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STEREOSELECTIVE CARBONYL OLEFINATION VIA ORGANOSILICON COMPOUNDS. BORON AND TITANIUM REAGENTS

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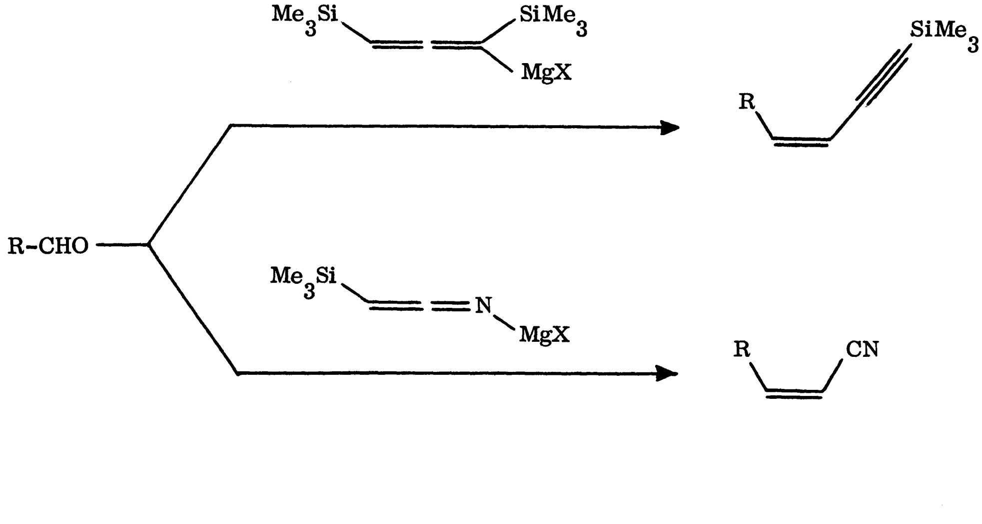
Boron reagents derived from trialkylsilylacetonitriles are effective for the synthesis of Z-α,β-unsaturated nitriles. Z-Terminal enyne units are synthesized from the titanium reagent from 1,3-bis-(trimethylsilyl)propyne and aldehydes.

We have recently described a new synthesis of Z-olefinic derivatives as exemplified in eq. 1.[1,2] It was demonstrated that the alkyl groups on silicon provide powerful steric screening effect which play an important role for the stereochemical course of the reaction.[1,2] It was also pointed out that the tightness of counterion has similar potential as a control element in stereochemistry:[1] to maximize the stereoselectivity of the reaction, "a tight chelate transition state" should be achieved, and, for example, magnesium chelate may be tighter than that for lithium, thus maximizing steric effect. Unfortunately, however, the elimination step of Peterson olefination seems to be easy · when lithium, sodium, or potassium derivatives are used, the magnesium derivatives being comparatively slow to undergo elimination.[3] This note deals with the reaction of α-silyl boron and titanium reagents with aldehydes to satisfy both of the above conflicting requirements.



(1)

Table 1 summarizes some of the results obtained in the reactions of several α-silylacetonitriles and carbonyl compounds under a variety of reaction conditions. Surprisingly, reaction of simple lithio reagent derived from (trimethylsilyl)acetonitrile[4] with cyclohexanecarbaldehyde at -78°C produced the Z-isomer with moderate stereoselectivity (entry 1).[5] In contrast to the previous observations of propargyl anions,[1] the stereochemical course of the reaction showed little dependence on the steric screening effect of silyl group, but the nature of the metal ion was crucial. Thus, the boron reagent of (trimethylsilyl)acetonitrile which is readily obtained in THF solution by sequential treatment of (trimethylsilyl)acetonitrile first with n-butyllithium[6] and then boron triisopropoxide, reacts with carbonyl compounds to produce Z-unsaturated nitriles with synthetically useful stereoselectivities. The lack of stereoselectivity with benzaldehyde as carbonyl compound was observed (entry 21-24) which may be due to the intervention of a competing electron transfer pathway[7,8] or an acyclic transition state.[9]

The following experimental procedure provides details of a typical preparation of Z-unsaturated nitriles: To a solution of (trimethylsilyl)acetonitrile (1.0 mmol) in dry THF (2 ml) was added dropwise over 5-min n-butyllithium (1.0 mmol) in hexane at -78°C. After 10 min, boron triisopropoxide (1.0 mmol) was added at -78°C and the solution was stirred there for an additional 10 min. Cyclohexanecarbaldehyde (1.0 mmol) in THF (0.5 ml) was added slowly and after 2 min dry HMPA (0.4 ml) was added to the reaction mixture and stirring was continued for 1 h. Addition of water at -78°C, extraction with ether repeatedly, concentration in vacuo, chromatography on silica gel, gave the α,β-unsaturated nitrile in 78% yield. GC analysis of the product revealed >23:1 Z-isomer.

Due to the observed high regioselectivities in the above investigations, we have sought to extend the study to the synthesis of enyne systems, Thus, 1,3-bis(trimethylsilyl)propyne was treated with tert-butyllithium (1.0 equiv, -78°C, THF, 1 h) and then with titanium tetraisopropoxide (1.0 equiv, -78°C, 10 min).[10] To the resulting solution was added cyclohexanecarbaldehyde (1.0 equiv) and the mixture was stirred at -78°C for 30 min and 25°C for 1 h. After the usual workup followed by column chromatoraphy on silica gel the Z-enyne was obtained in 87% yield (Z/E = ~20:1). Under the similar reaction conditions except using boron triisopropoxide rather than titanium tetraisopropoxide gave the Z-isomer with lower stereoselectivity (6:1) in 82% yield.[11]

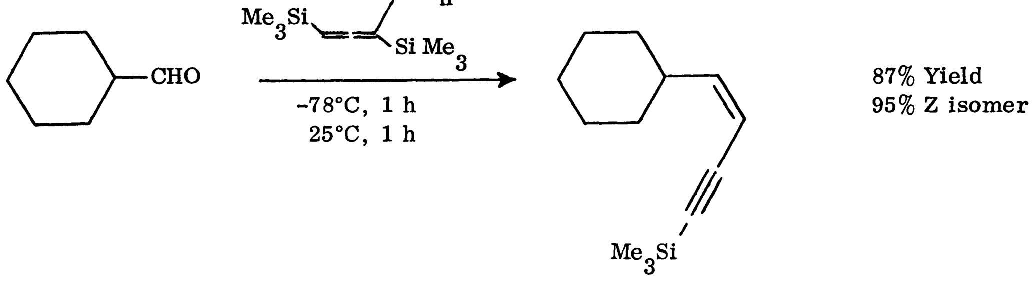


Table 1. Synthesis of α,β-Unsaturated Nitriles[a]

Entry	Aldehyde	Reagent	Metal	Conditions	% Yield[b]	Z/E[c]
1	Cyclohexanecarbaldehyde	Me_3SiCH_2CN	Li	-78°C, 1 h; 25°C, 30 min	82	7:1
2			Ti[f]	-78°C, 1 h; 25°C, 30 min	94	11:1
3			B	-78°C, 1 h; 25°C, 30 min	90	12:1
4			B	-78°C, 1 h	90	16:1
5			B	HMPA,[d] -78°C, 30 min	78	23:1
6		Ph_3SiCH_2CN	Mg	-78°C, 5 min; 50°C, 1 h[e]	80	9:1[1]
7			B	-78°C, 1 h	90	11:1
8		$^tBuMe_2SiCH_2CN$	Mg	-78°C, 5 min; 50°C, 1 h[e]	76	6:1[1]
9			B	-78°C, 1 h	85	15:1
10	Hexanal	Me_3SiCH_2CN	B	-78°C, 1 h; 25°C, 1 h	72	7:1
11			B	-78°C, 1 h	68	9:1
12			B	HMPA,[d] -78°C, 30 min	52	13:1
13		Ph_3SiCH_2CN	Mg	-78°C, 5 min; 50°C, 1 h[e]	63	5:1[1]
14			B	-78°C, 1 h	72	7:1
15	Hexenal	Me_3SiCH_2CN	Li	-78°C, 1 h	46	5:1
16			B	-78°C, 1 h	81	8:1
17			B	HMPA,[d] -78°C, 30 min	66	6:1
18		Ph_3SiCH_2CN	Li	-78°C, 1 h; 25°C, 2 h	60	2:1
19			B	-78°C, 1 h	84	6:1
20		$^tBuMe_2SiCH_2CN$	B	-78°C, 1 h	84	8:1
21	Benzaldehyde	Me_3SiCH_2CN	Li	-78°C, 1 h, 25°C, 1 h	86	3:1
22			B	-78°C, 1 h, 25°C, 1 h	90	3:1
23			B	HMPA,[d] -78°C, 30 min	71	2:1

[a] All reactions were performed as described in detail in the text.

[b] Values reported are for isolated product. NMR of RCH=CHCN (Z-isomer): R = Cyclohexyl: δ 5.15 (1H, d, J = 11 Hz), 6.23 (1H, dd, J = 10 and 11 Hz); R = n-C_5H_{11}: δ 5.22 (1H, d, J = 11 Hz), 6.37 (1H, dt, J = 7 and 11 Hz); R = $CH_3(CH_2)_2CH=CH$: δ 5.00 (1H, d, J = 10 Hz); R = Ph: δ 5.33 (1H, D, J = 12 Hz), 7.00 (1H, d, J = 12 Hz).

[c] Z/E ratio was determined by GC.

[d] HMPA was added after the addition of the aldehyde to the silylanions.

[e] Slightly higher temperature was necessary in the case of magnesio reagents.

[f] The lithio derivative was converted to Ti-reagent by the addition of $Ti(O^iPr)_4$, see ref. 10.

References

1) Y. Yamakado, M. Ishiguro, N. Ikeda, and H. Yamamoto, J. Am. Chem. Soc., 103, 5568 (1981).

2) Recently, 1,3-bis-(triisopropylsilyl)propyne was also shown to be an effective reagent for the synthesis of Z-enynes, see E. J. Corey and C. Rücker, Tetrahedron Lett., 23, 719 (1982).

3) I. Fleming in "Comprehensive Organic Chemistry, Vol. III," ed. by D. N. Jones, Pergamon Press, Oxford (1979), pp 640-644.

4) (a) I. Ojima, M. Kumagai, Y. Nagai, Tetrahedron Lett., 4005 (1974); (b) I. Matsuda, S. Murata, and Y. Ishii, J. Chem. Soc., Perkin Trans. 1, 26 (1978).

5) Longer reaction period at room temperature or the presence of excess base (lithium diisopropylamide) tends to decrease the stereoselectivity of the reaction.

6) Trimethylsilylacetonitrile was reported to undergo clean metallation with lithium diisopropylamide at low temperture (ref. 4). n-Butyllithium was found to be equally effective for the above transformation and the choice of reagent from a practical point of view.

7) The lack of stereoselectivity of the condensation of α-silylanions with aromatic aldehydes was observed previously, see ref. 1 and 2.

8) E. C. Ashby and A. B. Goel, J. Am. Chem. Soc., 103, 4983 (1981).

9) For an acyclic extended transition state of aldol reaction, see S. Murata, M. Suzuki, and R. Noyori, J. Am. Chem. Soc., 102, 3248 (1980).

10) The highly selective condensations of propargylic titanium reagents and aldehydes were reported; M. Ishiguro, N. Ikeda, and H. Yamamoto, J. Org. Chem., in press.

11) This work was partially assisted by the Asahi Glass Foundation.

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