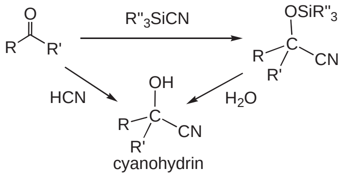
Iron-catalyzed Silylcyanation of Aldehydes and Ketones with Silyl Cyanide Prepared from Silane and Acetonitrile

Masumi Itazaki and Hiroshi Nakazawa*
Department of Chemistry, Graduate School of Science, Osaka City University, Sumiyoshi-ku, Osaka 558-8585

(Received May 6, 2005; CL-050586)

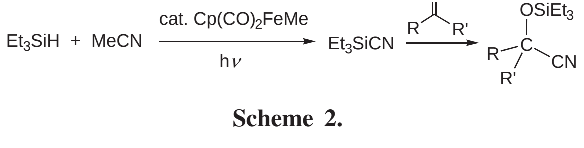
Silylcyanation of aldehyde or ketone was performed in a solution involving Et_3SiCN produced by photoreaction of Et_3SiH with MeCN in the presence of a catalytic amount of $Cp(CO)_2FeMe$ ($Cp = C_5H_5$). The iron complex derived from $Cp(CO)_2FeMe$ serves as a catalyst both for C–C bond cleavage of MeCN and concomitant Si–C bond formation and for Si–C bond cleavage in silylcyanation. The catalytic reaction mechanism has been discussed.

Cyanohydrin, RR′C(OH)CN, which is widely used in organic synthesis,[1] has been prepared mainly by hydrocyanation of aldehyde or ketone with hydrogen cyanide. Use of hydrogen cyanide is environmentally harmful because of its toxicity. Silyl cyanide has attracted considerable attention as an alternative CN source because it reacts with aldehyde and/or ketone to give the corresponding cyanohydrin silyl ether, which is readily convertible into cyanohydrin by hydrolysis (Scheme 1).



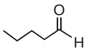
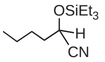
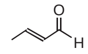
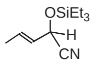
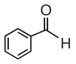
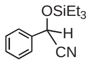
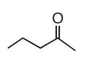
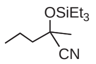
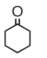
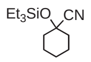
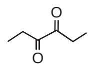
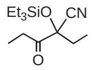
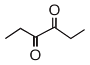
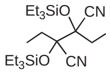
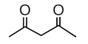
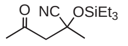
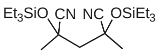
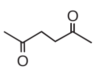
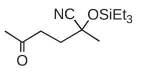
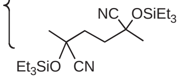
Scheme 1. Cyanohydrin formation.

This silylcyanation takes place under mild conditions using some iron catalysts such as $[Cp^*Fe(C_4H_4N)]$ ($Cp^* = C_5Me_5$) or their derivatives.[2] Without a catalyst the reaction undergoes very slowly (a half-life time of ca. 38 h).[2] Silyl cyanide is a useful CN source, but one of salient drawbacks is the use of HCN in its preparation. If silyl cyanide could be synthesized without HCN, silylcyanation of aldehyde[2,3] and ketone[3a–3c,3g,4] would become more environmentally acceptable. Recently we found a new synthetic route for preparation of silyl cyanide from silane and acetonitrile, promoted by $Cp(CO)_2FeMe$.[5] Herein we report silylcyanation reaction of aldehydes and ketones with silyl cyanide, which is prepared in situ from Et_3SiH and MeCN with an iron catalysis (Scheme 2).



Scheme 2.

Table 1. Silylcyanation of aldehydes and ketones with Et_3SiCN[a]

Entry	Substrate	Time/h	Product	Yield/%[b]
1		3		88
2		90		95
3		18		93
4		24		51
5		168		69
6		4		85
7		96		90
8		96		20
				56
9		96		19
				59

[a]Reaction conditions: triethylsilane (5.00 mmol), acetonitrile (50.00 mmol), $Cp(CO)_2FeMe$ (0.20 mmol), aldehyde (4.00 mmol) or ketone (2.00 mmol), THF (0.70 mL), room temperature, [b]Isolated yield based on the substrate.

In a typical reaction, valeraldehyde (4.00 mmol, 425 µL) was added to a solution of Et_3SiCN obtained by photolysis of a THF solution (0.70 mL) containing Et_3SiH (5.00 mmol, 0.80 mL), MeCN (50.00 mmol, 2.61 mL), and $Cp(CO)_2FeMe$ (0.20 mmol, 38.4 mg). The reaction mixture was stirred for 3 h at room temperature. After workup, $C_4H_9CH(OSiEt_3)(CN)$ was isolated in 88% yield based on valeraldehyde (Table 1, Entry 1). Table 1 presents the results of silylcyanation of several aldehydes and ketones. Both aliphatic and aromatic aldehydes are silylcyanated in excellent yields (Entries 1–3). The α,β-unsaturated aldehyde is selectively silylcyanated at the carbonyl position; no 1,4-addition product was produced (Entry 2). It is noteworthy that ketones are convertible into silylcyanated compounds in our system (Entries 4–9), but Fu reported that aliphatic ketones do not react with Et_3SiCN (catalyst: Bu_3SnCN).[3g] With α,β-diketones, a singly silylcyanated product was obtained as the main product (85% isolated yield) after the reaction for 4 h (Entry 6). In contrast, reaction for 96 h gave a doubly silylcya-

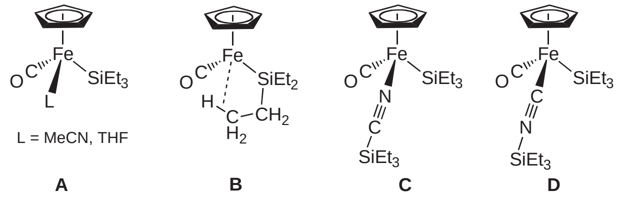
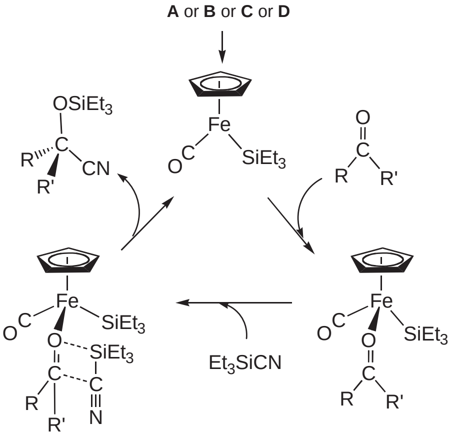


Figure 1. Plausible structures for the complex in the reaction mixture.

nated product in 90% yield (Entry 7). The ^{1}H and ^{13}C{^{1}H} NMR spectra revealed the formation of two diastereomers at 1.5:1 ratio. With α,γ-diketones and α,δ-diketones, both singly and doubly silylcyanated products were formed even after 4 h, increasing in amount with time with keeping the relative ratio, and finally (after 96 h) isolated with the latter predominating (yield: 20:56% for Entry 8, 19:59% for Entry 9). This is the first report of double silylcyanation for diketones catalyzed by a transition metal complex.[4b]

We infer that some compounds existing in our system work as catalysts. It is highly likely that a catalyst working for conversion of silane and acetonitrile into silylcyanide serves also as a catalyst for silylcyanation of aldehyde and ketone. Our previous report proposed Cp(CO)Fe($SiEt_3$) as an actual catalyst for formation of silyl cyanide.[5] The following attempts were conducted to pursue an actual catalyst. A solution of Et_3SiH (5.00 mmol, 0.80 mL), acetonitrile (50.00 mmol, 2.61 mL), and $Cp(CO)_2FeMe$ (0.50 mmol, 96.0 mg) in THF (0.7 mL) was photolyzed for 12 h and volatile compounds were removed under reduced pressure. The ^{1}H and ^{13}C{^{1}H} NMR spectra of the residue showed no signals attributable to $Cp(CO)_2FeMe$, and showed two signals attributable to Cp ring (^{1}H NMR (400 MHz, C_6D_6): $\delta = 4.42, 4.48$; ^{13}C{^{1}H} NMR (100.4 MHz, C_6D_6): δ 82.17 and 83.68). Exactly the same spectra were obtained when $Cp(CO)_2Fe(SiMe_3)$ was used in place of $Cp(CO)_2FeMe$. Addition of valeraldehyde to the above reaction mixture causes silylcyanation of the aldehyde group, giving $C_4H_9CH(OSiEt_3)(CN)$. Figure 1 displays the structures **A**–**D** which are possible for the complexes found in the reaction mixture (**A**: a solvated form, **B**: C–H agostic interactive form). Et_3SiNC contained in **D** is formed by the reaction of Et_3SiH with MeCN in the presence of Fe catalyst. Scheme 3 depicts a proposed catalytic cycle for silylcyanation. The cycle is initiated by coordination of aldehyde or ketone through its carbonyl oxygen to the 16e species, Cp(CO)Fe($SiEt_3$). Then, silyl cyanide comes near the complex to interact with O···Si and, concomitantly, with the carbonyl carbon···C in silyl cyanide, followed by completion of silylcyanation and its dissociation from the coordination sphere to regenerate Cp(CO)Fe($SiEt_3$). Recently, Shibasaki et al.[4e] and Feng et al.[4h] proposed a similar mechanism, but in these studies silyl isocyanide, instead of silyl cyanide, comes near the coordinated ketone. The possibility can not be ruled out in our case because silyl cyanide is reported to be in equilibrium with silyl isocyanide.[6]

Photoreaction of a THF solution containing Et_3SiH, MeCN, $Cp(CO)_2FeMe$, and valeraldehyde in the molar ratio shown in Table 1 caused only a trace amount of cyanohydrin silyl ether. This may be due to the reaction of active iron species (Cp(CO)FeMe or Cp(CO)Fe($SiEt_3$)) with the aldehyde rather than the acetonitrile.



Scheme 3. Plausible catalytic cycle of silylcyanation.

In summary, we found an unprecedented reaction system in which cyanohydrin silyl ether is prepared from silane, acetonitrile, and aldehyde or ketone. In this system, an iron compound, presumably Cp(CO)Fe($SiEt_3$), catalyzes both formation of silyl cyanide from silane and acetonitrile involving C–CN bond cleavage and C–Si bond formation and for silylcyanation of aldehyde and ketone involving C–Si bond cleavage.

This work was supported by a Grant-in-Aid (No. 15205010), by a Grant-in-Aid for Science Research on Priority Areas (No. 16033250, Reaction Control of Dynamic Complexes) from the Ministry of Education, Culture, Sports, Science and Technology, Japan, by the Sasagawa Scientific Research Grant from the Japan Science Society, and by the Yamada Science Foundation.

References

1 a) R. J. H. Gregory, *Chem. Rev.*, **99**, 3649 (1999). b) F. Effenberger, *Angew. Chem., Int. Ed. Engl.*, **33**, 1555 (1994). c) M. North, *Synlett*, **1993**, 807. d) M. North, *Tetrahedron: Asymmetry*, **14**, 147 (2003).

2 J. C. Ruble and G. C. Fu, *J. Org. Chem.*, **61**, 7230 (1996).

3 a) D. A. Evans, L. K. Truesdale, and G. L. Carroll, *J. Chem. Soc., Chem. Commun.*, **1973**, 55. b) D. A. Evans and L. K. Truesdale, *Tetrahedron Lett.*, **49**, 4929 (1973). c) W. Lidy and W. Sundermeyer, *Chem. Ber.*, **106**, 587 (1973). d) S. Hünig and H. Reichelt, *Chem. Ber.*, **119**, 1772 (1986). e) S. Kobayashi, Y. Tsuchiya, and T. Mukaiyama, *Chem. Lett.*, **1991**, 541. f) S. Kobayashi, Y. Tsuchiya, and T. Mukaiyama, *Chem. Lett.*, **1991**, 537. g) M. Scholl and G. C. Fu, *J. Org. Chem.*, **59**, 7178 (1994).

4 a) D. A. Evans, J. M. Hoffman, and L. K. Truesdale, *J. Am. Chem. Soc.*, **95**, 5822 (1973). b) M. Oda, A. Yamamuro, and T. Watabe, *Chem. Lett.*, **1979**, 1427. c) M. Golinski, C. P. Brock, and D. S. Watt, *J. Org. Chem.*, **58**, 159 (1993). d) Y. N. Belokon, B. Green, N. S. Ikonnikov, M. North, and V. I. Tararov, *Tetrahedron Lett.*, **40**, 8147 (1999). e) Y. Hamashima, M. Kanai, and M. Shibasaki, *J. Am. Chem. Soc.*, **122**, 7412 (2000). f) M. Bandini, P. G. Cozzi, P. Melchiorre, and A. Umani-Ronchi, *Tetrahedron Lett.*, **42**, 3041 (2001). g) S.-K. Tian, R. Hong, and L. Deng, *J. Am. Chem. Soc.*, **125**, 9900 (2003). h) F.-X. Chen, H. Zhou, X. Liu, B. Qin, X. Feng, G. Zhang, and Y. Jiang, *Chem.—Eur. J.*, **10**, 4790 (2004). i) H. Zhou, F.-X. Chen, B. Qin, X. Feng, and G. Zhang, *Synlett*, **2004**, 1077.

5 H. Nakazawa, K. Kamata, and M. Itazaki, Chem. Commun., in press.

6 a) J. S. Thayer, *Inorg. Chem.*, **7**, 2599 (1968). b) J. A. Seckar and J. S. Thayer, *Inorg. Chem.*, **15**, 501 (1976).

Published on the web (Advance View) June 25, 2005; DOI 10.1246/cl.2005.1054