Nickel/Lewis Acid Dual Catalysis for Carbocyanation Reactions of Alkynes and Alkenes

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Contents

Abbreviations

Ac	acetyl	eq.	equation
Anis	anisyl	equiv	equivalent
Ar	aryl	Et	ethyl
aq.	aqueous	FID	flame ionization detector
Bn	benzyl	FOXAP	ferrocenyloxazolinyl-phosphine
br	broad		
Bu	butyl	GC	gas chromatography
calcd	calculated	GPC	gel permeation chromatography
cat.	catalyst		
ChiraPhos	2,3-bis(diphenylphosphino)-butane	h	hour(s)
		Hex	hexyl
cod	1,5-cyclooctadiene	HPLC	high-performance liquid chromatography
Cp	cyclopentadienyl		
Cy	cyclohexyl	HRMS	high-resolution mass spectra
d	doublet		
δ	scale (NMR)	Hz	hertz
DCM	1,2-dichloromethane	*i*	iso
DIBAL–H	diisobutylaluminumhydride	IR	infrared spectroscopy
DME	1,2-dimethoxyethane	*J*	coupling constant
DMF	*N*,*N*-dimethylformamide	L	ligand
DMPE	1,2-bis(dimethylphosphino)-ethane	LA	Lewis acid
		LDA	lithium diisopropylamide
DMSO	dimethyl sulfoxide	lit.	literature
DPPB	1,4-bis(diphenylphosphino)-butane	LUMO	lowest unoccupied molecular orbital
DPPE	1,2-bis(diphenylphosphino)-ethane	m	multiplet
		M	metal or mol perliter
dr	diastereomeric ratio	MAD	methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenolate)
ed.	edition		
ee	enantiomeric excess		
EI	electron ionization	Me	methyl

Mes	mesityl	sat.	saturated
min	minute(s)	sept	septet
mL	milliliter	sext	sextet
μL	microliter	SPhos	2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl
mp	melting point		
n	normal	t	triplet
NMR	nuclear magnetic resonance	*t*, *tert*	tertiary
NOE	nuclear Overhauser effect	temp.	temperature
Pent	pentyl	Tf	triflate
Ph	phenyl	THF	tetrahydrofuran
Phth	phthalimide	THP	tetrahydropyranyl
Pr	propyl	TLC	thin layer chromatography
q	quartet	TM	transition metal
quint	quintet	TMS	trimethylsilyl
ref.	reference	TS	transition state
R_f	relative mobility	UV	ultraviolet
rt	room temperature	wt%	weight percent
s	singlet		

Chapter 1

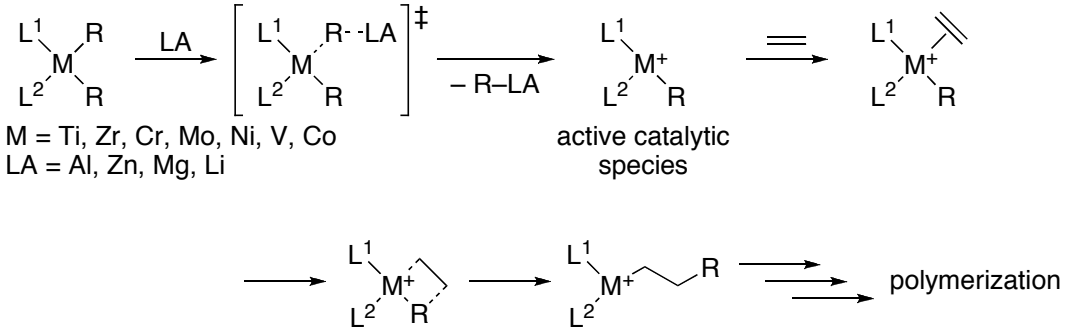
Introduction and General Summary

Organometallic catalysts have made the greatest contribution to development of a wide variety of organic transformations to allow synthesis of complex molecules that are hardly accessible by classical organic reactions. Particularly, transition metal catalysts and Lewis acid (LA) catalysts are representative. Reactions that employ transition metal catalysts allow to perform novel reactions such as cross-coupling, the Tsuji–Trost allylation, and hydro- and carbometalation. Catalysis in these transformations generally involves oxidation and reduction of transition metals, allowing activation and formation of a variety of bonds in revolutionary manners as compared with conventional organic reactions.

In contrast, LAs activate carbonyls and unsaturated bonds through binding to lone pair or π electrons of these substrates, mediating electrophilic transformations such as the Friedel–Crafts reaction, the ene reaction, the Diels–Alder reaction, and the Mukaiyama aldol reaction. Cooperative catalysis of these two different metal catalysts should be versatile to uncover novel transformations of organic molecules and to open a new paradigm in modern organic synthesis.

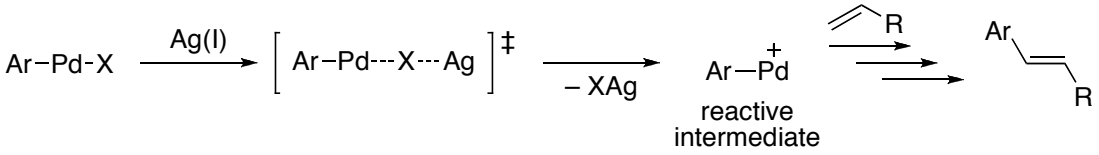
Activation of transition metal catalysts by Lewis a cids

Transition metal complexes upon co-use of LAs often generate highly reactive transition metal intermediates. For example, the Zieglar–Natta catalyst for olefin polymerization is typically made by treatment of transition metal salts like Ti(IV) and Zr(IV) with LAs like Me_2AlX to form the corresponding cationic transition metal species that serve as highly active catalysts for polymerization through sequential coordination and migratory insertion of olefin monomers (Scheme 1).[1]



Scheme 1. Zieglar–Natta-type catalysts in olefin polymerization.

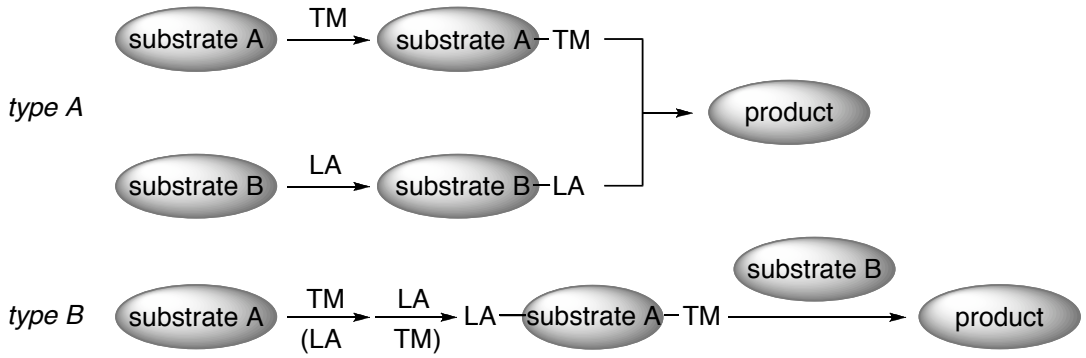
It is also well-known that a silver(I) ion abstracts a halogen ligand bound to palladium(II) intermediates in the Mizoroki–Heck reaction and enhances the electrophilicity. Indeed, the resulting cationic Pd(II) species bind more efficiently to alkene substrates to promote coordination and migratory insertion of the alkenes (Scheme 2).[2]



Scheme 2. Silver/palladium-promoted Mizoroki–Heck reaction.

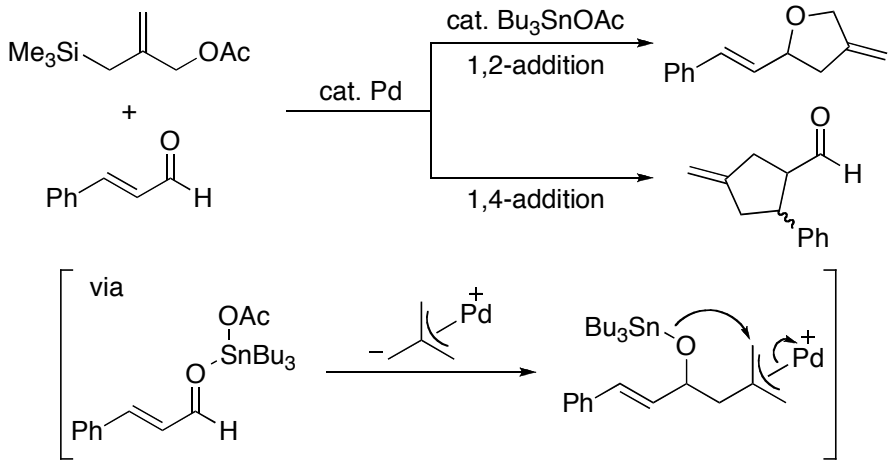
Activation of substrates by Lewis acids in transition metal-catalyzed reactions

Another type of combined use of transition metal and LA catalysts is exemplified by transition metal-catalyzed transformations of LA-activated substrates.[3] Such cooperative catalysis can be categorized further into two types shown in Scheme 3. One involves two or more substrates activated independently by a transition metal complex and LA to give respective reaction intermediates, which then react together to give a product (Scheme 3, type A). The other type is initiated by sequential reactions of a substrate with both a transition metal and LA, and the resulting intermediate further react with another substrate or reagent to give a product (Scheme 3, type B).



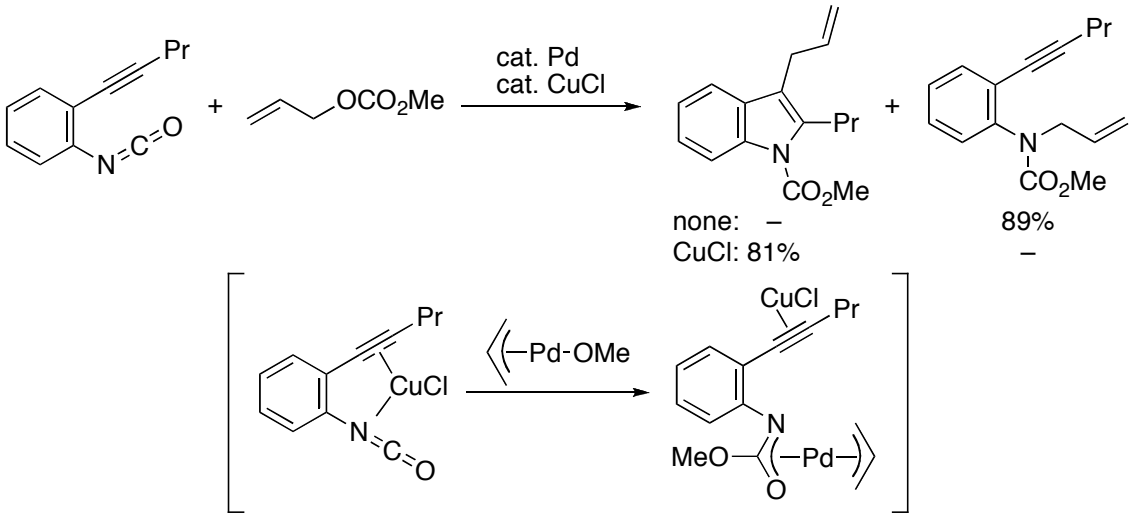
Scheme 3. Cooperative transition metal/LA catalysis for substrate activation.

An example of type A is the reaction of 2-(trimethylsilylmethyl)allyl acetate with α,β-unsaturated carbonyl compounds. Palladium/Bu_3SnOAc catalysis gives 1,2-adducts,[4] whereas Pd catalyst only gives 1,4-adducts (Scheme 4).[5] In the proposed catalytic cycle, palladium(0) activates the allylic acetate to give a palladium–trimethylenemethane (Pd–TMM) complex, which reacts with the electrophile activated by the tin(IV) LA in a 1,2-fashion.



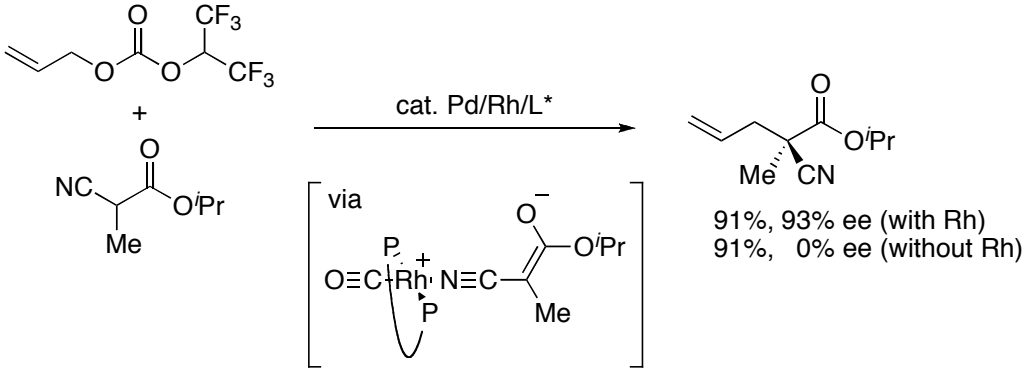
Scheme 4. Cycloaddition of 2-(trimethylsilylmethyl)allyl acetate to enals.

Another example of the heterobimetallic catalysis is found in the palladium/copper-catalyzed allylation reaction of *O*-alkynylphenyl isocyanates (Scheme 5).[6] A copper salt is supposed to act as the LA catalyst to activate the isocyanate and/or alkyne to react with a π-allylpalladium intermediate.



Scheme 5. Pd/Cu-catalyzed indole synthesis from isocyanates and allyl carbonates.

An enantioselective allylic alkylation is achieved by cooperative catalysis of palladium/rhodium and a chiral phosphorous ligand (Scheme 6).[7] The chiral rhodium catalyst is assumed to coordinate to the cyano group in α-cyanopropionate, and thereby controlling facial selectivity of the resulting prochiral enolates. In the absence of rhodium and in the presence of only Pd/L* the enantioselection is null.

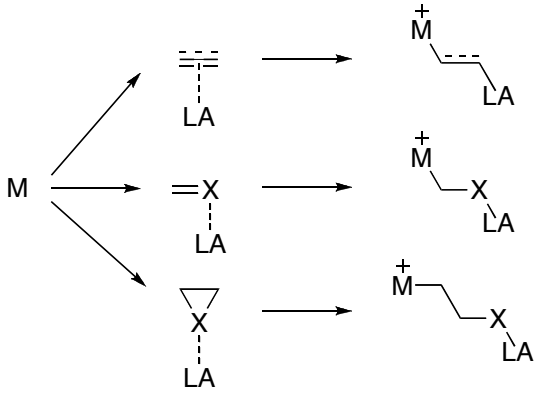


Scheme 6. Pd/Rh-catalyzed enantioselective allylation of α-cyanopropionate.

Examples of type B (Scheme 3) will be discussed in the subsequent sections.

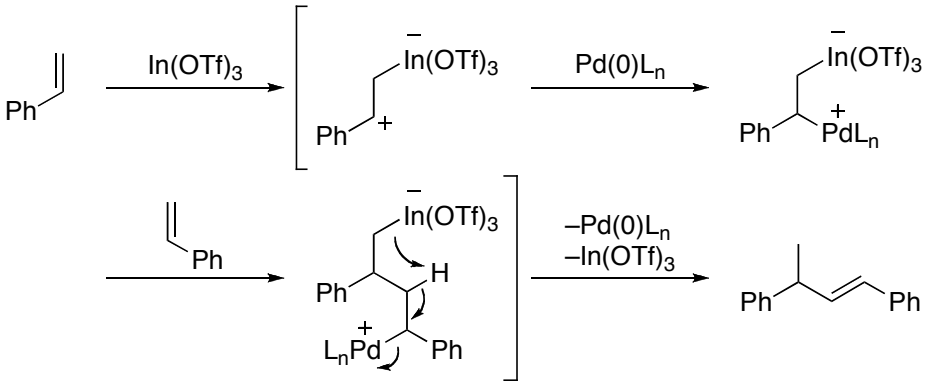
Combination of Lewis acid and nucleophilic transition metal complex

Nucleophilic activation of unsaturated bonds by transition metal catalysts and its application to synthetic transformations remain elusive compared with electrophilic activation typically observed in the Wacker oxidation. A few such examples involve activation of unsaturated C–C bonds, carbonyls/imines, and epoxides/aziridines by transition metal/LA catalysis to generate new organometallic species that undergo further transformations (Scheme 7).



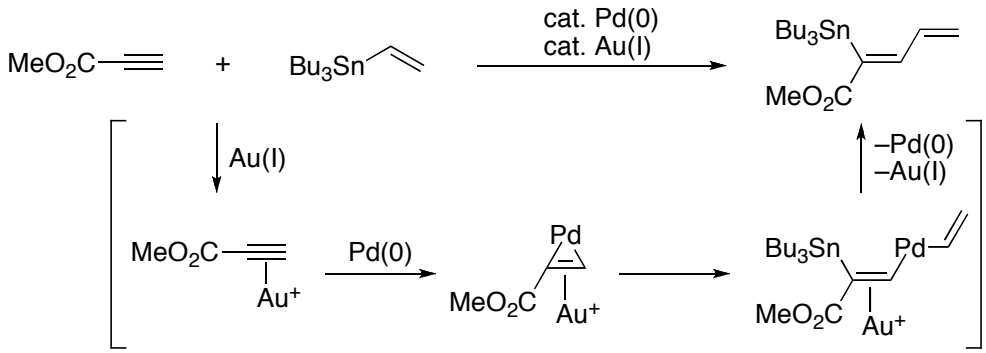
Scheme 7. Nucleophilic activation of LA–substrate complexes by transition metal complexes.

For example, vinylarenes undergo dimerization upon activation with palladium/$In(OTf)_3$ (Scheme 8).[8]



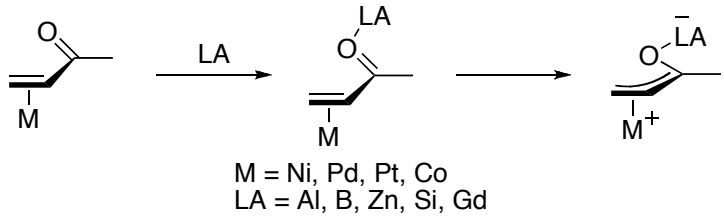
Scheme 8. Dimerization of vinylarenes catalyzed by palladium/$In(OTf)_3$.

Electron-poor alkynes also couple with organostannanes by Pd/Au dual catalysis to give alkyne–carbostannylation products (Scheme 9).[9] In both cases, LA catalysts are supposed to lower LUMO of the unsaturated bonds to promote oxidative addition of Pd(0) to the LA-activated vinylarenes and alkynes.



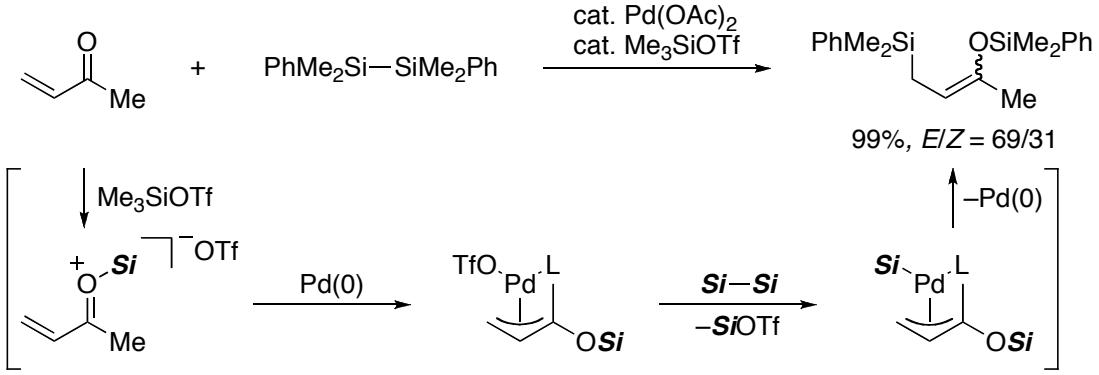
Scheme 9. Palladium/gold-catalyzed alkyne–vinylstannylation.

Activation of conjugate enones has been achieved by a wide variety of combinations of transition metals and LAs to afford η^3-oxoallylmetal complexes, which can be further applied to catalytic C–C, C–Si, and C–B bond forming reactions (Scheme 10).[10]



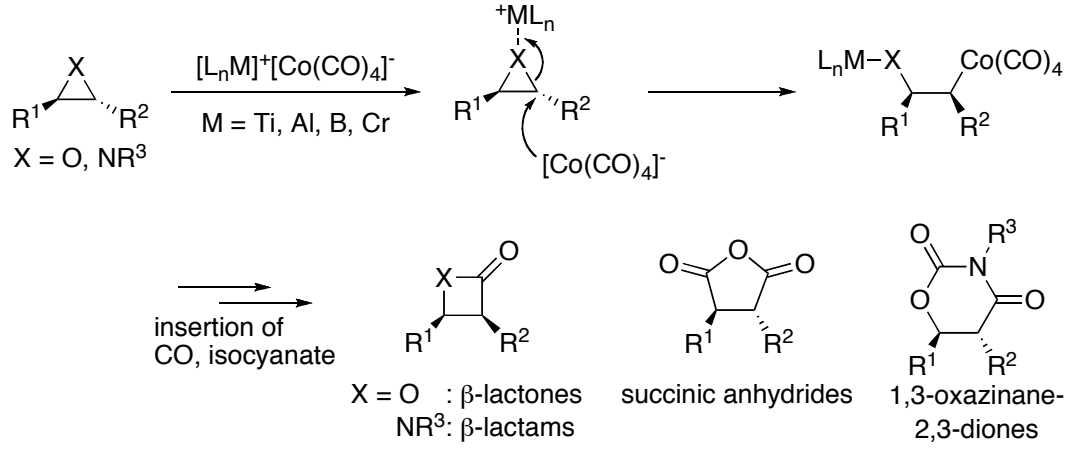
Scheme 10. Cooperative activation of conjugate enones by transition metal/LA.

Thus, palladium/Me_3SiOTf-catalyzed bissilylation of α,β-unsaturated carbonyl compounds is achieved through such cooperative activation of the electrophile (Scheme 11).[10f]



Scheme 11. Palladium/Me_3SiOTf-catalyzed bissilylation of 3-penten-2-one.

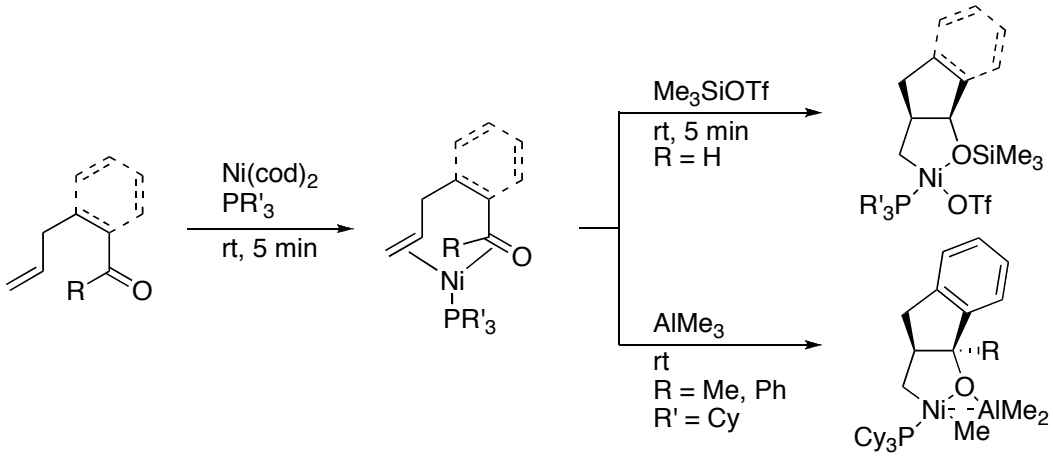
Anionic cobalt complexes oxidatively add to epoxides and aziridines upon activation by LA (Scheme 12).[11] The resulting organocobalt species undergo insertion of CO or isocyanates to give heterocycles such as β-lactone, β-lactam, succinic anhydride, and 1,3-oxazinane-2,4-dione derivatives.



Scheme 12. Cooperative activation of epoxides and aziridines by cobalt/LA catalysis.

Acceleration of oxidative cyclization of transition metals and unsaturated substrates by Lewis acid

Nickel-catalyzed multi-component reductive coupling reaction involving carbonyls and olefins/acetylenes has received increasing attention, because the transformation allows rapid assembly of complex carbon frameworks from simple substrates.[12] The oxidative cyclization on nickel(0) giving nickelacycle intermediates is proposed to be a crucial step and reported to be accelerated by LA. For example, intramolecular oxidative cyclization of alkenes and carbonyls is promoted significantly by LA, whereas the absence of LA requires higher temperatures and longer reaction times (Scheme 13).[13]



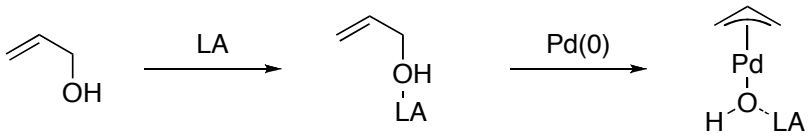
Scheme 13. Oxidative cyclization of alkene and carbonyl moieties by Ni(0) and LA.

Similar nickelacycle formation is accelerated by a zinc(II) as the LA cocatalyst as exemplified by the nickel-catalyzed coupling reaction of enones, alkynes and $ZnMe_2$.[14]

Lewis acid-promoted oxidative addition of carbon–oxygen or carbon–hydrogen bonds to transition metal complexes

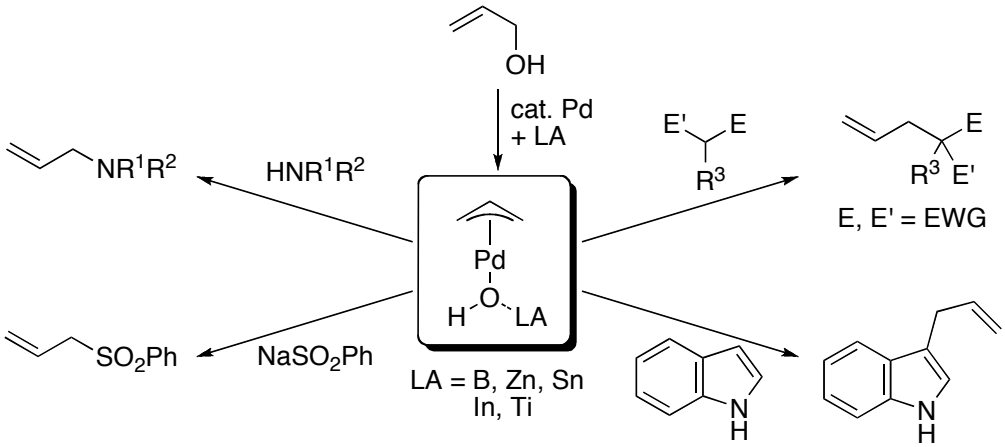
Oxidative addition is one of the most important and fundamental elemental step of transition metal catalysis. However, it is not common with unreactive bonds such as C–H, C–C, and C–O bonds. Thus, oxidative addition of such inert chemical bonds by transition metal/LA cooperative catalysis, if easily attained, would allow many novel catalytic transformations. For example, coordination of the hydroxy group in allylic alcohols to LA allows palladium complexes to undergo oxidative addition to the C–O

bonds directly to afford π-allylpalladium intermediates, which are otherwise generated only from allylic carboxylates or carbonates (Scheme 14). Enhancement of the leaving group potential of a hydroxy group by LA coordination is definitely responsible for this activation.



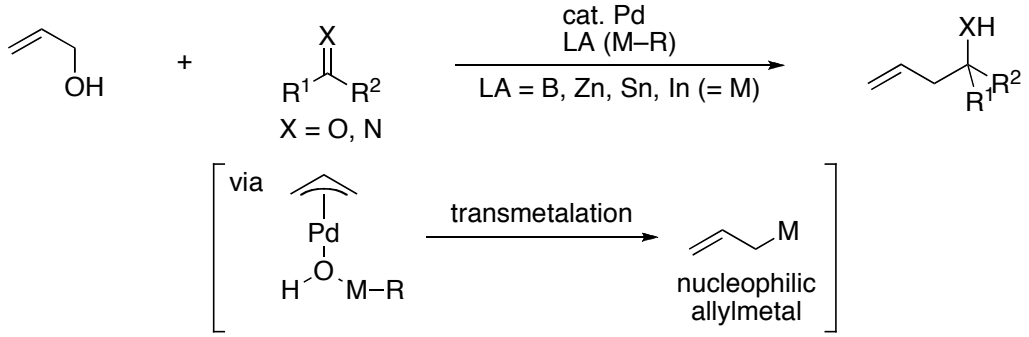
Scheme 14. Activation of C–O bond in allylic alcohols by palladium/LA.

The resulting π-allylpalladium intermediates can participate in a wide variety of transformations with nucleophiles including amines,[15,16] sulfinates,[17] malonates,[18] enolates,[19] and electron-rich hetreroarenes[20] (Scheme 15).



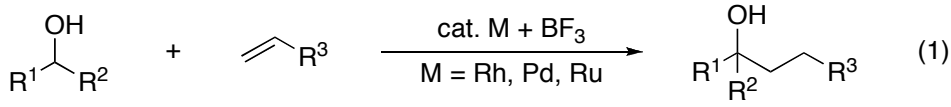
Scheme 15. Allylic substitution reactions by palladium/LA catalysis.

In the absence of nucleophiles, on the other hand, the π-allylpalladium intermediates undergo transmetalation with LA to give allylmetals,[21] which participate in nucleophilic carbonyl addition reactions to afford homoallylic alcohols[22] and amines[23] (Scheme 16). Thus, the overall transformation is umpolung of allylic reagents.



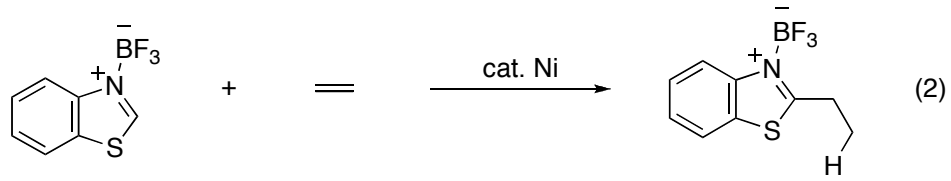
Scheme 16. Palladium/LA-mediated umpolung of allylic alcohols.

Oxidative addition of C–H bonds can also be assisted by LA. For example, activation of C–H bonds next to alcoholic oxygen is promoted by LA to effect transition metal-catalyzed α-alkylation of alcohols with an alkene as the alkylating agent (eq. 1).[24]



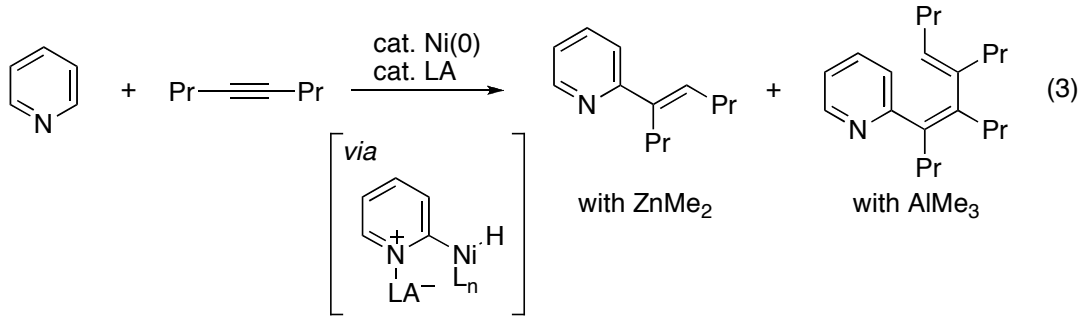
Similarly, rhodium-catalyzed C–H bond alkylation of cyclic ethers is promoted by LA.[25]

The C(2)–H bond in a benzothiazole–BF_3 complex is activated by a nickel catalyst through oxidative addition to allow direct C-2 ethylation using ethylene (eq. 2).[26] The BF_3 coordination likely enhances the acidity of the C(2)–H bond to undergo oxidative addition to nickel(0), whereas uncomplexed benzothiazole failed to undergo the alkylation under the similar conditions.



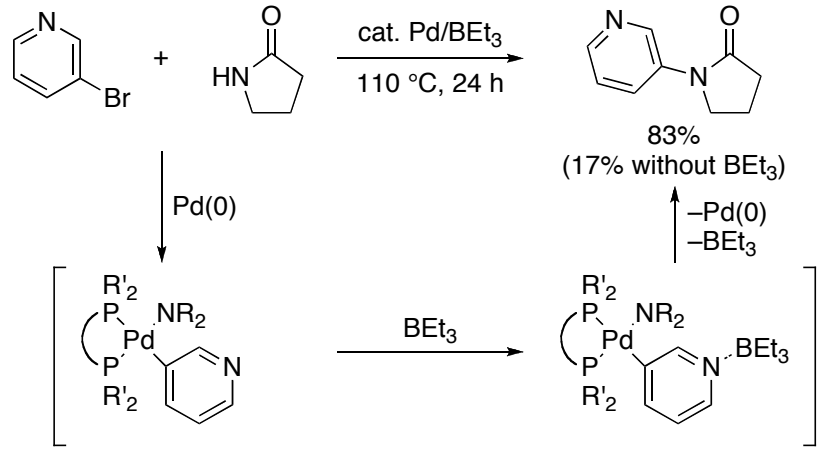
Even a catalytic amount of LA can effect similar nickel-catalyzed reactions of heteroarenes. For example, C(2)-alkenylation of pyridine is catalyzed cooperatively by nickel/LA (eq. 3).[27] Oxidative addition of the C(2)–H bond of pyridine coordinating to

LA catalysts is proposed. Similar Ni/LA catalysts are also effective for C–H alkenylation and alkylation of imidazoles,[28] pyridones,[29] and formamides.[30]



Reductive elimination promoted by Lewis acid

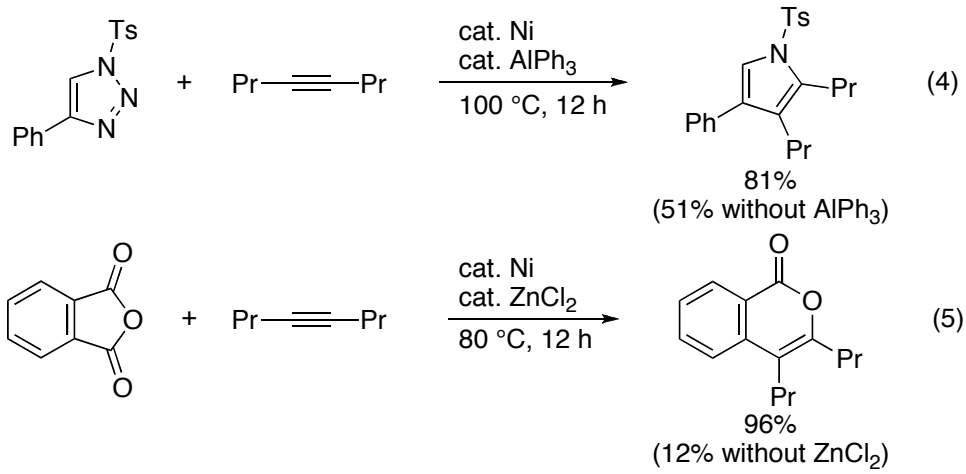
Reductive elimination reaction, a product-forming elemental step in many transition metal-catalyzed reactions, is also accelerated by LA. For example, reductive elimination of a C–N bond is dramatically accelerated by the presence of LA in the palladium-catalyzed coupling of heteroaryl bromides with amides. The reaction particularly proceeds through coordination of sp^2-nitrogen of an electron-withdrawing heteroaryl group (Scheme 17).[31]



Scheme 17. Palladium/LA-catalyzed coupling of heteroaryl halides with amides.

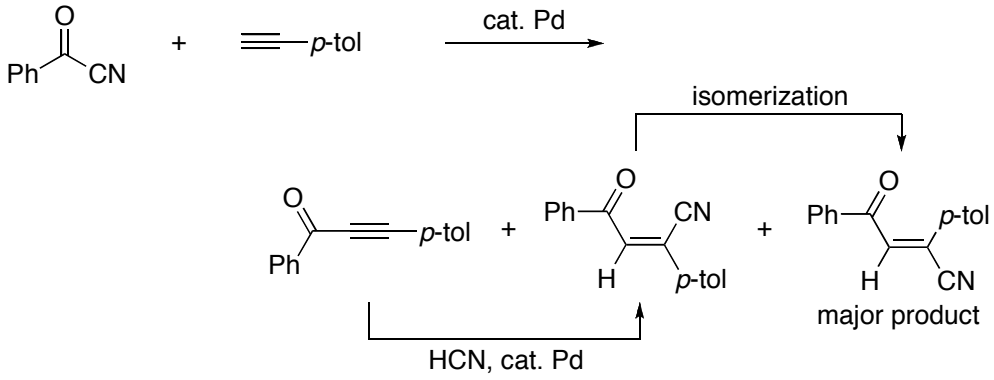
Similar acceleration of C–N and C–O bond-forming reductive elimination has also been suggested for nickel-catalyzed denitrogenative coupling of alkynes with *N*-sulfonyl-1,2,3-triazoles (eq. 4)[32] and decarbonylative coupling of alkynes with

anhydrides (eq. 5).[33] These reactions proceed smoothly only in the presence of LA cocatalysts. Thus, C–N and C–O bond-forming reductive elimination is suggested to be the rate-determining step.



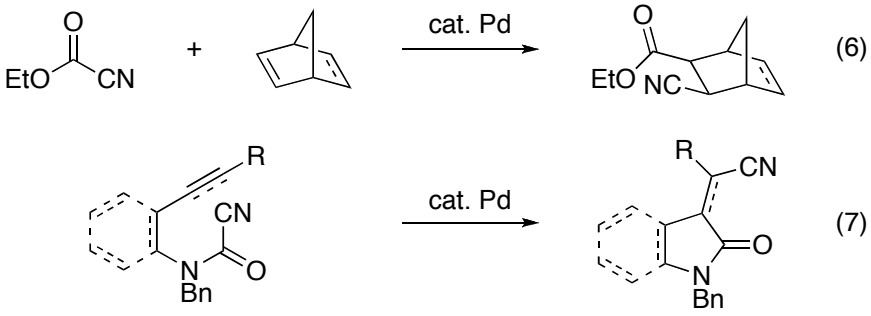
Transition metal-catalyzed carbocyanation reaction across unsaturated bonds

Cleavage of a C–CN bond[34–37] in nitriles followed by insertion of unsaturated bonds into the C–CN bond by transition metal catalysts, namely carbocyanation reaction, should be synthetically versatile, because the transformation allows simultaneous formation of both C–C and C–CN bonds without forming byproducts. A prototype of this transformation was first reported with benzoyl cyanide, terminal alkynes, and a palladium catalyst (Scheme 18).[38] However, this reaction has been suggested to proceed through benzoylation of the terminal alkynes, followed by hydrocyanation of the resulting alkynyl ketones and subsequent isomerization of the double bond thus formed. Therefore, scope of this reaction is severely limited to terminal alkynes.

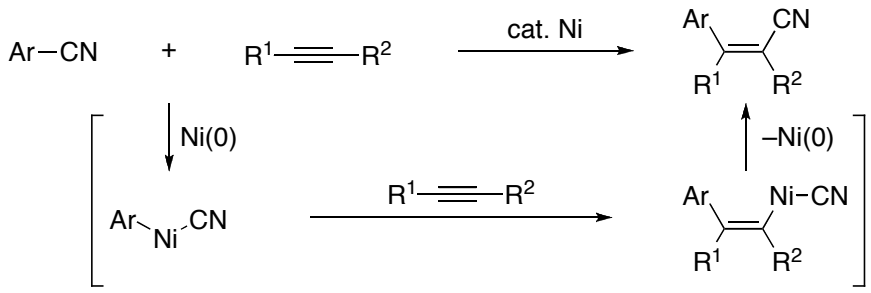


Scheme 18. Palladium-catalyzed benzoylcyanation reaction of terminal alkynes.

Recent studies have revealed that palladium catalysts are also effective for cyanoesterification of norbornadiene (eq. 6)[39] and intramolecular cyanocarbamoylation of alkynes and alkenes (eq. 7).[40]

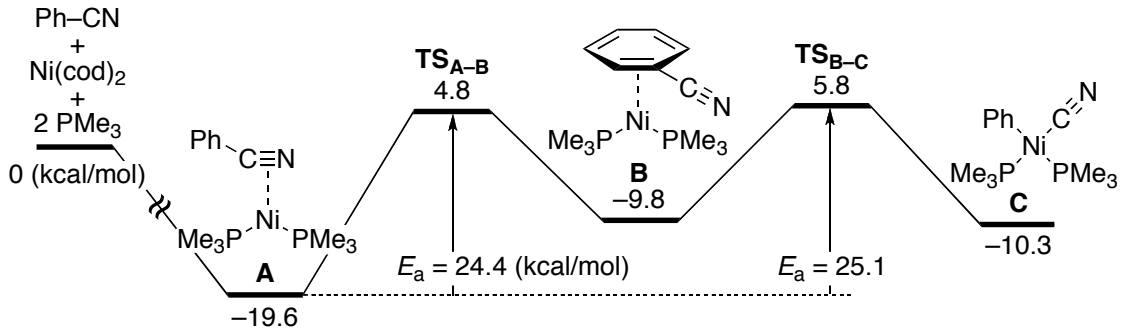


In 2004, the nickel-catalyzed addition reaction of aryl cyanides across alkynes was reported (Scheme 19).[41] A proposed catalytic cycle starts with oxidative addition of C–CN bonds of aryl cyanides to nickel(0). Subsequent coordination and insertion of alkynes followed by reductive elimination give arylcyanation products and regenerate nickel(0).



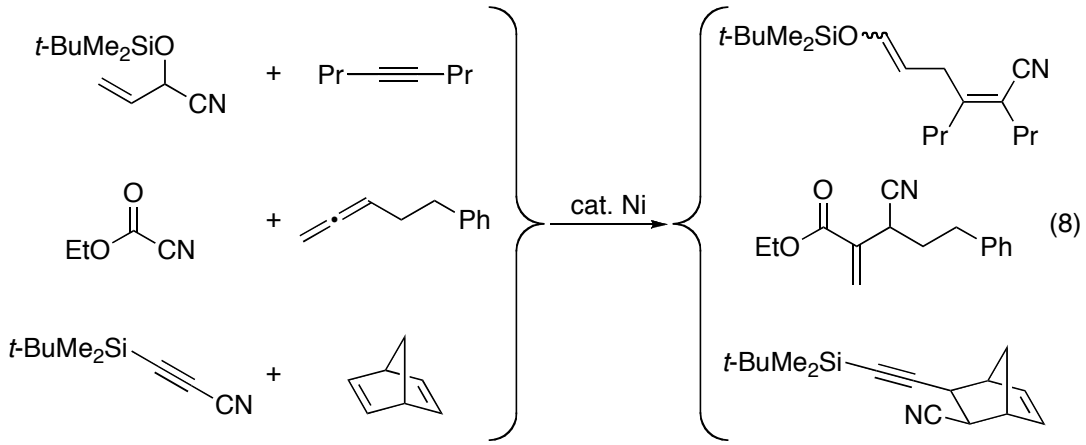
Scheme 19. Nickel-catalyzed arylcyanation reaction of alkynes.

All the intermediates as well as transition states of each elemental step have been fully identified by theoretical calculations.[42] These studies suggest that the oxidative addition of the C–CN bond to nickel(0) is rate-determining and proceeds stepwise through a formation of η^2-nitrile (**A**) and η^2-arene complex (**B**) (Scheme 20).[43]



Scheme 20. Theoretical studies on oxidative addition of Ar–CN bond to nickel(0).

Scope of nitriles for the nickel-catalyzed carbocyanation reaction is disclosed to be very broad: allyl cyanides,[44] alkoxycarbonyl cyanides,[45] and alkynyl cyanides[46] are found to participate in the reaction with alkynes, 1,2-dienes, and norbornadiene (eq. 8).

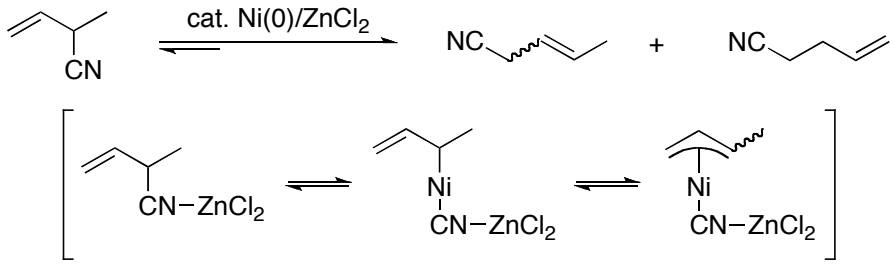


Nevertheless, the reactions required generally high catalyst loadings and harsh reaction conditions and other nitriles including alkenyl and alkyl cyanides could not be employed in this novel transformation. Accordingly, development of a more efficient catalyst system for the carbocyanation was desired.

Oxidative addition and reductive elimination of C–CN bond promoted by Lewis Acid

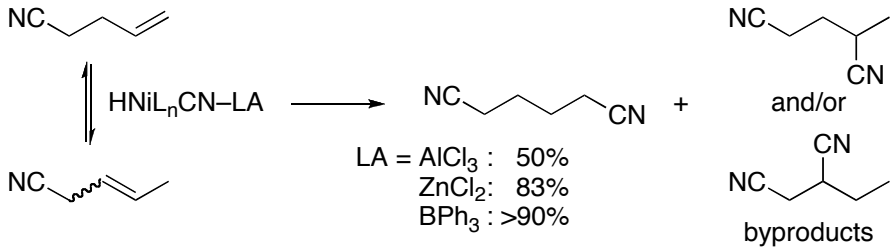
In the DuPont adiponitrile process, $ZnCl_2$ is an effective LA cocatalyst for isomerization of 2-methyl-3-butenenitrile, an initial product in the process, to

3-pentenenitrile and 4-pentenenitrile, an ultimate precursor for adiponitrile (Scheme 21).[47] This isomerization is assumed to be initiated by oxidative addition of the Zn(II)-coordinated C–CN bond to nickel(0).



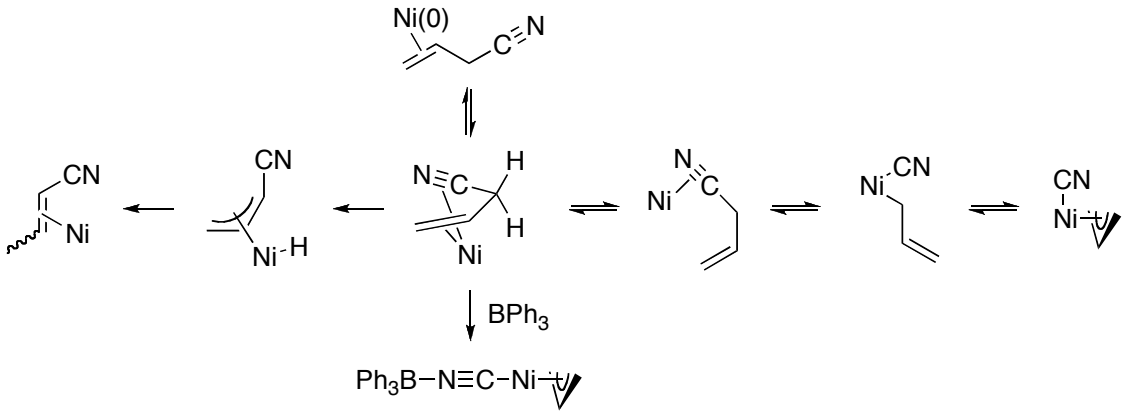
Scheme 21. Nickel/$ZnCl_2$-catalyzed isomerization of 2-methyl-3-butenenitrile to 3- and 4-pentenenitriles in the DuPont adiponitrile process.

In the above process, nickel/LA dual catalysts are considered to improve also regioselectivity of hydrocyanation of 3- and 4-pentenenitriles. A bulky LA cocatalyst like BPh_3 is suggested to be crucial for the selectivity over 90% (Scheme 22).[48]



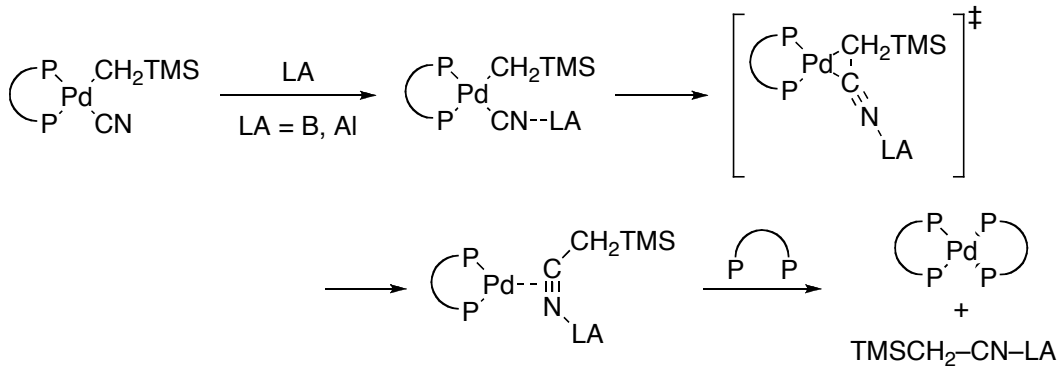
Scheme 22. Nickel/Lewis acid-catalyzed hydrocyanation of 3- and 4-pentenenitriles.

In the similar line, selective activation of the C–CN bond over the allylic C–H bond of allyl cyanide is observed with Ni/BPh_3. In the absence of BPh_3, oxidative addition to the C–CN bond competes with olefin-isomerization through C–H activation, whereas the presence of BPh_3 prefers C–CN bond activation exclusively (Scheme 23).[34q] Coordination of BPh_3 to allyl cyanide at *sp*-nitrogen enhances the electrophilicity of the C–CN bond and also stabilizes the resulting oxidative adduct, making the C–CN activation kinetically and thermodynamically favored.



Scheme 23. Oxidative addition of C–H vs. C–CN bonds in allyl cyanide to nickel(0).

Reductive elimination of a C–CN bond from (diphosphine)Pd(R)(CN) (R = CH_2TMS) is also accelerated by LA bound to the cyano group (Scheme 24).[49] The coordination induces partial positive charge on both the nitrogen and carbon atoms of the cyano group, to facilitate reductive elimination through nucleophilic attack of the alkyl group to the activated cyano carbon.

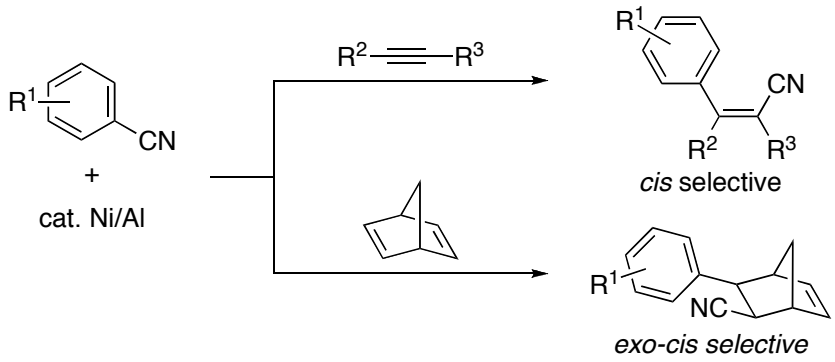


Scheme 24. Reductive elimination of C–CN bond from palladium promoted by LA.

Summary of the present Thesis

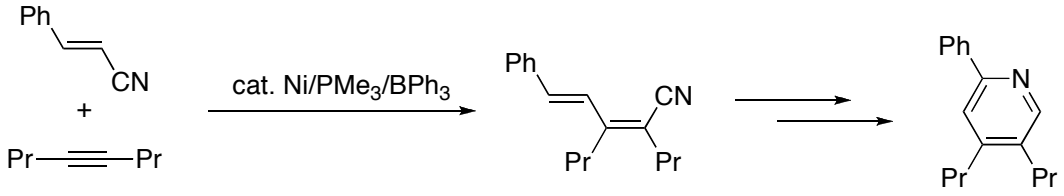
With these backgrounds in mind, the author envisioned that the co-use of a LA cocatalyst could improve the efficiency of the nickel-catalyzed carbocyanation reactions, hoping to broaden the scope of nitriles and unsaturated compounds. In fact, dramatic acceleration of the arylcyanation reaction of alkynes is achieved by nickel/LA cooperative catalysis as described in Chapter 2 (Scheme 25).[50] A wide variety of aryl

cyanides add across alkynes as well as norbornadiene in an exclusive *cis*-fashion.[51] Noteworthy is that highly electron-rich aryl cyanides, that are inert in the absence of LA, also gave the corresponding products.



Scheme 25. Nickel/LA-catalyzed arylcyanation of alkynes and norbornadiene.

Alkenyl cyanides are also found to add across alkynes for the first time to give 2,4-pentadienenitriles under a Ni/BPh_3 catalysis (Scheme 26). Some of the resulting adducts are readily converted to substituted pyridines through reduction of the cyano group followed by 6π–electrocyclization and oxidation.

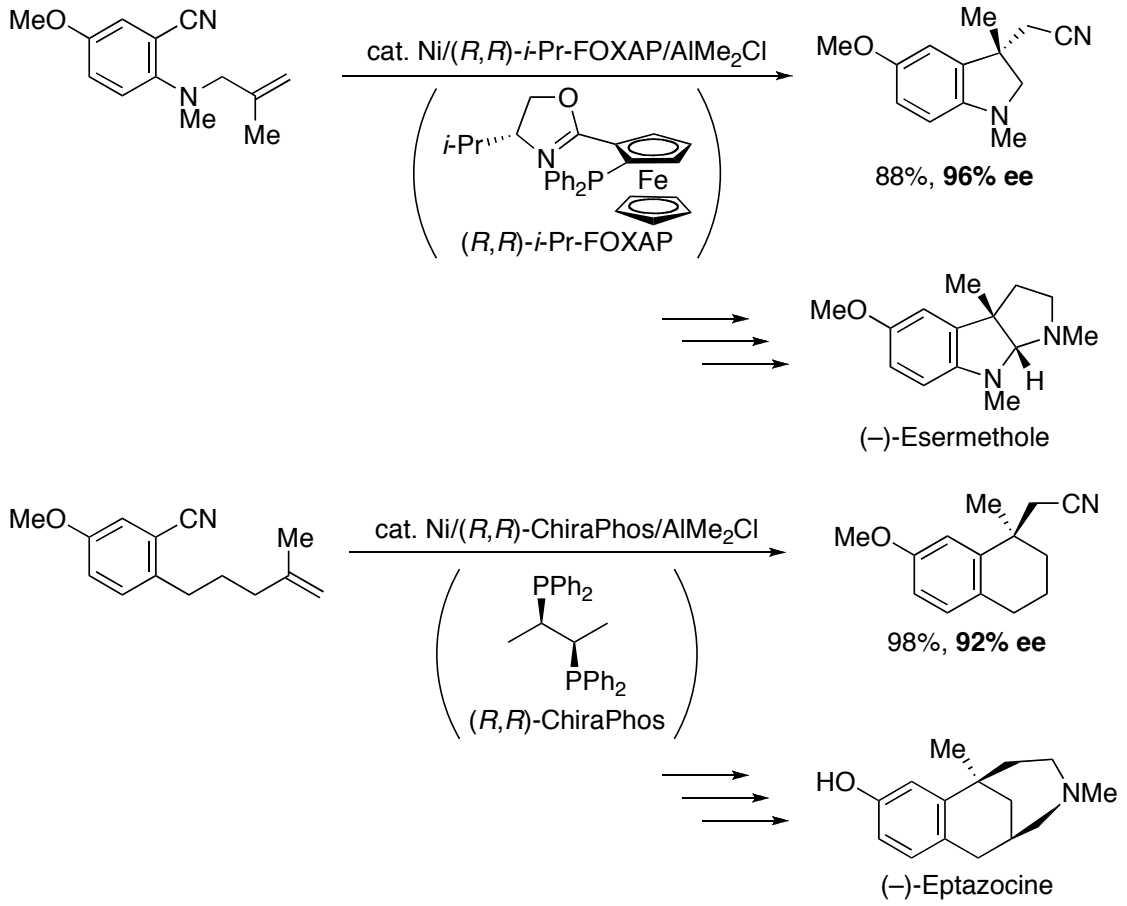


Scheme 26. Nickel/BPh_3-catalyzed alkenylcyanation of alkynes.

Demonstrated in Chapter 3 is intramolecular arylcyanation reaction of alkenes catalyzed cooperatively by nickel and $AlMe_2Cl$. The reaction allows simultaneous construction of both benzylic quaternary carbons and C–CN bonds in a single operation with high atom economy and stereospecificity (eq. 9).[52,53]

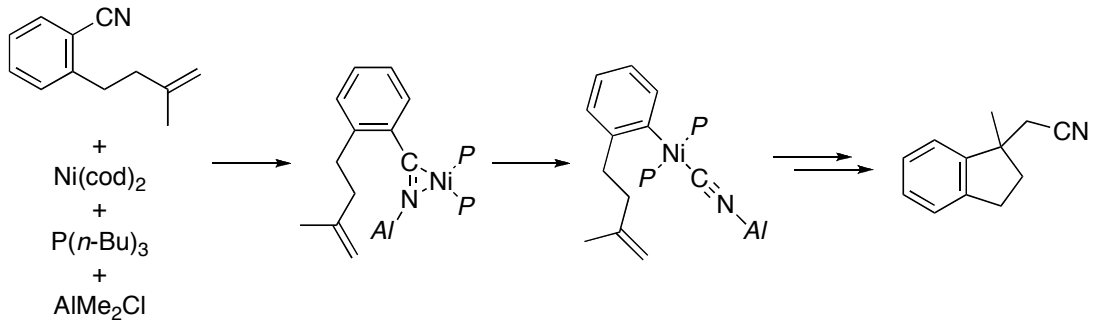
(9)

Two enantioselective examples of this reaction demonstrated below show chiral quaternary stereocenters as well as bicyclic structures are easily constructed. The products serve as synthetic intermediates for stereoselective formal synthesis of biologically active alkaloids (Scheme 27).



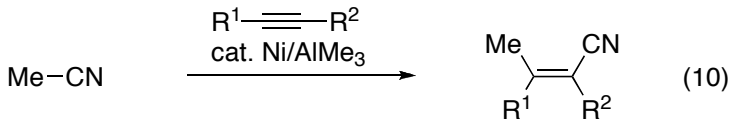
Scheme 27. Enantioselective intramolecular arylcyanation of alkenes

Mechanistic studies by stoichiometric reactions reveal two distinct structures of the reaction intermediates which are characterized unambiguously by NMR spectroscopy and X-ray crystallographic analysis. Monitoring experiments by NMR also suggest that either insertion of the double bond (carbonickelation) or substitution of the coordinating phosphorous by the double bond is a rate-determining step (Scheme 28).



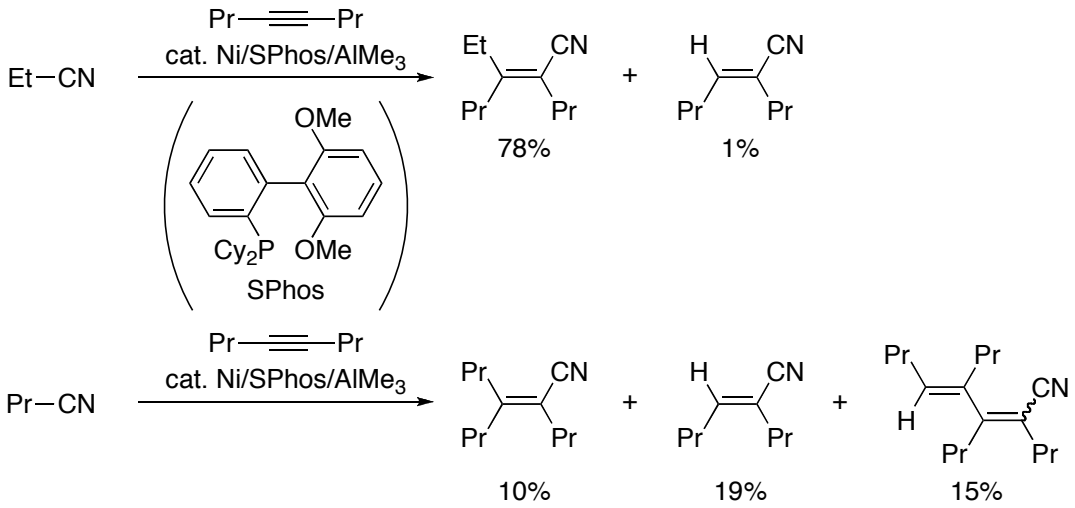
Scheme 28. Confirmed intermediates of intramolecular arylcyanation of alkenes.

The nickel/LA cooperative catalysis allows the activation of even C(sp^3)–CN bonds[54,55] of alkyl cyanides such as acetonitrile to allow alkylcyanation reactions of alkynes as described in Chapter 4 (eq. 10).[50a,56]



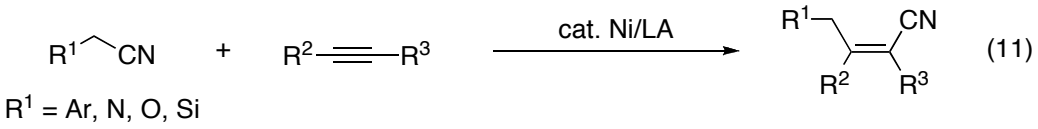
(10)

The similar reaction of propionitrile with 4-octyne is also achieved and the corresponding ethylcyanation products are isolated in good yield, whereas the reaction of butyronitrile gave significant amounts of hydrocyanation products possibly derived from β-hydride elimination of a propylnickel intermediate (Scheme 29).



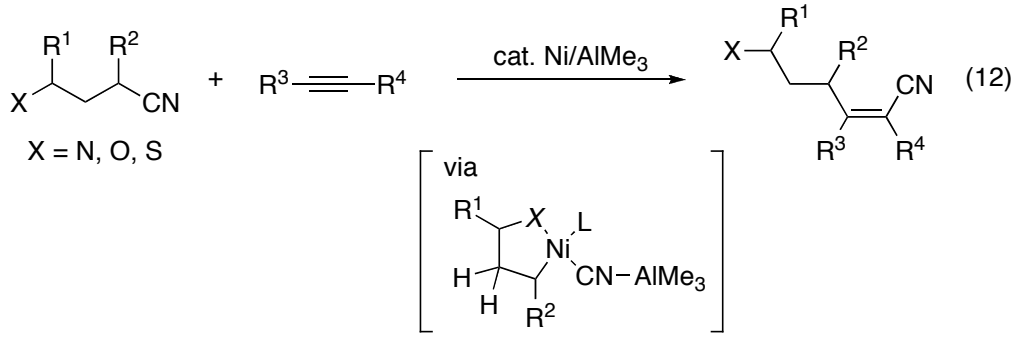
Scheme 29. Nickel/$AlMe_3$-catalyzed carbocyanation of 4-ocytne using propionitrile and butyronitrile.

Limited success in the alkylcyanation of alkynes turned the author's attention to the reaction of substituted acetonitriles that have no β-hydrogens. Gratifyingly, substituted acetonitriles such as aryl-, amino-, protected hydroxy-, and silylacetonitriles have been demonstrated to add across alkynes under the nickel/LA catalysis (eq. 11).



(11)

Another possible solution to suppress β-hydride elimination is formation of heteroatom-coordinated nickelacycles where C–H and C–Ni bonds cannot align syn-periplanar. Thus, the author studied the addition reactions of alkyl cyanides having a heteroatom such as nitrogen, oxygen, and sulfur across alkynes by the nickel/LA catalysis to give functionalized alkyl-substituted acrylonitriles with high stereo- and regioselectivity (eq. 12).[57] A 5-membered azanickelacycle is suggested to be a key reaction intermediate and responsible for suppression of β-hydride elimination. Details are described in Chapter 5.



(12)

In summary, the present Thesis demonstrates a dramatic effect of a LA cocatalyst on nickel-catalyzed carbocyanation reactions of unsaturated compounds. Scope of nitriles for the transformation has been broadened significantly to include aryl, alkenyl, and even alkyl cyanides. The nickel/LA cooperative catalysis allows a rapid and atom-economical access to various nitriles, which would be otherwise inaccessible and serve as useful building blocks.

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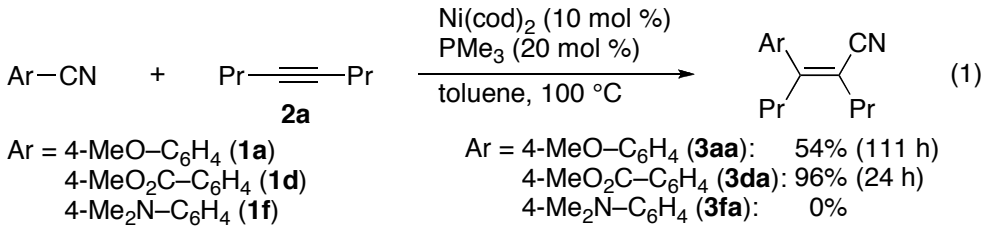
Chapter 2

Dramatic Effect of Lewis Acid Catalyst on Nickel-catalyzed Carbocyanation Reaction of Unsaturated Bonds Using Aryl and Alkenyl Cyanides

Lewis acid co-catalysts such as $AlMe_3$, $AlMe_2Cl$, and BPh_3 significantly improve the efficiency of the nickel-catalyzed arylcyanation of alkynes. Electron-rich aryl cyanides, which exhibit poor reactivity in the absence of Lewis acids, readily undergo the arylcyanation reaction under the newly disclosed conditions. Excellent chemoselectivity is observed for aryl cyanides having a chloro or bromo group, allowing a single-step preparation of the synthetic intermediate of P-3622, a squalene synthetase inhibitor. The scope of aryl cyanides for the arylcyanation of norbornadiene is also expanded significantly. The reaction across simple 1-alkenes gives arylethenes, Heck-type products, in low yields due to β-hydride elimination. Alkenylcyanation of alkynes is achieved under the nickel/Lewis acid dual catalysis for the first time to give cyano-substituted 1,3-dienes stereoselectively.

Introduction

Cleavage of the carbon–cyano bond in nitriles followed by addition reaction of the resulting two organic fragments across unsaturated bonds by transition metal catalysis should be useful, because such transformation allows simultaneous construction of carbon–carbon and carbon–cyano bonds without forming byproducts. The reaction, namely carbocyanation reaction, was recently achieved by nickel[1] and palladium[2,3] catalysts. Compared to palladium-catalyzed reactions, nickel catalysis allowes a wide variety of nitriles including aryl,[1a,c,d] alkoxycarbonyl,[1b,g] allyl,[1e,i] and alkynyl[1h] cyanides to participate in the reaction. Nevertheless, the reactions still require generally high catalyst loadings and harsh reaction conditions. For example, arylcyanation of alkynes using electron-rich aryl cyanides is feasible but generally sluggish: addition of 4-methoxybenzonitrile (**1a**) across 4-octyne (**2a**) in the presence of 10 mol % of a Ni/PMe_3 catalyst at 100 °C took 111 h for completion to give the corresponding adduct (**3aa**) in 54% yield, whereas that of methyl 4-cyanobenzoate (**1d**), an electron-deficient one, gave the adduct (**3da**) in 96% yield after 24 h (eq. 1).[1a,c] Moreover, highly electron-rich 4-dimethylaminobenzonitrile (**1f**) completely failed to give product **3fa** (eq. 1).



Based on the mechanism of the nickel-catalyzed arylcyanation reaction suggested by theoretical calculations,[4] oxidative addition of the C–CN bond to nickel(0) is likely rate-determining: an elemental step that proceeds through η^2-nitrile- and η^2-arenenickel complexes.[5] As LAs have been known to accelerate elemental steps such as oxidative addition[6] and reductive elimination[7] of C–CN bonds in a stoichiometric manner, investigated in this Chapter is the effect of a LA catalyst on arylcyanation reaction of alkynes. Indeed, the scope of aryl cyanides for the reaction with alkynes and norbornadiene is expanded significantly under the nickel/LA cooperative catalysis. Attempted reactions with simple 1-alkene are also described briefly. The cooperative metal catalysis allows the addition reaction of alkenyl cyanides across alkynes, giving

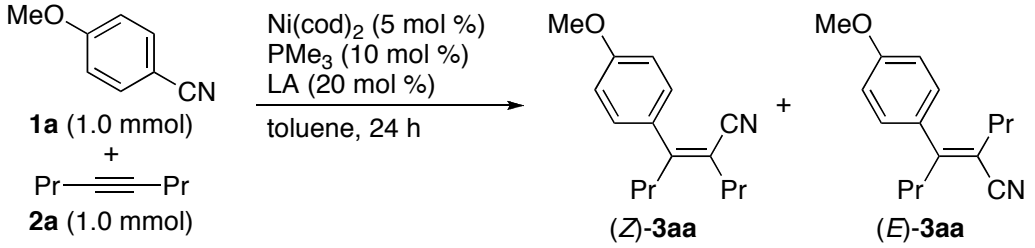
1-cyano-1,3-dienes with highly regio- and stereoselectively.

Results and discussion

Effect of Lewis acid cocatalyst on nickel-catalyzed arylcyanation of alkynes

The author first assessed an effect of various LA catalysts together with $Ni(cod)_2$ (5 mol %) and PMe_3 (10 mol %) as a ligand on the reaction of aryl cyanide (**1a**, 1.0 mmol) with 4-octyne (**2a**, 1.0 mmol) in toluene at 80 °C (Table 1). Of LAs examined, LAs of aluminum, boron, and zinc were found to significantly promote the reaction, giving (*Z*)-**3aa** in good to excellent yields (entries 3, 5, 10, 12, 17, 19, and 26), whereas the absence of the LA catalysts gave low yield of (*Z*)-**3aa** (entries 1 and 2). $AlMeCl_2$ was also found effective for the reaction, but significant amount of (*E*)-**3aa** was observed probably through isomerization of initially formed (*Z*)-**3aa** (entry 7). Stronger Lewis acidity would be responsible for such isomerization (*vide infra*). $Ti(O^iPr)_4$, $MgBr_2$, $LaCl_3$, and Me_3SiOTf were less effective (entries 29–32). Other LAs including indium, copper, iron, cobalt, gold, and zirconium LAs inhibited the reaction. Some of LAs including $AlMe_3$, $AlMe_2Cl$, $AlMeCl_2$, and BEt_3 are still effective even at 50 °C (entries 4, 6, 8, and 18). In the case of $ZnCl_2$, formation of insoluble materials was observed after the reaction (entry 27). Finally, the author tested various combinations of LAs and ligands in the presence of 1 mol % of $Ni(cod)_2$, and found that ligands such as $PPhMe_2$, PPh_2Me, and PPh_2Cy give better results than PMe_3, giving (*Z*)-**3aa** in over 90% yield with only a trace amount of (*E*)-**3aa** (Table 2). From the view point of practicality, it is worth noting that a similar catalyst prepared in situ from air- and moisture-stable $(PhMe_2P)NiCl_2$ (1 mol %) and $AlMe_3$ (4 mol %) was equally effective to give (*Z*)-**3aa** in 96% yield after 19 h. In the reaction course, the Ni(II) catalyst is reduced to the Ni(0) catalytic species and simultaneously $AlMe_2Cl$ as the LA cocatalyst is generated (Scheme 1).

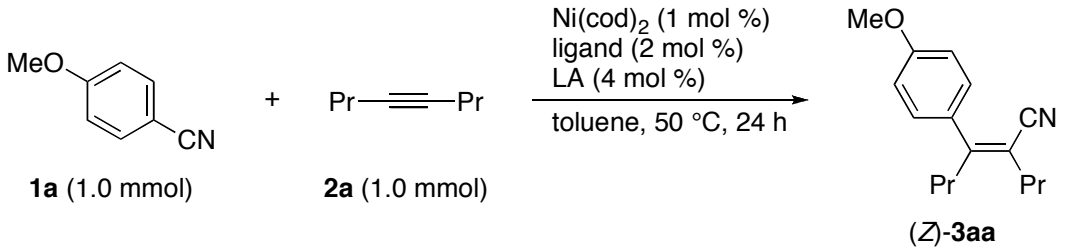
Table 1. Effect of LA cocatalyst on nickel-catalyzed arylcyanation of **2a** with **1a**.[a]



			yield (%)[b]	
entry	Lewis acid	temp (°C)	(*Z*)-**3aa**	(*E*)-**3aa**
1	none	80	36	1
2	none	50	7	0
3	$AlMe_3$	80	91	6
4	$AlMe_3$	50	61	0
5	$AlMe_2Cl$	80	79	21
6	$AlMe_2Cl$	50	94	1
7	$AlMeCl_2$	80	41	50
8	$AlMeCl_2$	50	82	4
9	$AlCl_3$	80	6	0
10	$AlPh_3$•OEt_2	80	90	3
11	$AlPh_3$•OEt_2	50	47	0
12	MAD[c]	80	82	10
13	MAD[c]	50	7	1
14	$Al(O^iPr)_3$	80	48	6
15	$Al(OPh)_3$	80	0	0
16	$Al(OTf)_3$	80	0	0
17	BEt_3	80	88	0
18	BEt_3	50	82	0
19	BPh_3	80	68	0
20	BPh_3	50	37	0
21	$B(C_6F_5)_3$	80	17	0
22	BF_3•OEt_2	80	1	0
23	$ZnEt_2$	80	0	0
24	$ZnPh_2$	80	8	0
25	$Zn(C_6F_5)_2$	80	2	0
26	$ZnCl_2$	80	86	1
27	$ZnCl_2$	50	68	0
28	$Zn(OTf)_2$	80	61	0
29	$Ti(O^iPr)_4$	80	42	1
30	$MgBr_2$•OEt_2	80	54	4
31	$LaCl_3$	80	39	3
32	Me_3SiOTf	80	21	4

[a] All the reaction was carried out using **1a** (1.0 mmol), **2a** (1.0 mmol), $Ni(cod)_2$ (50 μmol), PMe_3 (100 μmol), and Lewis acid (200 μmol) in toluene (1.0 mL) for 24 h. [b] Estimated by GC using dodecane as an internal standard. [c] Methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenolate).

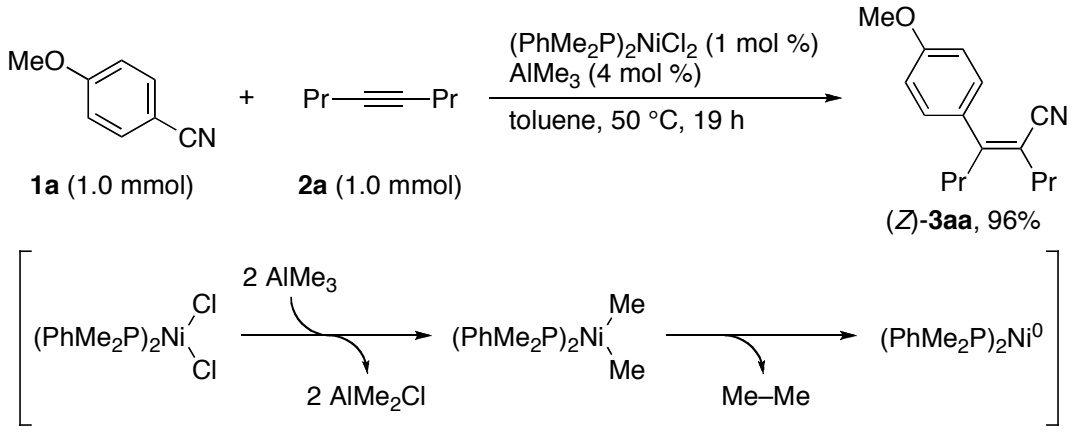
Table 2. Optimization of a combination of a LA and a ligand for the reaction of **1a** across **2a**.[a]



1a (1.0 mmol) **2a** (1.0 mmol) (*Z*)-**3aa**

	LA /yield of (*Z*)-**3aa** (%)[b]				
ligand	$AlMe_3$	$AlMe_2Cl$	$AlMeCl_2$	BPh_3	BEt_3
PMe_3	60	88	7	31	9
$P(n\text{-}Bu)_3$	63	41	5	39	<1
$PPhMe_2$	95	>99	8	78	6
PPh_2Me	92	98	<1	92	<1
PPh_2Cy	95	50	<1	79	1
$P(4\text{-}MeO\text{–}C_6H_4)_3$	29	6	<1	53	1
$Ph_2P(CH_2)_6PPh_2$	72	66	<1	60	<1

[a] All the reaction was carried out using **1a** (1.0 mmol), **2a** (1.0 mmol), $Ni(cod)_2$ (10 μmol), ligand (20 μmol), and LA (40 μmol) in toluene (1.0 mL) at 50 °C for 24 h. [b] Estimated by GC using dodecane as an internal standard.

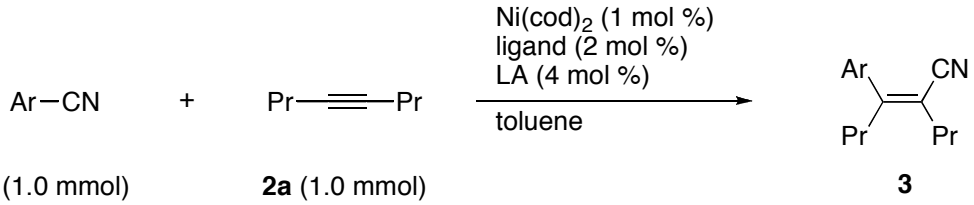


Scheme 1. The reaction of **1a** with **2a** using dichlorobis(dimethylphenylphosphine)-nickel(II) as a precatalyst.

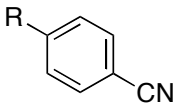
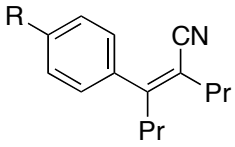
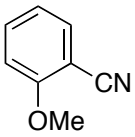
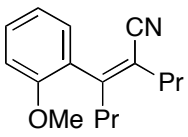
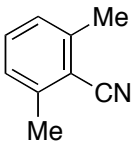
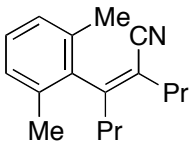
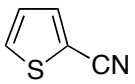
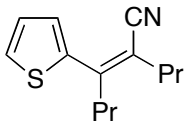
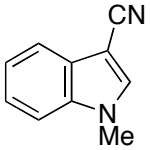
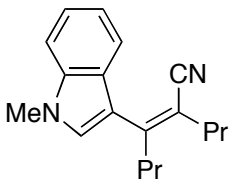
Nickel/Lewis acid-catalyzed arylcyanation of alkynes

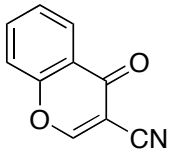
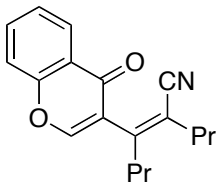
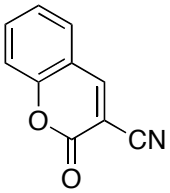
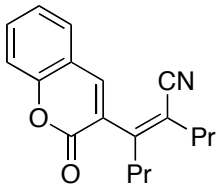
The new catalyst systems thus identified were then applied to the arylcyanation of **2a** using various aryl cyanides especially those unreactive under the LA-free conditions (Table 3). Under optimized reaction conditions, all the reaction gave adducts in an exclusive *cis*-fashion. *p*-Tolunitrile (**1b**) and benzonitrile (**1c**) added across **2a** in good to excellent yields (entries 2 and 3). Functional groups such as ester and a THP-protected [2-(hydroxymethyl)phenyl]dimethylsilyl group[8] also tolerated the reaction conditions (entries 4 and 5). Highly electron-rich 4-dimethylamino- (**1f**) and 4-diphenylaminobenzonitrile (**1g**) underwent the arylcyanation to give the corresponding adducts in good yields (entries 6 and 7). Selective activation of the Ar–CN bonds of 4-bromo- (**1h**), 4-chloro- (**1i**), and 4-fluorobenzonitrile (**1j**) over the Ar–halogen bonds is highly remarkable (entries 8–10). Even the sterically highly demanding Ar–CN bonds of 2-methoxybenzonitrile (**1k**) and 2,6-dimethylbenzonitrile (**1l**) participated in the reaction, although higher reaction temperatures (80–100 °C), higher loadings of catalysts, and/or prolonged reaction time were required (entries 11 and 12). Heteroaryl cyanides also successfully added across **2a** (entries 13–16). The selective activation of an Ar–CN bond over the C(2)–H bond in 1-methyl-3-cyanoindole (**1n**) demonstrates another chemoselective feature of the present Ni–LA catalysis (entry 14), the Ar–H bond being activated exclusively in the absence of LA.[9] Other heteroaryl cyanides such as 3-cyanochromone (**1o**) and 3-cyanocoumarin (**1p**) did not undergo carbocyanation reaction under the Ni/Al catalyst system, whereas Ni/BPh_3 catalyzed the reactions effectively to give adducts in good yields (entries 15 and 16).

Table 3. Nickel/LA-catalyzed arylcyanation of 4-octyne (**2a**).



1 (1.0 mmol) **2a** (1.0 mmol) **3**

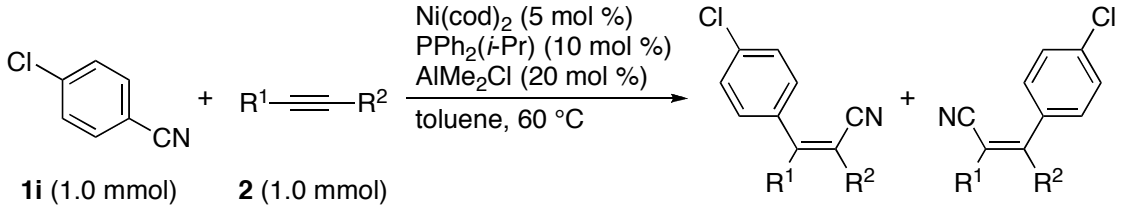
entry	aryl cyanide		cond.[a]	temp (°C)	time (h)	product, yield (%)[b]
						
1	R = MeO: **1a**		A	50	16	**3aa**, 96
2	Me: **1b**		A	60	20	**3ba**, 72
3	H: **1c**		B	50	16	**3ca**, 97
4	MeO_2C: **1d**		A	80	25	**3da**, 93
5	$ArMe_2Si$[c]: **1e**		B	50	42	**3ea**, 90
6	Me_2N: **1f**		A	80	21	**3fa**, 87
7	Ph_2N: **1g**		B	50	47	**3ga**, 91
8[d]	Br: **1h**		A	50	27	**3ha**, 72
9	Cl: **1i**		B	50	18	**3ia**, 94
10	F: **1j**		B	50	18	**3ja**, 95
11		**1k**	B	80	28	 **3ka**, 92
12[d]		**1l**	A	100	134	 **3la**, 78
13		**1m**	B	50	140	 **3ma**, 81
14		**1n**	A	50	116	 **3na**, 58

15[e]		**1o**	C	80	20		**3oa**, 91
16[e]		**1p**	C	80	20		**3pa**, 92

[a] Conditions A, $PPhMe_2$ and $AlMe_2Cl$; conditions B, PPh_2Cy and $AlMe_3$; condition C, $Ph_2P(CH_2)_4PPh_2$ and BPh_3. [b] Isolated yields. [c] Ar = 2-$(THPOCH_2)C_6H_4$. [d] The reaction was carried out using $Ni(cod)_2$ (50 μmol), $PPhMe_2$ (100 μmol), and $AlMe_2Cl$ (200 μmol). [e] The reaction was carried out using $Ni(cod)_2$ (40 μmol), DPPB (40 μmol), and BPh_3 (160 μmol).

The scope of internal alkynes was examined next with 4-chlorobenzonitrile (**1i**) (Table 4). Symmetrical alkynes such as 2-butyne (**2b**), 3-hexyne (**2c**), and 1,4-bis(trimethylsilyl)-2-butyne (**2d**) all participated in the reaction in good yields (entries 1–3). An unsymmetrical alkyne, 4,4-dimethyl-2-pentyne (**2f**), gave the corresponding adduct **3if** with good regioselectivity (entry 5), whereas that observed with 4-methyl-2-pentyne (**2e**) was modest (entry 4). The reactions gave the corresponding adducts having a larger substituent at the cyano-substituted carbon as major products. Internal alkynes with aryl- and silyl-substituents reacted with **1i** successfully with similar regioselectivity, although significant amounts of *trans*-adducts were also obtained through isomerization of the initial *cis*-adducts according to inconstant *E*/*Z* ratios (entries 6–8). The excellent chemoselectivity of the present Ni–LA catalysis allowed a single step access to **3ii**, which is a synthetic intermediate of P-3622, a squalene synthetase inhibitor (entry 8).[10] Under the same catalyst system, terminal alkynes failed to participate in the reaction due to rapid trimerization and/or oligiomerization.

Table 4. Nickel/$AlMe_2Cl$-catalyzed arylcyanation of internal alkynes with **1i**.



1i (1.0 mmol) **2** (1.0 mmol) **3** **3'**

entry	alkyne		time (h)	product(s)	yield (%),[a] (**3**:**3'**)[b]
1	Me—≡—Me	**2b**	12	**3ib**	88
2	Et—≡—Et	**2c**	6	**3ic**	92
3	Me_3Si—≡—$SiMe_3$	**2d**	6	**3id**	84
4	Me—≡—*i*-Pr	**2e**	5	**3ie** + **3'ie**	87 (64:36)
5	Me—≡—*t*-Bu	**2f**	19	**3if** + **3'if**	89 (91:9)
6[c]	Et—≡—*p*-Anis	**2g**	32	**3ig**, **3'ig**	**3ig**, 53%,[d] **3'ig**, 27%
7[e]	Me—≡—$SiMe_3$	**2h**	13	**3ih**, **3'ih**	**3ih**, 70%,[f] **3'ih**, 9%
8[g]	*p*-Anis—≡—$SiMe_3$	**2i**	37	**3ii**, **3'ii**	**3ii**, 73%,[h] **3'ii**, <5%

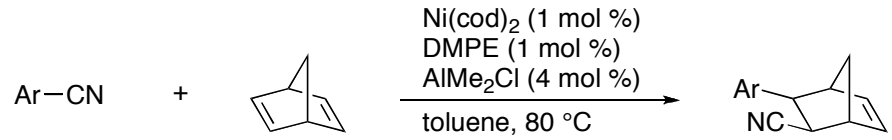
[a] Isolated yields. [b] Determined by ^{1}H NMR analysis. [c] PPh_2Me was used as a ligand. [d] (*E*)-**3ig** was also obtained in 5% yield. [e] Reaction run at 80 °C. [f] *E*/*Z* = 59:41 (78:22 at 5 h). [g] Reaction run with 1 mol % of catalyst. [h] *E*/*Z* = 47:53 (57:43 at 12 h).

Nickel/$AlMe_2Cl$-catalyzed arylcyanation of norbornadiene

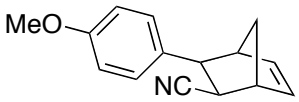
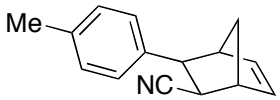
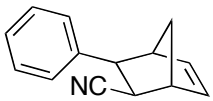
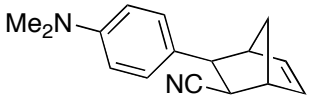
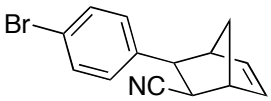
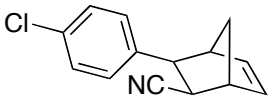
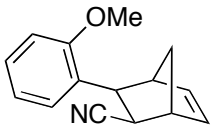
The author then turned his attention to arylcyanation of norbornadiene (**4**), because the original LA-free conditions were applicable only to electron-rich aryl cyanides.[11] The reaction of **1a** with **4** in the presence of the Ni/$AlMe_2Cl$ catalyst with $Me_2P(CH_2)_2PMe_2$ (DMPE) as a ligand in toluene at 80 °C proceeded successfully to afford *exo*-*cis*-arylcyanation product **5aa** in 69% yield after 4.5 h (entry 1 of Table 5).

Other ligands such as monodentate phosphine and bidentate DPPE were totally ineffective. The same catalyst system was further applied to the reactions of a wide variety of aryl cyanides, especially low-yielding cyanides in the absence of LA, to give the corresponding adducts in good yields (entries 2–7). No double addition products were observed in all cases. The resulting norbornene derivatives **5** would find further applications as precursors for functionalized cyclopenetanes[1d] or monomers for ring-opening metathesis polymerization.[12]

Table 5. Nickel/$AlMe_3$-catalyzed arylcyanation of norbornadiene (**4**).[a]



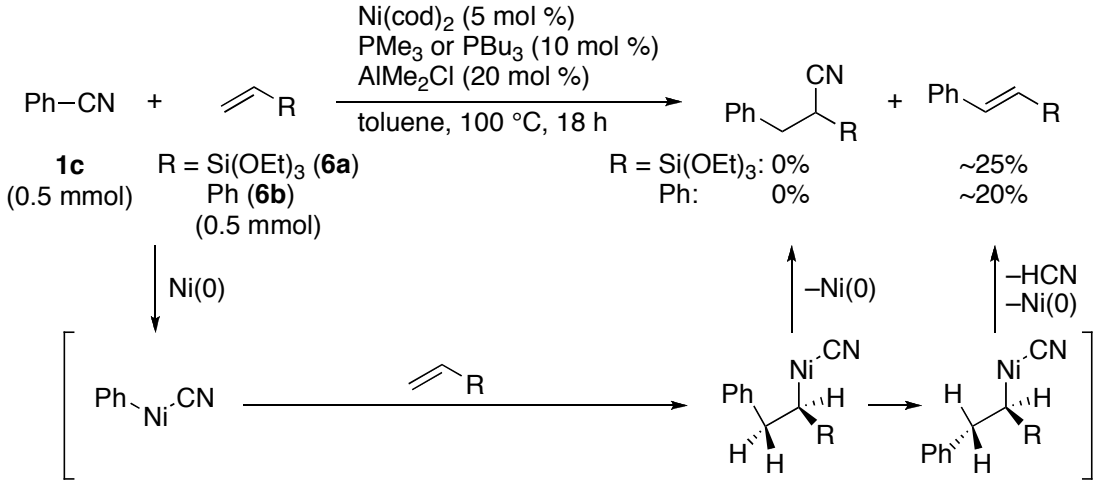
1 (1.0 mmol) **4** (1.5 mmol) **5**

entry	aryl cyanide	time (h)	product		yield (%)[b]
1	**1a**	4.5		**5aa**	69
2	**1b**	2		**5ba**	70
3	**1c**	2		**5ca**	68
4[c]	**1f**	2		**5fa**	57
5	**1h**	10		**5ha**	59
6	**1i**	2		**5ia**	69
7	**1k**	5.5		**5ka**	58

[a] All the reaction was carried out using **1** (1.0 mmol), **4** (1.5 mmol), $Ni(cod)_2$ (10 μmol), DMPE (10 μmol), and $AlMe_2Cl$ (40 μmol) in toluene (670 μL). [b] Isolated yields. [c] Reaction run at 100 °C.

Nickel/Lewis acid-catalyzed arylcyanation of 1-alkenes

The author then examined the arylcyanation reaction across simple 1-alkenes. Attempted reactions of benzonitrile (**1c**) with 1-alkenes such as triethoxy(vinyl)silane (**6a**) and styrene (**6b**) in the presence of diverse combinations of a ligand and a LA catalyst with $Ni(cod)_2$ disappointedly gave no arylcyanation product in any detectable amounts, and 1,2-disubstituted ethenes were obtained as a sole product probably through *β*-hydride elimination from an alkylnickel intermediate derived from insertion of the alkenes into the Ph–Ni bond of the oxidative adduct (Scheme 2). Possible solutions to avoid the unproductive *β*-hydride elimination are discussed in the following Chapters.



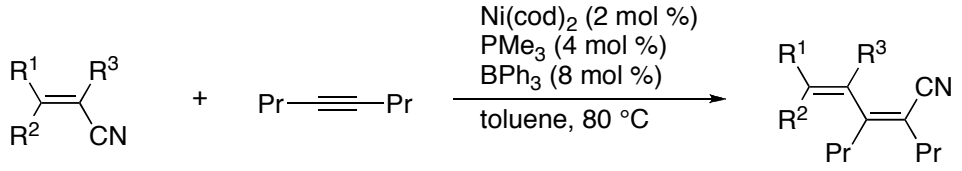
Scheme 2. Attempted arylcyanation of alkenes under nickel/LA dual catalyst.

Nickel/BPh_3-catalyzed alkenylcyanation of alkynes

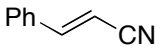
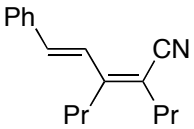
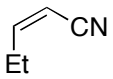
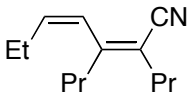
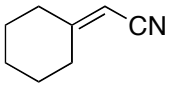
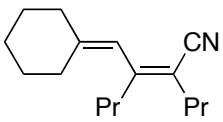
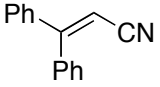
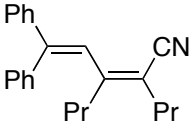
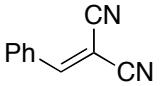
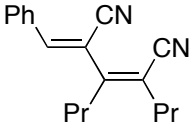
The author next turned his attention to the addition reaction of alkenyl cyanides across alkynes. After a brief survey of optimization of the reaction conditions for the reaction of (*E*)-cinnamonitrile (**7a**) with 4-octyne (**2a**), the author found that the combination of $Ni(cod)_2$ (2 mol %), PMe_3 (4 mol %), and BPh_3 (8 mol %) effectively catalyzed the expected alkenylcyanation reaction to give conjugated dienenitrile **8aa** in 94% yield (entry 1 of Table 6). LAs such as $AlMe_3$ and $AlMe_2Cl$ were also found effective for the reaction, but significant amount of 2*E*-isomer was observed. It is noteworthy that the catalyst differentiates precisely the alkenyl–CN bonds of starting alkenyl cyanides from those of products possibly by steric and/or electronic factors. Under the same reaction conditions, acrylonitrile failed to participate in the reaction,

giving a complex mixture. The reaction of (*Z*)-2-pentenenitrile (**7b**) resulted in contamination of 4*E*-isomer because of partial isomerization of **7b** to (*E*)-2-pentenenitrile before the addition reaction took place (entry 2). Disubstituted acrylonitriles gave tetrasubstituted 2,4-pentadienenitriles in good yields (entries 3–5). Especially, selective activation of the cyano group trans to the phenyl group in benzylidenemalononitrile (**7e**) is worth noting to give dicyanosubstituted 1,3-diene (**8ea**). The reaction of **7f** having two alkenyl cyanide moieties with 3 molar equivalents of **2a** gave double alkenylcyanation product **8fa** in 84% yield (eq. 2).

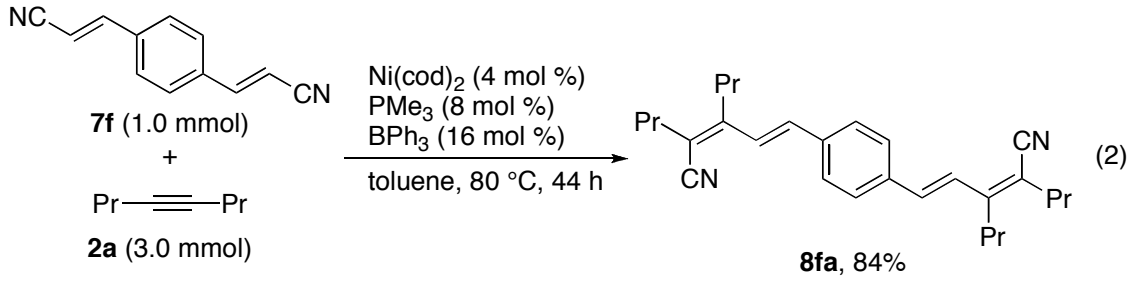
Table 6. Nickel/BPh_3-catalyzed alkenylcyanation across **2a**.[a]



7 (1.0 mmol) **2a** (1.2 mmol) **8**

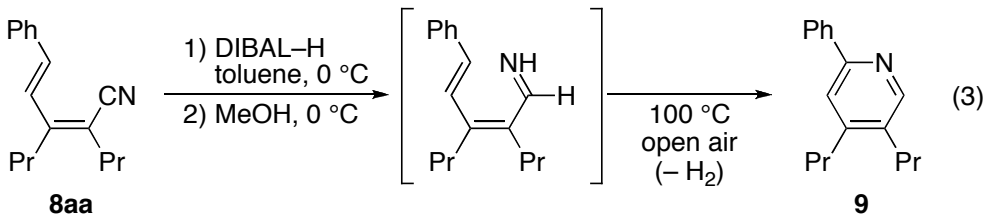
entry	alkenyl cyanide		time (h)	product, yield (%)[b]
1		**7a**	20	 **8aa**, 94
2		**7b**	15	 **8ba**, 78[c]
3		**7c**	21	 **8ca**, 91
4		**7d**	46	 **8da**, 94
5[d]		**7e**	13	 **8ea**, 81[e]

[a] All the reaction was carried out using **7** (1.0 mmol), **2a** (1.2 mmol), $Ni(cod)_2$ (20 μmol), PMe_3 (40 μmol), and BPh_3 (80 μmol) in toluene (1.0 mL) at 80 °C. [b] Isolated yield of isomerically pure product unless otherwise noted. [c] 4*Z*/4*E* = 84:16. [d] The reaction was carried out using $Ni(cod)_2$ (40 μmol), DPPB (40 μmol), and BPh_3 (160 μmol). [e] An isomer was also obtained in ~2% yield.



(2)

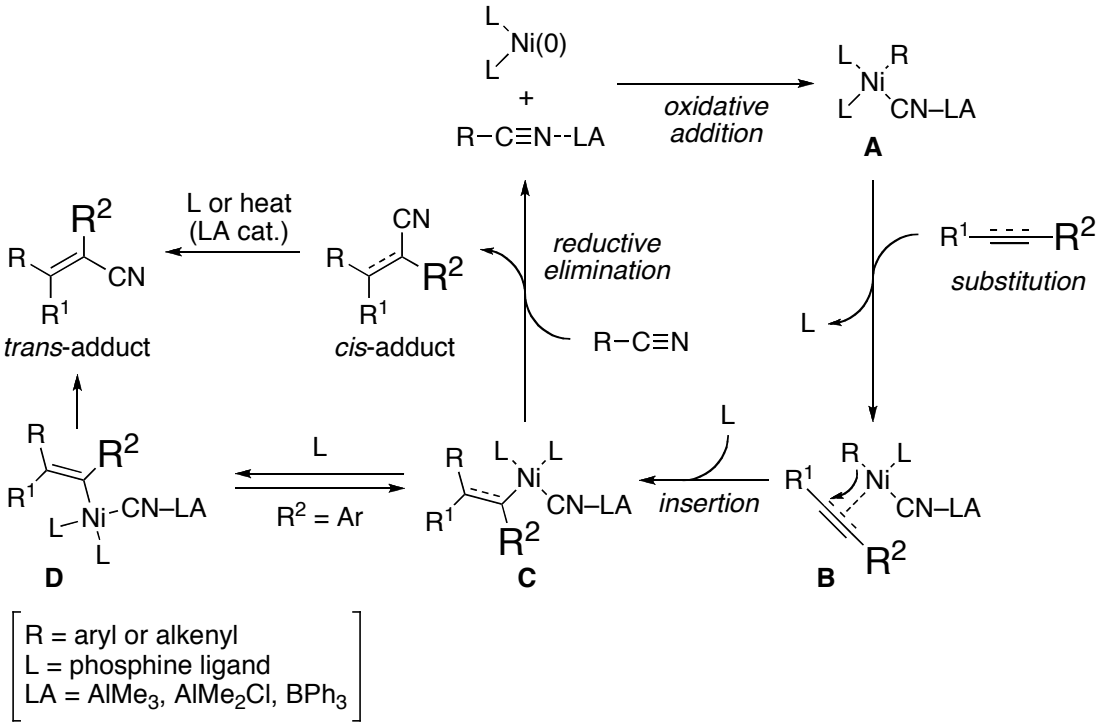
The substituted 2,4-pentadienenitriles thus obtained were readily converted to substituted pyridines via reduction with DIBAL–H, 6π electrocyclization followed by aerobic oxidation as exemplified by the reaction of **8aa** (eq. 3).



(3)

Reaction mechanism of aryl- and alkenylcyanation reactions

The observed dramatic effects of LA catalysis is attributed primarily to acceleration of oxidative addition of C–CN bonds by coordination of a cyano group to a LA catalyst as expected (Scheme 3).[6] Rate acceleration may be operative also reductive elimination of C–CN bonds[7] and/or other elemental steps. Coordination of an alkyne to a nickel center in the direction to minimize steric repulsion between bulkier R^2- and an aryl groups (**B**) should be responsible for the observed regioselectivity as was the case for the LA-free reaction.[1c] Trans adducts may be derived from phosphine- and/or heat-mediated isomerization of the initial cis adducts, because the stereoisomeric ratios depended on the reaction time and conditions. Stronger Lewis acid appears to induce such isomerization. A silyl group tends to further facilitate such isomerization.[1c] In the case of aryl-substituted alkynes, alkenylnickel species **C** may isomerize to its isomer **D** possibly through conjugated addition of phosphine ligand[13] followed by reductive elimination to give trans adducts.



Scheme 3. Plausible reaction mechanism.

Conclusion

In summary, the author has demonstrated a dramatic effect of LA catalysts on nickel-catalyzed arylcyanation of alkynes and norbornadiene. Lewis acids such as organoaluminum and -boron compounds significantly accelerate the whole catalytic cycle of the arylcyanation reaction to allow expansion of the scope of aryl cyanides. The binary catalysis is found applicable to the arylcyanation of norbornadiene, whereas that across simple 1-alkenes are still sluggish due to competitive β-hydride elimination. Also demonstrated is the first example of the addition reaction of alkenyl cyanides across alkynes by the Ni/BPh_3 cooperative catalysis to give variously substituted 2,4-dienenitriles stereoselectively.

Experimental Section

General remarks compatible to all the experimental part in the present Thesis

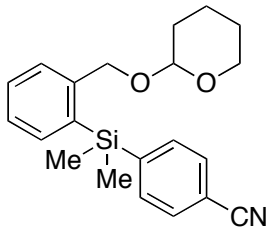
All manipulations of oxygen- and moisture-sensitive materials were conducted with a standard Schlenk technique or in a dry box under an argon or nitrogen atmosphere. Flash column chromatography was performed using Kanto Chemical silica gel (spherical, 40–50 μm) or Merck aluminum oxide 90 active neutral (4.8–5.0 wt% of water was added before use). Analytical thin layer chromatography (TLC) was performed on Merck Kieselgel 60 F_{254} (0.25 mm) plates. Visualization was accomplished with UV light (254 nm) and/or an aqueous alkaline $KMnO_4$ solution followed by heating. Proton and carbon nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a JEOL GSX-270S spectrometer, a Varian Mercury 400 spectrometer, or a Bruker DPX-400 spectrometer with Me_4Si or solvent resonance as the internal standard (^{1}H NMR, Me_4Si at 0 ppm, $CHCl_3$ at 7.26 ppm, or C_6D_5H at 7.16 ppm; ^{13}C NMR, Me_4Si at 0 ppm, $CDCl_3$ at 77.0 ppm, or C_6D_5H at 128.0 ppm). ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, br = broad, m = multiplet), coupling constants (Hz), and integration. Assignments of the resonances observed in ^{1}H and ^{13}C NMR spectra were carried out based on ^{1}H–^{1}H COSY, HMQC, and/or HMBC 2D NMR experiments. Phosphorus nuclear magnetic resonance spectra (^{31}P NMR) were recorded on a JEOL GSX-270S spectrometer (109 MHz) spectrometer with 85% H_3PO_4 (0 ppm) as the external standard. Infrared spectra (IR) recorded on a Shimadzu FTIR-8400 spectrometer are reported in cm^{-1}. Melting points (mp) were determined using a YANAKO MP-500D. Elemental analyses were performed by Elemental Analysis Center of Kyoto University. Chiral HPLC analyses were performed with a Shimadzu Prominence chromatograph. Optical rotations were measured on a JASCO DIP-360. High-resolution mass spectra were obtained with a JEOL JMS-700 (EI). X-ray crystallographic analysis data were collected with a Bruker SMART APEX diffractometer or a Rigaku RAXIS-RAPID Imaging Plate diffractometer. Preparative recycling silica gel chromatography was performed with a JAI LC-908 chromatograph equipped with Nacalai tesque 5SL-II (hexane–ethyl acetate as an eluent) or 5C18-MS-II [MeOH–phosphate buffer (pH 7.0) as an eluent]. GC analysis was performed on a Shimadzu GC 2014 chromatography equipped with an ENV-1 column (Kanto Chemical, 30 m x 0.25 mm, pressure = 31.7 kPa, detector = FID, 290 °C) with helium gas as a

carrier. Unless otherwise noted, commercially available reagents were used without purification. $Ni(cod)_2$ was purchased from Strem and used without further purification. Anhydrous toluene purchased from Kanto Chemical was degassed by purging vigorously with argon for 20 min and further purified by passage through activated alumina under positive argon pressure as described by Grubbs et al.[14] Benzene-d_6 was distilled from sodium benzophenone ketyl.

Chemicals

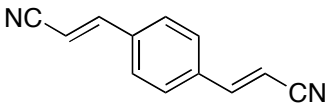
Aryl cyanides **1g**[15] and **1n**,[9] alkynes **2d**[16] and **2g**,[17] alkenyl cyanides **7c**,[18] and **7e**,[19] and dichlorobis(dimethylphenylphosphine)nickel(II)[20] were prepared according to the respective literature procedure.

4-Cyanophenyl-[2-(tetrahydro-2*H*-pyranoxymethyl)phenyl]dimethylsilane (1e). To



a mixture of 4-cyanophenyl[(2-hydroxymethyl)phenyl]dimethylsilane (525 mg, 2.0 mmol)[21] and 3,4-dihydro-2*H*-pyran (673 mg, 8 mmol) was added a drop of a 12 M HCl aqueous solution, and the whole was stirred for 10 min before addition of additional 4-cyanophenyl[(2-hydroxymethyl)phenyl]dimethylsilane (525 mg, 2.0 mmol) at rt. The reaction mixture was stirred at rt for 12 h and concentrated *in vacuo* to give a residue, which was purified by recrystallization from hexane–ethyl acetate (9:1) to give **1e** (772 mg, 55%) as a colorless solid, mp = 59.8–60.8 °C, R_f 0.25 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (m, 4H), 7.51 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.44 (td, *J* = 7.4, 1.3 Hz, 1H), 7.31 (td, *J* = 7.3, 1.5 Hz, 1H), 4.62 (d, *J* = 11.9 Hz, 1H), 4.43 (t, *J* = 3.5 Hz, 1H), 4.32 (d, *J* = 11.9 Hz, 1H), 3.73 (distorted td, *J* = 9.8, 3.1 Hz, 1H), 3.41 (m, 1H), 1.81–1.70 (m, 1H), 1.65–1.40 (m, 5H), 0.63 (s, 3H), 0.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.0, 143.9, 135.3, 134.35, 134.30, 130.8, 130.0, 128.7, 126.9, 118.9, 112.4, 97.7, 68.7, 62.1, 30.5, 25.5, 19.4, –1.1, −1.2. IR (KBr): 3470, 3051, 2942, 2864, 2226, 1937, 1589, 1566, 1543, 1493, 1464, 1451, 1437, 1414, 1400, 1385, 1350, 1321, 1314, 1281, 1254, 1200, 1184, 1163, 1155, 1128, 1117, 1098, 1078, 1055, 1032, 974, 909, 887, 870, 829, 826, 802, 781, 758, 748, 721, 689, 656, 557, 530, 496, 459, 444, 436 cm^{-1}. Anal. Calcd for $C_{21}H_{25}NO_2Si$: C, 71.75; H, 7.17. Found: C, 71.75; H, 7.17.

1,4-Di(cyanovinyl)benzene (7f). To a solution of NaH (756 mg, 32 mmol) in THF (60 mL) was added diethyl cyanomethylphosphonate (5.6 g, 32 mmol) dropwise at 0 °C, and the whole was stirred for 30 min. To this was added dropwise a solution of terephthalaldehyde (2.0 g, 15.0 mmol) in THF (10 mL), and the resulting mixture was stirred for 18 h before addition of the water (100 mL) at rt. The organic layer was separated; the aqueous layer was extracted three times with diethyl ether. The combined organic layers were washed twice with water and brine, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by recrystallization from methanol to give **7f** (565 mg, 21%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 4H), 7.39 (d, J = 16.7 Hz, 2H), 5.95 (d, J = 16.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.8, 135.7, 127.9, 117.5, 98.2.[22]

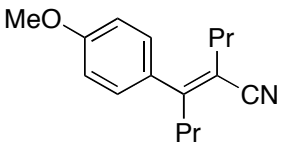


Nickel/Lewis acid-catalyzed arylcyanation of alkynes. *General procedure.* In a dry box, to a solution of $Ni(cod)_2$ (2.8–13.7 mg, 10–50 μmol) and a ligand (20–100 μmol) in toluene (1.0 mL) placed in a vial, were sequentially added an aryl cyanide (1.00 mmol), a Lewis acid (40–200 μmol), an alkyne (1.00 mmol), and dodecane (internal standard, 56 mg, 0.33 mmol). The vial was taken out from the dry box and heated at the temperature for the time specified in Tables 1–4. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography to give the corresponding arylcyanation products in yields listed in Tables 1–4. Regio- and/or stereoisomers were separated by preparative GPC or HPLC and characterized by spectrometry. The spectra of (*Z*)-**3aa**, **3ba**, **3ca**, **3da**, **3ja**, and **3ma** agreed well with those reported previously.[1a,c]

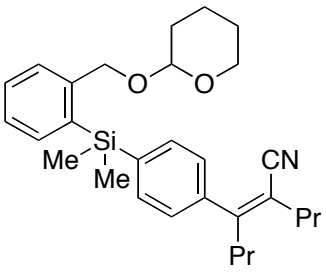
Nickel/Lewis acid-catalyzed arylcyanation of alkynes using dichlorobis(dimethylphenylphosphine)-nickel(II) as a precatalyst (Scheme 1). In a dry box, to **1a** (133 mg, 1.00 mmol) placed in a vial were added a solution of $(PhMe_2P)_2NiCl_2$ (4.1 mg, 10 mmol) in toluene (1.0 mL), **2a** (110 mg, 1.00 mmol), a 1.0 M solution of $AlMe_3$ in hexane (40 μL, 40 μmol), and dodecane (internal standard, 56 mg, 0.33 mmol). The vial was taken out from the dry box and heated at 50 °C for 19 h. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by

flash silica gel column chromatography (hexane–ethyl acetate = 8:1) to give (*Z*)-**3aa** (233 mg, 96%).

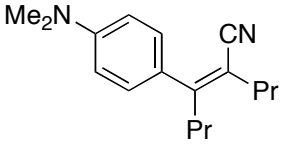
(*E*)-3-(4-Methoxyphenyl)-2-propylhex-2-enenitrile [(*E*)-3aa]. A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (dt, *J* = 8.8, 2.5 Hz, 2H), 6.91 (dt, *J* = 8.8, 2.4 Hz, 2H), 3.84 (s, 3H), 2.70 (t, *J* = 7.5 Hz, 2H), 2.10 (t, *J* = 7.6 Hz, 2H), 1.55 (sext, *J* = 7.5 Hz, 2H), 1.35 (sext, *J* = 7.4 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.85 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 158.2, 130.3, 128.6, 119.2, 113.7, 111.3, 55.3, 40.5, 32.7, 21.9, 21.2, 13.6, 13.5. IR (neat): 2961, 2934, 2872, 2837, 2207, 1607, 1574, 1510, 1464, 1443, 1412, 1381, 1304, 1288, 1250, 1177, 1109, 1034, 837, 739 cm^{-1}. HRMS (EI) Calcd for $C_{16}H_{21}NO$: M^+, 243.1623. Found: *m*/*z* 243.1624.



(*Z*)-3-(4-[2-(Tetrahydro-2*H*-pyran-2-oxymethyl)phenyl]dimethylsilylphenyl)-2-propylhex-2-enenitrile (3ea). A colorless oil, R_f 0.35 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.51–7.47 (m, 3H), 7.41 (td, *J* = 7.5, 1.5 Hz, 1H), 7.33–7.23 (m, 3H), 4.67 (d, *J* = 12.1 Hz, 1H), 4.48 (t, *J* = 3.5 Hz, 1H), 4.39 (d, *J* = 12.1 Hz, 1H), 3.84–3.74 (m, 1H), 3.49–3.39 (m, 1H), 2.49 (t, *J* = 7.8 Hz, 2H), 2.35 (t, *J* = 7.6 Hz, 2H), 1.83–1.40 (m, 8H), 1.30 (sext, *J* = 7.5 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H), 0.61 (s, 3H), 0.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 144.2, 140.6, 139.5, 135.7, 135.5, 134.0, 129.7, 128.5, 127.0, 126.8, 119.6, 111.5, 97.8, 68.8, 62.0, 35.6, 32.5, 30.4, 25.4, 21.7, 21.1, 19.3, 13.8, 13.5, –0.96, –1.11. IR (neat): 2959, 2872, 2361, 2210, 1458, 1437, 1389, 1350, 1258, 1202, 1119, 1078, 1028, 833, 814, 775, 756 cm^{-1}. Anal. Calcd for $C_{29}H_{39}NO_2Si$: C, 75.44; H, 8.51. Found: C, 75.53; H, 8.69.

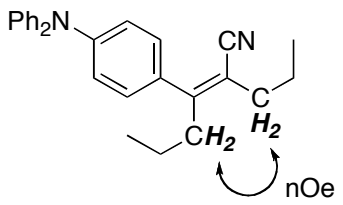


(*Z*)-3-(4-*N*,*N*-Dimethylaminophenyl)-2-propylhex-2-enenitrile (3fa). A colorless oil, R_f 0.61 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 9.0 Hz, 2H), 6.70 (d, *J* = 9.0 Hz, 2H), 2.98 (s, 6H), 2.49 (t, *J* = 7.7 Hz, 2H), 2.33 (t, *J* = 7.7 Hz, 2H),



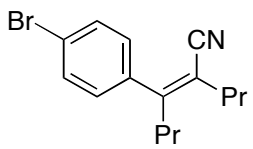
1.66 (sext, J = 7.5 Hz, 2H), 1.32 (sext, J = 7.5 Hz, 2H), 1.01 (t, J = 7.3 Hz, 3H), 0.86 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 150.5, 128.9, 127.3, 120.7, 111.6, 108.9, 40.2, 35.3, 32.7, 21.9, 21.4, 13.8, 13.5. IR (neat): 2961, 2932, 2872, 2205, 1611, 1524, 1454, 1445, 1360, 1229, 1202, 1167, 947, 820, 733 cm^{-1}. Anal. Calcd for $C_{17}H_{24}N_2$: C, 79.64; H, 9.44. Found: C, 79.64; H, 9.50.

(*Z*)-3-(4-*N*,*N*-Diphenylaminophenyl)-2-propylhex-2-enenitrile (3ga). A colorless oil,



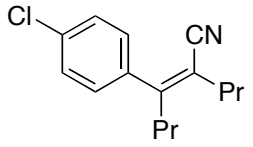
R_f 0.24 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.00 (m, 14H), 2.49 (t, J = 7.7 Hz, 2H), 2.34 (t, J = 7.6 Hz, 2H), 1.67 (sext, J = 7.5 Hz, 2H), 1.35 (sext, J = 7.5 Hz, 2H), 1.01 (t, J = 7.3 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 148.1, 147.3, 133.1, 129.3, 128.7, 125.0, 123.4, 122.0, 120.1, 110.5, 35.5, 32.7, 21.8, 21.3, 13.9, 13.5. IR (neat): 2963, 2932, 2872, 2208, 1591, 1506, 1493, 1327, 1277, 839, 754, 696 cm^{-1}. HRMS (EI) Calcd for $C_{27}H_{28}N_2$: M^+, 380.2252. Found: *m*/*z* 380.2244.

(*Z*)-3-(4-Bromophenyl)-2-propylhex-2-enenitrile (3ha). A colorless oil, R_f 0.53



(hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.6 Hz, 2H), 7.18 (d, J = 8.6 Hz, 2H), 2.48 (t, J = 7.7 Hz, 2H), 2.35 (t, J = 7.6 Hz, 2H), 1.67 (sext, J = 7.5 Hz, 2H), 1.30 (sext, J = 7.5 Hz, 2H), 1.01 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.5, 138.9, 131.7, 129.4, 122.8, 119.3, 112.3, 35.5, 32.4, 21.7, 21.0, 13.8, 13.5. IR (neat): 2963, 2932, 2872, 2210, 1587, 1487, 1458, 1393, 1381, 1101, 1072, 1011, 831, 785 cm^{-1}. HRMS (EI) Calcd for $C_{15}H_{18}BrN$: M^+, 291.0622. Found: *m*/*z* 291.0628.

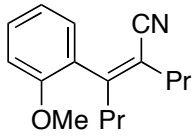
(*Z*)-3-(4-Chlorophenyl)-2-propylhex-2-enenitrile (3ia). A colorless oil, R_f 0.48



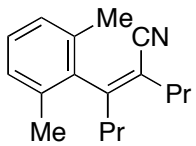
(hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 8.6 Hz, 2H), 2.49 (t, J = 7.7 Hz, 2H), 2.35 (t, J = 7.6 Hz, 2H), 1.67 (sext, J = 7.5 Hz, 2H), 1.30 (sext, J = 7.5 Hz, 2H), 1.02 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 57.5, 138.5, 134.6, 129.2, 128.7, 119.3, 112.3, 35.6, 32.4, 21.7, 21.0,

13.8, 13.5. IR (neat): 2963, 2932, 2874, 2210, 1593, 1491, 1458, 1092, 1015, 835 cm^{-1}. Anal. Calcd for $C_{15}H_{18}ClN$: C, 72.71; H, 7.32. Found: C, 72.97; H, 7.59.

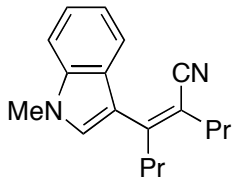
(*Z*)-3-(2-Methoxyphenyl)-2-propylhex-2-enenitrile (3ka). A colorless oil, R_f 0.34 (hexane–ethyl acetate = 7.5:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.8, 1.7 Hz, 1H), 7.09 (dd, *J* = 7.5, 1.8 Hz, 1H), 6.96 (td, *J* = 7.4, 1.0 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 3.81 (s, 3H), 2.47 (t, *J* = 7.8 Hz, 2H), 2.36 (t, *J* = 7.5 Hz, 2H), 1.67 (sext, *J* = 7.4 Hz, 2H), 1.30 (sext, *J* = 7.5 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 156.1, 129.72, 129.68, 129.4, 120.5, 119.4, 112.9, 111.1, 55.5, 35.0, 31.8, 21.7, 20.9, 14.0, 13.4. IR (neat): 2963, 2934, 2872, 2212, 1597, 1578, 1489, 1464, 1435, 1275, 1246, 1178, 1163, 1124, 1097, 1049, 1026, 799, 752 cm^{-1}. Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70. Found: C, 78.86; H, 8.67.



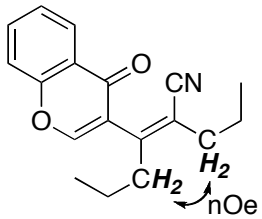
(*Z*)-3-(2,6-Dimethylphenyl)-2-propylhex-2-enenitrile (3la). A colorless oil, R_f 0.53 (hexane–ethyl acetate = 5:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 8.5, 6.5 Hz, 1H), 7.06 (d, *J* = 7.3 Hz, 2H), 2.45–2.35 (m, 4H), 2.22 (s, 6H), 1.70 (sext, *J* = 7.4 Hz, 2H), 1.42–1.29 (m, 2H), 1.05 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 139.5, 134.6, 127.9, 127.7, 118.7, 113.7, 36.2, 31.6, 21.6, 20.8, 19.8, 14.6, 13.6. IR (neat): 2963, 2932, 2872, 2212, 1464, 1379, 772 cm^{-1}. Anal. Calcd for $C_{17}H_{23}N$: C, 84.59; H, 9.60. Found: C, 84.38; H, 9.71.



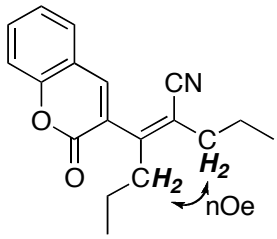
(*Z*)-3-(1-Methylindol-3-yl)-2-propylhex-2-enenitrile (3na). A pale yellow solid, mp = 74.7–75.3 °C, R_f 0.30 (hexane–ethyl acetate = 5:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.9 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.30–7.23 (m, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 3.81 (s, 3H), 2.66 (t, *J* = 7.8 Hz, 2H), 2.41 (t, *J* = 7.6 Hz, 2H), 1.71 (sext, *J* = 7.5 Hz, 2H), 1.36 (sext, *J* = 7.6 Hz, 2H), 1.05 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 152.4, 137.0, 129.0, 126.3, 122.0, 120.9, 120.2, 119.9, 114.3, 109.7, 109.4, 35.3, 33.0, 32.4, 22.0, 21.8, 13.9, 13.6. IR (KBr): 2961, 2870, 2201, 1614, 1605, 1537, 1477, 1466, 1385, 1331, 1244, 1134, 1105, 1090, 1015, 845, 741 cm^{-1}. Anal. Calcd for $C_{18}H_{22}N_2$: C, 81.16; H, 8.32. Found: C, 81.02; H, 8.47.



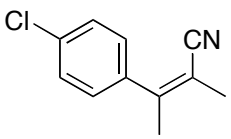
(*Z*)-3-(4-Oxo-4*H*-chromen-3-yl)-2-propylhex-2-enenitrile (3oa). A yellow oil, R_f 0.33 (hexane–ethyl acetate = 7:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.9 Hz, 1H), 7.89 (s, 1H), 7.70 (t, *J* = 7.9 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 2.60 (t, *J* = 7.8 Hz, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 1.69 (sext, *J* = 7.4 Hz, 2H), 1.38 (sext, *J* = 7.5 Hz, 2H), 1.04 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5, 156.0, 153.5, 151.0, 133.9, 125.9, 125.4, 124.4, 124.1, 118.6, 118.1, 115.3, 33.3, 32.0, 21.7, 21.2, 14.0, 13.6. IR (neat): 3069, 2963, 2932, 2872, 2212, 1649, 1616, 1572, 1466, 1377, 1350, 1321, 1304, 1296, 1221, 1165, 1148, 1107, 1096, 912, 887, 851, 762, 706, 538 cm^{-1}. HRMS (EI) Calcd for $C_{18}H_{19}NO_2$; M^+, 281.1416. Found: *m*/*z* 281.1418.



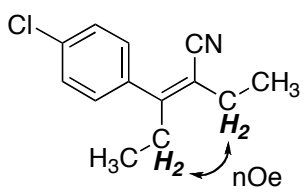
(*Z*)-3-(2-Oxo-2*H*-chromen-3-yl)-2-propylhex-2-enenitrile (3pa). A white solid, mp = 68.6–69.6 °C, R_f 0.23 (hexane–ethyl acetate = 7:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.59–7.51 (m, 2H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 1H), 2.60 (t, *J* = 7.8 Hz, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 1.70 (sext, *J* = 7.4 Hz, 2H), 1.40 (sext, *J* = 7.5 Hz, 2H), 1.05 (t, *J* = 7.3 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 153.7, 153.5, 142.5, 132.1, 128.1, 127.4, 124.6, 118.5, 118.4, 116.5, 115.2, 33.0, 32.0, 21.7, 21.4, 14.0, 13.7. IR (neat): 3036, 2961, 2932, 2872, 2211, 1713, 1611, 1570, 1489, 1458, 1381, 1368, 1252, 1225, 1186, 1126, 1076, 1065, 1036, 984, 972, 926, 910, 800, 764, 741 cm^{-1}. Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81. Found: C, 76.74; H, 6.75.



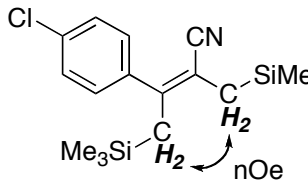
(*Z*)-3-(4-Chlorophenyl)-2-methylbut-2-enenitrile (3ib). A colorless oil, R_f 0.13 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dt, *J* = 9.0, 2.2 Hz, 2H), 7.31 (dt, *J* = 8.8, 2.2 Hz, 2H), 2.16 (q, *J* = 1.1 Hz, 3H), 2.41 (q, *J* = 1.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 139.1, 134.5, 128.57, 128.55, 119.9, 105.8, 105.8, 20.7, 17.7. IR (neat): 2997, 2926, 2862, 2211, 1906, 1620, 1593, 1491, 1441, 1398, 1294, 1265, 1186, 1094, 1061, 1013, 968, 947, 833, 725, 638, 613, 602, 579, 521 cm^{-1}. HRMS (EI) Calcd for $C_{11}H_{10}ClN$; M^+, 191.0502. Found: *m*/*z* 191.0497.



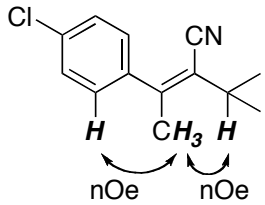
(*Z*)-3-(4-Chlorophenyl)-2-ethylpent-2-enenitrile (3ic). A colorless oil, R_f 0.13 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dt, *J* = 8.6, 2.2 Hz, 2H), 7.25 (dt, *J* = 8.4, 2.2 Hz, 2H), 2.53 (q, *J* = 7.6 Hz, 2H), 2.41 (q, *J* = 7.5 Hz, 2H), 1.24 (t, *J* = 7.5 Hz, 3H), 0.95 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 138.1, 134.5, 129.1, 128.6, 119.2, 113.0, 27.0, 24.0, 13.3, 12.6. IR (neat): 2974, 2936, 2876, 2211, 1906, 1618, 1593, 1491, 1460, 1397, 1379, 1317, 1269, 1180, 1096, 1053, 1013, 932, 856, 827, 731, 716, 577, 515 cm^{-1}. Anal. Calcd for $C_{13}H_{14}ClN$: C, 71.07; H, 6.42. Found: C, 71.10; H, 6.40.



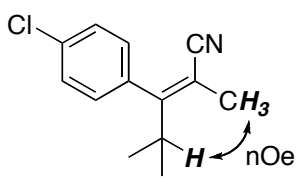
(*Z*)-3-(4-Chlorophenyl)-4-trimethylsilyl-2-[(trimethylsilylmethyl)but-2-enitrile (3id). A colorless solid, mp = 65.9–66.8 °C, R_f 0.45 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 2H), 2.03 (s, 2H), 1.77 (s, 2H), 0.17 (s, 9H), –0.10 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 139.8, 134.1, 129.3, 128.5, 120.8, 104.8, 27.6, 22.6, –0.7, –0.9. IR (KBr): 3437, 2955, 2899, 2203, 1906, 1599, 1589, 1489, 1466, 1397, 1304, 1296, 1246, 1202, 1165, 1152, 1134, 1090, 1030, 1013 903, 839, 789, 775, 766, 739, 725, 698, 675, 652, 629, 608, 521, 503 cm^{-1}. Anal. Calcd for $C_{17}H_{26}ClNSi_2$: C, 60.76; H, 7.80. Found: C, 60.54; H, 7.99.



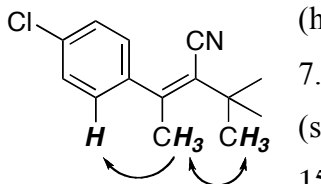
(*Z*)-3-(4-Chlorophenyl)-2-isopropylbut-2-enenitrile (3ie). A colorless oil, R_f 0.20 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dt, *J* = 8.7, 2.2 Hz, 2H), 7.29 (dt, *J* = 8.8, 2.2 Hz, 2H), 2.92 (sext, *J* = 6.8 Hz, 1H), 2.18 (s, 3H), 1.22 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.5, 139.5, 134.4, 128.7, 128.5, 118.9, 117.4, 29.2, 21.2, 20.5. IR (neat): 2970, 2932, 2872, 2211, 1904, 1613, 1593, 1491, 1464, 1398, 1389, 1366, 1292, 1263, 1094, 1076, 1047, 1007, 831, 797, 723, 700, 673, 631, 579, 532, 492 cm^{-1}. Anal. Calcd for $C_{13}H_{14}ClN$: C, 71.07; H, 6.42. Found: C, 71.36; H, 6.44.



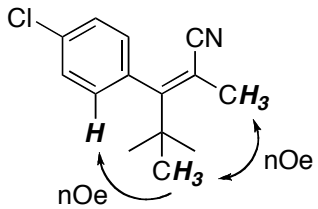
(*Z*)-3-(4-Chlorophenyl)-2,5-dimethylpent-2-enenitrile (3'ie). A colorless solid, mp = 97.8–98.8 °C, R_f 0.13 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dt, *J* = 8.8, 2.3 Hz, 2H), 7.05 (dt, *J* = 8.8, 2.2 Hz, 2H), 3.08 (sext, *J* = 6.9 Hz, 1H), 2.07 (s, 3H), 0.99 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 136.2, 134.1, 129.5, 128.4, 119.4, 107.0, 30.7, 20.5, 16.1. IR (KBr): 3447, 2974, 2932, 2872, 2209, 1908, 1624, 1589, 1489, 1466, 1391, 1364, 1329, 1113, 1103, 1090, 1049, 1015, 963, 878, 845, 814, 731, 723, 567, 548, 521, 469 cm^{-1}. Anal. Calcd for $C_{13}H_{14}ClN$: C, 71.07; H, 6.42. Found: C, 71.07; H, 6.37.



(*Z*)-3-(4-Chlorophenyl)-2-*tert*-butylbut-2-enenitrile (3if). A colorless oil, R_f 0.15 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dt, *J* = 8.4, 2.3 Hz, 2H), 7.21 (dt, *J* = 8.6, 2.2 Hz, 2H), 2.29 (s, 3H), 1.40 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 141.9, 134.1, 128.62, 128.55, 121.9, 118.7, 34.2, 30.6, 23.1. IR (neat): 2970, 2911, 2874, 2207, 1902, 1593, 1489, 1433, 1397, 1368, 1290, 1238, 1206, 1092, 1034, 1015, 831, 783, 687, 577, 532 cm^{-1}. Anal. Calcd [as a mixture with **3if** and **3'if**] for $C_{14}H_{16}ClN$: C, 71.94; H, 6.90. Found: C, 72.11; H, 6.90.



(*Z*)-3-(4-Chlorophenyl)-2,4,4-trimethylpent-2-enenitrile (3'if). A colorless solid, mp = 76.7–77.5 °C, R_f 0.15 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dt, *J* = 8.6, 2.2 Hz, 2H), 7.00 (dt, *J* = 8.6, 2.3 Hz, 2H), 2.21 (s, 3H), 1.18 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 140.2, 133.6, 128.6, 128.4, 120.1, 109.6, 36.9, 30.5, 19.1. IR (KBr): 3441, 2969, 2868, 2214, 1591, 1487, 1464, 1397, 1364, 1223, 1198, 1177, 1096, 1047, 1017, 968, 949, 939, 928, 860 841, 826, 791, 725, 718, 608, 563, 546, 530, 478 cm^{-1}.



(*Z*)-3-(4-Chlorophenyl)-2-(4-methoxyhenyl)pent-2-enenitrile [(*Z*)-3ig]. A colorless solid, mp = 109.8–110.5 °C, R_f 0.34 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.30 (m, 6H), 6.96 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 2.58 (q, *J* = 7.5 Hz, 2H), 0.93 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9, 159.8, 137.5, 135.0, 130.1, 129.3, 128.9, 126.4, 119.2, 114.2, 112.1, 55.4, 27.5, 12.8. IR (KBr): 2980, 2963, 2934, 2841, 2206, 1605, 1589, 1570, 1510, 1491, 1464, 1445, 1302, 1283, 1254, 1177, 1105, 1084, 1036, 1011, 845, 829, 689, 515 cm^{-1}. Anal. Calcd for $C_{18}H_{16}ClNO$: C, 72.60; H, 5.42. Found: C, 72.68; H, 5.67.

(*E*)-3-(4-Chlorophenyl)-2-(4-methoxyhenyl)pent-2-enenitrile [(*E*)-3ig]. A pale yellow oil, R_f 0.26 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.4 Hz, 2H), 7.03–6.97 (m, 4H), 6.70 (d, *J* = 8.8 Hz, 2H), 3.76 (s, 3H), 2.92 (q, *J* = 7.5 Hz, 2H), 1.06 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 158.2, 136.4, 134.3, 130.7, 129.9, 128.8, 125.7, 118.8, 113.8, 111.4, 55.2, 32.0, 12.6. IR (neat): 2972, 2936, 2212, 1607, 1510, 1489, 1464, 1294, 1254, 1178, 1092, 1034, 1015, 912, 826, 733 cm^{-1}. HRMS (EI) Calcd for $C_{18}H_{16}ClNO$: M^+, 297.0920. Found: *m*/*z* 297.0932.

(*Z*)-3-(4-Chlorophenyl)-3-(4-methoxyhenyl)-2-ethylacrylonitrile (3'ig). A pale yellow oil, R_f 0.26 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 3.83 (s, 3H), 2.42 (q, *J* = 7.5 Hz, 2H), 1.24 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 154.9, 138.7, 135.2, 130.9, 130.8, 130.6, 128.5, 119.7, 113.8, 113.0, 55.3, 25.8, 13.3. IR (neat): 2974, 2206, 1607, 1510, 1489, 1460, 1288, 1252, 1175, 1092, 1032, 1015, 908, 833, 824, 731 cm^{-1}; Calcd for $C_{18}H_{16}ClNO$: C, 72.60; H, 5.42. Found: C, 72.40; H, 5.24.

(*E*)-3-(4-Chlorophenyl)-2-trimethylsilylbut-2-enenitrile [(*E*)-3ih]. A colorless oil, R_f 0.14 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.33 (m, 4H), 2.31, (s, 3H), 0.39 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 140.5, 134.9, 128.6, 128.1, 120.1, 111.2, 24.5, –0.2. IR (neat): 2959, 2195, 1595, 1578, 1556, 1489, 1254, 1103, 1013, 845, 760, 673 cm^{-1}. Anal. Calcd [as a mixture with (*Z*)-**3ih** and **3'ih**] for $C_{13}H_{16}ClNSi$: C, 62.50; H, 6.46. Found: C, 62.75; H, 6.52.

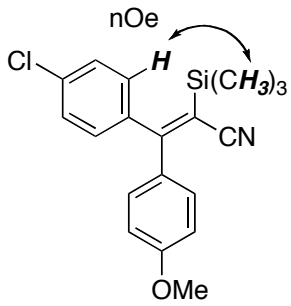
(*Z*)-3-(4-Chlorophenyl)-2-trimethylsilylbut-2-enenitrile [(*Z*)-3ih]. A colorless oil, R_f 0.14 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.6 Hz, 2H), 7.09 (d, *J* = 8.6 Hz, 2H), 2.46 (s, 3H), –0.01 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 140.3, 134.7, 128.5, 128.1, 119.7, 113.0, 28.2, –0.2. IR (neat): 2959, 2899, 2197, 1599, 1576, 1485, 1435, 1254, 1105, 1090, 1015, 982, 845, 762, 698, 633, 554 cm^{-1}.

(*E*)-3-(4-Chlorophenyl)-3-(trimethylsilyl)-2-methylpropenenitrile (3'ih). A colorless solid, mp = 67.2–67.9 °C, R_f 0.14 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 2.19 (s, 3H), 0.16 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 140.9, 132.9, 128.6, 127.7, 119.9, 118.3, 20.5, –0.2. IR (KBr): 2957, 2214, 1580, 1487, 1250, 1088, 1013, 908, 843, 800, 760, 521 cm^{-1}.

(*E*)-3-(4-Chlorophenyl)-3-(4-methoxyphenyl)-2-trimethylsilylacrylonitrile [(*E*)-3ii]. A colorless oil, R_f 0.38 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 4H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 0.10 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 160.6, 139.6, 135.7, 133.2, 130.8, 130.7, 128.3, 121.0, 113.5, 111.3, 55.4, 0.0. IR (neat): 2957, 2899, 2839, 2189, 1607,

1508, 1487, 1304, 1288, 1252, 1175, 1092, 1032, 1015, 845, 802, 760 cm^{-1}. Anal. Calcd for $C_{19}H_{20}ClNOSi$: C, 66.74; H, 5.90. Found: C, 66.92; H, 5.86.

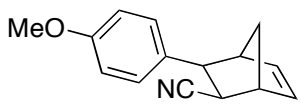
(*Z*)-3-(4-Chlorophenyl)-3-(4-methoxyphenyl)-2-trimethylsilylacrylonitrile [(*Z*)-3ii].



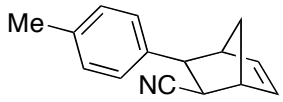
A colorless solid, mp = 98.7–99.6 °C, R_f 0.35 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 3.83 (s, 3H), 0.07 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 160.8, 139.8, 135.3, 132.9, 131.0, 130.7, 128.3, 121.1, 113.5, 110.1, 55.4, –0.01. IR (KBr): 2961, 2191, 1601, 1572, 1543, 1508, 1489, 1306, 1252, 1182, 1167, 1092, 1028, 860, 837 cm^{-1}. Anal. Calcd for $C_{19}H_{20}ClNOSi$: C, 66.74; H, 5.90. Found: C, 66.48; H, 5.97.

Arylcyanation of norbornadiene. *General procedure.* In a dry box, to an aryl cyanide (1.00 mmol) placed in a vial were sequentially added a solution of $Ni(cod)_2$ (2.8 mg, 10 μmol) and $Me_2P(CH_2)_2PMe_2$ (1.5 mg, 10 μmol) in toluene (0.67 mL), a 1.04 M solution of $AlMe_2Cl$ in hexane (39 μL, 40 μmol), norbornadiene (138 mg, 1.50 mmol), and dodecane (internal standard, 85 mg, 0.50 mmol). The vial was taken out from the dry box and heated at 80 °C for the time specified in Table 5. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography to give the corresponding arylcyanation products in yields listed in Table 5.

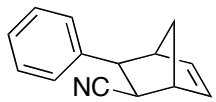
(2*R,3*S**)-2-Cyano-3-(4-methoxyphenyl)bicyclo[2.2.1]hept-5-ene (5aa).** A colorless



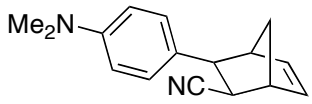
solid, mp = 67.3–68.1 °C, R_f 0.19 (hexane–ethyl acetate = 7:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dt, *J* = 8.4, 1.7 Hz, 2H), 6.90 (dt, *J* = 8.8, 2.6 Hz, 2H), 6.43 (dd, *J* = 5.7, 3.3 Hz, 1H), 6.18 (dd, *J* = 5.8, 3.0 Hz, 1H), 3.80 (s, 3H), 3.33 (s, 1H), 3.16 (d, *J* = 1.3 Hz, 1H), 3.03 (dd, *J* = 9.0, 1.5 Hz, 1H), 2.78 (dd, *J* = 9.1, 1.8 Hz, 1H), 2.11 (d, *J* = 9.3 Hz, 1H), 1.78 (dt, *J* = 9.4, 1.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 140.8, 135.3, 131.8, 129.0, 121.3, 114.0, 55.2, 48.2, 46.53, 46.47, 46.2, 36.5. IR (KBr): 2976, 2234, 1611, 1512, 1460, 1250, 1182, 1034, 835, 764, 729, 692 cm^{-1}. Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71. Found: C, 79.92; H, 6.74.

(2*R,3*S**)-2-Cyano-3-(4-methylphenyl)bicyclo[2.2.1]hept-5-ene (5ba).** A colorless solid, mp = 81.4–84.0 °C, R_f 0.20 (hexane–ethyl acetate = 10:1). 

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.43 (dd, *J* = 5.7, 3.1 Hz, 1H), 6.18 (dd, *J* = 5.7, 2.9 Hz, 1H), 3.33 (d, *J* = 0.6 Hz, 1H), 3.19 (d, *J* = 1.5 Hz, 1H), 3.04 (dd, *J* = 9.0, 1.5 Hz, 1H), 2.81 (dd, *J* = 9.1, 1.9 Hz, 1H), 2.34 (s, 3H), 2.11 (d, *J* = 9.3 Hz, 1H), 1.79 (dt, *J* = 9.3, 1.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.7, 136.8, 136.6, 135.3, 129.4, 127.9, 121.3, 48.2, 46.8, 46.3, 46.2, 36.5, 21.1. IR (KBr): 2978, 2922, 2234, 1514, 1456, 1327, 1263, 827, 758, 727, 696, 505 cm^{-1}. Anal. Calcd for $C_{15}H_{15}N$: C, 86.08; H, 7.22. Found: C, 86.27; H, 7.35.

(2*R,3*S**)-2-Cyano-3-phenylbicyclo[2.2.1]hept-5-ene (5ca).** A colorless solid, mp = 94.3–94.7 °C, R_f 0.21 (hexane–ethyl acetate = 10:1). 

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.34 (m, 2H), 7.30–7.24 (m, 3H), 6.44 (dd, *J* = 5.7, 3.3 Hz, 1H), 6.19 (dd, *J* = 5.7, 2.9 Hz, 1H), 3.34 (s, 1H), 3.22 (d, *J* = 1.3 Hz, 1H), 3.08 (dd, *J* = 9.1, 1.5 Hz, 1H), 2.83 (dd, *J* = 9.1, 1.9 Hz, 1H), 2.12 (d, *J* = 9.3 Hz, 1H), 1.80 (dt, *J* = 9.3, 1.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.7, 139.9, 135.3, 128.7, 128.0, 127.1, 121.1, 48.2, 47.2, 46.3, 46.2, 36.5. IR (KBr): 2996, 2951, 2230, 1451, 1327, 1263, 1098, 1076, 799, 723, 712, 700 cm^{-1}. Anal. Calcd for $C_{14}H_{13}N$: C, 86.12; H, 6.71. Found: C, 86.09; H, 6.65.

(2*R,3*S**)-2-Cyano-3-(4-*N*,*N*-dimethylaminophenyl)bicyclo[2.2.1]hept-5-ene (5fa).** A yellow solid, mp = 130.5–131.1 °C, R_f 0.28 (hexane–ethyl acetate = 5:1). 

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 7.9 Hz, 2H), 6.42 (dd, *J* = 5.7, 3.1 Hz, 1H), 6.16 (dd, *J* = 5.6, 3.0 Hz, 1H), 3.32 (s, 1H), 3.14 (d, *J* = 1.5 Hz, 1H), 2.99 (dd, *J* = 9.0, 1.5 Hz, 1H), 2.94 (s, 6H), 2.78 (dd, *J* = 9.0, 1.8 Hz, 1H), 2.12 (d, *J* = 9.3 Hz, 1H), 1.77 (dt, *J* = 9.4, 1.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.4, 140.8, 135.1, 128.6, 127.3, 121.5, 112.7, 48.1, 46.6, 46.4, 40.5, 36.5. IR (KBr): 2918, 2236, 1614, 1522, 1447, 1354, 1234, 1200, 1167, 1063, 951, 824, 729, 689 cm^{-1}. Anal. Calcd for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61. Found: C, 80.38; H, 7.59.

(2*R,3*S**)-2-Cyano-3-(4-bromophenyl)bicyclo[2.2.1]hept-5-ene (5ha).** A colorless solid, mp = 141.8–142.1 °C, R_f 0.30 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dt, *J* = 8.6, 2.3 Hz, 2H), 7.13 (dt, *J* = 8.2, 2.1 Hz, 2H), 6.43 (dd, *J* = 5.7, 3.3 Hz, 1H), 6.20 (dd, *J* = 5.6, 3.0 Hz, 1H), 3.35 (s, 1H), 3.17 (d, *J* = 1.5 Hz, 1H), 3.02 (dd, *J* = 9.1, 1.4 Hz, 1H), 2.82 (dd, *J* = 9.1, 1.9 Hz, 1H), 2.06 (d, *J* = 9.7 Hz, 1H), 1.80 (dt, *J* = 9.5, 1.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5, 139.0, 135.5, 131.8, 129.7, 121.1, 120.9, 48.2, 46.7, 46.20, 46.16, 36.4. IR (KBr): 2978, 2924, 2236, 1489, 1404, 1327, 1072, 1009, 835, 768, 716 cm^{-1}. Anal. Calcd for $C_{14}H_{12}BrN$: C, 61.33; H, 4.41. Found: C, 61.53; H, 4.62.

(2*R,3*S**)-2-Cyano-3-(4-chlorophenyl)bicyclo[2.2.1]hept-5-ene (5ia).** A colorless solid, mp = 147.4–148.3 °C, R_f 0.34 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dt, *J* = 8.4, 2.3 Hz, 2H), 7.19 (dt, *J* = 8.4, 2.0 Hz, 2H), 6.44 (dd, *J* = 5.6, 3.2 Hz, 1H), 6.20 (dd, *J* = 5.7, 2.9 Hz, 1H), 3.36 (s, 1H), 3.19 (d, *J* = 1.5 Hz, 1H), 3.04 (dd, *J* = 9.1, 1.4 Hz, 1H), 2.83 (dd, *J* = 9.1, 1.8 Hz, 1H), 2.08 (d, *J* = 9.5 Hz, 1H), 1.82 (dt, *J* = 9.3, 1.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5, 138.5, 135.5, 132.9, 129.4, 120.8, 48.2, 46.6, 46.24, 46.15, 36.4. IR (KBr): 2978, 2924, 2238, 1493, 1408, 1327, 1088, 1013, 839, 768, 719, 671 cm^{-1}. Anal. Calcd for $C_{14}H_{12}ClN$: C, 73.20; H, 5.27. Found: C, 73.11; H, 5.34.

(2*R,3*S**)-2-Cyano-3-(2-methoxyphenyl)bicyclo[2.2.1]hept-5-ene (5ka).** A colorless solid, mp = 98.0–98.5 °C, R_f 0.38 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (td, *J* = 7.8, 1.5 Hz, 1H), 7.23 (d, *J* = 7.7 Hz, 1H), 6.99 (td, *J* = 7.5, 1.0 Hz, 1H), 6.90 (dd, *J* = 8.2, 0.9 Hz, 1H), 6.39 (dd, *J* = 5.7, 3.1 Hz, 1H), 6.20 (dd, *J* = 5.7, 2.9 Hz, 1H), 3.85 (s, 3H), 3.31–3.26 (m, 2H), 3.15 (dd, *J* = 8.7, 1.7 Hz, 1H), 2.91 (dd, *J* = 8.8, 2.0 Hz, 1H), 1.97 (d, *J* = 9.2 Hz, 1H), 1.74 (dt, *J* = 9.2, 1.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8, 139.7, 135.7, 129.0, 128.1, 126.0, 121.5, 120.5, 110.0, 55.2, 48.0, 45.8, 44.0, 41.5, 35.7. IR (KBr): 2976, 2236, 1601, 1587, 1489, 1337, 1246, 1101, 1051, 1032, 750, 719, 706 cm^{-1}. Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71. Found: C, 80.23; H, 6.66.

Nickel/BPh_3-catalyzed alkenylcyanation of alkynes. *General procedure.* In a dry box, to a solution of $Ni(cod)_2$ (5.5 mg, 20 μmol) and PMe_3 (3.0 mg, 40 μmol) in toluene (1.0 mL) placed in a vial were added an alkenyl cyanide (1.00 mmol), BPh_3 (19.4 mg, 80 μmol), an alkyne (1.20 mmol), and dodecane (internal standard, 85 mg, 0.50 mmol). The vial was taken out from the dry box and heated at 80 °C for the time specified in Table 6. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography to give the corresponding alkenylcyanation products in yields listed in Table 6.

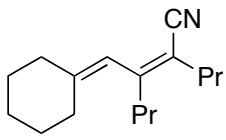
(2*Z*,4*E*)-5-Phenyl-2,3-dipropylpenta-2,4-dienenitrile (8aa). A pale yellow oil, R_f 0.13 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.1 Hz, 2H), 7.40–7.26 (m, 4H), 6.84 (d, *J* = 16.1 Hz, 1H), 2.46 (t, *J* = 8.0 Hz, 2H), 2.33 (t, *J* = 7.6 Hz, 2H), 1.66 (sext, *J* = 7.5 Hz, 2H), 1.53 (sext, *J* = 7.6 Hz, 2H) 1.02 (t, *J* = 7.5 Hz, 3H), 1.00 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 136.2, 133.5, 128.8, 128.7, 127.1, 127.0, 119.1, 112.4, 32.2, 29.9, 22.6, 21.8, 14.3, 13.6. IR (neat): 2963, 2934, 2874, 2203, 1692, 1450, 962, 754, 692 cm^{-1}. Anal. Calcd for $C_{17}H_{21}N$: C, 85.30; H, 8.84. Found: C, 85.54; H, 8.78.

(2*Z*,4*Z*)-2,3-dipropylhepta-2,4-dienenitrile [(*Z*)-8ba]. A colorless oil, R_f 0.15 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (d, *J* = 11.7 Hz, 1H), 5.66 (dt, *J* = 11.7, 7.3 Hz, 1H), 2.25 (t, *J* = 7.6 Hz, 2H), 2.20 (t, *J* = 7.7 Hz, 2H), 2.13 (qdd, *J* = 7.5, 7.3, 1.8 Hz, 2H), 1.62 (sext, *J* = 7.4 Hz, 2H), 1.42 (sext, *J* = 7.5 Hz, 2H), 1.03 (t, *J* = 7.5 Hz, 3H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 137.6, 126.8, 119.5, 111.5, 34.4, 31.8, 22.9, 21.9, 21.3, 14.1, 13.9, 13.7. IR (neat): 2964, 2934, 2874, 2208, 1458, 1379 cm^{-1}. HRMS (EI) Calcd for $C_{13}H_{21}N$: M^+, 191.1674. Found: *m*/*z* 191.1677.

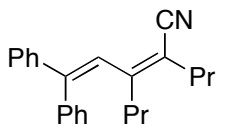
(2*Z*,4*E*)-2,3-dipropylhepta-2,4-dienenitrile [(*E*)-7ba]. A colorless oil, R_f 0.15 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.60 (dt, *J* = 15.6, 1.5 Hz, 1H), 6.07 (dt, *J* = 15.6, 6.7 Hz, 1H), 2.32 (t, *J* = 8.0 Hz, 2H), 2.28–2.19 (m, 4H), 1.61 (sext, *J* = 7.5 Hz, 2H), 1.44 (sext, *J* = 7.6 Hz, 2H), 1.07 (t, *J* = 7.4 Hz, 3H), 0.972 (t, *J* = 7.3 Hz, 3H), 0.966 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 138.3, 128.0, 119.2, 109.8, 32.0, 30.1, 26.4,

22.7, 21.9, 14.4, 13.8, 13.5. IR (neat): 2964, 2934, 2874, 2205, 1638, 1570, 1462, 1381, 1088, 966 cm^{-1}. HRMS (EI) Calcd for $C_{13}H_{21}N$: M^+, 191.1674. Found: *m*/*z* 191.1675.

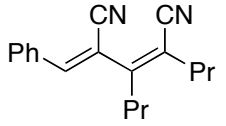
(*Z*)-2,3-Dipropyl-4-cyclohexylidene-2-butenenitrile (8ca). A pale yellow oil, R_f 0.28 (hexane–ethyl acetate = 40:1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.62 (s, 1H), 2.27–2.10 (m, 8H), 1.65–1.52 (m, 8H), 1.40 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 146.6, 121.0, 119.9, 111.1, 37.1, 34.7, 31.7, 30.6, 28.3, 27.1, 26.4, 21.8, 21.1, 14.0, 13.5. IR (neat): 2961, 2932, 2872, 2856, 2208, 1647, 1611, 1448, 1379, 1342, 1234, 1109, 1088, 833, 735 cm^{-1}. Anal. Calcd for $C_{16}H_{25}N$: C, 83.06; H, 10.89. Found: C, 82.85; H, 10.71.

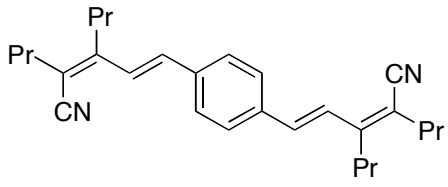


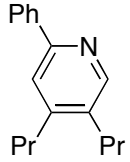
(*Z*)-5,5-Diphenyl-2,3-dipropylpenta-2,4-dienenitrile (8da). A colorless solid, mp = 58.1–58.7 °C, R_f 0.25 (hexane–ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.16 (m, 10H), 6.83 (s, 1H), 2.20 (t, *J* = 7.5 Hz, 2H), 1.89 (t, *J* = 7.8 Hz, 2H), 1.54 (sext, *J* = 7.5 Hz, 2H), 1.32 (sext, *J* = 7.5 Hz, 2H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.74 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 146.8, 142.2, 139.8, 129.9, 128.2, 128.0, 126.6, 119.5, 113.6, 32.8, 31.8, 22.0, 21.7, 13.9, 13.5. IR (KBr): 2963, 2932, 2870, 2203, 1599, 1493, 1445, 1375, 870, 779, 762, 696 cm^{-1}. Anal. Calcd for $C_{23}H_{25}N$: C, 87.57; H, 7.99. Found: C, 87.46; H, 8.04.



(2*Z*,4*Z*)-4-Cyano-5-phenyl-2,3-dipropylpenta-2,4-dienenitrile (8ea). A pale yellow oil, R_f 0.10 (hexane–ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.89–7.81 (m, 2H), 7.49–7.44 (m, 3H), 7.36 (s, 1H), 2.49 (t, *J* = 7.8 Hz, 2H), 2.36 (t, *J* = 7.7 Hz, 2H), 1.69 (sext, *J* = 7.5 Hz, 2H), 1.53 (sext, *J* = 7.5 Hz, 2H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.98 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 52.0, 148.2, 132.4, 131.3, 129.4, 128.9, 118.1, 116.3, 114.7, 109.6, 33.0, 32.8, 21.7, 21.4, 13.9, 13.7. IR (neat): 2964, 2933, 2874, 2212, 1605, 1574, 1448, 1381, 1092, 935, 758, 691 cm^{-1}. Anal. Calcd for $C_{18}H_{20}N_2$: C, 81.78; H, 7.63. Found: C, 81.83; H, 7.66.



Nickel/BPh_3-catalyzed addition reaction of 1,4-di(cyanovinyl)benzene (7f) across 2a (eq. 2).  In a dry box, to **7f** (180 mg, 1.00 mmol) placed in a vial were sequentially added a solution of $Ni(cod)_2$ (5.5 mg, 20 μmol) and PMe_3 (3.0 mg, 40 μmol) in toluene (1.0 mL), BPh_3 (19.4 mg, 80 μmol), **2a** (331 mg, 3.0 mmol). The vial was taken out from the dry box and heated at 80 °C for 44 h. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (hexane–toluene = 2:3 to toluene, then CH_2Cl_2) to give **8fa** (335 mg, 84%) as a yellow solid, mp = 147.2–148.2 °C, R_f 0.20 (hexane–toluene = 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 4H), 7.37 (d, *J* = 15.9 Hz, 2H), 6.82 (d, *J* = 15.9 Hz, 2H), 2.46 (distorted t, *J* = 8.0 Hz, 4H), 2.34 (t, *J* = 7.6 Hz, 4H), 1.67 (sext, *J* = 7.5 Hz, 4 H), 1.54 (sext, *J* = 7.6 Hz, 4 H), 1.03 (t, *J* = 7.4 Hz, 6H), 1.01 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.9, 136.5, 132.7, 127.4, 127.3, 119.0, 112.6, 32.3, 30.0, 22.7, 21.9, 14.5, 13.8. IR (KBr): 3428, 3040, 2959, 2934, 2872, 2199, 1614, 1574, 1516, 1479, 1464, 1454, 1433, 1422, 1379, 1335, 1285, 1209, 1161, 1115, 1086, 1071, 968, 903, 880, 822, 739, 658 552, 534 cm^{-1}. Anal. Calcd for $C_{28}H_{36}N_2$: C, 83.95; H, 9.06. Found: C, 83.99; H, 9.06.

Conversion of 8aa to 3,4-dipropyl-1-phenylpyridine (9) (eq. 3). To a solution of **8aa**  (72 mg, 0.30 mmol) in toluene (15 mL) was added a 1.5 M solution of DIBAL–H in toluene (0.40 mL, 0.60 mmol) at 0 °C, and the resulting mixture was stirred at the same temperature for 15 min. The reaction was quenched with MeOH (0.150 mL) at 0 °C and heated at 100 °C for 5 h in the open air. To the resulting mixture was added a slurry of SiO_2 (3.0 g) in water (0.90 mL), and the whole was stirred at rt for 45 min. Anhydrous $MgSO_4$ (0.50 g) and K_2CO_3 (0.50 g) were added, and the resulting mixture was further stirred for 90 min, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (hexane–ethyl acetate = 35:1) to give **9** (44 mg, 61%) as a pale yellow oil, R_f 0.43 (hexane–ethyl acetate = 7:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.99–7.93 (m, 2H), 7.50 (s, 1H), 7.48–7.42 (m, 2H), 7.41–7.34 (m, 1H), 2.68–2.59 (m, 4H), 1.74–1.58 (m, 4H), 1.02 (t, *J* = 7.3 Hz, 3H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0, 150.3, 149.8, 139.6, 134.5, 128.6, 128.4, 126.7,

120.7, 34.1, 31.8, 24.1, 23.5, 14.11, 14.07. IR (neat): 2959, 2932, 2870, 1597, 1477, 1377, 777, 694 cm^{-1}. Anal. Calcd for $C_{17}H_{21}N$: C, 85.30; H, 8.84. Found: C, 85.51; H, 9.12.

References and notes

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Chapter 3

Intramolecular Arylcyanation of Alkenes Catalyzed by Nickel/$AlMe_2Cl$

A catalyst system derived from nickel and cocatalytic $AlMe_2Cl$ effects the intramolecular arylcyanation of alkenes. The reaction takes place in an exclusive *exo*-trig manner to give a wide range of nitriles having a benzylic quaternary carbon in good yields. Detailed investigations are described on the scope and mechanism as well as asymmetric versions of the reaction to provide novel protocol to construct chiral quaternary stereocenters.

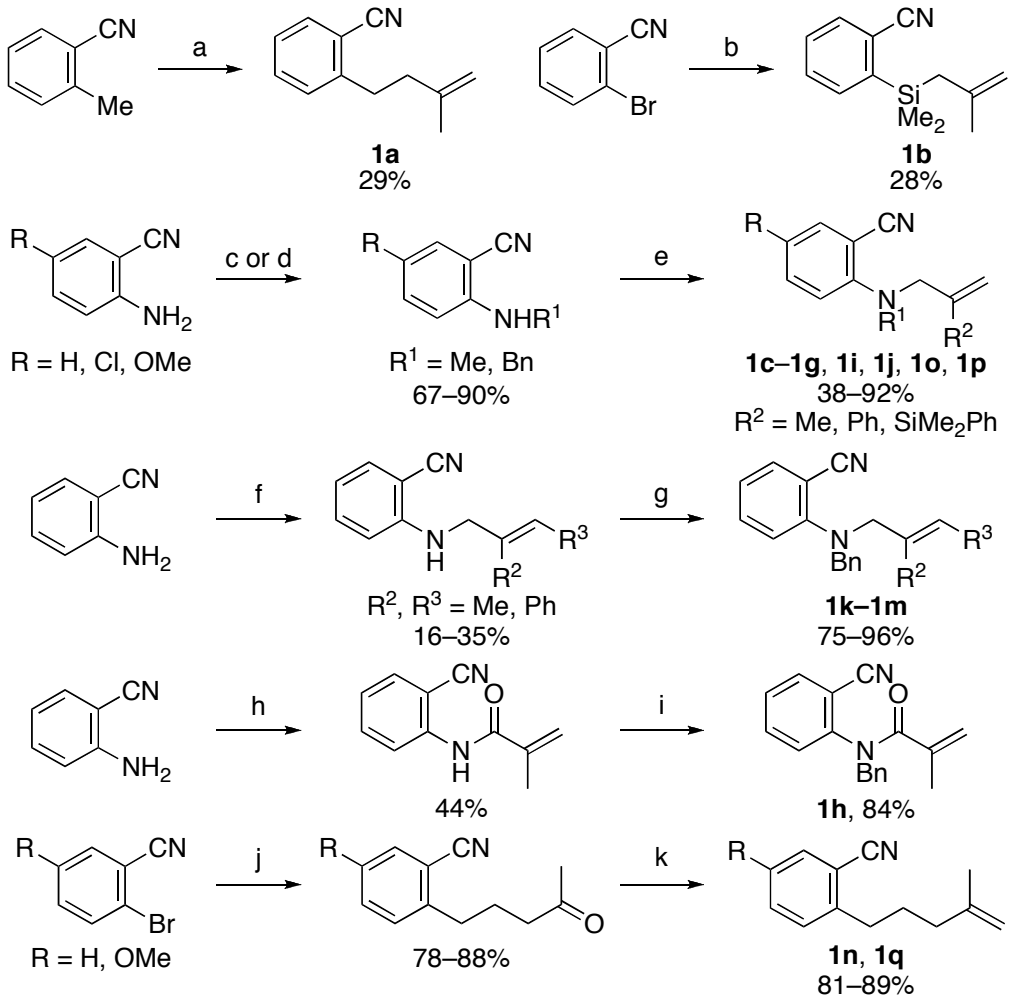
Introduction

In the previous Chapter, the author has disclosed that the arylcyanation reaction of alkynes[1] is significantly accelerated by LA cocatalysts,[2,3] whereas the attempted arylcyanation across simple 1-alkenes[4] such as styrene and vinylsilanes failed due possibly to β-hydride elimination from an alkylnickel intermediate derived from insertion of double bonds into Ar–Ni bond. Thus, the author turned his attention to an intramolecular version, which is discussed in this Chapter. The reaction allows simultaneous construction of both benzylic quaternary carbons and C–CN bonds in a single operation with high atom economy. The scope and mechanism as well as enantioselective versions of the reaction to provide novel access to asymmetric quaternary stereocenters are investigated.[5–7]

Results and discussion

Preparation of benzonitriles for intramolecular arylcyanation reaction

First, the author prepared various nitriles **1a**–**1q** to examine the feasibility of the intramolecular arylcyanation reaction across double bonds (Scheme 1). 2-(3-Methylbuta-3-en-1-yl)benzonitrile (**1a**) was prepared through lithiation of the benzylic position in *o*-tolunitrile by LDA followed by allylation with 3-bromo-2-methylpropene.[8] Halogen-lithium exchange of 2-bromobenzonitrile with butyllithium followed by the reaction with chlorodimethyl(2-methylpropen-1-yl)silane[9] gave silyl-substituted benzonitrile **1b** in 28% yield. All the 2-aminobenzonitrile derivatives were prepared by sequential *N*-alkylation[10,11] either by reductive amination or nucleophilic alkylation. The acylation of *o*-cyanoaniline with methyl methacrylate in the presence of $AlMe_3$[12] followed by *N*-benzylation afforded **1h**. The Mizoroki-Heck reaction of 2-bromobenzonitriles with 4-pentene-2-ol gave substituted 5-(2-cyanophenyl)pentan-2-ones,[13] which were then methylenated by the Wittig reaction, giving **1n** and **1q** in good yields.



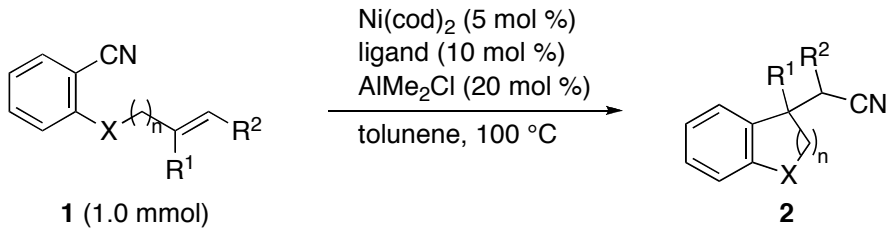
[a] Reagents and Conditions: (a) LDA (1.1 equiv), THF, –78 °C, 30 min; 3-bromo-2-methylpropene (1.2 equiv), –78 °C, 260 min, then rt, 15 h; (b) *n*-BuLi (1.1 equiv), THF, –78 °C, 2 h; chlorodimethyl(2-methylpropen-1-yl)silane (2.5 equiv), –78 °C, 2.5 h, then rt, 14 h; (c) PhCHO (1.3 equiv), AcOH, rt, 30 min; $NaBH_4$ (1.04 equiv), 0 °C to rt, 30 min; (d) $(CO_2Me)_2$ (1.5 equiv), *t*-BuOK (1.3 equiv), DMF, reflux, 11 h; (e) NaH (1.2 equiv), DMF, 0 °C to rt, 10 min; alkyl bromide or tosylate (1.1–1.5 equiv), 0–80 °C, 15 h–5 d; (f) (*E*)-2-methyl-2-butenal or (*E*)-2-methylcinnamaldehyde (1.2 equiv), $NaBH(OAc)_3$ (1.5–2.5 equiv), DCM/AcOH, 0 °C–reflux, 24 h–5 d; (g) NaH (1.2 equiv), DMF, 0 °C to rt, 10 min; BnBr (1.5 equiv), 0 °C to rt, 6 h; (h) $AlMe_3$ (1.5 equiv), benzene, 0 °C to rt, 1 h; mehyl metacrylate (1.2 equiv), 80 °C, 9 h; (i) NaH (1.2 equiv), DMF, 0 °C to rt, 5 min; BnBr (1.5 equiv), 0 °C to 80 °C, 15 h; (j) 4-penten-2-ol (1.5 equiv), $Pd(OAc)_2$ (25 mol %), *n*-Bu_4NCl (2.0 equiv), LiCl (1.0 equiv), $LiOAc•2H_2O$ (2.5 equiv), DMF, 100 °C, 24 h; (k) Ph_3PCH_3I (3.3–3.6 equiv), *t*-BuOK (2.8–3.0 equiv), THF, 0 °C to rt, 3–24 h.

Scheme 1. Preparation of nitriles for intramolecular arylcyanation reactions.[a]

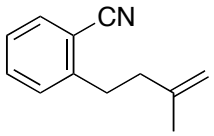
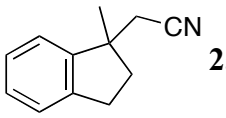
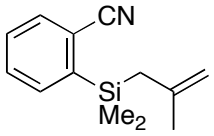
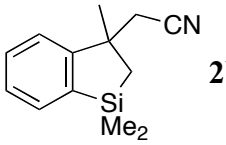
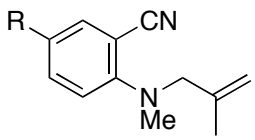
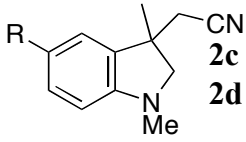
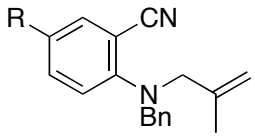
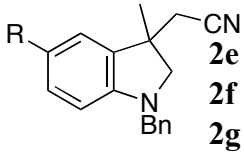
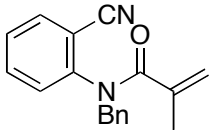
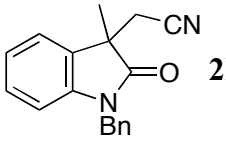
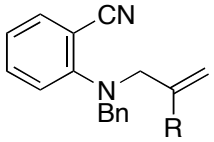
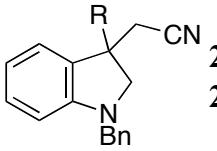
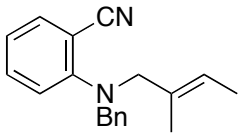
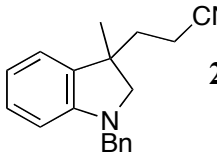
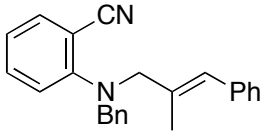
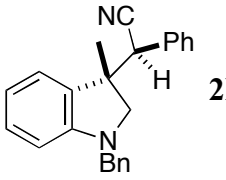
Nickel/$AlMe_2Cl$-catalyzed intramolecular arylcyanation of alkenes

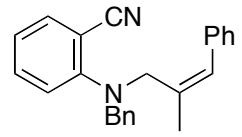
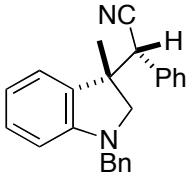
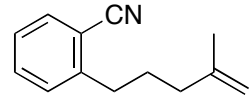
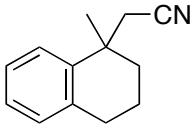
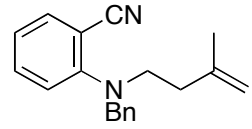
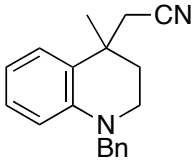
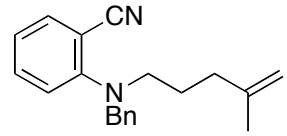
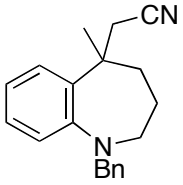
With a variety of terminal alkenyl-tethered benzonitriles in hand, the author then set out the intramolecular arylcyanation reaction of alkenes. Treatment of **1a** with $Ni(cod)_2$ (5 mol %), PMe_3 (10 mol %), and $AlMe_2Cl$ (20 mol %) in toluene at 100 °C for 7 h gave **2a** in 93% yield, which was derived from the insertion of the olefinic moiety into the Ar–CN bond in a 5-*exo*-trig fashion (entry 1 of Table 1). In the absence of $AlMe_2Cl$, only a trace amount of the adduct was observed. Silyl and alkylamino tethers as well as methoxy and chloro groups on the phenyl ring all tolerated these conditions to afford corresponding nitriles **2b**–**2g** in good yields (entries 2–8). In contrast, benzonitriles with acetylamino-, tosylamino-, and oxygen-tethers gave no desired products due to olefin isomerization and/or deallylation (Scheme 2). Disubstituted double bonds conjugated with a carbonyl and those having a phenyl or silyl substituent participated in the addition reaction (entries 9–12). Not only disubstituted double bonds, the addition reactions across trisubstituted ones also successfully took place (entries 13–16). The reaction of **1k** gave formal 1,3-arylcyanation product **2'k** together with small amounts of normal adduct **2k** and a decyanated olefin (*vide infra*). A high degree of stereospecificity was observed with **1l** and **1m**, giving respective diastereomers **2l** and **2m** (entries 14–16). Relative stereochemistry of **2l** was unambiguously determined by X-ray crystallography (Figure 1). Thus, the alkene-arylcyanation is shown to proceed in a *syn* stereochemical manner. Larger ring systems including six- and seven-membered compounds were successfully constructed (entries 17–21), whereas four-membered ring formation was not attained starting with 2-allylbenzonitrile. Instead, olefin isomerization as well as formation of 2-methylindene derived from *endo*-cyclization followed by *β*-hydride elimination were observed (Scheme 2). Under the identical conditions, the reaction of benzonitrile bearing a monosubstituted double bond (**1r**) resulted in olefin isomerization and 1-methylindene (**3**). In contrast, a palladium catalyst gave cyclization product **2r** albeit in a low yield (Scheme 3).

Table 1. Nickel/$AlMe_2Cl$-catalyzed intramolecular arylcyanation of alkenes.[a]

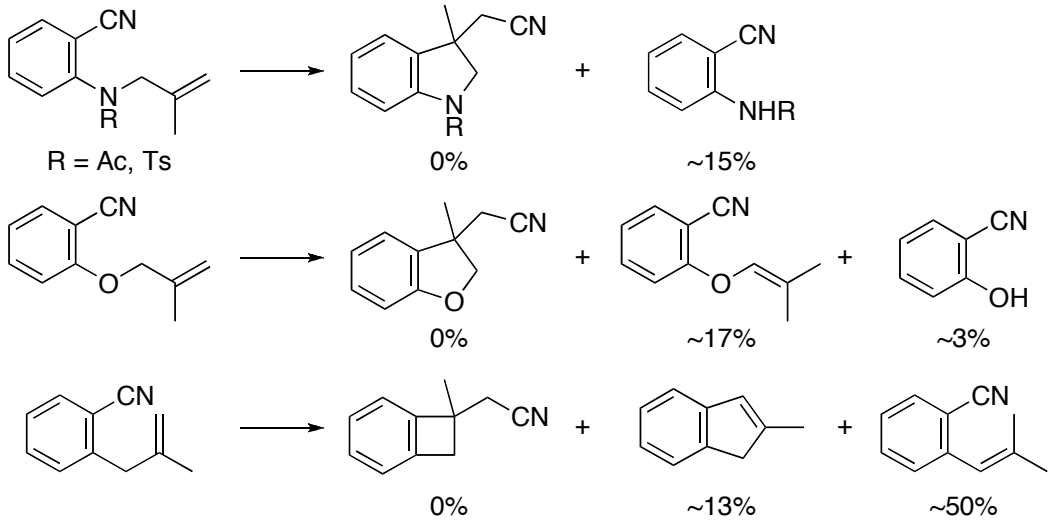


1 (1.0 mmol) **2**

enrty	substrate		ligand	time (h)	product	yield (%)[b]
1		**1a**	PMe_3	7	 **2a**	93
2		**1b**	PMe_3	20	 **2b**	18[c]
3			$PCyPh_2$	20		92
4[d]		R = H (**1c**)	PMe_3	4	 **2c**	86
5		MeO (**1d**)	PMe_3	3	**2d**	76
6		R = H (**1e**)	PMe_3	7	 **2e**	79
7		Cl (**1f**)	PMe_3	7	**2f**	82
8		MeO (**1g**)	PMe_3	7	**2g**	85
9		**1h**	PMe_3	3	 **2h**	71[c]
10			PMe_2Ph	3		74
11		R = Ph (**1i**)	PMe_3	6	 **2i**	89
12		$SiMe_2Ph$ (**1j**)	PMe_3	6	**2j**	84
13		**1k**[e]	PMe_3	3	 **2'k**	62
14		**1l**	PMe_3	0.5	 **2l**	48[c,f]
15			PMe_2Ph	0.5		88[f]

16		**1m**	PMe_2Ph	1		**2m**	76[g]
17		**1n**	PMe_3	3		**2n**	16[c]
18			DMPE[h]	3			91
19		**1o**	PMe_3	3		**2o**	96
20		**1p**	PMe_3	5		**2p**	9[c]
21			DMPE[h]	5			58

[a] The reactions were carried out using a substrate (1.0 mmol), $Ni(cod)_2$ (5 mol %), a ligand (10 mol %), and $AlMe_2Cl$ (20 mol %) in toluene at 100 °C. [b] Isolated yields. [c] Yields estimated by GC with 0.036–0.100 mmol scale. [d] Reaction run on a 3.0 mmol scale. [e] *E*/*Z* = 95:5. [f] dr = 98:2 (>99:1 after isolation). [g] dr = 97:3 (>99:1 after isolation). [h] $Me_2P(CH_2)_2PMe_2$ (5 mol %).



[a] Reagents and Conditions: $Ni(cod)_2$ (5 mol %), $PCyPh_2$ (10 mol %), $AlMe_2Cl$ (20 mol %), toluene, 100 °C, 23–50 h.

Scheme 2. Limitation of intramolecular arylcyanation of alkenes.[a]

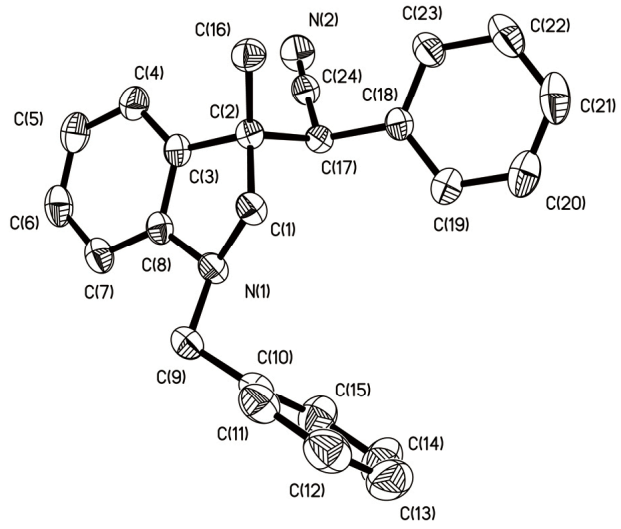
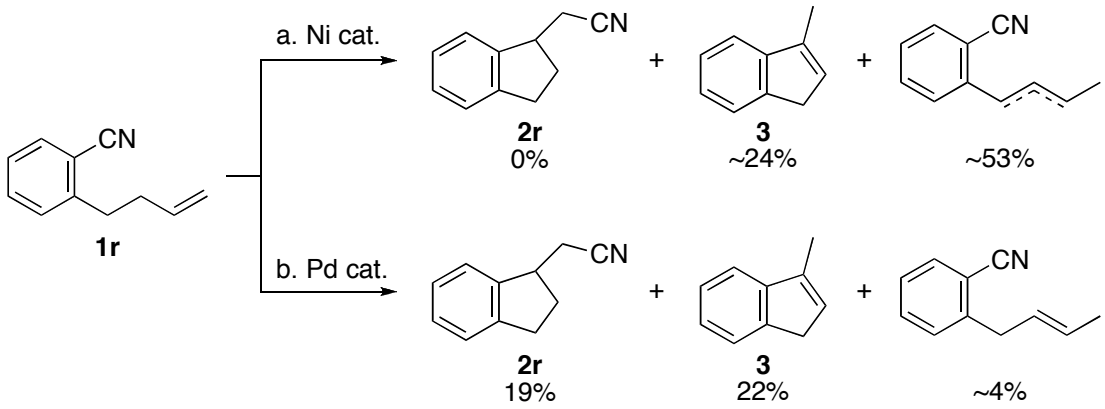


Figure 1. Molecular structure of **2l**.



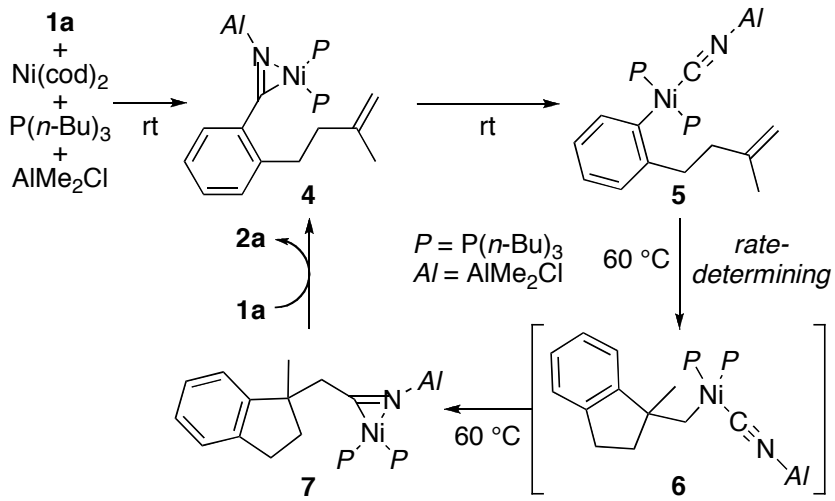
[a] Reagents and Conditions: (a) $Ni(cod)_2$ (5 mol %), $PMePh_2$ (10 mol %), $AlMe_2Cl$ (20 mol %), toluene, 100 °C, 30 h; (b) $CpPd(\pi\text{-allyl})$ (5 mol %), $PMePh_2$ (10 mol %), $AlMe_2Cl$ (20 mol %), toluene, 100 °C, 24 h.

Scheme 3. Transformations of 2-(but-3-en-1-yl)benzonitrile (**1r**) under the intramolecular arylcyanation conditions.[a]

Mechanism of intramolecular arylcyanation reaction

By monitoring the stoichiometric reaction of substrate **1a** with the catalyst system, some reaction intermediates were detected and characterized by NMR spectroscopy and/or by X-ray crystallographic analysis (Scheme 4). A mixture of $Ni(cod)_2$, $P(n\text{-Bu})_3$ (2 equiv), $AlMe_2Cl$, and **1a** gave immediately $AlMe_2Cl$-bounded η^2-nitrile complex **4**.[14,15] $AlMe_2Cl$ seems to promote the coordination of the cyano group to nickel(0),

because formation of no η^2-nitrile complex was observed in its absence. Oxidative addition of the Ar–CN bond in **4** proceeded at room temperature in 6 h to give **5**.[3] The molecular structures of **4** and **5** were unambiguously characterized by X-ray crystallography (Figure 2). Upon heating at 60 °C for 46 h, **5** was further converted to **7** presumably via **6**, the insertion step through a tetra- or penta-coordinate intermediate or the preceding ligand exchange step appearing to be rate-determining. Treatment of **7** with stoichiometric amount of **1a** resulted in regeneration of **4**, suggesting that the formation of the η^2-nitrile complex is more favorable for conjugated nitriles than alkyl cyanides because of the lower energy levels of the π^* orbitals of the conjugated cyano groups to better stabilize back-bonding interactions with nickel(0).[16]



Scheme 4. Plausible mechanism of the reaction.

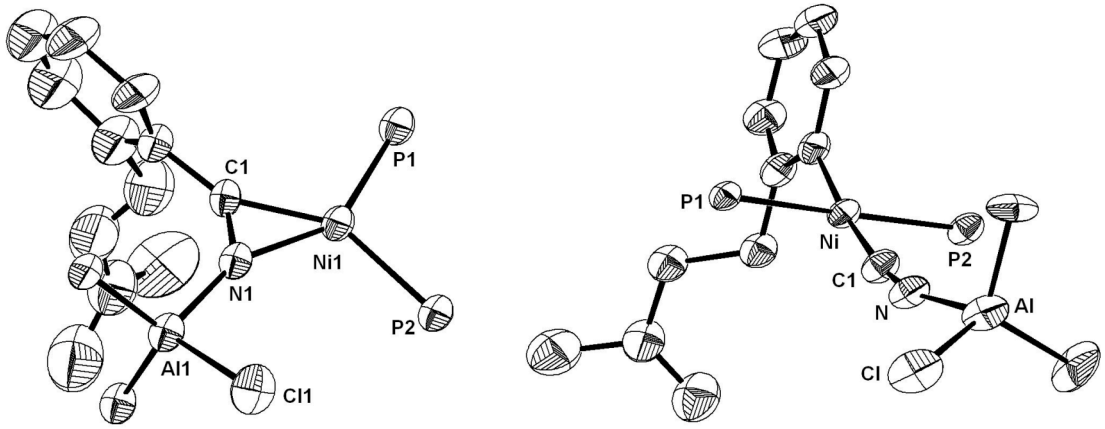
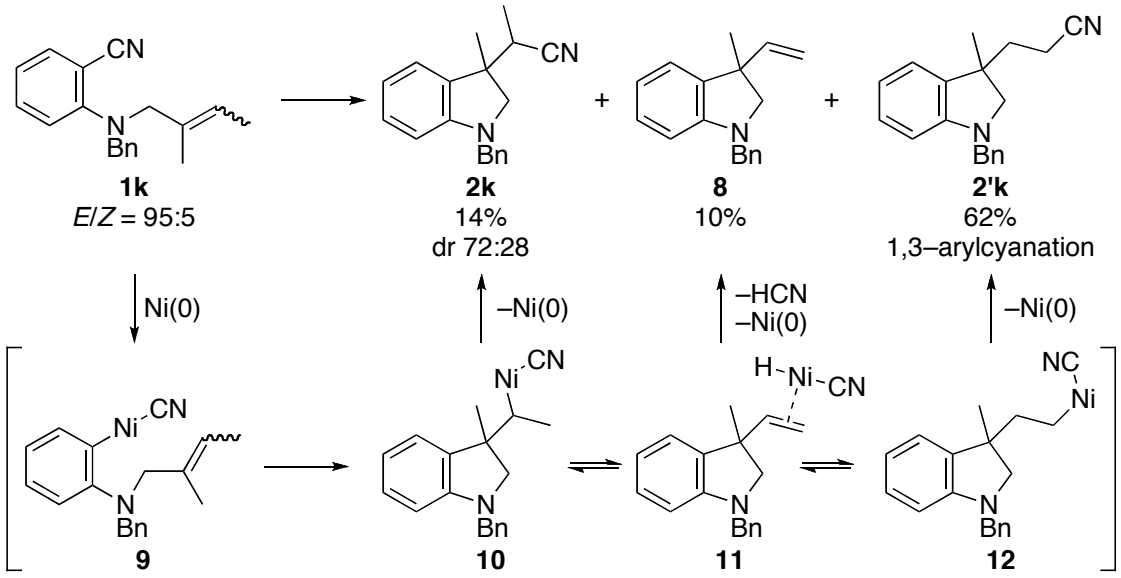


Figure 2. Molecular structures of **4** and **5**. Butyl groups on phosphorous are omitted.

The reaction mechanism for the 1,3-arylcyanation reaction using **1k** (entry 13 of Table 1) deserves to be noted (Scheme 5). Oxidative addition of the C–CN bond in **1k** to nickel(0) (**9**) and subsequent insertion of double bond into the C–Ni bond gives alkylnickel intermediate **10**, which then undergoes *β*-hydride elimination (**11**) followed by hydronickelation in an opposite direction to give **12**. Reductive elimination from **12** results in formal 1,3-arylcyanation product **2'k**. Partial loss of stereospecificity observed in **2k** contrasts to the reactions of in **1l** and **1m** (entries 14–16 of Table 1), and would support the presence of the equilibrium between **10** and **11**. Reaction profile showed **2'k** is a kinetic product, and gradually isomerizes to **2k**, whereas the amount of decyanated **8** was almost constant (Figure 3).



Scheme 5. Intramolecular 1,3-arylcyanation of alkene using **1k**.

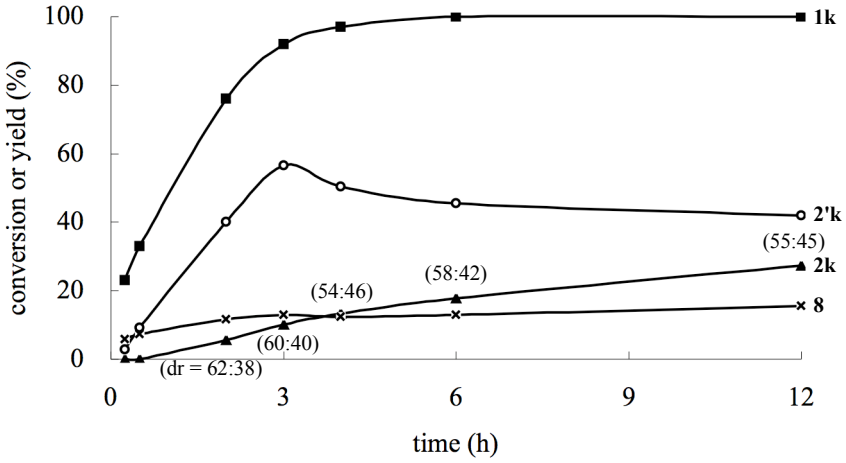
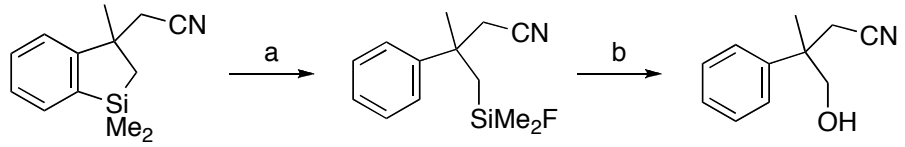


Figure 3. Monitoring experiment of the reaction of **1k**.

Transformation of 2b

Synthetic utility of the intramolecular arylcyanation products was examined briefly. Protonation followed by Tamao–Fleming oxidation[17] of C–Si bonds in **2b** gave cyano-substituted alcohol having a benzylic quaternary carbon **13** in 70% yield (Scheme 6).



2b **13** 70% (2 steps)

[a] Reagents and Conditions: (a) BF_3•2AcOH (2 equiv), DCM, 0 °C to rt, 25 h; (b) KF (3.0 equiv), $KHCO_3$ (3.0 equiv), aq. H_2O_2 (9.0 equiv), THF/MeOH, 0 °C to rt, 25 h.

Scheme 6. Transformations of the intramolecular arylcyanation product **2b**.[a]

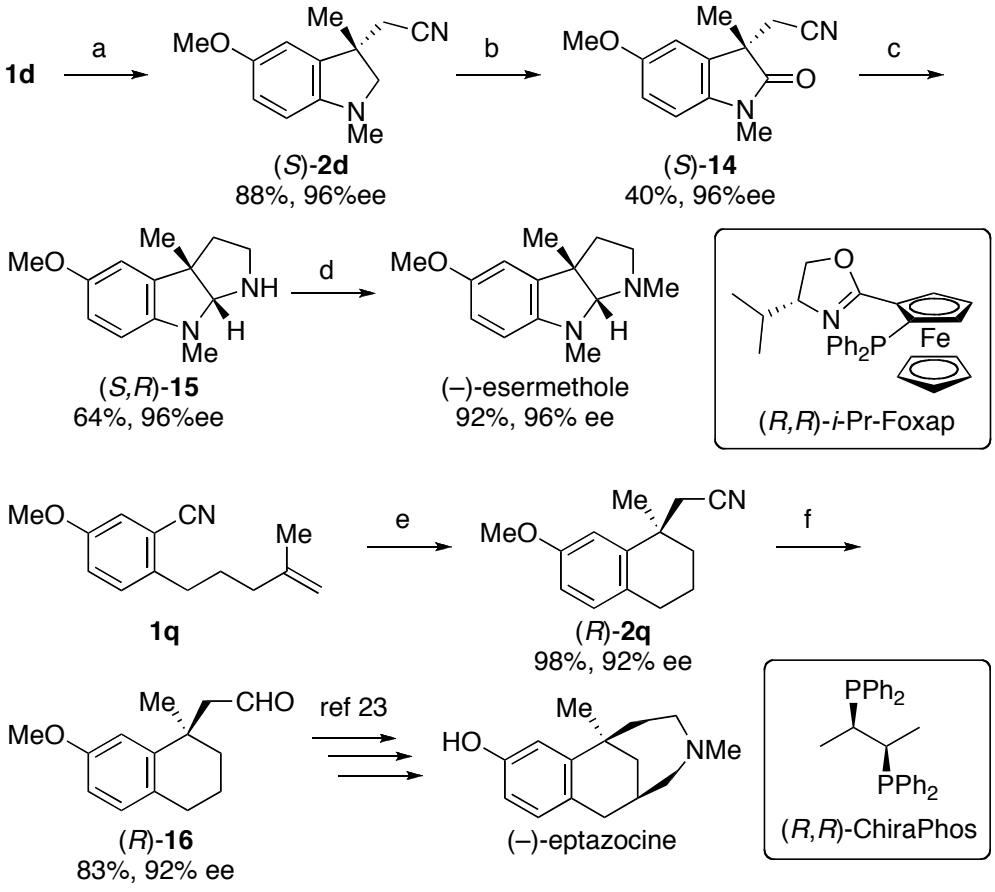
Enantioselective intramolecular arylcyanation of alkenes and synthetic elaboration for (–)-esermethole and (–)-eptazocine

With a broad substrate scope and mechanistic insights, the author focused on the asymmetric version of the reaction. After a brief survey of chiral ligands for the reaction of **1d**, phosphine-oxazoline ligand (*R*,*R*)-*i*-Pr-Foxap[18] was found effective to give (*S*)-**2d** in 96% ee and 88% yield (Scheme 7). Oxidation of the C-2 position of the indole framework gave (*S*)-**14**,[19] which was converted to (–)-esermethole through (*S*,*R*)-**15**,[7b,7c,20a] a synthetic precursor of potent acetylcholinesterase inhibitors such as (–)-physotigmine[21] and (–)-phenserine.[22] Moreover, the enantioselective formation of a six-membered ring was achieved with **1q** using (*R*,*R*)-ChiraPhos as a ligand to give (*R*)-**2q** in 92% ee and 98% yield. The cyano group of (*R*)-**2q** was reduced to give aldehyde (*R*)-**16**, which is a synthetic precursor of (–)-eptazocine, an analgesic substance available commercially.[23]

Conclusion

In summary, the author has demonstrated the intramolecular arylcyanation of alkenes catalyzed by nickel/$AlMe_2Cl$. The transformation should be a versatile protocol to synthesize a range of synthetically interesting nitriles having a benzylic quaternary

carbon. Mechanistic studies by stoichiometric reactions revealed two distinct structures of the reaction intermediates in the catalytic cycle. Monitoring experiments by NMR suggested that either insertion of the double bond or substitution of the coordinating phosphorous by the double bond is a rate-determining step. He has also achieved enantioselective version of the reaction, which was applied successfully to stereoselective formal synthesis of biologically active alkaloides.



[a] Reagents and Conditions: (a) $Ni(cod)_2$ (10 mol %), (*R*,*R*)-*i*-Pr-Foxap (20 mol %), $AlMe_2Cl$ (40 mol %), DME, 100 °C, 10 h; (b) PhIO (6.0 equiv), CH_2Cl_2, rt, 2.5 h; (c) $LiAlH_4$ (4.0 equiv), THF, rt, 1 h, then reflux, 0.5 h; (d) HCHO aq. (5.0 equiv), $NaBH(OAc)_3$ (5.0 equiv), MeOH, 0 °C to rt, 1.5 h; (e) $Ni(cod)_2$ (5 mol %), (*R*,*R*)-ChiraPhos (6 mol %), $AlMe_2Cl$ (20 mol %), 100 °C, 1 h; (f) DIBAL–H (2.0 equiv), toluene, –78 °C, 2 h, then 1 M HCl aq., THF, 0 °C to rt, 2 h.

Scheme 7. Enantioselective intramolecular arylcyanation and its application to natural product syntheses.[a]

Experimental Section

Chemicals

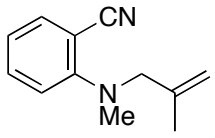
(*R*,*R*)-*i*-Pr-Foxap was prepared according to the literature procedure.[24]

2-(3-Methylbut-3-en-1-yl)benzonitrile (1a).[8] A 1.6 M solution of *n*-BuLi (36 mmol, 23 mL) in hexane was added dropwise to the solution of diisopropylamine (3.3 g, 33 mmol) in THF (300 mL) at –78 °C over 10 min, and the resulting mixture was stirred for 10 min. *o*-Tolunitrile (3.5 g, 30 mmol) was added dropwise to the solution over 10 min, and the whole was stirred for further 20 min to give a deep red solution, to which 3-bromo-2-methylpropene (4.9 g, 36 mmol) was added dropwise at –78 °C over 100 min. The color of the solution changed to yellow. The resulting mixture was stirred for additional 160 min at –78 °C, then at rt for further 15 h. The reaction mixture was evaporated and quenched with a saturated NH_4Cl aqueous solution, and the resulting mixture was extracted three times with ethyl acetate. The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 15:1) and further by distillation under vacuum to give the title compound (1.5 g, 8.6 mmol, 29%) as a colorless oil, bp 100–115 °C (0.02 mmHg), R_f 0.35 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.51 (td, *J* = 7.7, 1.3 Hz, 1H), 7.33 (d, *J* = 7.3 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 4.77 (s, 1H), 4.70 (s, 1H), 2.99 (t, *J* = 8.0 Hz, 2H), 2.37 (t, *J* = 8.0 Hz, 2H), 1.81 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8, 143.9, 132.7, 132.5, 129.3, 126.3, 117.9, 112.2, 111.1, 38.9, 33.0, 22.5. IR (neat) 3074, 2936, 2224, 1651, 1599, 1485, 1450, 1375, 891, 760 cm^{-1}. Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65. Found: C, 83.95; H, 7.88.

2-[Dimethyl(2-methylprop-2-en-1-yl)silyl]benzonitrile (1b). A 1.6 M solution of *n*-BuLi (22 mmol, 14 mL) in hexane was added dropwise to a solution of 2-bromobenzonitrile (3.6 g, 20 mmol) in THF (120 mL) at –78 °C over 10 min, and the resulting mixture was stirred for 2 h before dropwise addition of chlorodimethyl(2-methylpropen-1-yl)silane [7.4 g, 50 mmol, prepared from 3-bromo-2-methylpropene following the procedure for

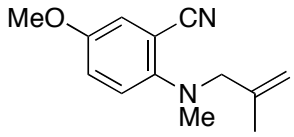
allyl(chloro)dimethylsilane[9]] over 30 min. The reaction mixture was stirred for 2 h at –78 °C then at rt for 14 h, and treated with water. The resulting mixture was extracted three times with ethyl acetate, and the combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and then concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 5:1) followed by distillation under vacuum to give the title compound (1.19 g, 5.5 mmol, 28%) as a colorless oil, bp 70–71 °C (0.02 mmHg), R_f 0.30 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dt, *J* = 7.7, 0.6 Hz, 1H), 7.59 (dt, *J* = 7.3, 0.6 Hz, 1H), 7.54 (td, *J* = 7.5, 1.4 Hz, 1H), 7.44 (td, *J* = 7.5, 1.4 Hz, 1H), 4.61 (s, 1H), 4.50 (s, 1H), 1.99 (s, 2H), 1.64 (s, 3H), 0.48 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 142.2, 134.8, 133.4, 131.4, 129.1, 119.9, 117.2, 109.5, 26.6, 25.2, –2.8. IR (neat) 3076, 2964, 2222, 1638, 1431, 1375, 1279, 1259, 1165, 1128, 1070, 874, 841, 762 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NSi$: C, 72.50; H, 7.96. Found: C, 72.31; H, 8.06.

2-[Methyl(2-methylprop-2-en-1-yl)amino]benzonitrile (1c). To a suspension of NaH



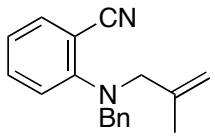
(0.23 g, 9.6 mmol) in DMF (20 mL) was added dropwise a solution of 2-(methylamino)benzonitrile[10] (1.06 g, 8.0 mmol) in DMF (20 mL) over 10 min at 0 °C. The mixture was allowed to warm up to rt, and 3-bromo-2-methylpropene (1.62 g, 12 mmol) was added dropwise at 0 °C over 10 min. The resulting mixture was stirred at 80 °C for 65 h, quenched with a saturated $NaHCO_3$ aqueous solution, and then extracted three times with ethyl acetate. The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 4:1) to give the title compound (1.39 g, 7.4 mmol, 93%) as a colorless oil, R_f 0.50 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 1.8, 7.9 Hz, 1H), 7.38 (td, *J* = 8.0, 1.6 Hz, 1H), 6.88 (d, *J* = 8.6 Hz, 1H), 6.82 (td, *J* = 7.5, 0.9 Hz, 1H), 4.94 (quint, *J* = 1.4 Hz, 1H), 4.89 (q, *J* = 0.8 Hz, 1H), 3.89 (s, 2H), 3.02 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 140.9, 135.0, 133.2, 119.7, 118.7, 117.1, 112.2, 100.3, 61.0, 40.1, 20.1. IR (neat) 2882, 2824, 2212, 1597, 1558, 1493, 1441, 1425, 1375, 1288, 1236, 1180, 1121, 1047, 986, 934, 901, 754 cm^{-1}. Anal. Calcd for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58. Found: C, 77.51; H, 7.63.

5-Methoxy-2-[methyl(2-methylprop-2-en-1-yl)amino]benzonitrile (1d). Following



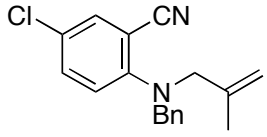
the procedure for **1c**, deprotonation of 3-methoxy-6-(methylamino)benzonitrile[10,25] (0.69 g, 4.3 mmol) followed by treatment with 3-bromo-2-methylpropene (0.86 g, 6.4 mmol) at rt for 16 h gave the title compound (0.91 g, 4.2 mmol, 98%) as a yellowish oil, R_f 0.33 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05–6.99 (m, 2H), 6.97–6.91 (m, 1H), 4.92 (s, 2H), 3.78 (s, 3H), 3.70 (s, 2H), 2.85 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 149.6, 141.7, 120.7, 120.1, 118.7, 117.6, 112.8, 104.3, 62.5, 55.8, 40.7, 20.2. IR (neat) 3076, 2945, 2837, 2220, 1653, 1609, 1568, 1504, 1445, 1412, 1310, 1286, 1242, 1219, 1161, 1126, 1038, 986, 903, 820 cm^{-1}. Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46. Found: C, 72.36; H, 7.43.

2-[Benzyl(2-methylprop-2-en-1-yl)amino]benzonitrile (1e). Following the procedure



for **1c**, deprotonation of 2-(benzylamino)benzonitrile[11] (2.1 g, 10 mmol) followed by treatment with 3-bromo-2-methylpropene (2.0 g, 15 mmol) gave the title compound (2.4 g, 9.1 mmol, 91%) as a yellowish oil, R_f 0.45 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, J = 7.9, 1.6 Hz, 1H), 7.38–7.22 (m, 6H), 6.93–6.86 (m, 2H), 4.94 (s, 1H), 4.90 (s, 1H), 4.55 (s, 2H), 3.87 (s, 2H), 1.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 141.0, 137.2, 134.9, 133.1, 128.3, 127.6, 127.1, 120.1, 119.5, 119.2, 112.9, 102.9, 58.0, 56.4, 20.4. IR (neat) 3065, 3028, 2972, 2937, 2914, 2845, 2218, 1653, 1595, 1556, 1487, 1445, 1373, 1362, 1288, 1223, 1180, 1167, 1097, 1076, 1047, 1028, 964, 939, 901, 808, 752, 700, 559, 532, 509 cm^{-1}. Anal. Calcd for $C_{18}H_{18}N_2$: C, 82.41; H, 6.92. Found: C, 82.59; H, 7.11.

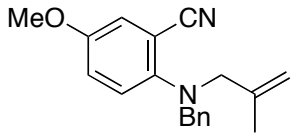
2-[Benzyl(2-methylprop-2-en-1-yl)amino]-5-chlorobenzonitrile (1f). Following the



procedure for **1c**, deprotonation of 2-(benzylamino)-5-chlorobenzonitrile[11] (1.94 g, 8.0 mmol) followed by treatment with 3-bromo-2-methylpropene (1.40 g, 10 mmol) at rt for 24 h gave the title compound (2.3 g, 7.6 mmol, 95%) as a yellowish oil, R_f 0.48 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 2.6 Hz, 1H), 7.35–7.20 (m, 6H), 6.83 (d, J = 9.0 Hz, 1H), 4.95 (s, 1H), 4.89 (s, 1H), 4.53 (s, 2H), 3.86 (s, 2H), 1.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.7, 140.6, 136.7, 133.9, 133.3, 128.5, 127.5,

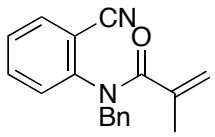
127.3, 124.7, 120.8, 117.9, 113.1, 103.8, 58.2, 56.5, 20.3. IR (neat) 2972, 2939, 2912, 2220, 1653, 1597, 1549, 1487, 1454, 1398, 1362, 1277, 1225, 1178, 1109, 1028, 901, 864, 812, 737, 698, 667, 502 cm^{-1}. Anal. Calcd for $C_{18}H_{17}ClN_2$: C, 72.84; H, 5.77. Found: C, 72.69; H, 5.78.

2-[Benzyl(2-methylprop-2-en-1-yl)amino]-5-methoxybenzonitrile (1g). Following



the procedure described for **1c**, deprotonation of 2-(benzylamino)-5-methoxybenzonitrile[11,25] (1.55 g, 6.5 mmol) followed by treatment with 3-bromo-2-methylpropene (1.23 g, 9.1 mmol) gave the title compound (1.65 g, 5.6 mmol, 87%) as a yellowish oil, R_f 0.28 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.20 (m, 5H), 7.05 (d, *J* = 2.6 Hz, 1H), 6.99–6.91 (m, 2H), 4.91 (s, 1H), 4.90 (s, 1H), 4.32 (s, 2H), 3.77 (s, 3H), 3.65 (s, 2H), 1.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 147.8, 141.8, 137.4, 128.3, 128.2, 127.1, 123.1, 120.1, 118.4, 117.6, 113.6, 107.8, 59.3, 57.8, 55.7, 20.6. IR (neat) 2940, 2837, 2222, 1502, 1454, 1313, 1283, 1232, 1207, 1161, 1038, 903, 700 cm^{-1}. Anal. Calcd for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89. Found: C, 77.97; H, 6.85.

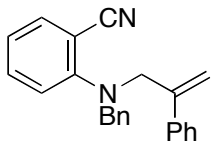
***N*-Benzyl-*N*-(2-cyanophenyl)methacrylamide (1h).** To a suspension of NaH (0.12 g,



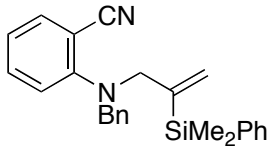
5.0 mmol) in DMF (30 mL) at 0 °C was added a solution of *N*-(2-cyanophenyl)methacrylamide (0.72 g, 4.2 mmol, prepared following the literature procedure[12] using 2-aminobenzonitrile and methyl methacrylate) in DMF (20 mL) dropwise over 5 min. The mixture was allowed to warm up to rt, and benzyl bromide (1.08 g, 6.3 mmol) was added dropwise at 0 °C over 10 min. The resulting mixture was stirred at 80 °C for 15 h before quenching with a saturated $NaHCO_3$ aqueous solution. The whole was extracted three times with ethyl acetate, and the combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, filtered through a Celite pad, and then concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 2:1) to give the title compound (0.98 g, 3.5 mmol, 84%) as a white powder, mp = 69.6–71.4 °C, R_f 0.21 (hexane–ethyl acetate = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.46 (td, *J* = 7.8, 1.6 Hz, 1H), 7.33 (td, *J* = 7.6, 0.9 Hz, 1H), 7.30–7.18 (m, 5H), 6.97 (d, *J* = 7.9 Hz, 1H), 5.38 (br, 1H), 5.11 (s, 1H), 5.02 (s, 1H), 4.75 (br, 1H), 1.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 145.2, 139.9,

136.0, 133.5, 133.2, 129.7, 128.9, 128.4, 127.73, 127.67, 119.9, 116.2, 112.7, 53.0, 20.3. IR (KBr) 3030, 2957, 2228, 1645, 1624, 1593, 1489, 1450, 1431, 1387, 1369, 1325, 1308, 1231, 1202, 1186, 1165, 1111, 1078, 934, 785, 745, 696, 623, 556 cm^{-1}. Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84. Found: C, 78.45; H, 5.97.

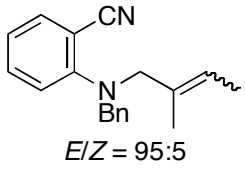
2-[Benzyl(2-phenylprop-2-en-1-yl)amino]benzonitrile (1i). Following the procedure described for **1c**, deprotonation of 2-(benzylamino)benzonitrile (2.5 g, 12 mmol) followed by the reaction with 3-bromo-2-phenylpropene[26] (3.2 g, 16 mmol) gave the title compound (1.95 g, 6.0 mmol, 48%) as a yellowish oil, R_f 0.38 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.35–7.23 (m, 11H), 6.87 (td, *J* = 7.5, 0.9 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 5.44 (d, *J* = 1.1 Hz, 1H), 5.23 (d, *J* = 1.3 Hz, 1H), 4.56 (s, 2H), 4.37 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 143.4, 139.3, 137.1, 134.8, 133.0, 128.4, 128.1, 127.67, 127.65, 127.2, 126.2, 120.2, 119.9, 119.1, 114.7, 103.0, 56.3, 55.7. IR (neat) 3061, 3028, 2854, 2216, 1595, 1558, 1495, 1445, 1362, 1288, 1223, 1182, 1165, 1094, 1074, 1028, 959, 908, 754, 704, 534 cm^{-1}. Anal. Calcd for $C_{23}H_{20}N_2$: C, 85.15; H, 6.21. Found: C, 85.44; H, 6.49.



2-{Benzyl[2-(dimethylphenylsilyl)prop-2-en-1-yl]amino}benzonitrile (1j). Following the procedure for **1c**, deprotonation of 2-(benzylamino)benzonitrile (0.62 g, 3.0 mmol) followed by the reaction with 2-(dimethylphenylsilyl)propen-3-yl *p*-toluenesulfonate (1.15 g, 3.3 mmol, prepared by standard tosylation of 2-(dimethylphenylsilyl)propen-1-ol[27]) at rt for 8 h, then at 50 °C for 102 h in THF afforded the title compound (0.61 g, 1.6 mmol, 53%) [2-(benzylamino)benzonitrile was also recovered in 37% yield] as a colorless oil, R_f 0.48 (hexane–ethyl acetate = 5:1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.45 (m, 3H), 7.39–7.18 (m, 7H), 7.14–7.07 (m, 2H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 5.91 (q, *J* = 1.9 Hz, 1H), 5.58 (d, *J* = 1.8 Hz, 1H), 4.51 (s, 2H), 3.92 (s, 2H), 0.40 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 145.3, 137.1, 136.9, 135.0, 133.7, 132.9, 128.9, 128.2, 127.8, 127.7, 127.6, 127.1, 119.7, 119.5, 119.3, 102.4, 56.8, 56.3, –3.0. IR (neat) 3067, 3028, 2955, 2216, 1595, 1556, 1487, 1443, 1427, 1360, 1288, 1250, 1221, 1180, 1111, 951, 835, 818, 777, 752, 733, 702 cm^{-1}. Anal. Calcd for $C_{25}H_{26}N_2Si$: C, 78.49; H, 6.85. Found: C, 78.77; H, 6.88.



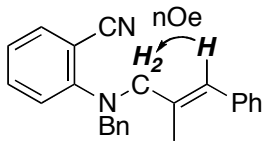
2-[Benzyl(2-methylbut-2-enyl)amino]benzonitrile (1k). Following the procedure for



1c, deprotonation of 2-[(2-methylbut-2-enyl)amino]benzonitrile (*E*/*Z* = 95:5) (1.49 g, 8.0 mmol, prepared following the literature procedure for *N*-allyl-*p*-anisidine[28]) followed by treatment with benzyl bromide (2.1 g, 12.0 mmol) gave a stereoisomeric mixture of the title compound (2.1 g, 7.7 mmol, 96%, *E*/*Z* = 95:5) as a colorless oil, R_f 0.45 (hexane–ethyl acetate = 5:1). ^{1}H NMR [spectra for (*E*)-**1k** (400 MHz, $CDCl_3$)] δ 7.52 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.39–7.18 (m, 6H), 6.93–6.84 (m, 2H), 5.38 (d, *J* = 6.6 Hz, 1H), 4.49 (s, 2H), 3.82 (s, 2H), 1.64 (s, 3H), 1.62 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR [spectra for (*E*)-**1k** (101 MHz, $CDCl_3$)] δ 153.7, 137.4, 134.8, 133.0, 131.5, 128.3, 127.7, 127.0, 122.2, 120.1, 120.0, 119.3, 103.5, 60.2, 55.7, 14.3, 13.4. IR (neat) 3028, 2916, 2858, 2218, 1595, 1556, 1487, 1445, 1381, 1362, 1286, 1223, 1180, 1165, 1088, 1076, 1042, 1028, 937, 756, 698, 530 cm^{-1}. Anal. Calcd for $C_{19}H_{20}N_2$: C, 82.57; H, 7.29. Found: C, 82.87; H, 7.52.

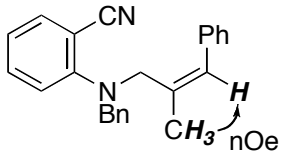
2-[Benzyl(2-methyl-3-phenylpropen-1-yl)amino]benzonitrile (1l and 1m). Following the procedure for **1c**, deprotonation of (*E*)-2-[(2-methyl-3-phenylpropen-1-yl)amino]benzonitrile [1.49 g, 6.0 mmol, prepared following the literature procedure[28] using 2-aminobenzonitrile and *(E)*-2-methylcinnamaldehyde] followed by treatment with benzyl bromide (1.54 g, 9.0 mmol) gave a stereoisomeric mixture of the title compound [1.53 g, 4.5 mmol, 75%, **1l**/**1m** (*E*/*Z*) = 96:4], which was further separated by preparative recycling HPLC (hexane–ethyl acetate = 7:1).

1l. A colorless powder, mp = 63.3–64.0 °C, R_f 0.43 (hexane–ethyl acetate = 5:1). ^{1}H



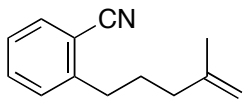
NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.42–7.18 (m, 11H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.92 (td, *J* = 7.6, 1.1 Hz, 1H), 6.39 (s, 1H), 4.59 (s, 2H), 4.01 (s, 2H), 1.90 (d, *J* = 1.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.5, 137.3, 137.1, 134.9, 134.2, 133.1, 128.7, 128.4, 128.0, 127.8, 127.4, 127.2, 126.3, 120.4, 120.0, 119.2, 103.6, 60.5, 56.3, 16.3. IR (KBr) 3061, 3026, 2912, 2851, 2218, 1595, 1556, 1487, 1445, 1360, 1286, 1225, 1180, 1167, 1096, 1076, 1028, 943, 746, 698, 513 cm^{-1}. Anal. Calcd for $C_{24}H_{22}N_2$: C, 85.17; H, 6.55. Found: C, 85.06; H, 6.57.

1m. A yellowish oil, R_f 0.44 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$)



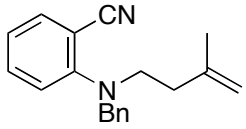
δ 7.56 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.35–7.16 (m, 9H), 7.69 (d, *J* = 7.5 Hz, 2H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.50 (s, 1H), 4.34 (s, 2H), 3.98 (s, 2H), 1.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.6, 137.2, 137.1, 135.5, 134.4, 132.8, 129.5, 128.7, 128.2, 128.1, 128.0, 127.1, 126.4, 121.4, 121.3, 118.8, 106.0, 57.9, 52.0, 22.2. IR (neat) 3061, 3026, 2918, 2853, 2220, 1701, 1595, 1487, 1445, 1379, 1362, 1290, 1211, 1167, 1134, 1096, 1074, 1043, 1028, 951, 930, 743, 698, 515 cm^{-1}. HRMS (EI) Calcd for $C_{24}H_{22}N_2$: M^+, 338.1783. Found: *m*/*z* 338.1789.

2-(4-Methylpent-4-en-1-yl)benzonitrile (1n). A mixture of



methyltriphenylphosphonium iodide (7.3 g, 18 mmol) and *t*-BuOK (1.68 g, 15 mmol) in THF (60 mL) was stirred for 30 min at rt. To this was added 2-(4-oxopentyl)benzonitrile (0.94 g, 5.0 mmol, prepared according to the literature procedure[13] using 2-bromobenzonitrile and 4-penten-2-ol) at 0 °C, and the resulting mixture was stirred at rt for 24 h before quenching with silica gel (ca. 50 g). The suspension thus obtained was diluted with hexane and filtered. The filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 10:1). The title compound (0.82 g, 4.4 mmol, 89%) was isolated as a colorless oil, R_f 0.48 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.7 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 7.35–7.25 (m, 2H), 4.76 (s, 1H), 4.72 (s, 1H), 2.84 (t, *J* = 7.9 Hz, 2H), 2.11 (t, *J* = 7.5 Hz, 2H), 1.83 (quint, *J* = 7.7 Hz, 2H), 1.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.3, 144.8, 132.7, 132.5, 129.4, 126.3, 118.0, 112.2, 110.4, 37.3, 34.2, 28.8, 22.4. IR (neat) 3072, 2937, 2866, 2224, 1649, 1599, 1485, 1448, 1375, 889, 762, 735 cm^{-1}. Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16. Found: C, 84.02; H, 8.24.

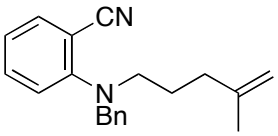
2-[Benzyl(3-methylbut-3-en-1-yl)amino]benzonitrile (1o). Following the procedure



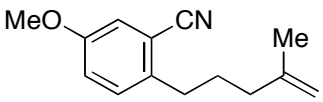
for **1c**, deprotonation of 2-(benzylamino)benzonitrile (4.2 g, 20 mmol) followed by the reaction with 3-methylbut-3-en-1-yl *p*-toluenesulfonate (5.8 g, 24 mmol, prepared by standard tosylation of 3-methylbut-3-en-1-ol) in THF at rt for 24 h afforded the title compound (2.1 g, 7.5 mmol, 38%) as a yellowish oil, R_f 0.35 (hexane–ethyl acetate = 10:1). ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.38 (td, *J* = 8.0, 1.8 Hz, 1H), 7.35–7.21 (m, 5H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.91 (td, *J* = 7.5, 0.9 Hz, 1H), 4.74 (t, *J* = 0.9 Hz, 1H), 4.65 (q, *J* = 1.0 Hz, 1H), 4.52 (s, 2H), 3.45 (t, *J* = 7.8 Hz, 2H), 2.32 (t, *J* = 7.7 Hz, 2H), 1.69 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 142.8, 137.3, 134.8, 133.1, 128.4, 127.7, 127.2, 120.4, 120.0, 119.1, 111.6, 104.3, 56.8, 51.1, 35.4, 22.7. IR (neat) 3069, 3028, 2968, 2936, 2853, 2218, 1647, 1595, 1558, 1487, 1447, 1362, 1288, 1204, 1180, 1167, 1138, 1099, 1074, 1047, 1028, 949, 891, 756, 698 cm^{-1}. Anal. Calcd for $C_{19}H_{20}N_2$: C, 82.57; H, 7.29. Found: C, 82.42; H, 7.42.

2-[Benzyl(4-methylpent-4-en-1-yl)amino]benzonitrile (1p). Following the procedure for **1c**, deprotonation of 2-(benzylamino)benzonitrile (4.2 g, 20 mmol) followed by treatment with 4-methylpent-4-en-1-yl *p*-toluenesulfonate (5.3 g, 21 mmol, prepared by standard tosylation of 4-methylpent-4-en-1-ol[29]) in THF at rt gave the title compound (5.1 g, 17.5 mmol, 88%) as a yellowish oil, R_f 0.30 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.37 (td, *J* = 7.9, 1.6 Hz, 1H), 7.34–7.21 (m, 5H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.90 (td, *J* = 7.5, 1.1 Hz, 1H), 4.68 (s, 1H), 4.62 (s, 1H), 4.51 (s, 2H), 3.31 (t, *J* = 7.6 Hz, 2H), 2.01 (t, *J* = 7.7 Hz, 2H), 1.75 (quint, *J* = 7.5 Hz, 2H), 1.68 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.5, 144.9, 137.4, 134.8, 133.1, 128.3, 127.7, 127.1, 120.3, 119.8, 119.2, 110.1, 104.0, 57.0, 52.0, 34.9, 25.3, 22.5. IR (neat) 3067, 3028, 2937, 2864, 2218, 1647, 1595, 1558, 1487, 1445, 1364, 1286, 1180, 1167, 1138, 1101, 1076, 1051, 1028, 945, 889, 752, 698 cm^{-1}. Anal. Calcd for $C_{20}H_{22}N_2$: C, 82.72; H, 7.64. Found: C, 82.46; H, 7.81.



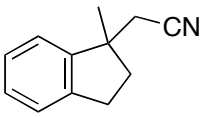
3-Methoxy-2-(4-methylpent-4-en-1-yl)benzonitrile (1q). Following the procedure for **1n**, the reaction of 5-methoxy-2-(4-oxopentyl)benzonitrile (2.8 g, 13.0 mmol, prepared according to the literature procedure[13] using 5-methoxy-2-bromobenzonitrile[30] and 4-penten-2-ol) gave the title compound (2.3 g, 11 mmol, 81%) as a colorless oil, R_f 0.39 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.6 Hz, 1H), 7.09 (d, *J* = 2.6 Hz, 1H), 7.06 (dd, *J* = 8.4, 2.7 Hz, 1H), 4.75 (q, *J* = 0.7 Hz, 1H), 4.71 (s, 1H), 3.82 (s, 3H), 2.77 (t, *J* = 7.8 Hz, 2H), 2.09 (t, *J* = 7.6 Hz, 2H), 1.79 (quint, *J* = 7.9 Hz, 2H), 1.74 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 144.9, 138.5, 130.5, 119.6,



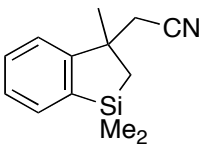
118.0, 116.6, 112.6, 110.3, 55.6, 37.3, 33.3, 29.0, 22.5. IR (neat): 3074, 2939, 2864, 2839, 2226, 1649, 1609, 1570, 1502, 1458, 1325, 1288, 1258, 1204, 1159, 1105, 1036, 889, 853, 833 cm^{-1}. HRMS (EI) Calcd for $C_{14}H_{17}NO$: M^+, 215.1310. Found: *m*/*z* 215.1312.

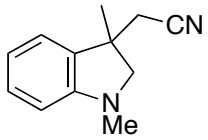
Nickel/$AlMe_2Cl$-catalyzed intramolecular arylcyanation of alkenes. *General procedure.* In a dry box, to a solution of $Ni(cod)_2$ (13.8 mg, 50 μmol) and a ligand (0.100 mmol) in toluene (1.00 mL) placed in a vial were sequentially added an aryl cyanide (1.00 mmol), a 1.04 M solution of $AlMe_2Cl$ in hexane (0.20 mL, 0.20 mmol), and dodecane (an internal standard, 57 mg, 0.33 mmol). The vial was taken out from the dry box and heated at 100 °C for the time specified in Table 1. The resulting mixture was filtered through a silica gel pad, and the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the corresponding arylcyanation products in yields listed in Table 1.

2-(1-Methyl-2,3-dihydro-1*H*-inden-1-yl)acetonitrile (2a). A colorless oil, R_f 0.38 (hexane–ethyl acetate = 5:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.27–7.20 (m, 4H), 3.04–2.90 (m, 2H), 2.57 (d, *J* = 7.8 Hz, 1H), 2.53 (d, *J* = 7.8 Hz, 1H), 2.17 (ddd, *J* = 13.0, 7.1, 5.9 Hz, 1H), 2.07 (dt, *J* = 13.0, 7.9 Hz, 1H), 1.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3, 142.5, 127.5, 126.7, 124.8, 122.2, 118.3, 45.8, 39.2, 29.9, 29.8, 26.1. IR (neat) 3069, 3020, 2957, 2868, 2245, 1479, 1454, 1421, 1379, 1321, 1099, 1009, 1024, 760, 725, 550 cm^{-1}. Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65. Found: C, 84.27; H, 7.80.

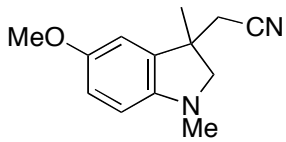


2-(1,1,3-Trimethyl-2,3-dihydro-1*H*-benzo[*b*]silol-3-yl)acetonitrile (2b). A colorless solid, mp = 45.6–46.5 °C, R_f 0.28 (hexane–ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.56–7.51 (m, 1H), 7.44–7.37 (m, 1H), 7.33–7.25 (m, 2H), 2.68 (d, *J* = 16.5 Hz, 1H), 2.59 (d, *J* = 16.5 Hz, 1H), 1.50 (s, 3H), 1.24 (d, *J* = 15.2 Hz, 1H), 1.16 (d, *J* = 15.2 Hz, 1H), 0.37 (s, 3H), 0.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 139.1, 132.2, 130.0, 126.9, 123.1, 118.5, 45.4, 33.9, 31.5, 27.0, –0.6, –0.7. IR (KBr) 3057, 2963, 2949, 2891, 2236, 1587, 1458, 1441, 1375, 1250, 1138, 1057, 845, 824, 808, 768, 727, 704, 648, 548, 453 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NSi$: C, 72.50; H, 7.96. Found: C, 72.50; H, 7.75.

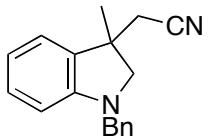


2-(1,3-Dimethylindolin-3-yl)acetonitrile (2c). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 5:1). 

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (td, *J* = 7.7, 1.3 Hz, 1H), 7.12 (dd, *J* = 7.3, 1.3 Hz, 1H), 6.76 (td, *J* = 7.4, 0.9 Hz, 1H), 6.53 (d, *J* = 7.9 Hz, 1H), 3.34 (d, *J* = 9.1 Hz, 1H), 3.05 (d, *J* = 9.1 Hz, 1H), 2.78 (s, 3H), 2.59 (d, *J* = 16.5 Hz, 1H), 2.56 (d, *J* = 16.5 Hz, 1H), 1.55 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.6, 133.8, 128.7, 122.0, 118.2, 118.0, 107.8, 67.6, 42.2, 35.6, 28.6, 23.4. IR (neat) 2959, 2862, 2812, 2247, 1715, 1682, 1607, 1493, 1454, 1423, 1383, 1333, 1304, 1281, 1258, 1215, 1157, 1117, 1103, 1022, 970, 745 cm^{-1}. HRMS (EI) Calcd for $C_{12}H_{14}N_2$: M^+, 186.1157. Found: *m*/*z* 186.1161.

2-(5-Methoxy-1,3-dimethylindolin-3-yl)acetonitrile (2d). A colorless oil, R_f 0.20 (hexane–ethyl acetate = 3:1). 

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.74 (s, 1H), 6.73 (dd, *J* = 8.2, 2.6 Hz, 1H), 6.46 (dd, *J* = 7.5, 1.6 Hz, 1H), 3.77 (s, 3H), 3.31 (d, *J* = 9.0 Hz, 1H), 2.96 (d, *J* = 9.0 Hz, 1H), 2.72 (s, 3H), 2.59 (d, *J* = 16.5 Hz, 1H), 2.55 (d, *J* = 16.5 Hz, 1H), 1.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 146.0, 135.4, 118.0, 113.4, 109.4, 108.6, 68.3, 56.1, 42.4, 36.7, 28.3, 23.1. IR (neat) 2953, 2858, 2806, 2247, 1595, 1495, 1468, 1454, 1421, 1383, 1279, 1240, 1215, 1186, 1153, 1111, 1059, 1032, 1005, 970, 870, 806, 745, 694, 685 cm^{-1}. Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46. Found: C, 72.05; H, 7.34

2-(1-Benzyl-3-methylindolin-3-yl)acetonitrile (2e). A brownish solid, mp = 40.7–41.5 °C, R_f 0.38 (hexane–ethyl acetate = 5:1). 

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.25 (m, 5H), 7.18–7.01 (m, 2H), 6.77 (t, *J* = 7.4 Hz, 1H), 6.57 (d, *J* = 8.2 Hz, 1H), 4.40 (d, *J* = 14.8 Hz, 1H), 4.16 (d, *J* = 14.6 Hz, 1H), 3.28 (d, *J* = 9.3 Hz, 1H), 3.10 (d, *J* = 9.3 Hz, 1H), 2.59 (s, 2H), 1.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.7, 137.5, 133.7, 128.8, 128.5, 127.7, 127.3, 122.3, 118.3, 117.9, 107.8, 65.3, 52.9, 42.2, 28.9, 23.7. IR (KBr) 3028, 2964, 2926, 2829, 2249, 1699, 1649, 1605, 1487, 1454, 1391, 1354, 1331, 1312, 1258, 1204, 1159, 1105, 1072, 1026, 827, 745, 700, 650 cm^{-1}. Anal. Calcd for $C_{18}H_{18}N_2$: C, 82.41; H, 6.92. Found: C, 82.66; H, 7.08.

2-(1-Benzyl-5-chloro-3-methylindolin-3-yl)acetonitrile (2f). A brownish solid, mp = 99.5–100.2 °C, R_f 0.33 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 7.11–7.06 (m, 2H), 6.46 (dd, *J* = 7.7, 1.1 Hz, 1H), 4.34 (d, *J* = 14.8 Hz, 1H), 4.17 (d, *J* = 14.8 Hz, 1H), 3.31 (d, *J* = 9.5 Hz, 1H), 3.13 (d, *J* = 9.5 Hz, 1H), 2.58 (s, 2H), 1.51 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 137.0, 135.4, 128.59, 128.56, 127.6, 127.4, 122.9, 122.7, 117.5, 108.6, 65.3, 52.8, 42.2, 28.8, 23.7. IR (KBr) 3065, 3030, 2961, 2924, 2839, 2239, 1601, 1489, 1468, 1452, 1418, 1393, 1366, 1317, 1273, 1244, 1190, 1151, 876, 829, 816, 766, 745, 706, 673, 638, 583, 473 cm^{-1}. Anal. Calcd for $C_{18}H_{17}ClN_2$: C, 72.84; H, 5.77. Found: C, 72.99; H, 5.94.

2-(1-Benzyl-5-methoxy-3-methylindolin-3-yl)acetonitrile (2g). A colorless solid, mp = 74.0–74.8 °C, R_f 0.33 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H), 6.78 (d, *J* = 2.6 Hz, 1H), 6.71 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.49 (d, *J* = 8.4 Hz, 1H), 4.33 (d, *J* = 14.5 Hz, 1H), 4.07 (d, *J* = 14.5 Hz, 1H), 3.78 (s, 3H), 3.25 (d, *J* = 9.1 Hz, 1H), 3.01 (d, *J* = 9.3 Hz, 1H), 2.59 (s, 2H), 1.52 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 145.1, 137.7, 135.2, 128.4, 127.8, 127.2, 117.9, 113.3, 109.6, 108.6, 66.0, 56.1, 54.1, 42.3, 28.5, 23.3. IR (KBr) 3028, 2957, 2831, 2247, 1595, 1493, 1470, 1454, 1435, 1420, 1366, 1317, 1286, 1252, 1244, 1217, 1204, 1188, 1175, 1155, 1070, 1040, 997, 872, 827, 806, 775, 754, 719, 702, 617, 588, 490, 467 cm^{-1}. Anal. Calcd for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89. Found: C, 78.24; H, 6.82.

2-(1-Benzyl-3-methyl-2-oxoindolin-3-yl)acetonitrile (2h).[7b] A yellowish oil, R_f 0.28 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.0, 0.7 Hz, 1H), 7.37–7.20 (m, 6H), 7.10 (td, *J* = 7.5, 0.9 Hz, 1H), 6.80 (d, *J* = 7.9 Hz, 1H), 4.95 (s, 2H), 2.91 (d, *J* = 16.7 Hz, 1H), 2.67 (d, *J* = 16.5 Hz, 1H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.3, 141.5, 135.1, 130.7, 128.9, 128.7, 127.6, 127.0, 123.1, 123.0, 116.4, 109.6, 44.9, 43.9, 26.3, 22.6. IR (neat) 3061, 3032, 2972, 2928, 2249, 1713, 1614, 1487, 1470, 1454, 1381, 1360, 1302, 1178, 1109, 1080, 1028, 1005, 754, 698, 683, 629, 552, 490, 457 cm^{-1}. Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84. Found: C, 78.26; H, 6.06.

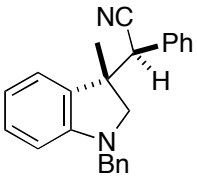
2-(1-Benzyl-3-phenylindolin-3-yl)acetonitrile (2i). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.26 (m, 10H), 7.21 (td, *J* = 7.7, 1.3 Hz, 1H), 7.14 (dd, *J* = 7.6, 0.9 Hz, 1H), 6.81 (td, *J* = 7.4, 0.9 Hz, 1H), 6.69 (d, *J* = 8.1 Hz, 1H), 4.46 (d, *J* = 14.6 Hz, 1H), 4.23 (d, *J* = 14.6 Hz, 1H), 3.51 (d, *J* = 9.5 Hz, 1H), 3.48 (d, *J* = 9.5 Hz, 1H), 3.08 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.1, 142.0, 137.3, 132.5, 129.0, 128.54, 128.51, 127.7, 127.3, 127.2, 126.6, 124.7, 118.7, 117.8, 108.1, 67.5, 52.9, 50.4, 27.3. IR (neat) 3059, 3028, 2922, 2833, 2247, 1603, 1495, 1487, 1454, 1360, 1246, 1159, 1026, 953, 743, 698, 610, 567, 542, 465 cm^{-1}. Anal. Calcd for $C_{23}H_{20}N_2$: C, 85.15; H, 6.21. Found: C, 85.12; H, 6.51.

2-[1-Benzyl-3-(dimethylphenylsilyl)indolin-3-yl]acetonitrile (2j). A colorless solid, mp = 100.4–101.1 °C, R_f 0.40 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.20 (m, 10H), 7.06 (tt, *J* = 7.7, 1.6 Hz, 1H), 6.77 (d, *J* = 7.3 Hz, 1H), 6.68 (tt, *J* = 7.4, 1.0 Hz, 1H), 6.47 (d, *J* = 7.9 Hz, 1H), 4.40 (d, *J* = 14.8 Hz, 1H), 4.00 (d, *J* = 14.8 Hz, 1H), 3.58 (dd, *J* = 9.1, 1.8 Hz, 1H), 3.25 (dd, *J* = 9.1, 2.0 Hz, 1H), 2.71 (dd, *J* = 17.0, 1.6 Hz, 1H), 2.57 (dd, *J* = 16.8, 1.5 Hz, 1H), 0.36 (t, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.5, 137.8, 134.4, 134.3, 131.7, 129.7, 128.4, 127.8, 127.7(2C), 127.1, 122.7, 118.0, 117.8, 107.3, 61.5, 53.5, 35.0, 24.3, –5.0, –5.5. IR (KBr) 3051, 2957, 2905, 2799, 2251, 1595, 1485, 1472, 1427, 1379, 1250, 1169, 1159, 1113, 1069, 1026, 951, 935, 835, 816, 775, 752, 737, 702, 648, 473, 459, 421 cm^{-1}. Anal. Calcd for $C_{25}H_{26}N_2Si$: C, 78.49; H, 6.85. Found: C, 78.55; H, 7.06.

3-(1-Benzyl-3-methylindolin-3-yl)propionitrile (2'k). A colorless oil, R_f 0.34 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H), 7.12 (tdd, *J* = 7.7, 1.3, 0.5 Hz, 1H), 6.99 (dt, *J* = 7.3, 0.6 Hz, 1H), 6.74 (t, *J* = 7.8 Hz, 1H), 6.55 (d, *J* = 7.9 Hz, 1H), 4.40 (d, *J* = 14.8 Hz, 1H), 4.10 (d, *J* = 14.6 Hz, 1H), 3.20 (d, *J* = 9.1 Hz, 1H), 3.06 (d, *J* = 9.1 Hz, 1H), 2.39–2.28 (m, 1H), 2.20–2.10 (m, 1H), 2.05–1.88 (m, 2H), 1.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.4, 137.8, 134.2, 128.5, 128.3, 127.7, 127.2, 122.3, 120.0, 118.1, 107.4, 65.1, 53.2, 43.1, 37.0, 25.7, 13.1. IR (neat) 3026, 2961, 2926, 2826, 2245, 1605, 1493, 1454, 1360, 1254, 1157, 1105, 1074, 1026,

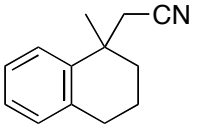
943, 910, 743, 700, 457 cm^{-1}. Anal. Calcd for $C_{19}H_{20}N_2$: C, 82.57; H, 7.29. Found: C, 82.31; H, 7.30.

(*S)-2-[(*S**)-1-Benzyl-3-methylindolin-3-yl]-2-phenylacetonitrile (2l).** A colorless solid, mp = 141.7–142.3 °C, R_f 0.25 (hexane–ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.09 (m, 12H), 6.84 (td, *J* = 7.4, 0.6 Hz, 1H), 6.55 (d, *J* = 7.9 Hz, 1H), 4.44 (d, *J* = 14.3 Hz, 1H), 3.92 (s, 1H), 3.87 (d, *J* = 14.3 Hz, 1H), 3.25 (d, *J* = 9.9 Hz, 1H), 2.73 (d, *J* = 9.9 Hz, 1H), 1.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.0, 137.6, 133.5, 132.4, 129.1, 128.9, 128.4, 128.2, 128.03, 127.99, 127.3, 123.6, 120.0, 118.4, 107.8, 62.3, 53.0, 47.1, 45.7, 20.6. IR (KBr) 3059, 3034, 2978, 2820, 2241, 1599, 1485, 1470, 1454, 1385, 1375, 1304, 1246, 1223, 1151, 1022, 945, 914, 748, 727, 702, 621, 579, 509, 471 cm^{-1}. Anal. Calcd for $C_{24}H_{22}N_2$: C, 85.17; H, 6.55. Found: C, 85.27; H, 6.60.



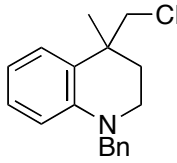
(*R)-2-[(*S**)-1-Benzyl-3-methylindolin-3-yl]-2-phenylacetonitrile (2m).** A yellowish oil, R_f 0.25 (hexane–ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.16 (m, 8H), 7.13 (td, *J* = 7.6, 1.5 Hz, 1H), 6.93 (d, *J* = 7.3 Hz, 2H), 6.61 (t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 7.5 Hz, 1H), 6.50 (d, *J* = 7.9 Hz, 1H), 4.35 (d, *J* = 14.8 Hz, 1H), 4.04 (d, *J* = 14.8 Hz, 1H), 3.98 (s, 1H), 3.60 (d, *J* = 9.7 Hz, 1H), 3.11 (d, *J* = 9.7 Hz, 1H), 1.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.5, 137.5, 132.3, 131.3, 129.4, 128.9, 128.4, 128.1, 127.9, 127.6, 127.2, 124.5, 120.1, 117.5, 107.7, 65.3, 53.1, 47.7, 45.8, 21.8. IR (neat) 3061, 3030, 2966, 2928, 2829, 2361, 2235, 1605, 1493, 1454, 1379, 1358, 1329, 1313, 1242, 1159, 1103, 1080, 1026, 947, 910, 741, 700 cm^{-1}. HRMS (EI) Calcd for $C_{24}H_{22}N_2$: M^+, 338.1783. Found: *m*/*z* 338.1776.

2-(1-Methyl-1,2,3,4-tetrahydronaphthalen-1-yl)acetonitrile (2n). A colorless oil, R_f 0.43 (hexane–ethyl acetate = 5:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.18 (td, *J* = 7.3, 1.5 Hz, 1H), 7.14 (td, *J* = 7.1, 1.6 Hz, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 2.88–2.75 (m, 2H), 2.65 (s, 2H), 2.06–1.76 (m, 4H), 1.48 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 136.4, 129.5, 126.5, 126.2, 125.9, 118.1, 36.3, 36.1, 32.0, 30.3, 29.1, 19.3. IR (neat): 3061, 3017, 2934, 2870, 2245, 1491, 1450, 1381, 1285, 1196, 1053, 1040, 785, 760, 729, 550,

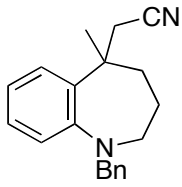


455 cm^{-1}. Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16. Found: C, 84.42; H, 8.24.

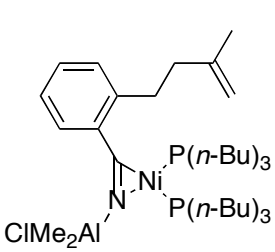
2-(1-Benzyl-4-methyl-1,2,3,4-tetrahydroquinolin-4-yl)acetonitrile (2o). A brownish solid, mp = 42.6–43.1 °C, R_f 0.35 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.22 (m, 5H), 7.18 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.04 (td, *J* = 7.8, 1.6 Hz, 1H), 6.67 (td, *J* = 7.4, 1.1 Hz, 1H), 6.57 (d, *J* = 8.2 Hz, 1H), 4.53 (s, 2H), 3.42 (dd, *J* = 7.9, 5.3 Hz, 2H), 2.68 (s, 2H), 2.10 (dt, *J* = 13.5, 5.2 Hz, 1H), 2.01 (dt, *J* = 13.9, 7.0 Hz, 1H), 1.56 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 137.9, 128.6, 128.2, 126.9, 126.3, 125.7, 125.3, 117.8, 116.2, 111.6, 55.0, 45.4, 34.4, 34.1, 30.5, 27.4. IR (KBr) 3061, 3028, 2959, 2934, 2885, 2831, 2241, 1601, 1506, 1448, 1356, 1342, 1298, 1244, 1196, 1173, 1136, 1055, 1030, 1015, 972, 870, 752, 743, 725, 696, 498, 457 cm^{-1}. HRMS (EI) Calcd for $C_{19}H_{20}N_2$: M^+, 276.1626. Found: *m*/*z* 276.1623.



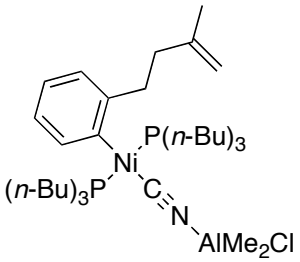
2-(1-Benzyl-5-methyl-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-5-yl)acetonitrile (2p). A colorless solid, mp = 74.3–75.1 °C, R_f 0.41 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.22 (m, 7H), 7.15 (d, *J* = 7.9 Hz, 1H), 7.04 (td, *J* = 7.5, 1.3 Hz, 1H), 4.40 (d, *J* = 13.0 Hz, 1H), 4.13 (d, *J* = 13.0 Hz, 1H), 3.56 (d, *J* = 16.5 Hz, 1H), 3.14–3.02 (m, 1H), 3.02 (d, *J* = 16.5 Hz, 1H), 2.53 (td, *J* = 11.4, 2.9 Hz, 1H), 1.97–1.84 (m, 1H), 1.80–1.45 (m, 3H), 1.65 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8, 138.7, 137.1, 128.7, 128.5, 128.0, 127.2, 126.8, 122.6, 119.1, 118.9, 59.1, 52.8, 40.6, 37.3, 29.1, 26.8, 26.2. IR (KBr) 3061, 3030, 2959, 2924, 2839, 2237, 1593, 1489, 1450, 1439, 1364, 1304, 1227, 1215, 1188, 1136, 1119, 1074, 1045, 976, 910, 883, 847, 827, 775, 764, 756, 741, 702, 625, 577, 556, 471 cm^{-1}. Anal. Calcd for $C_{20}H_{22}N_2$: C, 82.72; H, 7.64. Found: C, 82.58; H, 7.63.



Isolation of [P(*n*-Bu)$_3$]$_2$Ni{η^2-(κ^2-N,C)-*o*-C$_6$H$_4$[CH$_2$CH$_2$C(CH$_3$)=CH$_2$][CNAl(CH$_3$)$_2$Cl]} (4). To a toluene solution (3 mL) of Ni(cod)$_2$ (82 mg, 0.30 mmol) and P(*n*-Bu)$_3$ (150 μL, 0.60 mmol) was added 2-(3-methylbut-3-en-1-yl)benzonitrile (**1a**) (52.3 mg, 0.31 mmol) in benzene (3 mL) at rt. The color of the solution changed immediately from red to dark yellow. The reaction mixture was stirred for 10 min. A 1.0 M solution of AlMe$_2$Cl in hexane (0.30 mL, 0.30 mmol) was added to the solution and the mixture was stirred for 10 min. The mixture solution was concentrated *in vacuo*. To the residue was added hexane (1 mL) and cooled at –20 °C for 1 day to give **4** as yellow crystals (140 mg, 64%). ^{1}H NMR (400 MHz, C$_6$D$_6$) δ –0.26 (s, 6H, –Al(C***H***$_3$)$_2$Cl), 0.82–1.90 (m, 57H, *n*-Bu including 3H of –CH$_2$CH$_2$C(C***H***$_3$)=CH$_2$ at δ 1.80), 2.33 (brs, 2H, –CH$_2$C***H***$_2$C(CH$_3$)=CH$_2$), 2.79 (brs, 2H, –C***H***$_2$CH$_2$C(CH$_3$)=CH$_2$), 4.84 (s, 1H, –CH$_2$CH$_2$C(CH$_3$)=C***H***$_2$), 4.93 (s, 1H, –CH$_2$CH$_2$C(CH$_3$)=C***H***$_2$), 6.93–7.05 (m, 4H, Ph); ^{31}P NMR (109 MHz, C$_6$D$_6$) δ 7.4 (d, J_{pp} = 24.0 Hz), 18.1 (d, J_{pp} = 24.0 Hz); ^{13}C NMR (100 MHz, C$_6$D$_6$) δ –5.8 (s, –Al(***C***H$_3$)$_2$Cl), 13.9 (s, –P(CH$_2$CH$_2$CH$_2$***C***H$_3$)$_3$), 14.2 (s, –P(CH$_2$CH$_2$CH$_2$***C***H$_3$)$_3$), 23.0 (s, –CH$_2$CH$_2$C(***C***H$_3$)=CH$_2$), 24.9 (d, $^2J_{CP}$ = 13.1 Hz, –P(CH$_2$***C***H$_2$CH$_2$CH$_3$)$_3$), 25.0 (d, $^2J_{CP}$ = 13.1 Hz, –P(CH$_2$***C***H$_2$CH$_2$CH$_3$)$_3$), 25.2 (d, $^1J_{CP}$ = 23.1 Hz, –P(***C***H$_2$CH$_2$CH$_2$CH$_3$)$_3$), 25.7 (d, $^1J_{CP}$ = 20.1 Hz, –P(***C***H$_2$CH$_2$CH$_2$CH$_3$)$_3$), 27.0 (s, –P(CH$_2$CH$_2$***C***H$_2$CH$_3$)$_3$), 27.3 (s, –P(CH$_2$CH$_2$***C***H$_2$CH$_3$)$_3$), 33.1 (s, –***C***H$_2$CH$_2$C(CH$_3$)=CH$_2$), 38.8 (s, –CH$_2$***C***H$_2$C(CH$_3$)=CH$_2$), 110.4 (s, –CH$_2$CH$_2$C(CH$_3$)***C***H$_2$), 124.8 (s, Ph), 126.3 (s, Ph), 128.6 (s, Ph), 128.9 (s, Ph), 132.1 (dd, J_{CP} = 7.0 Hz, Ph), 137.1 (s, Ph), 145.5 (s, –CH$_2$CH$_2$***C***(CH$_3$)=CH$_2$), 183.9 (dd, J_{CP} = 10.6, 35.7 Hz, –***C***N).

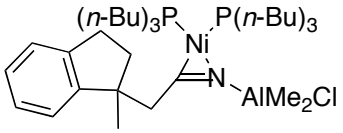


Isolation of *trans*-[P(*n*-Bu)$_3$]$_2$Ni[C$_6$H$_4$CH$_2$CH$_2$C(CH$_3$)=CH$_2$][CNAl(CH$_3$)$_2$Cl] (5). To a toluene solution (2 mL) of Ni(cod)$_2$ (100.6 mg, 0.37 mmol) and P(*n*-Bu)$_3$ (185 μL, 0.74 mmol) was added 2-(3-methylbut-3-en-1-yl)benzonitrile (**1a**) (63.2 mg, 0.37 mmol) in benzene (2 mL) at rt. The color of the solution changed immediately from red to dark yellow. The reaction mixture was stirred for 5 min. A 1.0 M solution of AlMe$_2$Cl in hexane (0.37 mL, 0.37 mmol) was added to the solution and the mixture was stirred for



6 h. The orange colored mixture was concentrated *in vacuo*, and the residue was dissolved in hexane (1 mL) and cooled at –20 °C for 1 day. The yellow precipitates were washed with small amount of hexane to give **5** (140 mg, 52%). A single crystal for X-ray diffraction analysis was prepared by recrystalization from hexane at –20 °C. ^{1}H NMR (400 MHz, C_6D_6) δ –0.06 (s, 6H, –Al(C***H***$_3$)$_2$Cl), 0.90–1.40 (m, 54H, *n*-Bu), 1.79 (s, 3H, –$CH_2CH_2C(C$***H***$_3$)=CH_2), 2.43 (m, 2H, –CH_2C***H***$_2C(CH_3)=CH_2$), 3.05 (m, 2H, –C***H***$_2CH_2C(CH_3)=CH_2$), 4.91 (s, 1H, –$CH_2CH_2C(CH_3)=C$***H***$_2$), 4.96 (s, 1H, –$CH_2CH_2C(CH_3)=C$***H***$_2$), 6.92 (m, 3H, Ph), 7.11 (brs, 1H, Ph); ^{31}P NMR (109 MHz, C_6D_6) δ 13.5 (s); ^{13}C NMR (100 MHz, C_6D_6) δ –6.8 (brs, –Al(***C***H$_3$)$_2$Cl), 14.0 (s, *n*-Bu), 23.2 (s, –$CH_2CH_2C($***C***H_3)=CH_2), 24.0 (t, J_{CP} = 13.6 Hz, *n*-Bu), 25.0 (t, J_{CP} = 6.5 Hz, *n*-Bu), 26.9 (s, *n*-Bu), 37.9 (s, –CH_2***C***$H_2C(CH_3)=CH_2$), 38.6 (s, –***C***$H_2CH_2C(CH_3)=CH_2$), 110.3 (s, –$CH_2CH_2C(CH_3)=$***C***H_2), 123.5 (s, Ph), 125.4 (s, Ph), 126.3 (s, Ph), 134.9 (t, J_{CP} = 4.0 Hz, Ph), 145.7 (s, –CH_2CH_2***C***$(CH_3)=CH_2$), 146.1 (t, J_{CP} = 3.0 Hz, Ph), 154.8 (t, J_{CP} = 23.1 Hz, –***C***N), 157.0 (t, J_{CP} = 28.2 Hz, Ph).

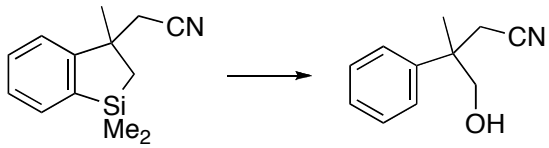
Reaction of 5. A solution of **5** (15.4 mg, 0.021 mmol) in C_6D_6 (0.5 mL) was heated at



60 °C for 46 h. The reaction was monitored by NMR spectroscopy, and the formation of **7** was observed. The complex was characterized on the basis of ^{1}H and ^{1}H–^{1}H COSY spectra as well as ^{31}P NMR spectrum, in which a doublet signal was observed at 4.8 ppm probably due to formation of an unidentifiable minor product. The other half of the doublet was obscured by the signal at δ 18.7. The reaction mixture was passed through a short silica gel column (hexane) to give **2a**. To a solution of **2a** in C_6D_6 (0.2 mL) was added a solution of Ni(cod)$_2$ (3.3 mg, 0.012 mmol) and P(*n*-Bu)$_3$ (6.0 μL, 0.024 mmol) in C_6D_6 (0.3 mL) at rt. Ni(cod)[P(*n*-Bu)$_3$]$_2$ was generated quantitatively and **2a** remained intact in this reaction. Addition of a 1.0 M solution of $AlMe_2Cl$ in hexane (12 μL, 0.012 mmol) led to the regeneration of **7**. After **1a** (2.1 mg, 0.012 mmol) was added to the reaction mixture, formation of complex **4** was confirmed by ^{1}H and ^{31}P NMR spectra. Spectral data for **7**: ^{1}H NMR (270 MHz, C_6D_6) δ 0.03 (s, 3H, –Al(C***H***$_3$)$_2$Cl), 0.04 (s, 3H, –Al(C***H***$_3$)$_2$Cl), 0.80–2.0 (m, 58H, P(*n*-Bu)$_3$ including 1H of –C***H***$_2$– at δ 1.75, and 3H of –C***H***$_3$), 2.40 (ddd, J_{HH} = 13.5, 8.1, 3.1 Hz, 1H, –C***H***$_2$–), 2.69 (ddd, J_{HH} = 16.2, 8.1, 3.1 Hz, 1H, –C***H***$_2$–), 2.97 (m, 1H, –C***H***$_2$–), 3.26 (dd, J_{HH} = 11.8, 5.4 Hz, 1H, –C***H***$_2$CN), 3.41 (dd, J_{HH} = 11.8, 5.4 Hz, 1H, –C***H***$_2$CN), 7.0–7.3 (m, 4H,

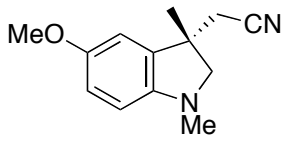
Ph);[31]P NMR (109 MHz, C_6D_6); δ 4.8 (d, J_{PP} = 24.0 Hz), 5.4 (d, J_{PP} = 27.3 Hz), 18.7 (d, J_{PP} = 27.3 Hz).

Tamao–Fleming oxidation of 2b.[17] To a solution of **2b** (138 mg, 0.64 mmol) in



1,2-dichloromethane (3.2 mL) was added boron trifluoride–acetic acid complex (301 mg, 1.6 mmol) over 3 min at 0 °C. After stirring at 0 °C for 8 min then rt for 25 h, the reaction was quenched with saturated $NaHCO_3$ aqueous solution. The resulting mixture was extracted three times with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered through a Celite pad, and concentrated *in vacuo* to give the crude fluorosilane (148 mg). This material was used directly for the next oxidation step. To a solution fluorosilane in THF/MeOH (1:1, 25 mL) were sequentially added potassium fluoride (112 mg, 1.9 mmol), powdered potassium bicarbonate (192 mg, 1.9 mmol) and 30 wt% H_2O_2 aqueous solution (178 mL, 5.8 mmol) at 0 °C. After stirring at 0 °C for 10 min then rt for 25 h, the solution was cooled to 0 °C and quenched with saturated $NaHCO_3$ aqueous solution. The resulting mixture was extracted three times with ethyl acetate. Combined organic layers were washed with brine and dried over anhydrous Na_2SO_4, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 2:1) to give the alcohol **13** [0.45 mmol, 70% (2 steps)] as a colorless oil, R_f 0.23 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.27 (m, 1H), 3.84–3.72 (m, 2H), 2.85 (d, *J* = 16.7 Hz, 1H), 2.83 (d, *J* = 16.7 Hz, 1H), 1.53 (s, 3H), 1.51 (t, *J* = 6.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.7, 128.8, 127.3, 125.8, 118.0, 70.1, 42.5, 26.8, 22.8. Spectra were identical to previously described material.[31]

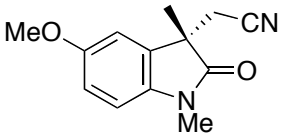
Enantioselective intramolecular arylcyanation of 1d. In a dry box, to a solution of



$Ni(cod)_2$ (28 mg, 0.100 mmol) and (*R*,*R*)-*i*-Pr-Foxap (96 mg, 0.20 mmol) in DME (2.0 mL) placed in a vial were sequentially added **1d** (0.22 g, 1.00 mmol), a 1.04 M solution of $AlMe_2Cl$ in hexane (0.40 mL, 0.40 mmol), and dodecane (an internal standard, 57 mg, 0.33 mmol). The vial was taken out from the dry box and heated at 100 °C for 10 h. The resulting

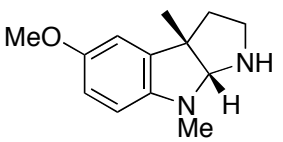
mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give (*S*)-**2d** (189 mg, 88%). Ee of the nitrile was determined on a Daicel Chiralpak AD-H column with hexane–2-propanol = 95:5, flow = 0.5 mL/min, detection by UV of 254 nm. Retention times: 16.4 min [(*S*)-enantiomer], 19.2 min [(*R*)-enantiomer]. 96% ee. $[\alpha]^{26}_{D}$ +62.2 (c 1.0, $CHCl_3$).

(*S*)-2-(5-methoxy-1,3-dimethyl-2-oxoindolin-3-yl)acetonitrile [(*S*)-14].[19] A solution



of (*S*)-**2d** (188 mg, 0.87 mmol) and iodosobenzene (1.15 g, 5.2 mmol) in CH_2Cl_2 (9.0 mL) was stirred at rt for 2.5 h. The reaction mixture was filtered through a glass filter and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 1:1) to give the title compound (80 mg, 40%) as a yellowish oil, R_f 0.30 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 2.4 Hz, 1H), 6.87 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 3.82 (s, 3H), 3.23 (s, 3H), 2.84 (d, *J* = 16.7 Hz, 1H), 2.58 (d, *J* = 16.7 Hz, 1H), 1.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 156.2, 135.8, 132.1, 116.5, 113.4, 110.4, 109.0, 55.9, 45.3, 26.7, 26.4, 22.3. IR (neat) 2959, 2936, 2837, 2249, 1713, 1601, 1504, 1472, 1454, 1435, 1379, 1362, 1292, 1236, 1123, 1042, 876, 810 cm^{-1}. HRMS (EI) Calcd for $C_{13}H_{14}N_2O_2$: M^+, 230.1055. Found: *m*/*z* 230.1057. Ee of the nitrile was determined on a Daicel Chiralpak AD-H column with hexane–2-propanol = 95:5, flow = 0.5 mL/min, detection by UV of 254 nm. Retention times: 34.8 min [(*R*)-enantiomer], 47.6 min [(*S*)-enantiomer]. 96% ee. $[\alpha]^{28}_{D}$ +54.0 (c 1.0, $CHCl_3$).

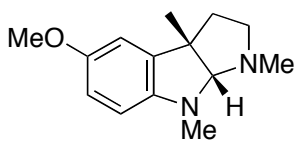
(3a*S*,8a*R*)-5-methoxy-3a,8-dimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole



[(*S*,*R*)-15].[20] A solution of (*S*)-**14** (78 mg, 0.34 mmol) and $LiAlH_4$ (52 mg, 1.36 mmol) in THF (12 mL) was stirred under an argon atmosphere at rt for 1 h, and then heated to reflux for 0.5 h. The reaction was quenched with 2 mL of THF–H_2O (10:1) solution at 0 °C, and the resulting mixture was diluted with CH_2Cl_2 and filtered through a glass filter. The resulting precipitates were washed thoroughly with CH_2Cl_2, and the filtrate was concentrated *in vacuo*. The residue was dissolved in ethyl acetate. To this was added 1 M HCl aqueous solution (5 mL). After stirring for 5 min, the solution was neutralized

by adding solid K_2CO_3, and then extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography neutral aluminum oxide ($CHCl_3$) to give the title compound (48 mg, 64%) as a yellowish oil, R_f 0.28 ($CHCl_3$–MeOH = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (d, *J* = 2.6 Hz, 1H), 6.64 (dd, *J* = 8.2, 2.6 Hz, 1H), 6.27 (d, *J* = 8.4 Hz, 1H), 4.44 (s, 1H), 3.75 (s, 3H), 3.07 (ddd, *J* = 10.4, 7.1, 2.9 Hz, 1H), 2.86–2.76 (m, 1H), 2.79 (s, 3H), 2.09 (br, 1H), 2.02 (ddd, *J* = 12.3, 6.4, 3.1 Hz, 1H), 1.79 (ddd, *J* = 12.3, 9.7, 7.3 Hz, 1H), 1.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 145.4, 137.2, 111.8, 110.4, 105.6, 93.2, 56.1, 52.3, 46.3, 42.3, 33.2, 26.2. IR (neat) 3333, 2953, 2864, 2829, 1593, 1495, 1454, 1433, 1277, 1223, 1171, 1117, 1067, 1032, 868, 845, 799 cm^{-1}. HRMS (EI) Calcd for $C_{13}H_{18}N_2O$: M^+, 218.1419. Found: *m*/*z* 218.1421. Ee of the product was determined on a Daicel Chiralpak AD-H column with hexane–2-propanol = 95:5, flow = 0.5 mL/min, detection by UV of 254 nm. Retention times: 17.3 min [(*R*,*S*)-enantiomer], 18.7 min [(*S*,*R*)-enantiomer]. 96% ee. $[\alpha]^{27}_D$ –46.9 (c 0.70, $CHCl_3$).

Synthesis of (–)-esermethole.[32] To a solution of (*S*,*R*)-**15** (47 mg, 0.21 mmol) in



MeOH (12 mL) was added HCHO aqueous solution (37 wt%, 79 μl, 1.07 mmol) at 0 °C under an argon atmosphere, and the whole was stirred for 5 min. $NaBH(OAc)_3$ (1.07 mmol, 230 mg) was added to the resulting mixture, and the solution was stirred at rt for 1.5 h. After complete conversion of (*S*,*R*)-**15** confirmed by TLC, the solution was diluted with ethyl acetate and concentrated *in vacuo*. The residue was treated with a saturated $NaHCO_3$ aqueous solution and extracted three times with CH_2Cl_2. Combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, filtered through a Celite pad, and then concentrated *in vacuo*. The residue was purified by flash column chromatography neutral aluminum oxide ($CHCl_3$) to give the title compound (46 mg, 92%) as a yellowish amorphous, R_f 0.68 ($CHCl_3$–MeOH = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68–6.62 (m, 2H), 6.36 (d, *J* = 8.4 Hz, 1H), 4.05 (s, 1H), 3.75 (s, 3H), 2.90 (s, 3H), 2.72 (dt, *J* = 8.8, 5.3 Hz, 1H), 2.64 (dt, *J* = 9.0, 7.4 Hz, 1H), 2.54 (s, 3H), 1.95 (dd, *J* = 7.5, 5.5 Hz, 2H), 1.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 146.4, 138.1, 112.0, 109.7, 107.3, 98.3, 56.0, 53.2, 52.8, 40.9, 38.3, 38.1, 27.6. Ee of the product was determined on a Daicel Chiralpak OD-H column with hexane–2-propanol = 98:2, flow

= 0.5 mL/min, detection by UV of 254 nm. Retention times: 11.0 min [(*S*,*R*)-enantiomer], 14.0 min [(*R*,*S*)-enantiomer]. 96% ee. $[\alpha]^{28}_{D}$ –114.5 (c 0.55, C_6H_6), [lit[33] $[\alpha]^{26.1}_{D}$ –136.9 (c 0.55, C_6H_6)]. Analyses were identical to previously described material.[7b]

Enantioselective intramolecular arylcyanation of 1q. In a dry box, to $Ni(cod)_2$ (13.8 mg, 50 μmol) and (*R*,*R*)-ChiraPhos (25.6 mg, 60 μmol) placed in a vial was added a 1.04 M solution of $AlMe_2Cl$ in hexane (192 μl, 0.20 mmol). The solution was stirred and concentrated *in vacuo* for 1 h. To the residue was added **1q** (215 mg, 1.00 mmol), and the vial was taken out from the dry box and heated at 120 °C for 1 h. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 4:1) to give (*R*)-2-(7-methoxy-1-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)acetonitrile [(*R*)-**2q**] (211 mg, 98%) as a colorless oil, R_f 0.30 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.4 Hz, 1H), 6.81 (d, *J* = 2.7 Hz, 1H), 6.73 (dd, *J* = 8.4, 2.7 Hz, 1H), 3.80 (s, 3H), 2.77–2.71 (m, 2H), 2.64 (s, 2H), 2.02–1.90 (m, 1H), 1,90–1.74 (m, 3H), 1.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8, 141.9, 130.3, 128.5, 118.1, 112.2, 111.6, 55.4, 36.33, 36.31, 32.1, 29.5, 29.1, 19.5. IR (neat) 2934, 2866, 2837, 2243, 1611, 1574, 1504, 1462, 1420, 1285, 1240, 1043, 878, 856, 812 cm^{-1}. HRMS (EI) Calcd for $C_{14}H_{17}NO$: M^+, 215.1310. Found: *m*/*z* 215.1312. Ee of the nitrile was determined determined on a Daicel Chiralpak OD-H column with hexane–2-propanol = 98:2, flow = 0.5 mL/min, detection by UV of 254 nm. Retention times: 21.7 min [(*S*)-enantiomer], 22.9 min [(*R*)-enantiomer]. 92% ee. $[\alpha]^{25}_{D}$ +16.8 (c 1.0, $CHCl_3$).

(*R*)-2-(7-methoxy-1-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)acetaldehyde [(*R*)-16]. To a solution of (*R*)-**2q** (82 mg, 0.38 mmol) in toluene (4.0 mL) was added dropwise a 1.5 M solution of DIBAL–H in toluene (0.51 mL, 0.76 mmol) at –78 °C under an argon atmosphere. After stirring for 2 h, the reaction was quenched with MeOH (1.0 mL) at –78 °C. The resulting mixture was diluted with Et_2O (10 mL) and then filtered through a glass filter. The resulting precipitates were washed thoroughly with CH_2Cl_2, and the combined filtrate was concentrated *in vacuo*. The residue was diluted with THF

(12 mL), and 1 M HCl aqueous solution was added at 0 °C. The solution was stirred for 2 h at rt before being quenched with a saturated $NaHCO_3$ aqueous solution. The resulting mixture was extracted with ethyl acetate, and the combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and then concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 5:1) to give the title compound (69 mg, 83%) as a colorless oil, R_f 0.43 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (dd, *J* = 3.5, 2.6 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.82 (d, *J* = 2.7 Hz, 1H), 6.70 (dd, *J* = 8.4, 2.7 Hz, 1H), 3.79 (s, 3H), 2.80 (dd, *J* = 15.2, 2.6 Hz, 1H), 2.73 (t, *J* = 6.2 Hz, 2H), 2.57 (dd, *J* = 15.2, 3.7 Hz, 1H), 1.93–1.71 (m, 4H), 1.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.1, 157.7, 143.4, 130.2, 128.7, 112.0, 111.5, 56.2, 55.3, 36.8, 36.6, 30.7, 29.6, 19.6. Ee of the aldehyde was determined on a Daicel Chiralpak AD-H column with hexane–2-propanol = 97:3, flow = 0.5 mL/min, detection by UV of 254 nm. Retention times: 12.0 min [(*R*)-enantiomer], 13.5 min [(*S*)-enantiomer]. 92% ee. $[\alpha]^{24}_D$ +46.2 (c 1.16, $CHCl_3$), [lit[23] $[\alpha]^{24}_D$ +56.4 (c 1.16, $CHCl_3$), lit[34] $[\alpha]^{20}_D$ +57.5 (c 2.6, $CHCl_3$)]. Analyses were identical to previously described material.[20]

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Chapter 4

Nickel/Lewis Acid-catalyzed Carbocyanation of Alkynes Using Acetonitrile and Substituted Acetonitriles

Nickel/Lewis acid dual catalysis is found to effect the carbocyanation reaction of alkynes using acetonitrile and substituted acetonitriles to give a range of variously substituted acrylonitriles. The reaction of optically active α-phenylpropionitrile suggests a reaction mechanism that involves oxidative addition of a C–CN bond with retention of its absolute configuration. The addition of propionitrile across alkynes is also demonstrated briefly to give the corresponding ethylcyanation products in good yields, whereas the reaction of butyronitrile suffers from β-hydride elimination of a propylnickel intermediate to give hydrocyanation products in significant amounts.

Introduction

Nickel/Lewis acid (LA) dual catalysis allows, as described in Chapter 2, a wide variety of aryl cyanides to add across unsaturated compounds. The author further anticipated the carbocyanation reaction using alkyl cyanides might be feasible under the similar dual catalysis, because some alkyl cyanides were reported to undergo oxidative addition to nickel(0) through the activation of C(sp^3)–CN σ-bonds.[1] In this Chapter, he demonstrates the carbocyanation reaction of alkynes with acetonitrile under nickel/$AlMe_3$ dual catalysis. The reactions of propionitrile and butyronitrile with alkynes are also described briefly. Also demonstrated is the addition reaction of substituted acetonitriles such as aryl-, protected amino-, hydroxy-, and silylacetonitrile to give a wide variety of tri- and disubstituted acrylonitriles having an allylic functional group regio- and stereoselectively.

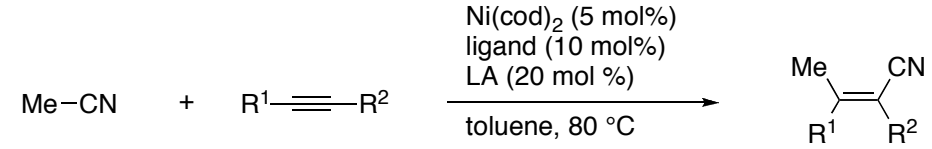
Results and Discussion

Nickel/Lewis acid-catalyzed carbocyanation of alkynes using acetonitrile

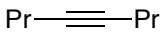
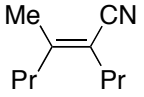
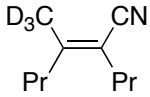
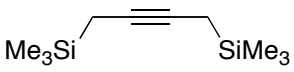
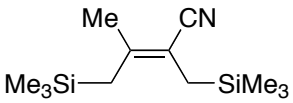
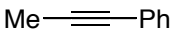
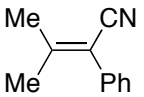
First, the author investigated the reaction of acetonitrile (**1a**) with 4-octyne (**2a**) in the presence of a nickel/LA cooperative catalyst, and found that $AlMe_3$, $AlMe_2Cl$, and BPh_3 were effective as a LA cocatalyst. After screening several combinations of catalysts conditions, he found that the reaction of **1a** (10 mmol) with **2a** (10 mmol) proceeded in the presence of $Ni(cod)_2$ (5 mol %), PPh_2(*t*-Bu) (10 mol %), and $AlMe_3$ (20 mol %) in toluene at 80 °C to afford the corresponding *cis*-methylcyanation product **3aa** in 71% yield after 4 h (entry 1 of Table 1). Exclusive *cis*-addition of **1a** was unambiguously confirmed by nOe experiments. In the absence of the LA cocatalyst, the methylcyanation product was not observed in any detectable amount. Use of CH_3CN-d_3 as a nitrile substrate gave **3aa**-d_3 of 99% deuteration, suggesting that the methyl group in **3aa** was full derived from acetonitrile and definitely not from $AlMe_3$ (entry 2). Under the same reaction conditions, 1,4-bis(trimethylsilyl)-2-butyne (**2b**) also underwent methylcyanation to give bis(silylmethyl)-substituted crotonitrile **3ab** in 91% yield (entry 3). Partial isomerization of the initially formed *cis*-adduct was observed to give a 12:88 mixture of *E*/*Z* stereoisomers. Methylcyanation of unsymmetrical alkynes gave a single regioisomer but as a mixture of stereoisomers (entries 4–9). Addition to 1-phenyl-1-propyne (**2c)** and 1-phenyl-1-butyne (**2d**) proceeded in the presence of a slightly modified catalyst with PMe_3 as a ligand in

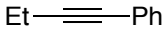
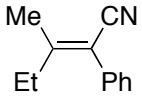
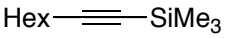
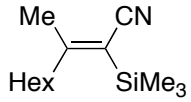
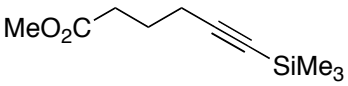
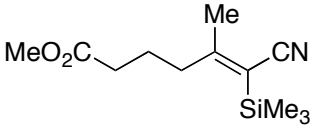
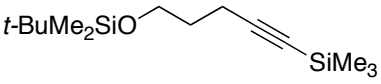
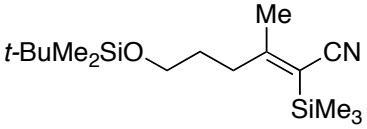
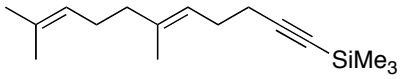
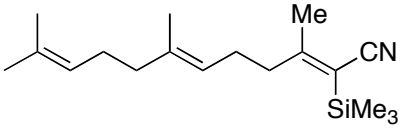
acetonitrile as a solvent to give methylcyanation products **3ac** and **3ad** in 53% and 49% yield, respectively (entries 4 and 5). In the latter case, *E*/*Z* ratio remained constant throughout the reaction, implying a mechanism leading to *trans*-adduct (*vide infra*). Silyl-substituted acetylenes **2e**–**2h** also underwent the methylcyanation reaction in the presence of a Ni/$PPhCy_2$/$AlMe_2Cl$ catalyst (entries 6–9). Functional groups such as ester, silyloxy, and internal double bond were compatible with the reaction conditions. Formation of formal *trans*-adducts was ascribed to isomerization of the initial *cis*-adducts based on inconstant *E*/*Z* ratios during the reaction (entries 6–9). The isomerization could be induced by conjugate addition of a phosphorus ligand as a nucleophile. The presence of a LA catalyst, which could interact with the cyano group of the methylcyanation products, might further promote the isomerization. Indeed, exposure of an isolated sample of (*Z*)-**3ae** to the reaction conditions in the presence or absence of a LA catalyst revealed such promotion of the isomerization.

Table 1. Nickel/Lewis acid-catalyzed carbocyanation of alkynes with acetonitrile.



1a (1.0 mmol) **2a–2h** **3**

entry	alkyne (mmol)	cond.[a]	time (h)	major product, yield (%),[b] *E*/*Z*
1[c]	 **2a** (10.0)	A	4	 **3aa**, 71
2[d]	**2a** (1.0)	A	5	 **3aa**-d_3, 66[e]
3	 **2b** (1.0)	A	10	 **3ab**, 91, 12:88[f]
4[g]	 **2c** (1.0)	B	19	 **3ac**, 53

5[g]	 **2d** (1.0)	B	23	 **3ad**, 49, 61:39[h]
6[i]	 **2e** (2.0)	C	12	 **3ae**, 74, 9:91[j]
7[i]	 **2f** (2.0)	C	21	 **3af**, 38, 9:91
8[i]	 **2g** (2.0)	C	24	 **3ag**, 60, 25:75
9[i]	 **2h** (2.0)	C	18	 **3ah**, 63, 14:86

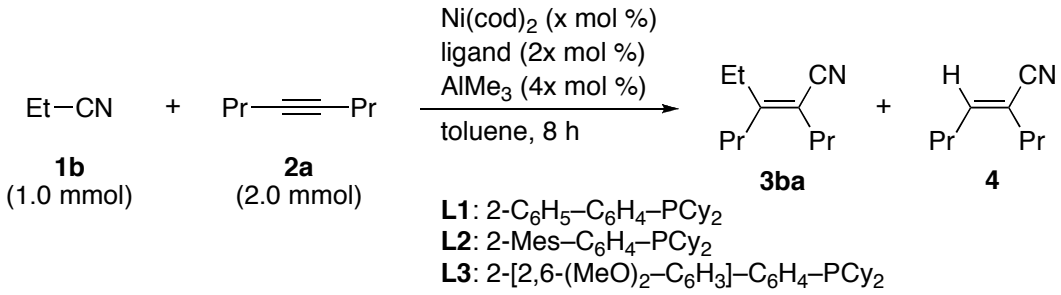
[a] Conditions A, $PPh_2(t\text{-Bu})$ and $AlMe_3$; conditions B, PMe_3 and $AlMe_3$; conditions C, $PPhCy_2$ and $AlMe_2Cl$. [b] Isolated yields. [c] Reaction run in a 10 mmol scale. [d] d_3-Acetonitrile was used. [e] 99% Deuteration. [f] E/Z = 6:94 at 6 h. [g] Reaction run with 1.0 mL of acetonitrile as a solvent. [h] E/Z = 61:39 at 8 h. [i] Run with 10 mol % of $Ni(cod)_2$. [j] E/Z = 7:93 at 3 h.

Nickel/$AlMe_3$-catalyzed carbocyanation of alkynes using propionitrile and butyronitrile.

The author then examined the reaction of propionitrile (**1b**) with **2a**. Under the optimal reaction conditions for the methylcyanation reaction, no trace amount of ethylcyanation product **3ba** was observed. Instead, hydrocyanation product **4** was obtained in 3% yield probably through *β*-hydride elimination from an ethylnickel intermediate (entry 1 of Table 2). To suppress the unproductive *β*-hydride elimination and to optimize reaction conditions for general alkylcyanation, he screened several ligands, especially focusing on bulky phosphines (entries 2–6). Of the ligands

examined, Buchwald's ligands[2] such as 2-Mes–C_6H_4–PCy_2 (**L2**)[2b] and 2-[2,6-$(MeO)_2$–C_6H_3]–C_6H_4–PCy_2 (**L3**)[2c] were found to be effective to give **3ba** in modest yields accompanied by small amounts of **4** (entries 5 and 6). Use of $Ni(cod)_2$ (10 mol %) with **L3** as a ligand at 50 °C significantly improved yield of **3ba** up to 78%, and only a trace amount of **4** was detected by GC (entry 8). The improvement may be attributed to lower reaction temperature and methoxy substituents in **L3** that can coordinate to the nickel center of the reaction intermediates to suppress *β*-hydride elimination. Under the same conditions, ethylcyanation of **2b** also proceeded to give the corresponding adduct (**3bb**) in 83% yield, although partial isomerization of the *cis*-adduct was again observed (eq. 1). These results prompted the author to examine the reaction of butyronitrile (**1c**) with **2a** under the similar conditions. However, an expected propylcyanation product was obtained only in 10% yield, and by-products **4** and **5** derived from *β*-hydride elimination were obtained as major components (eq. 2).

Table 2. Nickel/$AlMe_3$-catalyzed carbocyanation of 4-octyne with propionitrile (**1b**).[a]

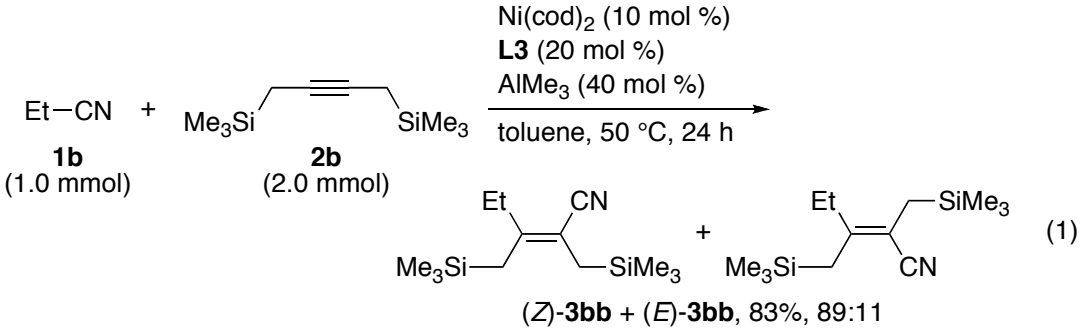


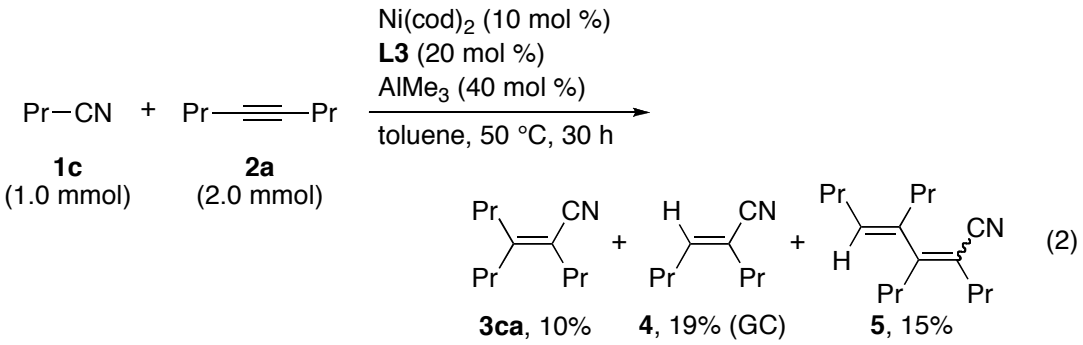
1b (1.0 mmol) **2a** (2.0 mmol) **3ba** **4**

L1: 2-C_6H_5–C_6H_4–PCy_2
L2: 2-Mes–C_6H_4–PCy_2
L3: 2-[2,6-$(MeO)_2$–C_6H_3]–C_6H_4–PCy_2

				product, yield (%)[b]	
entry	ligand	x	temp (°C)	**3ba**	**4**
1	PPh_2(*t*-Bu)	5	80	0	3
2	P(*t*-Bu)$_3$	5	80	11	5
3	PCy_3	5	80	2	4
4	**L1**	5	80	21	1
5	**L2**	5	80	22	1
6	**L3**	5	80	39	1
7	**L3**	5	50	36	0
8	**L3**	10	50	78[c]	1

[a] All the reaction was carried out using **1b** (1.0 mmol) and **2a** (2.0 mmol) in toluene (1.0 mL). [b] Estimated by GC using dodecane as an internal standard. [c] Isolated yield.

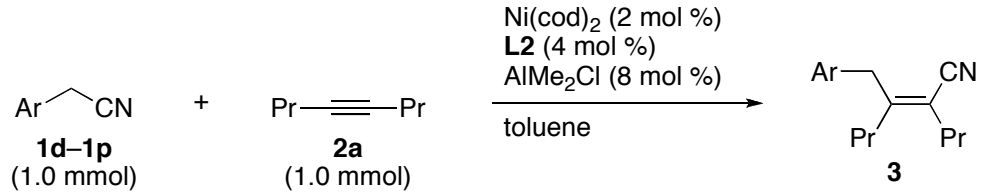


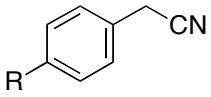
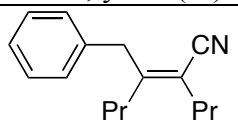
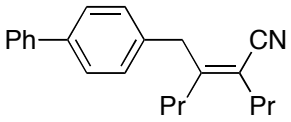
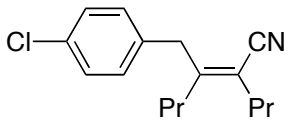
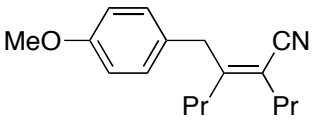
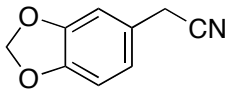
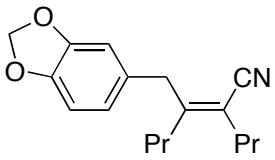
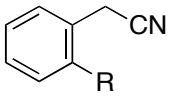
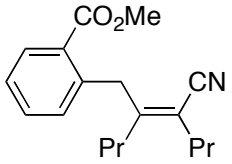
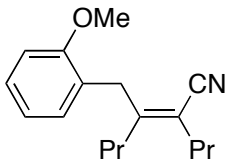


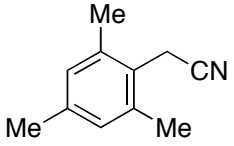
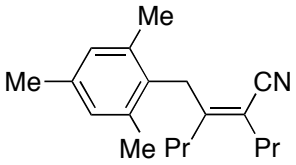
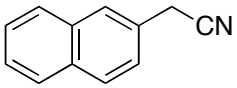
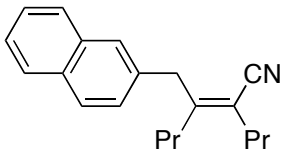
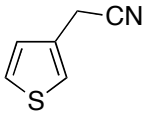
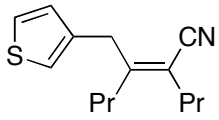
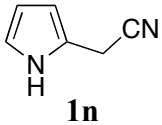
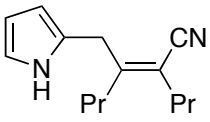
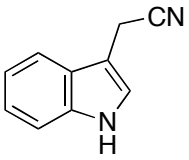
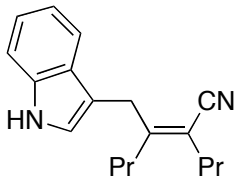
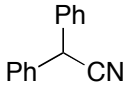
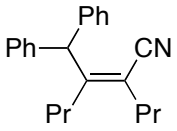
Nickel/AlMe$_2$Cl-catalyzed carbocyanation of alkynes using arylacetonitriles

With the limited success in the carbocyanation of alkynes with alkyl cyanides, the author turned his attention to the reaction of substituted acetonitriles, which would not suffer from *β*-hydride elimination. At the onset, he used arylacetonitriles for carbocyanation, because relatively high reactivity was expected for the oxidative addition of their C–CN bonds to nickel(0) as compared with related reactions of allyl cyanides.[3] After a brief survey of reaction conditions with benzyl cyanide (**1d**, 1.0 mmol) and 4-octyne (**2a**, 1.0 mmol), he found that the combination of Ni(cod)$_2$ (2 mol %), **L2** (4 mol %), and AlMe$_2$Cl (8 mol %) effectively catalyzed the desired benzylcyanation reaction at 35 °C to afford **3da** in 90% yield after 8 h (entry 1 of Table 3). He further studied the scope of benzyl cyanide having a substituent on the phenyl ring and found that a range of functional groups, such as chloro, acetal, and ester were compatible with both the electron-rich nickel(0) and LA catalysis, C–CN bonds being activated exclusively to give various (*Z*)-3-arylmethyl-2,3-dipropylacrylonitriles (entries 2–8). Heteroarylacetonitriles also participated in the reaction (entries 9–12). Notably, no *N*-protecting group was necessary for pyrrolyl- and indolylacetonitriles (entries 11 and 12). The sterically hindered C–CN bond in diphenylacetonitrile (**1p**) also was activated to give the corresponding adduct **3pa** having a tertiary carbon albeit in a low yield (entry 13).

Table 3. Carbocyanation of 4-octyne with arylacetonitriles.



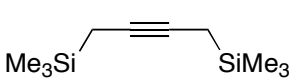
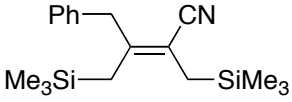
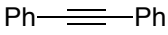
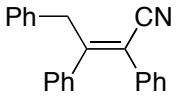
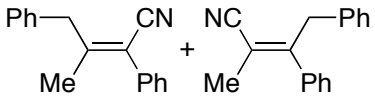
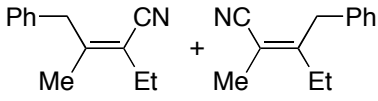
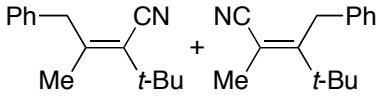
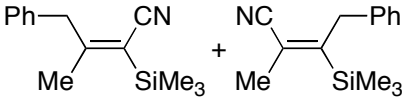
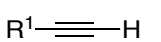
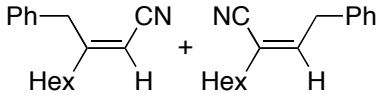
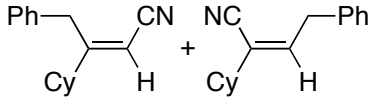
entry	arylacetonitrile	temp (°C)	time (h)	product, yield (%)[a]
1	 R = H: **1d**	35	8	 **3da**, 90
2	Ph: **1e**	35	8	 **3ea**, 90
3	Cl: **1f**	80	18	 **3fa**, 74
4	MeO: **1g**	35	8	 **3ga**, 93
5	 **1h**	35	24	 **3ha**, 96
6	 R = CO_2Me: **1i**	80	5	 **3ia**, 56
7	MeO: **1j**	35	24	 **3ja**, 83

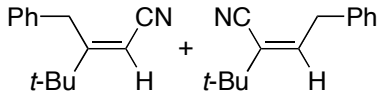
8	 **1k**	80	2	 **3ka**, 85
9	 **1l**	35	96	 **3la**, 85
10	 **1m**	80	2	 **3ma**, 95
11[b]	 **1n**	35	10	 **3na**, 54
12[b]	 **1o**	35	48	 **3oa**, 69
13[b]	 **1p**	100	12	 **3pa**, 22

[a] Isolated yields. [b] The reaction was carried out using $Ni(cod)_2$ (10 mol %), **L2** (20 mol %), and $AlMe_2Cl$ (40 mol %).

The scope of alkynes toward benzyl cyanide (**1d**) is summarized in Table 4. A symmetrical alkyne, 1,4-bis(trimethylsilyl)-2-butyne (**2b**), participated in the benzylcyanation reaction to afford **3db** in 93% yield in an exclusive *cis*-fashion (entry 1), whereas the addition reaction across diphenylacetylene (**2i**) gave a mixture of stereoisomers (entry 2). The stereochemistry of (*Z*)-**3di** was unambiguously confirmed by X-ray crystallography (Figure 1). Internal unsymmetrical alkynes with sterically different substituents reacted with modest to excellent regio- and stereoselectivities (entries 3–6). Whereas the regioselection across 2-pentyne (**2j**) was modest because of small steric difference in the substituents (entry 4), 1-phenyl-1-propyne (**2c**), 4,4-dimethyl-2-pentyne (**2k**), and trimethyl(1-propynyl)silane (**2l**) all reacted regioselectively to give preferentially isomers having a cyano group at the carbon substituted by a larger group (entries 3, 5 and 6). Use of $PMePh_2$ as a ligand allowed terminal alkynes to undergo the benzylcyanation to give adducts in good to excellent regioselectivity (entries 7–9). In the presence of the nickel/**L2** catalyst, tri- and/or oligomerization of terminal alkynes took place rapidly, and no trace amount of the corresponding benzylcyanation products was detected. Interestingly, the observed regioselectivity was opposite to that with internal alkynes, giving preferentially isomers with a cyano group at the carbon having a smaller substituent (hydrogen). This reversal of regiochemistry might be ascribed to the difference of the ligand. However any reasonable explanation is available at present. Also observed was formation of 10–20% of structurally unidentified 1:2 adducts, when **2m** and **2n** were employed as an alkyne substrate. Formation of the 1:2 adducts may be attributed to double migratory insertion of 1-octyne into a C–Ni bond (*vide infra*) based on the experimental fact that isolated **3dm** did not react with **2a** under the same reaction conditions.

Table 4. Carbocyanation of alkynes with phenylacetonitrile.

entry	alkyne	temp (°C)	time (h)	product(s), yield (%),[a] ratio[b]
1	 **2b**	80	70	 **3db**, 93
2	 **2i**	80	73	 **3di**, 86[c]
3	R^2 = Ph: **2c**	35	24	 **3dc**, **3'dc**, 85, 92:8
4	Et: **2j**	35	8	 **3dj**, **3'dj**, 69, 59:41
5	*t*-Bu: **2k**	35	21	 **3dk**, **3'dk**, 94, >99:1
6[d]	$SiMe_3$: **2l**	35	53	 **3dl**, **3'dl**, 56, 81:19
7[e]	 R^1 = Hex: **2m**	35	11	 **3dm**, **3'dm**, 48,[f] 88:12
8[e]	Cy: **2n**	35	9	 **3dn**, **3'dn**, 61,[f] 92:8

9[e]		*t*-Bu: **2o**	35	9	 **3do**, **3'do**, 54, >99:1

[a] Isolated yields. [b] Estimated by ^{1}H NMR of a crude product. [c] *E*/*Z* = 79:21 (82:18 at 1.5 h). [d] The reaction was carried out using Ni(cod)$_2$ (10 mol %), **L2** (20 mol %), and AlMe$_2$Cl (40 mol %). [e] The reaction was carried out using 3.0 equiv. of alkyne, Ni(cod)$_2$ (10 mol %), PMePh$_2$ (20 mol %), and AlMe$_2$Cl (40 mol %). [f] 10–20% of a isomeric mixture of 1:2 adducts were also detected.

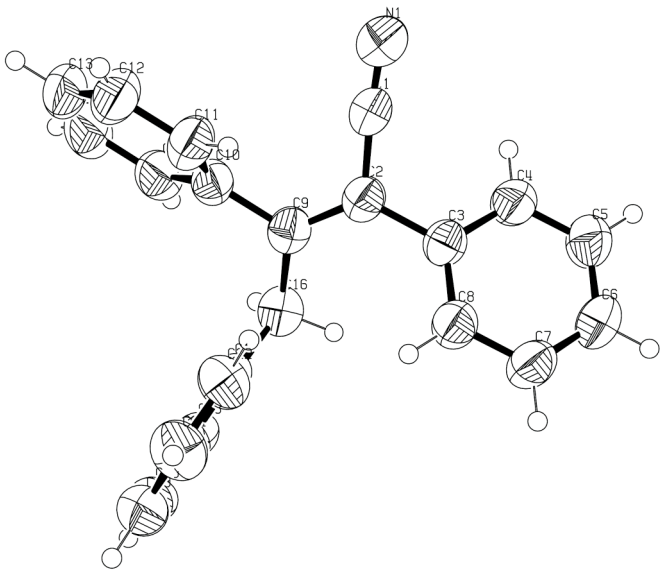


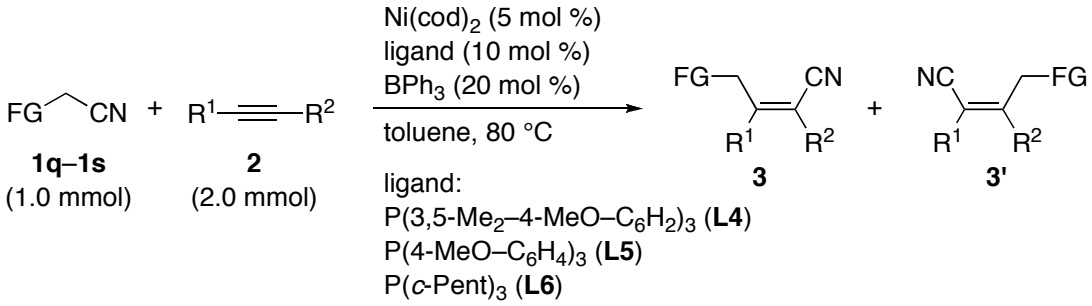
Figure 1. ORTEP drawing for (*Z*)-**3di**.

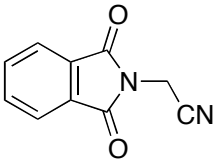
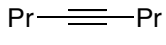
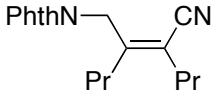
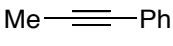
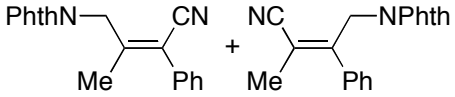
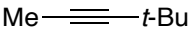
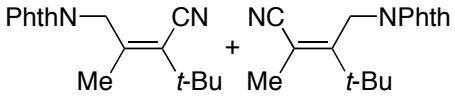
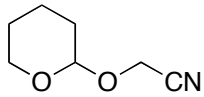
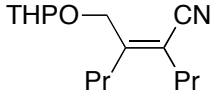
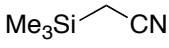
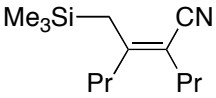
Nickel/BPh$_3$-catalyzed carbocyanation of alkynes with functionalized acetonitriles

Having established a broad scope of the carbocyanation of alkynes with arylacetonitriles, the author next examined the reaction using other functionalized acetonitriles. He envisioned that the addition of amino- and alkoxyacetonitriles across alkynes would straightforwardly give highly functionalized polysubstituted allylic amines and alcohols with defined stereochemistry. To verify this strategy, he first examined the reaction of *N*-(cyanomethyl)phthalimide (**1q**) with 4-octyne (**2a**). After brief screening of ligands and LA using Ni(cod)$_2$ (5 mol %) in toluene at 80 °C, he found the combination of P(3,5-Me$_2$–4-MeO–C$_6$H$_2$)$_3$ (10 mol %) and BPh$_3$ (20 mol %) was the best, and obtained protected trisubstituted (*Z*)-allylic amine **3qa** in 64% yield

(entry 1 of Table 5). Unsymmetrical alkynes, **2c** and **2k**, also underwent the addition of **1q** with the same regioselectivity observed for the benzylcyanation reaction (entries 2 and 3). In the case of 1-phenyl-1-propyne (**2c**), a small amount of stereoisomer (*E*)-**3qc** was obtained, which should be derived from isomerization of initially formed (*Z*)-**3qc**.

Table 5. Carbocyanation of alkynes with protected functionalized acetonitriles.



entry	nitrile	alkyne	ligand	time (h)	product(s), yield (%),[a] ratio[b]
1	 **1q**	 **2a**	**L4**	30	 **3qa**, 64[c]
2	**1q**	 **2c**	**L4**	30	 **3qc**, **3'qc**, 60,[c] 92[d]:8
3	**1q**	 **2k**	**L4**	30	 **3qk**, **3'qk**, 79, >99:1
4[e,f]	 **1r**	**2a**	**L5**	3	 **3ra**, 82[c]
5[f]	 **1s**	**2a**	**L6**	13	 **3sa**, 89

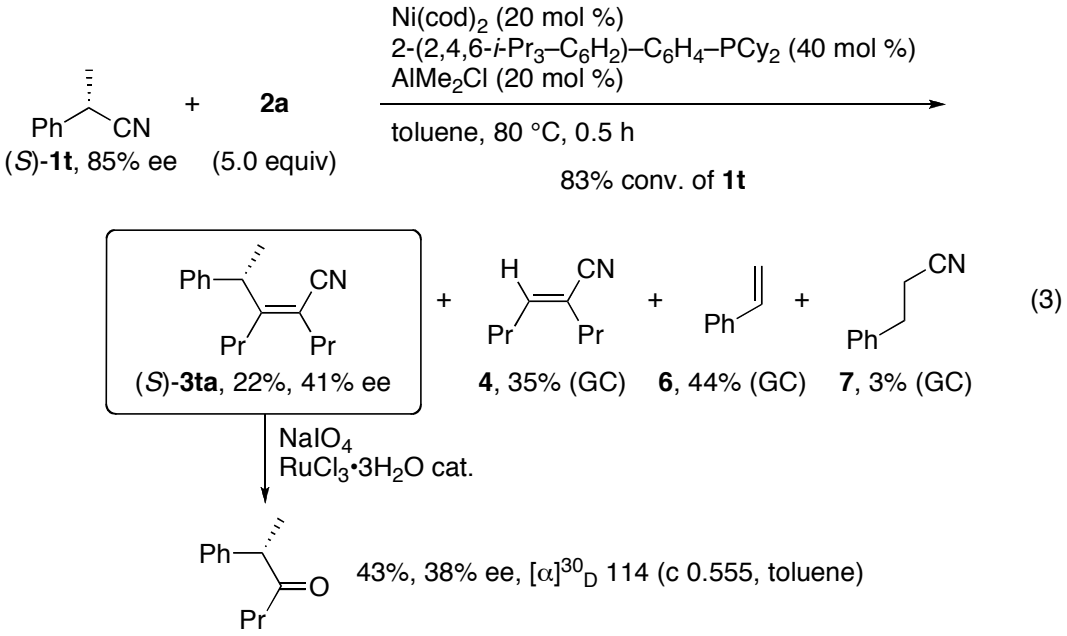
[a] Isolated yields. [b] Estimated by ^{1}H NMR of a crude product. [c] An isomeric mixture of 1:2 adducts (10–20%) also was detected. [d] *E*/*Z* = 13:87 (5:95 at 6 h). [e] The reaction was carried out using Ni(cod)$_2$ (10 mol %), **L5** (20 mol %), and BPh$_3$ (40 mol %). [f] **2a** (1.5 mmol) was used.

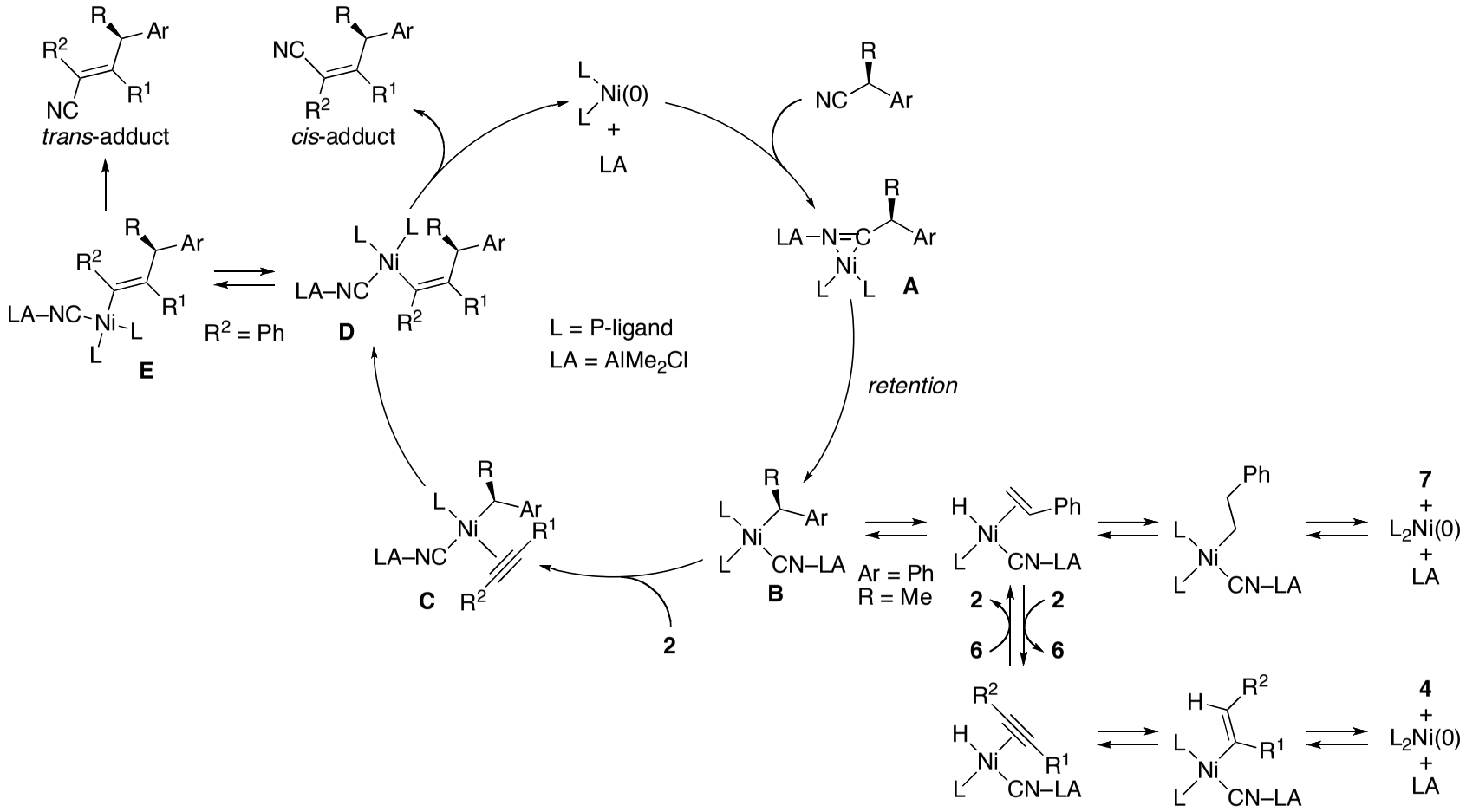
Exposure of the isolated sample of (*Z*)-**3qc** to the present reaction conditions indeed caused the isomerization. THP-protected hydroxyacetonitrile (**1r**) also served as a substrate of the alkyne-carbocyanation reaction under slightly modified conditions to give the corresponding THP-protected allylic alcohol **3ra** in a stereoselective manner (entry 4). For silylmethylcyanation of **2a** with (trimethylsilyl)acetonitrile (**1s**), BPh_3 was a more effective cocatalyst than $AlMe_2Cl$.[4] A milder Lewis-acidity of BPh_3 would be favorable for the reactions of particular nitriles **1q**–**1s** that give products with acid-sensitive functional groups.

Reaction mechanism

To gain a mechanistic insight, (*S*)-α-phenylpropionitrile [(*S*)-**1t**] of 85% ee was reacted with **2a** under slightly modified conditions using $Ni(cod)_2$ (20 mol %), 2-(2,4,6-*i*-Pr_3–C_6H_2)–C_6H_4–PCy_2 (**L7**, 40 mol %),[2d] and $AlMe_2Cl$ (20 mol %) (eq. 3). The corresponding adduct (*S*)-**3ta** of 41% ee was obtained in 22% yield, the absolute configuration being determined based on the reported optical rotation of (*R*)-2-phenyl-3-hexanone[5] after oxidative cleavage of the double bond. Also obtained were hydrocyanation product **4**, styrene **6**, and hydrocinnamonitrile **7** in 35%, 44%, and 3% yields, respectively as estimated by GC. Recovered **1t** showed 80% ee, suggesting that back-ground racemization of **1t** under these conditions appears to be slower than the carbocyanation event. The author also confirmed that no further racemization of **3ta** took place under the present conditions. Accordingly, these results clearly suggest a mechanism shown in Scheme 1, which should start with oxidative addition of a C–CN bond with *retention* of configuration through LA adduct of η^2-nitrilenickel species **A**[6] to give **B**.[1d] Oxidative addition of acetonitrile to nickel(0) with retention of configuration has also been suggested by theoretical calculations,[1j] in contrast to the nonstereospecific oxidative addition of benzyl halides to nickel(0).[7] The details of the mechanism may be understood in terms of the following steps. Coordination and then migratory insertion of alkynes into the $ArCH_2$–Ni bond in **B** give **D** via **C**. Reductive elimination from **D** gives rise to a carbocyanation product and regenerate nickel(0) species. The absolute configuration is retained during these elemental steps.[8] The partial loss of %ee during the addition reaction may be ascribed to β-hydride elimination followed by reinsertion. Particularly, the formation of **4**, styrene, and hydrocinnamonitrile is in accord with these side reactions. In the case of

phenyl substituted alkynes, **D** may isomerize to **E** possibly through conjugate addition of phosphorus ligands[9] followed by reductive elimination to give *trans*-adduct. A LA catalyst would primarily accelerate the oxidative addition step,[3a,4,6,10] though other elemental steps may also be facilitated by its coordination to a cyano group.[1d,11]





Scheme 1. Plausible reaction mechanism.

Conclusion

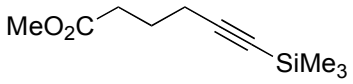
In summary, the author has demonstrated the nickel/Lewis acid-catalyzed methylcyanation of alkynes proceeds with high *cis*-selectivity and high regioselectivity. Extension of this catalysis to propionitrile as an alkyl cyanide substrate also meets success by employing bulky phosphorous ligand **L3** having a hemilabile methoxy group, whereas propylcyanation reaction of 4-octyne using butyronitrile proceeded only sluggishly even with the improved catalyst system due to competitive β-hydride elimination. Instead, a general substrate scope of the carbocyanation reaction with arylacetonitriles has been established under mild reaction conditions with nickel/$AlMe_2Cl$ catalysts. Moreover, functionalized acetonitriles such as protected amino- and hydroxyacetonitriles as well as silylacetonitrile have been demonstrated to add across alkynes in stereo- and regioselective manners under nickel/BPh_3 catalysis, affording a wide variety of polysubstituted acrylonitriles having an allylic functionality. Using (*S*)-α-phenylpropionitrile, the mechanism of the carbocyanation reaction including the oxidative addition of C–CN bonds with retention of its absolute configuration has been elucidated.

Experimental Section

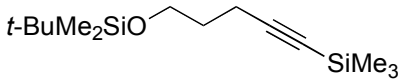
Chemicals

2-Mes–C_6H_4–PCy_2 (**L2**),[2b] 2-(2,4,6-*i*-Pr_3–C_6H_2)–C_6H_4–PCy_2 (**L7**),[2d] 1,4-bis(trimethylsilyl)-2-butyne (**2b**),[12] 2-pyrrolylaceonitrile (**1n**),[13] (*S*)-α-phenylpropionitrile [(*S*)-**1t**] [using (*R*,*S*)-Josiphos as a ligand],[14] *N*-(cyanomethyl)phthalimide (**1q**),[15] and tetrahydro-2*H*-pyranoxyacetonitrile (**1r**)[16] were prepared according to the respective literature procedure.

Methyl 6-trimethylsilyl-5-hexynoate (2f). A 1.6 M solution of *n*-BuLi (34 mmol, 22 mL) in hexane was added dropwise to a solution of methyl 5-hexynoate (3.6 g, 29 mmol) in THF (29 mL) at –78 °C, and the resulting mixture was stirred for 30 min before dropwise addition of chlorotrimethylsilane (3.4 g, 32 mmol). The reaction mixture was stirred at rt for 19 h before quenching with a saturated NH_4Cl aqueous solution. The resulting mixture was extracted three times with diethyl ether, and the combined organic layers were dried over anhydrous $MgSO_4$, filtered through a Celite pad, and then concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 30:1) and further by distillation under vacuum to give the title compound (1.13 g, 5.7 mmol, 20%).[17]

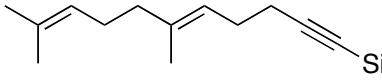


5-*tert*-Butyldeimethylsilyloxy-1-trimethylsilyl-1-pentyne (2g). To a suspension of NaH (0.86 g, 36 mmol) in THF (150 mL) was added dropwise 4-pentyn-1-ol (2.8 g, 33 mmol) at 0 °C. The resulting mixture was stirred at rt for 30 min, cooled at 0 °C, and treated with *tert*-butyldimethylchlorosilane (5.4 g, 30 mmol). The whole mixture was stirred at rt for 15 h, and then quenched with water. The resulting mixture was extracted three times with hexane, and the combined organic layers were washed three times with water, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and then concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 50:1) to give 1-*tert*-butyldimethylsilyloxy-4-pentyne (3.6 g, 18.3 mmol, 61%).[18] To a solution of the silyl ether (3.6 g, 18.3 mmol) in THF (37 mL) was added dropwise a 1.6 M solution of *n*-BuLi (20 mmol, 13 mL) in hexane at –78 °C. The resulting mixture was stirred for 30 min before dropwise addition of

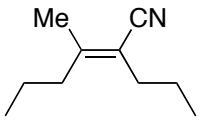


chlorotrimethylsilane (2.4 g, 22.0 mmol). After stirring at rt for 13 h, the reaction was quenched with a saturated NH_4Cl aqueous solution. The resulting mixture was extracted three times with hexane, and the combined organic layers were washed three times with water, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and then concentrated *in vacuo*. The residue was purified by distillation under vacuum to give the title compound (4.5 g, 16.6 mmol, 90%).[19]

(*E*)-6,10-Dimethyl-1-trimethylsilyl-5,9-undecadien-1-yne (2h). A 1.6 M solution of *n*-BuLi (24 mmol, 15 mL) in hexane was added dropwise to a solution of (*E*)-6,10-dimethyl-5,9-undecadien-1-yne (3.5 g, 20 mmol, prepared[20] from (*E*)-1-chloro-3,7-dimethyl-2,6-octadiene) in THF (40 mL) at –78 °C, and the resulting mixture was stirred for 15 min before dropwise addition of chlorotrimethylsilane (3.3 g, 30 mmol). After stirring at rt for 3 h, the reaction was quenched with water. The resulting mixture was extracted three times with hexane, and the combined organic layers were washed three times with water, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and then concentrated *in vacuo*. The residue was purified by distillation under vacuum to give the title compound (4.6 g, 18.5 mmol, 92%).[21]



Methylcyanation of 4-octyne (2a). In a dry box, acetonitrile (**1a**, 0.41 g, 10.0 mmol), a 1.0 M solution of $AlMe_3$ in hexane (2.0 mL, 2.0 mmol), and **2a** (1.10 g, 10.0 mmol) were added sequentially to a solution of $Ni(cod)_2$ (138 mg, 0.50 mmol) and PPh_2(*t*-Bu) (0.24 g, 1.00 mmol) in toluene (10 mL) placed in a vial. The resulting mixture was stirred at 80 °C for 4 h, filtered through a silica gel pad, and concentrated *in vacuo*. The residue was distilled to give (*E*)-3-methyl-2-propylhex-2-enenitrile (**3aa**, 1.08 g, 71%) as a pale yellow oil, bp 80 °C (20 mmHg), R_f 0.18 (hexane–ethyl acetate = 40:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21–2.12 (m, 4H), 2.05 (s, 3H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.46 (sext, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 119.3, 109.7, 35.6, 31.5, 22.6, 21.9, 21.0, 14.1, 13.6. IR (neat): 2964, 2934, 2874, 2208, 1630, 1466, 1381, 1138, 1094, 741 cm^{-1}. Anal. Calcd for $C_{10}H_{17}N$: C, 79.41; H, 11.33. Found: C, 79.47; H, 11.47.



Carbocyanation of alkynes with acetonitrile.

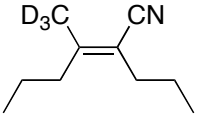
General procedure A. In a dry box, acetonitrile (41 mg, 1.00 mmol), a 1.0 M solution of $AlMe_3$ in hexane (0.20 mL, 0.20 mmol), and an alkyne (1.00 mmol), and dodecane (internal standard, 85 mg, 0.50 mmol) were added sequentially to a solution of $Ni(cod)_2$ (14 mg, 50 μmol) and PPh_2(*t*-Bu) (24 mg, 0.10 mmol) in toluene (1.0 mL) placed in a vial. The vial was taken out from the dry box and heated at 80 °C for the time specified in Table 1. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash silica gel column chromatography to give the corresponding alkylcyanation products in yields listed in Table 1.

General procedure B. In a dry box, a 1.0 M solution of $AlMe_3$ in hexane (0.20 mL, 0.20 mmol), and an alkyne (1.00 mmol), and dodecane (internal standard, 85 mg, 0.50 mmol) were added sequentially to a solution of $Ni(cod)_2$ (14 mg, 50 μmol) and PMe_3 (7.6 mg, 0.10 mmol) in acetonitrile (1.0 mL) placed in a vial. The vial was taken out from the dry box and heated at 80 °C for the time specified in Table 1. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash silica gel column chromatography to give the corresponding alkylcyanation products in yields listed in Table 1.

General procedure C. In a dry box, acetonitrile (82 mg, 2.00 mmol), a 1.0 M solution of $AlMe_2Cl$ in hexane (0.40 mL, 0.40 mmol), and an alkyne (1.00 mmol), and dodecane (internal standard, 85 mg, 0.50 mmol) were added sequentially to a solution of $Ni(cod)_2$ (28 mg, 0.10 mmol) and $PPhCy_2$ (55 mg, 0.20 mmol) in toluene (1.0 mL) placed in a vial. The vial was taken out from the dry box and heated at 80 °C for the time specified in Table 1. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash silica gel column chromatography to give the corresponding alkylcyanation products in yields listed in Table 1.

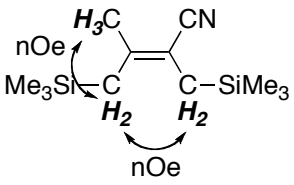
Regio- and/or stereoisomers were separated by preparative GPC or HPLC and characterized by spectrometry. The spectra of **3ac**, and **3ad** agreed well with those reported previously.[22]

(*E*)-3-($^2H_3$)Methyl-2-propylhex-2-enenitrile (3aa-*d*$_3$). A colorless oil, R_f 0.20 (hexane–ethyl acetate = 40:1). ^1H NMR (400 MHz, $CDCl_3$) δ 2.21–2.11 (m, 4H), 1.55 (sext, *J* = 7.5 Hz, 2H), 1.45 (sext, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101



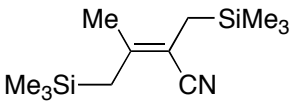
MHz, $CDCl_3$) δ 155.2, 119.3, 109.7, 35.5, 31.5, 21.9, 21.0, 14.1, 13.6. IR (neat): 2963, 2934, 2874, 2208, 1624, 1466, 1381, 1090, 1042, 739 cm^{-1}. HRMS (EI) Calcd for $C_{10}H_{14}D_3N$: M^+, 154.1549. Found: *m*/*z* 154.1557.

(*Z*)-3-Methyl-4-(trimethylsilyl)-2-(trimethylsilyl)methylbut-2-enenitrile [(*Z*)-3ab].



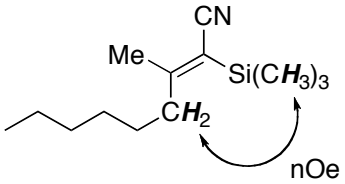
A colorless oil, R_f 0.20 (hexane–ethyl acetate = 30:1). ^1H NMR (400 MHz, $CDCl_3$) δ 2.04 (s, 3H), 1.70 (s, 2H), 1.56 (s, 2H), 0.11 (s, 9H) 0.09 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.2, 120.8, 102.1, 27.4, 24.8, 21.0, –0.4, –1.1. IR (neat): 2955, 2899, 2205, 1614, 1418, 1250, 1196, 1175, 1144, 1086, 1011, 928, 845, 762, 696, 627, 606, 594, 565, 478, 442 cm^{-1}. Anal. Calcd for $C_{12}H_{25}NSi_2$: C, 60.18; H, 10.52. Found: C, 60.09; H, 10.62.

(*E*)-3-Methyl-4-(trimethylsilyl)-2-(trimethylsilyl)methylbut-2-enenitrile [(*E*)-3ab].



A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 30:1). ^1H NMR (400 MHz, $CDCl_3$) δ 2.02 (s, 2H), 1.75 (s, 3H), 1.64 (s, 2H), 0.12 (s, 9H) 0.11 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.1, 121.1, 102.2, 31.1, 21.2, 21.0, –0.4, –1.1. IR (neat): 2955, 2899, 2207, 1614, 1416, 1377, 1248, 1179, 1152, 1096, 1015, 920, 841, 762, 694 cm^{-1}. HRMS (EI) Calcd for $C_{12}H_{25}NSi_2$: M^+, 239.1526. Found: *m*/*z* 239.1521.

(*Z*)-3-Methyl-2-trimethylsilylnon-2-enenitrile [(*Z*)-3ae]. A colorless oil, R_f 0.15 (hexane–ethyl acetate = 30:1). ^1H NMR (400 MHz, $CDCl_3$) δ 2.25 (t, *J* = 8.0 Hz, 2H), 2.15 (s, 3H), 1.50–1.40 (m, 2H), 1.37–1.24 (m, 6H) 0.90 (t, *J* = 6.9 Hz, 3H), 0.28 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.2, 120.3, 108.7, 38.7, 31.7, 29.5, 28.4, 24.4, 22.6, 14.1, 0.1. IR (neat): 2957, 2930, 2858, 2197, 1583, 1466, 1377, 1254, 843, 762 cm^{-1}. Anal. Calcd for $C_{13}H_{25}NSi$: C, 69.88; H, 11.28. Found: C, 69.81; H, 11.42.



(*E*)-3-Methyl-2-trimethylsilylnon-2-enenitrile [(*E*)-3ae]. A colorless oil, R_f 0.15 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (t, *J* = 7.8 Hz, 2H), 1.97 (s, 3H), 1.55–1.46 (m, 2H), 1.39–1.26 (m, 6H) 0.89 (t, *J* = 6.9 Hz, 3H), 0.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.2, 120.0, 108.3, 41.0, 31.7, 29.1, 28.1, 22.63, 22.56, 14.2, –0.2. IR (neat): 2957, 2930, 2858, 2195, 1583, 1462, 1377, 1254, 843, 760 cm^{-1}. Anal. Calcd for $C_{13}H_{25}NSi$: C, 69.88; H, 11.28. Found: C, 69.98; H, 11.08.

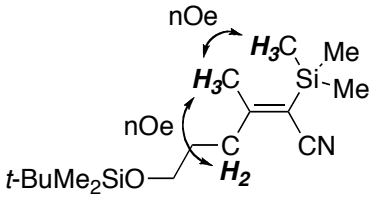
(*Z*)-Methyl 6-cyano-5-methyl-6-trimethylsilylhex-5-enoate [(*Z*)-3af]. A colorless oil, R_f 0.25 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, 3H), 2.34 (t, *J* = 7.3 Hz, 2H), 2.30 (t, *J* = 8.1 Hz, 2H), 2.17 (s, 3H), 1.79 (quint, *J* = 7.7 Hz, 2H), 0.28 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 172.3, 120.0, 110.1, 51.7, 37.6, 33.6, 24.2, 23.4, 0.0. IR (neat): 2955, 2901, 2195, 1740, 1584, 1437, 1375, 1254, 1200, 1157, 1088, 1045, 1007, 905, 843, 762, 698, 631 cm^{-1}. Anal. Calcd for $C_{12}H_{21}NO_2Si$: C, 60.21; H, 8.84. Found: C, 59.99; H, 8.69.

(*E*)-Methyl 6-cyano-5-methyl-6-trimethylsilylhex-5-enoate [(*E*)-3af]. A colorless oil, R_f 0.25 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 3H), 2.54 (t, *J* = 7.8 Hz, 2H), 2.37 (t, *J* = 7.5 Hz, 2H), 1.99 (s, 3H), 1.86 (quint, *J* = 7.7 Hz, 2H), 0.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 172.4, 119.7, 109.7, 51.7, 40.0, 33.4, 23.2, 22.4, –0.3. IR (neat): 2955, 2195, 1740, 1586, 1437, 1375, 1254, 1200, 1175, 1157, 1088, 1045, 1003, 845, 762, 698, 640 cm^{-1}. HRMS (EI) Calcd for $C_{12}H_{21}NO_2Si$: M^+, 239.1342. Found: *m*/*z* 239.1343.

(*Z*)-6-(*tert*-Butyldimethylsilyloxy)-3-methyl-2-trimethylsilylhex-2-enenitrile [(*Z*)-3ag]. A colorless oil, R_f 0.10 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (t, *J* = 5.9 Hz, 2H), 2.35 (t, *J* = 8.1 Hz, 2H), 2.17 (s, 3H), 1.70–1.60 (m, 2H), 0.90 (s, 9H), 0.29 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 120.3, 109.1, 62.7, 35.4, 31.5, 26.0, 24.5, 18.4, 0.0,

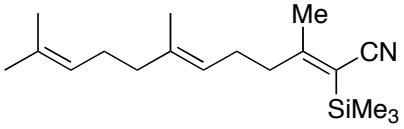
–5.2. IR (neat): 2955, 2930, 2897, 2858, 2197, 1583, 1472, 1462, 1437, 1408, 1387, 1362, 1256, 1099, 1022, 1005, 947, 908, 839, 777, 762, 696, 662, 629 cm^{-1}. Anal. Calcd for $C_{16}H_{33}NOSi_2$: C, 61.67; H, 10.67. Found: C, 61.51; H, 10.66.

(*E*)-6-(*tert*-Butyldimethylsilyloxy)-3-methyl-2-trimethylsilylhex-2-enenitrile



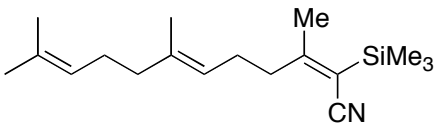
[(*E*)-3ag]. A colorless oil, R_f 0.13 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (t, *J* = 6.4 Hz, 2H), 2.55 (t, *J* = 8.0 Hz, 2H), 2.00 (s, 3H), 1.77–1.69 (m, 2H), 0.91 (s, 9H), 0.29 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 119.8, 108.7, 62.5, 37.5, 31.3, 26.0, 22.7, 18.4, –0.3, –5.1. IR (neat): 2955, 2930, 2897, 2858, 2195, 1585, 1472, 1462, 1408, 1389, 1362, 1254, 1103, 1007, 839, 775, 760 cm^{-1}. Anal. Calcd for $C_{16}H_{33}NOSi_2$: C, 61.67; H, 10.67. Found: C, 61.95; H, 10.75.

(2*Z*,6*E*)-3,7,11-Trimethyl-2-trimethylsilyldodeca-2,6,10-trienenitrile [(*Z*)-3ah]. A



colorless oil, R_f 0.18 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.11–5.02 (m, 2H), 2.30 (t, *J* = 8.0 Hz, 2H), 2.22–2.14 (m, 2H), 2.18 (s, 3H), 2.11–1.97 (m, 4H), 1.69 (s, 3H), 1.62 (s, 3H), 1.61 (s, 3H), 0.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 136.5, 131.4, 123.9, 122.1, 120.2, 109.3, 39.7, 38.5, 26.8, 26.6, 25.9, 24.3, 17.8, 16.2, 0.1. IR (neat): 2965, 2916, 2857, 2195, 1667, 1582, 1445, 1377, 1327, 1254, 1109, 1042, 984, 893, 843, 760, 696, 629 cm^{-1}. Anal. Calcd for $C_{18}H_{31}NSi$: C, 74.67; H, 10.79. Found: C, 74.76; H, 11.01.

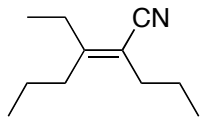
(2*E*,6*E*)-3,7,11-Trimethyl-2-trimethylsilyldodeca-2,6,10-trienenitrile [(*E*)-3ah]. A



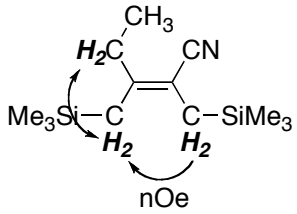
colorless oil, R_f 0.23 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.17–5.06 (m, 2H), 2.53 (t, *J* = 7.6 Hz, 2H), 2.23 (q, *J* = 7.4 Hz, 2H), 2.12–2.04 (m, 2H), 2.02–1.96 (m, 2H), 1.98 (s, 3H), 1.69 (s, 3H), 1.62 (s, 3H), 1.61 (s, 3H), 0.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 136.6, 131.3, 124.1, 122.2, 119.9, 108.8, 40.8, 39.8, 26.8, 26.7, 25.8, 22.9, 17.8, 16.2, –0.3. IR (neat): 2963, 2918, 2857, 2193, 1584, 1451, 1375, 1254, 1109, 1042, 843, 760, 696, 644, 629 cm^{-1}. HRMS (EI) Calcd for $C_{18}H_{31}NSi$: M^+, 289.2226. Found: *m*/*z* 289.2225.

Ethylcyanation of alkynes using propionitrile (entry 8 of Table 2 and eq. 1). *General procedure.* In a dry box, propionitrile (60 mg, 1.00 mmol), a 1.0 M solution of $AlMe_3$ in hexane (0.40 mL, 0.40 mmol), and an alkyne (2.00 mmol), and dodecane (internal standard, 85 mg, 0.50 mmol) were added sequentially to a solution of $Ni(cod)_2$ (28 mg, 0.10 mmol) and 2-[2,6-$(MeO)_2$–C_6H_3]–C_6H_4–PCy_2 (**L3**, 82 mg, 0.20 mmol) in toluene (1.0 mL) placed in a vial. The vial was taken out from the dry box and heated at 50 °C for 8 h (for **2a**) or 24 h (for **2b**). The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give the corresponding carbocyanation products in yields listed in entry 8 of Table 2 and eq. 1. Stereoisomers were separated by preparative HPLC and characterized by spectrometry.

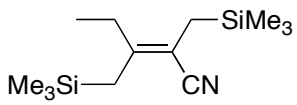
(*Z*)-3-Ethyl-2-propylhex-2-enenitrile (3ba). A colorless oil, R_f 0.18 (hexane–ethyl acetate = 40:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (q, *J* = 7.5 Hz, 2H), 2.17 (t, *J* = 7.3 Hz, 2H), 2.15 (t, *J* = 7.9 Hz, 2H),1.57 (sext, *J* = 7.4 Hz, 2H), 1.43 (sext, *J* = 7.6 Hz, 2H), 1.09 (t, *J* = 7.6 Hz, 3H), 0.944 (t, *J* = 7.3 Hz, 3H), 0.940 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 119.1, 109.2, 33.0, 31.5, 29.3, 21.9, 21.4, 14.3, 13.6, 13.2. IR (neat): 2964, 2936, 2874, 2208, 1624, 1464, 1379, 1138, 1057, 797, 741 cm^{-1}. Anal. Calcd for $C_{11}H_{19}N$: C, 79.94; H, 11.59. Found: C, 79.91; H, 11.71.



(*Z*)-2,3-Bis(trimethylsilylmethyl)pent-2-enenitrile [(*Z*)-3bb]. A colorless oil, R_f 0.16 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (q, *J* = 7.5 Hz, 2H), 1.70 (s, 2H), 1.55 (s, 2H), 1.10 (t, *J* = 7.5 Hz, 3H), 0.11 (s, 9H), 0.09 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.5, 120.6, 101.3, 31.2, 24.5, 21.0, 13.7, –0.4, –1.1. IR (neat): 2955, 2899, 2203, 1607, 1464, 1418, 1400, 1375, 1250, 1184, 1173, 1142, 1063, 1044, 978, 912, 843, 791, 772, 696, 673, 606, 525 cm^{-1}. Anal. Calcd for $C_{13}H_{27}NSi_2$: C, 61.59; H, 10.73. Found: C, 61.76; H, 10.99.



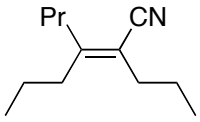
(*E*)-2,3-Bis(trimethylsilylmethyl)pent-2-enenitrile [(*E*)-3bb]. A colorless oil, R_f 0.16 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.06 (q, *J* = 7.5 Hz, 2H), 2.00 (s, 2H), 1.64 (s, 2H), 1.01 (t, *J* =



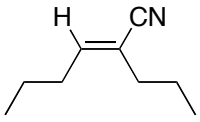
7.5 Hz, 3H), 0.12 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.7, 121.3, 101.5, 27.6, 26.7, 20.4, 12.0, –0.5, –1.1. IR (neat): 2955, 2895, 2205, 1605, 1452, 1418, 1244, 1171, 1150, 1069, 1038, 976, 905, 839, 791, 766, 704, 694, 648 cm^{-1}. HRMS (EI) Calcd for $C_{13}H_{27}NSi_2$: M^+, 253.1682. Found: *m*/*z* 253.1694.

Propylcyanation of 2a using butyronitrile (eq. 2). In a dry box, butyronitrile (69 mg, 1.00 mmol), a 1.0 M solution of $AlMe_3$ in hexane (0.40 mL, 0.40 mmol), and 4-octyne (220 mg, 2.00 mmol), and dodecane (internal standard, 85 mg, 0.50 mmol) were added sequentially to a solution of $Ni(cod)_2$ (28 mg, 0.10 mmol) and 2-[2,6-$(MeO)_2$–C_6H_3]–C_6H_4–PCy_2 (**L3**, 82 mg, 0.20 mmol) in toluene (1.0 mL) placed in a vial. The vial was taken out from the dry box and heated at 50 °C for 30 h. GC analysis of the reaction mixture showed the formation of hydrocyanation product **4** in 19% yield. The mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash column chromatography on silica gel followed by preparative HPLC to give 2,3-dipropylhex-2-enenitrile (**3ca**, 18 mg, 10%) and the isomeric mixture of 1:2 adducts (38 mg, 15%).

2,3-Dipropylhex-2-enenitrile (3ca). A colorless oil, R_f 0.10 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (t, *J* = 7.6 Hz, 2H), 2.19 (t, *J* = 7.6 Hz, 2H), 2.14 (t, *J* = 7.9 Hz, 2H), 1.58 (sext, *J* = 7.5 Hz, 2H), 1.52 (sext, *J* = 7.5 Hz, 2H), 1.43 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 119.3, 110.0, 38.0, 33.4, 31.6, 21.9, 21.8, 21.5, 14.3, 14.0, 13.6. IR (neat): 2963, 2934, 2874, 2207, 1624, 1458, 1381, 1341, 1258, 1136, 1094, 1076, 895, 743 cm^{-1}. Anal. Calcd for $C_{12}H_{21}N$: C, 80.38; H, 11.81. Found: C, 80.41; H, 11.61.

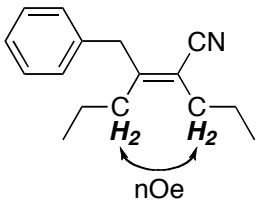


(*E*)-2-Propylhex-2-enenitrile (4). A colorless oil, R_f 0.18 (hexane–ethyl acetate = 40:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (t, *J* = 7.6 Hz, 1H), 2.17 (quint, *J* = 7.5 Hz, 4H), 1.58 (sext, *J* = 7.4 Hz, 2H), 1.46 (sext, *J* = 7.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9, 120.1, 114.8, 30.5, 30.4, 21.9, 21.4, 13.8, 13.5. IR (neat): 2963, 2934, 2874, 2216, 1634, 1460, 1381, 1067, 908 cm^{-1}. HRMS (EI) Calcd for $C_9H_{15}N$: M^+, 137.1204. Found: *m*/*z* 137.1209.

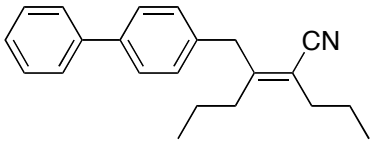


Carbocyanation of alkynes with arylacetonitriles. *General procedure.* In a dry box, to a stirred mixture of an arylacetonitrile (1.00 mmol), an alkyne (1.00 mmol), and tetradecane (internal standard, 99 mg, 0.50 mmol) placed in a vial were added a solution of $Ni(cod)_2$ (5.5 mg, 20 μmol), 2-Mes–C_6H_4–PCy_2 (**L2**, 15.7 mg, 40 μmol) and a 1.0 M solution of $AlMe_2Cl$ in hexane (80 μL, 80 μmol) in toluene (1.0 mL) placed in a vial. The vial was taken out from the dry box and stirred at 35 °C for the time specified in Tables 3 and 4. The resulting mixture was filtered through a Florisil pad, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give the corresponding carbocyanation products in yields listed in Tables 3 and 4. Regio- and/or stereoisomers were separated by preparative GPC or HPLC and characterized by spectrometry.

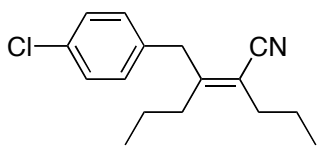
(*Z*)-3-Benzyl-2-propylhex-2-enenitrile (3da). A colorless oil, R_f 0.41 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (tt, *J* = 7.1, 1.5 Hz, 2H), 7.27–7.19 (m, 3H), 3.74 (s, 2H), 2.24 (t, *J* = 7.6 Hz, 2H), 2.04 (t, *J* = 8.0 Hz, 2H), 1.63 (sext, *J* = 7.5 Hz, 2H), 1.38 (sext, *J* = 7.6 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 137.8, 128.7, 128.6, 126.7, 119.6, 111.2, 42.0, 32.7, 31.6, 21.8, 21.3, 14.1, 13.5. IR (neat): 2963, 2932, 2872, 2206, 1624, 1603, 1495, 1454, 1381, 1086, 1030, 737, 702 cm^{-1}. Anal. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31. Found: C, 84.46; H, 9.39.



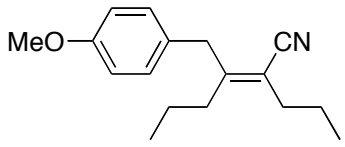
(*Z*)-3-(Biphenyl-4-ylmethyl)-2-propylhex-2-enenitrile (3ea). A colorless oil, R_f 0.41 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.56 (m, 2H), 7.53 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.34 (tt, *J* = 7.4, 1.5 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 3.78 (s, 2H), 2.26 (t, *J* = 7.6 Hz, 2H), 2.09 (t, *J* = 8.0 Hz, 2H), 1.65 (sext, *J* = 7.5 Hz, 2H), 1.42 (sext, *J* = 7.6 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 140.7, 139.6, 136.9, 129.1, 128.7, 127.3, 127.2, 126.9, 119.6, 111.3, 41.6, 32.7, 31.6, 21.7, 21.3, 14.1, 13.5. IR (neat): 3028, 2963, 2932, 2872, 2361, 2343, 2206, 1487, 1458, 1408, 1381, 1009, 910, 735, 698, 421 cm^{-1}. Anal. Calcd for $C_{22}H_{25}N$: C, 87.08; H, 8.30. Found: C, 87.34; H, 8.36.



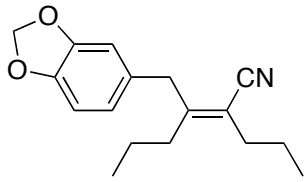
(*Z*)-3-[(4-Chlorophenyl)methyl]-2-propylhex-2-enenitrile (3fa). A colorless oil, R_f 0.34 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (dt, *J* = 8.6, 2.3 Hz, 2H), 7.14 (dt, *J* = 8.4, 2.1 Hz, 2H), 3.70 (s, 2H), 2.24 (t, *J* = 7.6 Hz, 2H), 2.03 (t, *J* = 7.9 Hz, 2H), 1.62 (sext, *J* = 7.5 Hz, 2H), 1.37 (sext, *J* = 7.6 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 136.3, 132.6, 130.0, 128.7, 119.4, 111.7, 41.2, 32.7, 31.6, 21.7, 21.3, 14.1, 13.4. IR (neat): 2963, 2932, 2872, 2341, 2208, 1624, 1491, 1466, 1408, 1381, 1092, 1016, 912, 800, 735 cm^{-1}. Anal. Calcd for $C_{16}H_{20}ClN$: C, 73.41, H, 7.70. Found: C, 73.62, H, 7.94.



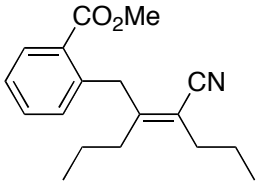
(*Z*)-3-[(4-Methoxyphenyl)methyl]-2-propylhex-2-enenitrile (3ga). A colorless oil, R_f 0.13 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (dt, *J* = 8.8, 2.6 Hz, 2H), 6.83 (dt, *J* = 8.8, 2.6 Hz, 2H), 3.79 (s, 3H), 3.67 (s, 2H), 2.23 (t, *J* = 7.6 Hz, 2H), 2.03 (t, *J* = 8.0 Hz, 2H), 1.62 (sext, *J* = 7.5 Hz, 2H), 1.37 (sext, *J* = 7.6 Hz, 2H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 158.2, 129.7, 129.6, 119.6, 113.9, 110.7, 55.1, 41.0, 32.5, 31.5, 21.6, 21.2, 14.0, 13.4. IR (neat): 2963, 2934, 2872, 2835, 2361, 2343, 2206, 1611, 1512, 1464, 1441, 1302, 1250, 1178, 1115, 1036, 816 cm^{-1}. Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01. Found: C, 79.50; H, 9.03.



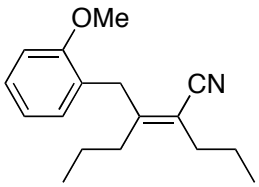
(*Z*)-3-[(3,4-Methylenedioxyphenyl)methyl]-2-propylhex-2-enenitrile (3ha). A colorless oil, R_f 0.39 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.74 (d, J = 7.9 Hz, 1H), 6.69 (d, J = 1.8 Hz, 1H), 6.66 (dd, J = 7.9, 1.6 Hz, 1H), 5.94 (s, 2H), 3.65 (s, 2H), 2.23 (t, J = 7.7 Hz, 2H), 2.04 (t, J = 7.9 Hz, 2H), 1.62 (sext, J = 7.5 Hz, 2H), 1.37 (sext, J = 7.6 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 147.8, 146.3, 131.4, 121.7, 119.5, 111.1, 108.9, 108.2, 100.9, 41.5, 32.5, 31.5, 21.7, 21.3, 14.1, 13.4. IR (neat): 2963, 2932, 2874, 2206, 1504, 1489, 1443, 1246, 1186, 1097, 1040, 928, 810, 773 cm^{-1}. Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.25; H, 7.80. Found: C, 75.45; H, 7.89.



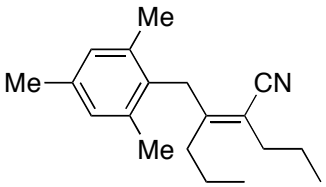
(*Z*)-3-[(2-Methoxycarbonylphenyl)methyl]-2-propylhex-2-enenitrile (3ia). A yellow oil, R_f 0.31 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, J = 7.8, 1.4 Hz, 1H), 7.44 (td, J = 7.6, 1.5 Hz, 1H), 7.33–7.22 (m, 2H), 4.22 (s, 2H), 3.91 (s, 3H), 2.26 (t, J = 7.6 Hz, 2H), 1.99 (t, J = 8.0 Hz, 2H), 1.64 (sext, J = 7.5 Hz, 2H), 1.33 (sext, J = 7.6 Hz, 2H), 0.98 (t, J = 7.3 Hz, 3H), 0.84 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 157.8, 139.0, 132.1, 130.8, 130.2, 130.1, 126.7, 119.5, 112.0, 52.2, 38.8, 33.0, 31.7, 21.8, 21.5, 14.1, 13.5. IR (neat): 2963, 2874, 2206, 1720, 1435, 1265, 1192, 1109, 1078, 739 cm^{-1}. Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12 Found: C, 75.82; H, 8.27.



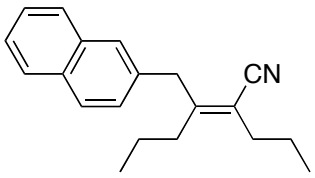
(*Z*)-3-[(2-Methoxyphenyl)methyl]-2-propylhex-2-enenitrile (3ja). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (td, *J* = 8.1, 1.8 Hz, 1H), 7.13 (dd, *J* = 7.3, 1.6 Hz, 1H), 6.89 (td, *J* = 7.5, 1.1 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 3.83 (s, 3H), 3.76 (s, 2H), 2.23 (t, *J* = 7.5 Hz, 2H), 2.02 (t, *J* = 8.0 Hz, 2H), 1.61 (sext, *J* = 7.5 Hz, 2H), 1.37 (sext, *J* = 7.6 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8, 157.5, 129.9, 127.9, 126.2, 120.4, 119.6, 110.9, 110.2, 55.1, 35.8, 32.6, 31.6, 21.7, 21.4, 14.1, 13.3. IR (neat): 2963, 2934, 2872, 2837, 2361, 2343, 2206, 1624, 1599, 1587, 1493, 1464, 1439, 1290, 1246, 1123, 1051, 1030, 754 cm^{-1}. Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01. Found: C, 79.21; H, 9.18.



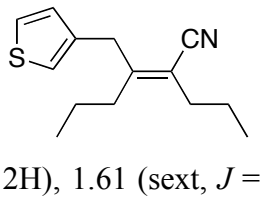
(*Z*)-3-[(2,4,6-Trimethylphenyl)methyl]-2-propylhex-2-enenitrile (3ka). A colorless oil, R_f 0.37 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 2H), 3.82 (s, 2H), 2.27 (s, 6H), 2.26 (s, 3H), 2.22 (t, *J* = 7.7 Hz, 2H), 1.86 (t, *J* = 8.2 Hz, 2H), 1.62 (sext, *J* = 7.5 Hz, 2H), 1.22 (sext, *J* = 7.8 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.81 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.5, 137.3, 136.1, 131.3, 129.2, 119.2, 110.0, 36.4, 32.4, 31.7, 22.1, 21.6, 20.8, 20.4, 14.3, 13.6. IR (neat): 2963, 2932, 2872, 2206, 1614, 1456, 1379, 912, 851, 735 cm^{-1}. Anal. Calcd for $C_{19}H_{27}N$: C, 84.70; H, 10.10 Found: C, 84.92; H, 10.23.



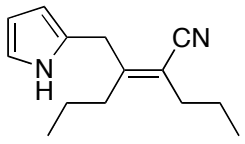
(*Z*)-3-(2-Naphthylmethyl)-2-propylhex-2-enenitrile (3la). A colorless oil, R_f 0.42 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86–7.71 (m, 3H), 7.64 (s, 1H), 7.51–7.42 (m, 2H), 7.35 (dd, *J* = 8. 4, 1.8 Hz, 1H), 3.91 (s, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 2.07 (t, *J* = 8.0 Hz, 2H), 1.66 (sext, *J* = 7.5 Hz, 2H), 1.41 (sext, *J* = 7.6 Hz, 2H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 135.3, 133.4, 132.3, 128.3, 127.6, 127.5, 127.2, 126.8, 126.1, 125.6, 119.6, 111.4, 42.1, 32.6, 31.6, 21.7, 21.3, 14.0, 13.4. IR (neat): 2963, 2932, 2872, 2206, 1624, 1601, 1508, 1458, 818, 756 cm^{-1}. Anal. Calcd for $C_{20}H_{23}N$: C, 86.59; H, 8.36. Found: C, 86.50; H, 8.58.



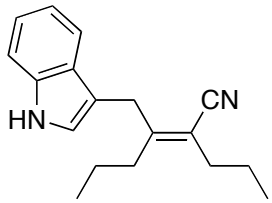
(*Z*)-2-Propyl-3-(3-thienylmethyl)hex-2-enenitrile (3ma). A colorless oil, R_f 0.46 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.24 (m, 1H), 7.02 (dd, *J* = 1.8, 0.9 Hz, 1H), 6.96 (d, *J* = 4.9 Hz, 1H), 3.73 (s, 2H), 2.23 (t, *J* = 7.7 Hz, 2H), 2.08 (t, *J* = 8.0 Hz, 2H), 1.61 (sext, *J* = 7.4 Hz, 2H), 1.38 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 137.7, 127.9, 125.8, 121.7, 119.2, 110.9, 36.6, 32.8, 31.4, 21.6, 21.2, 14.0, 13.3. IR (neat): 2963, 2932, 2872, 2206, 1624, 1464, 1381, 1082, 787, 745 cm^{-1}. Anal. Calcd for $C_{14}H_{19}NS$: C, 72.05; H, 8.21. Found: C, 72.29; H, 8.11.



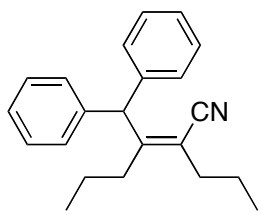
(*Z*)-2-Propyl-3-(pyrrol-2-ylmethyl)hex-2-enenitrile (3na). A slightly brown oil, R_f 0.23 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (br s, 1H), 6.70 (ddd, *J* = 2.7, 1.5, 1.3 Hz, 1H), 6.12 (dd, *J* = 5.9, 2.7 Hz, 1H), 6.02–5.96 (m, 1H), 3.69 (s, 2H), 2.20 (t, *J* = 7.7 Hz, 2H), 2.13 (t, *J* = 7.9 Hz, 2H), 1.60 (sext, *J* = 7.5 Hz, 2H), 1.40 (sext, *J* = 7.6 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 127.5, 119.8, 117.5, 110.6, 108.4, 107.1, 34.4, 33.2, 31.5, 21.7, 21.2, 14.1, 13.5. IR (neat): 3373, 2963, 2932, 2872, 2208, 1624, 1566, 1466, 1381, 1121, 1094, 1026, 912, 883, 795, 716 cm^{-1}. Anal. Calcd for $C_{14}H_{20}N_2$: C, 77.73; H, 9.32. Found: C, 77.87; H, 9.07.



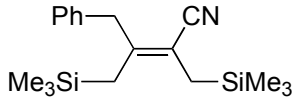
(*Z*)-3-(Indol-3-ylmethyl)-2-propylhex-2-enenitrile (3oa). A slightly brown oil, R_f 0.24 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (br s, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.05 (s, 1H), 3.89 (s, 2H), 2.26 (t, *J* = 7.6 Hz, 2H), 2.12 (t, *J* = 7.9 Hz, 2H), 1.65 (sext, *J* = 7.4 Hz, 2H), 1.43 (sext, *J* = 7.6 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 136.0, 127.2, 122.4, 122.0, 119.6, 119.5, 118.8, 112.3, 111.0, 110.1, 32.9, 32.1, 31.8, 21.9, 21.6, 14.3, 13.7. IR (neat): 3414, 2963, 2932, 2872, 2206, 1620, 1456, 1433, 1339, 1232, 1094, 1011, 910, 737, 648 cm^{-1}. Anal. Calcd for $C_{18}H_{22}N_2$: C, 81.16; H, 8.32. Found: C, 81.07; H, 8.33.



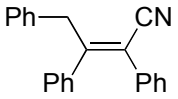
(*Z*)-3-(Diphenylmethyl)-2-propylhex-2-enenitrile (3pa). A colorless oil, R_f 0.37 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.23 (m, 6H), 7.16 (d, *J* = 5.1 Hz, 4H), 5.70 (s, 1H), 2.28 (t, *J* = 7.7 Hz, 2H), 2.20 (t, *J* = 8.0 Hz, 2H), 1.68 (sext, *J* = 7.5 Hz, 2H), 1.01 (t, *J* = 7.3 Hz, 3H), 0.73–0.59 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 140.7, 129.1, 128.4, 126.9, 118.9, 113.1, 57.4, 33.5, 32.1, 22.7, 21.6, 14.6, 13.6. IR (neat): 2963, 2932, 2872, 2206, 1601, 1495, 1454, 1379, 1115, 1078, 1032, 910, 733, 698 cm^{-1}. Anal. Calcd for $C_{22}H_{25}N$: C, 87.08; H, 8.30. Found: C, 86.85; H, 8.43.



(*Z*)-3-Benzyl-4-trimethylsilyl-2-(trimethylsilyl)methylbut-2-enenitrile (3db). A colorless oil, R_f 0.25 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (tt, *J* = 7.1, 1.3 Hz, 2H), 7.26–7.19 (m, 3H), 3.69 (s, 2H), 1.64 (s, 2H), 1.61 (s, 2H), 0.12 (s, 9H), 0.11 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 138.4, 128.6, 128.4, 126.5, 121.0, 103.4, 43.7, 24.2, 21.4, –0.2, –0.9. IR (neat): 3063, 3028, 2955, 2899, 2203, 1603, 1495, 1454, 1437, 1418, 1250, 1219, 1173, 1142, 1084, 1030, 957, 847, 762, 727, 700, 610, 552 cm^{-1}. Anal. Calcd for $C_{18}H_{29}NSi_2$: C, 68.50; H, 9.26. Found: C, 68.73; H, 9.09.

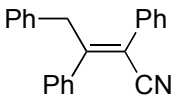


(*E*)-2,3,4-Triphenylbut-2-enenitrile [(*E*)-3di]. A colorless solid, mp = 105.0–106.0 °C,



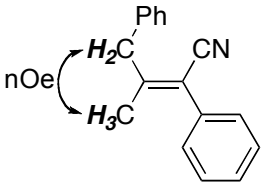
R_f 0.23 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.11 (m, 13H), 6.95–6.89 (m, 2H), 4.27 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 137.5, 136.6, 133.4, 129.4, 128.7, 128.5, 128.4, 128.3, 128.14, 128.09, 126.7, 119.2, 112.8, 44.9. IR (KBr): 3439, 3057, 3028, 2915, 2218, 1966, 1954, 1896, 1881, 1821, 1805, 1755, 1599, 1575, 1493, 1454, 1441, 1431, 1219, 1184, 1107, 1069, 1030, 1001, 976, 945, 926, 910, 854, 833, 773, 750, 702, 677, 637, 600, 561, 517, 488, 461 cm^{-1}. Anal. Calcd for $C_{22}H_{17}N$: C, 89.46; H, 5.80. Found: C, 89.42; H, 5.74.

(*Z*)-2,3,4-Triphenylbut-2-enenitrile [(*Z*)-3di]. A yellow solid, mp = 103.5–104.3 °C,



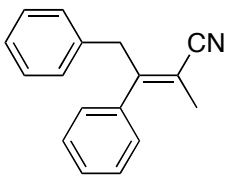
R_f 0.15 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.32 (m, 10H), 7.22–7.11 (m, 3H), 6.95 (d, *J* = 6.6 Hz, 2H), 3.96 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.8, 138.7, 136.9, 134.0, 129.1, 129.0, 128.83, 128.80, 128.5, 128.4, 128.2, 128.0, 126.4, 119.0, 113.8, 40.0. IR (KBr): 3443, 3061, 3028, 2207, 1981, 1960, 1888, 1809, 1763, 1603, 1591, 1570, 1495, 1445, 1290, 1277, 1244, 1180, 1157, 1074, 1030, 999, 947, 920, 893, 791, 777, 766, 731, 708, 698, 567, 517, 490, 461, 446 cm^{-1}. Anal. Calcd for $C_{22}H_{17}N$: C, 89.46; H, 5.80. Found: C, 89.29; H, 5.84.

(*Z*)-3-Methyl-2,4-diphenylbut-2-enenitrile (3dc). A colorless oil, R_f 0.33



(hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.26 (m, 10H), 3.91 (s, 2H), 1.81 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5, 137.3, 133.8, 129.1, 128.73, 128.70, 128.5, 128.3, 126.9, 119.0, 111.6, 44.5, 19.2. IR (neat): 3061, 3028, 2210, 1601, 1493, 1447, 1375, 1076, 1030, 1005, 989, 912, 767, 750, 700 cm^{-1}. HRMS (EI) Calcd for $C_{17}H_{15}N$: M^+, 233.1204. Found: *m*/*z* 233.1214.

(*E*)-2-Methyl-3,4-diphenylbut-2-enenitrile (3'dc). A colorless oil, R_f 0.33



(hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 3H), 7.23–7.14 (m, 3H), 7.07–7.02 (m, 2H), 6.96–6.90 (m, 2H), 4.04 (s, 2H), 1.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 137.4, 136.8, 128.7, 128.3, 128.2, 128.1, 127.6,

126.5, 119.9, 106.5, 44.5, 17.9. IR (neat): 3061, 3028, 2924, 2855, 2361, 2343, 2210, 1601, 1493, 1443, 1375, 1076, 1030, 1005, 912, 779, 766, 735, 702, 565 cm^{-1}. HRMS (EI) Calcd for $C_{17}H_{15}N$: M^+, 233.1204. Found: *m*/*z* 233.1195.

(*Z*)-2-Ethyl-3-methyl-4-phenylbut-2-enenitrile (3dj). A colorless oil, R_f 0.31 (hexane–ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.20 (m, 5H), 3.71 (s, 2H), 2.28 (q, *J* = 7.6 Hz, 2H), 1.73 (s, 3H), 1.17 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 137.7, 128.7, 128.6, 126.8, 119.3, 112.0, 44.4, 23.4, 17.6, 12.8. IR (neat): 3028, 2974, 2936, 2876, 2208, 1630, 1603, 1495, 1454, 1377, 752, 704 cm^{-1}. HRMS (EI) Calcd for $C_{13}H_{15}N$: M^+, 185.1204. Found: *m*/*z* 185.1199.

(*Z*)-3-Benzyl-2-methylpent-2-enenitrile (3'dj). A colorless oil, R_f 0.31 (hexane–ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.20 (m, 5H), 3.74 (s, 2H), 2.10 (q, *J* = 7.6 Hz, 2H), 1.96 (s, 3H), 0.95 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 137.5, 128.7, 128.5, 126.7, 120.2, 104.5, 41.7, 24.1, 16.1, 12.0. IR (neat): 3028, 2966, 2934, 2874, 2361, 2341, 2208, 1603, 1489, 1454, 1379, 912, 735, 702 cm^{-1}. HRMS (EI) Calcd for $C_{13}H_{15}N$: M^+, 185.1204. Found: *m*/*z* 185.1196.

(*Z*)-2-*tert*-Butyl-3-methyl-4-phenylbut-2-enenitrile (3dk). A colorless oil, R_f 0.43 (hexane–ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (tt, *J* = 7.1, 1.6 Hz, 2H), 7.27–7.19 (m, 3H), 3.76 (s, 2H), 1.91 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 137.8, 128.6, 128.5, 126.7, 120.4, 119.3, 46.5, 33.6, 30.6, 19.8. IR (neat): 2970, 2206, 1601, 1495, 1454, 1367, 914, 735, 700, 428 cm^{-1}. Anal. Calcd for $C_{15}H_{19}N$: C, 84.46; H, 8.98. Found: C, 84.55; H, 9.03.

(*E*)-3-Methyl-4-phenyl-2-trimethylsilylbut-2-enenitrile (3dl). A colorless oil, R_f 0.42 (hexane–ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (tt, *J* = 7.2, 1.6 Hz, 2H), 7.28–7.20 (m, 3H), 3.82 (s, 2H), 1.88 (s, 3H), 0.31 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 137.5, 128.8, 128.7, 126.8, 120.4, 110.0, 46.7, 22.1, –0.4. IR (neat): 3029,

2959, 2901, 2193, 1582, 1495, 1454, 1375, 1254, 1028, 880, 845, 762, 745, 700, 633, 559 cm^{-1}. Anal. Calcd for $C_{14}H_{19}NSi$: C, 73.30; H, 8.35. Found: C, 73.56; H, 8.37.

(*E*)-2-Methyl-4-phenyl-3-trimethylsilylbut-2-enenitrile (3'dl). A colorless oil, R_f 0.47 (hexane–ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.17 (m 3H), 7.11 (d, *J* = 7.0 Hz, 2H), 3.87 (s, 2H), 2.17 (s, 3H), 0.08 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 137.9, 128.8, 128.4, 126.5, 119.3, 118.8, 43.0, 20.5, –0.4. IR (neat): 3028, 2955, 2901, 2855, 2206, 1587, 1495, 1452, 1254, 1080, 1030, 843, 760, 739, 700 cm^{-1}. Anal. Calcd for $C_{14}H_{19}NSi$: C, 73.30; H, 8.35. Found: C, 73.56; H, 8.37.

(*Z*)-3-Benzylnon-2-enenitrile (3dm). A pale yellow oil, R_f 0.33 (hexane–ethyl acetate = 15:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.25–7.20 (m, 5H), 5.21 (s, 1H) 3.74 (s, 2H), 2.08 (td, *J* = 7.7, 1.3 Hz, 2H), 1.48–1.20 (m, 8H), 0.87 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 136.9, 128.64, 128.59, 126.8, 117.4, 95.4, 41.1, 35.5, 31.5, 28.8, 27.1, 22.6, 14.1. IR (neat): 3086, 3063, 3028, 2955, 2930, 2857, 2216, 1624, 1601, 1495, 1454, 1379, 1076, 1030, 827, 737, 700 cm^{-1}. Anal. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31. Found: C, 84.79; H, 9.27.

(*Z*)-2-(2-Phenylethynylidene)octanenitrile (3'dm). A colorless oil, R_f 0.38 (hexane–ethyl acetate = 15:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.4 Hz, 2H), 7.27–7.17 (m, 3H), 6.26 (t, *J* = 7.7 Hz, 1H), 3.69 (d, *J* = 7.7 Hz, 2H), 2.24 (t, *J* = 7.5 Hz, 2H), 1.62–1.51 (m, 2H), 1.37–1.23 (m, 6H), 0.89 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 137.7, 128.7, 128.3, 126.7, 117.6, 115.3, 37.8, 34.3, 31.5, 28.4, 28.1, 22.6, 14.1. IR (neat): 3030, 2955, 2928, 2859, 2214, 1603, 1495, 1454, 1435, 1379, 1261, 1105, 1076, 1030, 797, 739, 698, 569 cm^{-1}. HRMS (EI) Calcd for $C_{16}H_{21}N$: M^+, 227.1674. Found: *m*/*z* 227.1676.

(*Z*)-3-Cyclohexyl-4-phenyl-2-butenenitrile (3dn). A colorless oil, R_f 0.16 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (tt, *J* = 7.1, 1.5 Hz, 2H), 7.25–7.19 (m, 3H), 5.24 (s, 1H), 3.78 (s, 2H), 1.98 (t, *J* = 11.2 Hz, 1H), 1.80–1.62 (m, 5H), 1.30–1.00 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 136.9, 128.6, 126.7, 117.7, 94.6, 43.3, 40.4, 32.1, 26.3, 26.0. IR (neat): 3061, 3028, 2930, 2853, 2216, 1618, 1601, 1584, 1495, 1451, 1300, 1269, 1182, 1144, 1076, 1030, 980, 893, 827, 816, 775, 737, 700 cm^{-1}. Anal. Calcd for $C_{16}H_{19}N$: C, 85.28; H, 8.50. Found: C, 85.38; H, 8.61.

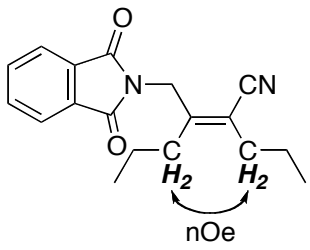
(*Z*)-2-Cyclohexyl-4-phenylbut-2-enenitrile (3'dn). A colorless oil, R_f 0.23 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.1 Hz, 2H), 7.24 (tt, *J* = 7.5, 2.2 Hz, 1H), 7.19 (d, *J* = 7.3 Hz, 2H), 6.26 (td, *J* = 7.7, 0.9 Hz, 1H), 3.69 (d, *J* = 7.7 Hz, 2H), 2.15 (td, *J* = 11.2, 3.0 Hz, 1H), 1.82 (t, *J* = 11.8 Hz, 4H), 1.42–1.10 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 137.8, 128.6, 128.3, 126.6, 121.3, 117.2, 42.6, 37.7, 31.8, 26.0, 25.6. IR (neat): 3063, 3028, 2928, 2853, 2214, 1603, 1495, 1451, 1350, 1076, 1030, 990, 936, 891, 741, 689, 646, 573, 513 cm^{-1}. HRMS (EI) Calcd for $C_{16}H_{19}N$: M^+, 225.1517. Found: *m*/*z* 225.1524.

(*E*)-3-Benzyl-4,4-dimethylpent-2-enenitrile (3do). A colorless oil, R_f 0.31 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.25–7.19 (m, 3H), 5.52 (s, 1H), 3.87 (s, 2H), 1.07 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 137.3, 128.4, 128.0, 126.4, 117.8, 96.7, 38.3, 38.2, 29.5. IR (neat): 3063, 3028, 2969, 2870, 2216, 1609, 1495, 1479, 1468, 1454, 1397, 1366, 1260, 1215, 1196, 1096, 1076, 1030, 978, 926, 824, 764, 719, 696, 671 cm^{-1}. Anal. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60. Found: C, 84.38; H, 8.56.

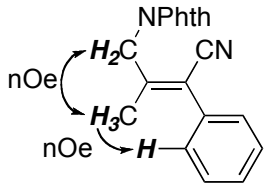
Carbocyanation of alkynes with functionzalized acetonitriles. *General procedure.* In a dry box, to a solution of $Ni(cod)_2$ (14 mg, 50 μmol) and a ligand (0.10 mmol) in toluene (1.0 mL) placed in a vial were sequentially added a substituted acetonitrile (1.00 mmol), BPh_3 (48 mg, 0.20 mmol), an alkyne (2.0 mmol), and dodecane (internal standard, 85 mg, 0.50 mmol). The vial was taken out from the dry box and heated at

80 °C for the time specified in Table 5. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give the corresponding carbocyanation products in yields listed in Table 5. Regio- and/or stereoisomers were separated by preparative GPC or HPLC and characterized by spectrometry.

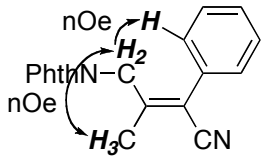
(*Z*)-3-(Phthalimidoylmethyl)-2-propylhex-2-enenitrile (3qa). A colorless solid, mp = 38.1–38.7 °C, R_f 0.12 (hexane–ethyl acetate = 7:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.1 Hz, 2H), 4.62 (s, 2H), 2.25 (t, J = 7.6 Hz, 2H), 2.08 (t, J = 8.0 Hz, 2H), 1.63 (sext, J = 7.5 Hz, 2H), 1.47 (sext, J = 7.6 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 151.2, 134.1, 131.7, 123.4, 117.8, 113.8, 41.7, 32.1, 31.6, 21.55, 21.51, 14.2, 13.6. IR (KBr): 2964, 2934, 2874, 2212, 1773, 1717, 1466, 1425, 1396, 1350, 953, 926, 712, 530 cm^{-1}. Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80. Found: C, 72.78; H, 6.83.



(*Z*)-3-Methyl-2-phenyl-4-phthalimidoylbut-2-enenitrile [(*Z*)-3qc]. A colorless solid, mp = 104.1–104.8 °C, R_f 0.13 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, J = 5.4, 3.0 Hz, 2H), 7.77 (dd, J = 5.5, 2.9 Hz, 2H), 7.43–7.31 (m, 5H), 4.81 (s, 2H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 150.3, 134.2, 133.2, 131.7, 128.9, 128.7, 128.6, 123.5, 117.3, 113.4, 43.2, 17.6. IR (KBr): 2214, 1773, 1713, 1418, 1396, 1348, 930, 766, 729, 714, 700 cm^{-1}. Anal. Calcd for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67. Found: C, 75.45; H, 4.78.



(*E*)-3-Methyl-2-phenyl-4-phthalimidoylbut-2-enenitrile [(*E*)-3qc]. A colorless solid, mp = 111.0–111.8 °C, R_f 0.16 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, J = 5.5, 2.9 Hz, 2H), 7.74 (dd, J = 5.5, 3.1 Hz, 2H), 7.49–7.39 (m, 4H), 7.38–7.32 (m, 1H), 4.45 (s, 2H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 150.5, 134.2, 132.7, 131.5, 129.0, 128.81, 128.77, 123.4, 117.8, 114.0, 40.1, 20.0. IR (KBr): 2208, 1776, 1713, 1427, 1396, 1340, 1317, 930, 764, 731, 712, 700, 530 cm^{-1}.



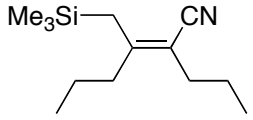
HRMS (EI) Calcd for $C_{19}H_{14}N_2O_2$: M^+, 302.1055. Found: *m*/*z* 302.1054.

(*Z*)-2-Methyl-3-phenyl-4-phthalimidoylbut-2-enenitrile (3'qc). A colorless solid, mp = 131.7–132.6 °C, R_f 0.17 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J = 5.6, 3.0 Hz, 2H), 7.65 (dd, J = 5.7, 2.9 Hz, 2H), 7.31–7.21 (m, 3H), 7.11 (dt, J = 6.4, 1.5 Hz, 2H), 4.93 (q, J = 1.3 Hz, 2H), 1.88 (t, J = 1.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 151.6, 134.5, 133.9, 131.4, 128.7, 128.4, 127.6, 123.2, 118.3, 108.8, 42.8, 18.3. IR (KBr): 2926, 2214, 1773, 1717, 1466, 1421, 1394, 1342, 1325, 1119, 1013, 945, 727, 714, 696, 530 cm^{-1}. HRMS (EI) Calcd for $C_{19}H_{14}N_2O_2$: M^+, 302.1055. Found: *m*/*z* 302.1058.

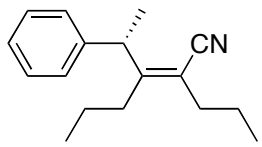
(*Z*)-2-*tert*-Butyl-3-methyl-4-phthalimidoylbut-2-enenitrile (3qk). A colorless solid, mp = 125.4–126.1 °C, R_f 0.18 (hexane–ethyl acetate = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, J = 5.6, 3.0 Hz, 2H), 7.75 (dd, J = 5.5, 3.1 Hz, 2H), 4.67 (s, 2H), 1.92 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 148.2, 134.1, 131.6, 123.4, 122.3, 117.5, 45.2, 34.1, 30.5, 17.5. IR (KBr): 2976, 2206, 1774, 1717, 1423, 1398, 1348, 1119, 924, 729, 712 cm^{-1}. Anal. Calcd for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43. Found: C, 72.59; H, 6.51.

(*Z*)-2-Propyl-3-(tetrahydro-2H-pyran-2-oxymethyl)hex-2-enenitrile (3ra). A colorless oil, R_f 0.15 (hexane–ethyl acetate = 15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 (t, *J* = 3.4 Hz, 1H), 4.46 (d, *J* = 12.3 Hz, 1H), 4.26 (d, *J* = 12.3 Hz, 1H), 3.92–3.82 (m, 1H), 3.61–3.51 (m, 1H), 2.32–2.21 (m, 4H), 1.89–1.69 (m, 2H), 1.67–1.41 (m, 8H), 0.97 (t, *J* = 7.0 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9, 118.1, 112.3, 98.5, 68.4, 62.3, 31.8, 31.7, 30.5, 25.4, 21.6, 21.4, 19.4, 14.3, 13.6. IR (neat): 2961, 2872, 2210, 1630, 1464, 1456, 1383, 1350, 1261, 1202, 1182, 1157, 1119, 1078, 1057, 1034, 972, 907, 870, 816 cm^{-1}. Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.02. Found: C, 71.62; H, 10.23.

(*Z*)-3-(Trimethylsilyl)methyl-2-propylhex-2-enenitrile (3sa). A pale yellow oil, R_f 0.18 (hexane–ethyl acetate = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (t, *J* = 7.5 Hz, 2H), 2.08 (t, *J* = 7.8 Hz, 2H), 2.02 (s, 2H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.44 (sext, *J* =7.6 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H), 0.11 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 120.4, 105.7, 35.7, 31.4, 28.8, 22.3, 21.6, 14.2, 13.6, –0.6. IR (neat): 2961, 2874, 2203, 1611, 1464, 1421, 1379, 1250, 1148, 1078, 853, 766, 694 cm^{-1}. Anal. Calcd for $C_{13}H_{25}NSi$: C, 69.88; H, 11.28. Found: C, 70.18; H, 11.17.



Carbocyanation of 2a with (*S*)-1t (eq. 3). In a dry box, to a solution of $Ni(cod)_2$ (55 mg, 0.2 mmol) and 2-(2,4,6-*i*-Pr_3–C_6H_2)–C_6H_4–PCy_2 (**L7**, 191 mg, 0.4 mmol) in toluene (1.0 mL) placed in a vial were sequentially added (*S*)-**1t** (131 mg, 1.00 mmol), a 1.0 M solution of $AlMe_2Cl$ in hexane (0.20 mL, 0.20 mmol), **2a** (0.55 g, 5.0 mmol), and tridecane (internal standard, 92 mg, 0.50 mmol). The vial was taken out from the dry box and heated at 80 °C for 0.5 h. GC analysis of the mixture showed the formation of hydrocyanation product **4**, styrene **6**, and hydrocinnnamonitrile **7** in 35%, 44%, and 3% yield, respectively. The mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel followed by preparative HPLC to give (*S*)-(*Z*)-3-(1-phenylethyl)-2-propylhex-2-enenitrile [(*S*)-**3ta**] (54 mg, 22%) and (*S*)-**1t** (17 mg, 13%). (*S*)-**3ta**: A colorless oil, R_f 0.27 (hexane–ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.20 (m, 5H), 4.46 (q, *J* = 7.1 Hz, 1H), 2.18 (t, *J* = 7.6 Hz, 2H), 1.91 (t, *J* = 8.2 Hz, 2H), 1.64 (sext, *J* = 7.5 Hz, 2H), 1.47 (d, *J* = 7.1 Hz, 3H), 1.27–1.09 (m, 1H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.91–0.73 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 141.6, 128.3, 127.4, 126.8, 119.3, 110.2, 45.6, 31.7, 30.9, 23.1, 21.5, 17.1, 14.6, 13.5. IR (neat): 2964, 2934, 2874, 2206, 1601, 1495, 1450, 1379, 1123, 1090, 1022, 912, 735, 700 cm^{-1}. Anal. Calcd for $C_{17}H_{23}N$: C, 84.59; H, 9.60. Found: C, 84.78; H, 9.59. The enantiomeric excess (ee) was determined by HPLC analysis on a Daicel Chiralcel OB-H column with hexane, flow rate = 0.5 ml/min, detection by UV of 254 nm. Retention times: 14.5 min [(*S*)-enantiomer], 17.2 min [(*R*)-enantiomer]. 41% ee. $[\alpha]^{30}_D$ –145.97 (c 1.055, toluene). (*S*)-**1t**: Ee was determined by HPLC analysis on a Daicel Chiralcel OD-H column with hexane, flow rate = 0.5 ml/min, detection by UV of 258 nm. Retention times: 37.4 min



[(*S*)-enantiomer], 43.8 min [(*R*)-enantiomer]. 80% ee.

Ruthenium catalyzed oxidation of (*S*)-3ta. To a solution of (*S*)-**3ta** (42 mg, 0.18 mmol) in CCl_4–CH_3CN–H_2O (1.0:1.0:1.5, 1.4 mL) were added $NaIO_4$ (0.38 g, 1.6 mmol) and $RuCl_3 \cdot 3H_2O$ (2.1 mg, 7.9 μmol) at 0 °C, and the resulting mixture was stirred at rt for 5 h. Water was added, and the resulting aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give (*S*)-2-phenyl-3-hexanone (14 mg, 43%) as a pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.30 (m, 2H), 7.28–7.19 (m, 3H), 3.75 (q, *J* = 7.0 Hz, 1H), 2.33 (t, *J* = 7.5 Hz, 2H), 1.58–1.47 (m, 2H), 1.40 (d, *J* = 7.0 Hz, 3H), 0.80 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.6, 140.6, 128.7, 127.7, 126.9, 53.0, 43.0, 17.6, 17.4, 13.7. IR (neat): 3028, 2964, 2932, 2874, 1713, 1601, 1493, 1452, 1373, 1130, 1070, 1015, 762, 700 cm^{-1}. HRMS (EI) Calcd for $C_{12}H_{16}O$: M^+, 176.1201. Found: *m/z* 176.1203. Ee of the ketone was determined by HPLC analysis on a Daicel Chiralcel OD-H column with hexane, flow rate = 0.5 ml/min, detection by UV of 254 nm. Retention times: 17.2 min [(*S*)-enantiomer], 18.8 min [(*R*)-enantiomer]. 38% ee. $[\alpha]^{30}_D$ +113.51 (c 0.555, toluene) [lit.[5] $[\alpha]^{20}_D$ –234 (c 0.281, toluene) for 91% ee of (*R*)-enantiomer].

References and notes

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Chapter 5

Heteroatom-directed Alkylcyanation of Alkynes

Alkanenitriles having a heteroatom such as nitrogen, oxygen, and sulfur at the γ-position are found to add across alkynes stereo- and regioselectively by nickel/Lewis acid catalysis to give highly substituted acrylonitriles. The heteroatom functionalities likely coordinate to the nickel center to make oxidative addition of the C–CN bonds of the alkyl cyanides kinetically favorable, forming a five-membered nickelacycle intermediate and thus preventing β-hydride elimination to allow the alkylcyanation reaction.

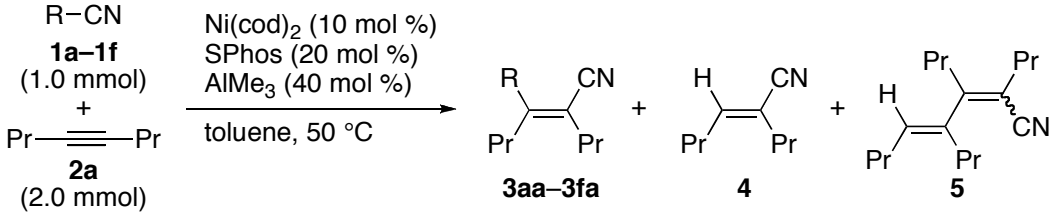
Introduction

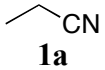
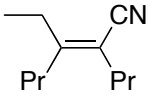
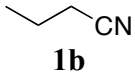
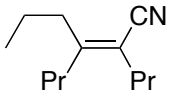
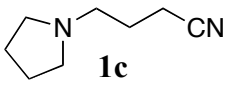
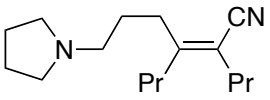
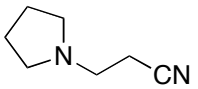
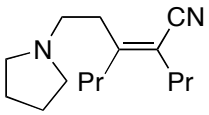
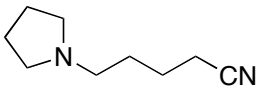
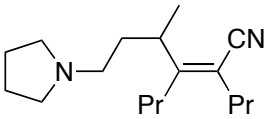
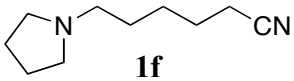
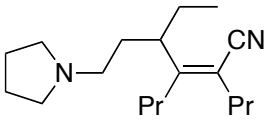
As described in Chapter 4, alkylcyanation of alkynes using acetonitrile was achieved with the aid of nickel/LA dual catalysis. Propionitrile also participated in the reaction only in the presence of a bulky phosphine ligand, whereas butyronitrile was reluctant due to competitive *β*-hydride elimination of a propylnickel intermediate. The author then focused on use of aza(oxa or thia)alkanenitrile, as intramolecular coordination of the heteroatom to a nickel center, he envisioned, could suppress the *β*-hydride elimination by occupying a vacant coordination site. This Chapter demonstrates alkylcyanation of alkynes using alkyl cyanides having coordinating functional groups at the *γ*-position. A 5-membered azanickelacycle is suggested to be key reaction intermediates responsible for successful suppression of *β*-hydride elimination.

Results and discussion

In Chapter 4, methylcyanation of alkynes using acetonitrile is shown to successfully proceed by nickel/$AlMe_3$ dual catalysis using PPh_2(*t*-Bu) as a ligand. Under the identical conditions, propionitrile (**1a**) was found to react sluggishly, and a hydrocyanation product was obtained in a fair amount. Formation of such byproduct was suppressed to some extent partially by employing highly bulky ligands such as SPhos. For example, the reaction of **1a** (1.0 mmol) and 4-octyne (**2a**, 2.0 mmol) in the presence of $Ni(cod)_2$ (10 mol %), SPhos (20 mol %), and $AlMe_3$ (40 mol %) in toluene at 50 °C for 9 h to give a *cis*-ethylcyanation product (**3aa**) in 78% yield (entry 1 of Table 1), whereas, under the same condition, butyronitrile (**1b**) still suffered from formation of competitive hydrocyanation products **4** and **5** in 19% and 15% yield respectively and afford propylcyanation product **3ba** only 10% yield (entry 2). A dramatic improvement of the product selectivity was observed by introducing a secondary amino group at the *γ*-position in **1b** to give corresponding *cis*-alkylcyanation product **3ca** in 86% yield and no trace amount of **4** and **5** (entry 3). The observed effect of the *γ*-amino group, however, did not work at all with *β*-aminopropionitrile **1d** (entry 4), whereas *δ*-aminovaleronitrile **1e** and *ε*-aminohexanenitrile **1f** reacted with **2a** exclusively at the *γ*-position from the pyrrolidyl group to give adducts of secondary alkyl groups (entries 5 and 6). In addition, the author observed that *γ*-aminonitrile **1c** reacted much faster than **1a** based on the results from their competitive reaction with **2a** (entry 7).

Table 1. Nickel/$AlMe_3$-catalyzed alkylcyanation of 4-octyne (**2a**).

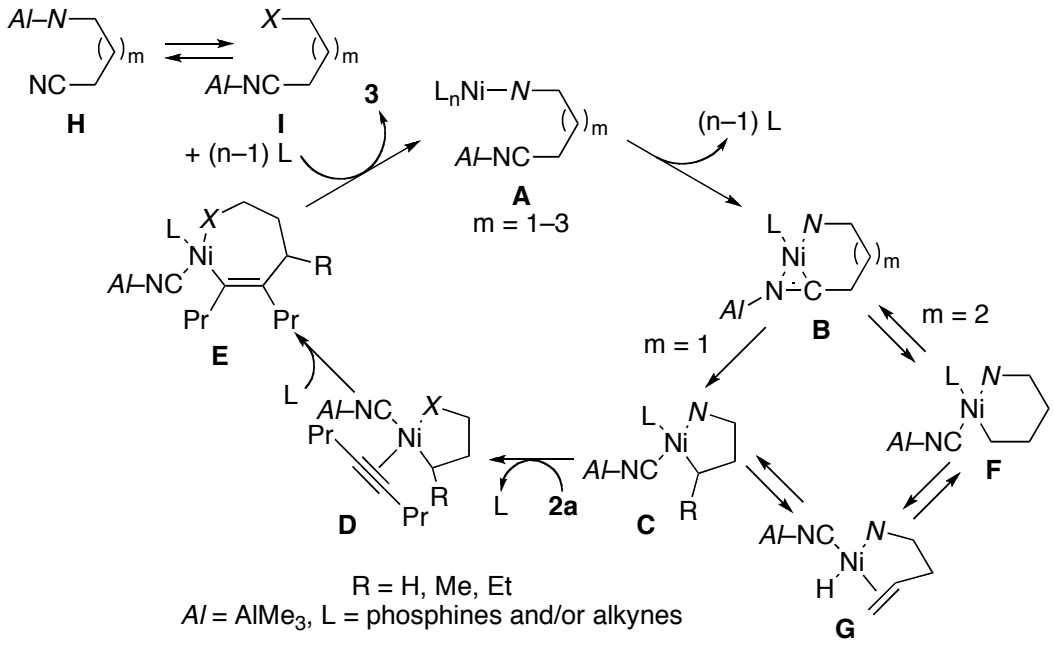


entry	alkyl cyanide	time (h)	product(s), yield[a]
1	 **1a**	9	 **3aa**, 78%
2	 **1b**	30	 **3ba**, 10% + **4**, 19%[b] + **5**, 15%
3	 **1c**	9	 **3ca**, 86%
4[c]	 **1d**	21	 **3da**, <5%
5[c]	 **1e**	11	 **3ea**, 77%
6[c,d]	 **1f**	45	 **3fa**, 45% + **4**, 9%[b]
7[c,e]	**1a** + **1c** (1:1)	6	**3aa**, <5%[b] + **3ca**, 57%[b]

[a] Isolated yields based on **1**. [b] Estimated by GC using dodecane as an internal standard. [c] Run at 80 °C. [d] Run with 60 mol % of $AlMe_3$. [e] Run with 0.5 mmol of **2a**.

All the data described above suggest a catalytic cycle involving 5-membered azanickelacycle **C** as a key intermediate generated by rapid oxidative addition of the C–CN bond of **1c** to nickel(0) through coordination of the amino group to nickel(0) (**A**) and intramolecular η^2-coodination of the cyano group (**B**), wherein the cyano nitrogen is bound to $AlMe_3$ (Scheme 1).[1] Subsequent ligand exchange (**D**), alkylnickelation (**E**), and reductive elimination give rise to **3ca** and regenerate **A**. The fact that no observed adduct was derived from **1d** is attributed to lack of the possibility of a 5-membered chelate and clearly suggests that 4-membered ring formation is not effective for the

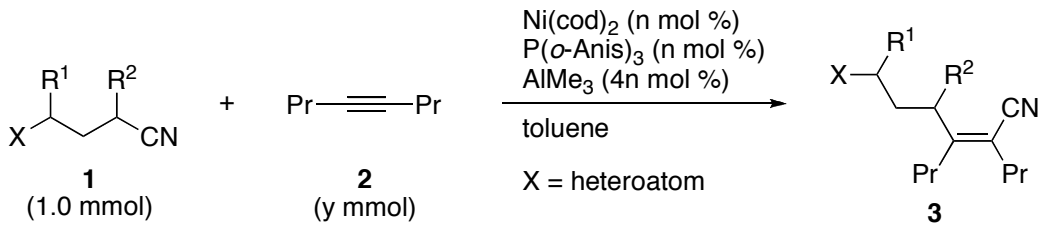
catalytic cycle, whereas a possible 6-membered nickelacycle **F** derived from **1e** would be reluctant to proceed the subsequent elemental steps and undergo *β*-hydride elimination (**G**) followed by hydronickelation in an opposite direction to give 5-membered intermediate **C** (R = Me),[2] which appears to be responsible for the formation of **3ea**. Similar isomerization should also be operative with **1f** through multiple *β*-hydride elimination–hydronickelation sequences to finally give **3fa** through **C** (R = Et). The amino group can also interact with $AlMe_3$, but the resulting species **H** would not be involved in the present catalytic cycle and in equilibrium with cyano-coordinating one **I**, that can participate in the catalysis.

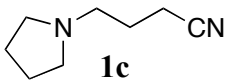
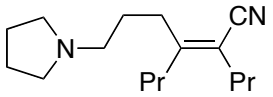
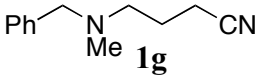
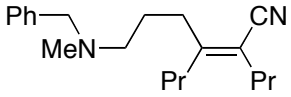
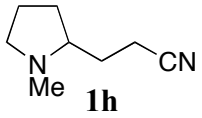
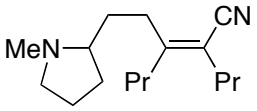
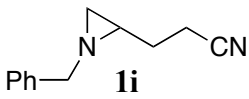
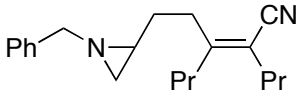
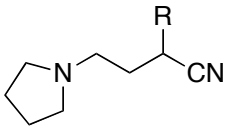
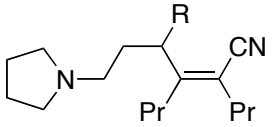
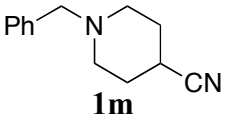
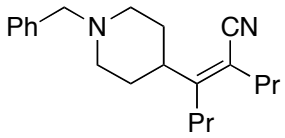
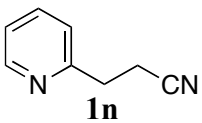
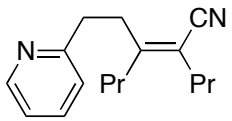
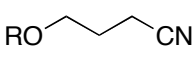
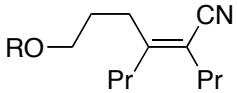


Scheme 1. Plausible mechanism.

The amino effect for promotion of the alkylcyanation reaction was further tested under slightly modified reaction conditions using P(2-MeO–C_6H_4)$_3$ as a ligand (Table 2). Other cyclic and acyclic amino moieties were equally effective (entries 2 and 3): even labile aziridine-containing substrate **1i**[3] gave the corresponding alkylcyanation product (**3ia**) without ring opening (entry 4). The formation of **3ea** and **3fa** (Table 1) prompted the author to examine secondary alkyl cyanides, challenging substrates for the alkylcyanation.[4] To his delight, a range of α-substituents in **1c** did not interfere in the reaction to give branched carbocyanation products in modest to good yields (entries 5–8), whereas α-silyl, cyano, and ester substituted aminobutyronitrile did interfere.

Table 2. Carbocyanation of 4-octyne with alkanenitriles having a coordinating group.



entry	1	y	n	temp (°C)	time (h)	product	yield (%)[a]
1	 **1c**	1.4	3	80	9		88 (**3ca**)
2	 **1g**	1.4	5	80	20		88 (**3ga**)
3	 **1h**	1.4	5	80	9		82 (**3ha**)
4	 **1i**	1.4	5	80	3		79 (**3ia**)
							
5	R = Et: **1j**	2.0	10	60	8	R = Et: **3fa**	89
6	Ph: **1k**	2.0	10	60	31	Ph: **3ka**	90
7	$OSiMe_2t$-Bu: **1l**	2.0	10	60	3	$OSiMe_2t$-Bu: **3la**	90
8	 **1m**	2.0	10	60	111		49 (**3ma**)
9	 **1n**	1.1	5	50	4		94 (**3na**)
							
10	R = CH_2Ph: **1o**	2.0	10	50	20	R = CH_2Ph: **3oa**	64
11	$SiMe_2t$-Bu: **1p**	2.0	10	50	40	$SiMe_2t$-Bu: **3pa**	65

12	R = CH_2: **1q**	2.0	10	50	40	R = CH_2: **3qa**	47
13	O: **1r**	2.0	10	50	22	O: **3ra**	66
14[b]	**1s**	1.4	5	50	24		79 (**3sa**)

[a] Isolated yields based on **1**. [b] Run with P(*t*-Bu)$_3$ as a ligand.

Attempted addition of tertiary alkyl cyanides was totally futile even with the aid of an amino group. A pyridyl sp^2-nitrogen in **1n** also served as a directing group (entry 9). Moreover, ether, acetal, and thioether functionalities assisted the reaction to give the corresponding alkylcyanation products (entries 10–14). In contrast, the reaction of alkanenitriles having phenylamino, phthalimidoyl, aminocarbonyl, imidazolyl, oxazolinyl, and alkoxycarbonyl substituents failed due probably to lower coordination abilities of nitrogen atom to nickel center. Nitriles having allylamino, diethoxy phosphinyl, and diphenylphosphino groups decomposed under the reaction conditions. Epoxide and dithioacetal[5] groups apparently decomposed the nickel catalyst (Figure 1).

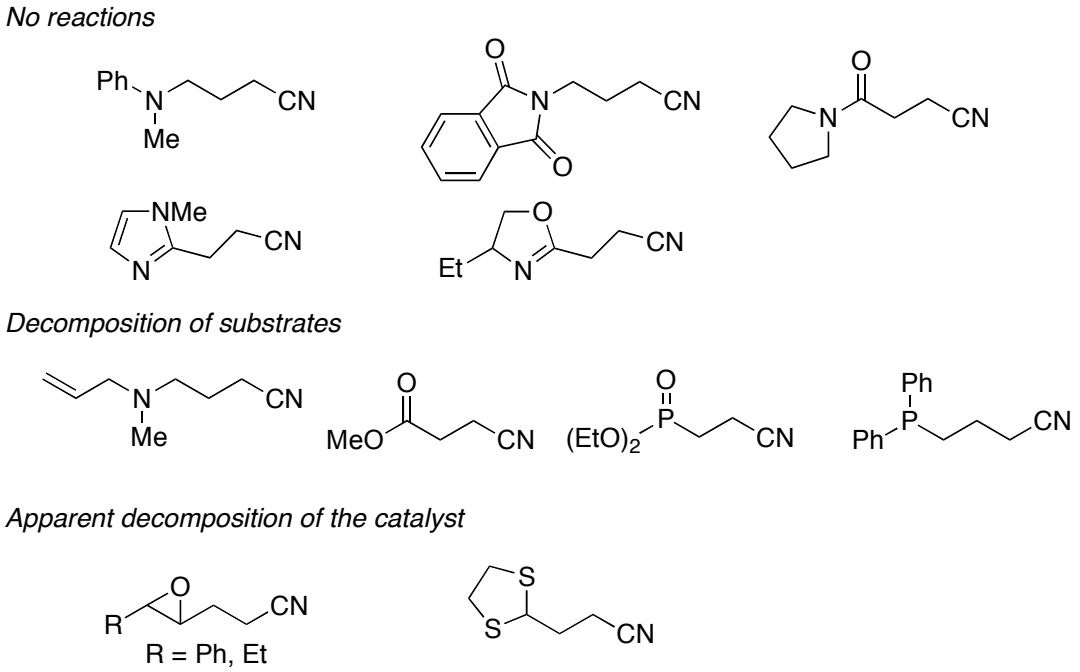
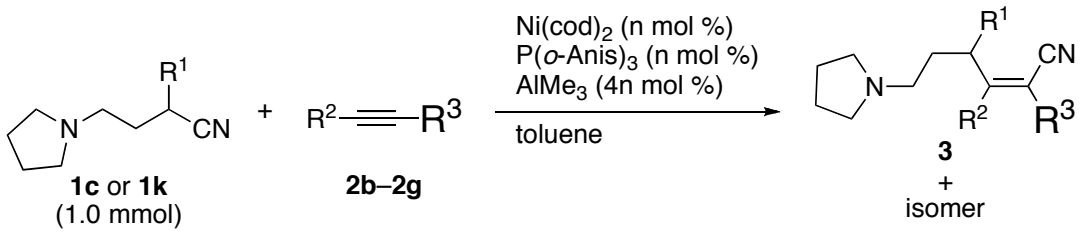
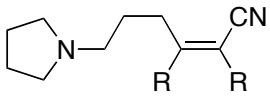
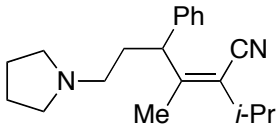
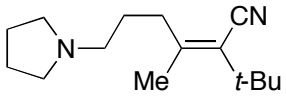
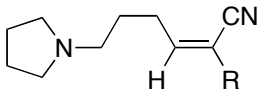


Figure 1. Alkanenitriles that did not give alkylcyanation products.

Table 3. Carbocyanation of alkynes with γ-aminonitriles.



entry	**1**	**2** (mmol)	n	temp (°C)	time (h)	major product	yield (%)[a]
		R—≡—R					
1[b]	**1c**	R = Me: **2b** (2.0)	10	50	10	R = Me: **3cb**	72
2	**1c**	CH_2SiMe_3: **2c** (1.4)	3	80	5	CH_2SiMe_3: **3cc**	94
3	**1k**	Me—≡—*i*-Pr **2d** (2.0)	10	60	14		87 (**3kd**)[c]
4	**1c**	Me—≡—*t*-Bu **2e** (2.0)	3	80	13		88 (**3ce**)[d]
		H—≡—R					
5[e]	**1c**	R = *t*-Bu: **2f** (1.4)	3	50	26	R = *t*-Bu: **3cf**	74[d]
6[e,f]	**1c**	Ph: **2g** (2.0)	3	50	10	Ph: **3cg**	73[d]

[a] Isolated yields based on **1**. [b] Run with 60 mol % of $AlMe_3$. [c] Contaminated with 9% of regioisomer **3'kd**. [d] Contaminated with <5% of regio- and/or stereoisomers. [e] Run with $AsPh_3$ (6 mol %) and $B(C_6F_5)_3$ (12 mol %). [f] Run with slow addition of **2g** over 7.5 h and additional stirring for 2.5 h.

The scope of alkynes was examined briefly using **1c** and **1k** as the nitrile substrates (Table 3). In addition to other symmetrical dialkylacetylenes (entries 1 and 2), internal alkynes with sterically different substituents reacted successfully with stereo- and regioselectivities similar to common alkyne-carbocyanation reactions,[7] and adducts are produced having a larger alkyne-substituent and the cyano group bound to the same sp^2-carbon (entries 3 and 4). Use of less electron-donating triphenylarsine as a ligand was found effective for the addition across terminal alkynes (entries 5 and 6); nickel catalysts with an electron-donating phosphine were apt to induce trimerization and/or oligomerization of terminal alkynes.

Conclusion

In summary, the author has demonstrated that nickel/LA catalyzed regio- and stereoselective alkylcyanation of alkynes is achieved by introduction of a coordinating heteroatom in alkanenitriles. Accordingly, the scope of alkylcyanation reaction is broadened significantly to allow stereoselective synthesis of various tri- and tetra-substituted ethenes having an alkyl group containing various heteroatom functionalities, that allow further elaboration of the adducts.

Experimental Section

Chemicals

2-Cyanoethylpyrrolidine (**1d**),[8] 1-benzyl-2-(2-cyanoethyl)-aziridine (**1i**),[9] and 3-(tetrahydrofuran-2-yl)propanenitrile (**1q**)[10] were prepared according to the respective literature procedure.

5-(Pyrrolidin-1-yl)pentanenitrile (1e). A mixture of 5-bromovaleronitrile (2.4 g, 15.0 mmol), pyrrolidine (1.12 g, 15.8 mmol), potassium carbonate (2.2 g, 15.8 mmol), and potassium iodide (125 mg, 0.75 mmol) in acetonitrile (15 mL) was stirred at rt for 13 h before quenching by addition of water. The organic layer was separated; the aqueous layer was extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by distillation under vacuum (120 °C, 1.0 mmHg) to give the title compound (1.64 g, 72%) as a pale yellow oil, R_f 0.10 (CH_2Cl_2–MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51–2.43 (m, 6H), 2.38 (t, J = 6.9 Hz, 2H), 1.82–1.61 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 119.6, 55.3, 54.2, 28.0, 23.7, 23.5, 17.2. IR (neat) 2959, 2876, 2791, 2245, 1462, 1427, 1393, 1385, 1352, 1327, 1292, 1236, 1209, 1148, 1128, 1067, 880, 735 cm^{-1}. Anal. Calcd for $C_9H_{16}N_2$: C, 71.01; H, 10.59. Found: C, 70.77; H, 10.84.

6-(Pyrrolidin-1-yl)hexanenitrile (1f). A mixture of 6-bromohexanenitrile (1.76 g, 10.0 mmol), pyrrolidine (747 mg, 10.5 mmol), potassium carbonate (1.45 g, 10.5 mmol), and potassium iodide (83 mg, 0.50 mmol) in acetonitrile (10 mL) was stirred at rt for 12 h. To the reaction mixture was added a saturated $NaHCO_3$ aqueous solution. The resulting mixture was extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous $MgSO_4$, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on neutral aluminum oxide (CH_2Cl_2–MeOH = 50:1) to give the title compound (0.71 g, 43%) as a brown oil, R_f 0.13 (CH_2Cl_2–MeOH = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50–2.39 (m, 6H), 2.34 (t, J = 7.0 Hz, 2H), 1.81–1.72 (m, 4H), 1.68 (quint, J = 7.3 Hz, 2H), 1.59–1.43 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 119.6, 56.1, 54.2, 28.4, 26.8, 25.4, 23.5, 17.2. IR (neat) 2936, 2874, 2789, 2245, 1458, 1427, 1389, 1350, 1327, 1292, 1234, 1204, 1146, 1128, 1072, 905, 880, 731 cm^{-1}.

HRMS (EI) Calcd for $C_{10}H_{18}N_2$: M^+, 166.1470. Found: *m/z* 166.1466.

4-[Benzyl(methyl)amino]butanenitrile (1g). A mixture of 4-bromobutyronitrile (1.48 g, 10.0 mmol), benzylmethylamine (1.27 g, 10.5 mmol), potassium carbonate (1.45 g, 10.5 mmol), and potassium iodide (83 mg, 0.50 mmol) in acetonitrile (10 mL) was stirred at rt for 12 h. The reaction mixture was treated with a saturated $NaHCO_3$ aqueous solution and then extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, filtered through a Celite pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 1:1) followed by distillation (100 °C, 1.4 x 10^{-3} mmHg) to give the title compound (1.60 g, 85%) as a pale brown oil, R_f 0.30 (hexane–ethyl acetate = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.23 (m, 5H), 3.50 (s, 2H), 2.49 (t, *J* = 6.5 Hz, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 2.20 (s, 3H), 1.84 (quint, *J* = 6.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 128.7, 128.1, 127.0, 119.8, 62.5, 55.3, 42.0, 23.6, 14.9. IR (neat) 3063, 3028, 2945, 2797, 2247, 1601, 1495, 1454, 1422, 1368, 1352, 1319, 1300, 1261, 1215, 1180, 1136, 1076, 1026, 962, 910, 862, 839, 737, 700 cm^{-1}. Anal. Calcd for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57. Found: C, 76.47; H, 8.70.

3-(1-Methylpyrrolidin-2-yl)propanenitrile (1h).[11] Methanesulfonyl chloride (3.2 g, 28 mmol) was added to a mixture of 2-(1-methylpyrrolidin-2-yl)ethanol (2.6 g, 20 mmol) and triethylamine (2.8 g, 28 mmol) in CH_2Cl_2 (32 mL) at 0 °C, and the resulting mixture was stirred for 10 min. The reaction mixture was treated with water (100 mL) and a saturated $NaHCO_3$ aqueous solution and then extracted three times with CH_2Cl_2. Combined organic layers were dried over anhydrous Na_2SO_4, filtered through a Celite pad, and concentrated *in vacuo*. The residue dissolved in DMF (30 mL). To this solution was added NaCN (1.96 g, 40 mmol), and the mixture was stirred at 60 °C for 14 h before quenching with a saturated $NaHCO_3$ aqueous solution. The organic layer was separated; the aqueous layer was extracted three times with diethyl ether. Combined organic layers were dried over anhydrous Na_2SO_4, filtered through a Celite pad, and then concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2–MeOH = 10:1) to give the title compound (318 mg, 12%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.04 (ddd, 9.3, 7.1, 2.6 Hz,

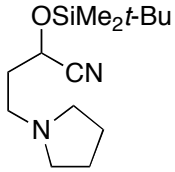
1H), 2.48–2.38 (m, 1H), 2.36–2.12 (m, 6H), 2.01–1.90 (m, 2H), 1.81–1.58 (m, 3H), 1.50–1.40 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 119.8, 64.3, 57.2, 40.5, 29.9, 29.1, 22.2, 13.7.

2-Ethyl-4-(pyrrolidin-1-yl)butanenitrile (1j). Butyronitrile (1.04 g, 15.0 mmol) was added dropwise to a solution of LDA (15.0 mmol, prepared from *n*-BuLi and diisopropylamine) in THF (20 mL) at –78 °C, and the whole was stirred at 0 °C for 1 h. To the mixture was added 1-(2-chloroethyl)pyrrolidine [2.2 g, 16.2 mmol, freed from 1-(2-chloroethyl)pyrrolidine hydrochloride with potassium carbonate] dropwise at –78 °C, and the resulting mixture was stirred at rt for 6 h then heated to reflux for 10 h. A saturated $NaHCO_3$ aqueous solution was added, and the aqueous layer was extracted three times with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2–NEt_3 = 98:2 then CH_2Cl_2–MeOH = 15:1) and then neutral aluminum oxide (hexane–ethyl acetate = 4:1) followed by distillation (110 °C, 1.0 mmHg) to give the title compound (1.23 g, 49%) as a pale yellow oil, R_f 0.13 (CH_2Cl_2–MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68–2.44 (m, 7H), 1.86–1.69 (m, 6H), 1.65 (quint, *J* = 7.6 Hz, 2H), 1.09 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 122.0, 54.2, 53.5, 31.3, 31.2, 25.6, 23.5, 11.7. IR (neat) 2967, 2878, 2793, 2236, 1462, 1387, 1354, 1294, 1219, 1153, 1138, 1117, 1030, 939, 905, 880, 862 cm^{-1}. Anal. Calcd for $C_{10}H_{18}N_2$: C, 72.24; H, 10.91. Found: C, 72.08; H, 10.89.

2-Phenyl-4-(pyrrolidin-1-yl)butanenitrile (1k). Sodium amide (0.66 g, 16.8 mmol) was added portionwise to a solution of phenyacetonitrile (1.76 g, 15.0 mmol) and 1-(2-chloroethyl)pyrrolidine (2.1 g, 15.9 mmol) in toluene (10 mL) at 80 °C, and the resulting mixture was stirred for 4 h before addition of cold water (15 mL) at rt. The aqueous layer was separated, and the organic layer was treated with a 12 M HCl aqueous solution (15 mL). The aqueous layer was separated and treated with a 7.5 M NaOH aqueous solution to make the whole mixture alkaline. The resulting mixture was extracted three times with diethyl ether, and the combined organic layers were dried over anhydrous Na_2SO_4, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column

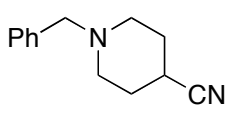
chromatography on silica gel (CH_2Cl_2–NEt_3 = 98:2 then CH_2Cl_2–MeOH = 10:1) and then neutral aluminum oxide (hexane–ethyl acetate = 100:1 to ethyl acetate) followed by distillation (120 °C, 3.0 x 10^{-3} mmHg) to give the title compound (2.2 g, 64%) as a colorless oil, R_f 0.15 (CH_2Cl_2–MeOH = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.29 (m, 5H), 4.03 (dd, *J* = 8.4, 6.6 Hz, 1H), 2.64 (dt, *J* = 12.2, 7.1, Hz, 1H), 2.54–2.46 (m, 5H), 2.20–2.09 (m, 1H), 2.02 (sext, *J* = 7.0 Hz, 1H), 1.84–1.74 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 128.9, 127.8, 127.2, 120.9, 54.0, 52.7, 35.1, 34.8, 23.6. IR (neat) 3063, 3030, 2961, 2876, 2795, 2239, 1601, 1495, 1454, 1385, 1356, 1339, 1292, 1244, 1215, 1148, 1125, 1078, 1061, 1030, 955, 905, 878, 854, 758, 698 cm^{-1}. Anal. Calcd for $C_{14}H_{18}N_2$: C, 78.46; H, 8.47. Found: C, 78.32; H, 8.44.

2-(*tert*-Butyldimethylsilyloxy)-4-(pyrrolidin-1-yl)butanenitrile (1l).[12] Acrolein (0.67



g, 12.0 mmol) was added dropwise to a mixture of pyrrolidine (0.85 g, 12.0 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (18.0 mg, 0.12 mmol) in THF (4.0 mL) at –15 °C, and the whole was stirred for 30 min. To this mixture was added THF (8.0 mL) and 2,8,9-triisopropyl-2,5,8,9-tetraaza-1-phosphabicyclo[3.3.3]undecane (180 mg, 0.60 mmol). A solution of *tert*-butyldimethylsilyl cyanide (2.0 g, 14.4 mmol) in THF (1.0 mL) was added dropwise at –15 °C, and the resulting mixture was stirred for 15 h, during which time the mixture was allowed to warm up to rt. The mixture was concentrated *in vacuo*, and the residue was purified by flash column chromatography on silica gel (CH_2Cl_2–MeOH = 10:1) followed by distillation (90 °C, 1.5 x 10^{-3} mmHg) to give the title compound (2.9 g, 90%) as a pale yellow oil, R_f 0.28 (CH_2Cl_2–MeOH = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.63 (t, *J* = 6.5 Hz, 1H), 2.66 (dt, *J* = 12.1, 7.3 Hz, 1H), 2.58–2.41 (m, 5H), 1.99 (q, *J* = 6.9 Hz, 2H), 1.82–1.72 (m, 4H), 0.92 (s, 9H), 0.20 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 120.2, 59.9, 54.1, 50.8, 35.7, 25.6, 23.6, 18.2, –5.0, –5.3. IR (neat) 2957, 2932, 2859, 2795, 1472, 1464, 1391, 1362, 1294, 1256, 1190, 1142, 1113, 1015, 1007, 939, 839, 781, 727, 669 cm^{-1}. Anal. Calcd for $C_{14}H_{28}N_2OSi$: C, 62.63; H, 10.51. Found: C, 62.36; H, 10.80.

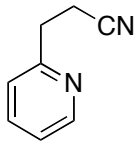
1-Benzyl-4-cyanopiperidine (1m).[13] To a solution of 1-benzyl-4-piperidinecarbox-



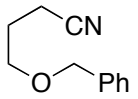
amide[13] (3.3 g, 15.0 mmol) in $CHCl_3$ (40 mL) was added thionyl chloride (17.8 g, 150 mmol). The mixture was stirred at the reflux

temperature for 29 h before evaporation of the solvent and excess thionyl chloride under reduced pressure. The residue was dissolved in CH_2Cl_2 (30 mL), and then treated with a 5% NH_4OH (60 mL) aqueous solution. The mixture was stirred for 15 min, and then the aqueous layer was separated and extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were washed with water (2 x 30 mL) and brine, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2–MeOH = 40:1 to 20:1) followed by distillation (120 °C, 0.12 mmHg) to give the title compound (2.7 g, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.23 (m, 5H), 3.51 (s, 2H), 2.66 (br s, 3H), 2.32 (br s, 2H), 1.99–1.82 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 128.8, 128.1, 127.0, 121.7, 63.1, 51.4, 28.9, 26.3.

2-(2-Cyanoethyl)pyridine (1n).[14] A solution of 2-(2-pyridyl)ethyl tosylate[15] (4.2 g, 15.0 mmol) and potassium cyanide (1.95 g, 30 mmol) in DMF (38 mL) was stirred at 60 °C for 14 h. The resulting mixture was diluted with diethyl ether, and the whole was washed with a saturated $NaHCO_3$ aqueous solution and then with water twice. The aqueous layer was extracted five times with CH_2Cl_2, and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 1:2 to 1:4) followed by distillation (150 °C, 1.0 mmHg) to give the title compound (1.44 g, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 4.8 Hz, 1H), 7.64 (td, J = 7.7, 1.8 Hz, 1H), 7.22 (d, J = 7.9 Hz, 1H), 7.19 (dd, J = 7.9, 5.3 Hz, 1H), 3.13 (t, J = 7.3 Hz, 2H), 2.85 (t, J = 7.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 149.5, 136.6, 123.0, 122.1, 119.3, 33.5, 16.8.

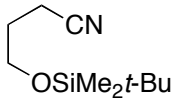


4-(Benzyloxy)butanenitrile (1o). A solution of benzyl 3-bromopropyl ether[16] (3.7 g, 16.0 mmol) and potassium cyanide (1.25 g, 19.2 mmol) in ethylene glycol (16 mL) was stirred at 100 °C for 3 h. The resulting mixture was extracted three times with CH_2Cl_2, and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 5:1) followed by distillation (120 °C, 3.0 x 10^{-3} mmHg) to give the title compound (2.3 g, 82%) as a colorless oil, R_f 0.23 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H),



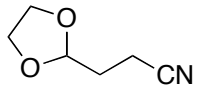
4.53 (s, 2H), 3.59 (td, J = 5.7, 1.0 Hz, 2H), 2.50 (td, J = 7.1, 0.9 Hz, 2H), 1.95 (quint, J = 6.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7, 128.3, 127.6, 127.5, 119.4, 73.2, 67.6, 25.9, 14.3. IR (neat) 3509, 3063, 3030, 2936, 2862, 2799, 2249, 1495, 1479, 1454, 1424, 1368, 1312, 1287, 1206, 1107, 1028, 909, 739, 698, 613 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48. Found: C, 75.60; H, 7.49.

4-(*tert*-Butyldimethylsilyloxy)butanenitrile (1p).[17] To a mixture of



tert-butyldimethylsilyl chloride (2.7 g, 18.0 mmol) and imidazole (1.28 g, 18.8 mmol) in THF (10 mL) was added a solution of 3-bromo-1-propanol (2.1 g, 15.0 mmol) in THF (10 mL) at 0 °C, and the whole was stirred at rt for 24 h. The resulting mixture was diluted with diethyl ether, and the whole was washed with a saturated $NaHCO_3$ aqueous solution twice and a 3 M HCl aqueous solution twice, dried over anhydrous $MgSO_4$, filtered through a Celite pad, and concentrated *in vacuo*. The residue was then added to a mixture of potassium cyanide (1.22 g, 18.8 mmol) and potassium iodide (249 mg, 1.50 mmol) in DMSO (20 mL), and the whole was stirred at 100 °C for 12 h. The resulting mixture was cooled down to rt, and then poured into water (75 mL). The whole was extracted three times with ethyl acetate, and combined organic layers were washed with brine, dried over $MgSO_4$, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 25:1 to 10:1) followed by distillation (130 °C, 1.0 mmHg) to give the title compound (1.88 g, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (t, J = 5.7 Hz, 2H), 2.46 (t, J = 7.0 Hz, 2H), 1.85 (quint, J = 6.4 Hz, 2H), 0.90 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 119.6, 60.6, 28.6, 25.9, 18.4, 13.9, –5.3.

2-(2-Cyanoethyl)-1,3-dioxolane (1r).[18] A mixture of 2-(2-bromoethyl)-1,3-dioxolane

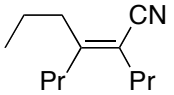


(2.7 g, 15.0 mmol) and potassium cyanide (1.25 g, 18.0 mmol) in ethylene glycol (12 mL) and water (2.0 mL) was stirred at 100 °C for 3 h. The resulting mixture was extracted three times with $CHCl_3$, and the combined extracts were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 1:1) followed by distillation (80 °C, 1.0 mmHg) to give the title compound (1.32 g, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.98 (t, J = 3.8 Hz, 1H), 4.03–3.94 (m, 2H), 3.93–3.84 (m,

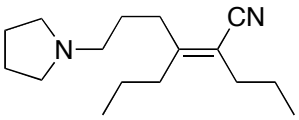
2H), 2.46 (t, J = 7.4 Hz, 2H), 2.04 (td, J = 7.4, 3.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 119.3, 101.6, 65.2, 29.3, 11.3.

4-(Benzylthio)butanenitrile (1s).[19] To a mixture of benzyl mercaptan (1.86 g, 15.0 mmol) and 4-bromobutyronitrile (2.2 g, 15.0 mmol) in triethylamine (15 mL) was added $RhCl(PPh_3)_3$ (0.69 g, 0.75 mmol), and the whole mixture was stirred at 50 °C for 12 h before filtration through a Celite pad with hexane as an eluant followed by concentration *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 5:1) followed by distillation (200 °C, 0.04 mmHg) to give the title compound (2.3 g, 80%) as a colorless oil, R_f 0.25 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.22 (m, 5H), 3.72 (s, 2H), 2.55 (t, J = 6.9 Hz, 2H), 2.45 (t, J = 7.1 Hz, 2H), 1.87 (quint, J = 7.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7, 128.6, 128.4, 127.0, 119.0, 36.2, 29.9, 24.9, 16.1. IR (neat) 3061, 3028, 2922, 2247, 1495, 1452, 1422, 1283, 1240, 1200, 1072, 1028, 918, 770, 704, 565 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NS$: C, 69.07; H, 6.85. Found: C, 69.16; H, 7.02.

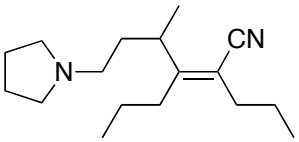
Nickel/Lewis Acid-catalyzed Alkylcyanation of Alkynes. *General procedure.* In a dry box, to a solution of $Ni(cod)_2$ (8.3–27.5 mg, 30–100 μmol) and a ligand (30–200 μmol) in toluene (1.00 mL) placed in a vial were sequentially added an alkyl cyanide (1.00 mmol), a 1.08 M solution of $AlMe_3$ in hexane (111–556 μL, 0.12–0.60 mmol), and dodecane (an internal standard, 85 mg, 0.50 mmol). The vial was taken out from the dry box and heated at the temperature for the time specified in Tables 1 and 2. The resulting mixture was filtered through a silica gel pad (hexane–NEt_3 = 98:2 then MeOH) and concentrated *in vacuo*. The residue was dissolved in hexane, and the solution was filtered through a Celite pad. Concentration *in vacuo* gave a residue, which was purified by flash column chromatography on silica gel or neutral aluminum oxide to give the corresponding alkylcyanation products in yields listed in Tables 1 and 2. Regioisomers were separated by preparative HPLC and characterized by spectrometry. The spectra of **3aa** and **4** were reported previously.[20]

2,3-Dipropylhex-2-enenitrile (3ba). A colorless oil, R_f 0.10 (hexane–ethyl acetate = 30:1). 

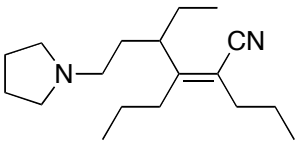
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (t, *J* = 7.6 Hz, 2H), 2.19 (t, *J* = 7.6 Hz, 2H), 2.14 (t, *J* = 7.9 Hz, 2H), 1.58 (sext, *J* = 7.5 Hz, 2H), 1.52 (sext, *J* = 7.5 Hz, 2H), 1.43 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 119.3, 110.0, 38.0, 33.4, 31.6, 21.9, 21.8, 21.5, 14.3, 14.0, 13.6. IR (neat): 2963, 2934, 2874, 2207, 1624, 1458, 1381, 1341, 1258, 1136, 1094, 1076, 895, 743 cm^{-1}. Anal. Calcd for $C_{12}H_{21}N$: C, 80.38; H, 11.81. Found: C, 80.41; H, 11.61.

(*Z*)-2,3-Dipropyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3ca). A brown oil, R_f 0.30 (CH_2Cl_2–MeOH = 10:1). 

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56–2.40 (m, 8H), 2.20–2.12 (m, 4H), 1.84–1.51 (m, 8H), 1.44 (sext, *J* = 7.7 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 119.2, 110.1, 56.0, 54.2, 34.2, 33.4, 31.6, 27.9, 23.5, 21.9, 21.5, 14.3, 13.6. IR (neat) 2961, 2934, 2874, 2787, 2206, 1622, 1462, 1381, 1348, 1327, 1292, 1238, 1209, 1146, 1109, 1088, 883, 800, 741 cm^{-1}. Anal. Calcd for $C_{16}H_{28}N_2$: C, 77.36; H, 11.36. Found: C, 77.16; H, 11.55.

(*Z*)-2,3-Dipropyl-4-methyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3ea). A brown oil, R_f 0.28 (CH_2Cl_2–MeOH = 10:1). 

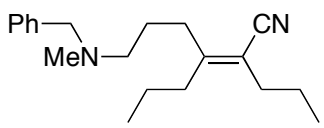
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.03 (sext, *J* = 7.0 Hz, 1H), 2.55–2.40 (m, 5H), 2.38–2.26 (m, 1H), 2.23–1.96 (m, 4H), 1.83–1.72 (m, 4H), 1.69–1.54 (m, 4H), 1.40 (sext, *J* = 7.6 Hz, 2H), 1.09 (d, *J* = 7.0 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 119.0, 110.2, 54.6, 54.3, 40.0, 34.5, 31.7, 30.7, 23.5, 23.3, 21.7, 19.4, 15.0, 13.6. IR (neat) 2959, 2876, 2791, 2245, 1462, 1427, 1393, 1385, 1352, 1327, 1292, 1236, 1209, 1148, 1128, 1067, 880, 735 cm^{-1}. Anal. Calcd for $C_{17}H_{30}N_2$: C, 77.80; H, 11.52. Found: C, 77.95; H, 11.76.

(*Z*)-2,3-Dipropyl-4-ethyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3fa). A brown oil, R_f 0.23 (CH_2Cl_2–MeOH = 10:1). 

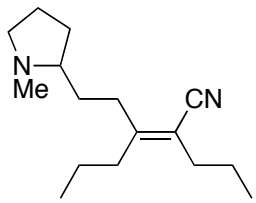
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81 (sept, *J* = 4.9 Hz, 1H), 2.54–2.38 (m, 5H), 2.29 (td, *J* = 11.6, 5.1 Hz, 1H), 2.20 (t, *J* = 7.6 Hz, 2H), 2.02 (distorted t, *J* = 8.6 Hz, 2H), 1.84–1.34 (m, 12H), 0.972 (t, *J* = 7.2 Hz, 3H), 0.967 (t, *J* = 7.4 Hz, 3H),

0.86 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 119.1, 112.1, 54.7, 54.3, 47.9, 32.9, 31.8, 30.6, 26.7, 23.5, 23.2, 21.7, 15.1, 13.7, 12.2. IR (neat) 2961, 2934, 2874, 2789, 2207, 1695, 1616, 1462, 1381, 1350, 1292, 1263, 1236, 1140, 1121, 1092, 905, 878, 779, 741 cm^{-1}. HRMS (EI) Calcd for $C_{18}H_{32}N_2$: M^+, 276.2565. Found: *m/z* 276.2574.

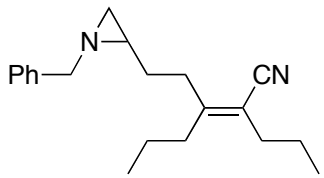
(*Z*)-6-[Benzyl(methyl)amino]-2,3-dipropylhex-2-enenitrile (3ga). A brown oil, R_f 0.70 (CH_2Cl_2–MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.20 (m, 5H), 3.50 (s, 2H), 2.42 (t, J = 7.3 Hz, 4H), 2.20 (s, 3H), 2.19–2.10 (m, 4H), 1.69 (quint, J = 7.6 Hz, 2H), 1.56 (sext, J = 7.5 Hz, 2H), 1.43 (sext, J = 7.5 Hz, 2H), 0.943 (t, J = 7.3 Hz, 3H), 0.937 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 138.9, 128.8, 128.0, 126.8, 119.2, 110.0, 62.4, 57.0, 42.2, 34.0, 33.5, 31.6, 26.5, 21.9, 21.5, 14.3, 13.6. IR (neat) 3063, 3028, 2961, 2872, 2789, 2207, 1682, 1622, 1495, 1462, 1454, 1379, 1366, 1350, 1258, 1126, 1074, 1059, 1026, 966, 909, 845, 737, 698 cm^{-1}. Anal. Calcd for $C_{20}H_{30}N_2$: C, 80.48; H, 10.13. Found: C, 80.27; H, 10.37.



(*Z*)-2-Propyl-3-(*N*-methylpyrrolidin-2-yl)ethylhex-2-enenitrile (3ha). A yellow oil, R_f 0.28 (CH_2Cl_2–MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.05 (td, J = 8.4, 2.0 Hz, 1H), 2.46–2.32 (m, 2H), 2.31 (s, 3H), 2.21–2.09 (m, 5H), 2.08–1.94 (m, 2H), 1.86–1.32 (m, 9H), 0.94 (t, J = 7.3 Hz, 3H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 119.1, 109.9, 65.7, 57.4, 40.5, 33.4, 33.1, 32.6, 31.5, 30.7, 22.0, 21.8, 21.4, 14.3, 13.5. IR (neat) 2938, 2872, 2778, 2207, 1622, 1456, 1379, 1364, 1352, 1213, 1126, 1115, 1049, 893, 799, 741 cm^{-1}. Anal. Calcd for $C_{16}H_{28}N_2$: C, 77.36; H, 11.36. Found: C, 77.06; H, 11.38.

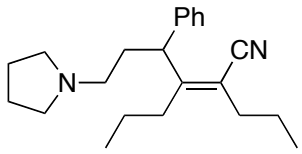


(*Z*)-3-(*N*-Benzylaziridin-2-yl)ethyl-2-propylhex-2-enenitrile (3ia). A yellow oil, R_f 0.20 (CH_2Cl_2–MeOH = 40:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.22 (m, 5H), 3.47 (d, J = 13.0 Hz, 1H), 3.38 (d, J = 13.2 Hz, 1H), 2.49–2.39 (m, 1H), 2.38–2.28 (m, 1H), 2.21–2.12 (m, 4H), 1.67–1.48 (m, 6H), 1.45 (d, J = 5.9 Hz, 1H), 1.37 (sext, J = 6.6 Hz, 2H), 0.94 (t, J = 7.3 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C

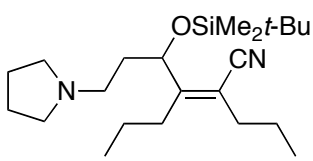


NMR (101 MHz, $CDCl_3$) δ 158.9, 139.1, 128.2, 128.0, 126.9, 119.1, 110.1, 64.7, 39.2, 34.03, 33.96, 33.3, 32.0, 31.5, 21.8, 21.4, 14.2, 13.6. IR (neat) 3030, 2963, 2932, 2872, 2207, 1620, 1495, 1454, 1379, 1356, 1254, 1161, 1067, 1028, 910, 889, 843, 818, 733, 698 cm^{-1}. HRMS (EI) Calcd for $C_{20}H_{28}N_2$: M^+, 296.2252. Found: *m/z* 296.2258.

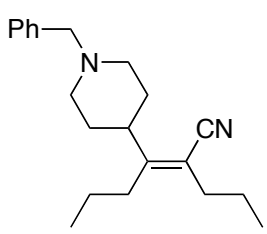
(*Z*)-2,3-Dipropyl-4-phenyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3ka). A brown oil, R_f 0.25 (CH_2Cl_2–MeOH = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.19 (m, 5H), 4.31 (dd, *J* = 8.4, 6.6 Hz, 1H), 2.59–2.39 (m, 6H), 2.26–1.74 (m, 10H), 1.64 (sext, *J* = 7.4 Hz, 2H), 1.21–1.07 (m, 1H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.74 (t, *J* = 7.0 Hz, 3H), 0.71–0.58 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 140.4, 128.3, 127.6, 126.8, 119.3, 111.0, 54.5, 54.3, 50.2, 31.8, 31.0, 30.5, 23.5, 23.1, 21.6, 14.8, 13.6. IR (neat) 2961, 2874, 2789, 2207, 1686, 1616, 1601, 1495, 1452, 1379, 1352, 1292, 1234, 1146, 1128, 1086, 1032, 883, 762, 739, 702 cm^{-1}. HRMS (EI) Calcd for $C_{22}H_{32}N_2$: M^+, 324.2565. Found: *m/z* 324.2570.



(*Z*)-4-(*tert*-Butyldimethylsilyloxy)-2,3-dipropyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3la). A brown oil, R_f 0.40 (CH_2Cl_2–MeOH = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 4.80 (dd, *J* = 8.1, 5.5 Hz, 1H), 2.57 (td *J* = 11.1, 4.6 Hz, 1H), 2.52–2.43 (m, 4H), 2.38–2.03 (m, 5H), 1.90–1.35 (m, 10H), 0.96 (t, *J* = 7.3 Hz, 6H), 0.89 (s, 9H), 0.11 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 118.0, 110.1, 73.8, 54.2, 52.6, 36.3, 31.7, 29.8, 25.9, 23.5, 23.3, 21.4, 18.2, 15.0, 13.7, –4.5, –4.9. IR (neat) 2961, 2932, 2874, 2859, 2785, 2209, 1462, 1381, 1360, 1350, 1258, 1153, 1078, 1015, 1005, 984, 959, 939, 858, 837, 804, 777, 667 cm^{-1}. Anal. Calcd for $C_{22}H_{42}N_2OSi$: C, 69.78; H, 11.18. Found: C, 69.98; H, 11.10.

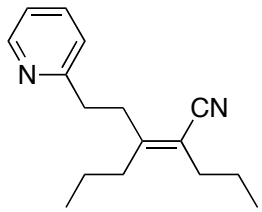


(*Z*)-2-Propyl-3-(*N*-benzylpiperidin-4-yl)hex-2-enenitrile (3ma). A pale yellow oil, R_f 0.23 (CH_2Cl_2–MeOH = 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.22 (m, 5H), 3.51 (s, 2H), 2.95 (d, *J* = 11.3 Hz, 2H), 2.80 (tt, *J* = 12.0, 3.8 Hz, 1H), 2.19–2.01 (m, 6H), 1.69 (qd, *J* = 12.3, 3.8 Hz, 2H), 1.63–1.51 (m, 4H), 1.45–1.28 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz,

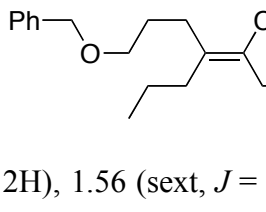


$CDCl_3$) δ 162.6, 138.1, 129.1, 128.0, 126.8, 118.9, 109.9, 63.4, 53.5, 44.9, 31.6, 31.1, 30.4, 23.0, 21.7, 14.7, 13.6. IR (neat) 2960, 2872, 2801, 2760, 2207, 1613, 1495, 1466, 1454, 1395, 1379, 1366, 1343, 1314, 1288, 1269, 1250, 1148, 1121, 1092, 1074, 1028, 991, 972, 955, 909, 839, 789, 739, 698 cm^{-1}. Anal. Calcd for $C_{21}H_{30}N_2$: C, 81.24; H, 9.74. Found: C, 81.30; H, 9.73.

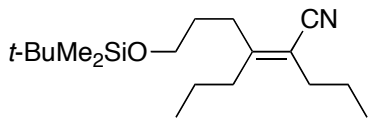
(*Z*)-2-Propyl-3-[2-(pyridin-2-yl)ethyl]hex-2-enenitrile (3na). A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 2.5:1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.8 Hz, 1H), 7.59 (td, *J* = 7.6, 1.8 Hz, 1H), 7.22 (d, *J* = 7.7 Hz, 1H), 7.11 (dd, *J* = 7.4, 4.8 Hz, 1H), 2.95 (dd, *J* = 10.1, 6.2 Hz, 2H), 2.79 (dd, *J* = 9.6, 6.5 Hz, 2H), 2.21–2.13 (m, 4H), 1.53 (sext, *J* = 7.5 Hz, 2H), 1.46 (sext, *J* = 7.6 Hz, 2H), 0.93 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 158.6, 149.0, 136.3, 122.8, 121.2, 119.0, 110.7, 37.1, 36.2, 33.5, 31.5, 21.8, 21.4, 14.2, 13.5. IR (neat) 2963, 2934, 2872, 2207, 1620, 1591, 1570, 1474, 1435, 1379, 1341, 1148, 1113, 1084, 1051, 993, 889, 750, 627 cm^{-1}. Anal. Calcd for $C_{16}H_{22}N_2$: C, 79.29 H, 9.15. Found: C, 79.07; H, 9.33.



(*Z*)-2,3-Dipropyl-6-(benzyloxy)hex-2-enenitrile (3oa). A colorless oil, R_f 0.13 (hexane–ethyl acetate = 30:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.25 (m, 5H), 4.52 (s, 2H), 3.51 (t, *J* = 6.4 Hz, 2H), 2.48 (t, *J* = 7.9 Hz, 2H), 2.21–2.12 (m, 4H), 1.86–1.75 (m, 2H), 1.56 (sext, *J* = 7.4 Hz, 2H), 1.44 (sext, *J* = 7.6 Hz, 2H), 0.942 (t, *J* = 7.4 Hz, 3H), 0.937 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 138.2, 128.2, 127.6, 127.4, 119.1, 110.2, 73.0, 69.7, 33.4, 32.9, 31.5, 28.7, 21.8, 21.5, 14.3, 13.6. IR (neat) 2961, 2934, 2872, 2207, 1721, 1622, 1497, 1454, 1379, 1363, 1273, 1204, 1103, 1028, 737, 698 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NO$: C, 79.95; H, 9.53. Found: C, 79.80; H, 9.57.

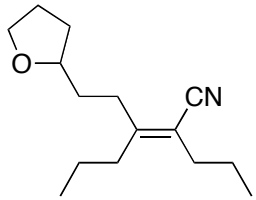


(Z)-6-(*tert*-Butyldimethylsilyloxy)-2,3-dipropylhex-2-enenitrile (3pa). A yellow oil, R_f 0.43 (hexane–ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 3.64 (t, *J* = 6.3 Hz, 2H), 2.43 (distorted t, *J* = 8.0 Hz, 2H), 2.17 (q, *J* =7.5 Hz, 4H), 1.68 (distorted quint, *J* = 7.1 Hz, 2H), 1.57 (sext, *J* = 7.4 Hz, 2H), 1.44 (sext, *J* = 7.5 Hz, 2H), 0.945 (t,

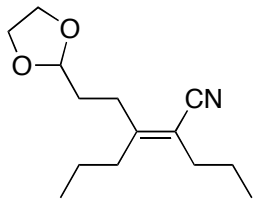


J = 7.3 Hz, 3H), 0.937 (t, J = 7.5 Hz, 3H), 0.90 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 119.1, 110.0, 62.6, 33.5, 32.6, 31.7, 31.6, 26.0, 21.9, 21.4, 18.4, 14.3, 13.6, –5.1. IR (neat) 2959, 2932, 2859, 2209, 1624, 1464, 1381, 1362, 1256, 1190, 1103, 1007, 970, 939, 837, 814, 775, 718, 662 cm^{-1}. Anal. Calcd for $C_{18}H_{35}NOSi$: C, 69.84; H, 11.40. Found: C, 69.59; H, 11.44.

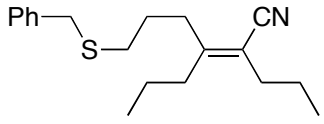
(Z)-2-propyl-3-[2-(tetrahydrofuran-2-yl)ethyl]hex-2-enenitrile (3qa). A brown oil, R_f 0.38 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90–3.77 (m, 2H), 3.73 (q, J =12.1 Hz, 1H), 2.51–2.37 (m, 2H), 2.22–2.10 (m, 4H), 2.18–1.98 (m, 1H), 1.96–1.81 (m, 2H), 1.79–1.68 (m, 1H), 1.66–1.38 (m, 6H), 0.94 (t, J = 7.4 Hz, 3H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 119.1, 110.0, 78.7, 67.7, 34.4, 33.6, 32.9, 31.5, 31.2, 25.8, 21.8, 21.4, 14.2, 13.5. IR (neat) 2963, 2872, 2207, 1622, 1460, 1379, 1343, 1132, 1063, 1022, 920, 799, 743 cm^{-1}. Anal. Calcd for $C_{15}H_{25}NO$: C, 76.55; H, 10.71. Found: C, 76.37; H, 10.87.



(*Z*)-2-Propyl-3-[2-(1,3-dioxolan-2-ly)ethyl]hex-2-enenitrile (3ra). A colorless oil, R_f 0.23 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89 (t, J = 4.5 Hz, 1H), 4.02–3.92 (m, 2H), 3.90–3.81 (m, 2H), 2.50 (distorted t, J = 8.1 Hz, 2H), 2.20–2.12 (m, 4H), 1.86–1.78 (m, 2H), 1.56 (sext, J = 7.4 Hz, 2H), 1.43 (sext, J = 7.5 Hz, 2H), 0.934 (t, J = 7.3 Hz, 3H), 0.930 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 118.9, 110.3, 103.5, 65.0, 33.4, 32.5, 31.6, 30.3, 21.8, 21.4, 14.2, 13.5. IR (neat) 3522, 2963, 2934, 2874, 2207, 1809, 1732, 1622, 1462, 1454, 1435, 1408, 1393, 1383, 1188, 1142, 1074, 1042, 972, 945, 901, 743 cm^{-1}. HRMS (EI) Calcd for $C_{14}H_{23}NO_2$: M^+, 237.1729. Found: *m/z* 237.1731.



(*Z*)-2,3-Dipropyl-6-(benzylthio)hex-2-enenitrile (3sa). A colorless oil, R_f 0.20 (hexane–ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.21 (m, 5H), 3.73 (s, 2H), 2.45 (t, J = 7.7 Hz, 2H), 2.44 (t, J = 8.6 Hz, 2H), 2.16 (t, J = 7.6 Hz, 2H), 2.09 (distorted t, J = 7.9 Hz, 2H), 1.71 (quint, J = 7.6 Hz, 2H), 1.56 (sext, J = 7.4 Hz, 2H), 1.41 (sext, J = 7.5 Hz, 2H), 0.94 (t, J = 7.3 Hz, 3H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR



(101 MHz, $CDCl_3$) δ 158.5, 138.2, 128.7, 128.3, 126.8, 119.0, 110.5, 36.4, 35.3, 33.4, 31.5, 31.1, 28.1, 21.8, 21.4, 14.2, 13.6. IR (neat) 3061, 3028, 2961, 2932, 2872, 2207, 1622, 1601, 1495, 1454, 1379, 1341, 1304, 1240, 1200, 1144, 1086, 1071, 1028, 916, 883, 802, 770, 739, 700, 565 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NS$: C, 75.69; H, 9.03. Found: C, 75.72; H, 8.85.

(*Z*)-2,3-Dimethyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3cb). A brown oil, R_f 0.18 (CH_2Cl_2–MeOH = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 2.56–2.41 (m, 8H), 1.87 (s, 3H), 1.82 (s, 3H), 1.81–1.76 (m, 4H), 1.71 (quint, J = 7.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 119.6, 103.6, 55.8, 54.1, 36.4, 27.3, 23.5, 18.1, 16.3. IR (neat) 2953, 2876, 2789, 2211, 1634, 1447, 1385, 1352, 1327, 1292, 1240, 1215, 1144, 1109, 1090, 1032, 955, 905, 874 cm^{-1}. HRMS (EI) Calcd for $C_{12}H_{20}N_2$: M^+, 192.1626. Found: *m/z* 192.1634.

(*Z*)-2,3-Bis(trimethylsilylmethyl)-6-(pyrrolidin-1-yl)hex-2-enenitrile (3cc). A pale yellow oil, R_f 0.40 (CH_2Cl_2–MeOH = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 2.55–2.44 (m, 6H), 2.37 (t, J = 7.8 Hz, 2H), 1.83–1.66 (m, 8H), 1.57 (s, 2H), 0.12 (s, 9H), 0.09 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 120.6, 102.2, 55.9, 54.2, 35.8, 28.5, 24.7, 23.5, 21.2, –0.3, –1.0. IR (neat) 2955, 2787, 2203, 1607, 1462, 1447, 1416, 1348, 1327, 1250, 1171, 1142, 1057, 939, 843, 770, 696, 606 cm^{-1}. HRMS (EI) Calcd for $C_{18}H_{36}N_2Si_2$: M^+, 336.2417. Found: *m/z* 336.2426.

(*Z*)-2-Isopropyl-3-methyl-4-phenyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3kd). A pale yellow oil, R_f 0.40 (CH_2Cl_2–MeOH = 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.21 (m, 5H), 4.29 (dd, J = 9.1, 6.0 Hz, 1H), 2.74 (sept, J = 6.8 Hz, 1H), 2.65–2.37 (m, 6H), 2.20 (sept, J = 5.9 Hz, 1H), 2.13–1.99 (m, 1H), 1.87–1.77 (m, 4H), 1.63 (s, 3H), 1.16 (d, J = 6.8 Hz, 3H), 1.12 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 140.6, 128.4, 127.4, 126.8, 117.7, 117.5, 54.3, 50.0, 30.1, 28.3, 23.5, 21.4, 21.1, 13.5. IR (neat) 2965, 2874, 2791, 2207, 1620, 1601, 1495, 1454, 1387, 1366, 1354, 1294, 1234, 1146, 1125, 1088, 1032, 905, 883, 758, 702 cm^{-1}. Anal. Calcd for $C_{20}H_{28}N_2$: C, 81.03; H, 9.52. Found: C, 80.83; H, 9.42 (as a mixture

with **3'kd**).

(*Z*)-3-Isopropyl-2-methyl-4-phenyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3'kd). A pale yellow oil, R_f 0.40 (CH_2Cl_2–MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 4H), 7.25–7.19 (m, 1H), 4.32 (dd, *J* = 8.7, 6.1 Hz, 1H), 2.65–2.44 (m, 7H), 2.28–2.01 (m, 5H), 1.86–1.76 (m, 4H), 1.15 (d, *J* = 7.5 Hz, 3H), 0.62 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 139.9, 128.2, 127.7, 126.8, 120.7, 105.5, 54.5, 54.2, 50.8, 29.8, 29.2, 23.5, 20.8, 17.9. IR (neat) 3064, 3024, 2963, 2934, 2872, 2803, 2776, 2749, 2207, 1622, 1599, 1584, 1497, 1479, 1462, 1451, 1391, 1377, 1366, 1352, 1327, 1298, 1279, 1236, 1217, 1204, 1196, 1180, 1153, 1140, 1123, 1105, 1084, 1030, 1015, 964, 951, 901, 885, 862, 847, 762, 704, 581, 550 cm^{-1}.

(*Z*)-2-*tert*-Butyl-3-methyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3ce). A brown oil, R_f 0.15 (CH_2Cl_2–MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53–2.40 (m, 8H), 2.00 (s, 3H), 1.82–1.65 (m, 6H), 1.28 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8, 119.1, 118.7, 55.8, 54.2, 39.1, 33.5, 30.7, 27.7, 23.5, 20.3. IR (neat) 2967, 2876, 2789, 2207, 1605, 1462, 1397, 1368, 1352, 1327, 1292, 1273, 1219, 1204, 1148, 1132, 1072, 905, 878 cm^{-1}. HRMS (EI) Calcd for $C_{15}H_{26}N_2$: M^+, 234.2096. Found: *m/z* 234.2091.

(*Z*)-2-*tert*-Butyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3cf). A yellow oil, R_f 0.23 (CH_2Cl_2–MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14 (t, *J* = 7.5 Hz, 1H), 2.51–2.36 (m, 8H), 1.80–1.72 (m, 4H), 1.64 (quint, *J* = 7.5 Hz, 2H), 1.15 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.5, 125.5, 116.9, 55.7, 54.2, 34.8, 29.8, 28.9, 28.3, 23.5. IR (neat) 2965, 2874, 2212, 1479, 1462, 1368, 1352, 1292, 1263, 1206, 1148, 1036, 905, 878, 667, 660 cm^{-1}. HRMS (EI) Calcd for $C_{14}H_{24}N_2$: M^+, 220.1939. Found: *m/z* 220.1940.

(*Z*)-2-Phenyl-6-(pyrrolidin-1-yl)hex-2-enenitrile (3cg). A brown oil, R_f 0.23 (CH_2Cl_2–MeOH = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.0 Hz, 2H), 7.47–7.35 (m, 3H), 6.86 (t, *J* = 7.8 Hz, 1H), 2.64 (q, *J* =7.5 Hz, 2H), 2.58–2.40 (m, 6H), 1.84–1.73 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.5, 133.0, 128.8, 128.7, 125.4, 116.4, 115.8, 55.7, 54.2, 30.5, 28.2, 23.5. IR (neat) 2957, 2876, 2791, 2218, 1684, 1597, 1497, 1449, 1385, 1352, 1292, 1238, 1211, 1148, 1107, 1078, 1032, 1001, 966, 905, 878, 762, 692 cm^{-1}. HRMS (EI) Calcd for $C_{16}H_{20}N_2$: M^+, 240.1626. Found: *m/z* 240.1618.

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List of Publications

I. Parts of the present Thesis have been or are to be published in the following journals.

Chapters 2

(1) A Dramatic Effect of Lewis-Acid Catalysts on Nickel-Catalyzed Carbocyanation of Alkynes
Nakao, Y.; Yada, A.; Ebata, S.; Hiyama, T. *J. Am. Chem. Soc.* **2007**, *129*, 2428–2429.

(2) Dramatic Effect of Lewis Acid Catalyst on Nickel-catalyzed Carbocyanation Reaction of Unsaturated Bonds Using Aryl and Alkenyl Cyanides
Yada, A.; Ebata, S.; Idei, H.; Zhang, D.; Nakao, Y.; Hiyama, T. manuscript in preparation.

Chapter 3

(3) Intramolecular Arylcyanation of Alkenes Catalyzed by Nickel/$AlMe_2Cl$
Nakao, Y.; Ebata, S.; Yada, A.; Hiyama, T.; Ikawa, M.; Ogoshi, S. *J. Am. Chem. Soc.* **2008**, *130*, 12874–12875.

Chapter 4

(4) Nickel/$AlMe_2Cl$-catalysed Carbocyanation of Alkynes Using Arylacetonitriles
Yada, A.; Yukawa, T.; Nakao, Y.; Hiyama, T. *Chem. Commun.* **2009**, 3931–3933.

(5) Nickel/Lewis Acid-catalyzed Carbocyanation of Alkynes Using Acetonitrile and Substituted Acetonitriles
Yada, A.; Yukawa, T.; Idei, H.; Nakao, Y.; Hiyama, T. manuscript in preparation.

Chapter 5

(6) Heteroatom-directed Alkylcyanation of Alkynes
Nakao, Y.; Yada, A.; Hiyama, T. manuscript in preparation.

II. Following publications are not included in this Thesis.

(7) Alkenyl- and Aryl[2-(hydroxymethyl)phenyl]dimethylsilanes: An Entry to Tetraorganosilicon Reagents for the Silicon-Based Cross-Coupling Reaction
Nakao, Y.; Imanaka, H.; Sahoo, A. K.; Yada, A.; Hiyama, T. *J. Am. Chem. Soc.* **2005**, *127*, 6952–6953.

(8) Alkenyl- and Aryl[2-(hydroxymethyl)phenyl]dimethylsilanes: Tetraorganosilanes for the Practical Cross-Coupling Reaction
Nakao, Y.; Sahoo, A. K.; Imanaka, H.; Yada, A.; Hiyama, T. *Pure Appl. Chem*. **2006**, *78*, 435–440.

(9) Arylcyanation of Norbornene and Norbornadiene Catalyzed by Nickel
Nakao, Y.; Yada, A.; Satoh, J.; Ebata, S.; Oda, S.; Hiyama, T. *Chem. Lett.* **2006**, 790–791.

(10) Arylcyanation of Alkynes Catalyzed by Nickel
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