A New Simple Synthesis of Isomerically Pure α,β-Unsaturated Nitriles *via* Hydroboration of Alkynes

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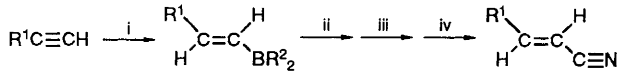
Terminal alkynes are converted into (*E*)-1-cyanoalk-1-enes in good yields *via* hydroboration followed by reaction with copper(I) cyanide and copper(II) acetate in the presence of a small amount of water, in hexamethylphosphoric triamide.

Although many useful synthetic reactions using organoboranes have been reported,[1] these do not include a procedure for synthesis of α,β-unsaturated nitriles. Previously we reported the first synthesis of one-carbon homologated secondary alkanenitriles from internal alkenes by use of sodium trialkylcyanoborates followed by reaction with sodium cyanide and lead(IV) acetate.[2] Recently we also reported a high yield synthesis of primary alkanenitriles from terminal alkenes *via* hydroboration followed by reaction with copper(I) cyanide, copper(II) acetate monohydrate, and acetylacetonatocopper(II) in tetrahydrofuran (THF).[3]

Applications of the above procedures without modification to a synthesis of α,β-unsaturated nitriles, potentially useful intermediates in organic synthesis, from alkynes *via* alkenyldialkylboranes, failed to give satisfactory results (20–30% yields in the latter procedure). However, a minor modification of the latter procedure was found to be effective for the synthesis of such unsaturated nitriles. Thus, treatment of (*E*)-hex-1-enylbis(1,2-dimethylpropyl)borane,[4] prepared by hydroboration of hex-1-yne with bis(1,2-dimethylpropyl)borane in THF, with excess of copper(I) cyanide and copper(II) acetate in the presence of hexamethylphosphoric triamide (HMPT) and a small amount of water gave (*E*)-1-cyanohex-1-ene in 88% yield (estimated by GLPC), unaccompanied by any by-product (for example 2,3-dimethylbutanenitrile which could have been formed from the 1,2-dimethylpropyl group on the boron atom) (Scheme 1). A similar reaction with dicyclohexylborane[5] also afforded (*E*)-1-cyanohex-1-ene, together with cyclohexanecarbonitrile in 3% yield as a by-product. The presence of a small amount of water is essential[3,6] for formation of the cyanoalkene. The presence of HMPT as the co-solvent markedly promoted the reaction.[7]†



Scheme 1 *Reagents and conditions*: i, R^2_2BH, THF, −15 °C for 30 min then 0–5 °C for 3 h; ii, CuCN and THF, −15 °C for 30 min then 20 °C for 1 h; iii, $(Me_2N)_3P(O)$, −15 °C for 30 min then 20 °C for 1 h; iv, $Cu(OAc)_2$, THF and H_2O, −15 °C for 30 min then 20 °C for 15 h. R^1 = alkyl or phenyl, R^2 = 1,2-dimethylpropyl or cyclohexyl.

Similarly good yields of the corresponding cyanoalkenes were obtained by reactions using representative terminal alkynes as the starting materials. In the reaction employing hex-3-yne, an internal alkyne, the yield of (*E*)-3-cyanohex-3-ene was slightly lower. The cyanoalkenes thus obtained were isolated from the worked-up[8] reaction mixtures by simple column chromatography.‡ Results are in Table 1.

For comparison we attempted to synthesize (*Z*)-1-cyanoalk-1-enes by similar reactions employing (*Z*)-1-alkenyldialkylboranes.[9] The desired (*Z*)-isomers were produced with good stereoselectivity (*E*:*Z*, *ca.* 6:94), though the yields were unsatisfactory (*ca.* 35%), and modifications are required to increase the yields.

Existing methods for synthesis of (*E*)-1-cyanoalk-1-enes are based on cyanation of (*E*)-1-haloalk-1-enes using metal cyanides catalysed by transition metals;[10] (*Z*)-1-cyanoalk-1-

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† The solubilities of the copper reagents increased by the presence of HMPT. In addition, the basicity of HMPT is likely to depress the protonation[1] of the alkenyl groups by acetic acid generated during the reaction.

‡ After filtration the reaction mixtures was washed and extracted with aqueous NH_4Cl and diethyl ether, followed by oxidation with $NaBO_3{\cdot}4H_2O$ in H_2O and THF.[8] Then the mixture was washed and extracted with brine and diethyl ether, and dried over anhydrous Na_2SO_4. The pure product isolated from the worked-up reaction mixture (consisting of the cyanoalkene and an almost quantitative amount of alcohol derived from the residual dialkly groups) by flash column chromatography (silica gel, pentane–dichloromethane) gave satisfactory spectral data (IR, ^1H NMR, ^{13}C NMR, mass).

Table 1 Synthesis of cyanoalkenes from alkynes *via* hydroboration by dialkylboranes[a]

		Yield[c] (%)	
Alkyne	Nitrile[b]	*A*[d]	*B*[e]
Hex-1-yne	(*E*)-Bu^{n}CH=CHCN	10[f]	
		22[g]	25[g]
		65[h]	
		86(81)[i,j]	88(82)[i,k]
Oct-1-yne	(*E*)-C_6H_{13}CH=CHCN	85	87(84)[i,k]
Cyclohexylacetylene	(*E*)-(c-C_6H_{11})CH=CHCN	84	86(83)[i,k]
tert-Butylacetylene	(*E*)-Bu^{t}CH=CHCN	81	84(78)[i,k]
Phenylacetylene	(*E*)-PhCH=CHCN	72[l]	73[l](71)[i,k]
Hex-3-yne	(*E*)-EtCH=C(Et)CN	62	65(58)[i,k,m]

[a] The reactions were carried out using the dialkylborane (20 mmol), alkyne (20 mmol), $Cu_2(CN)_2$ (60 mmol), $Cu(OAc)_2$ (80 mmol), H_2O (20 mmol), $(Me_2N)_3P{=}O$ (10 ml), and THF (total, 100 ml) under argon. [b] The *Z*-isomers were not detected by GLPC. [c] By GLPC based on alkynes employed. [d] By use of dicyclohexylborane. [e] By use of bis(1,2-dimethylpropyl)borane. [f] In the absence of H_2O. [g] In the absence of HMPT. [h] By use of $Cu(OAc)_2{\cdot}H_2O$ (80 mmol); without addition of H_2O. [i] Isolated. [j] The purity is 96%. [k] The purities are above 98%. [l] As a by-product, a 22% yield of styrene is produced. [m] As a by-product a 25% yield of (*E*)–EtCH=C(Et)OAc eluted after the nitrile.

enes are generally synthesized from aldehydes by reactions using trialkylsilylacetonitriles.[11]

Previously Zweifel and co-workers reported an interesting synthesis of (*E*)-α,β-unsaturated nitriles *via* hydroalumination of alkynes followed by cyanation employing cyanogen.[12] Our method seems to be easier and more practical than Zweifel's, because it uses the simple hydroboration procedure; also, the cyanation procedure does not require carefully controlled conditions.

Thus, the present reaction provides a simple synthesis of 1-cyanoalk-1-enes, valuable synthetic intermediates, from terminal alkynes in an anti-Markownikow manner.

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