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CYANATION OF ACETALS WITH t-BUTYL ISOCYANIDE—$TiCl_4$ SYSTEM

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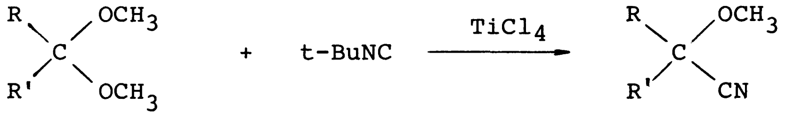
Cyanation of acetals was achieved by t-butyl isocyanide in the presence of $TiCl_4$, producing cyanohydrin ethers in good yields. β-(Trimethylsilyl)ethyl isocyanide in the combination with $TiCl_4$ effected the cyanation as well.

Cyantion is an important synthetic reaction which introduces one carbon unit into the substrate. Methods utilizing metal cyanides such as diethylaluminum cyanide[1)] and trimethylsilyl cyanide[2)] have been developed for cyanation reactions. Recently, we reported a novel conjugate hydrocyanation of α,β-unsaturated ketones with t-butyl isocyanide in combination with $TiCl_4$.[3)] The equivalency of t-butyl isocyanide to HCN in the cyanation reaction is not only mechanistically interesting but also practically useful.

Now we wish to describe here a new cyanation of acetals with the t-butyl isocyanide—$TiCl_4$ system.



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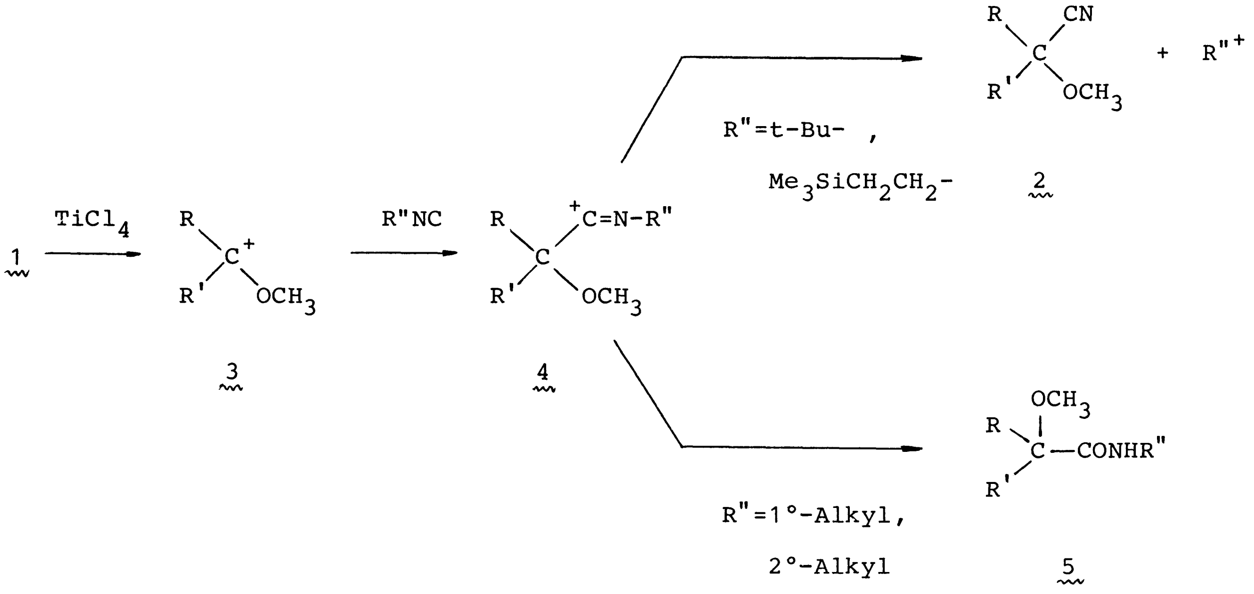
The procedure of cyanation with t-butyl isocyanide—$TiCl_4$ system is quite simple, which is carried out as follows. To a stirred solution of 288 mg (2 mmol) of cyclohexanone dimethyl acetal and 0.22 mL (2 mmol) of $TiCl_4$ in 6 mL of methylene chloride, 166 mg (2 mmol) of t-butyl isocyanide was dropwise added at -70 °C, and then allowed to warm up to 20 °C over 2-3 h, and finally quenched with aqueous

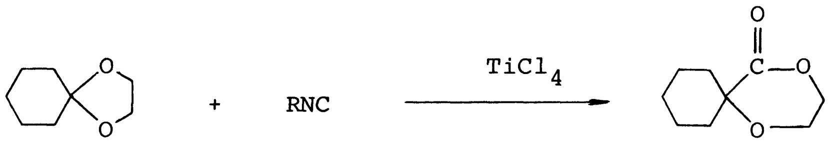
$NaHCO_3$. Extractive workup with methylene chloride followed by Kugel Rohr distillation afforded cyclohexanone cyanohydrin methyl ether (92% yield). Some results of cyanation of acetals are summarized in Table 1.

Use of primary and secondary alkyl isocyanides instead of t-butyl isocyanide in the present reaction did not afford cyanohydrin ether 2, but it gave N-alkyl α-alkoxycarboxamide 5 as already reported by Mukaiyama.4) However, β-(trimethylsilyl)ethyl isocyanide5) in combination with $TiCl_4$ effectuated the cyanation of acetal as well. These findings are consistent with the following mechanism involving N-substituted imidoyl cation intermediate 4, followed by β-elimination.



It is conceivable that the so-called β-effect of silicon6) facilitates the elimination of β-(trimethylsilyl)ethyl carbonium ion from intermediate 4.

The reaction of ethylene acetals with t-butyl isocyanide or β-(trimethylsilyl) ethyl isocyanide in the presence of $TiCl_4$ gave spiro-lactones7,8) in high yields, after aqueous workup.



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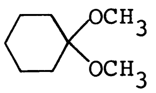
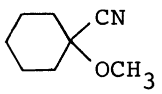
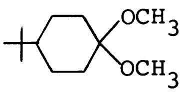
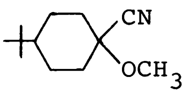
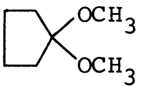
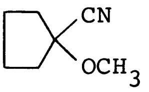
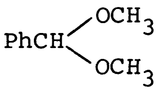
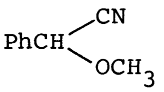
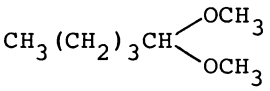
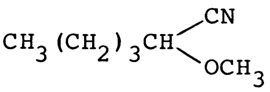
R = t-Bu	82%
R = $Me_3SiCH_2CH_2$	75%

Table 1. A Cyanation of Acetals with Isonitrile-$TiCl_4$ System

Acetal	Isonitrile	Cyanohydrin ether	(Yield/%)
	t-BuNC		(92)
	$Me_3SiCH_2CH_2NC$[a]		(88)
	t-BuNC		(95)[b]
	$Me_3SiCH_2CH_2NC$[a]		(90)[c]
	t-BuNC		(86)
 $PhCH(OCH_3)_2$	t-BuNC	 $PhCH(CN)OCH_3$	(96)
 $CH_3(CH_2)_3CH(OCH_3)_2$	t-BuNC	 $CH_3(CH_2)_3CH(CN)OCH_3$	(81)
	$Me_3SiCH_2CH_2NC$[a]		(82)

a) Cyanation with $Me_3SiCH_2CH_2NC$ was performed by stirring the reaction mixture at -78 °C to room temperature over 6 h.

b) Axial cyanide : Equatorial cyanide = 73 : 27[2c] c) Axial cyanide : Equtorial cyanide = 69 : 31[2c]

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References

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2) a) D. A. Evans, L. K. Truesdale, and G. L. Carroll, J. Chem. Soc., Chem. Commun., 1973, 55.

b) K. Utimoto, M. Obayashi, Y. Shishiyama, M. Inoue, and H. Nozaki, Tetrahedron Lett., 1978, 3389.

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3) Y. Ito, H. Kato, H. Imai, and T. Saegusa, J. Am. Chem. Soc., 104, 6449 (1982).

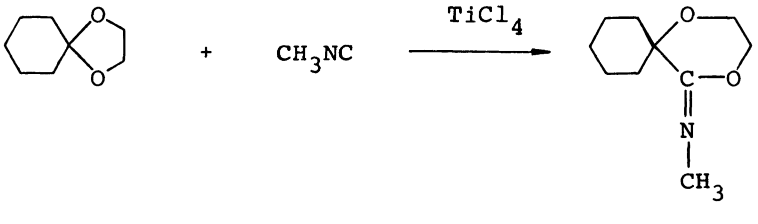
4) T. Mukaiyama, K. Watanabe, and M. Shiono, Chem. Lett., 1974, 1457.

5) β-(Trimethylsilyl)ethyl isocyanide was prepared by a reaction of α-lithiomethyl isocyanide with trimethylsilylmethyl chloride. [IR(neat) 2150, 1250, 840 cm^{-1}; NMR ($CDCl_3$) δ 0.07 (s, 9H), 1.02 (tt, 2H), 3.39 (tt, 2H)]

6) E. W. Colvin, "Silicon in Organic Synthesis," Butterworths (1981), pp. 15 - 20.

7) 6 : IR (neat) 1735, 1105 cm^{-1}; NMR ($CKCl_3$) δ 0.8 - 2.2 (m, 10H), 3.44 (t, 2H), 4.11 (t, 2H)

8) Reaction of cyclohexanone ethylene acetal with methyl isocyanide—$TiCl_4$ system afforded spiro-N-methyliminolactone (7). 7 : IR (neat) 1680, 1105 cm^{-1}; NMR ($CDCl_3$) δ 1.0 - 2.0 (m, 10H), 2.75 (s, 3H), 3.6 - 4.2 (A_2B_2 m, 4H).



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