TABLE I

ISOMERIZATION OF METHYLBIPHENYLS WITH WATER-PROMOTED ALUMINUM CHLORIDE AT 50°

Reaction time	—% methylbiphenyl isomer distribution— (normalized) *ortho*	*meta*	*para*
	2-Methylbiphenyl		
0 min	99.7	0.3	0
5 min	98.9	1.1	0
10 min	89.2	10.6	0.2
15 min	77.2	22.6	0.2
20 min	65.4	34.4	0.2
25 min	59.5	40.3	0.2
30 min	56.1	42.7	1.2
40 min	50.3	46.5	3.2
1 hr	37.1	54.6	8.3
2.5 hr	15.1	75.6	9.3
4.5 hr	15.3	72.1	12.6
6.5 hr	15.2	70.4	14.4
24 hr	15.6	65.3	19.1
72 hr	15.8	58.1	26.1
	3-Methylbiphenyl		
0 min	0	95.4	4.7
5 min	0.7	95.4	4.1
15 min	0.3	92.7	7.0
20 min	0.4	91.8	7.8
45 min	1.1	89.8	9.1
1 hr	0.8	82.0	17.2
1.5 hr	0.7	78.2	21.1
2 hr	1.2	75.4	23.4
2.5 hr	1.8	73.6	24.6
3 hr	2.3	72.3	25.4
4 hr	3.6	71.2	25.3
5 hr	4.5	70.3	25.2
6 hr	5.9	68.2	25.9
8 hr	8.1	64.4	27.5
24 hr	15.1	58.0	26.9
48 hr	15.3	57.8	26.9
72 hr	15.8	57.8	26.4
	4-Methylbiphenyl		
0 min	0.3	0	99.7
5 min	0.3	2.1	97.6
10 min	0.3	8.3	91.4
20 min	0.3	23.5	76.2
30 min	0.4	37.0	62.6
40 min	0.5	47.0	52.5
50 min	0.5	52.1	47.4
1 hr	0.5	54.9	44.6
2 hr	0.6	63.9	35.5
2.5 hr	0.8	64.5	34.7
3 hr	0.8	70.4	28.8
4 hr	1.1	71.2	27.7
5 hr	1.3	70.5	28.6
6 hr	2.4	68.7	28.9
8 hr	3.3	67.6	29.1
24 hr	6.3	66.6	27.1
48 hr	15.2	57.8	27.0
72 hr	15.7	56.3	28.0

Experimental Section

Materials.—*o*-, *m*-, and *p*-methylbiphenyl were obtained from Chemical Procurement Laboratories, College Point, N. Y., and were used without further purification.

Isomerization Procedure.—Isomerizations were carried out in stoppered glass flasks, magnetically stirred and thermostated at 50 ± 0.5°. The amounts of substrate and catalyst in each experiment were 0.2 mole of aluminum chloride/mole of methylbiphenyl. To this mixture 1 ml of water was added as a promoter. Samples were withdrawn periodically, the reaction was stopped with water, and the organic material was extracted with ether. The dried ether extracts were analyzed by gas-liquid partition chromatography (glpc).

Glpc Analysis.—The analyses were carried out by glpc on a Perkin-Elmer Model 226 Vapor Fractometer using a 150-ft, 0.01-in. diameter open-tubular column coated with Apiezon L and a hydrogen flame-ionization detector. At a column temperature of 165° and He carrier gas pressure of 30 psi the isomeric methylbiphenyls had the following retention times: *o*-methylbiphenyl, 16.0 min; *m*-methylbiphenyl, 24.7 min; and *p*-methylbiphenyl, 26.0 min. Biphenyl under the same conditions has a retention time of 15.6 min and the isomeric dimethylbiphenyls (not further identified concerning isomeric distribution) between 30.9 and 41 min (at 200° column temperature). Peak areas were determined by the use of an Infotronics Model CRS-1 high-speed electronic integrator.

The accuracy of the glpc analytical method, as established from the analysis of isomer mixtures of known composition was better than ±5 relative % for all isomers.

Reactions Catalyzed by Potassium Fluoride. V. The Kinetics of the Knoevenagel Reaction

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Received September 9, 1965

There are numerous examples of exchange reactions reported for the preparation of fluorinated organic compounds in which sodium or potassium fluorides are refluxed with chloro compounds.[1-3] In an attempt to prepare trifluoroacetic acid from trichloroacetic acid and potassium fluoride, Nesmeyanov[4] discovered that, rather than the expected exchange, the fluoride served to catalyze decarboxylation to afford chloroform, a procedure ordinarily requiring bases such as hydroxide or amines. This apparent basic property of potassium fluoride was further exemplified by Midorikawa and co-workers[5] who reported examples of catalysis of the Knoevenagel reaction, and by LeGoff[6] in preparing dihydrohexaphenylpentalene *via* a Michael–Knoevenagel sequence from 1,2,3-triphenylcyclopentadiene and 1,2,3-triphenylpropenone. It was further demonstrated[7] that rubidium and cesium fluorides were more effective as catalysts than potassium fluoride for the Knoevenagel reaction in both polar and nonpolar solvents.

The kinetics and mechanism of the uncatalyzed reaction of ethyl cyanoacetate with aromatic aldehydes in various solvent mixtures have been determined by Patai and Zabicky.[8] Their data indicate that the reaction sequence is governed by a initial dissociation of the active methylene, although this dissociation is not the rate-determining step for the over-all reaction whose steps are given in Chart I.

(1) J. T. Maynard, *J. Org. Chem.*, **28**, 112 (1963).

(2) A. L. Henne, *Org. Reactions*, **2**, 49 (1944).

(3) M. Hudlický, "Chemistry of Organic Fluorine Compounds," The MacMillan Co., New York, N. Y., 1962, p 87 ff.

(4) A. N. Nesmeyanov, K. A. Pecherskaya, and G. Y. Uretskaya, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 240 (1948).

(5) (a) H. Baba, H. Midorikawa, and S. Aoyama, *J. Sci. Res. Inst.* (Tokyo), **52**, 99 (1958); (b) H. Igarashi, H. Midorikawa, and S. Aoyama, *ibid.*, **52**, 105 (1958); (c) A. Sakurai, H. Midorikawa, and S. Aoyama, *ibid.*, **52**, 112 (1958); (d) H. Yasuda, H. Midorikawa, and S. Aoyama, *ibid.*, **53**, 19 (1959); (e) A. Sakurai, *ibid.*, **53**, 250 (1959).

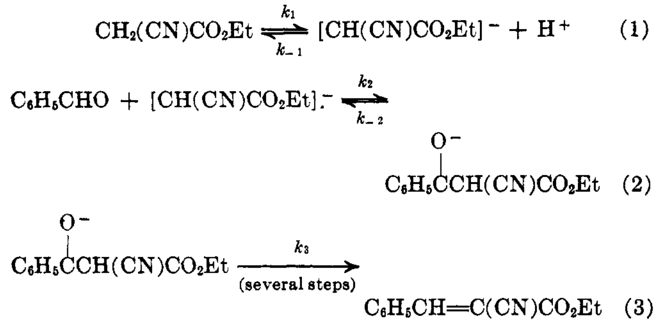
(6) E. LeGoff, *J. Am. Chem. Soc.*, **84**, 3975 (1962).

(7) L. Rand, J. V. Swisher, and C. J. Cronin, *J. Org. Chem.*, **27**, 3505 (1962).

(8) S. Patai and J. Zabicky, *J. Chem. Soc.*, 2030 (1960).

Chart I

Scheme of the Uncatalyzed Knoevenagel Reaction

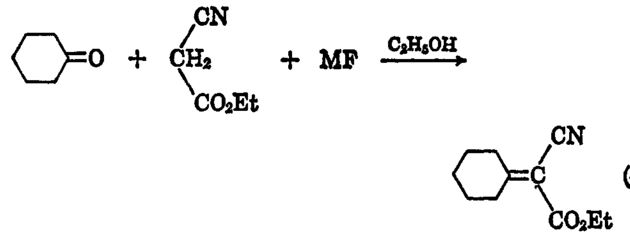


$$CH_2(CN)CO_2Et \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [CH(CN)CO_2Et]^- + H^+ \quad (1)$$

$$C_6H_5CHO + [CH(CN)CO_2Et]^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} C_6H_5\overset{O^-}{\overset{|}{C}}CH(CN)CO_2Et \quad (2)$$

$$C_6H_5\overset{O^-}{\overset{|}{C}}CH(CN)CO_2Et \xrightarrow[\text{(several steps)}]{k_3} C_6H_5CH{=}C(CN)CO_2Et \quad (3)$$

The role of the fluorides in the Knoevenagel reaction was not readily apparent, and a kinetic study was undertaken to elucidate the nature of the catalysis. Reaction rates were measured for the reaction of cyclohexanone with ethyl cyanoacetate in ethanol in the presence of potassium, rubidium, and cesium fluorides.



(4)

I

M = K, Rb, or Cs

Experimental Section

Materials.—Cyclohexanone and ethyl cyanoacetate were distilled before use and were chromatographically pure. Anhydrous potassium fluoride (Baker and Adamson) and anhydrous cesium and rubidium fluorides (American Potash and Chemical Corp.) were used as received. Absolute ethanol was used as the solvent. All weighing and transfer operations were conducted in a drybox. Ethyl cyclohexylidenecyanoacetate (I) was prepared in 85% yield following the method of Bezzi:[9] bp 138° (6 mm), $n^{28}\text{D}$ 1.4958 (lit.[9] bp 150–151° (9 mm), $n^{25}\text{D}$ 1.4950). The product colored slightly upon standing and was distilled prior to use.

Determination of Standard Curve.—The standard curve was obtained by measuring the absorbancy of I at λ_{max} 237 mμ (ε 14,200). A plot of the concentration of I against absorbancy was found to be linear and followed the expression

$$y = 1.5x \quad (5)$$

where y = absorbancy at 237 mμ, and x = concentration of the product in grams per liter. The reactants are transparent in this region.

Rate Measurements.—The general procedure for obtaining the rate data involved the preparation of a solution of ethyl cyanoacetate and fluoride in ethanol in a volumetric flask. The solution was brought to temperature in a water bath (±0.1°). Cyclohexanone, previously brought to the same temperature, was added, and the volume was brought to the mark by the addition of solvent. The flask was periodically shaken and at appropriate intervals, 1.00-ml samples were withdrawn and diluted with a 10,000-fold quantity of ethanol. An aliquot portion was transferred to an absorption cell, and the absorbance was measured at 237 mμ. The product concentration was then obtained from the standard curve. The rate function was plotted and the rate constant was obtained by measurement of the slope of the line.

Conductance Determinations.—Conductance measurements of ethanolic solutions of reactants were made with an Industrial Instruments conductivity bridge, Model RC-1682. The cell constant,[10] determined by measuring the conductance of a 0.01 N KCl solution in water at 30°, was 0.01. Conductance measurements were made of solutions of potassium, rubidium, and cesium fluorides in absolute ethanol and also of alcoholic solutions of each fluoride and ethyl cyanoacetate. The cell was immersed in a water bath maintained at 30 ± 0.1°. The values are given in Table III.

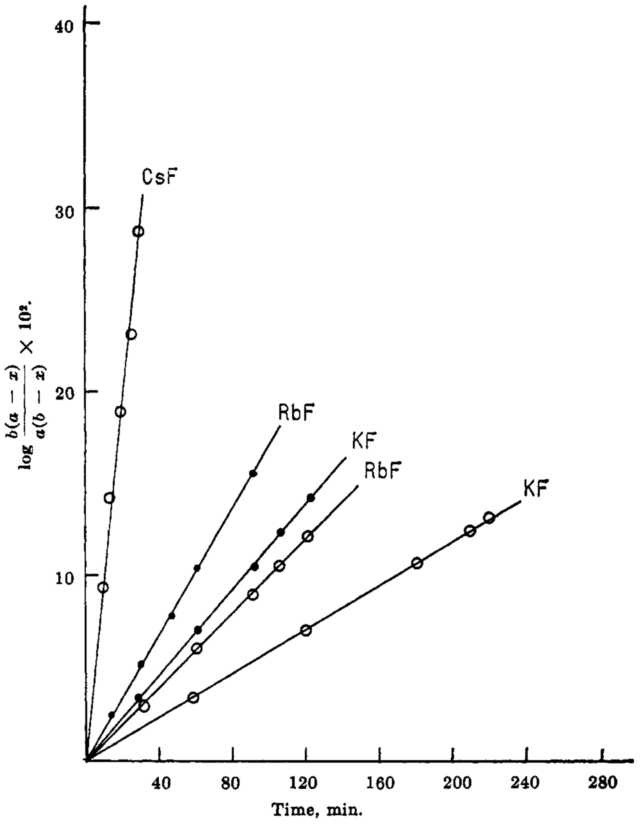


Figure 1.—Typical plot of the rate expression for the fluoride-catalyzed Knoevenagel reaction *vs.* time. ○, at 30°; ●, at 40°.

Results and Discussion

The rate of formation of the product was determined from the expression

$$\frac{dx}{dt} = k(a - x)^2c \quad (6)$$

for $a = b$ where a = initial concentration of cyclohexanone, b = initial concentration of ethylcyanoacetate, c = concentration of the metal fluoride, x = concentration of the product at time t. Plotting $x/ac(a - x)$ *vs.* t resulted in a straight line whose slope is the rate constant resulting from the integration of eq 6. A linear plot was obtained for $\log [b(a - x)/a(b - x)]$ *vs.* t when $a \neq b$. The slope[11] of this line is $c(a - b)k/2.303$. Typical plots are given in Figure 1. The rate data so obtained for the reaction between ethyl cyanoacetate and cyclohexanone in ethanol as a function of the fluoride concentration are given in Table I. For each run pseudo-second-order kinetics were found which correspond to an over-all third-order reaction, first order with respect to the fluoride.

On the basis of the rate data, it is reasonable to assume that the fluoride serves to promote the dissociation of the methylene compound as illustrated in eq 1.

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[9] S. Bezzi and A. Cocco, *Atti Ist. Veneto Sci.*, **106**, 75 (1948); *Chem. Abstr.*, **44**, 5826 (1950).

[10] "Operating Manual, Type RC Conductivity Bridges," Industrial Instruments, Inc., Cedar Grove, N. J., 1960, p 5.

[11] S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p 17 ff.

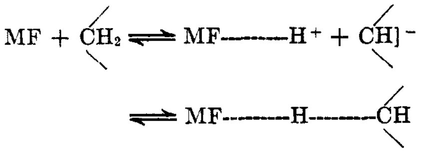
TABLE I

RATE CONSTANTS FOR THE ALKALI METAL FLUORIDE CATALYZED REACTION OF CYCLOHEXANONE (CH) WITH ETHYL CYANOACETATE (ECA) IN ETHANOL

Concn, *M*				Third-order constants
CH	ECA	KF	*T*, °C	$10k$, l.^{2} mole^{-2} min^{-1}
0.7500	0.7500	0.0300	30.0	1.05
0.5000	0.7500	0.0400	30.0	0.94
0.7500	0.5000	0.0500	30.0	1.05
0.5000	0.7500	0.0500	40.0	1.65
0.7500	0.5000	0.0700	40.0	1.59
0.5000	0.5000	0.0800	40.0	1.69
		RbF		
0.5000	0.7500	0.0800	30.0	1.15
0.7500	0.5000	0.1200	30.0	1.21
0.5000	0.5000	0.1500	30.0	1.20
0.7500	0.5000	0.0800	40.0	2.00
0.5000	0.5000	0.1200	40.0	2.10
0.5000	0.7500	0.1500	40.0	2.06
		CsF		
0.5000	0.5000	0.2500	30.0	1.50
1.0000	0.5000	0.3000	30.0	1.54
0.5000	1.0000	0.3500	30.0	1.31
0.5000	0.5000	0.0625	40.0	2.50
0.6000	0.3000	0.2000	40.0	2.30
0.5000	0.5000	0.2500	40.0	2.31
0.5000	0.7500	0.3500	40.0	2.19

It was shown, however, that the total yield of product from the Knoevenagel reaction does not require equimolar concentrations of the fluoride and the methylene compound, and that no evidence for the presence of hydrogen fluoride was found. It is interesting to note that an ethanolic solution of ethyl cyanoacetate and MF gives rise to an absorbance maximum at 247 $m\mu$ which corresponds to the anion of the methylene.[12] Intensity of the absorption increases with an increase in solution temperature, but is completely reversible when the temperature is lowered.[13] An attempt to establish the equilibrium constant for the dissociation of ethyl cyanoacetate in the presence of MF was made. Unfortunately, the value of the molar extinction coefficient for the carbanion, the latter resulting from reaction of equimolar concentrations of sodium ethoxide and ethyl cyanoacetate in ethanol, could not be measured with precision.

Two possible hydrogen-bonded[14] intermediates may be postulated on the basis of the experimental data as shown in eq 7 and 8. In eq 7, the abstracted proton from the active methylene group is hydrogen bonded to the fluoride of the metal fluoride ion pair. The alternative shown in eq 8 represents a hydrogen bond bridging between the metal fluoride ion pair and the methylene group.



$$MF + CH_2 \rightleftharpoons MF\text{-----}H^+ + CH]^- \quad (7)$$

$$\rightleftharpoons MF\text{-----}H\text{-----}CH \quad (8)$$

TABLE II

CONDUCTANCE MEASUREMENTS OF SOLUTIONS OF ALKALI METAL FLUORIDE WITH ETHYL CYANOACETATE (ECA) IN ETHANOL AT 30°

Catalyst concn, *M*	Measured resistance, ohms	Specific resistance, ohms	10^4 × specific conductance, ohms cm^{-1}
KF, 0.0300	35	3500	2.9
RbF, 0.0300	28	2800	3.6
CsF, 0.0300	30	3000	3.3
KF, 0.0300	34	3400	2.9
RbF, 0.0300	25	2500	4.0
CsF, 0.0300	26	2600	3.7

The conductance data, shown in Table II, reflect an increase in conductivity when ethyl cyanoacetate is added to a solution of the fluoride in ethanol. This increase would be more likely from the intermediate shown in eq 7.

The activation energies for the reaction with the three catalysts were calculated from the Arrhenius equation

$$\log \frac{k_2}{k_1} = \frac{E_a}{2.303R}\,\frac{T_2 - T_1}{T_1T_2} \qquad (9)$$

where k_2 and k_1 = rate constants determined at the absolute temperatures T_2 and T_1, R = molar gas constant, and E_a = Arrhenius activation energy. Within experimental error, the energies for each fluoride, given in Table III, are identical. This similarity argues for identical transition states with each fluoride which is not consistent with the intermediate postulated in eq 8.

TABLE III

ARRHENIUS ACTIVATION ENERGIES FOR THE ALKALI METAL FLUORIDE CATALYZED REACTION OF CYCLOHEXANONE WITH ETHYL CYANOACETATE IN ETHANOL

Catalyst	E_a, kcal/mole
KF	9.1
RbF	10.2
CsF	8.9

Acknowledgment.—Acknowledgment is gratefully made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the University Research Council for support of this research.

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[12] (a) A. Bruylants, E. Braye, and A. Schoone, *Helv. Chim. Acta*, **35**, 1127 (1952); (b) J. Segers and A. Bruylants, *ibid.*, **40**, 561 (1957).

[13] Unpublished results.

[14] It has been shown that the fluoride ion is an effective hydrogen-bond acceptor and that active methylene compounds are good donors. (a) A. Allerhand and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **85**, 1233 (1963); (b) *ibid.*, **85**, 1715 (1963).

The Reaction of Bis(2-methoxyethyl) Ether (Diglyme) with Hydrogen Fluoride–Boron Trifluoride

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Received September 2, 1965

We have observed that bis(2-methoxyethyl) ether (diglyme) treated with a mixture of HF and BF_3 evolves dimethyl ether. This happened very slowly from BF_3 solution and not at all from HF solution (see Table I). A substantial amount of dioxane and a lesser amount of 1,2-dimethoxyethane form also. Methanol was detected in only trace amounts. No scrambled products were detected when phenyl methyl ether or *n*-butyl ethyl ether were treated with HF–BF_3 in a similar manner.