Vinyl Carbanions. 2. Simultaneous Hydrogen–Deuterium Exchange and Addition of Ethyl [^{2}H]Alcohol to *trans*-Cinnamonitrile Catalyzed by Sodium Ethoxide

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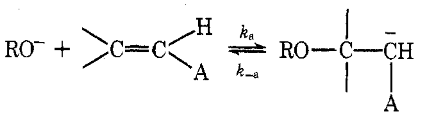
The kinetics of the simultaneous addition of ethyl [^{2}H]alcohol to *trans*-cinnamonitrile and the H–D exchange at C_α catalyzed by sodium ethoxide have been studied. The observed rate equation for the addition is $R = A[trans\text{-cinnamonitrile}] + B$, where A and B are constants which depend on the initial concentrations of olefin and base. The forward (k_1) and the backward (k_{-1}) rate constants of the nucleophilic addition step are $(3.72 \pm 0.51) \times 10^{-4}$ l. mol^{-1} s^{-1} and $(9.58 \pm 1.20) \times 10^4$ s^{-1}, respectively. The equilibrium constant for the overall addition reaction is $K = (3.9 \pm 0.2) \times 10^{-2}$ l. mol^{-1}. The H–D exchange is faster than the addition reaction and takes place via the vinyl carbanion derived from the olefin. Cis to trans isomerization occurs during the addition of ethyl [^{2}H]alcohol to *cis*-cinnamonitrile. Based on kinetic data, it is suggested that this isomerization takes place by an addition–elimination mechanism.

Kinetic studies of the addition of alcohols to activated olefins catalyzed by the derived sodium alkoxides have established that the rate-determining step is a nucleophilic attack of the alkoxide ion on the double bond followed by a fast protonation[1–4] as follows:



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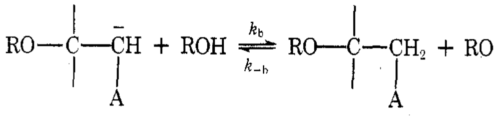

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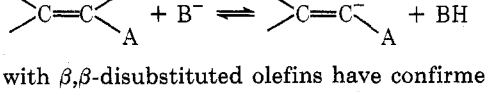
A = electronegative group

Equilibrium is established if the rate of decomposition of the intermediate carbanion is comparable with the rate of its protonation. This is the case in the addition of alcohols to vinyl sulfones,[5] to alkyl vinyl ketones,[6–9] and to β-nitrostyrene.[10]

Rate constants of the rate-limiting step (k_a) only and overall equilibrium constants were obtained from kinetic studies of the above-mentioned and some other Michael addition systems.[11] An appropriate treatment of the kinetic data in the case of the ethoxide-catalyzed addition of ethanol to β-nitrostyrene[10] made it possible to obtain the values of both k_a and k_{-a} as well as the overall equilibrium constant. This approach is being also used in the present work.

An acid–base type reaction may occur in Michael addition reaction systems in which an active olefin having an α-vinyl hydrogen is involved (eq 3). Recent kinetic and stereochemical



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studies with β,β-disubstituted olefins have confirmed that vinyl carbanions are intermediates in the base-catalyzed hydrogen–deuterium exchange of 2,2,4,6,6-pentamethylcyclohexylineneacetonitrile,[12] of the corresponding ketone,[13] and of fluorene-9-ylideneacetonitrile.[14] Active olefins which are not sterically hindered at C_β are subjected to nucleophilic attacks at this position, but vinyl carbanions are also involved in competing base-catalyzed reactions of such olefins. This has been suggested to be the case in the dimerization of acrylic[15] and crotonic[16] esters to yield such dimers as $CH_2{=}C(COOR)CH_2CH_2COOR$ and $CH_3CH{=}C(COOR)CH(CH_3)CH_2COOR$, respectively. A vinyl carbanion is also involved in a chain transfer reaction to monomer in the anionic polymerization of acrylonitrile.[17]

The acid–base type equilibrium (eq 3) has not been taken into account in any of the previous kinetic studies of Michael addition reactions. It was the purpose of the present work to study kinetically both the hydrogen–deuterium exchange at C_α and the nucleophilic addition reaction with such an olefin where these two may occur simultaneously.

Results and Discussion

The addition of ethyl [^{2}H]alcohol to *trans*-cinnamonitrile catalyzed by sodium ethoxide was accompanied by a simultaneous hydrogen–deuterium exchange reaction to yield the α-deuterated olefin *trans*-$PhCH{=}CDCN$. The rate of the exchange reaction was followed by infrared spetroscopy, and the rate of the addition reaction was followed by determined the concentrations of both the total (exchanged and unexchanged) olefin and the addition product by VPC. The rate of addition R_t was measured both as $-d[TCN]/dt$ and $d[add]/dt$, where [TCN] and [add] are the concentrations at time t of the total olefin and of the addition product, respectively. For each run a plot of R_t against [TCN] and against [add] gave straight lines with slopes A and A' and intercepts B and B', respectively (Figures 1 and 2). The experimental rate equations are

$$R_t = -d[\mathrm{TCN}]/dt = A[\mathrm{TCN}] + B \tag{4}$$

$$R'_t = d[\mathrm{add}]/dt = A'[\mathrm{add}] + B' \tag{5}$$

The values of R_t and R'_t for each run are the slopes of the conversion curves at different t values. On integration of eq 4 and 5, eq 6 and 7 are obtained:

$$[\mathrm{TCN}] = \frac{(A[\mathrm{TCN}]_0 + B)e^{-At} - B}{A} \tag{6}$$

$$[\mathrm{add}] = B'(e^{-A't} - 1)/A' \tag{7}$$

Using a computer, the best conversion curves were plotted according to eq 6 and 7, and the values of A, B, A', and B' were calculated. The deviations of the measured values of [TCN] from those computed according to eq 6 were small (±1%) indicating the reliability of the experimental method used. The same deviations for the adduct were somewhat higher (±3%). Detailed data for some of the kinetic runs are presented in the Experimental Section (Table II).[24]

In view of the evidence presented regarding the formation of vinyl carbanions in nucleophilic addition reactions to activated olefins,[12–17] the following reaction scheme may represent the ethoxide–*trans*-cinnamonitrile–ethyl [^{2}H]alcohol system.

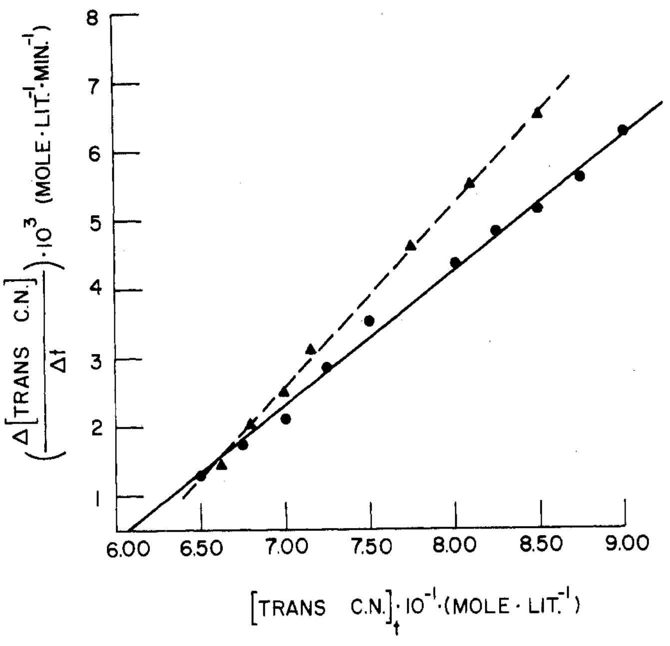
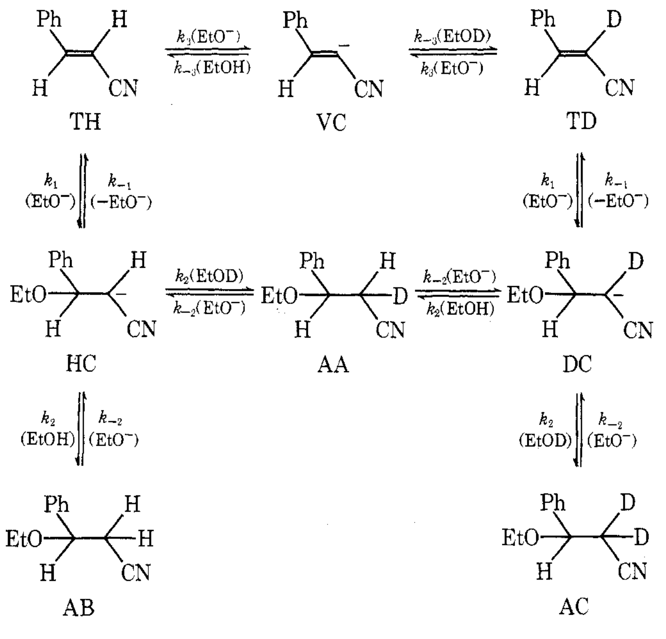


Figure 1. Plots of R_t, rate of addition of ethyl [^{2}H]alcohol to *trans*-cinnamonitrile (TCN), against $[\text{TCN}]_t$: ●, run 10; ▲, run 11.



This scheme takes into account only the nucleophilic addition and the hydrogen–deuterium exchange reactions, assuming that the trans to cis isomerization occurs to a negligible extent. This assumption will be justified later on presenting and discussing the problem of isomerization. The kinetic isotope effect is also being neglected for both the vinyl carbanion formation and the nucleophilic addition reaction. This is justified by the very low isotope effects observed in base-catalyzed hydrogen–isotope exchange in carbon acids.[18,19] This is also the case, for example, in the hydrogen–deuterium exchange of 2-methyl-3,3-diphenylpropionitrile[20] (k_H/k_D = 2.60), of 2,2-diphenylcyclopropanecarbonitrile[20] (k_H/k_D = 1.50), and of the α,β-unsaturated nitrile 2,2,4,6,6-pentamethylcyclohexylideneacetonitrile[12] (k_H/k_D = 2.05). Regarding the nucleophilic addition, it is quite reasonable to assume that the rate constants for this reaction involving either the hydrogen or the deuterium derivatives of the olefin are practically the same.

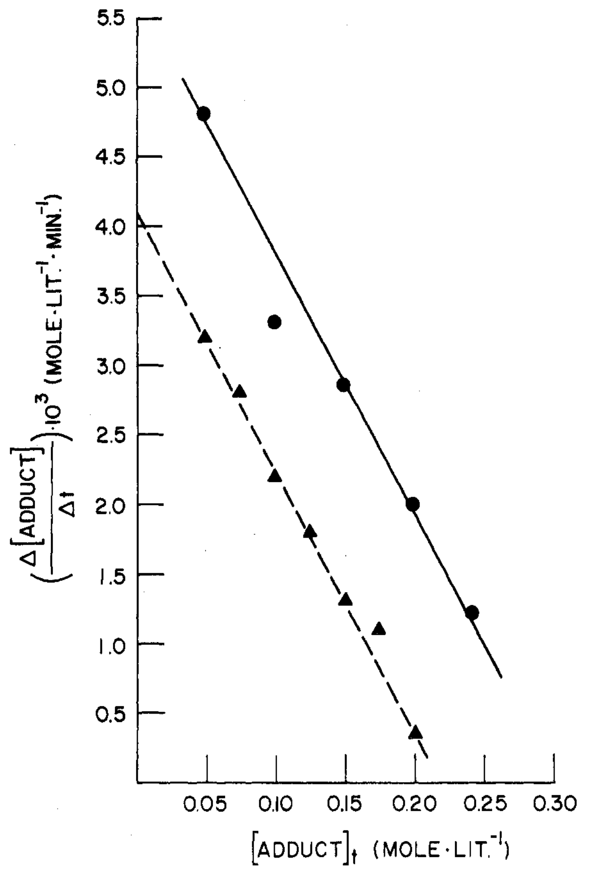


Figure 2. Plots of R_t, rate of addition of ethyl [^{2}H]alcohol to *trans*-cinnamonitrile, against $[\text{adduct}]_t$, the concentration of the addition product at time t: ●, run 6; ▲, run 7.

According to the above reaction scheme, the rates by which the olefins and adducts react are given by the following equations:

$$-d[\text{TH}]/dt = (k_1 + k_3)[\text{EtO}^-][\text{TH}] - k_1[\text{HC}] - k_3[\text{VC}][\text{EtOH}] \quad (8)$$

$$-d[\text{TD}]/dt = (k_1 + k_3)[\text{EtO}^-][\text{TD}] - k_{-1}[\text{DC}] - k_{-3}[\text{VC}][\text{EtOD}] \quad (9)$$

$$-d[\text{AA}]/dt = k_{-2}[\text{EtO}^-][\text{AA}] - k_2([\text{EtOD}][\text{HC}] + [\text{EtOH}][\text{DC}]) \quad (10)$$

$$-d[\text{AB}]/dt = k_{-2}[\text{EtO}^-][\text{AB}] - k_2[\text{EtOH}][\text{HC}] \quad (11)$$

$$-d[\text{AC}]/dt = k_{-2}[\text{EtO}^-][\text{AC}] - k_2[\text{EtOD}][\text{DC}] \quad (12)$$

The overall rate of addition of EtOD to *trans*-cinnamonitrile is given by

$$R_t = -d[\text{TCN}]/dt = -d[\text{TH}]/dt - d[\text{TD}]/dt \quad (13)$$
$$= (k_1 + k_3)([\text{TH}] + [\text{TD}])[\text{EtO}^-] + k_1([\text{HC}] + [\text{DC}]) - k_3[\text{VC}][\text{S}]$$

where [TCN] is the total concentration of *trans*-cinnamonitrile at time t and [S] = [EtOH] + [EtOD]. Assuming steady state conditions for the intermediate carbanions, namely d[HC]/dt = 0, d[DC]/dt = 0, and d[VC]/dt = 0, the corresponding expressions for the values of [HC], [DC], and [VC] can be derived. By substituting these values in eq 13 the following rate equation is obtained

$$-\frac{d[\text{TCN}]}{dt} = k_1[\text{TCN}][\text{EtO}^-] - \frac{k_1k_{-1}[\text{TCN}] + k_{-1}k_{-2}[\text{add}]}{k_2[\text{S}] + k_{-1}}[\text{EtO}^-] \quad (14)$$

Table I. Rate Constants for the Addition of Ethyl [^{2}H]Alcohol to *trans*-Cinnamonitrile Catalyzed by Sodium Ethoxide at 39 °C

Run no.	$[\mathrm{TCN}]_0$, mol l.$^{-1}$	$[\mathrm{EtO^-Na^+}]$, mol l.$^{-1}$	$10^2 A$ $10^3 B$	$10^4 A'$ $10^3 B'$	$10^4 k_1$,[a] l. mol^{-1} s^{-1}	$10^{-4} k_{-1}$,[a] s^{-1}	$10^4 k'_1$,[a] l. mol^{-1} s^{-1}	$10^{-4} k'_{-1}$,[a] s^{-1}	$10^2 \frac{-B}{[\mathrm{TCN}]_0[\mathrm{EtO^-}]}$
1	0.318	0.215	0.98 −1.71	−1.91 2.08	3.06	7.75	8.40	16.60	2.51
2	0.477		0.81 −2.22	−0.97 2.53	2.72	6.13	4.03	5.85	2.15
3	0.637	0.180	0.94 −3.21		3.07	7.13			2.78
4	0.637	0.215	1.13 −4.08	−1.80 4.18	3.33	9.20	5.08	15.10	3.00
5	0.795		1.63 −7.43	−1.83 5.58	5.07	12.93	5.72	14.38	4.35
6	0.954		1.21 −6.71	−1.51 5.28	3.75	9.58	4.28	12.68	3.27
7	1.114		1.27 −7.68	−1.49 6.67	4.30	9.42	4.63	11.80	3.21
8	0.954	0.180	1.23 −6.85	−1.20 4.45	4.73	11.38	4.32	11.60	4.00
9		0.240	1.44 −7.92	−0.92 3.80	3.53	10.83	2.77	6.22	3.47
10		0.320	2.00 −11.70	−3.15 11.14	4.18	11.46	6.38	18.42	4.02
11		0.414	2.21 −12.40	−3.45 11.18	3.30	9.52	4.72	15.58	3.47

[a] The average values of the rate constants are $k_1 = (3.72 \pm 0.51) \times 10^{-4}$ l. mol^{-1} s^{-1}; $k'_1 = (4.75 \pm 0.70) \times 10^{-4}$ l. mol^{-1} s^{-1}; $k_{-1} = (9.58 \pm 1.20) \times 10^4$ s^{-1}; $k'_{-1} = (12.8 \pm 3.20) \times 10^4$ s^{-1}.

where [add] is the total concentration of the addition products at time t: $[\mathrm{add}] = [\mathrm{AA}]_t + [\mathrm{AB}]_t + [\mathrm{AC}]_t$. Since an addition product is formed, it may be assumed that $k_2[\mathrm{S}] \gg k_{-1}$. Taking this into account and substituting $[\mathrm{TCN}]_0 - [\mathrm{TCN}]$ for [add], eq 14 changes into a rate equation which is similar to the experimental rate eq 4

$$-\frac{\mathrm{d}[\mathrm{TCN}]}{\mathrm{d}t} = \left(k_1 + \frac{k_{-1}k_{-2}}{k_2[\mathrm{S}]}\right)[\mathrm{EtO^-}]\,[\mathrm{TCN}] - \frac{k_{-1}k_{-2}}{k_2[\mathrm{S}]}\,[\mathrm{EtO^-}][\mathrm{TCN}]_0 \qquad (15)$$

where the constants A and B of eq 4 are given by

$$A = \left(k_1 + \frac{k_{-1}k_{-2}}{k_2[\mathrm{S}]}\right)[\mathrm{EtO^-}] \qquad (16)$$

$$B = -k_{-1}k_{-2}\,[\mathrm{EtO^-}][\mathrm{TCN}]_0/k_2[\mathrm{S}] \qquad (17)$$

A rate equation (eq 18) for the formation of the addition product can be derived in a similar way from the general reaction scheme:

$$\mathrm{d}[\mathrm{add}]/\mathrm{d}t = -(k_1 + k_{-1}k_{-2}/k_2[\mathrm{S}])[\mathrm{EtO^-}][\mathrm{add}] + k_1[\mathrm{EtO^-}][\mathrm{TCN}]_0 \qquad (18)$$

This rate equation is similar to the experimental rate eq 5 where A' and B' are therefore given by

$$A' = -(k_1 + k_{-1}k_{-2}/k_2[\mathrm{S}])[\mathrm{EtO^-}] \qquad (19)$$

$$B' = k_1[\mathrm{EtO^-}][\mathrm{TCN}]_0 \qquad (20)$$

Since the value of A, B, A', and B' were obtained experimentally for each kinetic run, the values of k_1 and k_{-1} could be calculated using eq 21 and 22, respectively, which were derived from eq 16, 17, 19, and 20. It can be shown that the ratio k_2/k_{-2} needed for these calculations is given by $k_2/k_{-2} = K_{\mathrm{a(EtOD)}}/K_{\mathrm{a[PhCH(OEt)CH_2CN]}}$. Since $K_{\mathrm{a(EtOD)}} \approx 10^{-18}$ and assuming that $K_{\mathrm{a[PhCH(OEt)CH_2CN]}}$ is equal to that of acetonitrile ($\mathrm{p}K_\mathrm{a} = 10^{-25}$), a value of $k_2/k_{-2} \approx 10^7$ is obtained. The calculated values of k_1 and k_{-1} for each run (Table I) are quite constant. This indicates that the reaction scheme and the derived rate equations (eq 15 and 18) indeed represent correctly the presently studied addition reaction of ethyl [^{2}H]alcohol to *trans*-cinnamonitrile. Experimentally found values of A, B, and B' and known concentrations of reagents appear in eq 21. As a result, the calculated values of k_1 should be quite accurate. k_{-1} is not as accurate as k_1 because only an approximate value of k_2/k_{-2} is available.

$$k_1 = \left(A + \frac{B}{[\mathrm{TCN}]_0}\right)/[\mathrm{EtO^-}] = B'/[\mathrm{EtO^-}][\mathrm{TCN}]_0 \qquad (21)$$

$$k_{-1} = -k_2B[\mathrm{S}]/k_{-2}[\mathrm{EtO^-}][\mathrm{TCN}]_0 = k_2[\mathrm{S}]\left(A' + \frac{B}{[\mathrm{TCN}]_0}\right)/k_{-2}[\mathrm{EtO^-}] \qquad (22)$$

Four distinct conditions may be associated with the suggested reaction scheme, from which rate eq 15 has been derived, namely (a) $k_1 \gg k_{-1}$, $k_2 \gg k_{-2}$; (b) $k_1 \gg k_{-1}$, $k_2 \ll k_{-2}$; (c) $k_1 \ll k_{-1}$, $k_2 \gg k_{-2}$; (d) $k_1 \ll k_{-1}$, $k_2 \ll k_{-2}$. If condition a holds, the result will be that $k_1 \gg k_{-1}k_{-2}/k_2[\mathrm{S}]$ and $k_1[\mathrm{EtO^-}][\mathrm{TCN}] \gg B$, so that rate eq 15 will change to a second-order rate equation $R = k_1[\mathrm{EtO^-}][\mathrm{TCN}]$, which is different from the observed rate eq 4. Condition a was found to apply in case of the addition of methanol and/or ethanol to acrylontrile,[2,4] acrylic esters,[4] and methacrylonitrile,[4] catalyzed by the derived sodium alkoxides. Conditions b and d cannot be applied at all since k_2 should be much larger than k_{-2} as $\mathrm{p}K_{\mathrm{a(AA)}} \gg \mathrm{p}K_{\mathrm{a(EtOD)}}$. As a consequence, condition c is the one which may hold for this reaction system. It requires that k_1 should be much smaller than k_{-1}, which is indeed the case.

The addition of ethyl alcohol to acrylonitrile catalyzed by sodium ethoxide was almost quantitative and much faster ($k_1 = 11.7 \times 10^{-2}$ l. mol^{-1} s^{-1} at 25 °C)[4] than the presently investigated addition of ethyl [^{2}H]alcohol to *trans*-cinnamonitrile [$k_1 = (3.72 \pm 0.51) \times 10^{-4}$ l. mol^{-1} s^{-1}]. This is of course due to the fact that $k_{-1} \gg k_1(k_1/k_{-1} \approx 10^{-8})$ resulting from the phenyl group at C_β. However, such steric hindrance does not necessarily lead to k_{-1} being larger than k_1. The reverse order was found for the addition of ethyl alcohol to β-nitrostyrene catalyzed by sodium ethoxide ($k_1/k_{-1} \approx 10^6$).[10] indicating that the electronegativity of the substituent at C_α also affects this ratio to a large extent. One can, in fact, predict the relation between k_1 and k_{-1} for such equilibrium nucleophilic additions of BH to activated olefins catalyzed by the conjugate base, by comparing the acidities of BH and of the addition product. It is obvious, in line with the above-mentioned conditions associated with the reaction scheme, that if the addition product is more acidic than BH ($k_2 \gg k_{-2}$) k_1 should be larger than k_{-1}, and if the reverse is true ($k_2 \gg k_{-2}$), k_1 should be smaller than k_{-1}. In accordance with these considerations, it was found for the addition of ethyl alcohol to β-nitrostyrene[10] (for which $k_2 \ll k_{-2}$) that $k_1 \gg k_{-1}$.

The equilibrium concentrations of the addition product and of *trans*-cinnamonitrile are given by $[\text{add}]_{\text{eq}} = B'/A'$ and $[\text{TCN}]_{\text{eq}} = B/A$, respectively (eq 4 and 5). The equilibrium

$$trans\text{-Ph} + \text{CH}{=}\text{CH} + \text{CN} + \text{C}_2\text{H}_5\text{OD} \xrightleftharpoons{K(\text{EtO}^-)} \text{C}_2\text{H}_5\text{O} + \text{CH(Ph)} + \text{CH}_2\text{CN} \quad (23)$$

constant K for the overall addition reaction (eq 23) is given by

$$K = [\text{add}]_{\text{eq}}/[\text{TCN}]_{\text{eq}}[\text{S}] = \text{A'B'/A'B[S]} \quad (24)$$

By substituting the expressions of A, B, A', and B' (as derived from eq 17, 18, 20, and 21) in eq 24 this equation is changed to

$$K = k_1k_2/k_{-1}k_{-2} \quad (25)$$

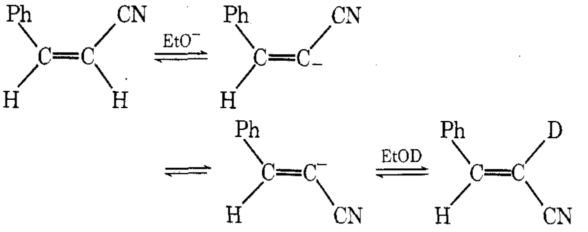
The value of $K = (3.9 \pm 0.2) \times 10^{-2}$ l. mol^{-1} obtained from eq 24 is relatively more accurate than the value of $K = (4.1 \pm 0.7) \times 10^{-2}$ l. mol^{-1} obtained from eq 25. This is due to the fact that A, A', B, and B' are experimentally obtained data, whereas some inaccuracy is involved in the values of k_{-1} and k_2/k_{-2}.

Hydrogen–Deuterium Exchange. As mentioned, a simultaneous hydrogen deuterium exchange of the α-vinyl hydrogen occurred during the addition of ethyl [2H]alcohol to *trans*-cinnamonitrile catalyzed by sodium ethoxide. Two alternative pathways are possible for this exchange, namely via the derived vinyl carbanion[12–14] or by an addition–elimination mechanism (see scheme). The exchange reaction is faster than the addition reaction, as can be seen from the corresponding conversion curves (Figure 3).[24] This by itself cannot be regarded as evidence in favor of the vinyl carbanion mechanism. It is obvious that such a behavior may also result from an addition–elimination mechanism, only if the addition product is unstable and decomposes at a relatively high rate to *trans*-cinnamonitrile. This, in turn, can be the case only if the condition $k_1 \ll k_{-1}k_{-2}/k_2[\text{S}]$ holds for the rate eq 26.

$$-\text{d[TCN]}/\text{d}t = (k_1[\text{TCN}] - k_{-1}k_{-2}[\text{add}]/k_2[\text{S}])[\text{EtO}^-] \quad (26)$$

Equation 26 is obtained from eq 15 by substituting $[\text{add}] = [\text{TCN}]_0 - [\text{TCN}]$. It follows from eq 17 that $k_{-1}k_{-2}/k_2[\text{S}] = -B/[\text{TCN}]_0[\text{EtO}^-]$, so that the value of $k_{-1}k_{-2}/k_2[\text{S}]$ can be calculated for each run. It was found by this way that $k_{-1}k_{-2}/k_2[\text{S}] \approx k_1$ (see Table I), which means that the above-mentioned condition does not apply for the exchange reaction. It should, therefore, be concluded that the hydrogen–deuterium exchange in the presently investigated system and its relatively higher rate as compared to that of the addition reaction is not due to an addition–elimination mechanism, but to the alternative vinyl carbanion mechanism. This depression of the addition–elimination mechanism is due to the combined effects of the steric hindrance to the nucleophilic attack ($k_1 \ll k_{-1}$, see Table I), to the fact that $k_2 \gg k_{-2}$, and to the lower value of k_{-2} as compared to k_3 (which is assumed by us to be so).

Isomerization. Isomerization was observed while carrying out kinetic rate measurements of the addition of ethyl [2H] alcohol to *cis*-cinnamonitrile. In a typical run, starting with the cis isomer, the percentage of *trans*-cinnamonitrile in the mixture of the unreacted cis and trans isomers increased gradually up to a value of 55% at equilibrium (Figure 4).[24] It has been shown that vinyl carbanions derived from α,β-unsaturated nitriles have a very high configurational stability.[12–14] It may be therefore assumed that this cis to trans isomerization does not occur via the derived vinyl carbanion (eq 27) but rather by an addition–elimination mechanism (eq 28).



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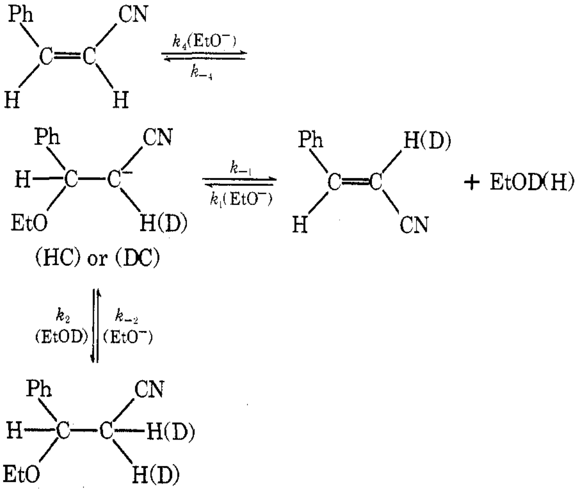

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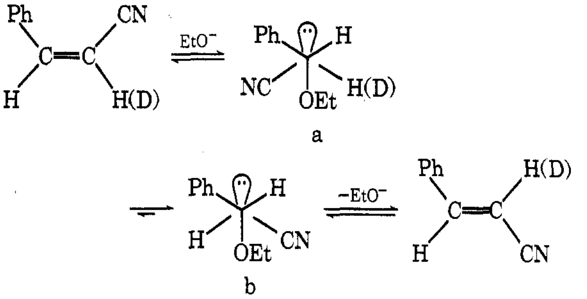
The isomerization involves an inversion of the carbanionic intermediate and rotation of the C_α–C_β bond (eq 29). The



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activation energy for the inversion of the carbanion is very low (~10^{-2} kcal/mol).[21]

It is obvious that the conformational equilibrium of the anionic intermediates a and b is highly in favor of b. In accordance with this, very small amounts of the cis isomer were detected while measuring the rates of addition of ethyl [2H]alcohol to *trans*-cinnamonitrile. At equilibrium the mixture of olefins consisted only of 4–6% of the cis isomer, its concentration being practically constant for each run during the whole reaction period (Table II).[24]

The transformation of the carbanionic intermediate a to b may be regarded as practically irreversible so that the backward reaction (k_{-4}) of (HC) or (DC) (eq 28) to the cis isomer is assumed to be negligible. The rate of the nucleophilic addition involving *cis*-cinnamonitrile (CCN) should therefore be given by

$$-\text{d[CCN]}/\text{d}t = k_4[\text{EtO}^-][\text{CCN}] \quad (30)$$

A detailed representative kinetic run is given in Table II.[24] First-order rate plots of log $[CCN]_t/[CCN]_0$ against t yielded straight lines in all cases studied (Figure 5).[24] The second-order rate constants were determined by dividing the pseudo-first-order rate constants by base concentration.

It may be argued that the trans olefin does indeed isomerize to the cis olefin, but that the very minor accumulation of the cis isomer is due to its faster consumption in the addition reaction, as compared to that of the trans olefin. This, however, is not the case as is evident from the fact that the second-order rate constants for the nucleophilic attack step of the ethoxide anion on the *cis*- and on the *trans*-cinnamonitrile are about the same: $k_4 \approx 3.50 \times 10^{-4}$ l. mol^{-1} s^{-1} and $k_1 = (3.72 \pm 0.51) \times 10^{-4}$ l. mol^{-1} s^{-1}.

Experimental Section

The infrared spectra were obtained with a Perkin-Elmer Model 257 spectrophotometer. NMR spectra were recorded on a JEOL 60 MHz spectrometer. VPC measurements were done on a Varian Aerograph Model 1800 gas chromatograph. Mass spectra were recorded on a Hitachi Perkin-Elmer Model RMV-6 (70 eV) mass spectrometer.

Materials. A mixture of *cis*- and *trans*-cinnamonitrile was synthesized[22] and separated by distillation on a spinning band column. The cis and trans isomers were each obtained at 98% purity (VPC). Absolute dry ethyl [^{2}H]alcohol (Miles-Yeda), 99.9% isotopically pure, was used. Ethanolic sodium ethoxide solutions were prepared by adding sodium metal to ethyl [^{2}H]alcohol under reflux and nitrogen. The base concentration was determined by titration with hydrochloric acid. Liquid materials and solutions were kept under pure nitrogen in flasks fitted with self-sealing rubber caps. Aliquot portions were removed from these flasks with syringes by applying nitrogen pressure.

Kinetic Runs. The reactions of *trans*-cinnamonitrile with ethyl [^{2}H]alcohol catalyzed by sodium ethoxide were carried out in a 150-ml flask connected to high vacuum and nitrogen lines. The flask was fitted with a self-sealing rubber cap through which liquids were introduced by syringes. The system was dried, evacuated, and flushed with dry nitrogen prior to the introduction of solvent and reactants. The required amounts of cinnamonitrile and ethyl [^{2}H]alcohol were introduced into the flask which was then immersed in a constant-temperature bath at (39 ± 0.5) °C. A solution of sodium ethoxide in ethyl [^{2}H]alcohol was then introduced and time recorded. Portions of the homogeneous mixture were withdrawn at measured intervals through a capillary stopcock, by applying a nitrogen pressure. The samples withdrawn were quenched with excess acetic acid and subjected to quantitative VPC and ir measurements. Some representative results of kinetic rate measurements of the addition reaction are presented in Table II.[24] The kinetic rate measurements of the addition of ethyl [^{2}H]alcohol to *cis*-cinnamonitrile and its simultaneous isomerization to the trans isomer were followed by VPC.

Quantitative Ir Analysis. The baseline density method[23] was used to determine the percentage of deuterium (% D) in the samples withdrawn from the reaction mixture. The ir spectrum of each of several mixtures composed of weighted amounts of α-deuterated and nondeuterated *trans*-cinnamonitrile was recorded using no solvent in sodium chloride cells (0.025 cm thickness). The transmittance T at 975 cm^{-1} (due to the C=CH bond) and the transmittance T' at 955 cm^{-1} (due to the C=CD bond) were determined. The % D of each of the same samples was determined from their mass spectra. A standard curve for the quantitative ir analysis was prepared by plotting log T/T' against % D. Solvents (ethyl [^{2}H]alcohol and acetic acid) were evaporated from each of the quenched samples withdrawn from the reaction mixture and the residue was distilled under vacuum into a cooled trap. This distillate consisted of a mixture of the addition product of ethyl [^{2}H]alcohol to *trans*-cinnamonitrile and the α-deuterated and nondeuterated olefins. The ir spectrum of the liquid was recorded, log T/T' determined, and the % D then directly read from the standard curve.

Registry No.—Ethyl [^{2}H]alcohol, 925-93-9; *trans*-cinnamonitrile, 1885-38-7; sodium ethoxide, 141-52-6; *cis*-cinnamonitrile, 24840-05-9.

Supplementary Material Available. Figures 3, 4, and 5 and Table II describing the addition of ethyl [^{2}H]alcohol to *trans*- and *cis*-cinnamonitrile (4 pages). Ordering information is given on any current masthead page.

References and Notes

(1) C. A. Fyfe, "The Chemistry of the Hydroxyl Group", S. Patai, Ed., Interscience, New York, N.Y., 1971, p 62.
(2) B. A. Feit and A. Zilkha, *J. Org. Chem.*, **28**, 3245 (1963).
(3) R. N. Ring, G. G. Tesoro, and R. R. Moore, *J. Org. Chem.*, **32**, 1091 (1967).
(4) B. A. Feit and Z. Bigon, *J. Org. Chem.*, **34**, 3942 (1969).
(5) W. G. Davies, E. W. Hardisty, T. P. Nevell, and R. H. Peters, *J. Chem. Soc. B*, 998 (1970).
(6) N. Ferry and F. McQuillin, *J. Chem. Soc.*, 103 (1962).
(7) P. Chamberlain and G. H. Whitham, *J. Chem. Soc. B*, 1131 (1969).
(8) R. Luft, S. Delattre, and J. Basso, *C. R. Acad. Sci., Ser. C*, **271**, 1623 (1970).
(9) R. Luft, S. Delattre, and J. E. Armando, *Bull. Soc. Chim. Fr.*, 1317 (1971).
(10) B. A. Feit and L. Bohor, *J. Chem. Soc., Perkin Trans. 2*, 1823 (1974).
(11) S. Patai and Z. Rappaport, "The Chemistry of Alkenes", S. Patai, Ed., Interscience, New York, N.Y., 1964, p 469.
(12) H. M. Walborsky and L. M. Turner, *J. Am. Chem. Soc.*, **94**, 2273 (1972).
(13) J. F. Arnett and H. M. Walborsky, *J. Org. Chem.*, **37**, 3678 (1972).
(14) B. A. Feit, L. Bohor, and S. Rubinraut, *J. Chem. Soc., Perkin Trans. 2*, 253 (1976).
(15) B. A. Feit, *Eur. Polym. J.*, **3**, 523 (1967).
(16) J. Shabtai and H. Pines, *J. Org. Chem.*, **30**, 3854 (1965).
(17) B. A. Feit and A. Zilkha, *J. Appl. Polym. Sci.*, **7**, 287 (1963).
(18) D. J. Cram and L. Gosser, *J. Am. Chem. Soc.*, **85**, 3696 (1963).
(19) R. Stewart, J. P. O'Donell, D. J. Cram, and B. Rickborn, *Tetrahedron*, **18**, 917 (1962).
(20) H. M. Walborsky and J. M. Motes, *J. Am. Chem. Soc.*, **92**, 2445 (1970).
(21) G. W. Koeppl, D. S. Sagatys, G. S. Krishnamurthy, and S. I. Miller, *J. Am. Chem. Soc.*, **89**, 3396 (1967).
(22) J. Goshes, *Bull. Soc. Chim. Belg.*, **41**, 477 (1932).
(23) C. N. R. Rao in "Chemical Applications of Infrared Spectroscopy", Academic Press, New York, N.Y., 1963, p 538.
(24) See paragraph at end of paper regarding supplementary material.

Regioselective Nucleophilic Addition to 3,4-Lutidine

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The usual orientation of nucleophilic addition at the 2 position of a 3-alkylpyridine can be changed by increasing the steric requirements of the nitrogen substituent. Thus the addition of phenylmagnesium bromide to the alkyl chloroformate ester salts of 3,4-lutidine is regioselective giving up to 90% addition of the aryl group at the 6 position. The large steric requirements of the 1-phenoxycarbonyl group or an ortho-substituted phenyl Grignard reagent gave 95% or greater regioselectivity of reaction at the less hindered α position of the 3,4-lutidine salt.

The reactions of nucleophiles with pyridines and pyridine derivatives may occur by addition at the 2, 4, or 6 position of the ring.[1] When the nucleophile is an organometallic reagent the addition usually takes place adjacent to the nitrogen, at the 2 or 6 positions,[2] and with the unsymmetrical ring having a 3-alkyl group, the addition is primarily at the 2 position.