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Cyanoesterification of 1,2-Dienes Catalyzed by Nickel

Yasuhiro Hirata, Tomohiko Inui, Yoshiaki Nakao,* and Tamejiro Hiyama*

Department of Material Chemistry, Graduate School of Engineering, Kyoto University,
Kyoto 615-8510, Japan

Received February 10, 2009; E-mail: yoshiakinakao@npc05.mbox.media.kyoto-u.ac.jp;
thiyama@z06.mbox.media.kyoto-u.ac.jp

Abstract: Cyanoformate esters add across 1,2-dienes in the presence of a nickel/PMe_2Ph catalyst to afford β-cyano-α-methylenealkanoates regioselectively, which are kinetically favored and readily isomerize to thermodynamically favored α-cyanomethyl-α,β-unsaturated carboxylates at high temperature under the nickel catalysis, possibly through oxidative addition of the C−CN bond. Similar cyanoesterification products are produced from chloroformate esters, trimethylsilyl cyanide, and 1,2-dienes in the presence of a nickel/dppp catalyst. The resulting cyanoesterification products have a structure of allylic cyanide and thus undergo further allyl cyanation reaction across alkynes with the aid of a nickel/$P(4\text{-}CF_3-C_6H_4)_3$ catalyst to afford highly substituted acrylonitrile derivatives.

Introduction

Transition metal catalyzed direct insertion of unsaturated bonds into C−C bonds should be an ultimately ideal transformation in view of atom economy, because it is not necessary to prefunctionalize substrates and no byproducts are formed.[1−3] However, the scope of such reactions is severely limited. In this regard, we have demonstrated nickel or nickel/Lewis acid catalyzed addition of nitriles across alkynes, namely a carbocyanation reaction.[4−7] The carbocyanation reaction of alkynes allows introduction of cyano and other various organic groups simultaneously through direct cleavage of C−CN bonds followed by insertion of alkynes to give highly substituted acrylonitriles with high regio- and stereoselectivities. Various nitriles such as acyl,[4] aryl,[5,7] allyl,[6] alkenyl,[7] alkynyl,[8] and alkyl cyanides[7] participate in the reaction successfully. The carbocyanation of alkenes should also be an attractive method for preparation of various alkanenitriles. However, the alkene functionalization suffers from reluctant reductive elimination of $C(sp^3)$−CN bonds and competes with β-hydride elimination.[9] Accordingly, examples of this transformation involve intramolecular reactions[10,11] and intermolecular reactions across strained alkenes such as norbornene,[9,12] all relying on alkylnickel intermediates having

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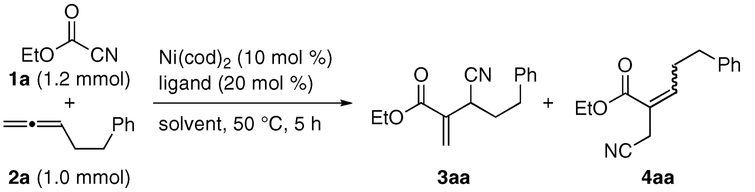
10.1021/ja9010282 CCC: $40.75

Table 1. Cyanoesterification of 5-Phenyl-1,2-pentadiene (**2a**) Using Ethyl Cyanoformate (**1a**)[a]



entry	ligand	solvent	yield of **3aa** (%)[b]	yield of **4aa** (%) (*E*/*Z*)[b]
1	PMe_3	toluene	0	0
2	PBu_3	toluene	0	0
3	PCy_3	toluene	0	0
4	P*t*-Bu_3	toluene	0	0
5	PMe_2Ph	toluene	77[d]	10[d] (5:>95)[e]
6	$PMePh_2$	toluene	73	5 (5:>95)
7	PPh_3	toluene	7	2 (50:50)
8	dppp[c]	toluene	18	3 (64:36)
9	PMe_2Ph	DMF	11	2 (5:>95)
10	PMe_2Ph	1,4-dioxane	23	4 (5:>95)
11[f]	PMe_2Ph	toluene	<5	78[d] (83:17)[e]

[a] All the reaction was carried out using **1a** (1.20 mmol), **2a** (1.00 mmol), $Ni(cod)_2$ (0.100 mmol), and a ligand (0.20 mmol) in toluene (2.0 mL) at 50 °C. [b] Estimated by GC using tetradecane as an internal standard. [c] 1,3-Bis(diphenylphosphino)propane (dppp) (0.100 mmol) was used. [d] Isolated yield. [e] Estimated by ^1H NMR analysis of an isolated product. [f] The reaction was carried out using **1a** (1.00 mmol) and **2a** (1.20 mmol) at 50 °C for 3 h and then at 100 °C for 24 h.

no chance for β-hydride elimination. We therefore envisioned the use of 1,2-dienes as an alkene surrogate. Insertion of the double bond of 1,2-dienes into C−M bonds often results in π-allylmetal intermediates, which are reluctant to undergo β-hydride elimination.[8,13] We report herein a full account of the carbocyanation of 1,2-dienes with cyanoformate esters to afford variously substituted β-cyano-α-methylenealkanoates.[14] We demonstrate that initially formed kinetic adducts isomerize to thermodynamically favored adducts through oxidative addition of the C−CN bonds and perform regiocontrol by simply changing the molar ratio of nitriles to 1,2-dienes and the reaction temperature. Also shown is that 1,2-diene-cyanoesterification products bearing various alkoxycarbonyl groups can be synthesized alternatively by a nickel-catalyzed three-component coupling reaction of chloroformate esters, 1,2-dienes, and trimethylsilyl cyanide. Synthetic transformations of the resulting β-cyano-α-methylenealkanoates including an allylcyanation reaction of alkynes are also demonstrated briefly.

Results and Discussion

Nickel-Catalyzed Cyanoesterification of 1,2-Dienes. We first examined the reaction of ethyl cyanoformate (**1a**, 1.2 mmol) with 5-phenyl-1,2-pentadiene (**2a**, 1.0 mmol) in toluene at 50 °C in the presence of a catalyst prepared in situ from $Ni(cod)_2$ (0.10 mmol) and various phosphine ligands (Table 1). Oligomerization of **2a** was predominant, when trialkylphosphine ligands such as PMe_3, PBu_3, PCy_3, or P*t*-Bu_3 were employed (entries 1−4). After thorough screening, PMe_2Ph was found to be the most effective for the desired cyanoesterification reaction to give ethyl 3-cyano-2-methylene-5-phenylpentanoate (**3aa**) and (*Z*)-ethyl 2-(cyanomethyl)-5-phenylpent-2-enoate [(*Z*)-**4aa**] in 77% and 10% yield, respectively (entry 5). Comparable yields of **3aa** and **4aa** were also obtained by use of $PMePh_2$ (entry 6), whereas use of PPh_3, dppp, and such polar solvents as DMF and 1,4-dioxane retarded the reaction (entries 7−10). While the ratio of **3aa** to **4aa** did not change after a prolonged reaction time and/or at a higher temperature, it was reversed by changing the molar ratio of **1a**:**2a** to 1.0:1.2 and by the running reaction at 50 °C for 3 h and then at 100 °C for 24 h to afford a stereoisomeric mixture of **4aa** as a major product (entry 11). These data provide mechanistic insights including the reversibility of reductive elimination and relative thermodynamic stability of **3aa** and **4aa**. $Pd(PPh_3)_4$, a catalyst of choice for the cyanoesterification of norbornene and norbornadiene,[12] was completely ineffective for the reaction across 1,2-dienes.

With the optimized catalyst in hand, we next examined the scope of 1,2-dienes using ethyl cyanoformate (**1a**) (Table 2). While the addition reaction across allene (**2b**) was sluggish due to rapid oligomerization of **2b** under the present reaction conditions (entry 1), the reactions with monosubstituted allenes having primary, secondary, and tertiary alkyl groups all proceeded with good yields and regioselectivity (entries 2−4). Higher regioselectivity was observed with a bulkier alkyl group. Substituents such as protected hydroxy, cyano, *N*-phthalimidoyl, ester, and a terminal double bond were tolerant under the reaction conditions to give highly functionalized β-cyanomethylacrylate esters (entries 5−10). Diastereoselectivity observed with 4-siloxy-1,2-pentadiene **2h** was modest (80:20) (entry 7). To our surprise, the reaction with 1,2-diene derived from diethyl malonate **2k** showed low regioselectivity (entry 10). Benzyl cyanoformate (**1b**) also participated in the reaction with **2a** in an acceptable yield under similar conditions (entry 11). Disubstituted allenes such as 3-methyl-1,2-butadiene (**2l**) and 5,6-

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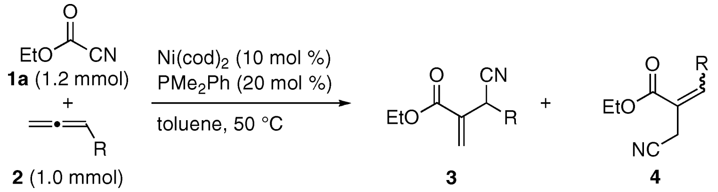
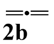
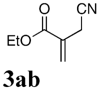
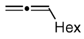
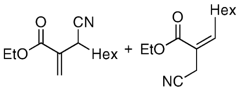
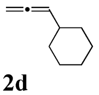
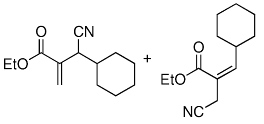
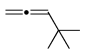
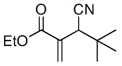
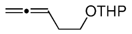
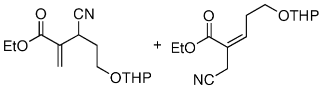
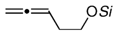
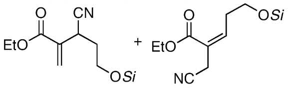
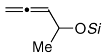
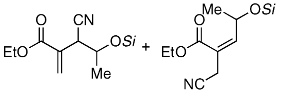
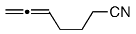
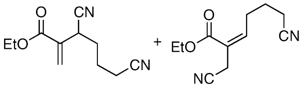
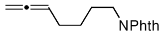
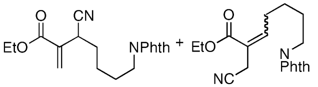
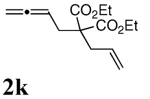
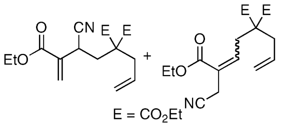
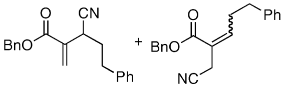
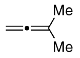
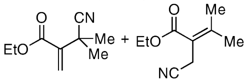
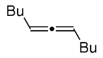
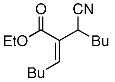
Table 2. Nickel-Catalyzed Cyanoesterification of 1,2-Dienes[a]



entry	2	time (h)	product(s) (*E*/*Z* of **4**)	yield (%)[b] (**3**:**4**)[c]
1[d]	 **2b**	9	 **3ab**	17 (—)
2	 **2c**	5	 **3ac**, (*Z*)-**4ac** (5:>95)	84 (89:11)
3	 **2d**	5	 **3ad**, (*Z*)-**4ad** (5:>95)	93 (90:10)
4	 **2e**	6	 **3ae**	70 (>95:5)
5	 **2f**	4	 **3af**, (*Z*)-**4af** (5:>95)	75 (83:17)
6	 *Si* = SiMe$_2$*t*-Bu **2g**	5	 **3ag**, (*Z*)-**4ag** (5:>95)	78 (82:18)
7	 **2h**	24	 **3ah**, (*Z*)-**4ah** (5:>95)	74 (86[e]:14)
8	 **2i**	5	 **3ai**, (*Z*)-**4ai** (5:>95)	79 (81:19)
9	 **2j**	4	 **3aj**, **4aj** (10:90)[f]	91 (84:16)
10	 **2k**	9	 E = CO$_2$Et **3ak**, **4ak** (58:42)[f]	59 (51:49)
11[g]	**2a**	18	 **3ba**, **4ba** (9:91)[f]	61 (84:16)
12	 **2l**	9	 **3al**, **4al** (—)	61 (84:16)
13	 **2m**	24	 **3am**	45 (—)

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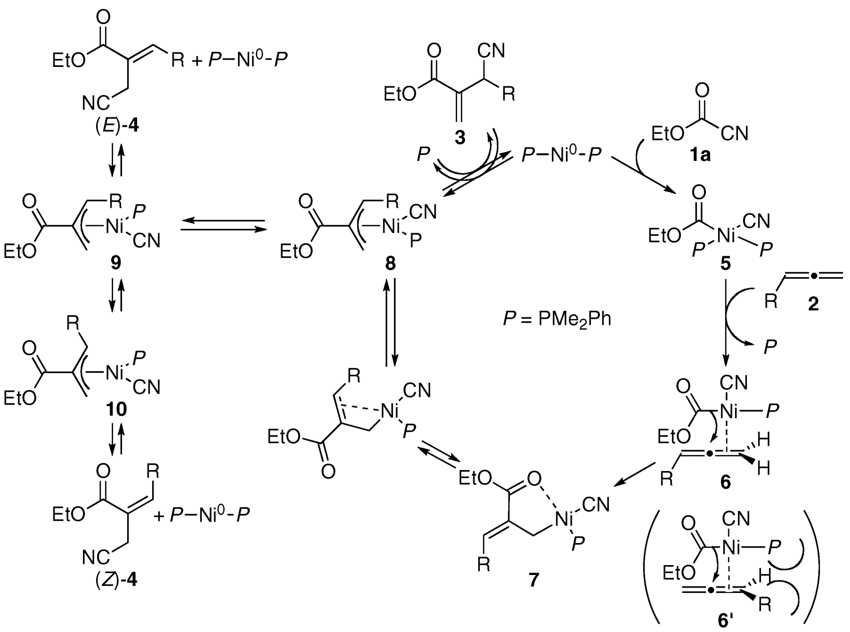
[a] All the reaction was carried out using **1a** (1.20 mmol), **2** (1.00 mmol), Ni(cod)$_2$ (0.100 mmol), and PMe$_2$Ph (0.20 mmol) in toluene (2.0 mL) at 50 °C. [b] Isolated yield. [c] Calculated based on yields of isolated products. [d] The reaction was carried out under an atmosphere of **2b** (1 atm). [e] dr = 80:20 as estimated by ^{1}H NMR analysis of an isolated product. Relative stereochemistry has not been identified. [f] Estimated by ^{1}H NMR analysis of an isolated product. [g] The reaction was carried out using benzyl cyanoformate (**1b**, 1.00 mmol) instead of **1a**.

Scheme 1. Plausible Mechanism for the Nickel-Catalyzed Cyanoesterification of 1,2-Dienes



undecadiene (**2m**) also underwent the reaction albeit in modest yields (entries 12 and 13).

In a manner similar to other carbocyanation reactions, the cyanoesterification reaction should be initiated by oxidative addition of an EtOC(O)−CN bond to nickel(0) (Scheme 1).[12,15] The sterically less hindered terminal double bond of a 1,2-diene coordinates to the nickel center,[13,16] and then the ethoxycarbonyl group migrates to a cumulative carbon of the coordinating 1,2-diene to give σ-allylnickel intermediate **7**, which isomerizes rapidly to π-allylnickel complex **8**. Reductive elimination finally produces **3** to regenerate nickel(0). Regioisomer **4** would be formed through coordination of 1,2-dienes in an opposite direction as shown in **6′** followed by similar steps involving π-allylnickel intermediates **9** or **10** under kinetically controlled conditions. Since **3** has an allyl cyanide substructure and oxidative addition of allyl cyanides to nickel(0) is feasible,[17] the reductive elimination, the product-forming step, would be reversible. Thus, under thermodynamically controlled conditions (entry 11 of Table 1), **3** undergoes further oxidative addition to nickel(0), isomerizaton of the resulting π-allylnickel **8** to **9** or **10**, and then reductive elimination to give (*E*)- or (*Z*)-**4**, which would be in equilibrium with **3**. Treatment of an isolated sample of **3aa** with Ni(cod)$_2$ (10 mol %) and PMe$_2$Ph (10 mol %) in toluene at 100 °C indeed caused the isomerization to a stereoisomeric mixture of **4aa**, whereas that with cyanide sources such as KCN, Et$_4$NCN, and Me$_3$SiCN in the presence of PMe$_2$Ph (20 mol %) in toluene at 100 °C resulted in decomposition of **3aa** to give an oligomeric product.[18] These results would support the proposed isomerization pathway. The equilibrium should lead to (*E*)-**4** over **3** and (*Z*)-**4** after a longer reaction time at higher temperature, according to the relative order of their thermodynamic stability. Nevertheless, the presence of **1a** in excess (entry 5 of Table 1) would inhibit the oxidative addition of **3** because of the higher reactivity of **1a** than **3** toward oxidative addition of a C−CN bond to reduce the chance of **3** to isomerize even at elevated temperature.

Nickel-Catalyzed Cyanoesterification of 1,2-Dienes by Three-Component Coupling. Cyanoformate esters are often synthesized from the corresponding chloroformate esters and metal cyanides such as KCN, NaCN, CuCN, and Me$_3$SiCN.[19] Therefore, a three-component coupling reaction of chloroformate esters, metal cyanides, and 1,2-dienes would be a practically straightforward way for the cyanoesterification of 1,2-dienes.[16] To realize this alternative protocol, we first examined the reaction of **2a** with ethyl chloroformate (**11a**) and trimethylsilyl cyanide (**12a**) in toluene in the presence of Ni(cod)$_2$ (10 mol%) and PMe$_2$Ph (20 mol%) (entry 1 of Table 3) to observe formation of **3aa** and **4aa** in only a small amount. Because a mechanistic scenario for the three-component approach was possibly different from that for the direct cyanoesterfication initiated by the oxidative addition of cyanoformate esters, we briefly examined the effect of other phosphine ligands and found that nickel/dppp effectively catalyzed the three-component reaction to give **3aa** and a stereoisomeric mixture of **4aa** (entry 3). Other bidentate phosphine ligands with a different bite angle, dppe and dppb, showed inferior catalytic activity (entries 2 and

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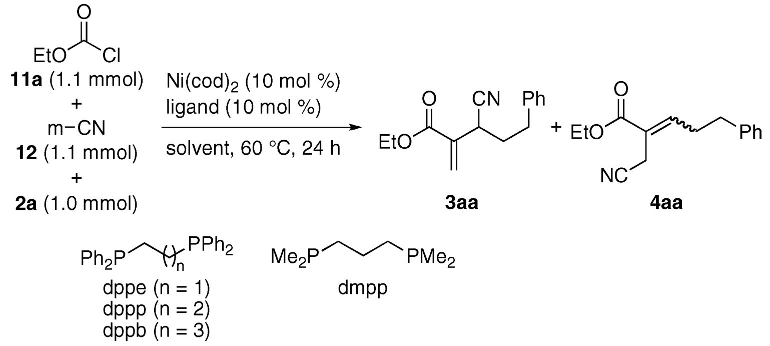
(16) Wu, M.-S.; Rayabarapu, D. K.; Cheng, C.-H. *J. Am. Chem. Soc.* **2003**, *125*, 12426–12427.

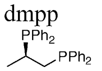
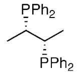
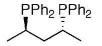
(17) (a) McKinney, R. J. In *Homogeneous Catalyst*; Parshall, G. W., Ed.; Wiley: New York, 1992; pp 42−50. (b) Chaumonnot, A.; Lamy, F.; Sabo-Etienne, S.; Donnadieu, B.; Chaudret, B.; Barthelat, J.-C.; Galland, J.-C. *Organometallics* **2004**, *23*, 3363–3365. (c) Brunkan, N. M.; Brestensky, D. M.; Jones, W. D. *J. Am. Chem. Soc.* **2004**, *126*, 3627–3641. (d) van der Vlugt, J. I.; Hewat, A. C.; Neto, S.; Sablong, R.; Mills, A. M.; Lutz, M.; Spek, A. L.; Müller, C.; Vogt, D. *Adv. Synth. Catal.* **2004**, *346*, 993–1003. (e) Wilting, J.; Müller, C.; Hewat, A. C.; Ellis, D. D.; Tooke, D. M.; Spek, A. L.; Vogt, D. *Organometallics* **2005**, *24*, 13–15. (f) Acosta-Ramírez, A.; Flores-Gaspar, A.; Muñoz-Hernández, M.; Arévalo, A.; Jones, W. D.; García, J. J. *Organometallics* **2007**, *26*, 1712–1720. (g) Acosta-Ramírez, A.; Muñoz-Hernández, M.; Jones, W. D.; García, J. J. *Organometallics* **2007**, *26*, 5766–5769. (h) Acosta-Ramírez, A.; Flores-Álamo, M.; Jones, W. D.; García, J. J. *Organometallics* **2008**, *27*, 1834–1840. (i) Swartz, B. D.; Reinartz, N. M.; Brennessel, W. W.; García, J. J.; Jones, W. D. *J. Am. Chem. Soc.* **2008**, *130*, 8548–8554.

(18) For phosphine-catalyzed nucleophilic substitution reactions of allylic acetates derived from Morita−Baylis−Hillman adducts, see:(a) Cho, C.-W.; Krische, M. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 6689–6691. (b) Cho, C.-W.; Kong, J.-R.; Krische, M. J. *Org. Lett.* **2004**, *6*, 1337–1339.

(19) Childs, M. E.; Weber, W. P. *J. Org. Chem.* **1976**, *41*, 3486–3487.

Table 3. Nickel-Catalyzed Cyanoesterification of **2a** by Three-Component Coupling Reaction[a]



entry	12	ligand	solvent	yield of **3aa** (%)[b]	yield of **4aa** (%) (*E*/*Z*)[b]
1	Me_3SiCN (**12a**)	PMe_2Ph[c]	toluene	1	5 (87:13)
2	**12a**	dppe	toluene	56	26 (76:27)
3	**12a**	dppp	toluene	78[d]	21[d] (62:38)[e]
4	**12a**	dppb	toluene	9	11 (82:18)
5	**12a**	dmpp	toluene	0	0
6[f]	**12a**		toluene	0	0
7[f]	**12a**		toluene	0	0
8[f]	**12a**		toluene	0	0
9	KCN (**12b**)	dppp	toluene	0	0
10	**12b**	dppp	DMF	0	0
11[g]	**12b**	dppp	DMF	0	0
12[h]	**12b**	dppp	DMF	0	0
13	CuCN (**12c**)	dppp	toluene	0	0
14	**12c**	dppp	DMF	0	0
15	$Zn(CN)_2$ (**12d**)	dppp	toluene	0	0
16	**12d**	dppp	DMF	0	0

[a] All the reaction was carried out using **11a** (1.10 mmol), **12** (1.10 mmol), **2a** (1.00 mmol), $Ni(cod)_2$ (0.100 mmol), and a ligand (0.100 mmol) in toluene (0.67 mL). [b] Estimated by GC using tetradecane as an internal standard. [c] PMe_2Ph (0.20 mmol) was used. [d] Isolated yield. [e] Calculated based on yields of isolated products. [f] Reaction run with a 0.30 mmol-scale. [g] 18-crown-6 (1.10 mmol) was used. [h] Bu_4NBr (1.10 mmol) was used.

4). An electron-donating variant having dimethylphosphino groups completely retarded the reaction (entry 5). Chiral analogues of dppp and dppe were not effective unfortunately (entries 6−8). Other metal cyanides such as KCN, CuCN, and $Zn(CN)_2$ were not effective in toluene or DMF even in the presence of a crown ether or a phase-transfer catalyst (entries 9−16).

With the nickel/dppp catalyst, we next examined the scope of the three-component cyanoesterification of **2a** and found that those having an internal triple bond, methoxyethyl, chloroethyl, and (−)-mentyl all participated in the three-component reaction (Table 4). To our regret, however, no diastereoselection (50:50) was attained with optically pure chloroformate ester **11e** (entry 4).

The scope of 1,2-dienes for the three-component strategy was found to be broad as is demonstrated in Table 5. Ethyl chloroformate (**11a**) and trimethylsilyl cyanide (**12a**) reacted with primary, secondary, and tertiary alkyl-substituted allenes in yields and with regioselectivity both comparable to the direct cyanoesterification (entries 1−3). Similar functional group tolerance was also observed (entries 4−8). The reaction with **2h** showed the diastereoselectivity similar to that observed with the reaction using ethyl cyanoformate (entry 5). On the other hand, 1,2-dienes **2l** and **2n**−**2p** showed reversed regioselectivities (entries 9−12). Phenylallene (**2o**) and chiral *N*-allenyloxazolidinone **2p** were applicable to this three-component reaction to give linear adducts **4**, while no trace amount of adducts was obtained in the direct cyanoesterification of these 1,2-dienes (entries 10 and 11). No trace amount of adduct, however, was obtained with 5,6-dodecadiene (**2m**).

The following experiments were performed to gain a mechanistic insight into the three-component coupling reaction. Reaction of ethyl cyanoformate (**1a**) with **2a** in the presence of trimethylsilyl chloride did not proceed at all (eq 1). This together with the observed poor activity of nickel/dppp for the reaction of **1a** with **2a** (entry 8 of Table 1) excludes a reaction path that goes through in situ generation of **1a** from **11a** and **12a** and its subsequent addition across 1,2-dienes. An alternative pathway involving chloroesterification of 1,2-dienes[20] with **11a** followed by cyanation of the resulting substituted allylic chloride is unlikely based on the fact that no chloroesterification products were obtained by the reaction of **11a** with **2a** under the nickel/dppp catalysis (eq 2), though ethyl *β*-chloromethylacrylate underwent a cross-coupling reaction with **12a** in the presence of the nickel/dppp catalyst to give **3ab** in 71% yield (eq 3). Finally, a reaction sequence may involve nickel-catalyzed silylcyanation of **2a**[21] with **12a** followed by cross-coupling of the resulting alkenylsilanes with chloroformate esters. Because

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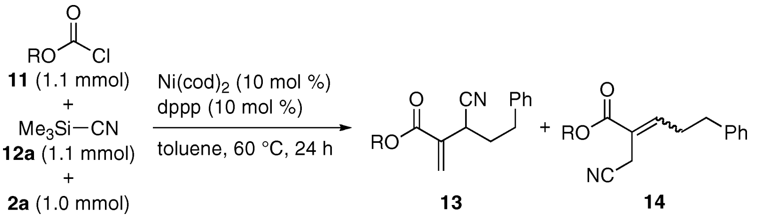
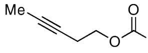
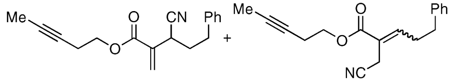
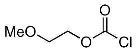
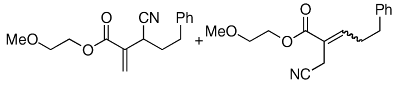
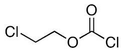
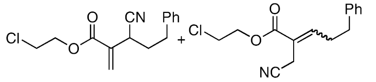
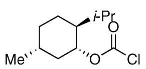
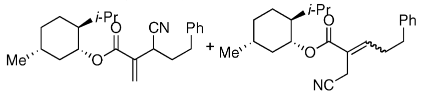
(20) Hua, R.; Tanaka, M. *Tetrahedron Lett.* **2004**, *45*, 2367–2370.

(21) Chatani, N.; Takeyasu, T.; Hanafusa, T. *Tetrahedron Lett.* **1986**, *27*, 1841–1844.

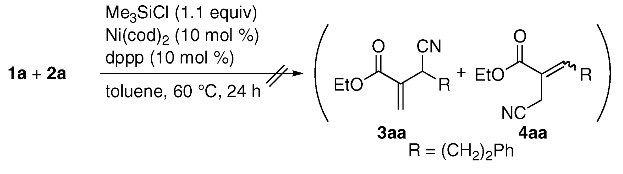
Table 4. Nickel-Catalyzed Cyanoesterification of **2a** by Three-Component Coupling Reaction: Scope of Chloroformate Esters[a]



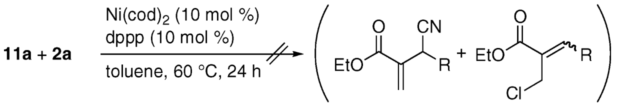
entry	11	products (*E*/*Z* of **14**)[b]	yield (%)[c] (**13**:**14**)
1	 **11b**	 **13ba**, **14ba** (75:25)	72 (61:39)
2	 **11c**	 **13ca**, **14ca** (65:35)	69 (83:17)
3	 **11d**	 **13da**, **14da** (72:28)	96 (81:19)
4	 **11e**	 **13ea**, **14ea** (67:33)	75 (84[d]:16)

[a] All the reaction was carried out using **11** (1.10 mmol), **12a** (1.10 mmol), **2a** (1.00 mmol), Ni(cod)$_2$ (0.100 mmol), and dppp (0.100 mmol) in toluene (0.67 mL). [b] Calculated based on isolated yields of (*E*)- and (*Z*)-**14**. [c] Isolated yield of **13** and **14**. [d] dr = 50:50 as estimated by ^{1}H NMR analysis of an isolated product.

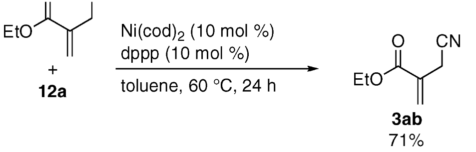
no silylcyanation of **2a** was observed with the nickel/dppp catalyst (eq 4), this possibility can also be ruled out.



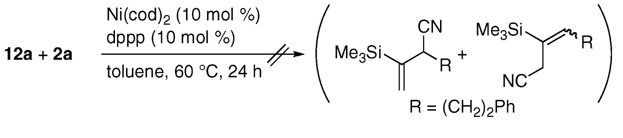
(1)



(2)



(3)



(4)

Based on these results, two reaction pathways (path A and path B) are suggested in Scheme 2. In each cycle, catalysis should be initiated by oxidative addition of a C−Cl bond in **11** to nickel(0) to give **15**. Subsequent coordination of 1,2-dienes to the nickel center in **15** would give **16** rather than **19** due to the sterics. Migratory insertion of the alkoxycarbonyl group on nickel affords π-allylnickel chloride intermediate **17**, which undergoes transmetalation with **12a** to give π-allylnickel cyanide **18**. Reductive elimination of **18** gives **3** and regenerates nickel(0)/dppp (path A). Alternatively, transmetalation may precede migratory insertion to give **20**, which then undergoes coordination of 1,2-dienes followed by migratory insertion of the coordinating 1,2-dienes and reductive elimination (path B). Formation of regioisomer **4** would be derived from such coordination of 1,2-dienes in an opposite direction as depicted in **19** or π-allylnickel intermediate **22**, both intermediates suffering from steric repulsion between R^2 and diphenylphosphino groups.

In cases of 1,2-dienes **2k** and **2n**−**2p**, reductive elimination from π-allylnickel intermediate **18** may be hampered by intramolecular coordination of carbonyl or phenyl groups (Scheme 3) to allow σ−π−σ isomerization to π-allynickel intermediates **22b**, which reductively eliminate **4** as a major product with these particular 1,2-dienes.

In the case of **2l**, the nickel center of 1,2-diene-nickel species **23** coordinated by two diphenylphosphino groups of dppp (Scheme 4) would suffer from a greater steric bulk compared with related intermediate **6** having a monophosphine ligand (Scheme 1). Therefore, migratory insertion followed by reductive elimination of **4al** from intermediate **24** would be favored rather than formation of π-allylnickel intermediate **25**, which would be responsible for formation of **3al**.

Transformations of 1,2-Diene-Cyanoesterification Products. The cyanoesterification products thus obtained have both α,β-unsaturated ester and allylic cyanide functionalities, which can be transformed orthogonally (Scheme 5). Cyanoesterification product **3al**

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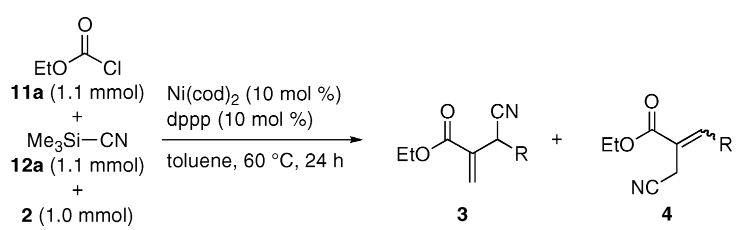
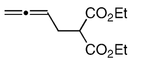
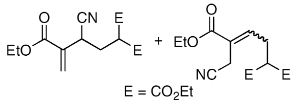
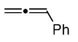
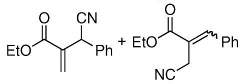
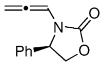
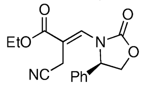
(22) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1978**, *100*, 3240–3241.

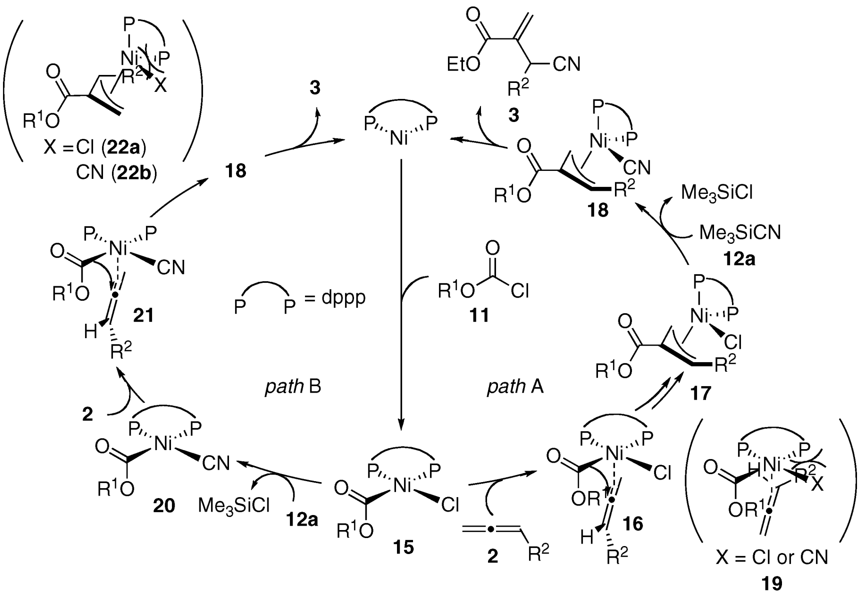
Table 5. Nickel-Catalyzed Cyanoesterification of 1,2-Dienes by Three-Component Coupling[a]



entry	2	product(s) (E/Z of **4**)[b]	yield (%)[c] (**3**:**4**)
1	**2c**	**3ac**, **4ac** (60:40)	84 (88:12)
2	**2d**	**3ad**, **4ad** (75:25)	84 (86:14)
3	**2e**	**3ae**, **4ae** (87:13)	77 (99:1)
4	**2g**	**3ag**, **4ag** (57:43)	81 (83:17)
5	**2h**	**3ah**, **4ah** (72:28)	84 (69[d]:31)
6	**2i**	**3ai**, **4ai** (50:50)	91 (80:20)
7	**2j**	**3aj**, **4aj** (60:40)	84 (85:15)
8	**2k**	**3ak, 4ak** (>95:5)	82 (49:51)
9	**2l**	**3al**, **4al** (—)	84 (17:83)
10	 **2n**	 **3an**, **4an** (66:34)	80 (49:51)
11	 **2o**	 **3ao**, **4ao** (87:13)	54 (13:87)
12	 **2p**	 (E)-**4ap** (>95:5)	28 (5:>95)

[a] All the reaction was carried out using **11a** (1.10 mmol), **12a** (1.10 mmol), a 1,2-diene (1.00 mmol), Ni(cod)$_2$ (0.100 mmol), and dppp (0.100 mmol) in toluene (0.67 mL). [b] Calculated based on isolated yields of **4**. [c] Isolated yield of **3** and **4**. [d] dr = 81:19 as estimated by ^{1}H NMR analysis of an isolated product.

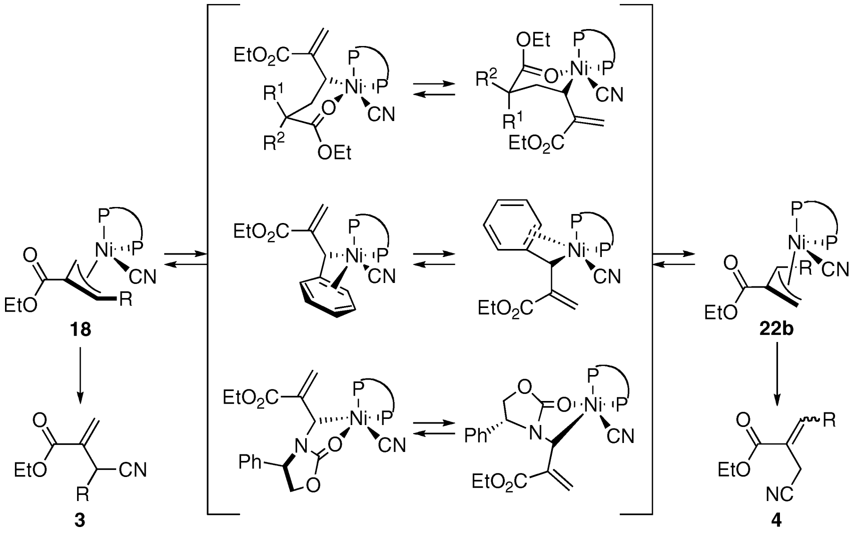
Scheme 2. Plausible Mechanism of Cyanoesterification of 1,2-Dienes by Three-Component Coupling



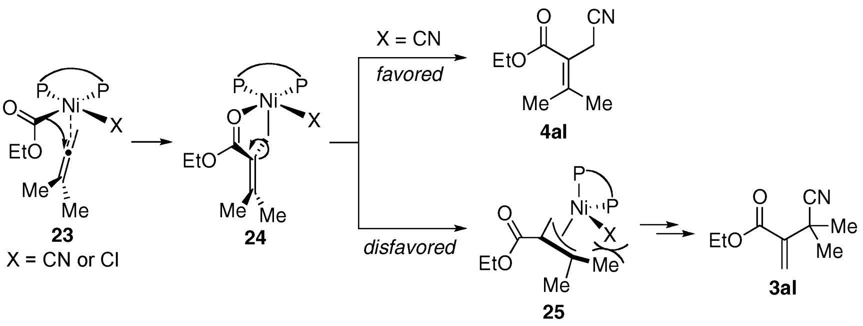
underwent 1,4-addition reactions with butylcopper/BF$_3$·OEt$_2$[22] or sodiomalonate to give the corresponding β-cyano esters **26a** and **26b**, respectively. Subsequent treatment of **26a** with NaBH$_4$ in the presence of CoCl$_2$ afforded γ-lactam **27** through reduction of the cyano group to aminomethyl followed by lactamization.[23]

The allylic cyanide moiety can participate in the carbocyanation reaction across alkynes. For example, cyanoesterification product **3aa** added across 4-octyne in the presence of a nickel/P(4-CF$_3$−C$_6$H$_4$)$_3$

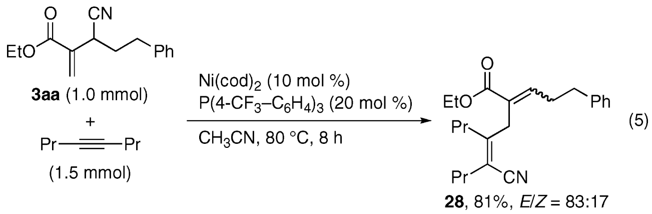
Scheme 3. Plausible Mechanism for the Formation of **4** from **2k** and **2n**−**2p**



Scheme 4. Plausible Mechanism for the Formation of **4al** from **2l** through the Three-Component Coupling



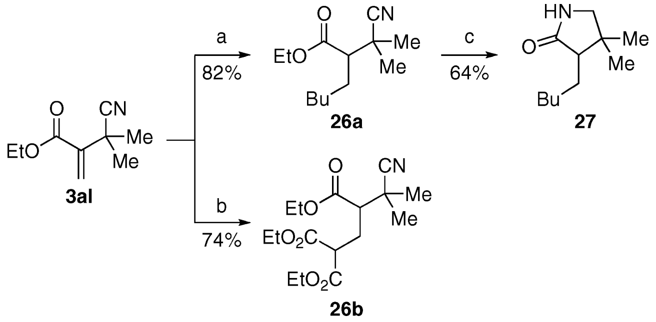
catalyst to regioselectively give trisubstituted acrylonitrile **28** in 81% yield as a mixture of stereoisomers (eq 5).[6]



Conclusion

Cyanoformates are demonstrated to add across 1,2-dienes regio- and stereoselectively in the presence of a nickel/PMe$_2$Ph catalyst. Accordingly, preparation of variously functionalized β-cyano-α-methylene alkanoates is achieved regioselectively. Cyanoesterification of 1,2-dienes has been attained also by the three-component coupling of chloroformate esters, trimethylsilyl cyanide, and 1,2-dienes with a nickel/dppp catalyst as an alternative and convenient protocol to introduce various alkoxycarbonyl and cyano groups to 1,2-dienes in a single operation. The resulting cyanoesterification products would serve as synthetically useful building blocks for γ-aminobutyric acid, β-amino acids,[24] and 1,2-dicarboxylic acid derivatives.

Scheme 5. Transformations of the Cyanoesterification Products[a]



[a] Reagents and Conditions: (a) BuLi, CuI, BF$_3$·OEt$_2$, Et$_2$O, −70 °C to rt, 5 h; (b) NaCH(CO$_2$Et)$_2$, THF, 0 °C to rt, 1 h; (c) NaBH$_4$, CoCl$_2$, EtOH, 0 °C to rt, 9 h.

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

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