# 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**



(L = H or $R_2Al$)
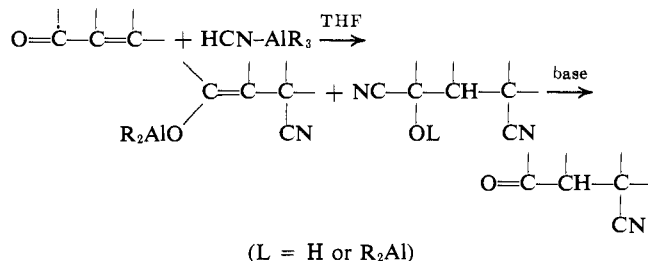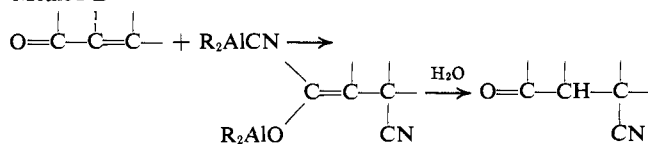
**Method B**



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 hy-

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

drocyanation 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.

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.

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

## 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.
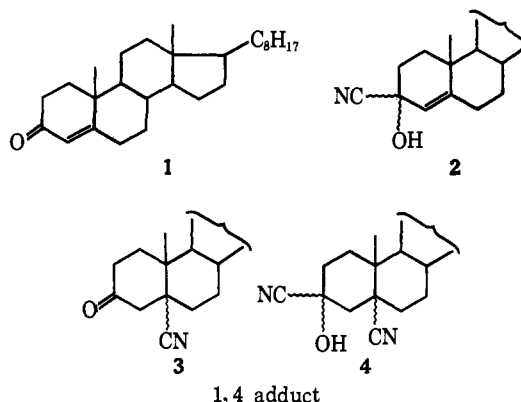


1, 4 adduct

Let us define the following relative concentrations

$$[\text{enone}] = [\mathbf{1}]/[\mathbf{1}]_i, \quad [1,2 \text{ adduct}] = [\mathbf{2}]/[\mathbf{1}]_i$$

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

$$[\text{enone}] + [1,2 \text{ adduct}] + [1,4 \text{ adduct}] = 1$$

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

(2) Apparently, each of 2, 3, and 4, though treated as homogeneous in the kinetics, is a mixture of epimeric α- and β-carbonitriles.
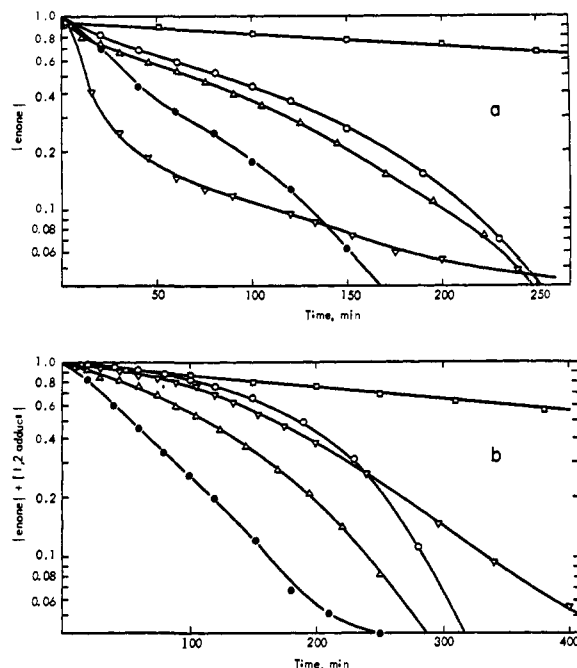
Figure 1. Plots of relative concentrations [enone] (a) and [enone] + [1,2 adduct] (b), as a function of time for hydrocyanation of 1(0.04 $M$) with HCN (0.28 $M$) and the following $AlR_3$ (0.28 $M$) in THF at 25°: □, $EtAlCl_2$; △, $Et_2AlCl$; ●, $AlEt_3$ + $H_2O$ (0.026 $M$); ○, $AlEt_3$; ▽, $AlMe_3$.



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 $M$).

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

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

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 $M$.

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.

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.

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
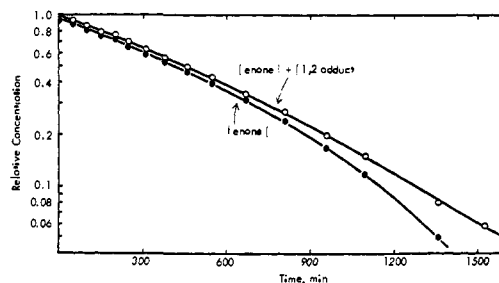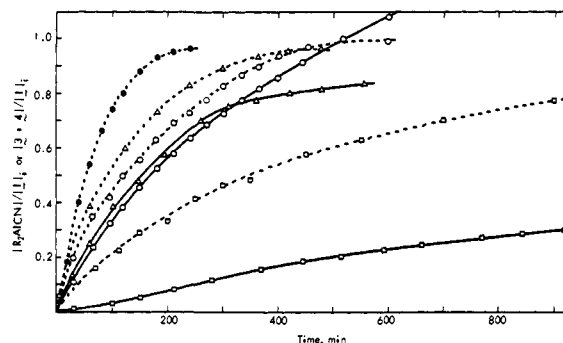
in the reaction of water with an excess of $AlEt_3$.

**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]

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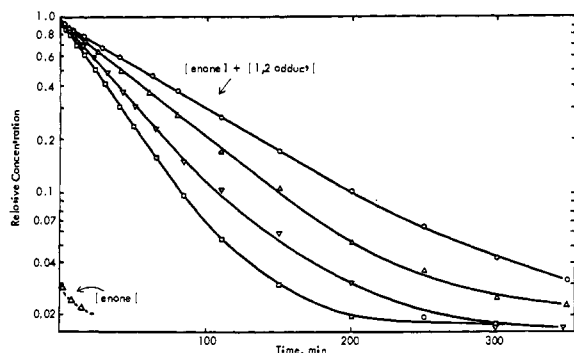
Figure 4. Plots of relative concentrations, [enone] + [1,2 adduct] (solid lines) and [enone] (dotted line), $vs.$ time for hydrocyanation of 1 (0.01 $M$) with $Et_2AlCN$ at the following concentrations (as [$Et_2AlCN^*$] in $M$] in THF–$i$-$Pr_2O$ (4:1) at 0°: O, 0.07; △, 0.13; ▽, 0.27; □, 0.433.
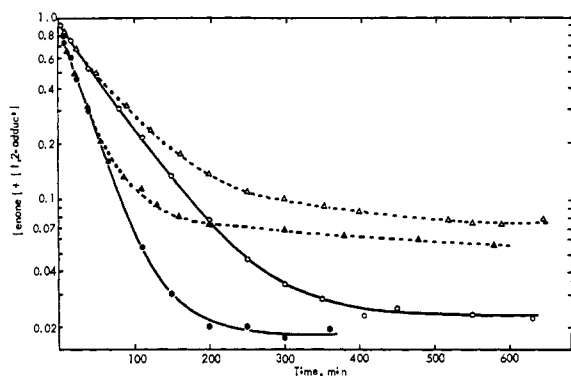


Figure 5. Effect of a trace of water on hydrocyanation of 1 (0.01 $M$) with $Et_2AlCN$ in THF–$i$-$Pr_2O$ (4:1) at 0°: O, [$Et_2AlCN^*$] = 0.09 $M$; △, [$Et_2AlCN^*$] = 0.09 $M$ and [$H_2O$] = 0.0002 $M$; ●, [$Et_2AlCN^*$] = 0.44 $M$; ▲, [$Et_2AlCN^*$] = 0.44 $M$ and [$H_2O$] = 0.0002 $M$.

(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



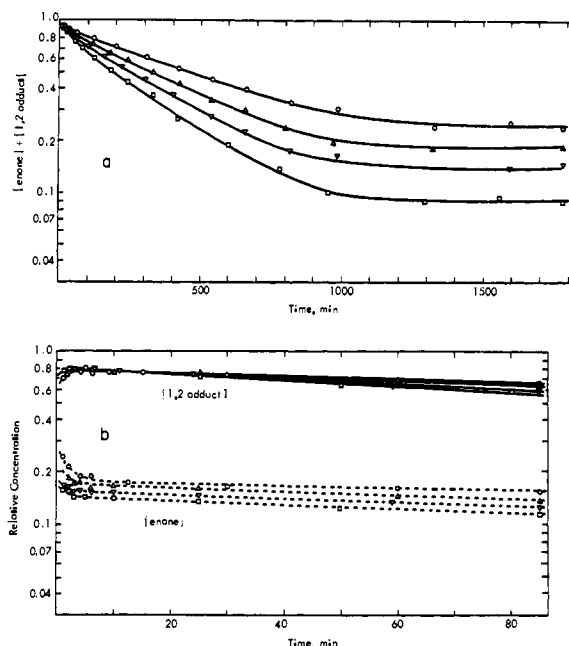Figure 6. Plots of relative concentrations, [enone] + [1,2 adduct] (a), [1,2 adduct] (b, solid lines), and [enone] (b, dotted lines), as a function of time for hydrocyanation of 5 (0.01 $M$) with $Et_2AlCN$ at the following concentrations (as [$Et_2AlCN^*$] in $M$) in THF–$i$-$Pr_2O$ (4:1) at 0°: O,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

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.

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

$$\text{enone} \underset{\diagdown\diagdown 1,4\text{ adduct}}{\overset{\diagup\diagup 1,2\text{ adduct}}{\rightleftharpoons}} \tag{3}$$
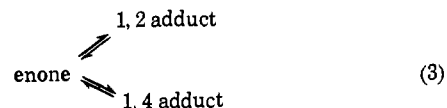
as the substrate, the concentration of the enone at an initial stage of reaction, [enone]$_0$, and the combined equilibrium concentrations of the enone and the 1,2 adduct, [enone]$_\infty$ + [1,2 adduct]$_\infty$, are too low to be analyzed accurately (Figure 4). We searched, therefore, for another substrate, suitable for an examination of the dependence of the reagent concentration on [enone]$_0$ and [enone]$_\infty$ + [1,2 adduct]$_\infty$, and $B$-nor-
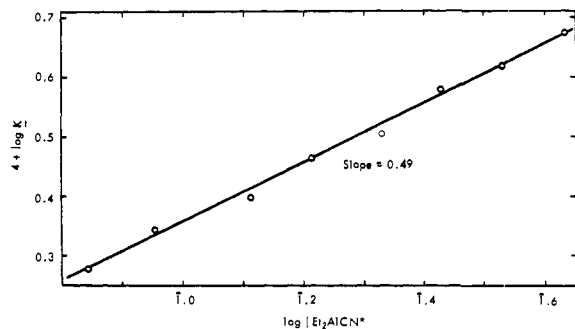
Figure 7. Linear plot of logarithm of the apparent pseudo-first-order rate costant, $K$, and of the $Et_2AlCN^*$ concentration for conjugate hydrocyanation of 1 (0.01 $M$) with $Et_2AlCN$ in THF-$i$-$Pr_2O$ (4:1) at 0°.



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°: O, 0.09; △, 0.165; ▽, 0.270; □, 0.44.
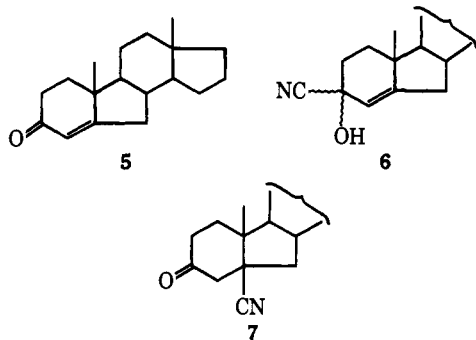
androst-4-en-3-one (5) was found suitable for this examination.

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

$$[enone] = [5]/[5]_i, [1,2 \text{ adduct}] = [6]/[5]_i$$

$$[1,4 \text{ adduct}] = [7]/[5]_i \qquad (4)$$

$$[enone] + [1,2 \text{ adduct}] + [1,4 \text{ adduct}] = 1$$

where $[5]_i$ is the initial concentration of 5.



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

$$[1,4 \text{ adduct}]_\infty \ln \frac{[1,4 \text{ adduct}]_\infty}{[1,4 \text{ adduct}]_\infty - [1,4 \text{ adduct}]} =$$

$$Kt + [1,4 \text{ adduct}]_\infty \ln \frac{[1,4 \text{ adduct}]_\infty}{[1,4 \text{ adduct}]_\infty - [1,4 \text{ adduct}]_0}$$

$$(5)$$

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

In the hydrocyanation of 1 (Figure 4), [1,4 adduct]$_\infty$ = {1 − ([enone]$_\infty$ + [1,2 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 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 adduct]$_0$ can be obtained by extrapolating the curve to $t = 0$.

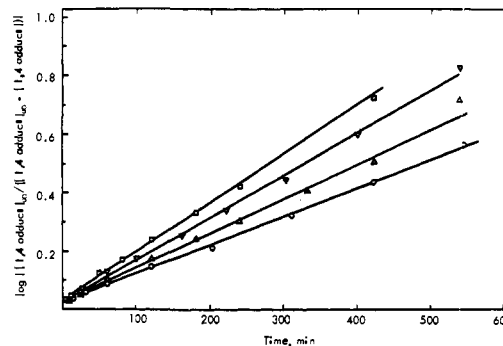Table IV. Apparent Pseudo-First-Order Rate Constants $K$ for Conjugate Hydrocyanation of 1 (0.01 $M$) with $Et_2AlCN$ at Various Concentrations in THF-$i$-$Pr_2O$ (4:1) at 0°

| [$Et_2AlCN^*$], $M$ | $\tau_{0.5}$, 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 adduct]$_\infty$/([enone]$_\infty$ + [1,2 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
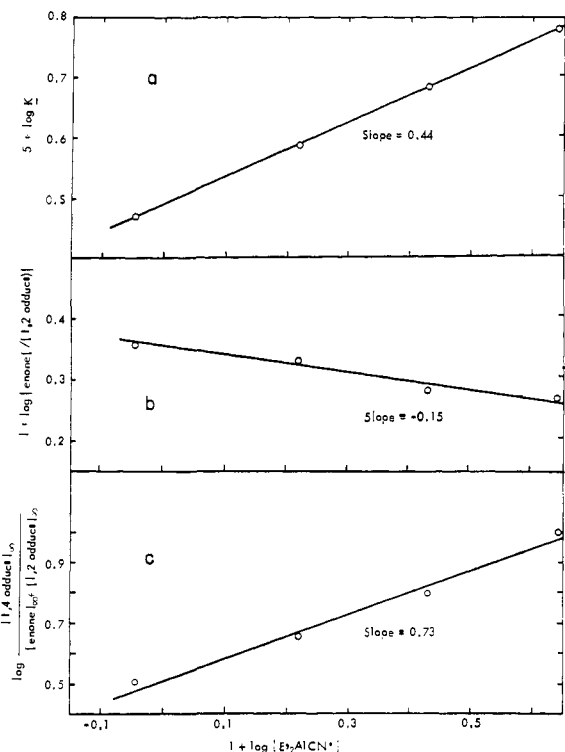
Figure 9. Dependence of Et₂AlCN* concentration of $K$ (a), [enone]/[1,2 adduct] (b), and [1,4 adduct]_∞/([enone]_∞ + [1,2 aduct]_∞) (c) for hydrocyanation of 5 with Et₂AlCN in THF-$i$-Pr₂O (4:1) at 0°.

**Table VI.** Time Variation in the Ratio [enone]/[1,2 adduct] for Hydrocyanation of 5 (0.01 $M$) with Et₂AlCN* (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 R₂AlCN (0.10 $M$) in THF-$i$-Pr₂O (4:1)

| R₂AlCN | Temp, °C | $K$, sec⁻¹ | Relative rate |
|---|---|---|---|
| Et₂AlCN | 0.0 | 2.27 × 10⁻⁴ | 1.0[a] |
| Et₂AlCN | 15.0 | 1.96 × 10⁻³ | 1.0[a] |
| Me₂AlCN | 15.0 | 1.64 × 10⁻⁴ | 0.084 |
| $i$-Bu₂AlCN | 0.0 | 1.17 × 10⁻³ | 5.15 |

[a] Taken as the standard.

reagent R₂AlCN on the 1,4-addition rate. The solvent effect on the rate for conjugate hydrocyanation of 1 with Et₂AlCN 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-AlR₃-THF) and method-B (R₂AlCN) 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, AlR₃, AlR₃-HCN, and R₂AlCN were measured and time dependence on electric conductivities of HCN-
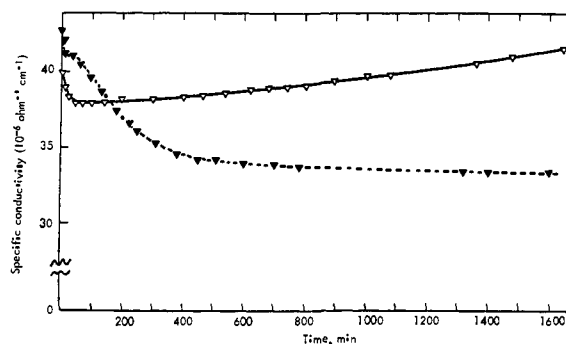


Figure 10. Plots of specific conductivity of HCN-EtAlCl₂ (0.28–0.28 $M$) (▽) and of 1-HCN-EtAlCl₂ (0.1-0.28-0.28 $M$) (▼) as a function of time in THF at 25°.

**Table VIII.** Solvent Effect in Conjugate Hydrocyanation of 1 (0.005 $M$) with Et₂AlCN

| Solvent | [Et₂-AlCN*], $M$ | Temp, °C | $\tau_{0.5}$, sec | Relative rate |
|---|---|---|---|---|
| THF-$i$-Pr₂O (4:1) | 0.045 | 0.0 | 4,800 | 1.0[a] |
| $i$-Pr₂O | 0.045 | 0.0 | 60 | 80 |
| THF-$i$-Pr₂O (7:1) | 0.095 | 10.0 | 950 | 1.0[a] |
| Dioxane-$i$-Pr₂O (4:1) | 0.095 | 10.0 | 25 | 38 |
| THF-$i$-Pr₂O (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-AlR₃ and R₂AlCN

| Reagent | Solvent | Relative rate |
|---|---|---|
| HCN-EtAlCl₂ | THF | 1.0 |
| HCN-Et₂AlCl | THF | 5.5 |
| HCN-AlEt₃-H₂O[a] | THF | 8.0 |
| HCN-AlEt₃ | THF | 4.5 |
| HCN-AlMe₃ | THF | 3.9 |
| Me₂AlCN | THF | 15 |
| ($i$-Bu)₂AlCN | THF | 950 |
| Et₃AlCN | THF[b] | 180 |
| Et₂AlCN | Dioxane[b] | 6,800 |
| Et₂AlCN | $i$-Pr₂O | ca. 14,000 |
| Et₂AlCN | Toluene | >85,000 |

[a] The molar ratio of water to HCN-AlEt₃ is 1:11. [b] Contains a small amount of $i$-Pr₂O.

EtAlCl₂ and 1-HCN-EtAlCl₂ was examined. The results are indicated in Table X and Figure 10.

**Discussion**

**Features of Ideal Method-A Hydrocyanation.** Participation of R₂AlCN in method-A hydrocyanation as estimated from the data shown in Figure 3 is in the following increasing order: HCN-EtAlCl₂ < HCN-AlEt₃-H₂O < HCN-Et₂AlCl < HCN-AlEt₃ < HCN-AlMe₃. The concentration-time pattern for hydrocyanation of 1 with HCN-EtAlCl₂ is almost linear, indicating that the reaction is substantially pseudo-first-order. Thus, the combination HCN-EtAlCl₂ represents the ideal method-A reagent. With other combinations, participation of more reactive R₂AlCN 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 |
| EtAlCl₂ | 0.28 | THF | 30 |
| Et₂AlCl | 0.28 | THF | 1.7 |
| AlEt₃ | 0.28 | THF | 0.37 |
| EtAlCl₂–HCN | 0.28–0.28 | THF | 40 |
| Et₂AlCl–HCN | 0.28–0.28 | THF | 2.4 |
| AlEt₃–HCN | 0.28–0.28 | THF | 0.78 |
| AlEt₃–H₂O–HCN | 0.28–0.026–0.28 | THF | 3.0 |
| Me₂AlCN | 0.28 | THF–i-Pr₂O (3:2) | 8.7 |
| i-Bu₂AlCN | 0.28 | THF–i-Pr₂O (3:2) | 4.7 |
| Et₂AlCN | 0.28 | THF–i-Pr₂O (3:2) | 4.6 |
| Et₂AlCN | 0.28 | THF–i-Pr₂O (6:1) | 9.3 |
| Et₂AlCN | 0.28 | i-Pr₂O | 0.21 |
| Et₂AlCN | 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–EtAlCl₂ 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–AlR₃ reaction.

**(b) Formation of Dinitrile 4 and Irreversibility of the Reaction.** Except for reaction with HCN–AlMe₃ in which the participation of Me₂AlCN 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–EtAlCl₂, the dinitrile formation is characteristic of the ideal HCN–AlR₃ 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–AlR₃ into dinitrile vi *via* v is



L = H or R₂Al
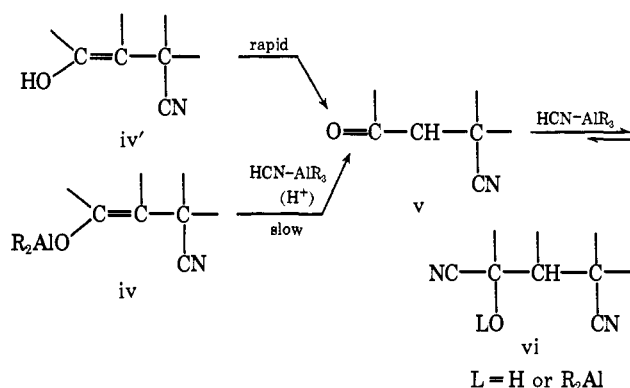
illustrated in Table III. Apparently, this conversion is effected by proton generated from HCN–AlR₃. The transformation of iv and iv' to v makes the 1,4 addition irreversible in method-A hydrocyanation. The irreversible and kinetic nature of the reaction is well demonstrated by the cis–trans equilibrium study of 1,4 adducts in an accompanying paper.[4]

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

**(c) Rate Acceleration by Water.** Addition of a small amount of water in the reaction of **1** with HCN–AlEt₃ 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–AlR₃ reaction. The data given in Table II indicate that water reacts with an excess of AlEt₃ very rapidly to give diethylaluminum hydroxide (Et₂AlOH) which slowly reacts with AlEt₃ to give bis(diethylaluminum) oxide (Et₂AlOAlEt₂).[5] Since the Et₂AlCN formation is not affected by the addition of water, the rate acceleration by water is due to the catalytic action of Et₂AlOH and Et₂AlOAlEt₂.

**(d) Catalytic Nature of AlR₃.** It has been shown in the previous paper[1] that AlR₃ acts as a catalyst in method-A hydrocyanation. Since AlR₃ eventually reacts with HCN to give R₂AlCN, the HCN addition would be catalyzed by both AlR₃ and R₂AlCN.

**Proposed Mechanism of Ideal HCN–AlR₃ 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–EtAlCl₂ combination that represents the ideal method-A reagent. A high electric conductivity (Table X) of EtAlCl₂ 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)].

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

$$R_3Al + HCN \rightleftharpoons H^+ + (R_3AlCN)^- \qquad (8)$$
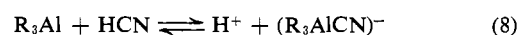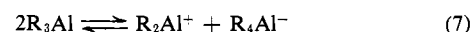
The assumption that the cations activate the enone system and (R₃AlCN)⁻ ion acts as the cyanating species is supported by the observation that the ionic species (conductivity) decrease as the hydrocyanation of **1** proceeds (Figure 10). The rate-determining step would be the attack of (R₃AlCN)⁻, since the combination HCN–AlCl₃ having a very high activating power has a poor hydrocyanating ability,[1] indicating that the reaction rate depends on the cyanating ability of (R₃AlCN)⁻.

This consideration, the catalytic nature of AlR₃, the irreversibility, and the product composition have led us to propose a probable mechanism (Scheme I) for ideal HCN–AlR₃ hydrocyanation which involves activation of enone with a cation L⁺ (H⁺ or R₂Al⁺), rate-determining, nucleophilic attack of the cyanoaluminate anion (R₃AlCN)⁻ to give the initial 1,4-adduct iv and regenerate AlR₃, 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, R₃Al is R₂AlOH or R₂AlOAlR₂) increasing the ideal HCN–AlR₃ reaction. The increase of ionic species is supported by the conductivity data (Table X).

(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 R₂Al)
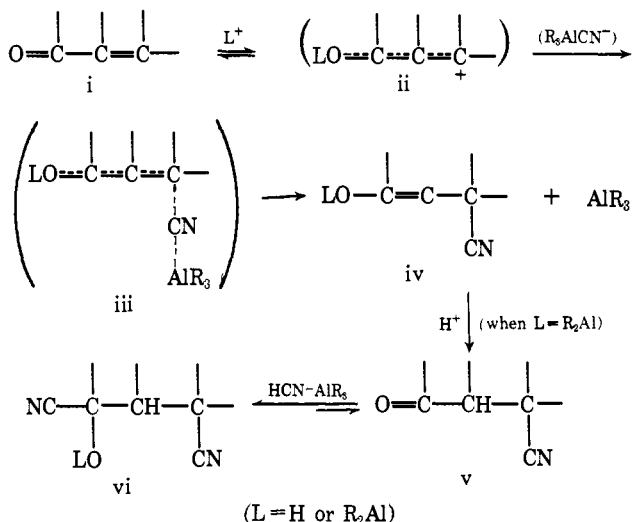
## Mechanism of Method-B Hydrocyanation.

When enone i reacts with Et₂AlCN, 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 Et₂AlCN to establish a fast preequilibrium with regards to the 1,2 addition, i.e., i ⇌ 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)
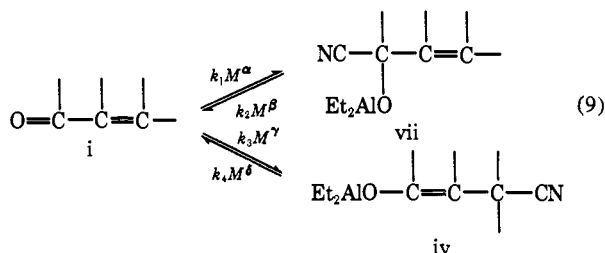
(7) A referee suggested a possible competitive S$_N$2' route (vii → iv). This possibility may be excluded by the finding that 1,2-adduct derivative **8** did not give 1,4-adduct **9** on treatment with Et₂AlCN. Compound **8**, mp 98–105°, was prepared by reaction of 1,2 adduct **2**[8] with dihydropyran and phosphorus oxychloride.
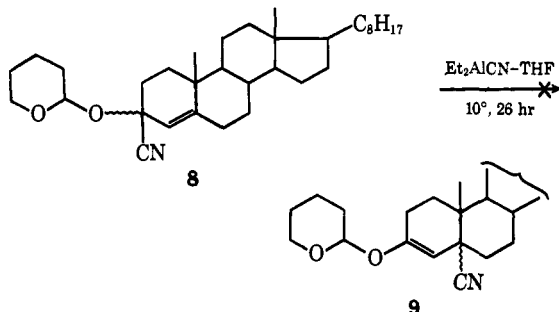


(8) Accompanying paper: W. Nagata, M. Yoshioka, and M. Murakami, *J. Amer. Chem. Soc.*, **94**, 4654 (1972).

where $k_i$ represents the rate constant of the specified step, $M$ is the effective concentration of the reagent [Et₂AlCN*], and the exponents $\alpha$, $\beta$, $\gamma$, and $\delta$ 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]∞/([enone]∞ + [1,2 adduct]∞) as given in eq 10–12. These equations are easily derived from eq 29, 20, and 30 (Appendix) by substituting $k_1M^\alpha$, $k_2M^\beta$, $k_3M^\gamma$, and $k_4M^\delta$ for $k_i$.

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

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

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

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]∞/([enone]∞ + [1,2 adduct]∞) 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 $\delta$ would suggest that the reagent Et₂AlCN 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 $\delta$ 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 $\beta$ value should be zero. With $\beta$ as zero, the $\alpha$ value is derived to be 0.15. This small $\alpha$ value indicates that the 1,2-addition i → vii would be effected by a minimum unit of reagent, i.e., monomeric "Et₂AlCN" and that $\alpha$ should be $^1/_3 \sim ^1/_2$ (cf. discussion below). This correction leads to a $\gamma$ 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 R₂AlCN 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 Et₂AlCN in various solvents (Table VIII) are antiparallel to the ion concentrations (conductivity) and that Me₂AlCN having the higher conductivity than Et₂AlCN and $i$-Bu₂AlCN 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 R₂AlCN itself. Ebullioscopic molecular weight deter-

(9) One possible such species is an oxygenated aluminum compound which is formed by reaction of Et₂AlCN 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 Et₂AlCN in the reverse reaction should be ruled out.

**Scheme II**
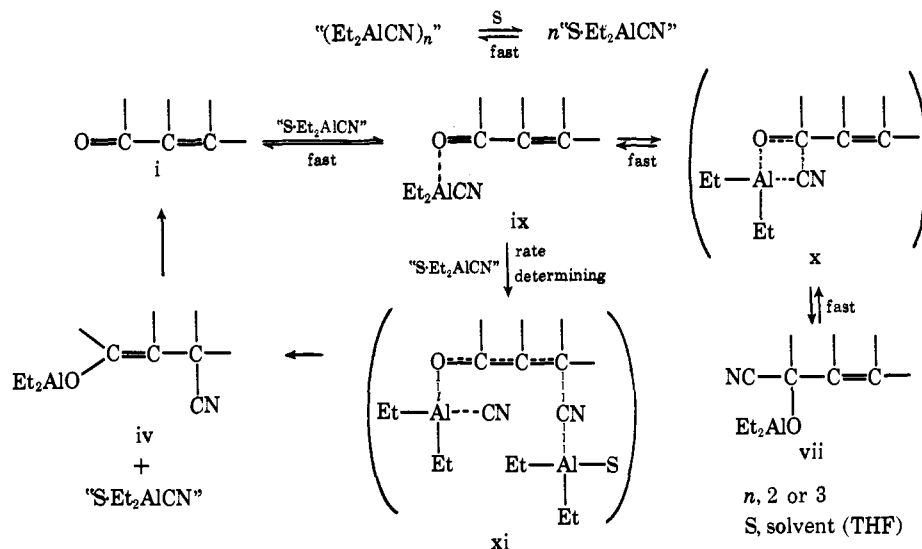


mination[1] indicates that degree of association of $Et_2$-AlCN is 1.86 at 66° and at low concentrations (0.038 and 0.076 $M$) in THF-$i$-$Pr_2O$ (13:1),[3] 4.7 in benzene at 80°, and 5.0 in $i$-$Pr_2O$ at 68°. The ir $C\equiv N$ stretching absorption at a lower frequency (2211 cm$^{-1}$, neat)[1] is in accord with the $C\equiv N$ bridged linear structure.[10]
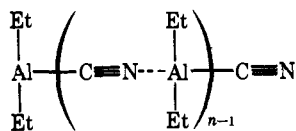


One may assume from this structure that there is no associated species of special stability (like the dimer for dimethylaluminum chloride)[11] and the cyanide is present as a mixture of associated species with rapid interconversion. Since the associated species of this type would be more stable at a 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 $\alpha$ value of $^1/_3 \sim {}^1/_2$ and the $\gamma$ 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

(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
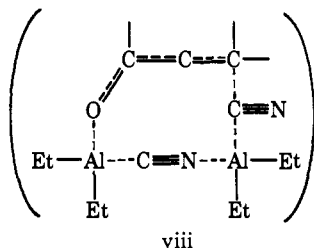


viii

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

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 "$S \cdot Et_2AlCN$," and a fast equilibrium exists between the solvated reagent and the substrate enone as suggested for the Grignard reaction.[15]

Participation of two monomeric "$S \cdot Et_2AlCN$" in the 1,4-addition is easily accounted for by the consideration that the first "$S \cdot Et_2AlCN$" 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 "$S \cdot Et_2AlCN$," 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 "$S \cdot Et_2AlCN$," the rate-determining step being the attack of "$S \cdot Et_2AlCN$" 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-

(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

$$
\begin{array}{c}
B \underset{k_2}{\overset{k_1}{\rightleftharpoons}} A \\
B \underset{k_4}{\overset{k_3}{\rightleftharpoons}} C
\end{array}
\tag{13}
$$

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

$$d[A]/dt = k_1[B] - k_2[A] \tag{14}$$

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

$$d[C]/dt = k_3[B] - k_4[C] \tag{16}$$

$$[A] + [B] + [C] = 1 \tag{17}$$

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 ⇌ A is in a fast equilibrium (eq 20) is pertinent from the data shown in Table VI.

$$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B \underset{k_4}{\overset{k_3}{\rightleftharpoons}} C \tag{18}$$
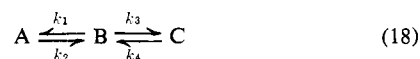
at $t = 0$, $[A] = [A]_0$; $[B] = [B]_0$; $[C] = [C]_0$ (19)

$$k_1[B] = k_2[A] \tag{20}$$

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

$$d[C]/dt = k_3[B] - k_4[C] \tag{21}$$

we have

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

where

$$K = k_3/(1 + k_1/k_2) = k_2k_3/(k_1 + k_2) \tag{23}$$

(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.

Integration under the condition given in eq 19 results in

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

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

At $t = \infty$

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

$$[C]_\infty = K/(K + k_4) \tag{26}$$

Substitution in eq 24 yields

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

Equation 28 can be obtained easily.

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

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

$$K = k_2k_3/k_1 \tag{29}$$

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

## 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-

(17) K. Ziegler, Belgium Patent, No. 616,188 (1962); *Chem. Abstr.*, **59**, 662e (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 AlR₃ 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 Et₂AlCN in THF–*i*-Pr₂O 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 τ₀.₅ = *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 AlR₃ 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.

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