Two experiments in which *t*-butylbenzene was heated at 50° (other conditions as above) for 1 hr and 3 hr., respectively, gave the following results: (1 hr.) 17 mole % conversion to isobutane, 10 wt. % recovery of alkylbenzenes, b.p. 100–200°, consisting of toluene (16%), ethylbenzene (47%), isopropylbenzene (34%), *sec*-/isobutylbenzene (5%), and *t*-butylbenzene (3%); (3 hr.) 35 mole % conversion to isobutane, 7 wt. % recovery of alkylbenzenes, b.p. 100–200°, consisting of toluene (17%), ethylbenzene (54%), isopropylbenzene (21%), *n*-propylbenzene (2%), and *sec*-/isobutylbenzene (6%).

Studies on the Changes in Dealkylation and Rearrangement Products from *sec*- and Isobutylbenzene with Time.—These experiments were carried out as described above (at 100°), except that the reactions were carried out for shorter periods of time and, at the end of each reaction, the gaseous products were swept into the receiver with a stream of helium so as to collect the total alkanes produced in a given time. The gaseous mixture was analyzed directly by v.p.c. The liquid reaction mixture was worked up in the usual way and the distillation fraction containing recovered *sec*- and isobutylbenzenes, b.p. 170–176°, was analyzed by infrared spectrophotometry. The results are presented in Table II.

The data given in the first lines of Table II (on the gases evolved in 1 min. and less after hydrocarbon was added to catalyst) were obtained in a special way. A syringe was inserted through a rubber bulb covering one neck of the reaction flask and samples were withdrawn about 10 sec. and 1 min. after the addition of the hydrocarbon to the catalyst. The volumes of gas produced at these times were estimated by extrapolation from the volumes at 5 and 10 min.

Tests were made in which pure *n*-butane and isobutane were passed into mixtures of aluminum chloride–water and benzene under the conditions of the dealkylation experiments. No isomerization of the butanes occurred.

Tests on Deactivation of the Catalyst toward Dealkylation. A.—*sec*-Butylbenzene (0.10 mole) was heated with aluminum chloride (0.033 mole) and water (0.017 mole) at 100° as described above. After 3 hr. the evolution of butane and isobutane, which had amounted to 29% of the theoretical amount, had virtually stopped. The apparatus was flushed with helium, and aluminum chloride (0.033 mole) and water (0.017 mole) were added. A brisk evolution of gas occurred immediately; it was mainly isobutane and *n*-butane, in the same proportions at different times as described in Table II, but about 4% of propane was present in the gas evolved during the first 10 min. after the second batch of catalyst was added. The volume of gas produced after 1 hr. corresponded to an additional 24% of dealkylation, and the evolution of gas had practically stopped again (an amount equivalent to only 0.5% occurred in an additional hour).

B.—Another reaction was run as in A. Five minutes after the reaction was initiated, *ca.* 9% dealkylation had occurred and the evolution of gas was steady. At this stage, 14.8 g. (0.10 mole) of melted pentamethylbenzene was added. The gas evolution stopped abruptly and no more occurred in the next 2 hr.

C.—A mixture of aluminum chloride (0.033 mole), water (0.017 mole), and pentamethylbenzene (0.10 mole) was stirred at 100° for 2 min. and then *sec*-butylbenzene (0.10 mole) was added. There was no evolution of gas either immediately or within the next 2 hr.

Isolation of *meso*-2,3-Diphenylbutane.—Reaction of 0.2 mole of *sec*-butylbenzene with aluminum chloride and water at 100° for 3 hr. was carried out and the liquid reaction mixture was decomposed with water as before. The organic material was distilled, 29 wt. % being obtained in the range 100–200° with a composition similar to that reported in Table I. The pot residue was distilled under reduced pressure, giving fractions a, b.p. 80–110° (3 mm.), 2.5 g.; b, b.p. 110–130° (3 mm.), 1.7 g.; c, b.p. 130–200° (3 mm.), 0.5 g.; residue, *ca.* 3 g. Fraction b crystallized partially upon prolonged standing. Recrystallized from ethanol, 0.42 g. of crystals, m.p. 124–126°, was obtained, identified as *meso*-2,3-diphenylbutane by mixture m.p. with authentic material and by identity of its infrared spectrum with that of authentic material.

Reaction of *meso*-2,3-Diphenylbutane with Aluminum Chloride.—A mixture of 10 g. (0.05 mole) of *meso*-2,3-diphenylbutane, 2.7 g. (0.02 mole) of aluminum chloride, and 1 drop of water was heated with stirring at 70° for 1 hr. The solid hydrocarbon formed a red, homogeneous solution within a few minutes after being mixed with aluminum chloride and warmed to 70°. The reaction mixture was poured into ice–water and extracted with two 50-ml. portions of ether. The ether extracts were washed with water, dried over calcium chloride, and distilled through an 80-cm. Nichrome spiral column. The distillate, b.p. 100–200°, 2.1 g., was shown by v.p.c. to consist of *sec*-/isobutylbenzene (50%), ethylbenzene (45%), isopropylbenzene (3%), and *n*-propylbenzene (2%).

Reactions of Pentylbenzenes. A. With Aluminum Chloride and Water.—These experiments were carried out as those with ethyl-, propyl-, and butylbenzenes, except that a mixture of the hydrocarbon (0.10 mole) and water (0.011 mole) was added to the aluminum chloride (0.033 mole) in a flask heated by an oil bath at 100°. Data on gaseous products are given in Table III and data on liquid products are given in Table IV.

B. **With Aluminum Chloride, Water, and Cyclohexane.**—These experiments were carried out as described above, except that a molar equivalent of cyclohexane was added, and the temperature was kept at 57–60°. Some butanes were identified in the gases evolved, and some lower alkylbenzenes were found in each liquid reaction mixture, in about the same proportions as in the absence of cyclohexane at 100°.

Analysis.—Vapor phase chromatographic analysis was made with a Beckman GC2A instrument, fitted with a 6-ft. column packed with silicone oil on firebrick. The carrier gas was helium at 30 p.s.i.; temperatures compatible with the boiling points of the samples were used.

Infrared analyses were made with a Beckman IR-5A instrument, with sodium chloride prism and cells. Quantitative analyses of mixtures of *sec*- and isobutylbenzene were carried out in isooctane solutions as described previously.[16]

Acknowledgment.—We wish to thank the National Science Foundation and the Robert A. Welch Foundation for grants which supported this research.

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[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACOLOGY, SCHOOL OF MEDICINE, YALE UNIVERSITY, NEW HAVEN, CONN.]

The Aminolysis of Thioacyl and Selenoacyl Analogs[1,2]

BY HENRY G. MAUTNER, SHIH-HSI CHU, AND WOLFGANG H. H. GÜNTHER

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The relative rates of the reaction of N,Se-dibenzoylselenocysteamine and of N,S-dibenzoylcysteamine with *n*-butylamine were investigated; the former compound was found to undergo aminolysis much more rapidly than the latter. This difference in reactivity was found to be due to a relatively favorable entropy of activation in the case of the selenoacyl compound.

Sulfur compounds as diverse as thiolesters, sulfonium compounds, and anhydrides of sulfuric and phosphoric acids play an important part in biological energy and group transfer reactions. While numerous comparative studies of the reactions of oxygen and sulfur analogs have been carried out, the interpretation of differences in reaction rates and mechanism have been complicated by differences in the atomic radii of oxygen and of sulfur.[3] This factor is of particular importance in obscuring the meaning of observed differences in the entropies of activation of oxygen and sulfur analogs. However, steric considerations play a less important part when the reactivities of sulfur and selenium analogs are compared, the atomic radii of sulfur and selenium being rather similar[3]

(1) A preliminary account of part of this material appeared in *J. Am. Chem. Soc.*, **83**, 3342 (1961). Portions of this work were presented before the I.U.P.A.C. Congress, London, July, 1963.

(2) We are indebted to the National Science Foundation and to the United States Public Health Service for their support of this work.

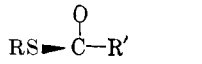
(3) L. Pauling in "The Nature of the Chemical Bond," 3rd. Ed., Cornell University Press, Ithaca, N. Y., 1960, pp. 246, 260.

	Tetrahedral covalent radius, Å.	van der Waals radius, Å.
Oxygen	0.66	1.40
Sulfur	1.04	1.85
Selenium	1.14	2.00

Differences in the reactivities of isologous sulfur and selenium compounds can, therefore, be attributed primarily to differences in electron distribution. Since lines based on three points tend to be more meaningful if less linear than lines drawn through two points, it would seem that correlations gained through a systematic study of isologous oxygen, sulfur, *and* selenium compounds should be useful in throwing light on the fundamental reasons for the differences in basicity and nucleophilicity seen on descending the sixth row of the periodic table.

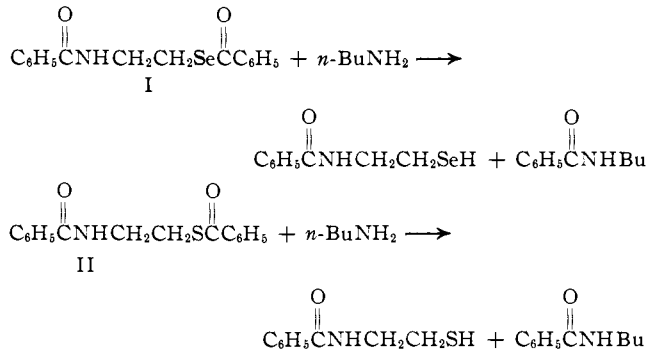
Since the recognition of the role played by thioacyl derivatives of coenzyme A in biological systems,[4] a great deal of attention has been centered on the mechanisms of the reactions of thiolesters.[5-10] While the rates of hydrolysis of thiolesters and of esters are similar, the rates of aminolysis of thiolesters exceed those of their oxygen analogs. For instance, ethyl *p*-nitrothiolbenzoate, but not ethyl *p*-nitrobenzoate, will undergo nucleophilic attack by butylamine.[10]

The high susceptibility of thioacyl compounds to aminolysis has been attributed to polarization of the electrons of the C–S bond in the direction of the sulfur, activating the carbonyl carbon to nucleophilic substitution[4]



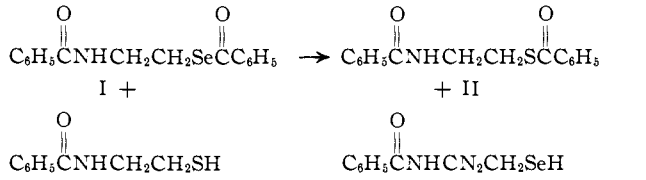
Infrared spectral evidence for resonance forms involving utilization of the d-orbitals of sulfur has been presented.[11]

Since during an investigation of isologous carbamyl, thiocarbamyl, and selenocarbamyl compounds the contribution of charge-separated structures was found to increase on descending the periodic table,[12-15] it seemed reasonable to expect that the C–Se bonds of selenolesters should be more highly polarized than the C–S bonds of comparable thiolesters, with a concomitant increase in the aminolysis rate of the selenoacyl compounds. Further interest in this problem was raised by the observation that selenopantethine,[16] 4′-phosphoselenopantethine, and dephosphoseleneocoenzyme A[17] could replace their naturally occurring sulfur analogs in some biological systems. Since the biological roles of coenzyme A are centered on the ability of this compounds' single sulfur atom to react with and transfer acyl groups, a study of the relative transacylating ability of thioacyl and selenoacyl analogs was undertaken. The following test system was used:



N,S-Diacyl and N,Se-diacyl derivatives of cysteamine and selenocysteamine, respectively, which contain some of the structural features of coenzyme A, were chosen as model compounds for kinetic studies. The ultraviolet absorption maxima of thiobenzoyl derivatives at 265 mμ and of selenobenzoyl derivatives at 285 mμ were found to be convenient for following the progress of the transacylation reactions. The benzoyl derivatives had the disadvantage of being only slightly soluble in water so that kinetic measurements had to be made in ethanol solution. The rate of aminolysis of the oxygen analogs could not be followed spectrophotometrically owing to interference by the ultraviolet absorption peak of the benzamido group.

In addition to comparative studies of the kinetics of the aminolysis of the thioacyl and selenoacyl compounds I and II, the ability of the selenoacyl compounds to react with mercaptans and disulfides to form thioacyl compounds was investigated by the use of the reaction



Experimental

N,Se-Dibenzoylselenocysteamine (I).—A mixture of 3.2 g. (0.01 mole) of selenocystamine dihydrochloride[18] and 1.68 g. (0.02 mole) of sodium bicarbonate was dissolved in 30 ml. of water. After the addition of 150 ml. of tetrahydrofuran and flushing of the apparatus with nitrogen, the diselenide was reduced by the addition in small portions of 0.37 g. (0.01 mole) of sodium borohydride, resulting in the disappearance of the yellow color of the solution. After the addition of 8.0 g. of sodium bicarbonate, 5.6 g. (0.04 mole) of benzoyl chloride was dropped into the vigorously stirred solution over a period of 15 min. Stirring was continued for 90 min. after which time the smell of benzoyl chloride had disappeared. The organic layer was separated and evaporated to dryness under reduced pressure. After recrystallization from 150 ml. of 50% methanol, 5.9 g. (89.4%) of I was obtained in the form of colorless needles. After recrystallization from benzene–petroleum ether (boil. range 60–80°) the product melted at 99–100° (uncor.); ultraviolet spectrum in absolute ethanol: λ_{max} 240, 285, 305 (inflect.) mμ; ϵ_{max} 21,630, 5520, 4390.

Anal. Calcd. for $C_{16}H_{15}NO_2Se$: C, 57.83; H, 4.55; N, 4.22; Se, 23.77. Found: C, 58.10; H, 4.56; N, 4.01; Se, 23.68.

Other Compounds.—N,N′-Dibenzoylselenocystamine,[18] N,S-dibenzoylcysteamine,[19] N,N′-dibenzoylcystamine,[20] N-benzoylcysteamine,[21] and *n*-butylbenzamide[22] were prepared and purified according to literature methods. *n*-Butylamine was redistilled from solid potassium hydroxide.

Reaction of N,Se-Dibenzoylselenocysteamine (I) **with *n*-Butylamine.**—To a solution of 47.6 g. (0.652 mole) of *n*-butylamine in 2 l. of absolute ethanol was added 0.12 g. (0.000362 mole) of I. The mixture was permitted to stand at room temperature for 18 hr., aerated for 30 min., and evaporated to

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(18) W. H. H. Günther and H. G. Mautner, *J. Am. Chem. Soc.*, **82**, 2762 (1960).

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(22) J. F. Bunnett and G. T. Davis, *J. Am. Chem. Soc.*, **82**, 665 (1960).

dryness under reduced pressure. Extraction of the yellow residue with three 10-ml. portions of dry ether, followed by evaporation, decolorization with Norit, and recrystallization, yielded 0.053 g. (81%) of *n*-butylbenzamide, the infrared spectrum of which was identical with that of authentic material. Neither the infrared spectrum nor gas chromatography showed the presence of a detectable amount of ethyl benzoate. The ether-insoluble residue on recrystallization from chloroform–petroleum ether gave 0.078 g. (92%) of N,N'-dibenzoylselenocystamine, m.p. 144–145°, which did not depress the m.p. of authentic material.

The reaction conditions described here duplicate conditions used in kinetic runs. Utilization of larger quantities of reagents and of more concentrated solutions gave quantitative yields of N,N'-dibenzoylselenocystamine and *n*-butylbenzamide.

Repetition of the above reaction in the presence of 27.4 g. (0.65 mole) of lithium chloride resulted again in the formation of N,N'-dibenzoylselenocystamine and *n*-butylbenzamide. No ethyl benzoate formation could be detected.

Heating an ethanolic solution of I to reflux temperature for 12 hr. in the presence or absence of lithium chloride resulted in no alteration of the spectrum of the original material.

Reaction of N,S-Dibenzoylcysteamine (II) with *n*-Butylamine.—To a solution of 47.6 g. (0.652 mole) of *n*-butylamine in 2 l. of absolute ethanol was added 0.103 g. (0.000362 mole) of II. After being permitted to stand at room temperature for 3 days, the mixture was worked up as described above to yield 0.061 g. (98%) of N,N'-dibenzoylcystamine and 0.062 g. (97%) of crude *n*-butylbenzamide. Gas chromatography failed to indicate the formation of ethyl benzoate.

Repetition of this reaction in the presence of 27.4 g. (0.65 mole) of lithium chloride yielded the same products in comparable yield.

Reaction of N,Se-Dibenzoylselenocysteamine (I) with N-Benzoylcysteamine.—A mixture of 0.0271 g. (0.00015 mole) of N-benzoylcysteamine and 0.05 g. (0.00015 mole) of I was dissolved in 220 ml. of 50% ethanol. The solution was permitted to reflux for 18 hr., aerated for 30 min., and evaporated to dryness under vacuum. The residue was extracted with three 10-ml. portions of dry ether. After evaporation to dryness of the ether extracts and recrystallization from a benzene–petroleum ether mixture 0.026 g. (60%) of II was obtained. The product which melted at 92–93° did not depress the m.p. of authentic II and had an identical infrared spectrum.

From the ether-insoluble residue 0.022 g. (60%) of crystalline N,N'-dibenzoylselenocystamine was isolated, the authenticity of which was proved by comparison with authentic material.

Repetition of the above reaction using N,N'-dibenzoylcystamine instead of N-benzoylcysteamine again resulted in the formation of II and of N,N'-dibenzoylselenocystamine.

Attempted Reaction of N,S-Dibenzoylcysteamine (II) with N,N'-Dibenzoylselenocystamine.—A mixture of 0.093 g. (0.00015 mole) of N,N'-dibenzoylselenocystamine and 0.0855 g. (0.0003 mole) of II in 200 ml. of 50% ethanol was heated to reflux temperature for 17 hr. At the end of this period ultraviolet absorption at 265 mμ corresponding to the thiobenzoyl group had not decreased, while absorption at 285 mμ corresponding to the selenobenzoyl group had not increased.

Kinetic Measurements.—Solutions of I and II in absolute ethanol were placed in thermostated stoppered quartz cuvettes. Stock solutions of ethanolic *n*-butylamine were permitted to reach the temperatures (±0.02°) at which the rate studies were to be conducted. Aliquots of amine solution were added as quickly as possible to the cuvettes followed by shaking and stirring. Reaction rates were followed by observing the disappearance of absorption at 265 mμ (II) or 285 mμ (I). A Cary model 15 ultraviolet spectrophotometer was utilized. Temperatures inside the thermostated cell compartment were determined by means of a telethermometer (YSI).

Plots of log ($O.D._{\infty} - O.D._{obsd}$) *vs.* time gave straight lines, the slopes of which multiplied by 2.303 yielded the pseudo-first-order rate constants. While $O.D._{\infty}$ at 285 mμ was negligible when the aminolysis of the selenobenzoyl compound I was studied, the situation was more complicated in studies involving the thiobenzoyl compound II. Here $O.D._{obsd\infty}$ at 265 mμ was considerable, owing to absorption by the benzamido group of N-benzoylcysteamine as well as that of butylbenzamide formed during the course of the reaction. To obtain absorption due to the presence of the thioacyl group, the following relationship had to be considered

$$O.D._{SCO} = O.D._{obsd} - O.D._{A} - O.D._{B}$$

where $O.D._{SCO}$ is absorption due to the thiobenzoyl group of II, $O.D._{A}$ is absorption due to the benzamido group of II or of N-benzoylcysteamine (a constant), and $O.D._{B}$ is absorption due to the benzamido group of *n*-butylbenzamide formed during the reaction. The values for $O.D._{A}$ and $O.D._{B\infty}$ were determined using solutions of the appropriate concentration of butylbenzamide and of N-benzoylcysteamine; $O.D._{obsd\infty}$ should and does equal the sum of $O.D._{A}$ and $O.D._{B\infty}$. Assuming that $O.D._{A}$ is constant, while $O.D._{B}$ increases from zero to $O.D._{B\infty}$ at a constant rate proportional to the rate at which $O.D._{SCO}$ decreases to $O.D._{SCO\infty}$, an empirical equation for obtaining $O.D._{SCO}$ in terms of $O.D._{obsd}$ and $O.D._{obsd\ initial}$ could be derived

$$O.D._{SCO} = 1.151\ O.D._{obsd} - 0.302O.D._{obsd\ initial}$$

The same result can be obtained graphically. Plots of log ($O.D._{SCO\infty} - O.D._{SCO}$) or of log ($O.D._{obsd\infty} - O.D._{obsd}$) against time yielded parallel straight lines from which the pseudo-first-order rate constants ($k_{SCO} = k_{obsd}$) were obtained.

All kinetic determinations were made in duplicate. Data from typical runs are shown in Table I.

TABLE I

REACTION OF N,Se-DIBENZOYLSELENOCYSTEAMINE WITH *n*-BUTYLAMINE IN ETHANOL AT 25.0°

Init. concentrations: RNH_2, 3.26×10^{-1} *M*; N, Se-dibenzoylselenocysteamine, 1.81×10^{-4} *M*

Time, sec.	$O.D._{obsd}$	Time, sec.	$O.D._{obsd}$
0	0.980	220	0.595
60	.846	260	.540
80	.810	340	.449
120	.750	380	.410
147	.700	420	.375
190	.640	1200	.075
		1800	.033

Pseudo-first order k_{obsd} $2.30 \pm 0.06 \times 10^{-3}$ sec.$^{-1}$

REACTION OF N,S-DIBENZOYLCYSTEAMINE WITH *n*-BUTYLAMINE IN ETHANOL AT 25°

Init. concentrations: RNH_2, 1.63×10^{-1} *M*; N,S-dibenzoylcysteamine, 0.905×10^{-4} *M*

Time, sec.	$O.D._{obsd}$	$O.D._{SCO}$	Time, sec.	$O.D_{obsd}$	$O.D._{SCO}$
0	0.892	0.756	126,000	0.476	0.277
18,000	.810	.661	144,000	.440	.235
36,000	.734	.574	162,000	.412	.203
54,000	.668	.498	180,000	.389	.177
72,000	.610	.431	198,000	.368	.153
90,000	.559	.372	216,000	.348	.130
108,000	.513	.319	540,000	.230	.005
			$O.D._{A} + O.D._{B\infty}$	.225	

Pseudo-first order k_{SCO} $7.88 \pm 0.23 \times 10^{-6}$ sec.$^{-1}$

Discussion of the Results

A striking difference in the rates of aminolysis of I and II was observed. It should be noted that in comparative studies of the aminolysis of analogous thioacyl and selenoacyl compounds not related to the cysteamine derivatives reported here, similar rate differences were observed. Thus, benzylselenobenzoate reacted with *n*-butylamine at 20° more than one hundred times as rapidly as did benzylthiobenzoate.

The pseudo-first-order coefficients of the aminolysis reactions were not dependent on the concentrations of the acyl compounds in the presence of constant, high amine concentration. A series of runs in which amine concentration was varied in the presence or absence of lithium chloride is summarized in Table II.

The pseudo-first-order rate coefficients of the aminolysis of the selenoacyl compound I are proportional to amine concentration over the range investigated both in the presence and in the absence of lithium chloride. On the other hand, while the pseudo-first-order rate coefficients of the thioacyl analog II were proportional to amine concentration in the presence of lithium chloride, in the absence of salt, a plot of rate coefficients against amine concentration yielded a curved line indicating that the aminolysis of this thiolester, similarly to the aminolysis of esters,[22] is not a first-order reaction with respect to amine concentration. It should be noted that, as in the study of the aminolysis of esters quoted by Bunnett,[22] reproducibility was not all that could be desired when amine concentration was varied. It is regrettable that the aminolysis of I was so

TABLE II

REACTION OF N,Se-DIBENZOYLSELENOCYSTEAMINE WITH *n*-BUTYLAMINE IN ETHANOL AT 20°

Initial concn. of N,Se-dibenzoylselenocysteamine, 1.81×10^{-4} *M*

No LiCl		LiCl, 3.26×10^{-1} *M*	
$BuNH_2$, *M*	$k_{obsd} \times 10^{-3}$ sec.$^{-1}$	$BuNH_2$, *M*	$k_{obsd} \times 10^{-3}$ sec.$^{-1}$
0.326	1.75	0.326	2.73
.163	0.79	.163	1.29
.081	0.39	.081	0.70

REACTION OF N,S-DIBENZOYLCYSTEAMINE WITH *n*-BUTYLAMINE IN ETHANOL AT 20°

Initial concn. of N,S-dibenzoylcysteamine, 0.905×10^{-4} *M*

No LiCl		LiCl, 1.63×10^{-1} *M*	
$BuNH_2$, *M*	$k_{SCO} \times 10^{-6}$ sec.$^{-1}$	$BuNH_2$, *M*	$k_{SCO} \times 10^{-6}$ sec.$^{-1}$
0.652	67.7	0.652	177.0
.326	20.1	.326	110.0
.163	6.8	.163	62.0
.081	2.8	.081	31.8

fast that at higher amine concentrations than the ones reported the reaction was too rapid for reproducible rate measurements to be made with the equipment available.

It can be seen that lithium chloride accelerated the aminolysis of the thioacyl compound II more than that of its selenoacyl analog I. The positive salt effect on the reaction of II with *n*-butylamine was most pronounced at relatively low amine concentrations.

The variations of pseudo-first-order rate coefficients with temperature are summarized in Table III.

TABLE III

EFFECT OF TEMPERATURE ON THE PSEUDO-FIRST-ORDER RATE COEFFICIENTS OF THE REACTION OF N,Se-DIBENZOYLSELENOCYSTEAMINE (I) AND N,S-DIBENZOYLCYSTEAMINE (II) WITH *n*-BUTYLAMINE

Initial concn.: aminolysis of I: RNH_2, 3.26×10^{-1} *M*; I, 1.81×10^{-4} *M*; LiCl, 3.26×10^{-1} *M*; aminolysis of II: RNH_2, 1.63×10^{-1} *M*; II, 0.905×10^{-4} *M*; LiCl, 1.63×10^{-1} *M*

	No LiCl		LiCl	
Temp., °C.	$k_{obsd} \times 10^{-3}$ (I)	$k_{SCO} \times 10^{-6}$ (II)	$k_{obsd} \times 10^{-3}$ (I)	$k_{SCO} \times 10^{-6}$ (II)
20.0	1.75	6.77	2.73	62.0
25.0	2.30	7.88	3.43	77.0
30.0	2.86	11.46	4.19	103.0
40.0	4.08	17.15	5.63	176.0

An Arrhenius plot summarizing these data is shown in Fig. 1. Enthalpies of activation ($\Delta H^{\pm}$) and entropies of activation ($\Delta S^{\pm}$), which were derived from the Arrhenius plot, are summarized in Table IV.

TABLE IV

ENTHALPIES AND ENTROPIES OF ACTIVATION FOR REACTION OF N,Se-DIBENZOYLSELENOCYSTEAMINE AND N,S-DIBENZOYLCYSTEAMINE WITH *n*-BUTYLAMINE

	No LiCl $\Delta H^{\pm}$, kcal.	LiCl $\Delta H^{\pm}$, kcal.	No LiCl $\Delta S^{\pm}$, e.u.	LiCl $\Delta S^{\pm}$, e.u.
Selenoacyl (I)	8.12	7.34[a]	−43.3	−45.2[a]
Thioacyl (II)	8.58	8.58	−53.1	−48.5

[a] Even though lithium chloride accelerated the aminolysis of I relatively little, rates at temperatures above 25° in the presence of salt were so rapid that it proved difficult to obtain reproducible results with the equipment available.

It can be seen that the very considerable differences in the susceptibility of the selenoacyl and thioacyl analogs to aminolysis in the absence of salt can be attributed primarily to differences between the entropies rather than to differences between the enthalpies of activation. Systems in which different substituent groups alter $\Delta S^{\pm}$ without altering $\Delta H^{\pm}$ are rare; a recent example has been reported by Bruice and Benkovic.[23]

(23) T. C. Bruice and S. J. Benkovic, *J. Am. Chem. Soc.*, **85**, 1 (1963).

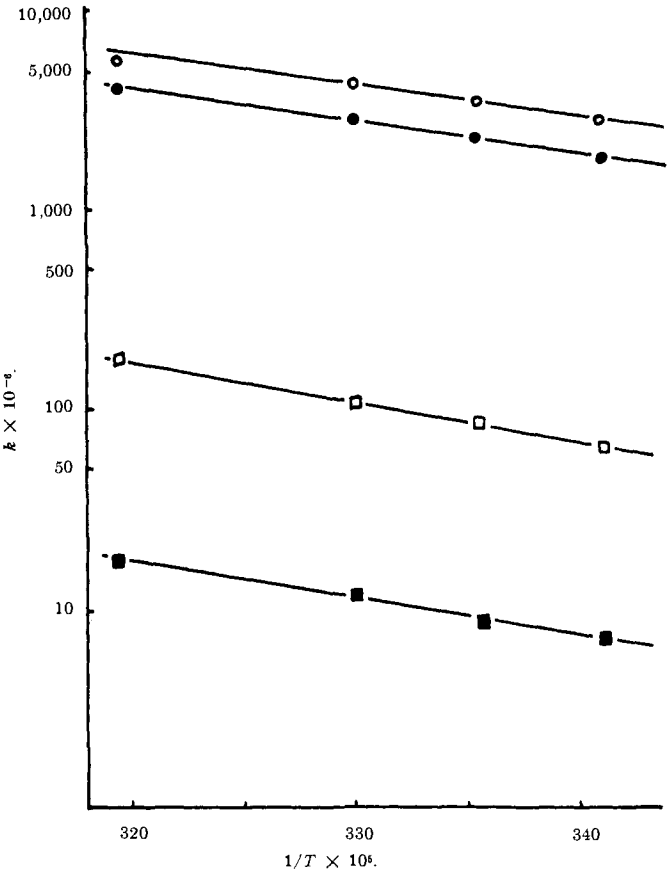


Fig. 1.—Arrhenius plot of aminolysis in EtOH:

O
||
RSeCR'
O, with LiCl
●, without LiCl

O
||
RSCR'
□, with LiCl
■, without LiCl

It is interesting to note that similar differences in entropy of activation were observed when the reactivities of thiolesters and oxygen esters were observed. Thus Schaefgen,[24] studying the alkaline hydrolysis of ethyl thiolacetate and of ethyl acetate, noted that the enthalpy and entropy of activation of the thiolester exceeded those of the ester. Similar differences in entropy of activation were noted by Rylander and Tarbell.[25] Differences in the entropy of activation of the reactions of thiolesters and of esters have been attributed to the greater size of the sulfur than of the oxygen atom,[25] to a relatively high ability of oxygen esters, compared to thiolesters, to be hydrated in the transition state,[24] and to the difficulty of forming resonance hybrids in which sulfur is partially double bonded to the carbonyl carbon.[25]

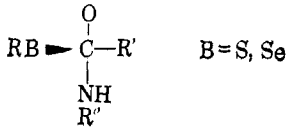
In comparing thiolesters and selenolesters, differences in the atomic sizes of sulfur and selenium seem inadequate to account for the very considerable differences in the entropies of activation noted. Relatively little is known about the comparative solvating abilities of thio and seleno analogs, although the observation that analogous sulfur and selenium compounds generally appear to have very similar crystal structures containing the same number of moles of water of hydration[12,13] and to exhibit similar partition coefficients[14] makes it unlikely that differences in solvation are the cause of the entropy differences noted.

If one assumes that sulfur and selenium activate the carbonyl carbon to nucleophilic attack to a different degree through differences of polarization in the direc-

(24) J. R. Schaefgen, *ibid.*, **70**, 1308 (1948).

(25) P. N. Rylander and D. S. Tarbell, *ibid.*, **72**, 3021 (1950).

tion of sulfur or selenium, respectively, one should expect both $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values to differ in comparing thio and seleno esters. Since, however, $\Delta H^{\ddagger}$ values for the aminolysis of I and II are quite similar, while the $\Delta S^{\ddagger}$ value of the selenoacyl compound is considerably less negative than that of its thioacyl analog, it seems more reasonable to postulate that the differences in reactivity and entropies of activation are related to leaving tendencies of the selenomercaptide as compared to that of the mercaptide group from the tetrahedral transition state



This postulate is reinforced by the observation that the addition of lithium chloride accelerates the aminolysis of the sulfur compound II more than that of its seleno analog I. In the latter case, the carbon–selenium bond is presumably polarized highly even in the absence of salt, while the carbon–sulfur bond, which in the transition state of the analogous thiolester is polarized to a lesser degree, is more susceptible to an increase in polarization induced by lithium chloride addition, which in turn alters the entropy of activation.

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Phosphorylations and Phosphonations of Glycerol by Recoil Atoms[1,2]

BY TATSUHIKO YAGI, S. A. EL-KINAWY,[3] AND A. A. BENSON[4]

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The labeled products of neutron activation of phosphorus oxyacids in glycerol were studied by paper chromatographic techniques. Irradiation of mixtures of phosphoric acid and glycerol produced P^{32}-labeled H_3PO_3, H_3PO_2, glycerophosphorous acid, 3-phosphinicopropanediol-1,2, and 1-phosphonoglycerol. Other C_2- and C_3-organic phosphorus compounds were suggested. Neither $H_3P^{32}O_4$ nor its esters was produced.

Introduction

Neutron irradiation of phosphorus oxyacids has, so far, suggested that most of the P^{32} *in statu nascendi* reverts to the oxidation level of the parent compounds. Thus, neutron activation of crystalline or aqueous ortho- and condensed phosphoric acids or their salts yielded mainly phosphoric acids-P^{32} or their salts,[5,6] the only change, if any, being that of the degree of polymerization.[6] Formation of more than trace amounts of reduced compounds such as phosphorous, hypophosphoric, or hypophosphorous acids was also repeatedly reported.[7] Lindner and Harbottle[8a] reported the neutron activation products of various phosphate salts as a mixture of oxyanions of phosphorus containing one, two, or three phosphorus atoms, in which distribution of P^{32} was critically dependent upon the irradiation conditions. Recent work by Campbell, *et al.*,[8b] defined the products of neutron activation of tributyl phosphate as di- and monobutyl phosphates, unchanged tributyl phosphate, and phosphoric and phosphorous acids. Studies of the radioactive products from PCl_3 reported formation of $P^{32}Cl_3$ in yields as high as 88% of the total radioactivity induced.[9]

A P^{32} nucleus, recoiling from the (n,γ) capture process, has more than enough energy to break its covalent chemical bonds. Except in the case of symmetrical distribution of γ-recoil momenta, a "hot atom" will be produced which can return to its original state only by proper recombination with ions and radicals formed in its path. When inorganic phosphorus oxyacids are activated in the presence of organic substances, combination of the recoiling nucleus and organic radicals may occur. Although labeling of organic molecules by recoiling atoms such as C^{14} or halogens has been extensively investigated,[10,11] syntheses of organic phosphorus compounds by such methods have been relatively unsuccessful.[12]

The present paper reports phosphorylations and phosphonations of the biologically important compound, glycerol, as a result of thermal neutron capture in mixtures of glycerol and phosphoric acid. Radiochromatographic techniques were applied in the elucidation of the structures of the products. Recognition

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(2) Neutron irradiations were provided by the staffs of the Nuclear Reactor Facility of the Pennsylvania State University and of the Engineering Nuclear Reactor, University of California, Los Angeles. We are indebted to Professor E. V. Jensen for a sample of 2,3-dihydroxypropylphosphonic acid (phosphonopropanediol).

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(4) Department of Marine Biology, Scripps Institution of Oceanography, University of California, San Diego, La Jolla, Calif.

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