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Synthesis of Substituted 1,3-Butadienes Via Cyanocuprate-Mediated Transmetalations of Vinylstannanes

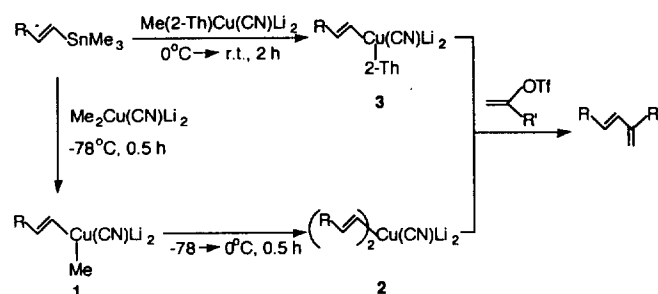
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Vinylstannanes have been widely used as masked vinyl anion equivalents in organic synthesis.¹ Transmetalation of vinylstannanes with $\text{Me}_2\text{Cu}(\text{CN})\text{Li}_2$ or $\text{Me}(2\text{-Th})\text{Cu}(\text{CN})\text{Li}_2$ (2-Th = 2-Thienyl) gives in situ generated vinyl mixed higher order(HO)cyanocuprate reagent, which is utilized for the conjugate addition of enone² and epoxide opening reaction³ in regiospecific manner. Palladium-catalyzed cross-coupling reaction of vinylstannanes with vinyl triflates⁴ or vinyl iodides⁵ is effective for the stereospecific synthesis of conjugated dienes. However, there has been no report on the cyanocuprate-mediated transmetalations of trimethylstannyl alkenes and their synthetic applications except 1,4-bis-trimethylstannyl-1,3-butadiene.⁶ Furthermore, coupling reaction⁷ of vinyl triflates with lithium dialkylcuprates affords to give the corresponding olefin, but it fails to prepare the substituted 1,3-butadienes.

In this paper we wish to report (i) in situ vinyl HO cyanocuprate formation from transmetalation of trimethylstannyl alkenes and (ii) stereospecific synthesis of substituted 1,3-



Scheme 1.

butadienes *via* coupling reaction of the vinyl HO cyanocuprates with vinyl triflates. Treatment of trimethylstannyl alkene⁸ with $\text{Me}_2\text{Cu}(\text{CN})\text{Li}_2$ in THF at -78°C for 0.5 h led to Cu/Sn exchange to give in situ generated mixed HO reagent 1 as shown in Scheme 1. Reaction of 1 with vinyl triflate at -78°C appeared to be proceeded with virtually completely selective substitution of methyl residue, whereas addition of an enone⁹ smoothly effected 1,4-addition of vinyl residue. For example, reaction of in situ $[\text{Ph}(\text{C}=\text{CH}_2)](\text{Me})\text{Cu}(\text{CN})\text{Li}_2$, generated from transmetalation of 1-phenyl-1-trimethylstannyl ethene and 1 equiv of $\text{Me}_2\text{Cu}(\text{CN})\text{Li}_2$ at -78°C , with 1-trifluoromethanesulfonyloxy-3,3,4,4-tetrahydronaphthalene gave 1-methyl-3,3,4,4-tetrahydronaphthalene in 81% yield with trace amount of the corresponding 1,3-butadiene.

Thus, it was necessary to produce in situ HO mixed cyanocuprate without methyl ligand for the exclusive vinyl substitution with vinyl triflates. Fortunately, treatment of trimethylstannyl alkenes with 0.55 equiv of $\text{Me}_2\text{Cu}(\text{CN})\text{Li}_2$ at -78°C $\sim 0^\circ\text{C}$ for 0.5 h gave reddish divinylcyanocuprate 2 in contrast with tributylstannyl alkenes and no interference was observed with tetramethyltin in the second transmetalation. Reaction of 2 with vinyl triflates smoothly proceeded with disappearing of red color and 0.75 equiv of the reagent was required for the completion of the reaction.

Anticipating the formation of in situ HO cyanocuprate not having methyl ligand, was also examined transmetalation of trimethylstannyl alkenes using $\text{Me}(2\text{-Th})\text{Cu}(\text{CN})\text{Li}_2$. In spite of somewhat slower process, $\text{Me}(2\text{-Th})\text{Cu}(\text{CN})\text{Li}_2$ was also found to undergo in situ ligand exchange with trimethylstannyl alkenes, and the resultant greenish vinyl HO cyanocuprate 3 coupled with vinyl triflates to give substituted 1,3-butadienes.

As shown in Table 1, various structurally different 1,3-butadienes could be prepared by this method without appreciable side products. The reaction worked well with 1 or 2-trimethylstannyl alkenes and aliphatic or cyclic vinyl triflates. Divinyl HO cyanocuprate generated in situ was more reactive than the corresponding (vinyl)(2-Th) $\text{Cu}(\text{CN})\text{Li}_2$ and tetramethyltin didn't interfere with the substitution of vinyl group during coupling reaction. Significantly, it has been shown that the transmetalation of trimethylstannyl alkenes and the coupling reaction with vinyl triflates occurred stereospecifically with respect to the double bond. Treatment of 2-trifluoromethanesulfonyloxy-1-heptene with $(\text{PhCH}=\text{CH})(\text{L})\text{Cu}(\text{CN})\text{Li}_2$ (L = PhCH=CH or 2-Th) gave (1E)-1-phenyl-3-pentyl-1,3-butadiene with none of the (1Z)-isomer detected by ¹H NMR. Similar treatment of 4-tert-butyl-1-trifluoromethanesulfonyloxy-1-cyclohexene with $(\text{PhCH}=\text{CH})_2\text{Cu}(\text{CN})\text{Li}_2$ gave

Table 1. Synthesis of Substituted 1,3-Butadienes from Vinyl Triflates and Trimethylstannyl Alkenes

Vinyl stannane	Vinyl triflate	Cyanocuprate	Product	Yield, % ^c
		Me ₂ Cu(CN)Li ₂ ^a		80
		Me(2-Th) Cu(CN)Li ₂ ^b		76
		Me ₂ Cu(CN)Li ₂		62
		Me(2-Th) Cu(CN)Li ₂		74
		Me ₂ Cu(CN)Li ₂		65 ^d
		Me(2-Th) Cu(CN)Li ₂		73 ^d
		Me ₂ Cu(CN)Li ₂		60 ^d

^a0.55 equiv was used. ^bThe transmetalation was carried out between 0 °C and room temperature for 1.5 h. ^cIsolated, chromatographically pure and all the compounds gave satisfactory spectral data. ^dStereochemically pure by ¹H NMR analysis.

only (1*E*)-1-styryl-4-*tert*-butylcyclohexene.

The typical experimental procedure is as follows. To a solution of copper cyanide (89.6 mg, 1.0 mmol) in THF (2 mL) was added methylolithium (1.40 mL, 1.50 M in diethyl ether, 2.1 mmol) at -20 °C under argon. After the reaction mixture was stirred for 20 min between -20° and 0 °C, the resultant colorless solution was cooled at -78 °C and 2-trimethylstannyl-1-heptene (474.2 mg, 1.82 mmol) in THF (2 mL) was added. The temperature rose to 0 °C for 0.5 h and 2-trifluoromethanesulfonyloxy-1-heptene (334.7 mg, 1.36 mmol) in THF (2 mL) was added. After 0.5 h, the reaction mixture was quenched with 10% NH₄OH/sat. NH₄Cl (30 mL) and the product was extracted with hexane (3×20 mL). The organic phase was dried over anhydrous MgSO₄, filtered, and evaporated to dryness under vacuum. The crude product was purified by silica gel column chromatography (hexane eluent) to give 211.3 mg (80%) of 2,3-dipentyl-1,3-butadiene. bp 85-90 °C/5.5 mm Hg (Kugelrohr distillation) [lit.¹⁰ 135 °C/45 mm Hg]; ¹H NMR (CDCl₃) δ 4.90 (br s, 2H_{olefin}), 4.77 (br s, 2H_{olefin}), 2.10 (t, 4H, *J*=7 Hz), 1.70-0.95 (m, 12H), 0.80 (t, 6H, *J*=7 Hz); IR (film) 3030 (=C-H), 2960, 2930, 2865, 1595 (C=C), 890 (1,1-disubstituted), 765 cm⁻¹.

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Aromatization of Hantzsch 1,4-Dihydropyridines with Pyridinium Dichromate

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Calcium channel blockers of the 3,5-bis(alkoxycarbonyl)-2,6-dimethyl-1,4-dihydropyridines (**1**, Hantzsch 1,4-DHP) are currently used for the treatment of cardiovascular disease. These compounds undergo oxidative metabolism in the liver to form the pyridine derivatives, which become biologically inactive.¹ In this respect, the convenient preparation of pyridines from 1,4-dihydropyridines is important for the identification of metabolites.

Aromatization of 1,4-DHP has been achieved using various oxidants² such as nitric acid,³ oxygen,⁴ HNO₂/bentonite,⁵ CrO₃/AcOH,⁶ pyridinium chlorochromate (PCC) adsorbed on a solid support,⁷ clay-supported cupric nitrate,⁸ cerium ammonium nitrate,⁹ MnO₂/bentonite¹⁰ or KMnO₄.¹¹ Previously, we reported that pyridinium dichromate (PDC) can be used as an oxidant for the aromatization of 2-pyrrolines.¹² To further illustrate the use of PDC-induced aromatization, the oxidation of Hantzsch 1,4-DHP was investigated in this work.

We found that Hantzsch 1,4-DHP **1**, prepared according to the known procedure,¹³ can be oxidized to pyridines **2**