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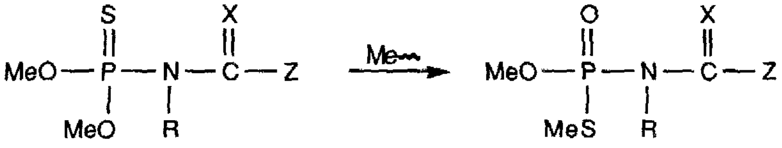
AN UNUSUAL REARRANGEMENT OF N-SUBSTITUTED THIOPHOSPHORYL CARBONYL MIXED IMIDES

Kenneth E. DeBruin* and Eric E. Boros

Department of Chemistry
Colorado State University
Fort Collins, Colorado 80523

Summary: N-Substituted O,O-dimethyl N-benzoyl phosphoramidothioates (**III**, R = Me, Ph but not H) undergo an uncatalyzed unimolecular rearrangement in an inert solvent; whereby, the carbonyl oxygen atom exchanges position with the thiophosphoryl sulfur atom (an O,S Switch) and forms O,O-dimethyl N-thiobenzoyl *phosphoramidates* (**IV**, *R = Me, Ph*).

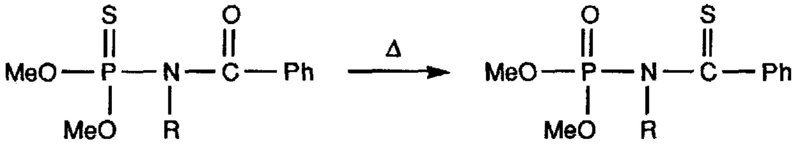
There is considerable mechanistic, biochemical, and industrial interest in mixed imides derived from phosphorus and carbon acids. Much of this interest is derived from the observations that compounds of general structure **II** and analogues have been developed or show promise as effective pest control agents.[1] We are interested in thiophosphoryl carbonyl mixed imides of structure **I** since they can serve as precursors to compounds of structure **II** (equation 1).[4] In addition, mechanistic studies on cleavage reactions of **I** can be compared to published results[5] on the phosphoryl analogue of **I**.



$$\mathrm{MeO{-}\underset{\underset{MeO}{|}}{\overset{\overset{S}{\|}}{P}}{-}\underset{\underset{R}{|}}{N}{-}\overset{\overset{X}{\|}}{C}{-}Z} \xrightarrow{\mathrm{Me}\sim} \mathrm{MeO{-}\underset{\underset{MeS}{|}}{\overset{\overset{O}{\|}}{P}}{-}\underset{\underset{R}{|}}{N}{-}\overset{\overset{X}{\|}}{C}{-}Z} \qquad (1)$$

I II

We have synthesized[6] N-benzoyl analogues of **I** (X = O, Z = Ph) with different substituents on nitrogen (R = H, Me, Ph) and would like to report the discovery that the tertiary imides (R = Me, Ph), but not the secondary imide (R = H), undergo a remarkable rearrangement. This rearrangement of O,O-dimethyl N-benzoyl phosphoramidothioates (**III**, R = Me, Ph) occurs uncatalyzed (as neat compound or in solution with an inert solvent) and involves a transpositioning of the thiophosphoryl sulfur atom with the carbonyl oxygen atom to quantitatively form O,O-dimethyl N-thiobenzoyl phosphoramidates (**IV**, R = Me, Ph). The process is shown in equation 2. Spectral data which verify the structure assignments are given in Table 1.



$$(MeO)_2P(S)N(R)C(O)Ph \xrightarrow{\Delta} (MeO)_2P(O)N(R)C(S)Ph \qquad (2)$$

III **IV**

Table 1. Spectral Data for Compounds **III** (R = H, Me, Ph) and **IV** (R = Me, Ph) of General Structure $(MeO)_2P(Y)N(R)C(X)Ph$.

	III (Y=S, X= O)			**IV** (Y=O, X=S)	
Spectrum	R = H[a]	R = Me[b,c]	R = Ph[b]	R = Me[a,c]	R = Ph[a]
Infrared: ν, cm^{-1}					
C(X)	1680	1665	1675	--------[d]	--------[d]
UV-Vis: λ_{max}, nm (ε)					
n -> π^*	--------[e]	--------[e]	--------[e]	438 (2×10^2)	456 (2×10^2)
^{1}H N.m.r.: δ, ppm (J_{HP}, Hz)					
$POCH_3$	3.95 (15)	3.63 (14)	3.72 (15)	3.59 (12)	3.55 (12)
PNR	--------[f]	3.13 (9)	7.19	3.54 (7)	7.27
^{13}C N.m.r.: δ, ppm					
$POCH_3$		53.9	54.8	53.2	54.3
PNC(X)		172.4	171.9	210.8	211.0
$PNCH_3$		34.0	-------	40.0	-------
^{31}P N.m.r.: δ, ppm					
$(MeO)_2P(Y)$		74.2	69.3	3.4	-1.9

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[a] Gave satisfactory elemental analysis. [b] Too unstable for elemental analysis. [c] Gave satisfactory mass spectrum. [d] Specific assignment uncertain. [e] Not distinguishable from the aromatic transitions. [f] Undetected. Possibly in the phenyl region.

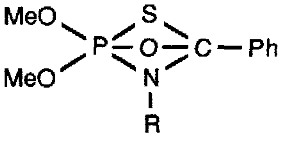
The rearrangements were followed kinetically in carbon tetrachloride by observing the appearance of the thiocarbonyl n->π* absorbance in the UV-Vis spectrum. Excellent first order rate constants were obtained over greater than four half-lives. The data is given in Table 2.

Table 2. Kinetic Data on the Rearrangement of **III** (R = Me, Ph) to **IV** (R = Me, Ph) in CCl_4.

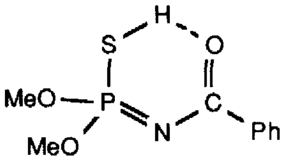
R	Temp, °C	10^5 k, sec-1[a]	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, cal/°K mol	$\Delta G^{\pm}$, kcal/mol
Me	60.0	38.3	21.1 (± 0.5)	-11 (± 1)	24.5 (± 0.5)
	40.0	4.97			
	20.0	0.531			
Ph	60.0	233	*21.2 (± 0.2)*	*-7 (± 1)*	*23.3 (± 0.3)*
	40.0	33.6			
	20.0	3.18			

a Average of triplicate determinations. Standard deviation < 5% of mean. Substrate concentration was *ca.* 10^{-3} M.

Several possible mechanisms can be postulated for the rearrangement. The observation of first order kinetics rules out the possibility of bimolecular exchange processes while the negative entropy indicates a more ordered transition state. An intriguing possibility involves the rate limiting formation or decomposition of the bicyclo species (**V**) *shown below. Since the nitrogen lone pair is* more localized in this intermediate than in the starting material, a phenyl group on nitrogen would provide more stabilization to the intermediate than reactant. Thus **III** (R = Ph) would react faster than **III** (R = Me) as is observed.



V



VI

No rearrangement of the parent mixed imide (**III**, R = H) was detected after one week in boiling carbon tetrachloride.[8] *The Infrared spectrum shows a peak at 2500* cm^{-1}; *characteristic of an S-H* bond. It seems reasonable, therefore, that **III** (R = H) exists sufficiently in the tautomeric form **VI** shown above to provide an additional barrier to rearrangement.[9]

Further studies are necessary to establish the generality or limitations of the rearrangement reported is this paper. Researchers interested in synthesizing mixed imides of phosphorothioates by the method of equation 1 need to be aware of the possibility for this competing side reaction. Alternatively, and more interestingly, this rearrangement may provide the method of choice for preparing certain phosphoryl thiocarbonyl mixed imides as useful chemicals.

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References and Footnotes

1. The discovery and development of Acephate (**II**, R = H, X = O, Z = Me) as a very effective pest control chemical provided the impetus for synthesizing other analogues and testing their activity. An extensive study appeared in 1974.[2] Numerous related compounds have since been investigated and reports largely appear in the patent literature.[3]
2. Magee, P. S., *Residue Reviews,* **1974**, *53*, 3.
3. For phosphonothioate examples, see: Fahmy, M. A. H., *Brit. UK Pat. Appl. GB 2,195,337,* **1988**; *Chem. Abstracts*, **1988**, *109*, 73665z.
4. Acephate and analogues have been prepared by this isomerization.[2]
5. (a) Mizrahi, V.; Modro, T. A., *J. Org. Chem.*, **1983**, *48*, 3030. (b) Hendrickse, T. F.; Mizrahi, V.; Modro, T. A., *Phosphorus and Sulfur*, **1984**, *20*, 93.
6. The mixed imides **III** (R = Me, Ph) were synthesized by preparing the sodium salt of the corresponding N-substituted O,O-dimethyl phosphoramidothioates with sodium hydride in dichloromethane and then adding benzoyl chloride dropwise with cooling.[7] The mixed imide **III** (R = H) was prepared by adding O,O-dimethyl phosphorothiochloridate to two equivalents of benzamide and sodium hydride in THF. Products were purified by chromotography on Silica Gel using a 3:1 mixture of dichloromethane and ethyl acetate as eluent and obtained in 85-90% yields.
7. This procedure is a modification of that used[5b] to react phosphoramidates with benzoyl chloride. We found that our reaction using phosphoramidothioates gave much higher yields.
8. A compound having the structure of **IV** (R = H) was reported[2] as a minor side product in a synthesis of **III** (R = H). Our results indicate that this product could not have arisen from the rearrangement reported in this paper.
9. Evidence for the existence of this tautomer in analogous phosphinothioate imides has been reported. See: Bodeker, V. J.; Zartner, H., *J. Prakt. Chem.*, **1976**, *318*, 149.

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