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Dimerization of terminal alkynes catalyzed by a nickel complex having a bulky phosphine ligand

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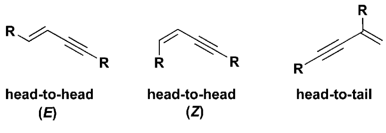
$Ni(cod)_2/P^tBu_3$ system catalyzed the dimerization of terminal alkynes to give (E)-head-to-head dimerization products, in which the stannylacetylene dimer could be applied to a one-pot synthesis of a conjugated enyne, when combined with Migita-Stille coupling.

The dimerization of terminal alkynes is one of the most useful and economical reactions to give conjugated enyne compounds, which are important for the synthesis of natural products.[1] However, only a limited number of highly selective syntheses of conjugated enynes by a dimerization have been reported[2] due to the competitive formation of undesired isomers (Scheme 1). In particular, the (*E*)-head-to-head dimerization is limited to aryl acetylene,[2a] silyl acetylene,[3a,b] or cyclohexenyl acetylene.[3c] Thus, a more efficient catalyst for the (*E*)-head-to-head dimerization remains to be developed.

In the (*E*)-head-to-head dimerization catalyzed by a Pd species bearing bulky $P(2,6\text{-}(MeO)_2C_6H_3)_3$[2a] or 1,3-dimesitylimidazolin-2-ylidene,[3c] the reaction course might be governed by the steric congestion in a coordination sphere. We envisaged that a tighter coordination sphere in the Group 10 metal complex would be more efficient for the dimerization of terminal alkynes to give (*E*)-head-to-head conjugated enynes and the steric effect of ligands on the reaction would be maximized by the smallest radius of nickel. Here, we report that regioselective (*E*)-head-to-head dimerization of terminal alkynes is catalyzed by a nickel catalyst having a bulky phosphine ligand.

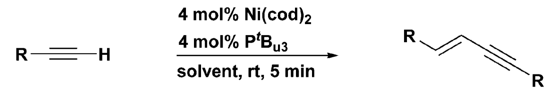
In the presence of 4 mol% of $Ni(cod)_2$ and P^tBu_3 (cone angle: 182°, pK_a: 11.4), the (*E*)-head-to-head dimerization of PhC≡CH proceeded very rapidly to give (*E*)-1,4-diphenylbut-3-en-1-yne (**1**) (57%) at room temperature for 5 min.[4] Although trimerization products (43%) were generated as by-products, the reaction proceeded extremely rapidly under very mild conditions and only one isomer was obtained among possible dimerization products. Various phosphine ligands were also examined for this dimerization reaction. (*E*)-Head-to-head dimerization proceeded to give compound **1** only in the presence of a very bulky (cone angle > 180°) and highly basic (pK_a > 9.3) phosphine, such as $P[2,6\text{-}(OMe)_2C_6H_3]_3$ (184°, 9.33, 42%) or $P[2,4,6\text{-}(OMe)_3C_6H_2]_3$ (184°, 11.0, 22%). The former requirement would be for the control of regiochemistry, and the latter would be for the strong coordination to nickel. The other ligands, P(*o*-tol)$_3$ (194°, 3.08), PCy_3 (170°, 9.70), PPh_3 (145°, 2.73), and P^nBu_3 (132°, 8.43), gave only a mixture of 1,3,5- and 1,2,4-triphenylbenzene.

The reaction can be applied to other alkynes (Table 1). Better selectivity was attained in a solution of C_6D_6/CD_3CN (1/1) at 80 °C than that in C_6D_6 (entries 1–4). The reaction of 2-methylphenylacetylene gave the corresponding dimer (**3**) in 92% yield, which indicates that a bulkier substituent group is more favorable for the (*E*)-head-to-head dimer (entries 3 and 5). 4-Methoxyphenylacetylene underwent the dimerization to give the dimer (**4**) in 88% yield, however the reaction of 4-chlorophenylacetylene gave the dimer (**5**) in 21% yield. 1-Octyne and 3,3-dimethyl-1-butyne also underwent dimerization to give **6** and **7** respectively, in moderate yields (entries 8 and 9).



Scheme 1 Possible isomers.

Table 1 Dimerization of alkyne



Entry	R	Conditions[a]	Product	Yield (%)
1	Ph	C_6D_6	**1**	57[b]
2	Ph	C_6D_6/CD_3CN (80 °C, 2 h)	**1**	73[b]
3	4-Me-C_6H_4	C_6D_6	**2**	70[b]
4	4-Me-C_6H_4	C_6D_6/CD_3CN (80 °C, 1 h)	**2**	87[b]
5	2-Me-C_6H_4	C_6D_6	**3**	92
6	4-MeO-C_6H_4	C_6D_6	**4**	88
7	4-Cl-C_6H_4	C_6D_6	**5**	21[b]
8	^{n}Hex	C_6D_6	**6**	28[c]
9	^{t}Bu	C_6D_6	**7**	51[c]
10	Me_3Si	C_6D_6	**8**	67[c]
11	Me_3Si	CD_3CN (2 h)	**8**	97
12	Me_3Si	neat (0.5 mol% cat., 1 h)	**8**	70(61)[d]
13	Me_2PhSi	CD_3CN (2 h)	**9**	95
14	$^nBu_3Sn$	C_6D_6 (60 °C, 0.5 h)	**10**	88
15	$^nBu_3Sn$	neat (1 mol% cat., 2 h)	**10**	99(98)[e]

[a] Reactions were carried out at room temperature for 5 min unless otherwise stated in parenthesis. [b] Trimerization product was obtained as by-product. [c] Oligomer was obtained as by-product. [d] Isolated yield. [e] Isolated yield of (*E*)-1-tributylstannylbut-1-en-3-yne.

The dimerization of silylacetylenes proceeded in CD_3CN much more effectively than the previous methods[3] to give quantitative yield of 1,4-bis(trimethylsilyl)but-1-en-3-yne (**8**) or 1,4-bis(dimethylphenylsilyl)but-1-en-3-yne (**9**) (entries 11,13), which are very useful compounds for a variety of transformations.[3a,5] The dimerization also proceeded under neat conditions to give **8** in 61% isolated yield after distillation of reaction mixture (entry 12).

Even tributylstannylacetylene underwent dimerization to give 1,4-bis(tributylstannyl)but-1-en-3-yne (**10**) in 88% yield (entry 14). This is the first example of the dimerization of stannylacetylene. Under neat conditions, the dimerization of tributylstannylacetylene proceeded much faster at room temperature to give **10** in 98% yield (entry 15).[6] Although the isolation of **10** by column chromatography failed due to destannylation on silica to give (*E*)-1-tributylstannylbut-1-en-3-yne (**11**), the reaction mixture containing **10** could be used as a reagent for further transformation without purification. In fact, the dimerization followed by Migita–Stille coupling reaction with bromobenzene or 4-chlorobromobenzene gave **1** (95%) or **7** (77%) in much better yield than that in the dimerization of the corresponding arylacetylene (eqn. (1)). Thus, this is a very useful method to prepare a series of (*E*)-1,

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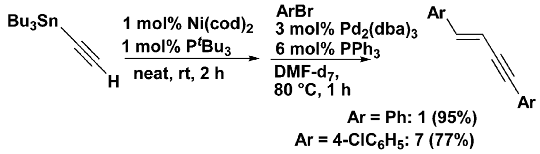
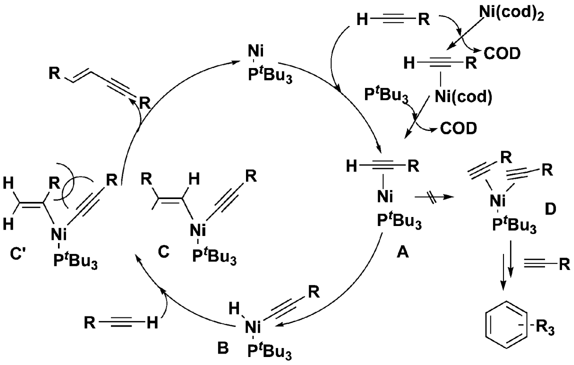
4-diarylbut-3-en-1-yne compounds.



(1)



Scheme 2

A plausible reaction path is depicted in Scheme 2. In the initial step of the reaction, the key intermediate (**A**) would be generated by the reaction of $\mathrm{P^tBu_3}$ with Ni(cod)(alkyne) concomitant with the dissociation of COD. The reaction of internal alkyne with $\mathrm{Ni(cod)_2}$ to give Ni(cod)(alkyne) had been also reported.[7] Moreover, we confirmed that $\mathrm{P^tBu_3}$ does not react with $\mathrm{Ni(cod)_2}$ even at 60 °C for 48 h in the absence of alkyne. The intermediate **A** may undergo the oxidative addition to give a hydride complex (**B**). For the (*E*)-head-to-head dimer to be formed selectively, the formation of **C** must predominate over the formation of more congested **C**′. The degree of such discrimination would become greater in the tighter coordination sphere. Therefore, the smaller transition metal, nickel, would be a better catalyst for the formation of (*E*)-head-to-head dimer. When $\mathrm{Pd(P^tBu_3)_2}$ was employed as a catalyst, the reaction required higher temperature and prolonged time (80 °C, 2 h, conversion 67%) to give a mixture of (*E*)-head-to-head (50%) and head-to-tail dimer (17%). This result shows a sharp contrast between nickel and palladium. In fact, although $\mathrm{Pd(P^tBu_3)_2}$ can be prepared easily, the corresponding $\mathrm{Ni(P^tBu_3)_2}$ was not obtained; $\mathrm{P^tBu_3}$ would be too large to form bisphosphine complex of Ni(0). It may well be that $\mathrm{Ni(P^tBu_3)}$ is involved in the catalytic cycle and has a tighter reaction site than that in the corresponding palladium complex $\mathrm{Pd(P^tBu_3)}$, if present.

For the formation of arene compounds by trimerization or oligomers to be suppressed, it seems essential to prevent unnecessary alkyne molecules from coordinating to the metal center as in **D**. In this respect the important role of acetonitrile in improving the selectivity would be the coordination to nickel. In fact, η^2-coordination of acetonitrile to nickel(0) complex has been known.[8] Similarly, introducing an electron donating group at the 4-position of the arene ring improved the selectivity, probably due to the lower coordination ability of the donating alkyne to the electron rich nickel(0) center.[9] In fact, the dimerization of 4-aminophenylacetylene, which has stronger electron donating group, can be catalyzed by even $\mathrm{Ni(CO)_2(PPh_3)_2}$ to give the corresponding (*E*)-head-to-head dimer (34%) as a mixture with trimerization products.[10] The palladium-catalyzed dimerization mentioned above[2a] is very efficient for less hindered and electron deficient aryl acetylenes, thus nickel and palladium are complementary to each other.

In conclusion, we reported the nickel-catalyzed dimerization of terminal alkynes, such as aryl-, alkyl-, silyl-, and stannylacetylene, to give the corresponding (*E*)-head-to-head dimers in moderate to excellent yields. The dimerization of tributylstannylacetylene was clean enough to be applied to a one-pot reaction, which can be a potential synthetic method for a variety of conjugated enyne compounds.

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4 To a solution of $\mathrm{Ni(cod)_2}$ (1.1 mg, 0.004 mmol) and $\mathrm{P^tBu_3}$ (0.8 mg, 0.004 mol) in $\mathrm{C_6D_6}$ (0.5 mL) was added phenylacetylene (10.2 mg, 0.1 mmol) at room temperature.

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