Arylcyanation of Norbornene and Norbornadiene Catalyzed by Nickel

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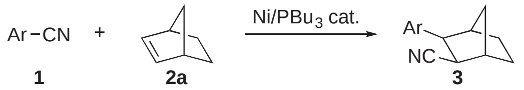
Aryl cyanides add to norbornene and norbornadiene under nickel catalysis to give (2*R**,3*S**)-3-aryl-2-cyanobicyclo[2.2.1]heptanes and (2*R**,3*S**)-3-aryl-2-cyanobicyclo[2.2.1]hept-5-enes in good yields with a general substrate scope. On the other hand, the reaction of an aryl cyanide with triethoxy(vinyl)silane gives a Heck-type arylation product, suggesting the arylnickelation pathway in the catalytic cycle.

Reactions that allow simultaneous formation of two C–C bonds in regio-, stereo-, and chemoselective manners should have innovative utility in organic synthesis. In this context, we have recently reported that direct addition reactions of aryl and allyl cyanides across alkynes and those of alkoxylcarbonyl and acyl cyanides across 1,2-dienes give variously functionalized nitriles in a single operation with perfect atom economy.[1] However, the corresponding reactions of alkenes have remained elusive, which would afford molecules endowed with two newly formed sp^3-carbon stereocenters having functional groups. Herein, we report that an aryl group and a cyano group add across norbornene and norbornadiene highly stereo- and chemoselectively under nickel catalysis, giving various (2*R**,3*S**)-3-aryl-2-cyanobicyclo[2.2.1]heptanes and (2*R**,3*S**)-3-aryl-2-cyanobicyclo[2.2.1]hept-5-enes.[2]

Initially, we examined the reaction of 4-trifluoromethylbenzonitrile (**1a**: 1.0 mmol) with norbornene (**2a**: 1.2 mmol) in toluene at 100 °C for 20 h in the presence of Ni(cod)$_2$ (5 mol %) and PBu$_3$ (10 mol %) and found that (2*R**,3*S**)-2-cyano-3-[4-(trifluoromethyl)phenyl]bicyclo[2.2.1]heptane (**3aa**) was produced in 95% yield (Table 1, Entry 1). The present conditions were found effective for the addition of a diverse range of aryl cyanides across **2a**. Electron-withdrawing functional groups including fluoro, keto, and ester were tolerated to give the corresponding adducts in good yields (Entries 2–4). In the case of 4-cyanobenzaldehyde (**1e**), use of PMe$_3$ as a ligand was important due presumably to competitive C–H activation of the formyl group under Ni/PBu$_3$ catalysis (Entry 5).[3] Electronically neutral 4-phenylbenzonitrile (**1f**) took longer reaction time for the completion of the reaction (Entry 6); electron-rich and ortho-substituted aryl cyanides required 10 mol % loadings of the catalyst to give the corresponding arylcyanation products in modest to good yields (Entries 7–11). Heteroaryl cyanides such as 3- and 4-pyridyl- and 2-furyl cyanide also participated in the reaction to give various (2*R**,3*S**)-2-cyano-3-heteroarylbicyclo[2.2.1]heptanes in good yields (Entries 13–15), whereas 2-cyanopyridine (**1l**) failed to react with **2a** and was recovered (Entry 12). 2-Cyanothiophene (**1p**) and 1-Boc-3-cyanoindole (**1q**) gave the adducts in good yields with PMe$_2$Ph as a ligand (Entries 16 and 17).

Table 1. Arylcyanation of norbornene (**2a**) catalyzed by Ni/PBu$_3$[a]



Entry	Ar	Time/h	Yield/%[b]
1	4-F$_3$C–C$_6$H$_4$ (**1a**)	20	95 (**3aa**)
2	4-F–C$_6$H$_4$ (**1b**)	20	91 (**3ba**)
3	4-Me(O)C–C$_6$H$_4$ (**1c**)	20	86 (**3ca**)
4	4-MeO$_2$C–C$_6$H$_4$ (**1d**)	20	89 (**3da**)
5[c]	4-H(O)C–C$_6$H$_4$ (**1e**)	38	56 (**3ea**)
6	4-Ph–C$_6$H$_4$ (**1f**)	54	67 (**3fa**)
7[d]	4-Me–C$_6$H$_4$ (**1g**)	77	84 (**3ga**)
8[d]	4-MeO–C$_6$H$_4$ (**1h**)	77	76 (**3ha**)
9[d]	3,4,5-(MeO)$_3$–C$_6$H$_2$ (**1i**)	54	66 (**3ia**)
10[d]	2-F$_3$C–C$_6$H$_4$ (**1j**)	77	55 (**3ja**)
11[d]	5-F-2-Me–C$_6$H$_3$ (**1k**)	77	73 (**3ka**)
12	2-Pyridyl (**1l**)	—	<5 (**3la**)
13	3-Pyridyl (**1m**)	48	88 (**3ma**)
14	4-Pyridyl (**1n**)	48	92 (**3na**)
15	2-Furyl (**1o**)	48	94 (**3oa**)
16[e]	2-Thienyl (**1p**)	48	90 (**3pa**)
17[e]	1-Boc-3-indolyl (**1q**)	48	71 (**3qa**)

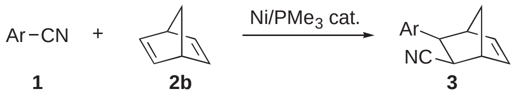
[a]Reactions were carried out in toluene (0.60 mL) using an aryl cyanide (1.00 mmol) and **2a** (1.20 mmol) in the presence of Ni(cod)$_2$ (50 µmol) and PBu$_3$ (0.100 mmol). [b]Isolated yields based on an aryl cyanide. [c]PMe$_3$ (0.100 mmol) was used as a ligand. [d]**2a** (1.50 mmol), Ni(cod)$_2$ (0.100 mmol), and PBu$_3$ (0.20 mmol) were used. [e]PMe$_2$Ph (0.100 mmol) was used as a ligand.

Carbocyanation of norbornadiene (**2b**) would be also synthetically valuable since the resulting (2*R**,3*S**)-2-cyano-3-organobicyclo[2.2.1]hept-5-enes would find further applications as precursors for functionalized cyclopentanes or monomers for ring-opening metathesis polymerization.[4] Although the standard conditions were not applicable to arylcyanation of **2b**, the expected arylcyanation product **3ab** was obtained in 77% yield when the reaction of **1a** with **2b** was conducted in the presence of Ni(cod)$_2$ (5 mol %) and PMe$_3$ (15 mol %) (Table 2, Entry 1).[5] The same catalyst system was further applied to the reactions of electron-poor aryl cyanides and heteroaryl cyanides to give the corresponding adducts in modest to good yields (Entries 2–7), whereas those of electron-neutral or -rich aryl cyanides were sluggish (<20%) due presumably to reluctant oxidative addition of unactivated aryl cyanides to Ni(0)/3PMe$_3$. None of double addition products were observed in all cases.

The arylcyanation product **3ab** underwent retro-Diels–Alder reaction at 190 °C in xylene to give (*Z*)-2-[4-(trifluoromethyl)-phenyl]acrylonitrile [(*Z*)-**5**] along with a small amount of (*E*)-**5** that might be derived from thermal isomerization of (*Z*)-**5**.[6] In addition, oxidative cleavage of the remaining double bond in **3ab** followed by treatment with Me$_3$SiCHN$_2$ afforded functionalized cyclopentane **6** in a stereospecific manner (Scheme 1).

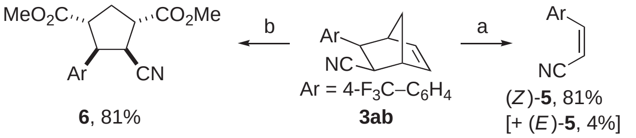
Although other bicyclic alkenes such as *N*-Boc-7-azabicyclo[2.2.1]heptene and bicyclo[2.2.2]octene as well as simple alkenes such as styrene, 1-hexene, and cyclopentene failed to give

Table 2. Arylcyanation of norbornadiene (**2b**) catalyzed by Ni/PMe_3[a]



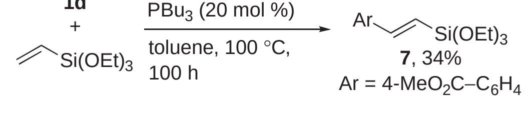
Entry	Ar	Time/h	Yield/%[b]
1	4-F_3C–C_6H_4 (**1a**)	21	77 (**3ab**)
2	4-Me(O)C–C_6H_4 (**1c**)	19	51 (**3cb**)
3	4-MeO_2C–C_6H_4 (**1d**)	24	52 (**3db**)
4	4-Pyridyl (**1n**)	20	60 (**3nb**)
5[c]	2-Furyl (**1o**)	21	81 (**3ob**)
6	2-Thienyl (**1p**)	35	79 (**3pb**)
7	1-Boc-3-indolyl (**1q**)	35	34 (**3qb**)

[a] Reactions were carried out in toluene (0.67 mL) using an aryl cyanide (1.00 mmol) and **2b** (1.50 mmol) in the presence of $Ni(cod)_2$ (50 µmol) and PMe_3 (0.150 mmol). [b] Isolated yields based on an aryl cyanide. [c] $Ni(cod)_2$ (0.100 mmol) and PMe_3 (0.30 mmol) were used.



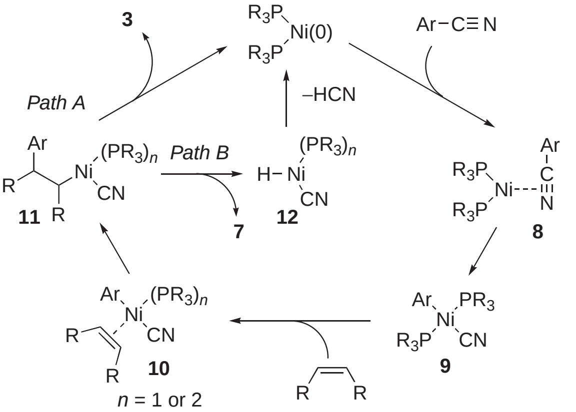
Scheme 1. Transformations of **3ab**. Reagents and Conditions: (a) xylene, 190 °C, 24 h; (b) $RuCl_3{\cdot}3H_2O$ cat., $NaIO_4$, CCl_4–CH_3CN–H_2O, 0 °C to rt, 1 h, then Me_3SiCHN_2, MeOH–C_6H_6, 35 °C, 1 h.

the desired product, methyl 4-cyanobenzoate (**1d**) reacted with triethoxy(vinyl)silane under the standard conditions and gave (*E*)-alkenylsilane **7** in 34% yield, possibly through the Heck-type reaction, the aryl cyanide acting as an arylating agent (eq 1). Formation of **7** clearly provides us with a clue on the mechanism: Arylnickelation should be involved in the catalytic cycle shown in Scheme 2. Thus, it is reasonable to assume that the reaction should be initiated by oxidative addition of an Ar–CN bond to Ni(0) giving **9** via **8**.[7] Insertion of norbornene or norbornadiene into the Ni–Ar bond followed by reductive elimination gives an arylcyanation product (path A), whereas that of triethoxy(vinyl)silane followed by *β*-hydrogen elimination appears likely to give alkenylsilane **7** (path B). As discussed previously,[8] the fact that electron density of the exo-face of norbornene is higher than that of the endo-face should be responsible for the exclusive exo-selectivity observed in the present reaction.



(1)

In summary, we have demonstrated that the arylcyanation reactions of norbornene and norbornadiene take place with a broad scope of substrates to allow a direct synthesis of (2*R**,3*S**)-3-aryl-2-cyanobicyclo[2.2.1]heptanes and (2*R**,3*S**)-3-aryl-2-cyanobicyclo[2.2.1]hept-5-enes. Also demonstrated was the Heck-type arylation of triethoxy(vinyl)silane using an aryl cyanide, suggesting that an arylnickelation pathway would be operative in the catalytic cycle. Further efforts to expand the scope of the reaction and to explore asymmetric versions are in progress.



Scheme 2. Plausible mechanism.

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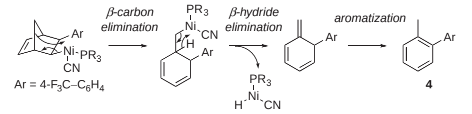
5 Use of 10 mol % of PMe_3 gave **3ab** in 48% yield and 2′-methyl-4-trifluoromethylbiphenyl (**4**) in 15% yield as estimated by ^{19}F NMR. The formation of **4** may be derived from *β*-carbon elimination followed by *β*-H elimination and aromatization as shown below. Addition of an extra amount of PMe_3 (total 15 mol %) might retard this scheme by inhibiting a requisite vacant coordination cite on the nickel center.



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