gave a mixture of regioisomers **3u** and **4u** (entry 20), whereas 4,4-dimethyl-2-pentyne gave adduct **3v** with complete regioselectivity (entry 21); 2-hexynyl methyl ether gave a 63:37 mixture of two regioisomers, **3w** and **4w** (entry 22). Terminal alkynes, such as 1-octyne and phenylacetylene, failed to participate in the reaction due presumably to rapid oligomerization and/or trimerization of alkynes.

We propose a mechanism involving the oxidative addition of a C−CN bond of arenecarbonitrile to Ni(0), giving Ni(II) complex **6** via possible π-coordinating intermediate **5** (Scheme 1).[7] Subsequent insertion of an alkyne takes place at the Ni−CN bond (cyanonickelation), giving alkenylnickel **7**, which reductively eliminates an arylcyanation product and regenerates the Ni(0). Although insertion of an alkyne into the Ni−Ar bond (arylnickelation) forming **8** cannot be ruled out, the cyanonickelation pathway better explains the regioselection that favors the formation of **3u** or **3v** over **4u** or **4v**, respectively (entries 20 and 21 of Table 2), by steric reason that the Ni center prefers to locate far from the bulky isopropyl or *tert*-butyl group.

In conclusion, we have demonstrated the first example of arylcyanation of alkynes giving β-aryl-substituted alkenenitriles,

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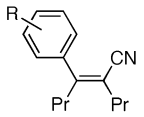
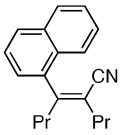
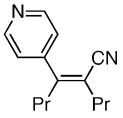
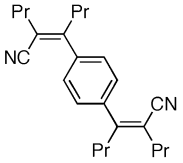
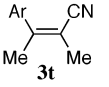
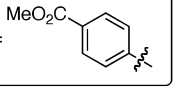
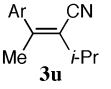
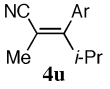
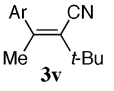
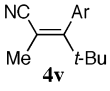
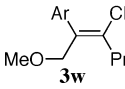
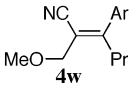
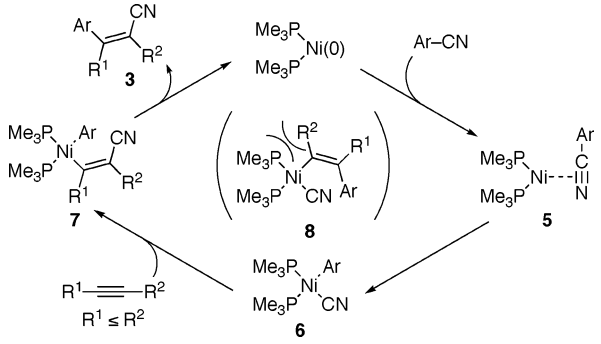
Table 2. Ni(cod)$_2$−PMe$_3$-Catalyzed Arylcyanation of Alkynes[a]

entry	product(s)		time (h)	yield (%)
1		R = 4-F (**3b**)	30	81
2		4-C(O)Me (**3c**)	30	73
3		4-CO_2Me (**3d**)	24	96
4		4-CHO (**3e**)	25	67
5		4-CN (**3f**)	19	67
6		H (**3g**)	45	64
7		4-Me (**3h**)	40	70
8		4-Ph (**3i**)	45	78
9		4-MeO (**3j**)	111	54
10		4-B(pin) (**3k**)	30	61
11		3-MeO (**3l**)	38	70
12		3,5-(MeO)$_2$ (**3m**)	92	76
13		3,4,5-(MeO)$_3$ (**3n**)	47	67
14		2-CF_3 (**3o**)	159	76
15		4-F-2-Me (**3p**)	26	62
16		**3q**	48	61
17		**3r**	24	85
18[b]		**3s**	22	80
19	 **3t**	Ar = 	20	70
20[c]	 **3u** + 62:38  **4u**		26	84
21[c]	 **3v** + >99:1  **4v**		86	59
22[c]	 **3w** + 63:37  **4w**		67	59

[a] Reactions were carried out using an aryl cyanide (1.0 mmol), an alkyne (1.0 mmol), Ni(cod)$_2$ (0.10 mmol), and PMe$_3$ (0.20 mmol) in toluene at 100 °C. [b] Performed with 2.0 mmol of **2a**. [c] Ratio of isomers was determined by GC analysis.

potential intermediates of biologically active compounds as well as organic materials. Efforts for expansion of the scope and elaboration of the detailed mechanism are currently under way in our laboratories.

Scheme 1. Plausible Mechanism of the Arylcyanation



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Supporting Information Available: Detailed experimental procedures including spectroscopic and analytical data. This material is available free of charge via the Internet at http:/pubs.acs.org.

References

(1) Trost, B. M. *Science* **1991**, *254*, 1471−1477.
(2) (a) Noyori, R.; Odagi, T.; Takaya, H. *J. Am. Chem. Soc.* **1970**, *92*, 5780−5781. (b) Noyori, R.; Kumagai, Y.; Umeda, I.; Takaya, H. *J. Am. Chem. Soc.* **1972**, *94*, 4018−4020. (c) Baba, A.; Ohshiro, Y.; Agawa, T. *J. Organomet. Chem.* **1976**, *110*, 121−127. (d) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1991**, *113*, 2771−2772. (e) Kondo, T.; Kaneko, Y.; Taguchi, Y.; Nakamura, A.; Okada, T.; Shiotsuki, M.; Ura, Y.; Wada, K.; Mitsudo, T. *J. Am. Chem. Soc.* **2002**, *124*, 6824−6825. (f) Murakami, M.; Itahashi, T.; Ito, Y. *J. Am. Chem. Soc.* **2002**, *124*, 13976−13977. (g) Matsuda, T.; Fujimoto, A.; Ishibashi, M.; Murakami, M. *Chem. Lett.* **2004**, 876−877.
(3) (a) Parshall, G. W. *J. Am. Chem. Soc.* **1974**, *96*, 2360−2366. (b) Morvillo, A.; Turco, A. *J. Organomet. Chem.* **1981**, *208*, 103−113. (c) Favero, G.; Morvillo, A.; Turco, A. *J. Organomet. Chem.* **1983**, *241*, 251−257. (d) Abla, M.; Yamamoto, T. *J. Organomet. Chem.* **1997**, *532*, 267−270. (e) Churchill, D.; Shin, J. H.; Hascall, T.; Hahn, J. M.; Bridgewater, B. M.; Parkin, G. *Organometallics* **1999**, *18*, 2403−2406. (f) García, J. J.; Brunkan, N. M.; Jones, W. D. *J. Am. Chem. Soc.* **2002**, *124*, 9547−9555. (g) Taw, F. L.; Mueller, A. H.; Bergman, R. G.; Brookhart, M. *J. Am. Chem. Soc.* **2003**, *125*, 9808−9813. (h) Nakazawa, H.; Kawasaki, T.; Miyoshi, K.; Suresh, C. H.; Koga, N. *Organometallics* **2004**, *23*, 117−126. (i) Liu, Q.-X.; Xu, F.-B.; Li, Q.-S.; Song, H.-B.; Zhang, Z.-Z. *Organometallics* **2004**, *23*, 610−614. (j) Brunkan, N. M.; Brestensky, D. M.; Jones, W. D. *J. Am. Chem. Soc.* **2004**, *126*, 3627−3641. (k) García, J. J.; Arévalo, A.; Brunkan, N. M.; Jones, W. D. *Organometallics* **2004**, *23*, 3997−4002.
(4) Murahashi, S.; Naota, T.; Nakajima, N. *J. Org. Chem.* **1986**, *51*, 898−901.
(5) (a) Miller, J. A. *Tetrahedron Lett.* **2001**, *42*, 6991−6993. (b) Miller, J. A.; Dankwardt, J. W. *Tetrahedron Lett.* **2003**, *44*, 1907−1910. (c) Miller, J. A.; Dankwardt, J. W.; Penney, J. M. *Synthesis* **2003**, 1643−1648. (d) Penney, J. M.; Miller, J. A. *Tetrahedron Lett.* **2004**, *45*, 4989−4992.
(6) Nozaki, K.; Sato, N.; Takaya, H. *J. Org. Chem.* **1994**, *59*, 2679−2681.
(7) This step has been studied in detail with (*i*-Pr)$_2$P(CH$_2$)$_2$P(*i*-Pr)$_2$ as a ligand by Jones and co-workers. See ref 3f.

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