

320 nm (Figure 4). Addition of alcohol converts the acyl hypobromite to the alkyl hypobromite immediately. Once the alkyl hypobromite has formed, the rate of formation of product is comparable to that observed in the silver acetate reaction.

In the absence of silver salts under the reaction conditions, the reaction of bromine with the alcohol is slow and no alkyl hypobromite is observed in the ultraviolet. The product formed is the ketone.

We therefore suggest that the difference in product observed in the alcohol-bromine-silver salt reaction between silver acetate and silver trifluoroacetate is a result of two competitive reactions rather than two products from a single reaction as reported previously.<sup>2</sup>

With silver acetate, the tetrahydrofuran product predominates, because of the facile formation of the acetyl hypobromite. Whereas with silver trifluoroacetate, which reacts slowly with bromine, the competitive reaction, to form the ketone via direct reaction of the alcohol with free bromine, can take place.

### Experimental Section

All spectrophotometric measurements were made on a Varian Series 634 spectrophotometer.

**Starting Materials.** Alcohols were commercial samples that gas chromatographic analysis indicated were better than 99% pure. They were used without further purification. The silver salts and bromine were also commercial samples and used without further purification.

Carbon tetrachloride (analytical reagent) was distilled with the fraction boiling 76-77 °C collected. The distillate was dried over anhydrous magnesium sulfate for at least 1 day and filtered immediately before use.

**Reaction Procedure.** The reactions were carried out in a three-neck flask (1000 mL) fitted with a Tru-bore stirrer.

The flask was wrapped in aluminum foil and placed in a constant-temperature bath at 25 °C. Alcohol and bromine solutions were prepared in separate volumetric flasks and stored in the constant-temperature bath until mixing.

Anhydrous sodium carbonate was added to the reaction flask (0.50 g/100 mL of reaction mixture) as well as the silver salts. After the addition of solids, the alcohol solution was added and the stirrer started. The bromine solution was then added.

Samples were taken from time to time with volumetric pipettes. The samples were placed in a quartz cuvette (1 cm), and the absorbance was measured immediately against a carbon tetrachloride blank scanning from 500 to 265 nm. In all cases, the stirrer was stopped long enough so that samples taken for spectrophotometric analysis did not contain suspended solids.

### Kinetics and Mechanism of the Conjugate Hydrocyanation of $\alpha,\beta$ -Unsaturated Ketones by the Potassium Cyanide-Ammonium Chloride System

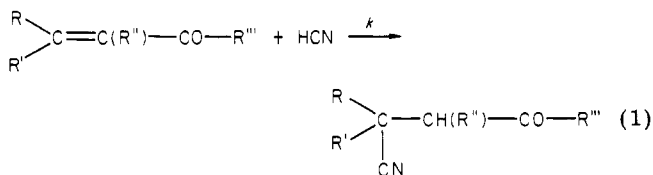
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In spite of their huge synthetic importance, nucleophilic additions to electrophilic double bonds were the subject of but a few kinetic studies. Thus, except for an early kinetic work,<sup>1</sup> the hydrogen cyanide addition to  $\alpha,\beta$ -unsaturated ketones has been examined from an almost exclusively stereochemical point of view.<sup>2,3</sup>

We recently described<sup>4</sup> a simple procedure for measuring the apparent rate constant of the potassium cyanide-ammonium chloride reaction with enones in dimethylformamide-water mixtures (eq 1). This method was then



applied to the elucidation of stereochemical problems.<sup>4</sup> Although the gross mechanistic features of conjugate hydrocyanation have been known for a long time,<sup>5</sup> it is the purpose of the present work to bring novel information concerning some physicochemical parameters related to the transition state location.

### Results and Discussion

**The  $\text{CN}^-$ - $\text{NH}_4^+$  System.** Prior to the reactions involving the enone molecule, there is a fast equilibrated reaction (eq 2) between cyanide and ammonium ions. In



the DMF-water mixture (9:1, v/v) this equilibrium (2) is shifted far to the right. It was indeed reported that the  $pK_a$ 's of  $\text{NH}_4^+$  and HCN, which are very similar in water, are respectively 10.5<sup>6a</sup> and 12.9<sup>6b</sup> in an aprotic medium ( $\text{Me}_2\text{SO}$ ). Under these conditions the experimental data show that the cyanide concentration remains constant during the first 50% of the hydrocyanation reaction (1):  $\text{CN}^-$  acts as a catalyst and HCN is consumed.

This assumption explains the pseudo-first-order rate constant in the rate law

$$\frac{d[\text{enone}]}{dt} = -\frac{k_{\text{ap}}}{1 + K_{\text{ap}}}[\text{enone}] \quad (3)$$

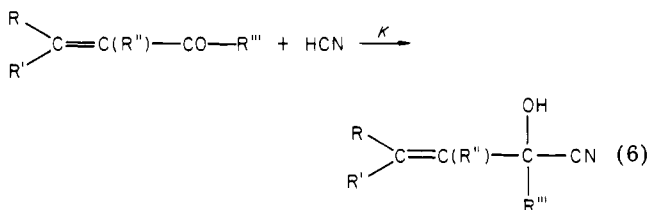
with

$$k_{\text{ap}} = k[\text{CN}^-] \quad (4)$$

and

$$K_{\text{ap}} = K[\text{HCN}] \quad (5)$$

$K$  being the equilibrium constant for the formation of the cyanohydrin (eq 6). It should be emphasized that in eq



3 the  $1 + K_{\text{ap}}$  term remains practically constant, thus allowing a simple integration of this equation:

$$\ln [\text{enone}] = -\frac{k_{\text{ap}}}{1 + K_{\text{ap}}}t + \ln [\text{enone}]_0 \quad (7)$$

(2) (a) Nagata, W.; Yoshioka, M. *Org. React.* 1977, 25, 255. (b) Agami, C.; Fadlallah, M.; Levisalles, J. *Tetrahedron* 1981, 37, 903, 909.

(3) Kinetics of hydrocyanation by Nagata's reagents ( $\text{HCN}$ - $\text{EtAlCl}_2$  and  $\text{Et}_2\text{AlCN}$ ) have been reported: Nagata, W.; Yoshioka, M.; Murakami, M. *J. Am. Chem. Soc.* 1972, 94, 4644.

(4) Agami, C.; Fadlallah, M.; Levisalles, J.; Cayzergues, P. *Tetrahedron* 1981, 37, 3723.

(5) Michael, A.; Weiner, N. *J. Am. Chem. Soc.* 1937, 59, 744.

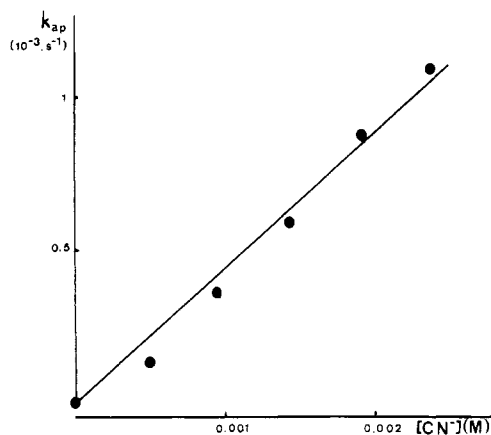
(6) (a) Kolthoff, I. M.; Chantooni, M. K., Jr.; Bhowmik, S. *J. Am. Chem. Soc.* 1968, 90, 23. (b) Ritchie, C. D.; Uschold, R. E. *Ibid.* 1967, 89, 1721.

(1) Jones, W. J. *J. Chem. Soc.* 1914, 105, 1547.

Table I. Variation of  $k_{ap}$  with the Weighted Molar Ratio of Reagents ([1-Cholesten-3-one] = 0.00475 M,  $T = 97^\circ\text{C}$ )

enone/KCN/ $\text{NH}_4\text{Cl}$	$10^3 k_{ap}, \text{s}^{-1}$
1:2:1.5	1.09
1:2:1.6	0.76
1:2:1.7	0.58
1:2:1.8	0.36
1:2:1.9	0.13
1:2:2	<i>a</i>

<sup>a</sup> Too small to be measured.

Figure 1. Variation of  $k_{ap}$  with actual cyanide concentration ([1-cholesten-3-one] = 0.00475 M,  $T = 97^\circ\text{C}$ ).

It has been checked that in all cases the 1-4 addition corresponding to eq 1 goes to completion, so that no account has to be taken of the reverse of the reaction 1.

Thus the weighed molar ratios (enone/ $\text{CN}^-/\text{NH}_4^+ = 1:2:1.5$ ) become after the establishment of equilibrium 2 the actual molar ratios 1:0.5:0. By a varying of the  $\text{NH}_4\text{Cl}$  weighed molar ratio at constant cholestenone and KCN weighed molar ratios,<sup>7</sup> it can be seen from Table I that  $k_{ap}$  decreases when the  $\text{NH}_4\text{Cl}$  weighed molar ratio is increased. Actually  $k_{ap}$  is linearly related to the KCN actual concentration, as shown in Figure 1, bearing out eq 3 and thus yielding the bimolecular rate constant  $k$  ( $0.44 \text{ M}^{-1} \text{ s}^{-1}$  at  $97^\circ\text{C}$ ).

This first-order dependence of  $k_{ap}$  on KCN concentration is also demonstrated when the bulk concentration of the reactants is modified while keeping constant the weighed molar ratios 1:2:1.5 (Table II, entries 1-3).

Equation 8 is verified by plotting  $\log k_{ap}$  vs.  $\log [\text{CN}^-]$

$$\log k_{ap} = n \log [\text{CN}^-] + \log k \quad (8)$$

( $[\text{CN}^-]$  is the actual cyanide concentration and not the weighed cyanide concentration). The graph exhibits a slope  $n = 0.99$  (correlation coefficient 0.986) and allows the calculation of the bimolecular rate constant ( $k = 1.05 \text{ M}^{-1} \text{ s}^{-1}$  at  $121^\circ\text{C}$ ).

**Ionic Strength and Solvent Effects.** The foregoing data also show that there is no appreciable ionic strength effect; this is not unexpected because transition state and reagents are almost equally charged. Kinetics of cyanohydrin formation were likewise reported<sup>9</sup> to be independent of salt effects.

(7) In our experimental conditions ( $T = 370 \text{ K}$ ,  $[\text{NH}_3] \leq 0.0071 \text{ M}$ ,  $[\text{HCN}] \leq 0.0071 \text{ M}$ ) ammonia and hydrogen cyanide remain in solution. Their respective calculated<sup>8</sup> partial vapor pressures are 0.03 and 0.004 atm.

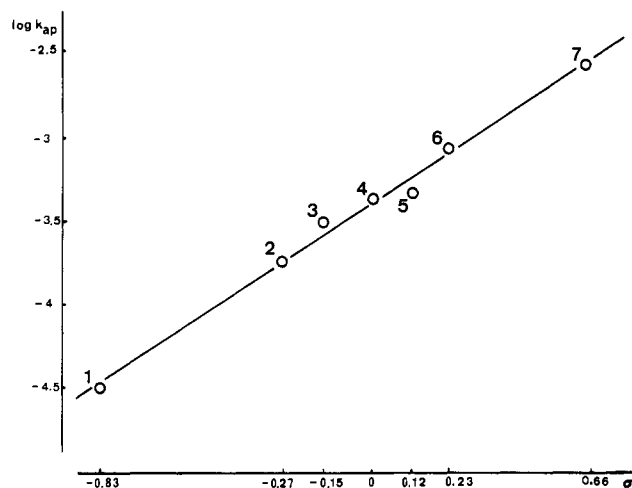
(8) Weast, R. C. "Handbook of Chemistry and Physics", 51st ed.; CRC Press: Cleveland, OH, 1970; D146.

(9) Svirbely, W. J.; Roth, J. F. *J. Am. Chem. Soc.* 1953, 75, 3106. See also ref 10.

Table II. Variation of  $k_{ap}$  with Physicochemical Parameters (Reagents' Concentration, Solvent Mixture, and Temperature). Reagents' Weighted Molar Ratio: Enone/KCN/ $\text{NH}_4\text{Cl} = 1:2:1.5$ 

entry	[enone], <sup>a</sup> M	DMF/ $\text{H}_2\text{O}$ (v:v)	T, K	$10^3 k_{ap}$ , $\text{s}^{-1}$
1	0.011	90:10	394	5.16
2	0.00475	90:10	394	2.82
3	0.00234	90:10	394	1.10
4	0.00475	95:5	370	1.02
5	0.00475	85:15	370	1.03
6	0.00475	90:10	370	1.09
7	0.00475	90:10	351	0.35

<sup>a</sup> Enone = 1-cholesten-3-one.

Figure 2. Hammett plots of the conjugate hydrocyanation of 4-phenyl-3-buten-2-ones at  $97^\circ\text{C}$  ( $k_{ap}$  values are expressed in  $\text{s}^{-1}$ ): [enone] = 0.017 M; reagents' weighted molar ratio, 1:2:1.5 enone/KCN/ $\text{NH}_4\text{Cl}$ . Substituents: 1, *p*- $\text{Me}_2\text{N}$ ; 2, *p*- $\text{CH}_3\text{O}$ ; 3, *p*-*iso*- $\text{C}_3\text{H}_7$ ; 4, H; 5, *m*- $\text{CH}_3\text{O}$ ; 6, *p*-Cl; 7, *p*-CN.

Concerning the solvent, it appears (Table II, entries 4-6) that the mixture composition is not crucial as there is no appreciable rate difference between 85%, 90%, and 95% DMF. Attempts to work on purified DMF without addition of water ("anhydrous" medium) were unsuccessful because of the low solubility of the inorganic reagents.

**Activation Parameters.** Entries 2, 6, and 7 of Table II allow the determination of the activation parameters for the conjugate hydrocyanation of 1-cholesten-3-one: From

$$\Delta H^\ddagger = 13.7 \pm 1.3 \text{ kcal mol}^{-1}$$

$$\Delta S^\ddagger = -23.4 \pm 3.5 \text{ cal mol}^{-1} \text{ K}^{-1}$$

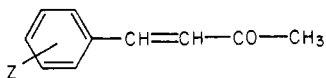
these it appears that the  $T\Delta S^\ddagger$  term makes an important contribution to the activation free energy. A similar phenomenon has already been reported for a cyanohydrin formation.<sup>10</sup> Owing to its small size, the cyanide should not contribute much to lowering the degrees of freedom. Despite its usual uncertainty—and the debatable property of this kind of argument<sup>11</sup>—the reported value of  $\Delta S^\ddagger$  could suggest a stoichiometric involvement of a solvent molecule (i.e., water).

**Structure-Reactivity Relationship.** Kinetic data with substituted 1-phenyl-3-buten-2-one<sup>12</sup> exhibit an excellent Hammett correlation:

(10) Schlesinger, G.; Miller, S. L. *J. Am. Chem. Soc.* 1973, 95, 3729.

(11) (a) Schaleger, L. L.; Long, F. A. *Adv. Phys. Org. Chem.* 1963, 1, 1. (b) Hammett, L. P. "Physical Organic Chemistry", 2nd ed.; McGraw Hill: New York, 1970; p 127.

(12) The *E* configuration of these enones is well-known: Brink, M. *Tetrahedron* 1969, 25, 995.

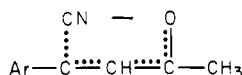


The plots of  $\log k_{ap}$  are linear over a wide range of  $\sigma$  values<sup>13</sup> (Figure 2).

The observed reaction constant is

$$\rho = +1.26 \pm 0.05 \quad (r^2 = 0.994)$$

Owing to the fact that the negative charge is delocalized over five atoms in the transition state (see I) and that the



enolate moiety is not directly located on the aromatic ring, the relatively high value of  $\rho$  implies a sizable charge redistribution. This result does not disagree with the hypothesis of a productlike transition state, which was put forward<sup>2,4</sup> on the basis of the Hammond postulate, in connection with stereochemical problems.

This reaction constant agrees well with the mean  $\rho$  value ( $1.35 \pm 0.23$ ,  $r^2 = 0.86$ ) found by Currie et al.<sup>14</sup> in a very intricate system in which hydrocyanation on benzalmonitriles occurred together with concomitant hydrolysis of the substrates.

In spite of the low degree of accuracy<sup>15</sup> expected for comparison of  $\rho$  values between different reactions, it is worth comparing the present value (1.26) for conjugate hydrocyanation with that reported<sup>16</sup> for the cyanohydrin formation from substituted benzaldehydes in 60% acetonitrile: 1.66. In the latter reaction, the negative charge in the transition state is less delocalized and much nearer to the aromatic ring. Also in that case, a late transition state appears from the Hammett correlation and the kinetic isotope effect.

### Conclusion

The present study confirms the expected bimolecular nature of the conjugate hydrocyanation reaction, while explaining the unexpected pseudo-first-order rate law, and demonstrates clearly that a late and highly ordered transition state is involved.

### Experimental Section

**Materials.** Dimethylformamide was purified by standard methods.<sup>17</sup> 1-Cholesten-3-one was prepared by following a published procedure.<sup>18</sup> The substituted 4-phenyl-3-buten-2-ones were obtained according to the classical Claisen-Schmidt reaction<sup>19</sup> from commercially available benzaldehydes and acetone. These enones were purified by running them several times through column chromatography on silica gel in order to obtain both the highest melting point and the highest UV extinction coefficient.

The UV kinetic measurements were performed at the following wavelengths (substituent,  $\lambda_{max}$  in nm,  $\epsilon$ ): H, 286, 22610; *p*-MeO, 318, 25950; *p*-Me<sub>2</sub>N, 375, 30150; *m*-MeO, 287, 18842; *p*-Cl, 295, 23166; *p*-*i*-Pr, 300, 24844; *p*-CN, 286, 29945; 1-cholesten-3-one, 237, 10634. Each  $\epsilon$  value is the average of five measures; the error

on  $\epsilon$  is about 1%. The spectra were obtained in 95% ethanol.

**General Procedure for the Preparation of the Cyano Ketones.** The enone (1 mmol) was dissolved in DMF-Water (9:1 v/v) (40 mL) containing KCN (130 mg) and NH<sub>4</sub>Cl (80 mg); the solution was heated at 100 °C for 4 h. A standard workup (extraction by ether) gave a crude product which was purified by column chromatography (SiO<sub>2</sub>; pentane-ether). Pure products were obtained in about 90% yields.

These reference cyano ketones exhibited no absorption at the UV wavelength used for the titration. The  $\beta$ -cyano derivatives of the substituted butenones showed the following <sup>1</sup>H NMR data (CDCl<sub>3</sub> solution, JEOL C 60 HL spectrometer) for the chemical shifts ( $\delta$ ) for COCH<sub>3</sub> (s), CH(CN) (t,  $J = 7$  Hz), CH<sub>2</sub> (dd,  $J = 7$ , and 16 Hz): H (mp 45 °C) 2.17, 4.35, 2.98, 3.22; *p*-MeO (mp 40 °C) 2.13, 4.25, 2.83, 3.20; *p*-Me<sub>2</sub>N (mp 82 °C) 2.13, 4.23, 2.93, 3.10; *m*-MeO (liquid) 2.17, 4.28, 2.92, 3.16; *p*-Cl (mp 92 °C) 2.17, 4.30, 2.94, 3.18; *p*-*i*-Pr (mp 77 °C) 2.15, 4.28, 2.90, 3.16; *p*-CN (mp 102 °C) 2.20, 4.43, 2.95, 3.21.

Elemental analysis of the aforementioned cyano ketones were performed by the Analysis Department of the P. and M. Curie University, and their results were within the accepted limits ( $\pm 0.4\%$ ).

**Kinetic Measurements.** Kinetics were studied by following our original procedure<sup>4</sup> with a Beckmann DK 2A spectrometer. The data were analysed by a linear least-squares treatment: (a) the correlation coefficients  $r^2$  for the rate constants measurements were always higher than 0.990; (b) the precision on the activation parameters was obtained by calculation of the standard deviation. The rate constants were not corrected for solvent expansion.

The rate data on which Figure 2 is based are the following: ( $10^{-4}$  s<sup>-1</sup>) 1-, 0.32; 2, 1.86; 3, 3.09; 4, 4.30; 5, 4.46; 6, 8.58; 7, 25.0.

**Registry No.** 4-[*p*-(Dimethylamino)phenyl]-3-buten-2-one, 5432-53-1; 4-(*p*-methoxyphenyl)-3-buten-2-one, 943-88-4; 4-(*p*-isopropylphenyl)-3-buten-2-one, 74389-78-9; 4-phenyl-3-buten-2-one, 122-57-6; 4-(*m*-methoxyphenyl)-3-buten-2-one, 20766-31-8; 4-(*p*-chlorophenyl)-3-buten-2-one, 3160-40-5; 4-(*p*-cyanophenyl)-3-buten-2-one, 51220-06-5; 1-cholesten-3-one, 50557-39-6; potassium cyanide, 151-50-8; ammonium chloride, 12125-02-9;  $\alpha$ -phenyl-4-oxopentenenitrile, 82323-82-8;  $\alpha$ -(4-methoxyphenyl)-4-oxopentenenitrile, 82323-83-9;  $\alpha$ -[4-(dimethylamino)phenyl]-4-oxopentenenitrile, 82323-84-0;  $\alpha$ -(3-methoxyphenyl)-4-oxopentenenitrile, 82323-85-1;  $\alpha$ -(4-chlorophenyl)-4-oxopentenenitrile, 82323-86-2;  $\alpha$ -(4-isopropylphenyl)-4-oxopentenenitrile, 82323-87-3;  $\alpha$ -(4-cyanophenyl)-4-oxopentenenitrile, 82323-88-4.

### Preparation of "Tied-Back" Functionalizable Derivatives of Tetra-*tert*-butylethylene<sup>1</sup>

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Investigations into the chemistry of strained organic molecules continue to generate new ideas on the nature of chemical bonding and reactivity.<sup>3</sup> Recent research has led to the preparation of a variety of molecular structures which cannot fail to astonish chemists familiar with the "normal" constraints of molecular geometries. Among these structures are very sterically crowded olefins containing torsionally distorted bonds. The ultimate synthetic

(13) The  $\sigma$  values were taken from the following: Hine, J. "Structural Effects on Equilibria in Organic Chemistry"; Wiley: New York, 1975; p 66.

(14) Pritchard, R. B.; Lough, C. E.; Reesor, J. B.; Holmes, H. L.; Currie, D. J. *Can. J. Chem.* 1967, 45, 775.

(15) McLennan, D. J. *Tetrahedron* 1978, 34, 2331.

(16) Young, P. R.; McMahon, P. E. *J. Am. Chem. Soc.* 1979, 101, 4678. See also: Ching, W. M.; Kallen, R. G. *Ibid.* 1978, 100, 6119.

(17) Gordon, A. J.; Ford, R. A. "The Chemist's Companion"; Wiley: New York, 1972; p 432.

(18) Johnson, H. E.; Crosby, D. J. *J. Org. Chem.* 1962, 27, 2205.

(19) Johnston, R. L.; Jones, L. A. *J. Chem. Eng. Data* 1971, 16, 112.

(1) Presented in part at the 2nd Chemical Conference of the North American Continent, Las Vegas, NV, Aug 1980.

(2) (a) Visiting Graduate Students, New Mexico State University, 1981-1982. (b) Present address: New Mexico State University.

(3) For recent reviews, see: (a) Leibman, J. F.; Greenberg, A. *Chem. Rev.* 1976, 76, 311. (b) Greenberg, A.; Leibman, J. F.; "Strained Organic Molecules"; Academic Press: New York, 1978. (c) Tidwell, T. T. *Tetrahedron* 1978, 1855. (d) Martin, S. F. *Ibid.* 1980, 419.