Hydrocyanation. V. Kinetics and Mechanism of Hydrocyanation of α,β-Unsaturated Ketones

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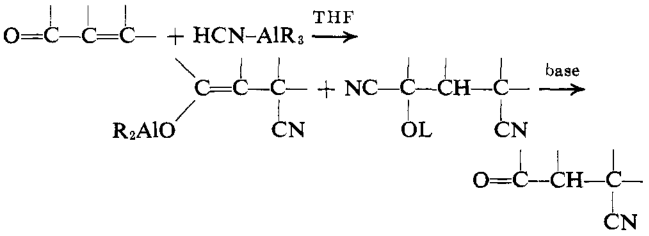
Abstract: Kinetics of hydrocyanation of cholest-4-en-3-one with combinations of hydrogen cyanide (HCN) and alkylaluminums (AlR_3) in tetrahydrofuran (method A) have revealed that HCN–$EtAlCl_2$ represents an ideal method-A reagent and with other combinations a secondarily formed alkylaluminum cyanide (R_2AlCN: method-B reagent) acts alongside with the ideal reagent. Clarifying the features of the ideal reaction, we have proposed an ionic mechanism for the ideal method-A hydrocyanation of α,β-unsaturated ketones which involves coordination of proton or an alkylaluminum cation (R_2Al^+) to the ketone oxygen to give an activated species, a rate-determining nucleophilic attack of a cyanoaluminate anion ($(R_3AlCN)^-$) at the β carbon to give a 1,4 adduct, irreversible transformation into a β-cyano ketone, and its conversion into a dicyano compound (*cf.* Scheme I). Kinetic data for hydrocyanation of cholest-4-en-3-one and *B*-norandrost-4-en-3-one with method-B reagents, R_2AlCN, have led us to propose a nonionic, reversible mechanism for method-B hydrocyanation of α,β-unsaturated ketones in tetrahydrofuran which involves activation of the enone with a monomeric solvated reagent, "$S \cdot R_2AlCN$," a preceding 1,2-addition preequilibrium, a rate-determining attack of a second "$S \cdot R_2AlCN$" at the β carbon to give a 1,4 adduct, and its partial reconversion into the starting enone (*cf.* Scheme II). Relative rates of conjugate hydrocyanation with these reagents have been presented also.

In the preceding paper,[1] we reported two new and useful methods for conjugate hydrocyanation of α,β-unsaturated ketones using alkylaluminum compounds.

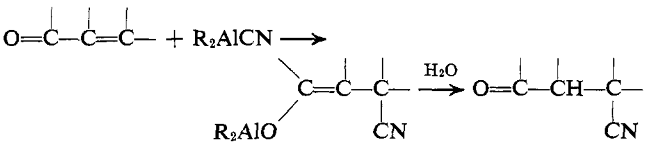
Method A



$$\mathrm{O{=}C{-}C{=}C{-}} + \mathrm{HCN\text{-}AlR_3} \xrightarrow{\mathrm{THF}} \mathrm{R_2AlO{-}C{=}C{-}C(CN){-}} + \mathrm{NC{-}C(OL){-}CH{-}C(CN){-}} \xrightarrow{\text{base}} \mathrm{O{=}C{-}CH{-}C(CN){-}}$$

(L = H or R_2Al)

Method B



$$\mathrm{O{=}C{-}C{=}C{-}} + \mathrm{R_2AlCN} \longrightarrow \mathrm{R_2AlO{-}C{=}C{-}C(CN){-}} \xrightarrow{\mathrm{H_2O}} \mathrm{O{=}C{-}CH{-}C(CN){-}}$$

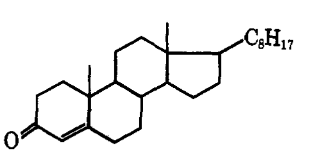
Since hydrogen cyanide (HCN) slowly reacts with an alkylaluminum (AlR_3) in tetrahydrofuran (THF) to give an alkylaluminum cyanide (R_2AlCN), the method-B reagent, according to eq 1, the actual method-A hydrocyanation is effected by the ideal HCN–AlR_3 reagent and the secondarily formed R_2AlCN reagent. The extent of the participation of the R_2AlCN will depend on reactivity of AlR_3 to HCN.

$$\mathrm{HCN} + \mathrm{AlR_3} \longrightarrow \mathrm{R_2AlCN} + \mathrm{RH} \qquad (1)$$

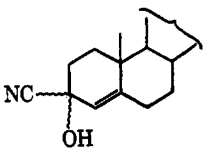
In the present paper, we report kinetics of method-A and -B hydrocyanations of cholest-4-en-3-one (**1**) and *B*-norandrost-4-en-3-one (**5**), rates of the R_2AlCN formation from HCN–AlR_3, and electric conductivities of the reagents and clarify the features and mechanisms of the ideal method-A and the method-B hydrocyanations of α,β-unsaturated ketones.

Results

Kinetic Data for Hydrocyanation of Cholest-4-en-3-one (1) with HCN–AlR_3 in THF (Method A). The product obtained by acid hydrolysis in an intermediate stage of method-A hydrocyanation of cholest-4-en-3-one (**1**) contains α-cyanohydrin **2**, cyano ketone **3**, and dinitrile **4**,[2] besides the starting enone **1**.



1



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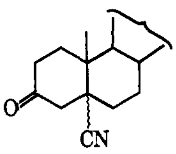

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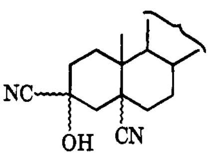

4

1, 4 adduct

Let us define the following relative concentrations

$$[\text{enone}] = [\mathbf{1}]/[\mathbf{1}]_i,\ [1{,}2\ \text{adduct}] = [\mathbf{2}]/[\mathbf{1}]_i$$
$$[1{,}4\ \text{adduct}] = [\mathbf{3} + \mathbf{4}]/[\mathbf{1}]_i \qquad (2)$$
$$[\text{enone}] + [1{,}2\ \text{adduct}] + [1{,}4\ \text{adduct}] = 1$$

where $(\mathbf{1})_i$ is the initial concentration of **1**. The concentrations of enone **1**, 1,2 adduct **2**, and 1,4 adduct (**3** + **4**) at time *t* were estimated by treatment of an aliquot with ethanolic hydrochloric acid or sodium hydroxide followed by ultraviolet analysis at 242 mμ to determine the enone concentration.

Figures 1a and b show plots of [enone] and [enone] + [1,2 adduct] as a function of time for hydrocyanation of **1** with method-A reagents at 25.0°. The effect of a

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[1] W. Nagata, M. Yoshioka, and S. Hirai, *J. Amer. Chem. Soc.*, **94**, 4635 (1972).

[2] Apparently, each of **2**, **3**, and **4**, though treated as homogeneous in the kinetics, is a mixture of epimeric α- and β-carbonitriles.

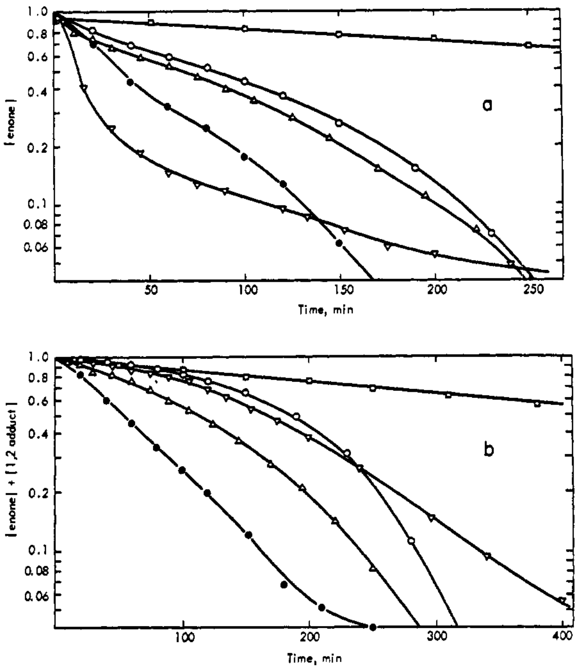

Figure 1. Plots of relative concentrations [enone] (a) and [enone] + [1,2 adduct] (b), as a function of time for hydrocyanation of 1(0.04 *M*) with HCN (0.28 *M*) and the following AlR_3 (0.28 *M*) in THF at 25°: □, $EtAlCl_2$; △, Et_2AlCl; ●, $AlEt_3$ + H_2O (0.026 *M*); ○, $AlEt_3$; ▽, $AlMe_3$.

small amount of water on the reaction is demonstrated also. In Figure 2 are shown concentration-time plots for hydrocyanation of 1 with HCN-$EtAlCl_2$ until the reaction is 95% complete. Plots of [1,2 adduct] and [1,4 adduct] are shown in the previous paper.[1] Since determination of the dinitrile distribution, [4]/([3] + [4]), is time consuming and of little kinetic significance, the distributions were determined only for the final products of the reactions (Table I). As clearly seen from Figures 1 and 2, different reagent species show different concentration–time patterns which prevent us from calculating rate constants for each reaction. Therefore, the relative rates of the 1,4 addition with different reagents were estimated from the reciprocals of 50 and 90% completion times, $\tau_{0.5}$ and $\tau_{0.9}$, the values for reaction with HCN–$EtAlCl_2$ being taken as the standard. The results are included in Table I.

Table I. Dinitrile Ratios, [4]/([3] + [4]), in the Products and Relative 1,4-Addition Rates in Hydrocyanation of 1[a] with Method-A Reagents in THF at 25°

Reagent[b]	[4]/([3] + [4])	Relative rate 50% completion	 90% completion
HCN-$EtAlCl_2$	0.93	1.0	1.0
HCN-Et_2AlCl	0.84	4.1	5.5
HCN-$AlEt_3$-H_2O[c]	0.81	7.9	8.0
HCN-$AlEt_3$	0.55	2.4	4.5
HCN-$AlMe_3$	0.30	2.8	3.9

[a] Initial concentration of 1 = $[1]_i$ = 0.04 *M*. [b] [HCN] = 0.28 *M*; $[AlR_3]$ = 0.28 *M*. [c] $[H_2O]$ = 0.026 *M*.

Figure 3 shows the formation of R_2AlCN from HCN–AlR_3 estimated from the evolution of ethane (eq 1) as compared with the formation of the 1,4 adduct. The concentration of the cyanide is expressed by the relative concentration $[R_2AlCN]/(1)_i$. The reaction of HCN and $AlMe_3$ was found to be considerably rapid. The cyanide formation curve in the $AlEt_3$–H_2O–HCN (0.28–0.026–0.28 *M*) reagent system was substantially the same as the curve in the $AlEt_3$–HCN (0.28–0.28 *M*) system when the amount of ethane formed from water was subtracted. In Table II is shown the gas formation in the reaction of water with an excess of $AlEt_3$.

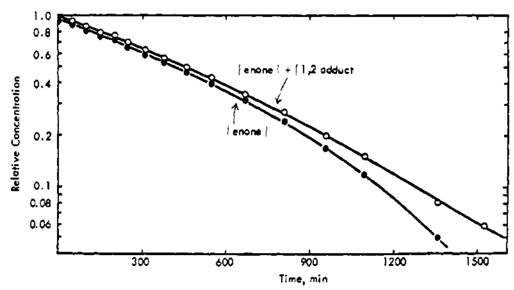

Figure 2. Plots of relative concentrations [enone] + [1,2 adduct] (○) and [enone] (●), as a function of time for hydrocyanation of 1 (0.04 *M*) with HCN (0.28 *M*) and $EtAlCl_2$ (0.28 *M*) in THF at 25°.

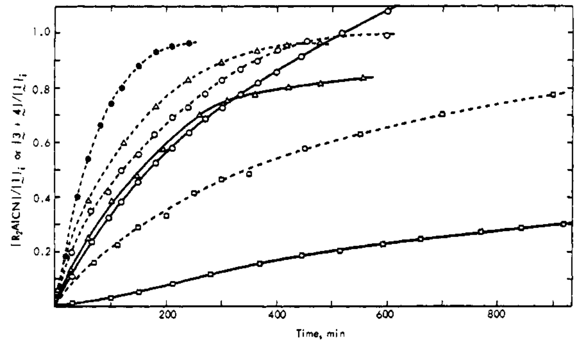

Figure 3. Relation between cyanide formation, $[R_2AlCN]/[1]_i$ (solid line), and formation of the 1,4 adduct, $[3 + 4]/[1]_i$ (dotted line), for hydrocyanation of 1 with HCN–AlR_3 at the following concentrations in THF at 25°: □, 1-HCN-$EtAlCl_2$ (0.15–0.30–0.45 *M*); △, 1-HCN-Et_2AlCl (0.15–0.30–0.45 *M*); ●, 1-HCN-$AlEt_3$-H_2O (0.04–0.28–0.28–0.026 *M*); ○, 1-HCN-$AlEt_3$ (0.10–0.28–0.28 *M*).

Table II. Formation of Ethane in Reaction of $AlEt_3$ (0.28 *M*) and H_2O (0.052 *M*)

Reaction time, min	Ethane evolved, %[a]	Reaction time, min	Ethane evolved, %[a]
0.5	77	20	150
1.0	103	70	170
7.0	138	300	187

[a] Based on the molar amount of H_2O added.

Kinetic Data for Hydrocyanation of Cholest-4-en-3-one (1) and *B*-Norandrost-4-en-3-one (5) with Diethylaluminum Cyanide (Method B). Figure 4 illustrates concentration *vs.* time plots for reaction of 1 with diethylaluminum cyanide (Et_2AlCN) in THF–*i*-Pr_2O[3]

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[3] Since Et_2AlCN slowly reacts with THF, isopropyl ether (*i*-Pr_2O) was used for preparation of a stock solution of the reagent. The presence of the less basic *i*-Pr_2O in a minor amount would not affect the high basicity of THF. Thus, the reaction in a mixture of THF and a small amount of *i*-Pr_2O would be essentially the same as that in THF alone.

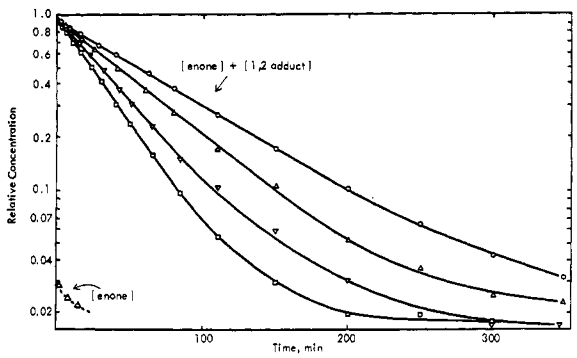


Figure 4. Plots of relative concentrations, [enone] + [1,2 adduct] (solid lines) and [enone] (dotted line), *vs.* time for hydrocyanation of **1** (0.01 *M*) with Et_2AlCN at the following concentrations (as [Et_2AlCN^*] in *M*] in THF-*i*-Pr_2O (4:1) at 0°: ○, 0.07; △, 0.13; ▽, 0.27; □, 0.433.

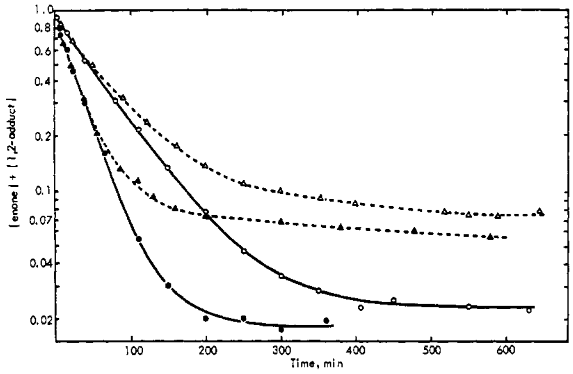


Figure 5. Effect of a trace of water on hydrocyanation of **1** (0.01 *M*) with Et_2AlCN in THF-*i*-Pr_2O (4:1) at 0°: ○, [Et_2AlCN^*] = 0.09 *M*; △, [Et_2AlCN^*] = 0.09 *M* and [H_2O] = 0.0002 *M*; ●, [Et_2AlCN^*] = 0.44 *M*; ▲, [Et_2AlCN^*] = 0.44 *M* and [H_2O] = 0.0002 *M*.

(4:1) at various reagent concentrations. Since the 1,2 addition is extremely rapid and amounts of the remaining enone are too small to be analyzed accurately, the change of [enone] was not followed except in a very early stage of the reaction. The plot of [enone] shown in the lower left corner is typical of the reaction at varying reagent concentrations. The reaction was carried out also at four other concentrations. The reagent concentration is based on the molecular formula Et_2AlCN and expressed as [Et_2AlCN^*], the effective concentration equal to [Et_2AlCN] − [substrate]. The use of the effective concentration is based on the observation that 1 molar equiv of the cyanide is consumed for the very rapid 1,2 addition, followed by slow 1,4 addition without substantial change in the remaining reagent concentration, irrespective of the progress of the 1,4 addition.

Although kinetic runs were carried out under a positive pressure of high-purity argon by using materials and equipment dried as completely as possible, one cannot exclude the possibility that traces of moisture and air would be contained in reaction system. A small amount of air was found to exert little effect on the reaction, whereas small amounts of water considerably affected the equilibrium concentration of **1** as shown in Figure 5.

In method-B hydrocyanation of **1**, the final product obtained by acid treatment consists of cyano ketone **3** and a small amount of 1,2 adduct **2**. Dinitrile **4**, the major product in method-A hydrocyanation, was not detected. However, compound **4** was formed when HCN–$AlEt_3$ was added to the method-B reaction mixture at a later stage of the reaction, as indicated in Table III.

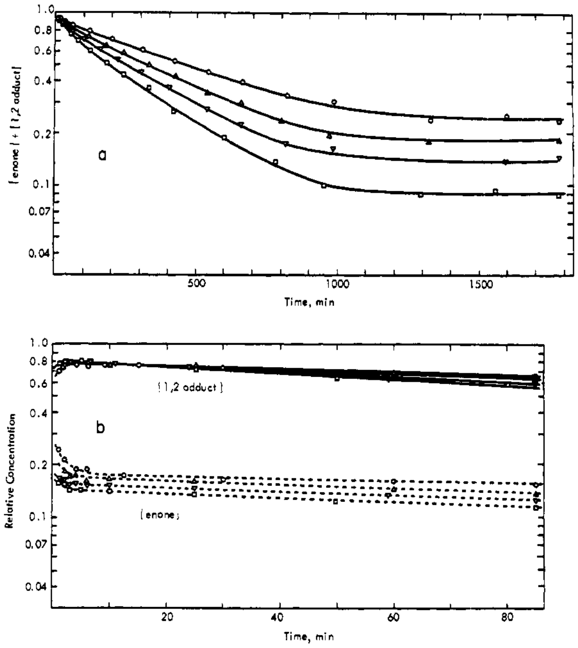


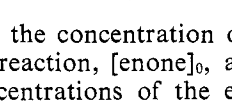
Figure 6. Plots of relative concentrations, [enone] + [1,2 adduct] (a), [1,2 adduct] (b, solid lines), and [enone] (b, dotted lines), as a function of time for hydrocyanation of **5** (0.01 *M*) with Et_2AlCN at the following concentrations (as [Et_2AlCN^*] in *M*) in THF-*i*-Pr_2O (4:1) at 0°: ○, 0.09; △, 0.165; ▽, 0.27; □, 0.44.

Table III. Effect of $AlEt_3$–HCN on the Dinitrile Distribution, [**4**]/([**3**] + [**4**]), in Hydrocyanation[a] of **1** with Et_2AlCN in THF-*i*-Pr_2O (8:1) at 25°

Time after addition of HCN-$AlEt_3$, min	[**4**]/([**3**] + [**4**])
0[b]	0
30	0.22
120	0.59
337	0.78

[a] [**1**], 0.04 *M*; [Et_2AlCN], 0.12 *M*; [HCN] and [$AlEt_3$], 0.28 *M*.
[b] The reagent HCN–$AlEt_3$ was added 1 hr after treatment of **1** with Et_2AlCN.

The kinetic data for method-B hydrocyanation of **1** indicate that the enone reacts with Et_2AlCN by two consecutive reversible reactions (*cf.* Discussion). With **1**



(3)

as the substrate, the concentration of the enone at an initial stage of reaction, $[\text{enone}]_0$, and the combined equilibrium concentrations of the enone and the 1,2 adduct, $[\text{enone}]_\infty + [1,2\ \text{adduct}]_\infty$, are too low to be analyzed accurately (Figure 4). We searched, therefore, for another substrate, suitable for an examination of the dependence of the reagent concentration on $[\text{enone}]_0$ and $[\text{enone}]_\infty + [1,2\ \text{adduct}]_\infty$, and *B*-nor-

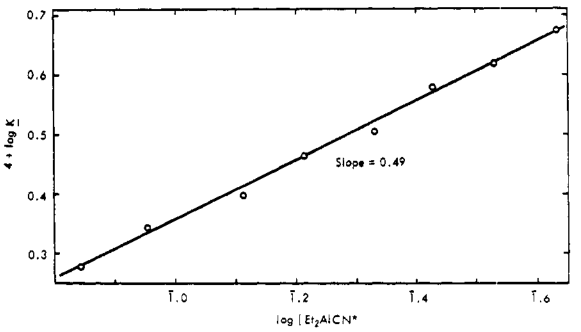


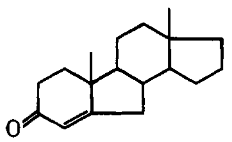
Figure 7. Linear plot of logarithm of the apparent pseudo-first-order rate costant, K, and of the Et_2AlCN^* concentration for conjugate hydrocyanation of **1** (0.01 M) with Et_2AlCN in THF–*i*-Pr_2O (4:1) at 0°.

androst-4-en-3-one (**5**) was found suitable for this examination.

Kinetic data for method-B hydrocyanation of **5** are indicated in Figure 6. The relative concentrations at time t are defined as

$$[\text{enone}] = [\mathbf{5}]/[\mathbf{5}]_i,\ [1{,}2\ \text{adduct}] = [\mathbf{6}]/[\mathbf{5}]_i$$
$$[1{,}4\ \text{adduct}] = [\mathbf{7}]/[\mathbf{5}]_i \qquad (4)$$
$$[\text{enone}] + [1{,}2\ \text{adduct}] + [1{,}4\ \text{adduct}] = 1$$

where $[\mathbf{5}]_i$ is the initial concentration of **5**.



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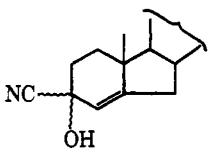

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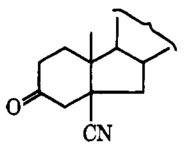

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As indicated in the Appendix (eq 27), the apparent pseudo-first-order rate constant K for the 1,4 addition can be calculated from the equation

$$[1{,}4\ \text{adduct}]_\infty \ln \frac{[1{,}4\ \text{adduct}]_\infty}{[1{,}4\ \text{adduct}]_\infty - [1{,}4\ \text{adduct}]} =$$
$$Kt + [1{,}4\ \text{adduct}]_\infty \ln \frac{[1{,}4\ \text{adduct}]_\infty}{[1{,}4\ \text{adduct}]_\infty - [1{,}4\ \text{adduct}]_0} \qquad (5)$$

where the subscripts 0 and ∞ represent initial and equilibrium concentrations, respectively.

In the hydrocyanation of **1** (Figure 4), $[1{,}4\ \text{adduct}]_\infty = \{1 - ([\text{enone}]_\infty + [1{,}2\ \text{adduct}]_\infty)\}$ is nearly equal to 1.0, and the curves are linear up to 90% completion. Thus, the 1,4 addition may be treated as a simple pseudo-first-order reaction. Let $\tau_{0.5}$ be the half-life when [1,4 adduct] = [enone] + [1,2 adduct]. Substitution of this and $[1{,}4\ \text{adduct}]_\infty = 1.0$ into eq 5 yields

$$K = \{0.693 + 2.303 \log (1 - [1{,}4\ \text{adduct}]_0)\}/\tau_{0.5} \qquad (6)$$

The value $[1{,}4\ \text{adduct}]_0$ can be obtained by extrapolating the curve to $t = 0$.

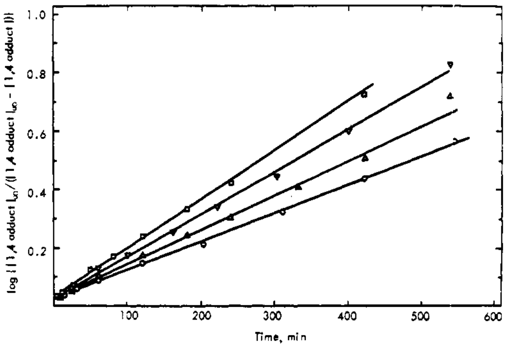


Figure 8. Linear plot for conjugate hydrocyanation of **5** (0.01 M) with Et_2AlCN at the following concentrations (as [Et_2AlCN^*] in M) in THF–*i*-Pr_2O (4:1) at 0°: ○, 0.09; △, 0.165; ▽, 0.270; □, 0.44.

Table IV. Apparent Pseudo-First-Order Rate Constants K for Conjugate Hydrocyanation of **1** (0.01 M) with Et_2AlCN at Various Concentrations in THF–*i*-Pr_2O (4:1) at 0°

[Et_2AlCN^*], M	$\tau_{0.5}$, sec	1 − [1,4 adduct]$_0$	$K \times 10^4$ sec^{-1}
0.07	3240	0.92	1.88
0.09	2760	0.92	2.21
0.130	2430	0.92	2.51
0.165	2100	0.92	2.91
0.215	2100	0.98	3.20
0.270	1710	0.96	3.81
0.340	1440	0.91	4.16
0.433	1380	0.96	4.73

In Table IV are summarized the apparent pseudo-first-order rate constants K for the 1,4 addition of Et_2AlCN to **1**, which were calculated from the data shown in Figure 4 by using eq 6. Figure 7 shows a linear relationship between log K and log [Et_2AlCN^*].

Apparent 1,4-addition rate constants K for the B-norsteroid **5** were calculated from the data shown in Figure 8 according to eq 5. The rate constants together with the values [enone]/[1,2 adduct] and $[1{,}4\ \text{adduct}]_\infty/([\text{enone}]_\infty + [1{,}2\ \text{adduct}]_\infty)$ which are necessary for the later discussion are listed in Table V.

Table V. Rate Data for Hydrocyanation of **5** (0.01 M) with Et_2AlCN in THF–*i*-Pr_2O (4:1) at 0°

[Et_2AlCN^*], M	$K \times 10^5$ sec^{-1}	[Enone]^a/[1,2 adduct]	[1,4 adduct]$_\infty$/ [enone]$_\infty$ + [1,2 adduct]$_\infty$
0.090	2.94	0.228	3.20
0.165	3.85	0.216	4.50
0.270	4.80	0.192	6.25
0.440	5.97	0.186	10.0

[a] Average of the [enone]/[1,2 adduct] values at t = 5–30 min.

Figure 9 shows dependence of the reagent concentration on these values.

Table VI shows a typical time variation in the ratio [enone]/[1,2 adduct] for the reaction of **5**, indicating that there is a rapid equilibrium between the enone and the 1,2 adduct.

1,4-Addition Rate Data for Hydrocyanation of Cholest-4-en-3-one (1) with Various Method-B Reagents (R_2AlCN) and with Et_2AlCN in Various Solvents. Table VII illustrates the effect of the alkyl group (R) of the

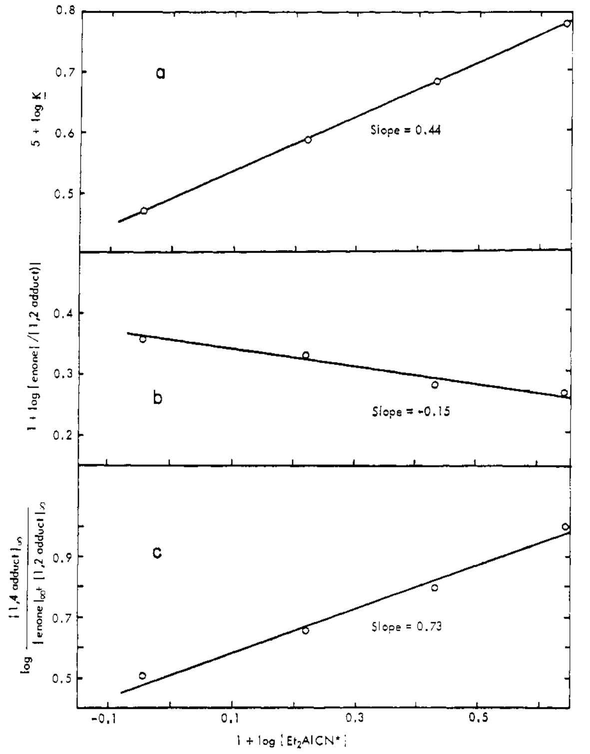


Figure 9. Dependence of Et_2AlCN^* concentration of K (a), [enone]/[1,2 adduct] (b), and $[1,4\ adduct]_\infty/([enone]_\infty + [1,2\ aduct]_\infty)$ (c) for hydrocyanation of **5** with Et_2AlCN in THF–*i*-Pr_2O (4:1) at 0°.

Table VI. Time Variation in the Ratio [enone]/[1,2 adduct] for Hydrocyanation of **5** (0.01 *M*) with Et_2AlCN^* (0.09 *M*)

Time, min	[Enone]/[1,2 adduct]	Time, min	[Enone]/[1,2 adduct]
1.0	0.343	60.0	0.238
4.0	0.250	120	0.219
9.0	0.228	310	0.236
15.2	0.229	422	0.213
30.2	0.227	544	0.295

Table VII. Relative Rates for Conjugate Hydrocyanation of **1** (0.05 *M*) with Various R_2AlCN (0.10 *M*) in THF–*i*-Pr_2O (4:1)

R_2AlCN	Temp, °C	K, sec^{-1}	Relative rate
Et_2AlCN	0.0	2.27×10^{-4}	1.0[a]
Et_2AlCN	15.0	1.96×10^{-3}	1.0[a]
Me_2AlCN	15.0	1.64×10^{-4}	0.084
i-Bu_2AlCN	0.0	1.17×10^{-3}	5.15

[a] Taken as the standard.

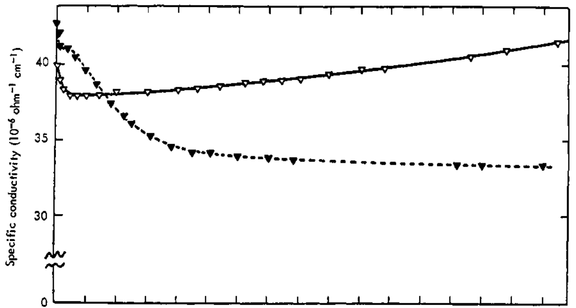


Figure 10. Plots of specific conductivity of HCN–$EtAlCl_2$ (0.28–0.28 *M*) (▽) and of **1**–HCN–$EtAlCl_2$ (0.1–0.28–0.28 *M*) (▼) as a function of time in THF at 25°.

Table VIII. Solvent Effect in Conjugate Hydrocyanation of **1** (0.005 *M*) with Et_2AlCN

Solvent	[Et_2-AlCN*], *M*	Temp, °C	$\tau_{0.5}$, sec	Relative rate
THF–*i*-Pr_2O (4:1)	0.045	0.0	4,800	1.0[a]
i-Pr_2O	0.045	0.0	60	80
THF–*i*-Pr_2O (7:1)	0.095	10.0	950	1.0[a]
Dioxane–*i*-Pr_2O (4:1)	0.095	10.0	25	38
THF–*i*-Pr_2O (20:1)	0.065	−5.0	11,000	1.0[a]
Toluene	0.065	−5.0	*ca.* 20	550

[a] Taken as the standard.

Table IX. Relative Rates of Conjugate Hydrocyanation of **1** with HCN–AlR_3 and R_2AlCN

Reagent	Solvent	Relative rate
HCN–$EtAlCl_2$	THF	1.0
HCN–Et_2AlCl	THF	5.5
HCN–$AlEt_3$–H_2O[a]	THF	8.0
HCN–$AlEt_3$	THF	4.5
HCN–$AlMe_3$	THF	3.9
Me_2AlCN	THF	15
(*i*-Bu)$_2$AlCN	THF	950
Et_3AlCN	THF[b]	180
Et_2AlCN	Dioxane[b]	6,800
Et_2AlCN	*i*-Pr_2O	*ca.* 14,000
Et_2AlCN	Toluene	>85,000

[a] The molar ratio of water to HCN–$AlEt_3$ is 1:11. [b] Contains a small amount of *i*-Pr_2O.

reagent R_2AlCN on the 1,4-addition rate. The solvent effect on the rate for conjugate hydrocyanation of **1** with Et_2AlCN is illustrated in Table VIII.

Relative Rates of Conjugate Hydrocyanation of Cholest-4-en-3-one (1) with Method-A and -B Reagents. Table IX summarizes relative rates of 1,4 addition of **1** (**1** → **3** + **4**) with method-A (HCN–AlR_3–THF) and method-B (R_2AlCN) reagents.

Electric Conductivities of Hydrocyanation Reagents and of a Reaction Mixture. To know ionic nature of method-A and -B reagents, electric conductivities of HCN, AlR_3, AlR_3–HCN, and R_2AlCN were measured and time dependence on electric conductivities of HCN–$EtAlCl_2$ and **1**–HCN–$EtAlCl_2$ was examined. The results are indicated in Table X and Figure 10.

Discussion

Features of Ideal Method-A Hydrocyanation. Participation of R_2AlCN in method-A hydrocyanation as estimated from the data shown in Figure 3 is in the following increasing order: HCN–$EtAlCl_2$ < HCN–$AlEt_3$–H_2O < HCN–Et_2AlCl < HCN–$AlEt_3$ < HCN–$AlMe_3$. The concentration–time pattern for hydrocyanation of **1** with HCN–$EtAlCl_2$ is almost linear, indicating that the reaction is substantially pseudo-first-order. Thus, the combination HCN–$EtAlCl_2$ represents the ideal method-A reagent. With other combinations, participation of more reactive R_2AlCN makes the kinetic patterns complex. Although the present kinetic data are not sufficient for deducing a logical reaction mechanism, they provide important information on features of ideal method-A hydrocyanation which are discussed here.

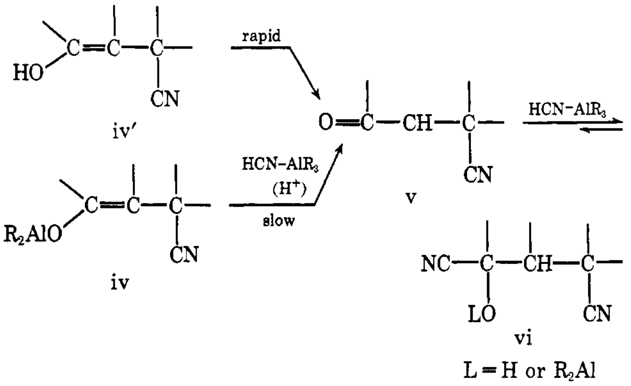
Table X. Specific Electric Conductivities at 25°

Compound(s)	Concn, *M*	Solvent	Specific conductivity,[a] 10^{-6} ohm^{-1} cm^{-1}
HCN	0.28	THF	*b*
$EtAlCl_2$	0.28	THF	30
Et_2AlCl	0.28	THF	1.7
$AlEt_3$	0.28	THF	0.37
$EtAlCl_2$–HCN	0.28–0.28	THF	40
Et_2AlCl–HCN	0.28–0.28	THF	2.4
$AlEt_3$–HCN	0.28–0.28	THF	0.78
$AlEt_3$–H_2O–HCN	0.28–0.026–0.28	THF	3.0
Me_2AlCN	0.28	THF–*i*-Pr_2O (3:2)	8.7
i-Bu_2AlCN	0.28	THF–*i*-Pr_2O (3:2)	4.7
Et_2AlCN	0.28	THF–*i*-Pr_2O (3:2)	4.6
Et_2AlCN	0.28	THF–*i*-Pr_2O (6:1)	9.3
Et_2AlCN	0.28	*i*-Pr_2O	0.21
Et_2AlCN	0.28	Toluene	*b*

[a] The measurement was made 3 min after mixing the compound(s) in the solvent. [b] Unmeasurably small.

(a) No Formation of the 1,2-Addition Product of Enone. As shown in Figure 2 (*cf.* ref 1), the formation of the enone 1,2-adduct **2** is negligible in the HCN–$EtAlCl_2$ reaction in contrast to an instantaneous and predominant formation of the 1,2 adduct in method-B hydrocyanation. Apparently, no 1,2-adduct formation is characteristic of the ideal HCN–AlR_3 reaction.

(b) Formation of Dinitrile 4 and Irreversibility of the Reaction. Except for reaction with HCN–$AlMe_3$ in which the participation of Me_2AlCN is large, the major component of the 1,4 adducts in method-A hydrocyanation of **1** is the dinitrile **4** (Table I). Since the dinitrile ratio is the highest with HCN–$EtAlCl_2$, the dinitrile formation is characteristic of the ideal HCN–AlR_3 reaction. The dinitrile formation is accounted for by irreversible transformation of the initial 1,4 adducts iv and iv′ into the cyano ketone v followed by 1,2 addition to the dicyano form vi. Conversion of enolate iv with HCN–AlR_3 into dinitrile vi *via* v is illustrated in Table III. Apparently, this conversion is effected by proton generated from HCN–AlR_3. The transformation of iv and iv′ to v makes the 1,4 addition irreversible in method-A hydrocyanation. The irreversible and kinetic nature of the reaction is well demonstrated by the cis–trans equilibrium study of 1,4 adducts in an accompanying paper.[4]



(c) Rate Acceleration by Water. Addition of a small amount of water in the reaction of **1** with HCN–$AlEt_3$ markedly increases the 1,4-addition rate (Figure 1b and Table I), decreases the formation of the 1,2-adduct **2** (Figure 1, see also ref 1), increases the dinitrile ratio in the product (Table I), and makes the 1,4 addition substantially pseudo-first-order (Figure 1b). All of these effects are characteristic of the ideal HCN–AlR_3 reaction. The data given in Table II indicate that water reacts with an excess of $AlEt_3$ very rapidly to give diethylaluminum hydroxide (Et_2AlOH) which slowly reacts with $AlEt_3$ to give bis(diethylaluminum) oxide ($Et_2AlOAlEt_2$).[5] Since the Et_2AlCN formation is not affected by the addition of water, the rate acceleration by water is due to the catalytic action of Et_2AlOH and $Et_2AlOAlEt_2$.

(d) Catalytic Nature of AlR_3. It has beens hown in the previous paper[1] that AlR_3 acts as a catalyst in method-A hydrocyanation. Since AlR_3 eventually reacts with HCN to give R_2AlCN, the HCN addition would be catalyzed by both AlR_3 and R_2AlCN.

Proposed Mechanism of Ideal HCN–AlR_3 Hydrocyanation. The above features of the ideal reaction coupled with the electric conductivity data lead us to propose a probable mechanism of ideal method-A hydrocyanation. Let us consider the HCN–$EtAlCl_2$ combination that represents the ideal method-A reagent. A high electric conductivity (Table X) of $EtAlCl_2$ in THF supports the dissociation of alkylaluminums (eq 7) to the ionic species as suggested by Bonitz,[6] and an increase in conductivity by the addition of HCN (HCN itself is not ionic in THF) indicates the formation of proton and a cyanoaluminate anion (eq 8) [see also the above discussion (b)].

$$2R_3Al \rightleftharpoons R_2Al^+ + R_4Al^- \qquad (7)$$

$$R_3Al + HCN \rightleftharpoons H^+ + (R_3AlCN)^- \qquad (8)$$

The assumption that the cations activate the enone system and $(R_3AlCN)^-$ ion acts as the cyanating species is supported by the observation that the ionic species (conductivity) decrease as the hydrocyanation of **1** proceeds (Figure 10). The rate-determining step would be the attack of $(R_3AlCN)^-$, since the combination HCN–$AlCl_3$ having a very high activating power has a poor hydrocyanating ability,[1] indicating that the reaction rate depends on the cyanating ability of $(R_3AlCN)^-$.

This consideration, the catalytic nature of AlR_3, the irreversibility, and the product composition have led us to propose a probable mechanism (Scheme I) for ideal HCN–AlR_3 hydrocyanation which involves activation of enone with a cation L^+ (H^+ or R_2Al^+), rate-determining, nucleophilic attack of the cyanoaluminate anion $(R_3AlCN)^-$ to give the initial 1,4-adduct iv and regenerate AlR_3, irreversible transformation to β-cyano ketone v, and conversion into dinitrile vi.

According to this mechanism, the rate acceleration due to water as described earlier can be easily accounted for by an increase of ionic species (in eq 7 and 8, R_3Al is R_2AlOH or $R_2AlOAlR_2$) increasing the ideal HCN–AlR_3 reaction. The increase of ionic species is supported by the conductivity data (Table X).

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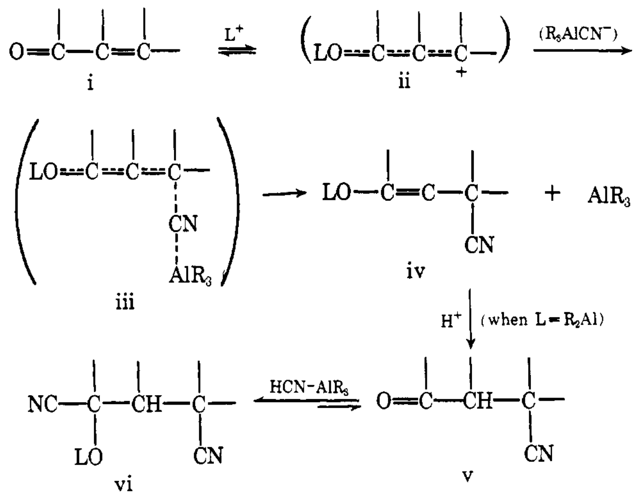
(4) W. Nagata, M. Yoshioka, and T. Terasawa, *J. Amer. Chem. Soc.*, **94**, 4672 (1972).

(5) (a) T. Saegusa, Y. Fujii, H. Fujii, and J. Furukawa, *Makromol. Chem.*, **55**, 232 (1962); (b) T. Saegusa, H. Imai, T Uejima, and J. Furukawa, *Catalyst (Tokyo)*, **7**, 43 (1965); (c) H. Tani, T. Araki, N. Oguni, and N. Ueyama, *J. Amer. Chem. Soc.*, **89**, 173 (1967).

(6) E. Bonitz, *Chem. Ber.*, **88**, 742 (1955).

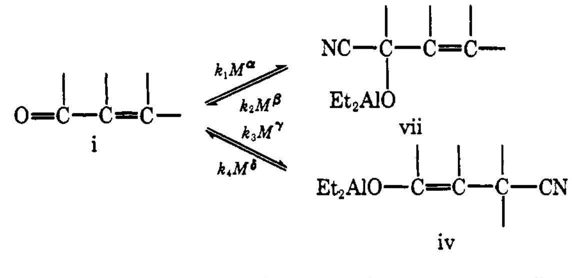
Scheme I



(L = H or R_2Al)

Mechanism of Method-B Hydrocyanation. When enone i reacts with Et_2AlCN, the reaction mixture contains the unchanged enone i, 1,2 adduct vii, and 1,4 adduct iv. The structures of 1,2 and 1,4 adducts before work-up are apparent from the discussion in the previous paper.[1] Thus, in the kinetics, [enone], [1,2 adduct], and [1,4 adduct] represent relative concentrations of i, vii, and iv. Kinetic data indicate that enone i rapidly reacts with Et_2AlCN to establish a fast pre-equilibrium with regards to the 1,2 addition, *i.e.*, i $\rightleftharpoons$ vii in an early stage of the reaction (Figure 6b and Table VI) and then 1,4 adduct iv forms gradually. The fact that the 1,4 addition is reversible is apparent from the observation that small but constant amounts of the enone counterparts ([enone] + [1,2 adduct]) remain at longer reaction times.

Thus, the method-B hydrocyanation is expressed by the following two consecutive, reversible, first-order reactions (eq 9) (*cf.* Appendix):[7]



(9)

where k_i represents the rate constant of the specified step, M is the effective concentration of the reagent [Et_2AlCN^*], and the exponents α, β, γ, and δ indicate kinetic orders with respect to the reagent. Since the 1,2 addition rate is too rapid to be measured, the kinetic data provide us with the apparent pseudo-first-order rate constant K for the 1,4 addition (i ⇀ iv), the reciprocal 1,2-addition equilibrium constant [enone]/[1,2 adduct] and the 1,4-addition equilibrium constant [1,4 adduct]$_\infty$/([enone]$_\infty$ + [1,2 adduct]$_\infty$) as given in eq 10–12. These equations are easily derived from eq 29, 20, and 30 (Appendix) by substituting k_1M^α, k_2M^β, k_3M^γ, and k_4M^δ for k_i.

$$K = (k_2k_3/k_1)M^{\beta+\gamma-\alpha} \qquad (10)$$

$$[\text{enone}]/[1{,}2\ \text{adduct}] = (k_2/k_1)M^{\beta-\alpha} \qquad (11)$$

$$[1{,}4\ \text{adduct}]_\infty/([\text{enone}]_\infty + [1{,}2\ \text{adduct}])_\infty = (k_2k_3/k_1k_4)M^{\beta+\gamma-\alpha-\delta} \qquad (12)$$

When cholest-4-en-3-one (**1**) is the substrate, only the 1,4-addition apparent rate constant K was measurable and from the linear plot given in Figure 7, we obtain $\beta + \gamma - \alpha = 0.49$.

With the B-norsteroid **5** as the substrate, dependences of K, [enone]/[1,2 adduct], and [1,4 adduct]$_\infty$/([enone]$_\infty$ + [1,2 adduct]$_\infty$) on the reagent concentration M were obtainable as shown in Figure 9 and the linear plots give $\beta + \gamma - \alpha = 0.44$, $\beta - \alpha = -0.15$, $\beta + \gamma - \delta - \alpha = 0.73$. Therefore $\gamma = 0.59$ and $\delta = -0.29$.

The unreasonable negative value of δ would suggest that the reagent Et_2AlCN does not directly participate in the 1,4-reverse addition iv → i, which is accelerated by an unknown species[9] whose effect is retarded with increasing reagent concentration. Therefore, the δ value should be taken as zero. Then, one would reasonably assume that the reagent does not participate also in the reverse reaction vii → i and the β value should be zero. With β as zero, the α value is derived to be 0.15. This small α value indicates that the 1,2-addition i → vii would be effected by a minimum unit of reagent, *i.e.*, monomeric "Et_2AlCN" and that α should be $^1/_3 \sim {}^1/_2$ (*cf.* discussion below). This correction leads to a γ value of $^2/_3 \sim 1$. The corrected values are summarized as follows: $\alpha = {}^1/_3 \sim {}^1/_2$, $\gamma = {}^2/_3 \sim 1$, and $\beta = \delta = 0$.

Now, a question arises as to the governing reacting species in method-B hydrocyanation. Although the conductivity data (Table X) indicate the presence of ionic species in solutions of R_2AlCN in ether solvents, the possibility that the reacting species are ionic can be excluded by the evidence that the relative 1,4-addition rates of cholestenone (**1**) with Et_2AlCN in various solvents (Table VIII) are antiparallel to the ion concentrations (conductivity) and that Me_2AlCN having the higher conductivity than Et_2AlCN and i-Bu_2AlCN is far less reactive than the latter reagents. This consideration leads us to conclude that the governing reacting species in method-B hydrocyanation is nonionic R_2AlCN itself. Ebullioscopic molecular weight deter-

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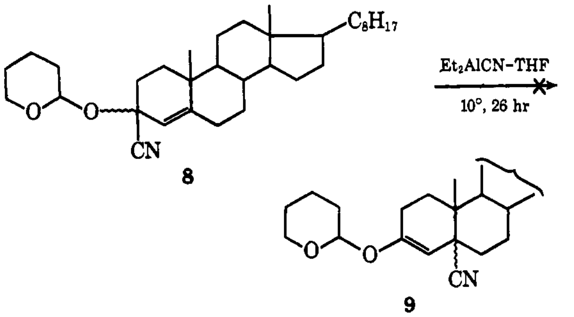
[7] A referee suggested a possible competitive S_N2' route (vii → iv). This possibility may be excluded by the finding that 1,2-adduct derivative **8** did not give 1,4-adduct **9** on treatment with Et_2AlCN. Compound **8**, mp 98–105°, was prepared by reaction of 1,2 adduct **2**[8] with dihydropyran and phosphorus oxychloride.



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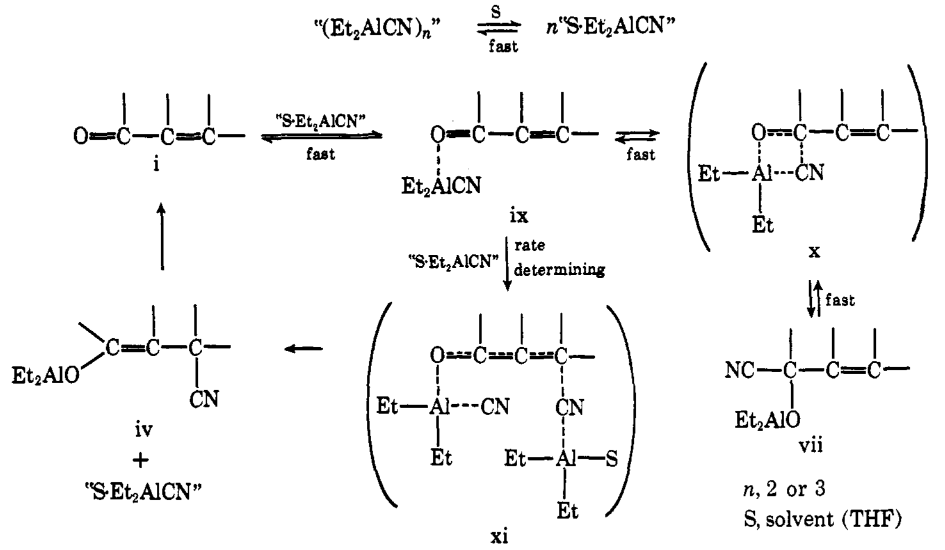
[8] Accompanying paper: W. Nagata, M. Yoshioka, and M. Murakami, *J. Amer. Chem. Soc.*, **94**, 4654 (1972).

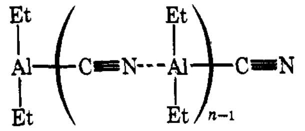
[9] One possible such species is an oxygenated aluminum compound which is formed by reaction of Et_2AlCN with water. The reagent and the reaction medium might be contaminated with a trace of water, despite great care to prevent any contamination. This possibility accords with the results shown in Figure 5 that indicate the addition of a small amount of water accelerates the reverse reaction and the effect is smaller at a higher reagent concentration. In any event, a direct participation of Et_2AlCN in the reverse reaction should be ruled out.

Scheme II



n, 2 or 3
S, solvent (THF)

mination[1] indicates that degree of association of Et_2AlCN is 1.86 at 66° and at low concentrations (0.038 and 0.076 *M*) in THF–*i*-Pr_2O (13:1),[3] 4.7 in benzene at 80°, and 5.0 in *i*-Pr_2O at 68°. The ir $C{\equiv}N$ stretching absorption at a lower frequency (2211 cm^{-1}, neat)[1] is in accord with the $C{\equiv}N$ bridged linear structure.[10]



$$Et_2Al\text{—}\left(C{\equiv}N\cdots AlEt_2\right)_{n-1}\text{—}C{\equiv}N$$

One may assume from this structure that there is no associated species of special stability (like the dimer for dimethylaluminum chloride)[11] and the cyanide is present as a mixture of associated species with rapid interconversion. Since the associated species of this type would be more stable at a lower temperature[12] and in a higher concentration,[13] the degree of association of Et_2AlCN in THF would be higher than the observed value of 1.86 under the conditions for kinetic runs (0°, 0.1–0.45 *M*) and be predominantly two or three.

With this consideration, the α value of $^1/_3 \sim {}^1/_2$ and the γ value of $^2/_3 \sim 1$ are consistent with the conclusion that the attacking species in the 1,2-addition step i → vii is a monomeric "Et_2AlCN" and in the 1,4 step i → iv two monomeric "Et_2AlCN."[14] Here, the marks " " are used to indicate the molecule of the specified degree of association to differentiate it from the expression R_2AlCN which illustrates merely the alkylaluminum cyanide molecule irrespective of the degree of association. The finding that the 1,4 addition is slowest in THF, the most basic solvent examined (Table IX), indicates that the reagent is solvated with THF, as expressed as "S·Et_2AlCN," and a fast equilibrium exists between the solvated reagent and the substrate enone as suggested for the Grignard reaction.[15]

Participation of two monomeric "S·Et_2AlCN" in the 1,4-addition is easily accounted for by the consideration that the first "S·Et_2AlCN" coordinates with the enone oxygen to activate the enone system and the second introduces the cyano group at position 4. This second step will be rate determining as evident from the very rapid 1,2 addition indicating an easy coordination of Et_2AlCN to the carbonyl, and from the structure–reactivity relationship[8] indicating that the 1,4-addition rate is dependent on the environment of position 4.

The above discussions are summarized as follows: (1) the method-B hydrocyanation consists of a very rapid reversible 1,2 addition (preequilibrium) and a slow reversible 1,4 addition; (2) the reacting species is monomeric and solvated in the both additions; (3) the 1,2 addition i → vii is first order both in enone and monomeric "S·Et_2AlCN," and the reverse 1,2 addition vii → i is first order in the 1,2-adduct vii and zero order in the reagent; (4) the 1,4-addition i → iv is first order in enone and second order in "S·Et_2AlCN," the rate-determining step being the attack of "S·Et_2AlCN" at position 4 of the enone coordinated with "Et_2AlCN"; (5) the reverse 1,4-addition iv → i is first order in the 1,4 adduct iv and zero order in the reagent.

In Scheme II is shown the mechanism for hydrocyanation of an enone with Et_2AlCN in THF which is consistent with the discussions described above. Since the rate-determining step of the 1,4 addition is preceded by the rapid 1,2-addition preequilibrium i ⇄ vii, the apparent 1,4-addition rate *K* is dependent on the 1,2-addition equilibrium constant k_2/k_1, as clearly seen from eq 10 and 11. The 1,2 adduct vii which predom-

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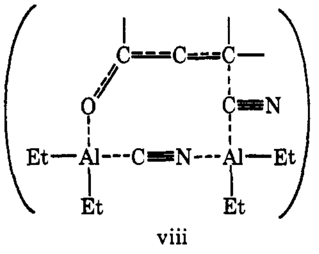
(10) D. A. Dows, A. Haim, and W. K. Wilmarth, *J. Inorg. Nucl. Chem.*, **21**, 33 (1961); *cf.* G. E. Coates and R. N. Mukherjee, *J. Chem. Soc.*, 229 (1963).

(11) Y. Sakurada, M. L. Huggins, and W. R. Anderson, *J. Phys. Chem.*, **68**, 1934 (1964).

(12) A. W. Laubengayer and W. F. Gilliam, *J. Amer. Chem. Soc.*, **63**, 477 (1941); M. B. Smith, *J. Phys. Chem.*, **71**, 364 (1967).

(13) E. C. Ashby and M. B. Smith, *J. Amer. Chem. Soc.*, **86**, 4363 (1964).

(14) The possibility that a dimeric species "$Et_4Al_2(CN)_2$" reacts with the enone as shown in viii may be ruled out from the experimental fact



viii

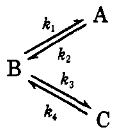
that the method-B conjugate hydrocyanation smoothly proceeds with many enones which are difficult to have the orientation viii.[8]

(15) (a) R. N. Lewis and J. R. Wright, *J. Amer. Chem. Soc.*, **74**, 1253 (1952); (b) H. Hashimoto, T. Nakano, and H. Okada, *J. Org. Chem.*, **30**, 1234 (1965); (c) A. A. Scales and E. I. Becker, *ibid.*, **30**, 3491 (1965).

inates in the early stage of the reaction is converted into the 1,4 adduct iv until an equilibrium is established between the enone i (usually negligible), the 1,2 adduct vii, and the 1,4 adduct iv (usually major). The reversibility of the 1,4 addition should be emphasized. With other R_2AlCN in THF and Et_2AlCN in solvents other than THF, the mechanism would be essentially the same as shown above, and the reactivity depends on difference in dissociation, the enone-activating ability, and the cyanating ability of R_2AlCN. The high reactivity of R_2AlCN may be attributed to the reagent nature that its abundant neutral species acts as an enone-activating as well as cyanating agent.

Appendix

Kinetic Equations. Consider the parallel reversible reactions shown in eq 13. If relative concentrations



(13)

with respect to the initial concentration of B are expressed by [A], [B], and [C], we obtain

$$d[A]/dt = k_1[B] - k_2[A] \qquad (14)$$

$$d[B]/dt = k_2[A] + k_4[C] - (k_1 + k_3)[B] \qquad (15)$$

$$d[C]/dt = k_3[B] - k_4[C] \qquad (16)$$

$$[A] + [B] + [C] = 1 \qquad (17)$$

Though general solutions are obtainable for the reaction under the condition that at time $t = 0$, $[A] = 0$, $[B] = 1$, $[C] = 0$, the solutions which are similar to those given by Lowry and John[16] are complicated and unpractical.

We have therefore derived simpler solutions in terms of the following approximations. First, the reactions shown in eq 13 are approximated to be the two consecutive reversible first-order reactions (eq 18) under the condition given in eq 19, since the data shown in Figure 8 indicate that a major amount of the substrate B, when mixed with an excess of the reagent, is very rapidly converted into the 1,2 adduct A and the 1,4 adduct C as if the three species were present at the start. The second approximation that the conversion B $\rightleftharpoons$ A is in a fast equilibrium (eq 20) is pertinent from the data shown in Table VI.

$$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B \underset{k_4}{\overset{k_3}{\rightleftharpoons}} C \qquad (18)$$

$$\text{at } t = 0,\ [A] = [A]_0;\ [B] = [B]_0;\ [C] = [C]_0 \qquad (19)$$

$$k_1[B] = k_2[A] \qquad (20)$$

By substitution into eq 21 with material balance (eq 17)

$$d[C]/dt = k_3[B] - k_4[C] \qquad (21)$$

we have

$$d[C]/dt = K - (K + k_4)[C] \qquad (22)$$

where

$$K = k_3/(1 + k_1/k_2) = k_2k_3/(k_1 + k_2) \qquad (23)$$

Integration under the condition given in eq 19 results in

$$\frac{1}{K + k_4} \ln \frac{K - (K + k_4)[C]_0}{K - (K + k_4)[C]} = t \qquad (24)$$

where $[C]_0$ may be obtained as the relative concentration of C when the step B $\rightleftharpoons$ A reaches equilibrium.

At $t = \infty$

$$K - (K + k_4)[C]_\infty = 0 \qquad (25)$$

$$[C]_\infty = K/(K + k_4) \qquad (26)$$

Substitution in eq 24 yields

$$[C]_\infty \ln \frac{[C]_\infty}{[C]_\infty - [C]} = Kt + [C]_\infty \ln \frac{[C]_\infty}{[C]_\infty - [C]_0} \qquad (27)$$

Equation 28 can be obtained easily.

$$\frac{[C]_\infty}{[A]_\infty + [B]_\infty} = \frac{[C]_\infty}{1 - [C]_\infty} = \frac{K}{k_4} = \frac{k_2k_3}{k_4(k_1 + k_2)} \qquad (28)$$

If $k_1 \gg k_2$, eq 23 and 24 may be simplified as

$$K = k_2k_3/k_1 \qquad (29)$$

$$[C]_\infty/([A]_\infty + [B_\infty]) = k_2k_3/k_1k_4 \qquad (30)$$

Experimental Section

For general directions see the accompanying paper.[8]

Materials. Cholest-4-en-3-one (**1**) obtained by the Oppenauer oxidation of cholesterol was purified by chromatography on alumina and repeated recrystallization from ethanol. The pure, snow-white crystals, mp 80.5–81.0°, were dried at 50° (2 mm) for 20 hr. *B*-Norandrost-4-en-3-one (**5**) was prepared as described in the accompanying paper[8] and purified in the same way as described above. The pure, snow-white crystals, mp 47–48°, were dried at room temperature and 2 mm for 20 hr. All solvents were distilled once from a dispersion of sodium, then refluxed for at least 4 hr with 5% of sodium dispersion and 1% of $AlEt_3$ (per cent based on the total volume of solvents). During this reflux period, high-purity argon was bubbled through the solvent mixtures. Then the solvents were distilled under argon through a 20-cm column packed with small, short, glass tubes. HCN was distilled from calcium chloride through a calcium chloride drying U-tube under nitrogen into a ice-cooled, tared flask. The dry HCN was diluted with THF to make a 7.0 *M* solution. $AlEt_3$ (Ethyl Corp., La.) was freed from an organoaluminum hydride contaminant (*ca.* 5%) in the following way. To a solution of 60 ml of $AlEt_3$ in 70 ml of THF was added a solution of 4.27 g of cyclohexanone in 10 ml of THF with ice cooling under nitrogen. After being kept overnight at room temperature, the mixture was concentrated by distillation, and the residue was distilled under reduced pressure to give 65 ml of triethylaluminum tetrahydrofuranate, bp 75° (0.3 mm) [lit.[17] bp 60.5–64° (0.005 mm)]. The vacuum was broken with argon, and the material was diluted with THF to make a 1.5 *M* solution of $AlEt_3$. Other alkylaluminums, Et_2AlCl, $EtAlCl_2$, and $AlMe_3$ (Ethyl Corp.), were purified by vacuum distillation. The concentrations of solutions of Et_2AlCl, $EtAlCl_2$, and $AlMe_3$ in THF were 1.83, 2.70, and 2.15 *M*, respectively. The dialkylaluminum cyanides, Et_2AlCN, Me_2AlCN, and *i*-Bu_2AlCN, were prepared as previously described[1] and purified by redistillation. Solutions (1–2 *M*) of the reagents in *i*-Pr_2O were prepared soon after the redistillation. A solution of $AlEt_3$ in toluene was also prepared and used for experiments carried out in toluene. The anhydrous solvents, neat alkylaluminums and the stock solutions of HCN, $AlEt_3$, $AlMe_3$, and the dialkylaluminum cyanides were stored at −20° in ampoules sealed in a stream of argon. The THF solutions of Et_2AlCl and $EtAlCl_2$ were prepared just before use. Nitrogen was purified by passing through reduced copper at 300° and then through Linde molecular sieves. High-purity argon (Takachiho Kagaku, Osaka) guaranteed 99.9999% purity was used without further purification.

Handling. All solvents and reagents were handled with hypodermic syringes (error below 1%) in an inert atmosphere of nitro-

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[16] T. M. Lowry and W. T. John, *J. Chem. Soc.*, **97**, 3337 (1910); *cf.* A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, p 175.

[17] K. Ziegler, Belgium Patent, No. 616,188 (1962); *Chem. Abstr.*, **59**, 662*e* (1963).

gen. All glassware and equipment used for purification and storage of solvents and reagents as well as for kinetics were dried at 100 and 150°, for method-A and -B operations, respectively, for at least 5 hr and cooled *in vacuo* or under nitrogen before use.

Kinetics. Kinetic Run for Method A. Cholest-4-en-3-one (**1**) was placed in a 25- or 30-ml volumetric flask fitted with an adaptor having a glass-stoppered opening and a side arm connected to a vacuum pump *via* an argon bubbler system. The flask was evacuated (0.05 mm) and refilled with argon several times. Fixed amounts of THF and an AlR_3 solution were added, and the flask was kept at 25 ± 0.05° for 30 min. A stock solution of HCN was then added with vigorous magnetic stirring when the reaction time was taken to be zero. The total volume was adjusted to 25 or 30 ml by the addition of a small amount of THF as rapidly as possible, and the stirring was continued for about 1 min. The reaction mixture was kept under a small positive pressure of argon. Aliquots were withdrawn by using 1-ml pipets connected with syringes by means of rubber tubing. When the reaction vessel was opened for transfer of THF and the reagents (or for withdrawal of aliquots), the opening was swept with a rapid stream of argon admitted through the side arm. The aliquots were analyzed as indicated later.

Kinetic Run for Method B. The same equipment as described above was used for the kinetic runs whose data are listed in Tables IV–VI. A stock solution of the enone **5** in THF was added to a solution of Et_2AlCN in THF–i-Pr_2O kept at 0 ± 0.005°. Four runs at every other different reagent concentrations (see Table VI) were carried out at the same time using the solvent, the reagent stock solution, and the stock solution of the enone **5**, each kept in the same ampoule. Other method-B kinetic runs were performed in a similar way except that a reagent stock solution was added to a thermostated solution of an enone. Analyses of the products were done as described below except for the reaction in toluene. The reaction in toluene was stopped by the addition of cold ethanolic hydrochloric acid as soon as possible after the reagent was added. The mixture was worked up and analyzed by ir spectroscopy as described below. The reaction at $-5°$ was 48 and 52% complete at $t = 14$ and 25 sec, respectively. We have estimated $\tau_{0.5} = ca.$ 20 sec from the data.

Analysis. The enones **1** and **5** showed uv absorption maxima at 242 mμ with molecular extinction coefficients (ϵ) of 16,200 and 15,100, respectively, whereas the coefficients of 1,2 adducts, **2** and **6**, and 1,4 adducts, **3**, **4**, and **7**, were less than 150. Therefore, concentrations of the enones could be analyzed by uv spectrometry without interference of the 1,2 and 1,4 adducts. To cancel small interference of the reagent and solvent, the reference solution for the uv measurement was prepared from a solution containing only the reagent in the solvent by the same work-up as used for the reaction aliquots. Thus, the enone concentrations were determined with a maximum error of 2%. The work-up of the aliquots for uv analysis was as follows. The aliquots were poured into 0.05 N ethanolic hydrochloric acid (prepared by adding concentrated hydrochloric acid to 95% ethanol) kept at $-50°$ in volumetric flasks. Aliquots from these ethanolic solutions were appropriately diluted with 0.05 N ethanolic hydrochloric acid and subjected to uv analysis at 242 mμ as soon as possible to determine the amount of the enone. Other aliquots from the ethanolic solutions were diluted with a five- to tenfold amount of 95% ethanol, made alkaline with 2 N sodium hydroxide, and made acid again with 0.05 N ethanolic hydrochloric acid after 3–5 min.[18] Uv analyses of these solutions gave the total amount of the enone counterparts.

The concentrations of enone **1** and 1,4 adduct **3** in an isolated product were analyzed by ir spectrometry with maximum error of 7% by measuring the absorption at 1665 and 1720 cm^{-1} in chloroform. The molecular extinction coefficients are 14.30 at 1665 cm^{-1} and 0.294 at 1720 cm^{-1} for enone **1** and 0.208 at 1665 cm^{-1} and 9.28 at 1720 cm^{-1} for 1,4 adduct **3**. The work-up of the reaction mixture was carried out as follows. The reaction mixture was poured into 2 N hydrochloric acid–ice and extracted with ether–dichloromethane (3:1). After the amount of the cyano ketone **3**, [**3**], in the product obtained by the usual work-up was analyzed by ir spectroscopy, the product was again dissolved in ether–dichloromethane (3:1). The solution was washed twice with ice cold 2 N sodium hydroxide and worked up in the usual way. Ir analysis of the product gave the total amount of the cyano ketone **3** and the dicyano compound **4**, [**3**] + [**4**].

Gas Evolution. A 50-ml flask was fitted with an adaptor having a glass-stoppered opening and a side arm connected to a 200-ml mercury gas buret. After crystals of pure cholestenone (**1**) were placed in the flask when necessary, the reaction system and the buret were evacuated (0.05 mm) and refilled with ethane (Takachiho Kagaku) several times. THF and a stock solution of AlR_3 were introduced into the flask while the opening was swept with a stream of ethane. After the solution was magnetically stirred at 25 ± 0.05° for 1 hr to saturate it with ethane, the glass stopper was replaced by a serum cap, through which a stock solution of HCN or water was added.

Conductivity Measurements. The conductivity measurements were made with a Yanagimoto conductivity apparatus model MY-7 at 800 Hz. The cell was a cylindrical glass container possessing two black platinum electrodes about 1 × 2 cm, placed 1 cm apart, and fitted with an adaptor as described for the kinetics. The cell constant was 0.175. The container was dried at 200° and 0.05 mm with a hot gun before use. The material, the reagent, and the reagent solution(s) were charged in the same way as described in method-A kinetics.

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(18) An aluminum compound precipitates from the alkaline solution upon standing for more than 30 min making the uv analysis impossible.