Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 48 (2007) 2299–2301
Tetrahedron Letters

One-pot synthesis of conjugated alkynenitriles from aldehydes

Joong-Gon Kim,[c] Eun Hwa Lee[a] and Doo Ok Jang[a,b,*]

[a] *Department of Chemistry, Yonsei University, Wonju 220-710, Republic of Korea*
[b] *Center for Bioactive Molecular Hybrids, Yonsei University, Seoul 120-749, Republic of Korea*
[c] *Biotechnology Division, Hanwha Chemical R&D Center, Daejeon 305-345, Republic of Korea*

Received 15 December 2006; revised 24 January 2007; accepted 30 January 2007

Abstract—A method of preparing conjugated alkynenitriles was developed from various aldehydes with CCl_3CN and PPh_3 in the presence of ^{t}BuLi. The reaction proceeded via α-chlorovinyl nitrile as an intermediate without any side reactions such as chlorination of starting aldehydes.

Conjugated alkynenitriles have been utilized for synthesizing various carbocyclic and heterocyclic compounds under nucleophilic addition and cycloaddition reaction conditions.[1] Many methods have been reported for preparing the conjugated alkynenitriles including the reaction of metallated acetylides with halocyanides,[2] and the dehydration of acetylenic carboxamates with dehydrating agents.[3] It has been reported that acetylenic halides or acetylene derivatives were transformed into the conjugated alkynenitriles by using cyanating reagents such as cuprous cyanide,[4] 1-cyanoimidazole,[5] or 1-cyanobenotriazole.[6] Recently, the intramolecular Wittig reaction of β-oxo-alkylidenetriphenylphosphoranes for the synthesis of the conjugated alkynenitriles was described by Rao.[7] However, these methods limit their applicability because of their drawbacks. The precursors had to be prepared or toxic reagents had to be used under difficult reaction conditions. Here we report an efficient one-pot procedure for converting aldehydes into the corresponding conjugated alkynenitriles with Ph_3P and CCl_3CN.

When reagent **1** which was prepared from Ph_3P and CCl_3CN in situ was treated with ^{t}BuLi at −78 °C, a brown color was immediately observed, indicating the formation of an ylide. After adding 4-nitrobenzaldehyde, the mixture was treated with ^{t}BuLi. This simple process furnished the product, 3-(4-nitrophenyl)propynenitrile, in 87% isolated yield (Table 1, entry 1).

We optimized the reaction by varying the bases and temperatures. Using an excess of the reagents did not affect the yields of the product (entries 2–4). The reaction did not proceed at −78 °C at the second step with ^{n}BuLi or ^{t}BuOK (entries 5 and 7). However, when the temperature of the second step was increased to room temperature, the reaction proceeded smoothly giving high yields of the product (entries 6 and 8). These experiments showed that low temperature was not necessary for the second step. The whole procedure could be carried out at room temperature.

The reaction proceeded via α-chlorovinyl nitrile, **5** ($R = 4\text{-}NO_2C_6H_4$), as an intermediate, which was isolated and characterized showing the *Z*-isomer exclusively. It has been reported that α-chlorovinyl nitrile was produced when **1** was treated with PPh_3 and an excess of aldehydes (Scheme 1).[8] However, the yield of the α-chlorovinyl nitrile was very poor (based on the amount of aldehydes), and an extra Ph_3PCl_2 was generated giving chlorinated products such as (dichloromethyl)benzene as a by-product. Therefore, the method is not suitable for the generation of α-chlorovinyl nitriles.

The present method was applied to the conversion of various aldehydes into the conjugated alkynenitriles to examine the generality of the reaction. The results are presented in Table 2. Benzaldehyde gave

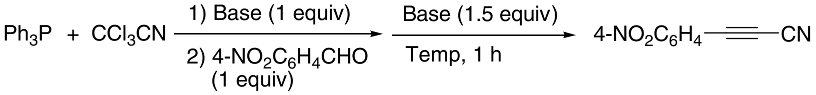
---

Keywords: Alkynenitrile; Aldehyde; Trichloroacetonitrile; Ylide; α-Chlorovinyl nitrile.

* Corresponding author. Tel.: +82 337602261; fax: +82 337602208; e-mail: dojang@yonsei.ac.kr

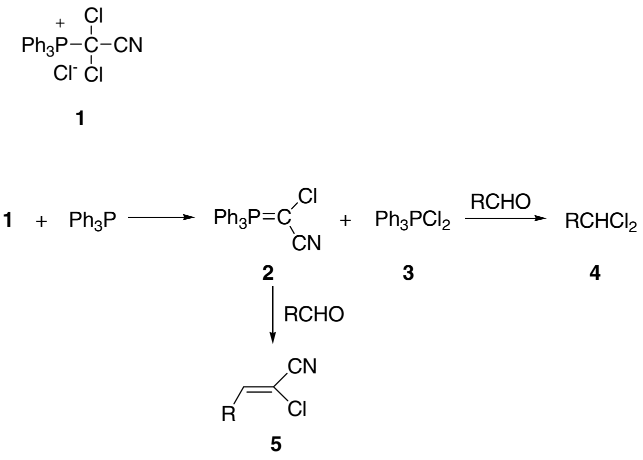
0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.01.157

Table 1. Reaction of 4-nitrobenzaldehyde with **1** under various reaction conditions



Entry	Ph_3P	CCl_3CN	Base	Temperature (°C)	Yield (%)
1	1	1	^{t}BuLi	−78	87
2	1	1	^{t}BuLi	−78	89[a]
3	2	2	^{t}BuLi	−78	88
4	2	2	^{t}BuLi	−78	90[a]
5	1	1	^{n}BuLi	−78	0
6	1	1	^{n}BuLi	rt	85
7	1	1	^{t}BuOK	−78	0
8	1	1	^{t}BuOK	rt	73

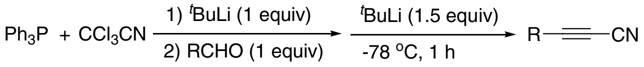
[a] 2 equiv of the base was used at the second step.

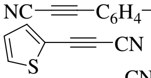
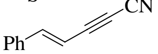
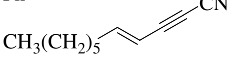


Scheme 1.

3-phenylpropynenitrile in 85% yield (entry 1). Benzaldehyde derivatives with an electron-donating group gave the corresponding alkynenitriles in somewhat lower yields (entries 2–6) than those with an electron-withdrawing group (entries 7–13). These results imply that the rate-determining step for the reaction is the addition step of ylide into aldehyde, which is very sensitive to the electronic effect. The α,β-unsaturated aldehydes were transformed into the corresponding alkynenitriles without isomerization of the double bonds (entries 15 and 16). The reaction with an aliphatic aldehyde such as octanal also proceeded smoothly (entry 17). When a sterically hindered aliphatic aldehyde such as pivalaldehyde was brought in to react under conditions, the corresponding product was obtained in low yield (entry 18). In the case of ketones such as acetophenone and isopropylacetone, the reaction did not afford the desired prod-

Table 2. Synthesis of conjugated alkynenitriles



Entry	R	Product	Yield[a] (%)
1	C_6H_5	$C_6H_5{-}\equiv{-}CN$	84
2	$2\text{-}MeOC_6H_4$	$2\text{-}MeOC_6H_4{-}\equiv{-}CN$	72
3	$3\text{-}MeOC_6H_4$	$3\text{-}MeOC_6H_4{-}\equiv{-}CN$	78
4	$4\text{-}MeOC_6H_4$	$4\text{-}MeOC_6H_4{-}\equiv{-}CN$	75
5	$3,4,5\text{-}(MeO)_3C_6H_2$	$3,4,5\text{-}(MeO)_3C_6H_2{-}\equiv{-}CN$	67
6	$4\text{-}Me_2NC_6H_4$	$4\text{-}Me_2NC_6H_4{-}\equiv{-}CN$	62
7	$3\text{-}ClC_6H_4$	$3\text{-}ClC_6H_4{-}\equiv{-}CN$	79
8	$4\text{-}ClC_6H_4$	$4\text{-}ClC_6H_4{-}\equiv{-}CN$	80
9	$2\text{-}NO_2C_6H_4$	$2\text{-}NO_2C_6H_4{-}\equiv{-}CN$	85
10	$3\text{-}NO_2C_6H_4$	$3\text{-}NO_2C_6H_4{-}\equiv{-}CN$	84
11	$4\text{-}NO_2C_6H_4$	$4\text{-}NO_2C_6H_4{-}\equiv{-}CN$	87
12	$4\text{-}NCC_6H_4$	$4\text{-}NCC_6H_4{-}\equiv{-}CN$	83
13	$4\text{-}CHO\text{-}C_6H_4$	$NC{-}\equiv{-}C_6H_4{-}\equiv{-}CN$	85[b]
14	2-Thiophenyl		70
15	Cinnamyl		91
16	(*E*)-Oct-1-enyl		81
17	$CH_3(CH_2)_6$	$CH_3(CH_2)_6{-}\equiv{-}CN$	77
18	^{t}Bu	^{t}Bu$-\equiv-$CN	47

[a] Spectroscopic data of ^1H NMR, ^{13}C NMR, and IR were in complete agreement with the assigned structures.

[b] The reaction was carried out with 2 equiv of PPh_3, 2 equiv of CCl_3CN, and 3 equiv of ^{t}BuLi.

ucts under the reaction conditions. The reactions are clean, and there are no side reactions such as chlorination of the starting aldehydes. The experimental procedure is quite simple, and the products are obtained in high isolated yields. The results show that the present procedure could be used as a general method of converting aldehydes in one-pot into the corresponding conjugated alkynenitriles.

In conclusion, we developed an efficient method of preparing conjugated alkynenitriles in one-pot manner directly from aldehydes with readily available CCl_3CN and PPh_3 in the presence of ^{t}BuLi. It is noteworthy that no side reaction such as chlorination of starting aldehydes was observed under the reaction conditions. The present process is clean and easy to perform, and it can be applied to the conversion of aldehydes into corresponding conjugated alkynenitriles.

A typical experimental procedure is as follows: ^{t}BuLi (2.94 mL, 1.7 M, 5 mmol) was added under argon at room temperature to a solution of reagent **1** which was prepared in situ by a reaction of PPh_3 (1.31 g, 5 mmol) with CCl_3CN (0.5 mL, 5 mmol) in THF (6 mL). The mixture was cooled to −78 °C, and ^{t}BuLi (4.41 mL, 1.7 M, 7.5 mmol) was added. 4-Nitrobenzaldehyde (760 mg, 5 mmol) in THF (4 mL) was added to the above mixture and the resulting mixture was stirred at −78 °C for 1 h. The mixture was then quenched with saturated aqueous NaCl (6 mL) and diluted with ether, washed with water, and dried over anhydrous $MgSO_4$. After evaporation, the residue was purified by column chromatography on silica gel eluting with hexane–EtOAc (8:2) to give 3-(4-nitrophenyl)propynenitrile (748 mg, 87%): mp 142–143 °C (lit.[7b] 139–141 °C); IR (Nujol) 2359 ($C\equiv N$), 2340 ($C\equiv C$), 1602, 1522 ($N=O$) 1463, 1346 ($N=O$) cm^{-1}; ${}^{1}H$ NMR ($CDCl_3$) δ 7.44 (d, $J = 7.9$ Hz, 2H), 7.94 (d, $J = 9.0$ Hz, 2H); ${}^{13}C$ NMR ($CDCl_3$) δ 66.6, 80.1, 104.9, 124.1, 124.2, 134.6, 149.3.

Acknowledgment

This work was supported by Center for Bioactive Molecular Hybrids at Yonsei University.

References and notes

1. (a) Sobenina, L. N.; Demenev, A. P.; Mikhaleva, A. I.; Elokhina, V. N.; Mal'kina, A. G.; Tarasova, O. A.; Ushakov, I. A.; Trofimov, B. A. *Synthesis* **2001**, 293; (b) Heard, N. E.; Turner, J. *J. Org. Chem.* **1995**, *60*, 4302; (c) Bloxham, J.; Dell, C. P. *Tetrahedron Lett.* **1991**, *32*, 4051; (d) Tanee Fomum, Z.; Forsche Asobo, P.; Landor, S. R.; Landor, P. D. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1078; (e) Merah, B.; Texier, F. *Bull. Soc. Chim. Fr.* **1980**, 552.
2. (a) Murray, R. E.; Zweifel, G. *Synthesis* **1980**, 150; (b) Compagnon, P. L.; Grosjean, B. *Synthesis* **1976**, 448.
3. (a) Mai, K.; Patil, G. *Tetrahedron Lett.* **1986**, *27*, 2203; (b) Liso, G.; Trapani, G.; Reho, A.; Latrofa, A.; Loiodice, F. *J. Chem. Soc., Perkin Trans. 1* **1983**, 567.
4. (a) Luo, F.-T.; Wang, R.-T. *Tetrahedron Lett.* **1993**, *34*, 5911; (b) Casarini, A.; Dembech, P.; Reginato, G.; Ricci, A.; Seconi, G. *Tetrahedron Lett.* **1991**, *32*, 2169.
5. Wu, Y.-Q.; Limburg, D. C.; Wilkinson, D. E.; Hamilton, G. S. *Org. Lett.* **2000**, *2*, 795.
6. Hughes, T. V.; Cava, M. P. *J. Org. Chem.* **1999**, *64*, 313.
7. (a) Rao, V. V. V. N. S. R.; Ravikanth, S.; Reddy, G. V.; Maitraie, D.; Yadla, R.; Rao, P. S. *Synth. Commun.* **2003**, *33*, 1523; (b) Yadla, R.; Rao, V. S.; Rao, J. M. *Indian J. Chem.* **1982**, *21B*, 1046; (c) Gough, S. T. D.; Trippett, S. *J. Chem. Soc.* **1962**, 2333.
8. Burton, D. J.; Greenwald, J. R. *Tetrahedron Lett.* **1967**, *8*, 1535.