

tion at 30°, the aflatoxins were extracted and separated chromatographically.¹ The RIC of the aflatoxin-B₁ was less than 0.01, whereas if phenylalanine were a precursor of aflatoxin an RIC of 1.0 would be expected. Thus, phenylalanine is clearly excluded as a precursor of aflatoxin B₁.

The possible involvement of shikimic acid was examined in a similar fashion using the parent strain and measuring the incorporation of labeled shikimic acid into aflatoxin B₁ as compared to its incorporation into the phenylalanine in the cellular protein. Since shikimic acid is an intermediate of aromatic amino acid biosynthesis,⁵ if it is also an intermediate in aflatoxin biosynthesis comparable specific activities should be observed when the cells are grown in the presence of [ring-¹⁴C]shikimic acid. Following growth, the aflatoxins were extracted and separated, and the cells were dried and hydrolyzed with HCl. The hydrolysate was dried and dissolved in 10% aqueous 2-propanol. Aliquots were chromatographed on silica gel G plates, and the phenylalanine was measured by a comparison with standards after spraying with ninhydrin. The radioactivity of the phenylalanine was measured by liquid scintillation counting of the spot after scraping into vials. The specific activity of the phenylalanine was found to be 11 μCi/mmol, while that of the aflatoxin-B₁ was 0.21 μCi/mmol. This indicates that shikimic acid is not a precursor of aflatoxin B₁.

As [1-¹⁴C]acetate has been found¹ to label aflatoxin-B₁ efficiently, it appeared likely that the molecule was derived in large part from acetate units. To examine this possibility, aflatoxin-B₁ was prepared from [1-¹⁴C]- and [2-¹⁴C]acetate by a procedure modified from that of Abye and Mateles¹ as follows.

Conidia of the parent strain were cultivated in 100 ml of synthetic medium¹ in 500-ml baffled erlenmeyer flasks at 25° on a rotary shaker at 200 rpm for 3 days. Mycelial pellets were collected on cheese cloth in a Büchner funnel, washed with distilled water, dispersed in distilled water with a Waring blender, refiltered, and resuspended in nitrogen-free resting cell medium. The suspension was filtered again, and 1 g of wet cake (containing about 12% dry cell mass) was resuspended in 10 ml of resting cell medium containing 50 μmol of glucose and 20 μmol of radioactive acetate. The culture was incubated at 25° for 12 hr on a rotary shaker at 250 rpm. The culture was filtered and the filtrate was extracted with chloroform. The washed chloroform extract was evaporated with a stream of nitrogen, and the aflatoxins were separated by thin layer chromatography.¹ In a typical preparative run, 1 mCi of [1-¹⁴C]-acetate yielded 57 μCi of aflatoxin-B₁ with an RIC of 1.48 (hypothetical volume 9). Such highly active aflatoxin was subjected to chemical degradation⁶ or used for metabolic studies in animals.^{7,8}

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Intramolecular Exchange in Phosphorus Pentahalide Molecules¹

Sir:

Pseudorotation of a trigonal-bipyramidal intermediate has been postulated recently by a number of investigators²⁻⁵ concerned with various aspects of phosphorus chemistry. We wish to report results defining the requirements for such a process for phosphorus pentahalide molecules (known to undergo intramolecular exchange) and provide useful criteria in analyzing possible related situations. What is being considered here is a process analogous in some respects to the inversion occurring in the ammonia molecule.⁶ In the case of trigonal-bipyramidal molecules an internal vibration is thought to lead to exchange of equatorial and axial positions, leaving the molecule rotated compared to its original state (Figure 1). This type of process was first postulated by Berry⁷

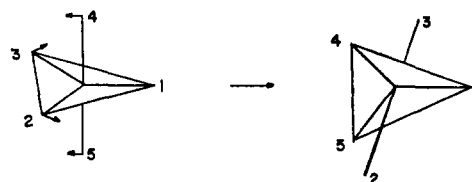
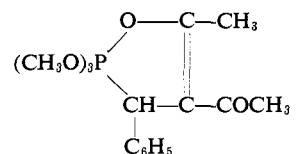


Figure 1. Pseudorotation.

to rationalize the appearance of equivalent fluorine environments in the ¹⁹F nmr spectrum⁸ of trigonal-bipyramidal PF₅. Nmr studies have now revealed examples of several trigonal-bipyramidal phosphorus compounds, PCl₂F₃,^{9,10} PH₂F₃,¹¹ (C₂H₅)₂NPF₄,^{10b} and



which have been shown to undergo exchange. In each case, a low-temperature pattern consistent with a non-exchanging structure transforms on increasing the temperature to a pattern showing averaging of fluorine atom magnetic environments with retention of P-F spin coupling.

Detailed considerations¹² of a vibrational exchange (pseudorotation), using a potential function¹³ based on

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Table I. Calculated Energy Barriers and Rate Constants (sec⁻¹) for Pentahalide Molecules

	Energy barrier, kcal/mol	-73°	27°	127°	Obsd exchange data (condensed state)	Ref
PF ₅	7.6	2.0 × 10 ⁴	1.7 × 10 ⁷	5.6 × 10 ⁸	Appreciable at -160° by ¹⁹ F nmr	8 ^a
PClF ₄	10.9	5.1	7.2 × 10 ⁴	9.2 × 10 ⁶	P-F doublet broadened at -157°	a
CH ₃ PF ₄	15.0	1.8 × 10 ⁻⁴	7.6 × 10 ¹	5.4 × 10 ⁴	Appreciable at -120° by ¹⁹ F nmr	10a
PCl ₅	13.5	6.6 × 10 ⁻³	8.5 × 10 ²	3.3 × 10 ⁵	Exchange not detected	10a ^b
SbCl ₅	9.4	2.2 × 10 ⁻²	8.7 × 10 ⁵	6.0 × 10 ⁷	Exchange not detected	

^a R. P. Carter, Jr., and R. R. Holmes, *Inorg. Chem.*, **4**, 738 (1965). ^b J. Downs and R. E. Johnson, *J. Chem. Phys.*, **22**, 143 (1954).

complete assignments of ir and Raman spectra,¹⁴ show that a tetragonal pyramid provides the lowest energy path leading to exchange. Actually only part of the potential function need be considered in the calculation, since the internal motions expected to lead to exchange, *i.e.*, vibrations involving predominantly equatorial or axial bending motions, belong to the same symmetry class (*e'* modes for D_{3h} molecules and a₁ modes for molecules of C_{2v} symmetry). The resulting normal coordinate calculations show, analogous to that for the ammonia molecule,¹⁵ that one normal mode dominates

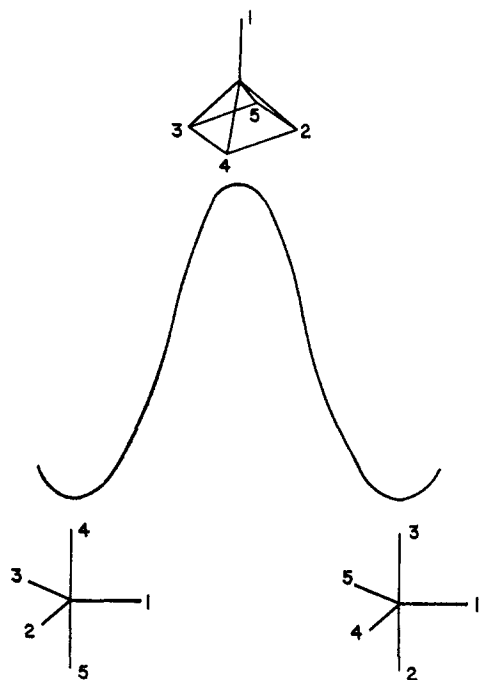


Figure 2. Potential well for trigonal bipyramids of type MX₅ and MX₄Y.

the exchange process for each of the pentahalide molecules considered here. This mode is the axial bending mode, a relatively low-frequency vibration with considerable amplitude in the ground vibrational state. The bending frequency, when the axial groups are fluorine atoms, has been observed^{13,14,16} to lie in the range 120–190 cm⁻¹. The eigenvector description (*L* matrix) (obtained by solution of the secular equation

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$GF - E\lambda_k L_k = 0$) shows that this normal mode is primarily made up of an axial bending coordinate with small contributions from equatorial bending and stretching coordinates.¹⁷

By allowing the amplitude of such a motion to increase, a tetragonal pyramid is formed (Figure 2). However, it is expected that as the amplitude of the motion increases anharmonicity should become increasingly more important. In the absence of detailed information, a correction amounting to 2% initially and then increasing slowly as the barrier maximum is approached was considered reasonable for vibrations of molecules of the type discussed. This procedure introduces a cubic and quartic term into the calculations and results in greater corrective effects for molecules having the larger barrier heights. The "corrected" barrier energies (Table I) range from 25 to 40% lower than those computed from the harmonic potential function.

Consideration of tunneling through the barrier and reaction over the barrier lead to the conclusion that for these molecules the latter process assumes importance at all but the lowest temperatures. Table II lists the symmetry force constants used, and Table I

Table II. Symmetry Force Constants (10⁵ dyn cm⁻¹) for Calculation of Exchange Barriers

	D _{3h} Symmetry					
	F ₃₅	F ₆₆	F ₇₇	F ₅₆		
PF ₅	5.55	0.785	0.0864	-0.1		
PCl ₅	2.49	0.349	0.104	-0.2		
SbCl ₅	2.20	0.160	0.0577	0.0		
	C _{2v} Symmetry					
	F ₁₁	F ₂₂	F _{5a,5a}	F _{6a,6a}	F _{7a,7a}	F _{5a,6a}
PClF ₄	10.44	5.34	1.90	0.612	0.121	-0.5
CH ₃ PF ₄	5.40	3.96	3.74	0.798	0.161	0.0

compares unimolecular rate constants, approximated as $(kT/h)e^{-\Delta E/RT}$, for several trigonal-bipyramidal molecules. A *relative* ordering in agreement with rates ascertained from nmr^{8,18} and exchange data¹⁹ is seen. The rates should be regarded as upper limits, since effects of "collisional complexes" which may serve to reduce the barrier height, especially in solution, have not been considered.

The magnitude of the calculated exchange rates (Table I) for trigonal-bipyramidal molecules as heavy

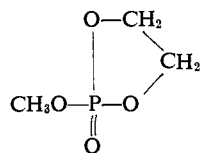
(17) Many possibilities of suitable exchange coordinates were considered such as combinations of normal modes. In all cases considerably higher barriers resulted compared to that discussed here except that about the same barriers were obtained by minimizing the symmetry coordinates S₅ and S₇.

(18) See Table I, footnote a.

(19) See Table I, footnote b.

as SbCl_5 at room temperature and above (where most kinetic processes have been studied) lies in the range 10^2 to 10^8 sec^{-1} . It seems altogether reasonable then that, in some mechanistic studies, pseudorotations of trigonal-bipyramidal intermediates must be considered in accounting for product distribution. The main requirement exists that the lifetime of the intermediate exceeds the exchange time.

In fact, in the hydrolysis of cyclic phosphate esters, for example



Dennis and Westheimer²⁰ postulate a pseudorotation of the trigonal-bipyramidal intermediate to account for the products formed. In their case, relatively light atoms are involved, and the reaction rate, $\sim 10^{-4} \text{ sec}^{-1}$ (mol/l.^{-1}) at room temperature, is slow enough for exchange to occur.

However, it is clear that for the molecules under consideration pseudorotation is possible only because the coordinate governing exchange has a low frequency and large amplitude motion (hence a correspondingly small force constant) associated with a molecule of comparatively low reduced mass. The latter conditions may apply for these trigonal-bipyramidal molecules because of the apparent weakness of axial bonds compared to equatorial bonds.

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The Molecular Geometry of Derivatives of 1H-Azepine in the Free and Complexed State¹

Sir:

The 1H-azepine molecule (**1a**) is isoelectronic with the cycloheptatrienide anion² and, if planar, may in actuality be antiaromatic.³ Interestingly, molecular quantum mechanical calculations for such a model predict marked polyenic character and strong localization of the π electrons on nitrogen and the double bonds of the seven-membered ring with little, if any, tendency for delocalization.⁴ Although the parent 1H-azepine (**1a**) remains to be synthesized, a few derivatives have been known since 1963.^{5,6} To the present time, however, no X-ray structural information has been obtained on these nitrogen-containing eight- π -electron systems. In an effort to elucidate the molecular

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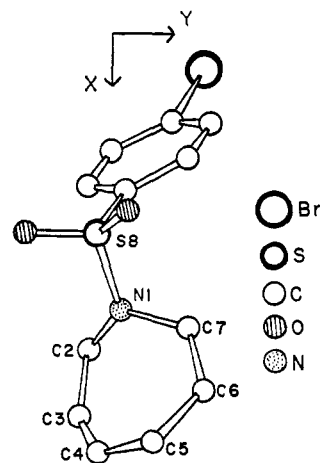
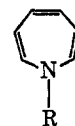


Figure 1. A view of **1b** looking along the z axis. Important distances are $\text{N}_1\text{-C}_2$ 1.43 Å, $\text{C}_2\text{-C}_3$ 1.38 Å, $\text{C}_3\text{-C}_4$ 1.44 Å, $\text{C}_5\text{-C}_6$ 1.46 Å, $\text{C}_6\text{-C}_7$ 1.37 Å, $\text{N}_1\text{-C}_7$ 1.45 Å, and $\text{N}_1\text{-S}_8$ 1.61 Å (estimated standard deviation ± 0.02 Å). The angles within the seven-membered ring are N_1 116°, C_2 118°, C_3 127°, C_4 123°, C_5 127°, C_6 124°, and C_7 121° (estimated standard deviation $\pm 1.5^\circ$). The $\text{S}_8\text{N}_1\text{C}_2$ and $\text{S}_8\text{N}_1\text{C}_7$ angles are 118 and 120°, respectively.

geometry of this seven-membered ring in the free state, and when complexed with iron tricarbonyl,⁷ we have carried out three-dimensional X-ray studies on **1b**⁸ and on the $\text{Fe}(\text{CO})_3$ complex of **1c**.⁸



1a, R = H

b, R = $\text{SO}_2\text{C}_6\text{H}_4\text{Br}$ -p

c, R = COOCH_3

1b crystallizes as lemon-yellow prisms, generally elongated along the b axis, and belongs to the orthorhombic system, with $a = 12.32$, $b = 5.96$, and $c = 16.53$ Å (Mo $\text{K}\alpha$, λ 0.7107 Å). There are four molecules of $\text{C}_{12}\text{H}_{10}\text{BrNO}_2\text{S}$ (mol wt 312.2) in the unit cell ($\rho_{\text{meas}} = 1.68 \text{ g cm}^{-3}$; $\rho_{\text{calcd}} = 1.71 \text{ g cm}^{-3}$). Systematic absences establish the space group as $\text{P2}_12_12_1$. The structure was determined by the heavy-atom method and has been refined by full-matrix least squares on 1274 independent intensities collected photographically (Cu $\text{K}\alpha$ radiation) to an R factor of 0.10. A view of the structure with important molecular dimensions is given in Figure 1.

The iron tricarbonyl complex of **1c** crystallizes as irregular orange prisms belonging to the triclinic system, with $a = 8.62$, $b = 6.47$, and $c = 10.90$ Å; $\alpha = 93.4^\circ$, $\beta = 93.0^\circ$, and $\gamma = 104.4^\circ$ (Mo $\text{K}\alpha$, λ 0.7107 Å). There are two molecules of $\text{C}_8\text{H}_9\text{NO}_2 \cdot \text{Fe}(\text{CO})_3$ (mol wt 291.0) in the unit cell ($\rho_{\text{meas}} = 1.60 \text{ g cm}^{-3}$; $\rho_{\text{calcd}} = 1.65 \text{ g cm}^{-3}$), and the structural analysis indicates that the space group is $\text{P}\bar{1}$. The structure has been refined by full-matrix least squares on 2008 independent intensities collected photographically (Mo $\text{K}\alpha$ radiation) to an R factor of 0.10. A view of the structure is shown in Figure 2.

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(8) The synthesis of this material will be published independently.