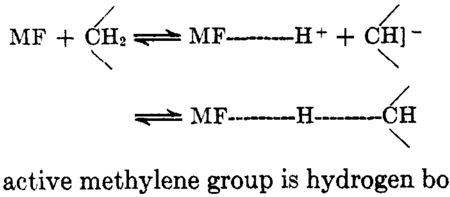
TABLE I

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	10*k*, 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 mμ 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



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

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

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.

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.

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

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

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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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.

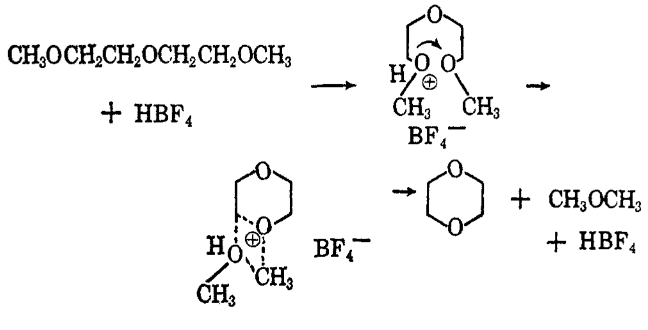
Table I

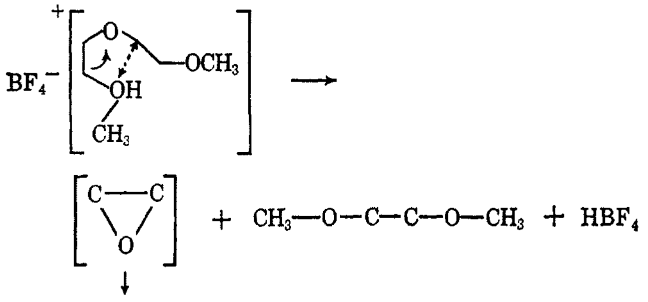
Formation of Dimethyl Ether from Bis(2-methoxyethyl) Ether

Diglyme, mole	BF_3, mole	HF, mole	Dimethyl ether formed, mole
0.40	0.08	None	0.005 in 5 days at 23°
0.40	0.20	None	0.037 in 3 days
0.40	0.20	0.20	0.25 in 21 hr
0.40	None	0.20	None in 5 days

Scheme I accommodates the above facts. Protonation of an ether oxygen occurs accompanied by partial charge separation in an adjacent C-O bond. Intramolecular attack of the resulting partially developed carbonium center on a nonprotonated ether oxygen forms an oxonium intermediate. This in turn breaks down into the observed products. If the incipient carbonium center resulting from protonation attacks the central oxygen (fifth atom in diglyme), Scheme I leads to 1,2-dimethoxyethane and ethylene oxide. In the presence of BF_3 ethylene oxide is known to form dioxane and a dark resinous product.[1] Should the central oxygen be protonated initially Scheme I leads to reformation of diglyme in which the positions of the specific carbon atoms are changed.

Scheme I





C-O-C-C-O-C-C-O-C → C-O-C-C-O-C-C-O-C
1 2 3 4 5 6 7 8 9 → 1 2 3 4 8 7 6 5 9

Experimental Section

Reaction of Bis(2-methoxyethyl) Ether with HF and BF_3.—Bis(2-methoxyethyl) ether (54 g, 0.40 mole) was placed in a weighed 200-ml round-bottom flask and cooled under nitrogen in an ice bath. Gaseous BF_3 was introduced (excluding atmospheric contact and moisture condensation as much as possible) until 13.6 g (0.20 mole) had been added. Then gaseous HF was cautiously introduced employing a plastic syringe barrel and flexible Teflon 17-gauge "needle" until 4.0 g (0.20 mole) had been added. Considerable heat is evolved during the step. The dark-colored reaction mixture flask was then connected directly to a volume-calibrated Dry Ice trap without delay. After 21 hr at room temperature (about 23°) the reaction mixture had lost 15 g in weight and about 17 ml of clear colorless liquid had been caught in the cold trap along with some colorless crystalline solids. The condensate was slowly bubbled through 25 ml of water and recondensed. The weight increase in the water (2.7 g) was assumed to be due principally to HF. One gram of liquid did not redistil at room temperature. The recondensed liquid (11.3 g) was shown to be dimethyl ether by comparison with known material on the three different gas chromatography columns and by proton nmr spectrum (single strong peak at τ 7.23).

The bulk of the reaction mixture was cautiously subjected to decreasing pressure until 1 mm at room temperature was achieved with no further bubbling. Volatiles removed during this process were caught in a Dry Ice cold trap. The liquid (at 23°) (14 g) trapped was placed in a soft glass vial and allowed to stand overnight. The dissolved HF reacted with the glass to form a white coating of solids. The remaining clear colorless liquid (11 g) was analyzed by gas chromatography on a 5-ft column of diatomaceous earth containing 10 wt % polypropylene glycol (mol wt 1000) at 90°. In this manner 0.10 mole of dioxane and 0.006 mole of 1,2-dimethyloxyethane were shown to be present. A trace of what was probably methanol could be seen when the polypropylene glycol column was employed but not when two other substrates were used.

A blackish slurry of the reaction mixture then remained. It was not further examined except to show that it contained a substantial amount of dark flocculent (in water) solids. Reaction mixtures in other experiments not stripped of product dioxane readily pick up water from the atmosphere if allowed. Well-formed colorless crystals of a dioxane–boron trifluoride–water complex then developed from the flask walls.

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(1) F. G. A. Stone and H. J. Emeleus, *J. Chem. Soc.*, 2758 (1950).

Alkaloids of *Cassia* Species. II. The Side Chain of Cassine[1]

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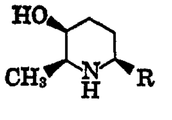
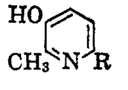
Characterization of the piperidine alkaloid cassine has led to the structure Ia.[1] Because condensation of the alkaloid with piperonal and benzaldehyde formed monopiperonylidine and monobenzylidine derivatives, respectively, it was inferred that the side chain was branched α to the ketone, and that structure Ib corresponded best to the degradative and spectral evidence available. The possibility of characterizing minute quantities of degradation products by mass spectrometry has now permitted further studies, which show



Ia, R = $C_{10}H_{20}COCH_3$
b, R = $(CH_2)_8CHCH_3COCH_3$
c, R = $(CH_2)_{10}COCH_3$
d, R = $(CH_2)_9CD_2COCD_3$



IIa, R = $(CH_2)_{10}COCH_3$
b, R = $(CH_2)_{11}CH_3$

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(1) Paper I: R. J. Highet, *J. Org. Chem.*, **29**, 471 (1964). Structure I corresponds to the mass spectral data noted in proof.

(2) After this work had been completed, we learned of synthetic studies which have subsequently confirmed these structures and established the absolute stereochemistry of cassine by the conversion of carpaine to the mirror image of N-methyl cassine. *Cf.* W. Y. Rice and J. L. Coke, *ibid.*, **31**, 1010 (1966). We are indebted to these authors for informing us of their results prior to publication.