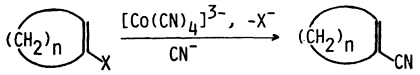
Cyanation of 1-Halocycloalkenes Catalyzed by Tetracyanocobaltate(I). Convenient Synthesis of 1-Cyanocycloalkenes

Takuzo FUNABIKI,* Hirohito KISHI, Yoshihiro SATO, and Satohiro YOSHIDA
Department of Hydrocarbon Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606
(Received July 30, 1982)

Synopsis. 1-Cyanocycloalkenes (1-cyanocyclopentene, -hexene, -heptene, and -octene) were readily synthesized by catalytic cyanation of the corresponding 1-halocycloalkenes with tetracyanocobaltate(I). Reactivities of methyl-substituted 1-chlorocyclohexenes were lower than that of 1-chlorocyclohexene, and 1-chloro-2-methylcyclohexene scarecely reacted. Hydrogenation and isomerization of 1-cyanocycloalkenes were observed only with 1-cyanocycloheptene and 1-cyano-6-methylcyclohexene, respectively.

Previously we have reported the convenient synthetic method of α,β-unsaturated nitriles by cyanation of vinyl halides with tetracyanocobaltate(I), which is formed in an aqueous alkaline solution of pentacyanocobaltate(II) under hydrogen atmosphere.[1] To extend the utility of this method, we have studied the reactivity of 1-halocycloalkenes. Alicyclic α,β-unsaturated nitriles serve as versatile intermediates in organic syntheses, and the methods of preparation of these nitriles may be applicable to the synthetic chemistry of natural products. The most conventional synthetic method of 1-cyanocycloalkenes is the addition of hydrogen cyanide to cycloalkanones to form cyanohydrins, which are dehydrated to nitriles.[2] This method was recently modified to a one-pot reaction by using trimethylsilyl cyanide.[3] Some other reactions have been reported mostly for synthesis of 1-cyanocyclohexene, but examples of synthesis of 1-cyanocyclopentene,[2a,b,e]-heptene,[2b,c,d] and -octene,[2c,3] are very few. The present reaction (Eq. 1) is applicable to 1-halocycloalkenes of various ring sizes, and high yields of 1-cyanocycloalkenes can be obtained under mild conditions from cycloalkenes or cycloalkanones as starting materials.


(1)

Results and Discussion

The reactions were performed in the same way as reported previously.[1] As shown in Table 1, 1-bromocycloalkenes were quantitatively converted into 1-cyanocycloalkenes. The reaction of 1-bromocyclopentene was fairly slower than other three bromides. The reaction proceeded catalytically, but the dropwise addition of the KCN solution at the controlled rate[1] was necessary for cyanation of a large excess of bromides as shown by the reaction of 1-bromocyclooctene. Interestingly, only 1-cyanocycloheptene was significantly hydrogenated. In the cyanation of alkenyl halides, the hydrogenation of acrylonitriles was observed with MeCH=CMeCN, but not with MeCH=CHCN, Me_2C=CHCN, and Me_2C=CMeCN.[1] The relation between the structure of acrylonitriles and facility for hydrogenation has not been clarified.

In order to find the effect of an alkyl substituent on the reactivity, we have studied the reactions of methyl-substituted 1-chlorocyclohexene. Results are shown in Table 2. 1-Chlorocyclohexene was cyanated at the similar rate to 1-bromocyclohexene, supporting that the reaction proceeds stepwise *via* a σ-vinyl cobalt complex and the C–X bond breaking is faster than the C–CN bond formation (Eqs. 2—4).[1] However, methyl-substituted 1-chlorocyclohexenes were less reactive than 1-chlorocyclohexene, regardless of the position of the methyl group, and, unexpectedly, 1-chloro-2-methylcyclohexene was hardly cyanated. In the case of alkenyl halides, the methyl substituent increased the reactivity of the halides, and the rapid reaction was observed with Me_2C=CHX and Me_2C=CMeX. The retardation effect of the methyl group observed with methyl-substituted 1-chlorocyclohexenes is not due to stabilization of the σ-complex (retarding the reaction (4)), but rather retardation or inhibition of the formation of the σ-complex. The result indicates that the rate of cyanation of alkyl-substituted 1-halocycloalkenes

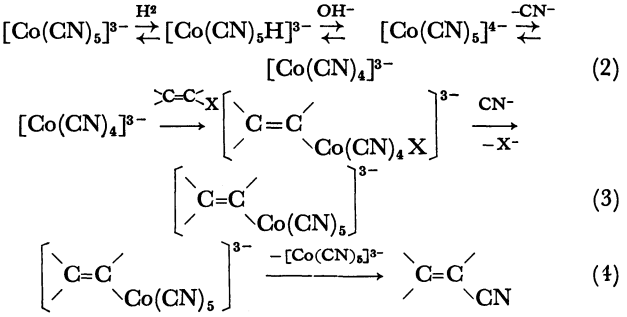

(2)
(3)
(4)

Table 1. Cyanation of 1-bromocycloalkenes

$(CH_2)_n$ Br n	Bromide[a] / Co	Time / h	Yield[b]	Nitriles(mol %) Composition $(CH_2)_n$ CN	$(CH_2)_{n+1}$ CN
3	2	8	70(81)	100	
4	2	4.5	85(96)	100	
5	1	1.5	80(99)	63	37[d]
5	2	4.5	85(99)	66	34[d]
6	2	4.5	90(100)	95	5
6	10[c]	14	68(73)	99	1

a) Mole ratio. b) Total isolated and GLC (in parentheses) yields based on bromides. c) Alkaline KCN solution was added dropwise. d) Yield of the saturated nitrile increased with the elapse of time.

Table 2. Cyanation of 1-chlorocyclohexenes

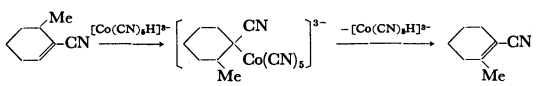
Chloride[a]	Time/h	Products and Yield (mol %)[b] Nitriles	Yield
1-Cl-C_6H_9	4.5	1-CN-C_6H_9	70(78)
1-Cl-2-Me-C_6H_8	24	1-CN-2-Me-C_6H_8	Trace(4)
1-Cl-3-Me-C_6H_8	8	1-CN-3-Me-C_6H_8	75(85)
1-Cl-4-Me-C_6H_8	12	1-CN-4-Me-C_6H_8	70(78)
1-Cl-5-Me-C_6H_8	8	1-CN-5-Me-C_6H_8	75(85)
1-Cl-6-Me-C_6H_8	24	1-CN-6-Me-C_6H_8 (61%)+ 1-CN-2-Me-C_6H_8 (39%)	75(83)

a) C_6H_8 denotes cyclohexene. Chloride/ Co=2. b) Isolated and GLC yields (in parentheses) based on chlorides.

is affected not only by the reaction (4), but also (3).

We have proposed that the C–X bond cleavage and the C–Co bond formation proceeds by an oxidative addition process *via* an electron-transfer interaction.[1] The electron-transfer may take place by the interaction of Co(I) with the π^* orbital of the C–C bond. Since the electronic effect of the methyl substituent may be similar both in alkenyl and cycloalkenyl halides, the retardation by the methyl group must be due to the steric effect of the methyl and methylene hydrogens of the rigid cycloalkene ring, hindering the approach of $[Co(CN)_4]^{3-}$ to the C=C bond.

We have observed the isomerization of 1-cyano-6-methylcyclohexene to 1-cyano-2-methylcyclohexene. This is one of the very few examples of the double bond migration catalyzed by $[Co(CN)_5H]^{3-}$.[4] 1-Cyano-6-methylcyclohexene was selectively formed in the initial stage, but the cyanation became very slow when the isomerization became the predominant reaction. The isomerization proceeds irreversively probably *via* a σ-complex (Eq. 5), which was suggested by broad ^{1}H NMR peaks (δ=1.1—2.2) of the reaction solution prepared in D_2O. The isomerization can be used to synthesize 1-cyano-2-methylcyclohexene which can not be formed from 1-chloro-2-methylcyclohexene.



(5)

Experimental

1-Bromocycloalkenes were synthesized by dehydrobromination of α,β-dibromocycloalkanes[5] with KOH (1-bromocyclopentene),[6] $NaNH_2$-*t*-BuOH (1-bromocyclohexene),[7] and morpholine (1-bromocycloheptene and -octene).[8] 1-Chlorocyclohexenes were synthesized by chlorination of corresponding cyclohexanones with CCl_4/PPh_3,[9] and mixtures (1-chloro-2- and -6-methylcyclohexenes from 2-methylcyclohexanone, and 1-chloro-3- and -5-methylcyclohexenes from 3-methylcyclohexanone) were separated by a preparative GLC. Nitriles obtained here are known compounds (1-cyano-3- and -5-methylcyclohexenes have been reported as a mixture)[10] and gave satisfactory elemental analyses, and identified by IR (JASCO IRA-2, observed as neat films) and ^{1}H and ^{13}C NMR spectroscopy (JEOL FX-100, observed in $CDCl_3$).

Cyanation of 1-Halocycloalkenes. The reaction was performed in the same fassion as described previously.[1] A typical procedure was as follows: $CoCl_2$ (1.00 mmol, 0.130 g), KCN (4.95 mmol, 0.322 g) and KOH (2.0 mmol, 0.12 g) were placed in a 20 cm^3 two-necked flask equipped with a cold-finger. H_2O (5 cm^3) was added under hydrogen atmosphere at 45 °C, and the solution was stirred magnetically for 30 min. *1-Bromocyclopentene* (0.21 cm^3, 2.0 mmol) was added with a microsyringe through a serum cap. It took 8 h to cyanate the added bromide, and the reaction mixture was extracted with dichloromethane. Dichloromethane was evaporated, and the residue was distilled *in vacuo* with a Kügelrohr apparatus to give 1-cyanocyclopentene (0.13 g, 1.4 mmol) bp 95 °C/28 mmHg† (oven temperature); IR 2220 cm^{-1} (CN); ^{1}H NMR δ=1.99 (q, 2H), 2.54 (m, 4H), 6.66 (m, 1H); ^{13}C NMR δ=22.8 (t), 33.7 and 34.2 (t), 115.3 (s), 116.7 (s, CN), 128.9 (d). *1-Bromo* and *-chlorohexene* (2 mmol) yielded 1-cyanocyclohexene (0.18 g, 1.7 mmol) and 0.15 g, 1.4 mmol), respectively, bp 120 °C/28 mmHg; IR 2204 cm^{-1} (CN); ^{1}H NMR δ=1.65 (m, 4H), 2.20 (m, 4H), 6.62 (q,1H); ^{13}C NMR δ=20.7 (t), 21.4 (t), 25.7 (t), 112.3 (s), 119.7 (s, CN), 145.2 (d). *1-Bromo-cycloheptene* (2 mmol) yielded a mixture of 1-cyanocycloheptene and cyanocycloheptane (0.21 g): 1-Cyanocycloheptene bp 60 °C/2 mmHg; IR 2204 cm^{-1}; ^{1}H NMR δ=1.62 (s, br, 6H), 2.34 (m, 4H), 6.78 (t, 1H);^{13}C NMR δ=25.3, 26.2, 29.6, 31.3, and 31.6 (t), 117.6 (s), 120.9 (s, CN), 150.3 (d): *Cyanocycloheptane* bp 60 °C/2 mmHg; IR 2220 cm^{-1}; ^{1}H NMR δ=1.60 (m, 8H), 1.87 (m, 4H), 2.87 (tt, 1H); ^{13}C NMR δ=25.4 and 31.6 (t), 27.6 (t), 30.1 (s), 123.3 (s, CN). *1-Bromocyclooctene* (2 mmol) yielded 1-cyanocyclooctene and cyclooctane (95 : 5, 0.24 g); 1-cyanocyclooctene bp 75 °C/0.5 mmHg; IR 2210 cm^{-1}; ^{1}H NMR δ=1.53 (s, br, 8H), 2.31 (m, 4H), 6.60 (t, 1H); ^{13}C NMR δ=25.5, 26.0, 27.1, 27.8, 28.3, and 28.8 (t), 115.1 (s), 120.3 (s, CN), 148.1 (d). *1-Chloro-2-methylcyclohexene* scarecely reacted, but *1-chloro-3-*, *-4-*, and *-5-methylcyclohexenes* (2 mmol) yielded selectively corresponding 1-cyano(methyl)-cyclohexenes bp 125 °C/28 mmHg; 1-cyano-3-methylcyclohexene (0.18 g, 1.5 mmol) Found: C, 79.01; H, 9.20; N, 79.60%; Calcd for $C_8H_{11}N$: C, 79.29; H, 9.15; N, 11.56%; IR 2210 cm^{-1}; ^{1}H NMR δ=1.05 (d, 3H), 1.75 (m, 4H), 2.20 (m, 3H), 6.46 (tt, 1H); ^{13}C NMR δ=21.2, 25.8, and 34.5 (t), 27.6 (t), 28.8 (d), 111.9 (s), 119.7 (s, CN), 144.7 (d); 1-cyano-4-methylcyclohexene (0.17 g, 1.4 mmol) IR 2210 cm^{-1}; ^{1}H NMR δ=0.98 (d, 3H), 1.32 (m, 1H), 1.72 (m, 3H), 2.23 (m, 3H), 6.59 (m, 1H); ^{13}C NMR δ=21.3 (t), 26.6 (t), 27.0 (d), 29.5 (t), 33.9 (q), 112.0 (s), 119.6 (s,CN), 144.7 (d); 1-cyano-5-methylcyclohexene (0.18 g, 1.5 mmol) Found: C, 79.05; H, 9.30; N, 11.68%; Calcd for $C_8H_{11}N$: C, 79.29; H, 9.15; N, 11.56%; IR 2210 cm^{-1}; ^{1}H NMR δ=1.00 (d, 3H), 1.73 (m, 4H), 2.23 (m, 3H), 6.67 (m, 1H); ^{13}C NMR δ=20.3 (t and q), 26.6 (t), 29.3 (t), 30.8 (d), 111.7 (s), 119.7 (s,CN), 150.5 (d). *1-Chloro-6-methylcyclohexene* (2 mmol) yielded a mixture of 1-cyano-6- and -2-methylcyclohexenes (61 : 39 after the 24 h reaction, 0.18 g, 1.5 mmol) bp 125 °C/28 mmHg; 1-cyano-6-methylcyclohexene IR 2205 cm^{-1}; ^{1}H NMR δ=1.19 (d, 3H), 1.69 (m, 4H), 2.15 (m, 3H), 6.60 (m, 1H); ^{13}C NMR δ=19.3 (t), 19.8 (q), 25.8 and 29.9 (t), 30.7 (d), 118.3 (s), 119.1 (s, CN), 145.0 (d); 1-cyano-2-methylcyclohexene IR 2202 cm^{-1}; ^{1}H NMR δ=1.63(m, 4H), 1.99 (s, 3H), 2.14 (m, 4H); ^{13}C NMR δ=21.5 (t), 21.6 (t), 23.0 (t), 27.1 (q), 31.3 (t), 106.2(s), 119.3 (s, CN), 153.4 (s).

† Throughout this paper 1 mmHg=133.322 Pa.

References

1) T. Funabiki, H. Hosomi, S. Yoshida, and K. Tarama, *J. Am. Chem. Soc.*, **104**, 1560 (1982).

2) a) S. M. McElvain and R. E. Starn, Jr., *J. Am. Chem. Soc.*, **77**, 4571 (1955); b) O. H. Wheeler and I. Lerner, *ibid.*, **78**, 63 (1956); c) J. Sicher, F. Sĭpoš, and J. Jonáš, *Collect. Czech. Chem. Commun.*, **26**, 262 (1961); *Chem. Abstr.*, **55**, 15372a (1961); d) K. C. Mathur, G. S. Saharia, *Indian J. Chem.*, **6**, 248 (1968); e) C. W. B. Cumper, S. K. Dev, and S. R. Landor, *J. Chem. Soc., Perkin Trans. 2*, **1973**, 537.

3) M. Oda, A. Yamamuro, and T. Watabe, *Chem. Lett.*, **1979**, 1427.

4) L. M. Jackman, J. A. Hamilton, and J. M. Lawlor, *J. Am. Chem. Soc.*, **90**, 1914 (1968).

5) H. R. Snyder and L. A. Brooks, *Org. Synth.*, Coll. Vol. II, 171 (1948).

6) P. I. Abell and C. Chiao, *J. Am. Chem. Soc.*, **82**, 3610 (1960).

7) P. Caubere and G. Coudert, *J. Chem. Soc., Chem. Commun.*, **1972**, 1289.

8) K. Schank and B. Eistert, *Chem. Ber.*, **99**, 1414 (1966).

9) N. Isaacs and D. Kirkpatrick, *J. Chem. Soc., Chem. Commun.*, **1972**, 443.

10) A. A. Petrov and A. F. Sapozhnikova, *J. Gen. Chem. (U.S.S.R)*, **18**, 424 (1948); *Chem. Abstr.*, **42**, 7221g (1948).