hydrochloric acid diazotization mixture, was divided into four portions. The first was dried and treated directly with ethyl glycinate at 2°; from it was isolated dipeptide, 0.10% racemic. The remaining portions were extracted at 2° with several portions of aqueous sodium bicarbonate; of these, one was treated at 2° with ethyl glycinate, another was allowed to warm to 20° 1 hr after addition of amine, and a fourth, treated at 2° with 1 equiv of acetic acid and 2 equiv of ethyl glycinate. The respective levels of racemate were 0.36, 0.31, and 0.27%. The inability of added acid to decrease the racemate level suggests that racemization occurs in part during extraction.

Acyl azide preparations which have been freed of traces of acid are particularly vulnerable to base-catalyzed racemization. After 10 min at 3° in ether containing 0.03 *M* triethylamine, the Young azide is racemized to the extent of 2.5%; the Anderson azide, after 15 min at 3° in DMF containing 0.2 *M* triethylamine, is racemized to the extent of 50.3%! *Extensive racemization may therefore occur whenever peptide azides are placed in strongly basic media, and reaction conditions which combine acyl azides and excesses of tertiary amines should be avoided.*[8]

Summary. The optically pure *N*-hydroxysuccinimide and 8-hydroxyquinoline esters have been found to be roughly comparable to the *p*-nitrophenyl esters[1] in extent of racemization during coupling. In our hands the addition of *N*-hydroxysuccinimide does not reduce the extent of racemization for carbodiimide couplings to an acceptable level, and addition of NHS is found to have an insignificant effect on racemization level for mixed anhydride couplings. Although these results have been obtained under a limited range of conditions for one model peptide, we feel they argue strongly against the use of *N*-hydroxysuccinimide as a racemization suppressor in fragment condensations involving these coupling agents. Under carefully defined conditions, the mixed anhydride procedure can rival the acyl azides and 3-acyloxy-2-hydroxy-*N*-ethylbenzamides[1] in yielding peptides of better than 99.9% chiral purity, but slight deviations from exact stoichiometry can result in an order of magnitude increase in racemate level.

(8) For earlier reports of tertiary amine catalyzed racemization of azides, see ref 1 and G. W. Anderson, J. E. Zimmerman, and F. M. Callahan, *J. Amer. Chem. Soc.*, **88**, 1338 (1966).

(9) A. P. Sloan Fellow, 1968–1970. Financial support from National Institutes of Health Grant No. GM 13453 is gratefully acknowledged.

(10) National Science Foundation Predoctoral Fellow, 1967–1970.

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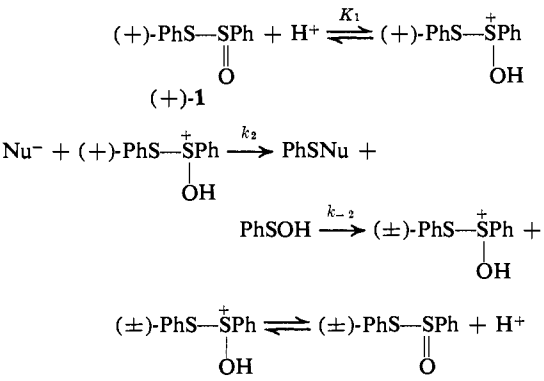
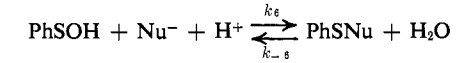
Acid- and Nucleophile-Catalyzed Oxygen-18 Exchange of Phenyl Benzenethiolsulfinate. New Insight into the Chemistry of Sulfenic Acids and Sulfenyl Derivatives[1]

Sir:

In aqueous dioxane optically active phenyl benzenethiolsulfinate, (+)-**1**, undergoes acid- and nucleophile-catalyzed racemization *via* the mechanism shown in eq 1–3, with k_2 rate determining.[2] One important



point unanswered previously was how rapidly PhSNu and PhSOH recombine to form thiolsulfinate (step k_{-2}) compared to the rate at which they are interconverted *via* the equilibrium shown in eq 4. We have



now investigated this point by studying the acid- and nucleophile-catalyzed ^{18}O exchange of PhS(^{18}O)SPh (**1**-^{18}O) under the same conditions. Our results, which reveal that exchange is generally considerably slower than racemization, provide some important new insights into the behavior of sulfenic acids and reactive sulfenyl derivatives in aqueous solution.

Labeled thiolsulfinate[3] (1.48 atom % ^{18}O) was subjected to exchange in 60% dioxane. Rates of exchange were determined by recovering the thiolsulfinate after varying periods of time and determining its ^{18}O content.[4] The results for the various nucleophiles studied as catalysts are shown in Table I. Besides the experi-

Table I. Rate of Oxygen-18 Exchange of Phenyl Benzenethiolsulfinate in 60% Dioxane[a]

Nucleophile	$[1]_0$, *M*	$[Nu^-] \times 10^2$, *M*	$[HClO_4]$, *M*	$k_{ex} \times 10^4$, sec^{-1}	(k_α/k_{ex})
Cl^-	0.050	10.0	0.40	1.0	2.3
Br^-	0.050	1.0	0.50	0.60	17
		3.0	0.50	1.53	19
n-Bu_2S	0.050	1.0	0.50	7.0	34
			0.10	1.5	31
		0.20	0.50	1.5	31
	0.025	0.20	0.10	0.63	15
	0.0125	0.20	0.10	0.83	11.3

[a] All runs at 39.6°. Ionic strength maintained constant at 0.5 by addition of lithium perchlorate where needed.

(1) This research was supported by the National Science Foundation, Grant No. GP-10732X.

(2) J. L. Kice and G. B. Large, *J. Amer. Chem. Soc.*, **90**, 4069 (1968).

(3) Prepared by reaction of thiophenol with labeled benzenesulfinyl chloride using the procedure of H. J. Backer and H. Kloosterziel, *Recl. Trav. Chim. Pays-Bas.*, **73**, 129 (1954). The labeled sulfinyl chloride was obtained by reaction of labeled acetic acid with $PhSCl_3$.

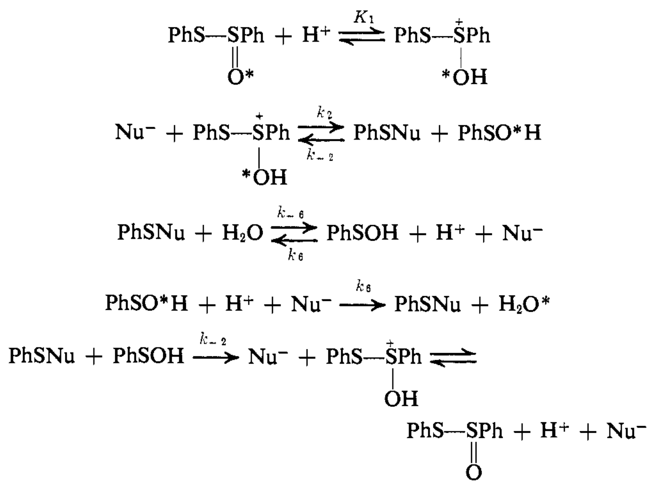
(4) Because the rates of acid- and nucleophile-catalyzed ^{18}O exchange are in several instances only about twice as fast as the rates of acid- and nucleophile-catalyzed disproportionation[5] of **1** to $PhSO_2SPh$ and PhSSPh under the same conditions,[6] some disproportionation occurs during the period while the exchange is being followed. Before analysis the recovered thiolsulfinate was separated from any thiolsulfonate and disulfide by preparative thin-layer chromatography on silica gel *via* a procedure shown in independent experiments not to lead to any exchange.

(5) J. L. Kice, C. G. Venier, G. B. Large, and L. Heasley, *J. Amer. Chem. Soc.*, **91**, 2028 (1969).

(6) J. P. Cleveland, unpublished results.

mental first-order rate constants for exchange, k_{ex}, values of (k_α/k_{ex}) are also tabulated, where k_α represents the first-order rate constant for racemization of (+)-**1** under the same reaction conditions.[2]

Acid- and nucleophile-catalyzed exchange of oxgyen-18 in **1**-^{18}O presumably proceeds by the mechanism shown in the following equations



This mechanism predicts k_{ex} should be given by the expression in eq 5, and (k_α/k_{ex}) by eq 6. Within

$$k_{ex} = \frac{k_2K_1[H^+][Nu^-]}{1 + \left\{\dfrac{k_2K_1}{k_6}\dfrac{k_{-2}[1]}{k_{-6}[H_2O]}\right\}^{1/2}} \quad (5)$$

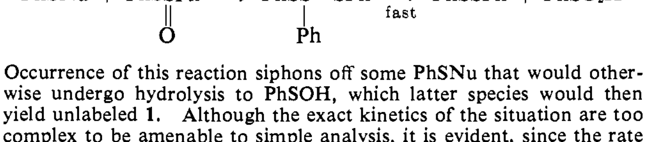
$$(k_\alpha/k_{ex}) = 1 + \left(\frac{k_2K_1}{k_6}\right)^{1/2}\left(\frac{k_{-2}}{k_{-6}[H_2O]}\right)^{1/2}[1]^{1/2} \quad (6)$$

experimental error k_{ex} is proportional to the first power of both hydrogen ion and nucleophile concentrations, as required by eq 5. The runs at different initial thiolsulfinate concentrations with n-Bu_2S as catalyst show that (k_α/k_{ex}) does depend on thiolsulfinate concentration, although the dependence, particularly at higher [**1**], is apparently somewhat more pronounced than the half-power dependence predicted by the mechanism. This apparently arises because the rate of acid- and nucleophile-catalyzed disproportionation[5] of **1** is not too much slower[6] than the rate of exchange, especially at the highest thiolsulfinate concentrations.[7]

The really important result here is what the values of (k_α/k_{ex}) suggest about the relative reactivity of PhSNu toward PhSOH and H_2O, steps k_{-2} and k_{-6}, respectively. Thus using the data for n-butyl sulfide as catalyst at the lowest thiolsulfinate concentration (0.0125 M), where there are no complications from the disproportionation of **1**,[6] $(k_2K_1/k_6)(k_{-2}/k_{-6}[H_2O])$ is calculated to be 9×10^3. Since there is no reason to believe that k_2K_1/k_6 should be significantly greater than unity, and since in 60% dioxane $[H_2O] \cong 20$ M, this suggests that $(k_{-2}/k_{-6}) \geqq 1.8 \times 10^5$. In other words, benzenesulfenic acid (PhSOH) is over 100,000 times more reactive as a nucleophile toward PhS-$S^+(n\text{-Bu})_2$ than is water. It is also presumably much more reactive than water toward PhSBr and somewhat more reactive than water toward PhSCl.

These results provide an explanation of why thiolsulfinates are invariably the first isolable product of the hydrolysis of reactive sulfenyl derivatives in water.[8] Since $k_{-2} \gg k_{-6}$, as soon as any PhSOH is formed by hydrolysis of PhSNu it reacts with some of the remaining PhSNu faster than the latter undergoes hydrolysis. Thus the inability to isolate sulfenic acids from the hydrolysis of sulfenyl derivatives may be less a matter of their inherent instability than of their high nucleophilic reactivity toward such sulfenyl derivatives.

(7) The rate-determining step of the acid- and nucleophile-catalyzed disproportionation[5] is given by



Occurrence of this reaction siphons off some PhSNu that would otherwise undergo hydrolysis to PhSOH, which latter species would then yield unlabeled **1**. Although the exact kinetics of the situation are too complex to be amenable to simple analysis, it is evident, since the rate of the disproportionation in 60% dioxane is proportional to $[1]^{3/2}$,[6] that the fraction of PhSNu prevented from undergoing eventual return to unlabeled **1** in this way will be larger the higher the concentration of **1**, thus causing (k_α/k_{ex}) to increase more rapidly with thiolsulfinate concentration than predicted by eq 6.

(8) E. Vinkler and F. Klivenyi, *Acta Chim. Acad. Hung.*, 22, 345 (1960).

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(10) National Institutes of Health Postdoctoral Fellow, 1969–1970.

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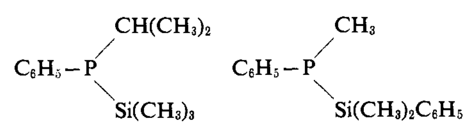
Barrier to Pyramidal Inversion in Silylphosphines[1]

Sir:

In contrast to the planar nitrogen atom in silylamines,[2] the phosphorus atom in trisilylphosphine possesses a normal pyramidal geometry characteristic of other phosphines.[3] However, we have found that the barrier to pyramidal inversion in silylphosphine **1** has the remarkably low value of $\Delta G^{\ddagger}_{62} = 18.9$ kcal/mol.[4] This observation demonstrates that a pronounced stabilization of the planar (relative to the pyramidal) geometry is a general phenomenon in mole-



1 **2**

cules having silicon bonded to an inversion center, and not one which is restricted to the first-row elements.[6,7]

(1) This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-B.

(2) K. Hedberg, *J. Amer. Chem. Soc.*, 77, 6491 (1955); E. A. V. Ebsworth, J. R. Hall, M. J. MacKillop, D. C. McKean, N. Sheppard, and L. A. Woodward, *Spectrochim. Acta*, 13, 202 (1958); G. Glidewell, D. W. H. Rankin, A. G. Robiette, and G. M. Sheldrick, *J. Mol. Struct.*, 4, 215 (1969); L. V. Wilkov and N. A. Tarasenko, *Chem. Commun.*, 1176 (1969).

(3) B. Beagley, A. G. Robiette, and G. M. Sheldrick, *J. Chem. Soc. A*, 3002 (1968); H. Siebert and J. Eints, *J. Mol. Struct.*, 4, 23 (1969).

(4) As compared to the barriers of comparable phosphines (*e.g.*, methylphenyl-*t*-butylphosphine) which fall in the range of 32–33 kcal/mol[5] at 130°.

(5) R. D. Baechler and K. Mislow, *J. Amer. Chem. Soc.*, 92, 3090 (1970).

(6) The temperature-dependent nmr spectrum of the cyclic tetramer $[Me_2SiAsMe]_4$ (E. W. Abel and J. P. Crow, *J. Organometal. Chem.*, 17, 337 (1969)) suggests the possibility that the barrier to inversion at