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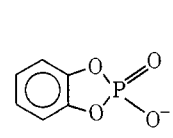
Structure and Enzymatic Reactivity of an Aromatic Five-Membered Cyclic Phosphate Diester. Biological Implications

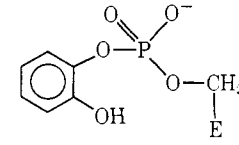
Sir:

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}.



I



II

(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).

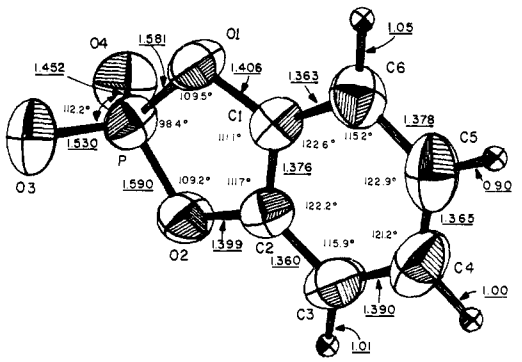


Figure 1. The molecular structure of catechol cyclic phosphate ($C_2H_5O_4P$). This compound crystallizes in space group *Pbca*, $a = 8.549 \pm 0.002$, $b = 15.041 \pm 0.003$, $c = 11.053 \pm 0.002$ Å; $Z = 8$. Its structure was solved by vector methods from diffractometer data (θ–2θ scan, λ 1.5418 Å) and refined by full-matrix least squares to $R_1 = 6.3\%$ for the 851 reflections above background. Anisotropic thermal motion, represented above by 50% probability thermal ellipsoids, was assumed for the P, O, and C atoms. Standard errors in bond distances and angles were computed from the least-squares variance–covariance matrix and are as follows: P–O, ±0.003; C–O, ±0.005; C–C, ±0.006 Å; O–P–O, ±0.2°; P–O–C, ±0.3°; O–C–C, ±0.4°, C–C–C, ±0.5°. The crystal contains an intermolecular O(3)–H···C(4) hydrogen bond of length 2.464 Å between molecules related by the *a* glide.

The phenolic hydroxyl groups in sulfonyl and acyl analogs of II have been shown to act as intramolecular nucleophiles, attacking, respectively, the carbonyl carbon or sulfonyl sulfur in these species.[4,5] Similarly, we have found that at pH 7.01 and 25.0° the rate constant k_{-2}[3] for the attack of the phenolic hydroxyl on the phosphoryl phosphorus of II has a value of 3.8×10^{-4} sec^{-1}.[6] The pseudo-first-order rate constant k_3[3] for the attack of water on II to give *o*-hydroxyphenylphosphoric acid and active α-chymotrypsin is less than 3.5×10^{-7} sec^{-1} under the same circumstances.

Our observations on the re-formation of compound I from II are particularly dramatic when the highly strained nature of the cyclic ester I is considered. Kinetic measurements have shown[7] that I is attacked by hydroxide ion nearly 10^7 faster than its open-chain analog, diphenyl phosphate, behavior paralleling that of the very reactive aliphatic five-membered cyclic phosphate esters.[8]

The enhanced rates of solvolysis observed for the latter compounds have been correlated with strain energies and molecular structure.[9] We have found now in an X-ray diffraction study of the structure of I that the endocyclic O–P–O bond angle in this compound is 98.4 ± 0.2°, a value close to those observed for very labile five-membered cyclic triesters, such as methyl ethylene phosphate[10] (99.1°), methyl pinacol phosphate[11] (98.4°), and acetoinenediol phosphate[12] (98.5°). The structure determination of I (Figure 1) is the first for a five-membered cyclic diester of phosphoric acid. In the six-membered cyclic diester uridine 3′,5′-phosphate[13] endocyclic O–P–O angles of 102.7 and 103.5° (for two independent molecules) were observed, whereas angles from 102 to 108° have been reported between the phosphorus–ester oxygen bonds in acyclic diesters.[14] The ring system of I is planar (within 0.17 Å); by contrast, in catechol cyclic sulfate[15] an unexpected puckering of the five-membered ring resulted in a structure where the sulfur atom was displaced 0.249 Å from the catecholate plane.

The analogy between the proximity effect of the phenolic hydroxyl group in the desulfonylation of 2-hydroxy-5-nitro-α-toluenesulfonyl-α-chymotrypsin and the effect of the amino group of the newly formed amino terminal acid present in the acyl-trypsin produced from the interaction of soybean trypsin inhibitor and trypsin has been noted.[4c,16] The proximity effects of the intramolecular nucleophiles present in these sulfonyl-α-chymotrypsin and acyl-trypsin species (phenolic hydroxyl or amino groups, respectively) allow the observation under suitable circumstances[4c] of the kinetically favored product (sultone or virgin inhibitor) rather than the thermodynamically favored product (sulfonic acid or hydrolyzed inhibitor).

The six-membered cyclic phosphate diester 3′,5′-cyclic adenylic acid (cyclic AMP) is thought to act as a second messenger in the action of many hormones.[17] We wish to suggest here that cyclic AMP may owe its effectiveness as a messenger in hormone action to its potential ability to phosphorylate enzymes reversibly in a manner similar to that we have described for the interaction of the highly strained cyclic phosphate diester I with α-chymotrypsin. In other words we propose that cyclic AMP can react with enzymes either at their active sites or allosteric sites with concomitant ring opening[18] to produce covalent phosphoryl–enzyme species.

(6) Preliminary studies on the pH dependence of the rate constant k_{-2} (unpublished work of T. W. S. Lee) show that in acidic solution the attack of the phenolic hydroxyl on the phosphoryl phosphorus is retarded. For example, at pH 6.35 and 25.0°, k_{-2} is 1.1×10^{-4} sec^{-1}.

(7) E. T. Kaiser and K. Kudo, *J. Amer. Chem. Soc.*, **89**, 6725 (1967).

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(12) D. Swank, C. N. Caughlan, F. Ramirez, O. P. Madan, and C. P. Smith, *ibid.*, **89**, 6503 (1967).

(13) C. L. Coulter, *Acta Crystallogr., Sect. B*, **25**, 2055 (1969).

(14) (a) J. D. Dunitz and J. S. Rollett, *ibid.*, **9**, 327 (1956); (b) M. Calleri and J. C. Speakman, *ibid.*, **17**, 1097 (1964); (c) S. Abrahamsson and I. Pascher, *ibid.*, **21**, 79 (1966); (d) M. S. J. Pletcher and B. Gustaffson, *ibid., Sect. B*, **26**, 114 (1970).

(15) F. P. Boer and J. J. Flynn, Jr., *J. Amer. Chem. Soc.*, **91**, 6604 (1969).

(16) H. F. Hixson, Jr., and M. Laskowski, Jr., *J. Biol. Chem.*, **245**, 2027 (1970).

(17) G. A. Robison, R. W. Butcher, and E. W. Sutherland, *Annu. Rev. Biochem.*, **37**, 149 (1968), and references therein.

(18) Cleavage of the 3′-phosphate bond in cyclic AMP has been demonstrated to be thermodynamically a very favorable process: P. Greengard, S. A. Rudolph, and J. M. Sturtevant *J. Biol. Chem.*, **244**, 4798 (1969). Semiquantitative support of our hypothesis for the action of cyclic AMP may be found from an examination of the relative Michaelis constants observed for the interactions of cyclic AMP and guanosine 3′,5′-cyclic phosphate (cyclic GMP) with bovine brain protein kinase. See: E. Miyamoto, J. F. Kuo, and P. Greengard, *ibid.*, **244**, 6395 (1969). Cyclic AMP binds more strongly to the enzyme by a factor of 80, which represents a free-energy difference of about 2.6 kcal/mol. The free energies of hydrolysis of cyclic AMP and cyclic GMP differ by 3.6 kcal/mol, and thus, one could account for the entire difference in binding strength by the difference in the expected values for k_2/k_{-2} if the cyclic nucleotides react with the kinase in a manner analogous to that we have observed for the interaction of I with α-chymotrypsin. Our comparisons between cyclic nucleotides and simple cyclic phosphate diesters involve data which are thermodynamic in the former case and kinetic in the latter. In the absence of reports on appropriate kinetic studies on cyclic nucleotides, we assume that the thermodynamic lability of cyclic AMP will be an approximate guide to its reactivity.

However, under appropriate conditions where kinetic control is favored, the hydroxyl group produced by ring opening, which remains covalently bound in close proximity to the phosphoryl function, can act as an intramolecular nucleophile, attacking the phosphorus, blocking the attack of water (which would cause the destruction of cyclic AMP), and causing re-formation of cyclic AMP with the release of free enzyme.[19] Our mechanistic proposal shows how cyclic AMP could regulate the action of many enzymes in a very effective way. We are actively investigating this hypothesis further.

(19) The re-formation of the six-membered cyclic ester, cyclic AMP, could be more favorable from a thermodynamic point of view than the cyclization reaction we have described for the five-membered system I.

(20) Fellow of the Alfred P. Sloan Foundation, 1968–1970.
(21) The studies at the University of Chicago were supported in part by the National Institute of General Medical Sciences.

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Photochemistry with Circularly Polarized Light. The Synthesis of Optically Active Hexahelicene

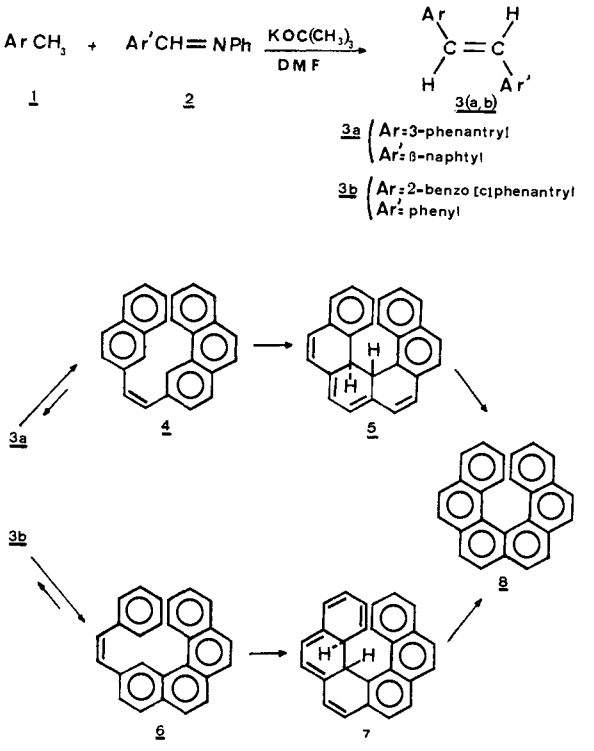
Sir:

The use of circularly polarized light in photochemistry has led to three types of asymmetric transformations: asymmetric photodestructions,[1] partial photoresolutions,[2] and asymmetric synthesis.[3,4] The latter until now have been unsuccessful, since the observed optical rotations have usually been very small and were always near the limit of the experimental error.

We now wish to report a synthesis of optically active hexahelicene **8** induced by circularly polarized light.[5] The method chosen for this synthesis is the photocyclization of 1,2-diarylethylenes to dihydrohelicenes. This reaction, if carried out in the presence of oxidants such as I_2 and O_2, has been shown to be an easy access to a series of helicenes.[6,7]

Our preliminary results concern the asymmetric synthesis of hexahelicene, starting from 1-(β-naphthyl)-2-(3-phenanthryl)ethylene (**3a**), or 1-(2-benzo[*c*]phenanthryl)-2-phenylethylene (**3b**),[8] which were prepared (Scheme I) from **1** and **2** by the method described by Siegrist and coworkers.[9] The alkene **3a** (162 mg) was irradiated[10] for 10 hr in 750 ml of benzene in the presence of 10 mg of iodine to give a maximum yield of 25% hexahelicene **8**. On the other hand, irradiation of the alkene **3b** (62 mg) for 6 hr under the same conditions

Scheme I



gave a maximum yield of 85% of hexahelicene **8**. After purifications by chromatography on alumina using *n*-hexane as an eluent, the optical rotations of hexahelicene (Table I) were directly measured without recrystallization. The optical yields thus obtained are

Table I. Optical Rotations of Hexahelicene **8** Synthesized by Photocyclization of Alkenes **3a** and **3b**

Alkene	Irradiations with right circularly polarized light, deg	Irradiations with left circularly polarized light, deg
3a	$[\alpha]^{23}°_{589} = -7.5 \pm 0.3$ $[\alpha]^{23}°_{436} = -30.0 \pm 0.3$ (*c* 2.08, $CHCl_3$)	$[\alpha]^{23}°_{589} = +7.9 \pm 0.6$ $[\alpha]^{23}°_{436} = +30.5 \pm 0.9$ (*c* 0.77, $CHCl_3$)
3b	$[\alpha]^{23}°_{589} = -1.8 \pm 0.4$ $[\alpha]^{23}°_{436} = -7.6 \pm 0.4$ (*c* 1.29, $CHCl_3$)	$[\alpha]^{23}°_{436} = +1.9 \pm 0.5$ $[\alpha]^{23}°_{436} = +8.4 \pm 0.5$ (*c* 0.99, $CHCl_3$)

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(2) (a) K. L. Stevenson and J. K. Verdieck, *J. Amer. Chem. Soc.*, **90**, 2974 (1968); (b) *Mol. Photochem.*, **1**, 271 (1969).
(3) T. L. Davis and J. Ackerman, *J. Amer. Chem. Soc.*, **67**, 486 (1945).
(4) T. L. Davis and R. Heggie, *ibid.*, **57**, 377, 1622 (1935).
(5) The reasons for having chosen helicenes and a discussion concerning the use of circularly polarized light in this type of photochemical synthesis will be given in a forthcoming publication.
(6) R. H. Martin, M. Flammang-Barbieux, J. P. Cosyn, and M. Gelbcke, *Tetrahedron Lett.*, 3507 (1968).
(7) R. H. Martin, M. Defay, H. P. Figeys, M. Flammang-Barbieux, J. P. Cosyn, M. Gelbcke, and J. J. Schurter, *Tetrahedron*, **25**, 4985 (1969).
(8) W. H. Laarhoven, Th. J. H. M. Cuppen, and R. J. F. Nivard, *ibid.*, **26**, 4865 (1970).
(9) A. E. Siegrist, P. Liechti, H. R. Meyer, and K. Weber, *Helv. Chem. Acta*, **52**, 2521 (1969).

(10) A mercury super-high-pressure arc lamp was used. After focalization with a quartz lens, the 290–370-nm band was isolated, using a nickel chloride–cobalt chloride solution (see W. W. Wladimiroff, *Photochem. Photobiol.*, **5**, 243 (1966)) as a filter, and then linearly polarized with a PL 40 filter (Polacoat, Inc.). Finally circular polarization was achieved by traversing the light beam through an isotrope silica plate, which was made birefractive by compression. All irradiations were carried out with a circularly polarized light at 313 nm. Therefore the ellipticity of the frontiers of the band are |1,16| for 290 nm and |0,79| for 370 nm. With this system we repeated Kuhn's asymmetric destruction experiment[1] and obtained optical rotations that were comparable to those reported. We are grateful to the "Laboratoire de Spectroscopie Herzienne" at the E.N.S. (Paris) for helpful suggestions that allowed us the realization of this system.