Table I. Products of Elimination of Ether-**1** and Ether-**2**

Entry	Base[a]	Solvent	Base concn, *M*	Temp, °C	Time, min	Substrate	Acenaphthylene Mol %	Acenaphthylene % d_0	Acenaphthylene % d_1	Acenaphthylene % d_2	Ether mol %
1	$(CH_3)_4N^+$	*tert*-BuOH	0.10	45	90	**1**	8	1.6	6.3	0.1	92
2	K^{+b}	*tert*-BuOH	0.021	45	617	**1**	5	1.2	3.7	0.1	95
3	Cs^+	*tert*-BuOH	0.20	86	31	**1**	10.5	7.8	2.6	0.1	89.5
4	Cs^+	*tert*-BuOH	0.22	86	31	**2**	15	3	11.5	0.5	85
5	K^+	*tert*-BuOH	0.43	86	74	**2**	15	2.0	12.5	0.5	85
6	Li^+	*tert*-BuOH	0.14	152	462	**2**	25	2	22	1	75
7	K^+	CH_3OH	0.48	152	45	**1**	23	11	12		77

[a] Present as the alkoxide salt. [b] Complexed with 0.021 *M* dicyclohexyl-18-crown-6.

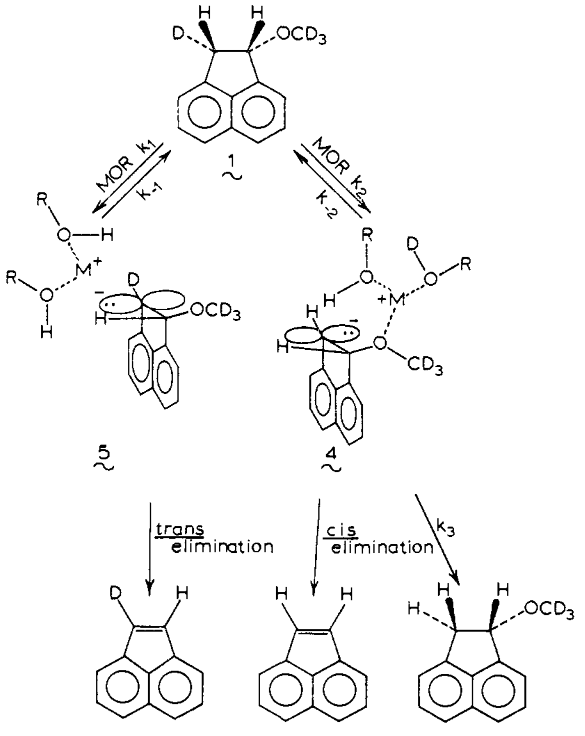
Table II. Effect of Cation on Relative Exchange and Elimination Rates

Entry	Base[a]	Ex/elim	Exchange k_{cis}/k_{trans}	Elimination k_{cis}/k_{trans}
8	$Li^+\bar{O}C(CH_3)_3$	0.4	≥ 16	≥ 13
9	$K^+\bar{O}C(CH_3)_3$	1.3	2.2	≥ 7
10	$Cs^+\bar{O}C(CH_3)_3$	2.1	0.9	≥ 5
11	$(CH_3)_4N^+\bar{O}C(CH_3)_3$	3.2	0.5	0.3
12	$K^+\bar{O}C(CH_3)_3{}^b$	3.2	0.6	0.3
13	$K^+\bar{O}CH_3$	5.1	1.0	0.6
14	$K^+\bar{O}CH_3{}^b$	3.4	1.0	

[a] Solvent is the conjugate acid. [b] Complexed with dicyclohexyl-18-crown-6-ether.

most reasonable to interpret the elimination reaction also in terms of carbanionic intermediates (E1cB).

As the results of Table II show, the ratio of cis/trans for both the exchange and elimination reactions varies by a factor of at least 30 (entries 8 and 11) from exclusive cis to dominant trans. The exchange and elimination stereoselectivity parallel each other closely except for Cs^+ and K^+ which show a greater cis to trans preference in elimination than in exchange.



Lithium cation shows a strong preference for cis reactions which can be interpreted in terms of a strong coordination between Li^+ of the base ion pair (or agglomerates) and the ether oxygen of substrate. This is shown in the simplified reaction scheme for **1**. The formation of **4** is greatly preferred over **5** with Li^+ present.

With K^+ and Cs^+, the coordinating ability is progressively reduced until **4** and **5** are produced in nearly equal amounts. However, from the elimination results it appears the cations enhance the decomposition into olefin and methoxide of **4** relative to **5**. The formation of a cation–methoxide ion pair from **4** seems to be an important factor in eliminations in *tert*-butyl alcohol.

In the absence of a coordinating cation (entries 11–14), intermediates **4** and **5** become near degenerate. A dramatic demonstration of this change is the large decrease in cis elimination and exchange when dicyclohexyl-18-crown-6-ether[6b] was added to potassium *tert*-butoxide (entries 9 and 12) and with tetramethylammonium cation.[8] In contrast, when dicyclohexyl-18-crown-6-ether is added to the already dissociated potassium methoxide in methanol (entries 13 and 14), there is no alteration in the stereochemistry of exchange.

These observations imply that there can be a significant role for cations in designing and interpreting elimination reactions in low polarity solvents.

Acknowledgment. The authors wish to thank the National Research Council of Canada for financial assistance.

[8] W. H. Saunders, D. G. Bushman, and A. F. Cockerill, *J. Amer. Chem. Soc.*, **90**, 1775 (1968).

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Hypofluorous Acid

Sir:

We have synthesized hypofluorous acid, HOF, by the reaction of fluorine with liquid or solid water in a Kel-F vessel. It is a volatile compound, stable enough to be transferred at room temperature under vacuum or in a gas stream.

Although the preparation of oxyacids of fluorine was reported in the early 1930's,[1,2] these results were soon

[1] L. M. Dennis and E. G. Rochow, *J. Amer. Chem. Soc.*, **54**, 832 (1932).

[2] L. M. Dennis and E. G. Rochow, *ibid.*, **55**, 2431 (1933).

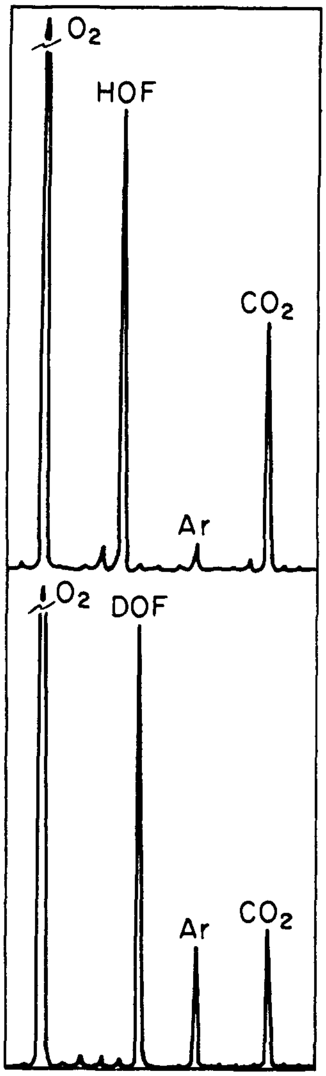

Figure 1. Positive-ion mass spectra of HOF (above) and DOF (below). The mass-to-charge ratios of the peaks corresponded to singly charged cations of the species indicated, *e.g.*, the peak identified as HOF had *m/e* 36, corresponding to HOF^+.

discredited as being due to chlorine impurity,[3] and no claims have subsequently been made for the isolation of such acids. Davis, *et al.*,[4] in 1949 observed that the reaction between fluorine and water vapor produced small amounts of materials whose properties did not seem to match those of any hitherto known compounds, but they were unable to identify these materials. In 1968 Noble and Pimentel[5] photolyzed a mixture of fluorine and water frozen into a nitrogen matrix at 14–20°K and observed infrared absorption bands that they attributed to HOF. From theoretical arguments, however, they concluded that the decomposition reaction

$$2HOF \longrightarrow 2HF + O_2 \qquad (1)$$

would probably be too rapid to permit the isolation of HOF.

We first detected hypofluorous acid in a Bendix time-of-flight mass spectrometer, and we used this instrument to monitor subsequent preparations. To confirm the mass spectrometric identification, preparations were carried out both with normal and with fully deuterated water. The positive-ion mass spectra appear in Figure 1. It is readily apparent that a prominent HOF peak at mass 36 is obtained with normal water, while an equally prominent DOF peak at mass 37 is obtained with deuterated water. The OF fragment is less than 5% as abundant as the parent, and its relative abundance appears to be somewhat less for DOF than for HOF. The fragments F, O, and OH are not readily distinguished because of the high oxygen, water, and HF background in the mass 16–20 region of the spectrum.

The proton on HOF was found to exchange rapidly with D_2O, at room temperature, with some evidence of exchange at much lower temperatures. Such exchange would be expected for an acidic hydrogen atom.

Although some HOF was formed from the reaction of fluorine with ice at temperatures at least as low as −40°, the best yields were obtained by bringing fluorine into contact with liquid water long enough for some, but not all, of the fluorine to react. If all the fluorine reacted, only O_2, HF, and some OF_2 remained. Oxygen difluoride did not appear to react with water or ice to yield HOF, nor was HOF found to decompose to OF_2.

On the basis of these observations, a simple Kel-F apparatus was designed to permit the preparation of milligram amounts of HOF. The reaction vessel consisted of a U tube packed with wet Teflon Raschig rings. It was cooled in an ice bath and fluorine was slowly pumped through it at pressures of 300 Torr or less. The fluorine stream was led through U tubes at −50 and −79° to trap water and then through one at −183° to trap the HOF. The −50° trap was needed to prevent a large fraction of the HOF from being caught with the water in the −79° trap. Most of the HF formed in the course of the reaction remained in the reaction vessel, although a small fraction was found in the −50 and −79° traps.

After the fluorine had all been removed, the −183° U tube was isolated from the preceding parts of the apparatus and was thoroughly evacuated to remove the traces of species volatile at this temperature such as O_2, F_2, and OF_2. Examination with the time-of-flight mass spectrometer confirmed that HOF was the predominant compound remaining in this U tube.

The HOF was analyzed by allowing the U tube to warm while a stream of argon was passed through it and bubbled into a 2 *M* sodium iodide solution cooled to 0°. The expected reaction is

$$HOF + 3I^- \longrightarrow I_3^- + OH^- + F^-$$

The base was titrated potentiometrically with acid and then the triiodide was titrated with thiosulfate. Of two typical samples, one generated 0.197 mmol of base and 0.207 mmol of triiodide, while the other generated 0.232 mmol of base and 0.247 mmol of triiodide. The relatively low base titers may reflect partial decomposition of the HOF to HF and O_2 prior to the analysis.

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(3) G. H. Cady, *J. Amer. Chem. Soc.*, **56**, 1647 (1934).

(4) W. Davis, Jr., F. D. Rosen, R. H. Winget, Jr., and R. H. Wiswall, Jr., Atomic Energy Commission Document 2827, Dec 27, 1949.

(5) P. N. Noble and G. C. Pimentel, *Spectrochim. Acta, Part A*, 24, 797 (1968).

The yield of HOF is dependent on the rate of flow of the fluorine through the reaction vessel. As the flow rate increases, more of the fluorine escapes reaction, but the HOF produced is a larger fraction of the fluorine that does react. In two typical experiments *ca.* 32 mmol of fluorine was passed through the reaction vessel at two different flow rates, and the fluorine consumed was roughly monitored by the amount of HF produced. At the slower flow rate 17 mmol of HF and 0.26 mmol of HOF were formed, while at the faster rate 1.7 mmol of HF and 0.11 mmol of HOF were formed. This suggests that a rapid and recirculating flow of fluorine might give a high yield of HOF.

The decomposition of HOF in a Kel-F vessel at 25–26° was monitored by periodically freezing the sample in liquid nitrogen, pumping off the oxygen evolved with a Toepler pump, measuring the volume of the oxygen, and analyzing it for purity mass spectrometrically. Half-lives for decomposition of HOF varied from 5 min to over 1 hr. The decomposition rate may very well be affected by variations in pressure and by traces of impurities such as water.

The amount of HF recovered after the decomposition of HOF was only about two-thirds that predicted by eq 1 on the basis of the O_2 evolved. Monitoring of the decomposition in the time-of-flight mass spectrometer showed the presence of various halocarbon molecules and some Cl_2, indicating that the HOF was attacking the Kel-F.

Hypofluorous acid reacts rapidly with water to produce HF, O_2, and H_2O_2. When *ca.* 200 mg of water was distilled onto *ca.* 0.1 mmol of HOF frozen at −196° and the mixture was allowed to warm, the principal products were HF and O_2. On the other hand, when an argon stream was used to bubble a sample of HOF into ice water, 0.185 mmol of HF and 0.173 mmol of H_2O_2 were formed, indicating that hydrolysis proceeded almost entirely according to the reaction

$$HOF + H_2O \longrightarrow HF + H_2O_2$$

The H_2O_2 was characterized by oxidation with Ce(IV) and by molybdate-catalyzed reduction with iodide, followed by titration with thiosulfate. The Ce(IV) and thiosulfate titers of aliquots of the same hydrolysate were identical within experimental uncertainty.

The HF formed by decomposition or hydrolysis of HOF was analyzed both by potentiometric titration with Th^{4+} or La^{3+}, using a fluoride sensitive electrode, and by potentiometric titration with base. The two titers agreed to within a few per cent, indicating the absence of significant amounts of acid other than HF.

Attempts to measure the vapor pressure of HOF with a Monel Bourdon gauge were not entirely successful because of decomposition of the compound. Hypofluorous acid appears to have a vapor pressure around 5 Torr at −64° and less than 1 Torr at −79°. However, detectable amounts of HOF can be distilled into the mass spectrometer from vessels cooled to temperatures as low as −140°. Condensed HOF is a white solid melting at about −117° to a colorless liquid.

In retrospect, it appears that early workers may have made HOF without recognizing their product. Credit for first identifying the compound, however, belongs to Noble and Pimentel,[5] provided that their assignment of the infrared spectrum is correct. We have attempted to confirm the work of Noble and Pimentel by measuring the gas-phase infrared spectrum of HOF, but because of the instability of the compound we have been unsuccessful. Efforts are now underway to measure the spectrum by codepositing HOF with a diluent gas in a low temperature matrix.

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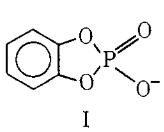
Structure and Enzymatic Reactivity of an Aromatic Five-Membered Cyclic Phosphate Diester. Biological Implications

Sir:

In the present communication we wish to describe the reaction of α-chymotrypsin with the aromatic five-membered cyclic phosphate diester, catechol cyclic phosphate (I).[1] Our results demonstrate for the first time that a newly introduced intramolecular nucleophile in an enzyme can be far more effective in attacking a phosphoryl phosphorus than the external nucleophile water and that a highly strained cyclic phosphate ester such as I can be synthesized from a covalent phosphoryl–enzyme species by a kinetically controlled pathway.

Catechol cyclic phosphate (I)[2] reacts stoichiometrically with α-chymotrypsin at pH 6.98 and 25.0° to form the inactive phosphorylated species II.[3] Under these conditions the value of k_2/K_s[3] is 3.0×10^2 M^{-1} sec^{-1}.



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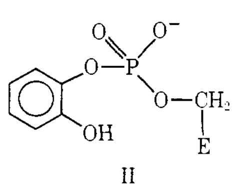

II

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[1] Although the organic chemistry of cyclic phosphate diesters has been explored thoroughly, relatively little is known about the mechanistic aspects of their reactions with enzymes except in the case of ribonuclease. See: D. A. Usher, D. I. Richardson, Jr., and D. G. Oakenfull, *J. Amer. Chem. Soc.*, **92**, 4699 (1970), and references therein.

[2] The method of H. Gross, S. Katzwinkel, and J. Gloebe, (*Chem. Ber.*, **99**, 2631 (1966)) with minor modifications was used for the preparation of I.

[3] The rates of phosphorylation by I and dephosphorylation of II were measured by techniques which have been described already in ref 4 and 5. The parameters k_2, k_{-2}, k_3, and K_s are defined in ref 4c.

[4] (a) J. H. Heidema and E. T. Kaiser, *J. Amer. Chem. Soc.*, **89**, 460 (1967); (b) *ibid.*, **90**, 1860 (1968); (c) *ibid.*, **92**, 6050 (1970).

[5] P. Tobias, J. H. Heidema, K. W. Lo, E. T. Kaiser, and F. J. Kézdy, *ibid.*, **91**, 202 (1969).