Table I. The $\Delta H°$ Values (in kcal/mol) for Some Reactions Showing Anomeric Effects and the Hardness (η) Values (in eV) for the Various Molecules Involved[a]

	reaction	$\Delta H°$
(i)	$2CH_3F = CH_4 + CH_2F_2$	−14[b]
η	9.4 10.3 7.84*	
(ii)	$2CH_3OH = CH_4 + CH_2(OH)_2$	−15 ± 1.5[c]
η	7.50* 10.3 7.58*	
(iii)	$CH_3F + CH_3OH = CH_4 + FCH_2OH$	−ve[d]
η	9.4 7.50* 10.3 7.55*	
(iv)	$CH_3NH_2 + CH_3OH = CH_4 + HOCH_2NH_2$	−ve[d]
η	7.2 7.50* 10.3 7.08*	
(v)	$2CH_3NH_2 = CH_4 + CH_2(NH_2)_2$	−ve[d]
η	7.2 10.3 6.47*	
(vi)	$CH_3NH_2 + CH_3F = CH_4 + FCH_2NH_2$	−ve[d]
η	7.2 9.4 10.3 6.99*	
(vii)	$2SiH_3F = SiH_2F_2 + SiH_4$	−8[b]
η	5.96* 5.71* 6.8	
(viii)	$2CF_2Cl_2 = CF_4 + CCl_4$	−16.3[e]
η	5.57* 9.02* 5.6	
(ix)	$3CH_3F = 2CH_4 + CHF_3$	−31.4[e]
η	9.4 10.3 7.92*	
(x)	$4CHF_3 = CH_4 + 3CF_4$	−22.9[e]
η	7.92* 10.3 9.02*	
(xi)	$4CH_3F = 3CH_4 + CF_4$	−63[f]
η	9.4 10.3 9.02*	
(xii)	$4CH_3Cl = 3CH_4 + CCl_4$	−6[f]
η	7.5 10.3 5.6	
(xiii)	$4CH_3OCH_3 = 3CH_4 + C(OCH_3)_3$	−52[f]
η	8.0 10.3 6.78*	
(xiv)	$4CF_3Cl = 3CF_4 + CCl_4$	−27.1[e]
η	6.27* 9.02* 5.6	
(xv)	$4CH_3CH_3 = 3CH_4 + C(CH_3)_4$	−13[f]
η	8.23* 10.3 8.3	
(xvi)	$4SiH_3F = 3SiH_4 + SiF_4$	−23[f]
η	5.96* 6.8 6.81*	
(xvii)[g]	$SiF_3H + CF_4 = SiF_4 + CF_3H$	−37[f]
η	6.07* 9.02* 6.81* 7.92*	
(xviii)	$C(OCH_3)_4 + SiH_4 = CH_4 + Si(OCH_3)_4$	−144[f]
η	6.78* 6.8 10.3 4.96*	

[a] The η values followed by an asterisk are calculated at the MNDO level (see text), and others are obtained experimentally (from refs 8 or 9). [b] From ref 1. [c] From: Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 6394. [d] As indicated by the ab initio study in: Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 6394. [e] The $\Delta H°$ value has been calculated by using the $\Delta H_{f,298}^{\circ}$ data taken from: Benson, S. W. *Angew. Chem., Int. Engl. Ed.* **1978**, *17*, 812. [f] From ref 5. [g] This reaction is an exception; see text.

shell species 2η is equal to the gap between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) (eq 3), where ϵ is

$$\eta = (\epsilon_{LUMO} - \epsilon_{HOMO})/2 \quad (3)$$

energy. The hardness of a species increases with increasing value of η. According to Pearson, the anomeric effect "refers to the stabilization caused by adding several hard substituents to the same" central atom. Herein we shall examine the various reactions listed in Table I in terms of the η values of the various molecules involved in order to identify the common driving factor in these reactions.

The η values used in our present study (Table I) are either experimental[8,9] or were calculated by the MNDO method of Dewar[10] according to eq 3. A standard MOPAC program has been used for the MNDO calculations. Elsewhere we have shown that η values calculated at the MNDO level usually lie within ±10% of the experimental η values.[11]

All reactions given in Table I proceed thermochemically from left to right. A survey of the η values of the various molecules involved in a particular reaction shows one common feature. The hardest species lies on the RHS, i.e., on the products' side. This observation, however, does not hold true for example xvii in Table I, where the hardest species is found on the reactants' side. It has been felt by several workers[12,13] in the area that η is an index of reactivity; the larger the value of η, the more reactive the species. Thus, as a general rule, it would be expected that all reactions would tend to generate the hardest possible species, so that the reactivities of the products are kept at the lowest possible level; otherwise the reverse reaction would take place. This notion is in complete agreement with all of the reactions listed in Table I, excluding xvii, which seems to be an exception. Earlier, while enumerating Pearson's hard–soft acid–base principle in terms of hardness, we found that an exchange reaction of the type shown in eq 4 also proceeds in a direction so as to produce the hardest possible species.[11]

$$PQ + XY = PX + QY \quad (4)$$

We have shown herein that the driving force behind all reactions in which anomeric effects are believed to be operative is the generation of the hardest possible species. Among the 18 reactions studied, we encountered only one exception to this rule. Interestingly, the examples of reaction 1 show that it is the hardness of CH_4, and not of the species of type XCH_2Y, that drives the reaction.

Our present observations can be related to the "maximum hardness principle" of Pearson which states that "there seems to be a general rule of nature that molecules arrange themselves so as to be as hard as possible".[14] Very recently, Parr and Chattaraj[15] have provided a theoretical proof of this statement by using statistical mechanics under certain constraints. Further proof has been provided by Pearson himself, together with Palke,[16] by means of case studies following the arguments of Parr and Chattaraj. Pearson's maximum hardness principle applies to an individual molecule. We can extend this concept to a chemical reaction by stating that in a chemical reaction molecules rearrange themselves so as to produce the hardest possible species.

Acknowledgment. Thanks are due to Prof. S. P. Bhattacharyya of the Department of Physical Chemistry for extending the computational facilities.

(8) Pearson, R. G. *Inorg. Chem.* **1988**, *27*, 734.
(9) Pearson, R. G. *J. Org. Chem.* **1989**, *54*, 1423.
(10) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.
(11) Datta, D. *Inorg. Chem.* **1992**, in press.
(12) Datta, D. *J. Phys. Chem.* **1992**, 2409 and references cited therein.
(13) Zhou, Z.; Parr, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 5720 and references cited therein.
(14) Pearson, R. G. *J. Chem. Educ.* **1987**, *64*, 561.
(15) Parr, R. G.; Chattaraj, P. K. *J. Am. Chem. Soc.* **1991**, *113*, 1854.
(16) Pearson, R. G.; Palke, W. E. *J. Phys. Chem.* **1992**, *96*, 3283.

A New Method of P–Se Bond Cleavage: Stereocontrolled Synthesis of P-Chiral Phosphoric–Trifluoroacetic Anhydrides

Lucyna A. Wozniak, Bozenna Krzyzanowska, and Wojciech J. Stec*

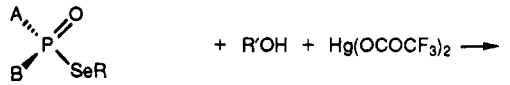
Polish Academy of Sciences, Centre of Molecular & Macromolecular Studies, Department of Bioorganic Chemistry, 90-363 Lodz, Sienkiewicza 112, Poland

Received April 30, 1992

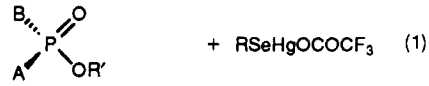
An earlier observation that reaction of *O,S,Se*-trimethyl phosphoroselenothioate with ethanol, catalyzed by silver nitrate, is chemoselective and gives exclusively *O,S*-dimethyl *O*-ethyl phosphorothioate[1] stimulated further at-

0022-3263/92/1957-6057$03.00/0

tempts to utilize *Se*-alkyl phosphoroselenoates as phosphorylating reagents. We have found that, besides silver nitrate, mercuric trifluoroacetate (1) can serve as an effective catalyst of phosphorylation. As in the case of silver nitrate, ethanolysis of *O,O,Se*-triethyl phosphoroselenoate (2) in the presence of $Hg(OCOCF_3)_2$ gives *O,O,O*-triethyl phosphate (3) in quantitative yield. Similarly, treatment of a methanol solution of *O,Se*-dimethyl *N*-phenylphosphoramidoselenoate (4) with 1 led to the formation of *O,O*-dimethyl *N*-phenylphosphoramidate (5). These

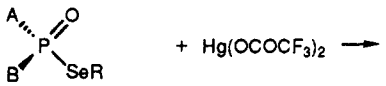


2: A = B = OEt, R = Et, R' = Et
4: A = OMe, B = NHPh, R' = Me

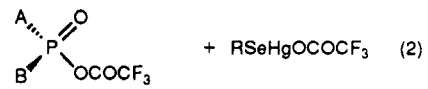


3: A = B = OEt, R = Et, R' = Et
5: A = OMe, B = NHPh, R' = Me

observations prompted detailed studies on the function of $Hg(OCOCF_3)_2$ in the above reactions. The reaction of acetonitrile solution of 2 with 1 gave *O,O*-diethyl *O*-trifluoroacetyl phosphate (6), while 4 under similar conditions was converted to *O*-methyl *O*-trifluoroacetyl *N*-phenylphosphoramidate (7). Both reactions, performed in either



2: A = B = OEt, R = Et
4: A = OMe, B = NHPh



6: A = B = OEt, R = Et
7: A = OMe, B = NHPh

acetonitrile or methylene chloride, were relatively fast[2] and accompanied by precipitation of $EtSeHgOCOCF_3$ or $MeSeHgOCOCF_3$, respectively. The anhydride structure of both 6 and 7 has been proved by their solvolysis. As expected, *O,O*-diethyl *O*-trifluoroacetyl phosphate (6), which in reaction with ethanol gave *O,O,O*-triethyl phosphate, reacted with aniline to provide anilinium *O,O*-diethyl phosphate and trifluoroacetanilide. Similarly, methanolysis of *O*-methyl *O*-trifluoroacetyl *N*-phenylphosphoramidate (7) led to the production of *O,O*-dimethyl *N*-phenylphosphoramidate (5). These preliminary results indicated that serendipiously we have discovered a *new method of cleavage of the P–Se bond and a new synthetic route to mixed phosphoric–trifluoroacetic anhydrides*, which in reaction with alcohols appeared to possess, as expected, phosphorylating properties.

To gain more information on the mechanistic aspects of the reaction between phosphoroselenoesters and 1, the stereochemistry of these reactions has been studied. As model compounds we used well-defined *cis*- and *trans*-2-(methylseleno)-2-oxo-4-methyl-1,3,2-dioxaphosphorinanes (8).[3] The reaction of *trans*-8 with 1 gives a single isomer of 2-(trifluoroacetoxy)-2-oxo-4-methyl-1,3,2-dioxaphosphorinane (9) ($\delta_{^{31}P}$ −16.44 ppm) and (methylseleno)-mercuric trifluoroacetate, $MeSeHgOCOCF_3$. *cis*-8 gave also an individual isomer of 9 ($\delta_{^{31}P}$ −16.29 ppm) and $MeSeHgOCOCF_3$, respectively. The identity of both compounds 9 has been confirmed by mass spectrometry.

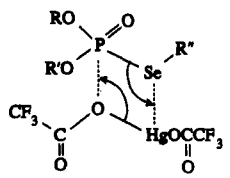
Moreover, separated isomers of 9 in a reaction with methanol afforded the corresponding phosphates (10) in almost quantitative yield. Interestingly, methanolysis of *trans*-9 gave almost exclusively *cis*-10, and the same product was obtained when the methanol solution of *trans*-8 was treated with an equimolar amount of 1. Similarly, methanolysis of *cis*-8 in the presence of 1 gave exclusively *trans*-10. Since the stereochemistry of the starting selenoloesters 8 and that of the products of their solvolysis, 10, is well documented,[3] the above results could be interpreted in terms of a stereoretentive reaction of the selenoloesters 8 with 1 leading to the mixed, phosphoric–trifluoroacetic anhydrides 9. The phosphorylating properties of mixed phosphoric–carboxylic anhydrides toward alcohols are well-known from earlier work.[4] In the light of the above results, as well as the earlier studies of Bartlett,[5] alcoholysis of 9 occurs with inversion of configuration at phosphorus.

Verification of the generality of our observation was shown by using another model system. It has been shown earlier that diastereoisomers of *O,Se*-dimethyl *N*-(α-methylbenzyl)phosphoramidoselenoates (11) react with ethanol in the presence of $AgNO_3$ with inversion of configuration.[1] The resultant *O*-methyl *O*-ethyl *N*-(α-methylbenzyl)phosphoramidate (12) in a reaction with NaH/CS_2, followed by methylation, gives the enantiomeric *O,S*-dimethyl *O*-ethyl phosphorothioate (13) of known absolute configuration.

Because the stereochemistry of each step of the conversion 11 → 13 is well-defined,[1] we decided to perform ethanolysis of the separated isomers (R_p,R_c)-11 ($\delta_{^{31}P}$ 22.86 ppm) and (S_p,R_c)-11 ($\delta_{^{31}P}$ 22.74 ppm) in the presence of 1. We have proved by means of ^{31}P NMR spectroscopy that ethanolysis of 11 in the presence of 1 occurs with inversion of configuration at phosphorus, most probably by stereoinvertive solvolysis of the intermediate mixed anhydride 14.[6]

A mechanistic interpretation of the reaction between selenoloesters of phosphorus acids and $Hg(OCOCF_3)_2$ is not simple. One can postulate a concerted mechanism involving simultaneous cleavage of both P–Se and Hg–O bonds, accompanied by simultaneous formation of P–O and Hg–Se bonds (15),[7] which leads to mixed anhydrides of type 3 with retention of configuration at phosphorus. Since mercury(II) is a soft acid, its interaction with a "soft" selenium atom seems to be more probable than that with the "hard" phosphoryl oxygen atom. Another proposal for the mechanism of formation of mixed phosphoric–trifluoroacetic anhydrides involves participation of the ion pair (16).

(1) Krzyzanowska, B.; Stec, W. J. *Heteroatom Chem.* **1991**, *2*, 123.
(2) Ethanolysis of 2 in the presence of equimolar amount of $Hg(OCOCF_3)_2$ is completed within 10 min in acetonitrile at −40 °C, whereas without catalyst it requires refluxing in ethanol for several days. Although alcoholysis is stereocontrolled process proceeding with inversion of configuration, prolonged reflux can lead to a mixture of cis and trans isomers; in the case of *cis*-8, the substrate is due to the different thermodynamic stabilities of isomers.
(3) (a) Stec, W. J.; Mikolajczyk, M. *Tetrahedron* **1973**, *29*, 538. (b) Stec, W. J.; Okruszek, A.; Michalski, J. *J. Org. Chem.* **1976**, *41*, 233.
(4) For a review, see: Ramage, R. in *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic Press: New York, 1979; Chapter 12.
(5) (a) Jacobson, N. E.; Bartlett, P. A. *J. Am. Chem. Soc.* **1983**, *105*, 1613. (b) Jacobson, N. E.; Bartlett, P. A. *J. Am. Chem. Soc.* **1983**, *105*, 1619.
(6) Detailed mechanistic studies of the reaction between 11 and alcohols in the presence of 1 will be described elsewhere.
(7) The equally hypothetic transition state, involving an equatorial–equatorial six-membered ring with the "carbonyl" oxygen atom of trifluoroacetyl group (equatorial "in") and alkylselenonium group (equatorial "out") interacting with phosphorus atom, has been suggested by anonymous referee.



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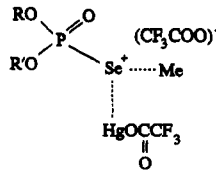

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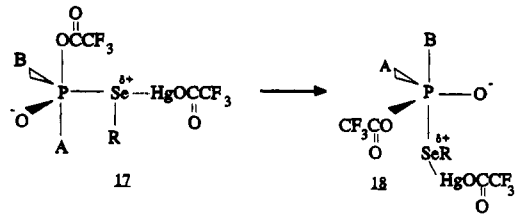
In such a case the trifluoroacetic ion attacks the phosphorus atom from the side opposite to the most apicophilic group, resulting in the formation of pentacoordinate intermediate (17), and a single pseudorotation is required for departure of the selenonium group from the apical position. The resulting compound (18) collapses via cleavage of the P–Se bond to give the mixed anhydride of type 3 or 14. Undoubtedly the mechanistic course of



17 18

$AgNO_3$-catalyzed solvolysis of phosphoroselenoesters of the type 2, 4, or 8 is different from that occurring in the presence of $Hg(OCOCF_3)_2$.[8] Selenoesters 2, 4, or 8 do not react with $AgNO_3$ itself, and methanolysis of 8 in the presence of $AgNO_3$ is a relatively slow process,[9] which supports earlier proposals concerning electrophilic assistance of silver ion in the solvolytic process of P–Se bond cleavage. On the contrary, $Hg(OCOCF_3)_2$ reacts rapidly with selenoesters giving isolable mixed anhydrides like 6, 7, or 9; they may undergo further reactions with any nucleophile present in the reaction medium. As expected, their methanolysis occurs with an exclusive attack at phosphorus, while aminolysis occurs via an attack at the carbonyl carbon atom.[10]

Although the detailed mechanism of the reaction between selenoloesters of phosphorus acids and $Hg(OCOCF_3)_2$ still remains obscure, we would like to emphasize here that, to our knowledge, we are able to present the first stereodefined method of the formation of mixed phosphoric–trifluoroacetic anhydrides[11] and their stereoinvertive alcoholysis. The only example of formation of phosphoric–(*N*-phenylimino)benzoic anhydride of well-defined stereochemistry was earlier reported from this laboratory, as the result of N → O phosphoryl group migration in N-benzoylated *O,O*-dialkyl *N*-phenylphosphoramidates, under the influence of electrophiles like benzoyl chloride or trimethylsilyl chloride.[12] Interestingly, methanolysis of dialkyl phosphoric–(*N*-phenylimino)benzoic anhydrides occurs via an exclusive attack of alcohol at the iminocarbonyl carbon atom.[13]

Besides the stereocontrolled synthesis of a P-chiral mixed phosphoric–trifluoroacetic anhydride, the novelty of our approach relies upon the development of a new stereocontrolled method of cleavage of P–Se bond, which complements four known methodologies: treatment of P–SeR with sodium alkoxides,[14] reaction with halogen in alcohol,[14] reaction with halogenating agents,[15] and reaction with silver nitrate in alcohol.[8]

Experimental Section

Solvents and commercial reagents were purified according to standard methods prior use.[16] Column chromatography and TLC analysis were performed on silica gel (230–400 mesh) and silica gel F_{254} plates (purchased from E. Merck). TMS and 80% H_3PO_4 were used as chemical shift standards. Gas chromatography experiments were performed with HP-1 capillary columns. All melting and boiling points are uncorrected. Reactions were performed under an argon atmosphere. Mercuric trifluoroacetate (1) was purchased from Aldrich Chemical Co. and was sublimed prior use (140 °C/0.1 mmHg).

***O,O,Se*-Triethyl phosphoroselenoate (2)** was prepared according to described procedure[17] and purified by distillation, bp 120 °C (20 mmHg) [lit.[17] bp 120 °C (17 mmHg)].

Diastereoisomers of 2-(methylseleno)-2-oxo-4-methyl-1,3,2-dioxaphosphorinane (8) were obtained by acid-catalyzed rearrangement[18] of appropriate selenoesters.[19]

trans-**8**: mp 59–60 °C [lit.[19] mp 58–60 °C)]; ^{31}P NMR δ 13.39 ppm, $^1J_{P-Se}$ = 468 Hz ($CDCl_3$).

cis-**8**: ^{31}P NMR δ 16.17 ppm, $^1J_{P-Se}$ = 499 Hz ($CDCl_3$).

***O,Se*-Dimethyl *N*-(α-methylbenzyl)phosphoramidoselenoate (11)** was prepared and isolated in diastereoisomerically pure form.[1]

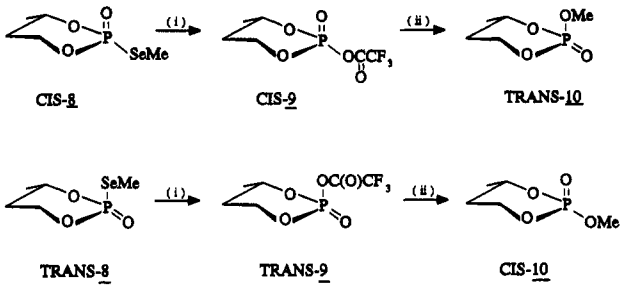
***O,Se*-Dimethyl *N*-Phenylphosphoramidoselenoate (4).** A solution of 6.43 g (0.05 mol) of *O,O*-dimethyl phosphorochloridite was added dropwise to a suspension of 3.95 g (0.05 mol) of selenium and 0.11 mol of aniline in dry benzene. The reaction mixture was stirred overnight. After extraction with 5% solution of hydrochloric acid, drying with $MgSO_4$, and concentration, a crude oily product was purified by means of silica gel chromatography, using chloroform as an eluent. The *O,O*-dimethyl *N*-phenylphosphoramidoselenoate $(MeO)_2(Se)NHPh$ (^{31}P NMR δ 72.58 ppm, $^1J_{P-Se}$ = 955 Hz) obtained was dissolved in dry benzene, and to this solution was added methyl iodide (14.2 g) in one portion. The reaction mixture was stirred at ambient temperature for 72 h. After concentration under reduced pressure, product 4 was purified by means of silica gel chromatography, using ethyl acetate as an eluent. Crystallization from benzene yielded 6.27 g (0.024 mol, 48%) of 4: ^{31}P NMR δ 21.35 ppm, $^1J_{P-Se}$ = 446 Hz; mp 123 °C; MS *m/z* 265 ($M^{\bullet+}$), 170 (100) $(M - MeSe)^{\bullet+}$, 92 $(PhNH)^+$.

1. Ethanolysis of *O,O,Se*-Triethyl Phosphoroselenoate (2) in the Presence of $Hg(OCOCF_3)_2$. Into a solution of 2 (0.024 g, 0.1 mmol) and ethanol (0.05 mL) in dry acetonitrile (0.5 mL) was added a solution of 1 (0.043 g, 0.1 mmol) in dry acetonitrile (0.1 mL) in one portion at room temperature. ^{31}P NMR spectra of reaction mixture recorded after 10 min indicated a complete disappearance of the signal of 2 at 25.66 ppm, accompanied by appearance of the signal of an exclusive product 3 at δ –0.81 ppm. The identity of 3 was confirmed by comparison with a genuine sample. Yield 100% (NMR).

2. Methanolysis of 4 in the Presence of $Hg(OCOCF_3)_2$. Into a solution of 4 (0.027 g, 0.1 mmol) and methanol (0.05 mL) in dry acetonitrile (0.5 mL) was added a solution of 1 (0.043 g, 0.1 mmol) in the same solvent (0.1 mL). The white precipitate of $MeSeHgOCOCF_3$, which appeared immediately, was filtered off, and the filtrate was concentrated to give almost exclusively 5 (^{31}P NMR δ 5.54 ppm): GC–MS (EI 70 eV) *m/z* 201 (100) ($M^{\bullet+}$), 169 $(M - MeOH)^{\bullet+}$.

(8) Stec, W. J. *Bull. Acad. Polon. Sci., Ser. Sci. Chim.* **1973**, *21*, 709.
(9) Methanolysis of 2 catalyzed by $AgNO_3$, under reaction conditions analogous to ones performed in the presence of 1, yielded after 24 h about 25% of required product.
(10) Jackson, A. G.; Kenner, G. W.; Moore, G. A.; Ramage, R.; Thorpe, W. D. *Tetrahedron Lett.* **1976**, 3627.
(11) For methods of synthesis of mixed anhydrides, see, for example: (a) *Houben-Weyl, Methoden der Organischen Chemie*, Georg Thieme Verlag: Stuttgart, 1982; pp 177, 257, 488. (b) Whitesides, G. M.; Siegel, M.; Garrett, P. *J. Org. Chem.* **1975**, *40*, 2516. (c) Whitesides, G. M.; Lewis, J. M.; Haynie, S. L. *J. Org. Chem.* **1979**, *44*, 864. (d) Helinski, J.; Skrzypczynski, Z.; Wasiak, J.; Michalski, J. *Phosphorus, Sulfur Silicon* **1990**, *54*, 225. (e) Dabkowski, W.; Michalski, J.; Wasiak, J.; Skrzypczynski, Z. *Croat. Chem. Acta* **1986**, *59*, 1951.
(12) Baraniak, J.; Stec, W. J. *Tetrahedron Lett.* **1991**, *32*, 137.
(13) Baraniak, J.; Stec, W. J. *Tetrahedron Lett.* **1991**, *32*, 4193.
(14) Hall, C. R.; Inch, Th. D. *Tetrahedron Lett.* **1976**, 3645.
(15) Krawiecka, B. *Rev. Heteroatom Chem.*, in press.
(16) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemical*; Pergamon Press: New York, 1980.
(17) Michalski, J.; Wieczorkowski, J. *Roczniki Chemii* **1959**, *33*, 105.
(18) Bruzik, K.; Stec, W. J. *J. Org. Chem.* **1981**, *46*, 1625.
(19) Mikolajczyk, M.; Luczak, J. *Tetrahedron* **1972**, *28*, 5411.

Scheme I[a]



[a] Reaction conditions: (i) mercuric trifluoroacetate (1 equiv), MeCN, rt, t = 5 min; (ii) methanol (4–10 equiv), rt, t = 5 min.

Co-injection of **5** and a genuine sample of **5**, prepared independently, additionally confirmed its identity (GC HP-1, t_R 8.7 min).

3. Synthesis of *O,O*-Diethyl *O*-Trifluoroacetyl Phosphate (6). Into a stirred solution of **2** (0.245 g, 1 mmol) in acetonitrile (5 mL) was added dropwise a solution of **1** (0.426 g, 1 mmol) in acetonitrile (1 mL) at room temperature. After 5 min dry hexane (5 mL) was poured into the reaction mixture, and a precipitate was filtered off under nitrogen. Solvents were carefully removed under reduced pressure. A residue was distilled under reduced pressure. The fraction boiling at 30–35 °C (0.1 mmHg) was collected and identified as **6** (^{31}P NMR δ −10.29 ppm C_6C_6/MeCN) [lit.[20] bp 25 °C (0.01 mmHg); ^{31}P NMR δ −9.6 ppm]: MS m/z 250 ($M^{\bullet+}$); yield 0.2 g (80%).

The reaction of **6** with an excess of ethanol in MeCN yielded **3** (^{31}P NMR δ −0.81 ppm), whereas aniline provided anilinium *O,O*-diethyl phosphate (^{31}P NMR δ −0.23 ppm) and trifluoroacetanilide, quantatively: MS m/z 189 ($M^{\bullet+}$) (100), 77 $(C_6H_5)^+$, 120 $(C_6H_5NHCO)^{\bullet+}$.

4. Reaction of *O,Se*-Dimethyl *N*-Phenylphosphoramidoselenoate (4) with $Hg(OCOCF_3)_2$. Into a solution of **4** (0.027 g, 0.1 mmol) in dry acetonitrile (0.5 mL) cooled to −40 °C was added a solution of **1** (0.043 g, 0.1 mmol) in acetonitrile (0.1 mL). The white precipitate of $MeSeHgOCOCF_3$ appeared instantly. The NMR spectrum of the filtrate indicated the formation of a single product **7** (^{31}P NMR δ −2.7 ppm). The spectrum recorded after addition of dry methanol (0.05 mL) confirmed a formation of **5**, as compared with a genuine sample (^{31}P NMR δ 5.54 ppm): MS m/z 201 ($M^{\bullet+}$), 169 (M − MeOH)$^{\bullet+}$.

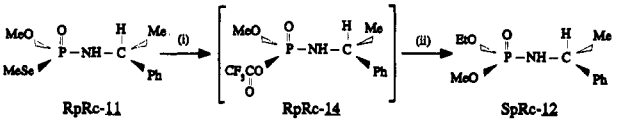
5. Synthesis of 2-(Trifluoroacetoxy)-2-oxo-4-methyl-1,3,2-dioxaphosphorinane (*cis*-9). Into a stirred solution of *cis*-**8** (0.230 g, 1 mmol) in dry acetonitrile (5 mL) was added a solution of **1** (0.426 g, 1 mmol) in dry acetonitrile in one portion at room temperature. After 5 min dry hexane (10 mL) was poured into the reaction mixture and a white precipitate was filtered off. Solvents were removed under reduced pressure, and the oily residue was distilled. The fraction distilling at 50–55 °C (0.1 mmHg) was collected and identified as *cis*-**9** (^{31}P NMR δ −12 ppm/C_6D_6): MS m/z 249 ($M^{\bullet+}$), 54 (100) $(C_4H_6)^{\bullet+}$, 55 (C_4H_7), 99 $(PO_4H_4)^+$, 136 (M − $CF_3COOH)^{\bullet+}$; yield 0.160 g (65%).

6. Methanolysis of 2-(Methylseleno)-2-oxo-4-methyl-1,3,2-dioxaphosphorinane (*cis*-8 and *trans*-8). Into a solution of *cis*-**8** (0.046 g, 0.2 mmol) and dry methanol (0.04 mL) was added a solution of **1** (0.08 g, 0.19 mmol) in dry acetonitrile (0.1 mL). After filtering off the precipitate, the reaction mixture was concentrated and analyzed. Beside the main product *trans*-**10**, unreacted *cis*-**8** was present in reaction mixture (10%).

trans-**10**: ^{31}P NMR δ −6.5 ppm [lit.[3] δ −6.4 ppm]; MS[21] m/z 166 ($M^{\bullet+}$), 54 (100) $(C_4H_6)^{\bullet+}$, 113 (M − $C_4H_5)^+$, 139 (M − $C_2H_3)^+$. In an analogous experiment with *trans*-**8** used as a substrate, the product *cis*-**10** was formed almost exclusively (^{31}P NMR δ −5.2 ppm; lit.[3] δ −5.1 ppm) with traces of pyrophosphates (δ −18.87 ppm, −19.87 ppm).

cis-**10**: MS m/z 166 ($M^{\bullet+}$), 113 (100) (M − $C_4H_5)^{\bullet+}$, 139 (M − $C_2H_3)^+$. Compound $MeSeHgOCOCF_3$ precipitating during the reaction course, formed a hygroscopic white powder. It was washed with dry diethyl ether, dried on vacuum line [50 °C (0.01 mm Hg)], and analyzed: ^{19}F NMR δ −69.15 ppm (pyridine-d_5). Elemental analysis confirmed the structure (Calcd: H, 0.74; C, 8.84. Found: H, 0.88; C, 8.89).

Scheme II[a]



[a] Reaction conditions: methanol (4–10 equiv), mercuric trifluoroacetate (1 equiv), MeCN, rt.

7. Reaction of 2-(Trifluoroacetoxy)-2-oxo-4-methyl-1,3,2-dioxaphosphorinane (*trans*-9) with Aniline. Into a solution of *trans*-**8** (0.046 g, 0.2 mmol) and **1** (0.08 g, 0.2 mmol) in acetonitrile (0.5 mL), resulting in the in situ formation of *trans*-**9**, as confirmed by means of ^{31}P NMR (δ −16.44 ppm), was added freshly distilled aniline (0.1 g, 0.11 mmol) in acetonitrile (0.1 mL). The precipitate was filtered off, and the filtrate containing anilinium salt of 2-hydroxy-2-oxo-4-methyl-1,3,2-dioxaphosphorinane was concentrated and its mass spectrum, after silylation with BSA, corresponded to 2-[(trimethylsilyl)oxy]-2-oxo-4-methyl-1,3,2-dioxaphosphorinane: m/z 224 ($M^{\bullet+}$). The identity of the second product presented in solution, namely trifluoroacetanilide, has been proved by GC–MS analysis (yield 100%): MS m/z 189 (100) ($M^{\bullet+}$); 77 $(C_6H_5)^+$; 120 $(C_6H_5NHCO)^{\bullet+}$; GC (HP-1) t_R 5.76 min.

Ethanolysis of *O,Se*-Dimethyl *N*-(α-Methylbenzyl)-phosphoramidoselenoates (11) in the Presence of 1. Into a solution of (R_p,R_c)-**11** (0.029 g, 0.1 mmol) in dry acetonitrile (0.5 mL) was added dropwise ethanol (0.04 mL), followed by a solution of **1** (0.043 g, 0.1 mmol), and then the mixture was stirred at ambient temperature for 0.5 h. The precipitate was filtered off, and the filtrate was concentrated and dissolved in $CDCl_3$. The ^{31}P NMR spectrum of resulting material contained only one signal at δ 9.32 ppm ($CDCl_3$), characteristic for (S_p,R_c)-**12** [lit.[1] ^{31}P NMR δ 9.38 ppm]: ^{1}H NMR δ 1.09 (t, 3 H, $^3J_{HH}$ = 6.8 Hz, CH_3CH_2O), 1.46, 1.50 (2 d, 3 H, $^3J_{HH}$ = 6.8 Hz, CH_3CH), 3.68 (d, 3 H, $^3J_{P\text{-}H}$ = 11.3 Hz, CH_3O), 3.80–3.90 (m, 2 H, CH_2O), 4.28 (m, 1 H, CH_3CH), 7.2–7.9 ppm (5 H_{arom}).

In the same way ethanolysis of mixture of (R_p,R_c)-**11** and (S_p,R_c)-**11** (1:2.7, respectively, ^{31}P NMR assay δ 27.0 and 26.4 ppm) was performed. Two signals in ^{31}P NMR spectrum in $CDCl_3$ were observed, δ 9.35 and 9.42 ppm in the ratio ca. 3:1, corresponding to (R_p,R_c)-**12** and (S_p,R_c)-**12**, respectively. Addition of pure (S_p,R_c)-**12** (0.01 g) gave rise to the expected change of ratio of diastereoisomers.

Acknowledgment. We are indebted to Dr. M. Sochacki for recording and interpretation of MS spectra. Discussions with Dr. Baraniak and the help of Dr. Zon (ABI, Foster City, CA) in preparation of the manuscript are highly appreciated. This paper is dedicated to Professor Fritz Eckstein, MPI for Experimental Medicine, Gottingen, Germany, on the occasion of this 60th birthday.

(20) Dabkowski, W. Ph.D. Thesis, CBMM PAN, 1985.
(21) Structural analysis was performed on the basis of mass spectra: Zielinska, B.; Stec, W. J. *Org. Mass Spectrom.* **1978**, *13*, 65.

Li$^+$ and Ca^{2+} Ions as Complementary Regulatory Elements for the Formation of Propeller-like Conformations

Izac Dayan, Yitzhak Tor, Jacqueline Libman, and Abraham Shanzer*

Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel

Received February 21, 1992

Regulation of molecular conformations is a key element in biochemical processes such as enzyme activity[1] or oxygen transport.[2] Conformational changes affect the structure

(1) Koshland, D. E.; Nee, K. E. *Annu. Rev. Biochem.* **1968**, *37*, 359.

0022-3263/92/1957-6060$03.00/0