one portion, and the mixture was stirred at room temperature for 20 h during which period a white solid gradually formed. The resulting mixture was carefully evaporated to dryness under reduced pressure and the residue was successively washed with water and methanol followed by repeated extraction with warm chloroform. The dried (anhydrous $MgSO_4$) chloroform solution was concentrated to ca. 10 ml and poured into a column of silica gel. The fractions eluted by benzene–petroleum ether (bp 50–75 °C) (1:4) on evaporation left a white solid which was recrystallized from benzene to give 130 mg (8%) of pure **4a**: mp 250–252 °C dec; NMR ($CDCl_3$) δ 6.84 (s, 1 H), 3.62 (s, 1 H); mass spectrum (70 eV) *m/e* 336 (M^+).

Acknowledgment. We are grateful to Mr. K. W. Ho for providing mass spectral data.

Registry No.—**1a**, 41563-69-3; **1b**, 42082-63-3; **1c**, 58074-29-6; **1d**, 58074-30-9; **1e**, 10074-13-2; **2a**, 27929-85-7; **2b**, 58074-31-0; **2c**, 58074-32-1; **2d**, 58074-33-2; **2e**, 58074-34-3; **3a**, 105-09-9; **3b**, 10519-84-3; **4a**, 58074-35-4; **4b**, 58074-36-5; NBS, 128-08-5.

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(3) All melting points were determined on a Koefler hot stage and are uncorrected. Nuclear magnetic resonance spectra were taken on a JEOL 60HL spectrometer using tetramethylsilane as internal standard. Mass spectral data were obtained on a Varian M66 instrument. Elemental analyses were performed by Australian Microanalytical Service, Melbourne.
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Protic Acid Catalyzed Thiono–Thiolo Rearrangements of Phosphorus Esters

Wojciech J. Stec,* Bogdan Uznański, Karol Bruzik, and Jan Michalski*

Centre of Molecular and Macromolecular Studies, Polish Academy of Science, Department of Heteroorganic Compounds, 90-362 Łódź, Boczna 5, Poland

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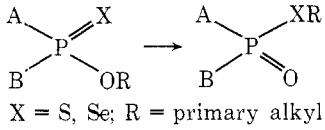
The thiono–thiolo rearrangement of organophosphorus thionoesters (eq 1) is known to be effected thermally as well as by alkyl halides, Lewis acids,[1] and electron impact.[2]

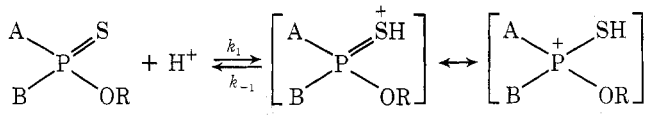


(1)

X = S, Se; R = primary alkyl

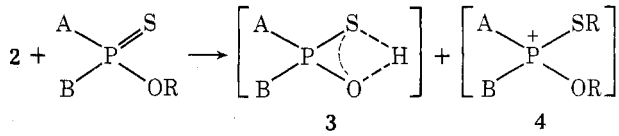
We have found that protic acids can also cause this type of rearrangement with the rate of reaction depending on the nature of the A, B, and R substituents and also on the strength of the acid used. The rearrangement can be monitored by means of either ^{31}P NMR[3] or by ^1H NMR.[4] The main limitation of our new procedure for thiono–thiolo rearrangements lies in its inapplicability to compounds with P–N bonds; such bonds are labile in acidic conditions.[5] Those esters when R is secondary or tertiary alkyl are also unsuitable reactants. The described method of rearrangement of phosphorothionates into isomeric phosphorothiolates under the influence of protic acids possesses one main advantage; it gives very clean and easily isolable products. Simple removal of trifluoroacetic acid by distillation and neutralization of the 1:1 complex[6] (>P=O·····$HOCOCF_3$) allows isolation of pure phosphorothiolate. For example, dissolving trimethyl phosphorothionate and trifluoro- or trichloroacetic acid (1:10 mol/mol) results in rearrangement to *O,O,S*-trimethyl phosphorothiolate. The half-life times $t_{1/2}$, measured at 55 °C, were 5.95 and 82.9 h, respectively. It has been also found that $t_{1/2}$ of conversion at 55 °C of trimethyl phosphorothionate, *O,O*-dimethyl phenylphosphonothionate, and *O*-methyl diphenylphosphonothionate diluted in trifluoroacetic acid (1:10 mol/mol) were respectively 0.46, 1.2, and 3.91 h.

Our preliminary observations allow us to draw some conclusions about the mechanism of the rearrangement. Intermolecular character has been demonstrated in the following experiment. The mixture of trimethyl and triethyl phosphorothionate (1:1) in trifluoroacetic acid solution gave the following products: $(MeO)_2P(O)SMe$, $(EtO)_2P(O)SEt$, $(MeO)_2P(O)SEt$, and $(EtO)_2P(O)SMe$. The last two compounds clearly indicate an intermolecular type of process. In addition $(EtO)_2P(O)SEt$ and $(MeO)_2P(O)SMe$, when stored in CF_3COOH solution under the same conditions, did not lead to detectable amounts of $(MeO)_2P(O)SEt$ or $(EtO)_2P(O)SMe$. It seems reasonable that the protonation of thiophosphoryl sulfur takes place in the first step of the reaction. The absorption band for the thiophosphoryl group, $\nu_{P=S}$ 635 cm^{-1} in $Ph_2P(S)OMe$ measured in CCl_4 solution (10%) shifts to 628 cm^{-1} when an equimolar amount of CF_3COOH is added, while the $\nu_{P=O}$ 1030 cm^{-1} of the bridging oxygen remains unchanged. Consequently, the formation of a quasi-phosphonium cation has to be considered:



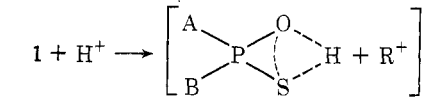
1 2

Equilibrium between **1** and **2** depends on the pK_a of the acid and the nature of the substituents A, B, and R. Quasi-phosphonium cation **2** possesses strong alkylating properties[7] and a "soft" base in the reaction medium would be immediately alkylated. The sulfur atom of the thiophosphoryl group can be considered as a "soft" base, which, in the presence of **2** would be alkylated immediately with formation of another ion **4** and free acid **3**.



3 4

Cationic species **4** would also possess alkylating properties[7] and could alkylate another molecule of thionoester **1** or the free thio acid **3**, with liberation of rearranged thioloester–trifluoroacetic acid complex. The formation of 1:1 complexes of phosphoryl compounds with protic acids is known.[6] It has to be emphasized that in several experiments the presence of dialkyl hydrogen phosphorothioate **3** has not been detected. Also methyl trifluoroacetate is not formed in the reactions investigated. *O-n*-Propyl diphenylphosphinothionate rearranges in CF_3COOH solution to *S-n*-propyl derivative. No traces of *S*-isopropyl ester were found among the reaction products. Thus, carbocation R^+ is then presumably not responsible for the S-alkylation process.



5

Table I. Isomerization of Alkyl Phosphoro(phosphino)thionates into Corresponding Phosphoro(phosphino)thiolates Catalyzed by Protic Acids

No.	Substrate	Temp, °C	Acid	Molar ratio substrate: acid	Yield, %	Product, ^{31}P NMR, bp or mp	Registry no.
1	$(CH_3O)_3P{=}S$	10	H_2SO_4	1:1	98	$(CH_3O)_2P(O)SCH_3$[c]	152-20-5
2	$(CH_3O)_3P{=}S$	20	CF_3COOH	1:2	92	$(CH_3O)_2P(O)SCH_3$	
3	$(CH_3)_2P(S)OCH_2CH{=}CHC_6H_5$	20	CF_3COOH	1:1	71	$(CH_3)_2P(O)SCH_2CH{=}CHC_6H_5$ $\delta_{^{31}P}$ −47.6 ppm (H_3PO_4) mp 73 °C (petroleum ether)	57969-75-2
4	$(CH_3)_2P(S)OCH_2CH{=}CD_2$	20	CF_3COOH	1:3	60	$(CH_3)_2P(O)SCH_2CH{=}CD_2$ bp 70 °C (0.001 mm) $\delta_{^{31}P}$ −51.5 ppm (H_3PO_4)	57969-76-3
5	$(CH_3O)_2P(S)OC(2,5\text{-}C_6H_3Cl_2){=}CHCl$	70	CF_3COOH	1:4	83	$CH_3OP(O)(SCH_3)OC(2,5\text{-}C_6H_3Cl_2){=}CHCl$ $\delta_{^{31}P}$ −27.5 ppm (H_3PO_4) mp 58–59 °C	57969-77-4
6	*trans*-$OCH_2CH_2CH(CH_3)OP(S)OCH_3$[a]	20	CF_3COOH	1:3	81	*cis*-$OCH_2CH_2CH(CH_3)OP(O)SCH_3$[d] $\delta_{^{31}P}$ −22.8 ppm (H_3PO_4) bp 110–115 °C (0.2 mm)	50902-83-5
7	*cis*-$OCH_2CH_2CH(CH_3)OP(S)OCH_3$[a]	20	CF_3COOH	1:3	82	*trans*-$OCH_2CH_2CH(CH_3)OP(O)SCH_3$[d] $\delta_{^{31}P}$ −14.0 ppm (H_3PO_4) bp 105–110 °C (0.1 mm)	50902-84-6
8	*trans*-$OCH_2CH_2CH(CH_3)OP(Se)OCH_3$[b]	20	CF_3COOH	1:3	80	*cis*-$OCH_2CH_2CH(CH_3)OP(O)SeCH_3$[b] $\delta_{^{31}P}$ −18.1 ppm (H_3PO_4) mp 77–77.5 °C (ether–acetone)	39826-74-9
9	*cis*-$OCH_2CH_2CH(CH_3)OP(Se)OCH_3$[b]	20	CF_3COOH	1:3	86	*trans*-$OCH_2CH_2CH(CH_3)OP(O)SeCH_3$[b] $\delta_{^{31}P}$ −10.8 ppm (H_3PO_4) mp 58–58.5 °C (ether–acetone)	39826-71-6

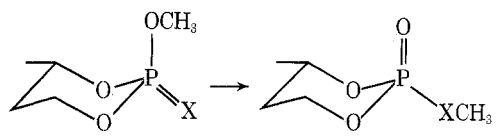
[a] C. L. Bodkin and O. Simpson, *J. Chem. Soc. B*, 1136 (1971). [b] M. Mikolajczyk and J. Luczak, *Tetrahedron*, **28**, 5411 (1972). [c] G. Hilgetag and H. Teichmann, *J. Prakt. Chem.*, **8**, 121 (1959). [d] B. Ziemnicka, *Zesz. Nauk. Politech. Lodz. Chem.*, **27**, 170 (1973); *Chem. Abstr.*, **80**, 107892 (1974).

In the light of the above overall explanation it is clear that secondary alkyl esters do not undergo this rearrangement because secondary and tertiary carbon atoms of R in **2** and/or **4** are less available for nucleophilic attack on the sulfur atom. Experimental results are collected in Table I.

Some experiments require further comments.

(a) Phosphoroselenoates (expt 7 and 8) undergo more facile rearrangement than their sulfur analogues owing to more enhanced nucleophilicity of the "soft" selenium atom.

(b) Fifty percent conversion of *cis*-2-methoxy-2-thiono-4-methyl-1,3,2-dioxaphosphorinane to *trans*-2-methylthio-2-oxo-4-methyl-1,3,2-dioxaphosphorinane ✓ (expt ✓6) ✓is achieved three times faster than that of *trans*- into *cis*-(expt 5). The faster rearrangement of the isomer with an axial sulfur atom may be explained in terms of an enhanced Lewis basicity of axially orientated sulfur relative to one in an equatorial position. This conclusion as applied to axial and equatorial oxygen has been reached by Verkade.[8]



trans, X = S, Se cis

(c) Rearrangement of *O*-allyl dimethylphosphinothionates proceeds much faster than that of other *O*-alkyl derivatives. However, rearrangement of *O*-γ-phenylallyl dimethylphosphinothioate (expt 3) gives exclusively *S*-γ-phenylallyl ester, without any trace of the *S*-α-phenyl isomer. The same product was obtained by thermal rearrangement of $Me_2P(S)OCH_2CH{=}CHC_6H_5$. Its structure was proved by ^1H NMR spectra: δ_{PSCH_2} −3.8 ppm, $^3J_{PSCH_2}$ = 12.3 Hz (2 H). The rearrangement of *O*-allyl-*3,3-d*$_2$ dimethylphosphinothionate (δ_{POCH_2} −4.56 ppm, $^3J_{POCH_2}$ = 10.9 Hz) gave *S*-allyl-*3,3-d*$_2$ dimethylphosphinothiolate [δ_{PSCH_2} −3.56 ppm, $^3J_{PSCH_2}$ = 11.9 Hz (2 H), Me_4Si internal standard]. These findings argue against a cyclic Claisen-type mechanism of rearrangement, postulated by Pudovik and Aladsheva[9] on the basis of their studies on the rearrangements of *O*-crotyl *O,O*-dimethylphosphorothionate. Enhanced reactivity of allyl esters may be explained in terms of known higher electrophilic reactivity of the allyl group toward nucleophiles.

Experimental Section

All melting and boiling points are uncorrected. Solvents and commercial reagents were distilled and dried by conventional methods before use. ^1H NMR spectra were recorded at 60 MHz with a JEOL C-60H spectrometer and Perkin-Elmer R12B. ^{31}P NMR spectra were obtained on a JEOL C-60H operating at 24.3 MHz with external H_3PO_4 as the reference. Mass spectra were obtained on an LKB-9000S spectrometer at 70 eV ionizing energy. GLC analyses were performed on a Varian Aerograph 1520. Ir spectra were obtained on a Zeiss-Jena UR-10.

General Procedure. At the temperature given in Table I the thionoester was added to the protic acid with intensive stirring and external cooling. Reactions were followed by means of ^1H and ^{31}P NMR. When the conversion of the substrate to the product reached 95%, excess of trifluoroacetic acid was removed under reduced pressure, the residue was diluted with either benzene or ether, and aqueous sodium carbonate was added for neutralization of the molar amount of acid involved in complex formation.[6] When H_2SO_4 was used, neutralization was done with gaseous ammonia. Following dilution by ether, ammonium sulfate was collected by filtration. The organic layer was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the product was distilled or crystallized from a suitable solvent. Satisfactory analyses were obtained for all reported compounds.

***O*-γ-Phenylallyl dimethylphosphinothionate** was obtained by reaction of cinnamyl alcohol with an equimolar amount of dimethyl phosphinobromothioate[10] in the presence of triethylamine. Attempts at its distillation caused rearrangement of the syrupy liquid to the thiolo isomer: ^{31}P NMR δ −91.3 ppm (external H_3PO_4); ^1H NMR δ_{POCH_2} −4.7 ppm, $^3J_{POCH_2}$ = 11.4 Hz.

***O*-Allyl-*3,3-d*$_2$ dimethylphosphinothionate** was prepared by condensation of allyl-*3,3-d*$_2$ alcohol[11] with dimethyl phosphinobromothioate in the presence of triethylamine. Distilled product, bp 35–40 °C (0.05 mmHg), was checked by ^{31}P NMR ($\delta_{^{31}P}$ −93 ppm, external H_3PO_4) and GC–MS.

Registry No.—**1**, 152-18-1; **3**, 57969-73-0; **4**, 57969-74-1; **5**, 1217-91-0; **6**, 23168-88-9; **7**, 23168-89-0; **8**, 33996-02-0; **9**, 33996-01-9; cinnamyl alcohol, 104-54-1; dimethyl phosphinobromothioate, 6839-93-6; allyl-*3,3-d*$_2$ alcohol, 16315-95-0.

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The Position of the Phenolic Function in Tiliacorine and Related Alkaloids[1]

Maurice Shamma* and James E. Foy

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

Tuticorin R. Govindachari and Narayana Viswanathan

CIBA-GEIGY Research Centre, Goregaon East, Bombay, India

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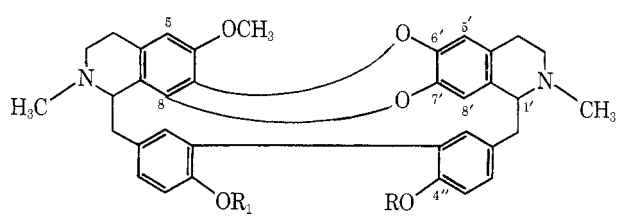
The bisbenzylisoquinoline alkaloid tiliacorine, found in *Tiliacora racemosa* Colebr. [*T. acuminata* (Lam.) Miers], has been assigned structure **1a** or **1b** since the exact position of the phenol in the lower half of the alkaloid was still uncertain.[2] We now wish to present evidence in favor of expression **1a** for tiliacorine.



1a, R = H; R_1 = CH_3
b, R = CH_3; R_1 = H
c, R = R_1 = CH_3
d, R = Ac; R_1 = CH_3

Our attention was called to this problem during a study of the selective oxidation of several bisbenzylisoquinolines using potassium permanganate in acetone. That investigation revealed that in every case oxidation occurred at the doubly benzylic bond of the isoquinoline moiety unsubstituted at C-8′ (or C-8) to afford an aldehydo lactam.[3]

Treatment of the known *O*-methyltiliacorine (**1c**)[2] with excess potassium permanganate in refluxing acetone fol-