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Palladium-Catalyzed Intramolecular Cyanosilylation of Alkynes Leading to Stereoselective Synthesis of α,β-Unsaturated Nitriles

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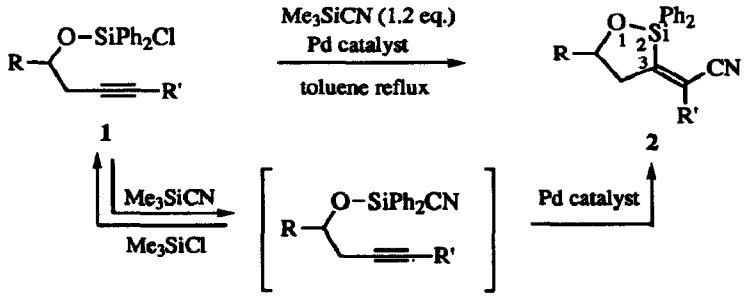
Abstract: Intramolecular cyanosilylation was achieved by the reaction of chlorodiphenylsilyl ether of homopropargylic alcohols with trimethylsilylcyanide in the presence of palladium catalyst. The reaction proceeded regio- and stereoselectively to give *(Z)*-3-(1-cyanoalkylidene)-2-silatetrahydrofurans, whose silyl group was transformed into various organic groups.

Palladium-catalyzed cyanosilylation of carbon-carbon triple bonds provides an attractive method for preparation of functionalized α,β-unsaturated nitriles.[1] The drawback of the reaction is, however, low regioselectivity in the case of internal alkynes. We herein wish to describe palladium-catalyzed intramolecular cyanosilylation of homopropargylic alcohols leading to regio- and stereoselective formation of *(Z)*-3-(1-cyanoalkylidene)-2-silatetrahydrofurans, whose silyl group was readily converted into various organic groups.

A mixture of chlorodiphenylsilyl ether[2] of homopropargylic alcohol **1** and 1.2 molar equivalent of trimethylsilylcyanide was heated in toluene under reflux in the presence of palladium catalyst to afford *(Z)*-3-(1-cyanoalkylidene)-2-silatetrahydrofurans **2** in moderate to good yields (eq.1, Table 1).[3]

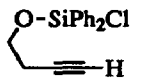
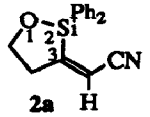
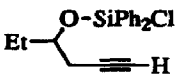
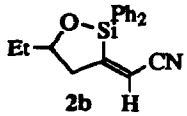
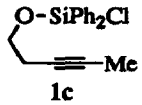
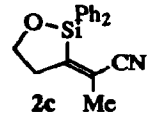
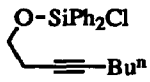
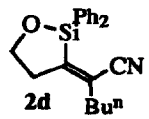
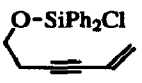
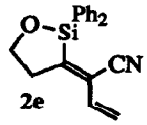


(1)

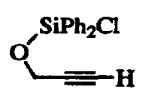
The cyanosilylation reaction proceeded stereoselectively via *exo*-ring closure. Any products derived from intermolecular cyanosilylation were not detected under the conditions. It may be presumed that cyano-chloro exchange between **1** and trimethylsilylcyanide took place prior to the palladium-catalyzed intramolecular cyanosilylation to carbon-carbon triple bond (eq.1).[4] Actually, 4-(cyanodiphenylsilyloxy)-1-butyne was distilled from the mixture of **1** and trimethylsilylcyanide. In contrast to the chlorodiphenylsilyl ethers, chlorodimethylsilyl ethers gave no cyclized products corresponding to **2**. Among palladium catalysts examined,

$Pd(acac)_2$ (acac = acetylacetonate) and $Pd_2(dba)_3CHCl_3$ (dba = dibenzylideneacetone) were the most effective, but $PdCl_2$/pyridine catalyst, which was employed for the intermolecular cyanosilylation, showed low activity.[1] Compared with terminal alkynes (entry 1,2), which are subject to oligomerization in the presence of palladium catalyst, internal alkynes underwent intramolecular cyanosilylation in better yields (entry 3,4). Conjugated enyne **1e** also cyclized via *5-Exo* ring closure to give 3-[cyano(vinyl)methylidene]-2-silatetrahydrofuran (**2e**) as a cis and trans mixture (4 : 1). The stereoselectivity was remarkably improved up to a cis/trans ratio of 13 : 1, when $Pd(acac)_2$ was used together with 1,1,3,3-tetramethylbutylisocyanide (isocyanide/Pd = 3 : 1) (entry 5).[5]

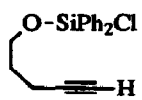
Table 1. Intramolecular Cyanosilylation of Alkynes

entry	substrate	catalyst (mol%Pd)	time (h)	product	yield (%)
1	 **1a**	$Pd_2(dba)_3CHCl_3$ (8)	10	 **2a**	57
2	 **1b**	$Pd_2(dba)_3CHCl_3$ (8)	10	 **2b**	64
3	 **1c**	$Pd(acac)_2$ (2)	5	 **2c**	84
4	 **1d**	$Pd(acac)_2$ (2)	10	 **2d**	80
5	 **1e**	$Pd(acac)_2$ (1) tOcNC (3)	12	 **2e**	65 (cis/trans =13/1)

Reactions of chlorodiphenylsilyl ethers **3** and **4** derived from propargyl alcohol and 4-pentyn-1-ol, respectively, with trimethylsilylcyanide under the conditions identical with those for **1a,b** (Table 1) did not afford any cyclized products but gave very complex mixtures. Consequently, only the formation of 5-membered ring was favorable for the intramolecular cyanosilylation.

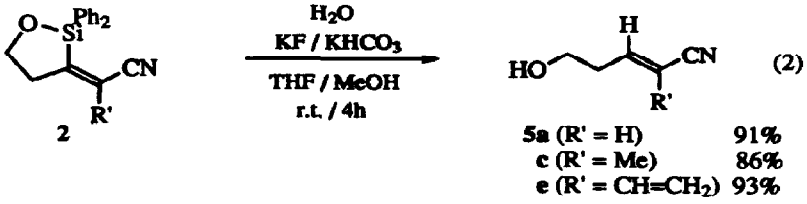


3



4

The cyclization products **2** underwent protodesilylation in the presence of KF at room temperature with retention of stereochemistry (eq.2). Thus, regio- and stereoselective hydrocyanation of homopropargylic alcohols was formally achieved by the intramolecular cyanosilylation-protodesilylation sequence.[6]



Synthetic elaboration of the cyanosilylation products is also feasible by palladium-catalyzed cross-coupling with organic halides.[7] Aryl and alkenyl iodide as well as allylic and benzylic bromide gave the corresponding coupling products **6a-d** in moderate to good yields by use of $(PPh_3)_2PdCl(CH_2Ph)$/CuI catalyst (eq.3, Table 2).[8] It is remarked that KF, which has failed to promote the palladium-catalyzed coupling reaction of alkoxy- and fluorosilylalkenes so far reported, was usable as fluoride source in the present coupling reaction. The high

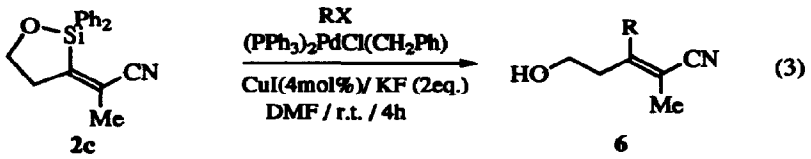
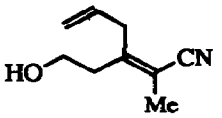
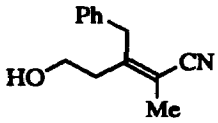
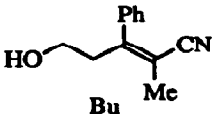
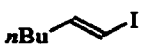
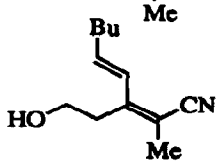


Table 2. Palladium-Catalyzed Cross-Coupling with Organic Halides

entry	organic halides	products		yield (%)
1			**6a**	90
2	$PhCH_2Br$		**6b**	67
3	PhI		**6c**	72
4			**6d**	79

reactivity of silicon-carbon bond in **2** may be given by strongly electron-withdrawing cyano group at its β-position.

The palladium-catalyzed intramolecular cyanosilylation of alkynes provides a new entry into the synthesis of regio- and stereodefined α,β-unsaturated nitriles.

General Experimental Procedure for Palladium-Catalyzed Intramolecular Cyanosilylation .
A mixture of trimethylsilylcyanide (0.84 mmol, 83 mg) , chlorodiphenylsilyl ether of homopropargylic alcohol **1** (0.70 mmol) and palladium catalyst in toluene (0.9 mL) was stirred under reflux for the period indicated above. Bulb-to-bulb distillation of the mixture (0.5 mmHg) gave cyclized product **2**.

REFERENCES AND NOTES

1) Chatani, N.; Takeyasu, T.; Horiuchi, N.; Hanafusa, T. *J. Org. Chem.* **1988**, *53*, 3539-3548.
2) **1** was prepared by simply mixing diphenyldichlorosilane and homopropargylic alcohol at 0°C under nitrogen bubbling, and isolated by distillation under reduced pressure. See also; Gillard, J. W.; Fortin, R.; Morton, H. E.; Yoakim, C.; Quesnelle, C. A.; Daignault, S.; Guindon, Y. *J. Org. Chem.* **1988**, *53*, 2602-2608.
3) Spectral data for **2**. **2a**: ^{1}H NMR (C_6D_6) δ 2.10 (dt, J = 1.6, 6.5 Hz, 2 H), 3.83 (t, J = 6.5 Hz, 2 H), 5.18 (t, J = 1.6 Hz, 1 H), 7.15-7.28 (m, 6 H), 7.87-7.95 (m, 4 H); ^{13}C NMR (C_6D_6) δ 38.0, 65.4, 106.7, 117.8, 127.6, 128.1, 131.1, 135.1, 167.7; IR (neat) 2220 , 1432, 1122 cm^{-1}. **2c**: ^{1}H NMR ($CDCl_3$) δ 2.03 (t, J = 1.6 Hz, 3 H), 2.82 (tq, J = 1.6, 6.6 Hz, 2 H), 4.33 (t, J = 6.6 Hz, 2 H), 7.38-7.59 (m, 6 H), 7.72-7.86 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 18.9, 34.7, 65.5, 117.0, 120.1, 128.0, 130.8, 130.9, 135.0, 159.1; IR (neat) 2212 , 1432, 1120 cm^{-1}. **2e**: ^{1}H NMR ($CDCl_3$) δ 3.19 (t, J = 6.5 Hz, 2 H), 4.35 (t, J = 6.5 Hz, 2 H), 5.32 (d, J = 10.3 Hz, 1 H), 5.71 (d, J = 16.9 Hz, 1 H), 6.29 (dd, J = 16.9, 10.3 Hz, 1 H), 7.39-7.56 (m, 6 H), 7.61-7.70 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 37.7, 65.6, 114.8, 119.8, 121.5, 128.4, 130.7, 131.2, 132.9, 135.0, 160.0; IR (neat) 2224 , 1432, 1122 cm^{-1}.
4) Moedritzer, K.; van Wazer, J. R. *J. Organomet. Chem.* **1966**, *6*, 242-248.
5) The isocyanide may work as ligand improving regioselectivity. See: (a) Ito, Y.; Suginome, M.; Murakami, M. *J. Org. Chem.* **1991**, *56*, 1948-1951. (b) Murakami, M.; Suginome, M.; Fujimoto, K.; Nakamura, H.; Andersson, P. G.; Ito, Y. *J. Am. Chem. Soc.* **1993**, *115*, 6487-6498.
6) (a) Jackson, W. R.; Lovel, C. G. *J. Chem. Soc., Chem. Commun.* **1982**, 1231-1232. (b) Jackson, W. R.; Perlmutter, P.; Smallridge, A. *Aust. J. Chem.* **1988**, *41*, 251-261.
7) (a) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918-920. (b) Tamao, K.; Kobayashi, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6051-6054.
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