meta isomers were removed in EtOH/HCl; however, conversion of the *o*-trimethylsilyl ether to the phenol required the use of tetra-*N*-butylammonium fluoride in THF.[21]

Syntheses of (Trimethylsilyl)anisoles. The bromoanisoles were reacted with Mg turnings (1 equiv) in anhydrous THF at reflux for 6 h. Trimethylsilyl chloride (1.5 equiv) was then added, and the reaction was refluxed overnight. The reaction mixtures were worked up as previously described.[22,23] Further purification of the products for the no-carrier-added radiohalogenations was accomplished by washing with 5% NaOH solution, followed by preparative TLC using 98:2 hexane/ethyl acetate to give products that were >99.5% pure by HPLC.

Syntheses of (Trimethylsilyl)phenyl Acetates. (Trimethylsilyl)phenols (6 mmol) were reacted in a mixture of 10 mL of pyridine and 10 mL of acetic anhydride at room temperature for 3 h. Removal of the pyridine and excess acetic anhydride by vacuum distillation yielded brown residues, which were purified by Kugelrohr distillation at 30–40 °C (10–50 μm) to give colorless oils[6,11] (meta isomer solidified at room temperature, mp 25–27 °C) in 66–86% yields.

Bromination of (Trimethylsilyl)phenols and (Trimethylsilyl)anisoles. To a solution of (trimethylsilyl)phenol or (trimethylsilyl)anisole (0.06 mmol) dissolved in 1.0 mL of MeOH was added 6 mg of NaBr (0.06 mmol) and 8 mg of NCS (0.06 mmol) at room temperature. The reaction progress was followed by HPLC and found to be over within 5 min (most were over instantaneously as halogen coloration of reaction solution was not seen).

p-(Trimethylsilyl)phenol yielded 80–90% of the *p*-bromophenol with several other unidentified species present.

o-(Trimethylsilyl)phenol yielded ~48% of the corresponding bromo compound and ~43% of a compound that had an HPLC retention time (~28 min) that was much longer than that of the starting material (~16 min) or the *o*-bromophenol (~4 min). GC/MS of this unidentified species had M = 244 and M + 2 = 246, which indicated that the bromine substitution had occurred without loss of the trimethylsilyl moiety. The following ^{1}H NMR spectrum was obtained: ($CDCl_3$) δ 7.39 (1 H, d, J = 1.5 Hz), 7.28 (1 H, dd, J = 1.5 Hz, J = 8.5 Hz), 6.55 (1 H, d, J = 8.5 Hz), 0.30 (9 H, s).

m-(Trimethylsilyl)phenol yielded none of the *m*-bromophenol (HPLC retention time ~4 min) but rather a new species that had a longer retention time (20 min) than the starting materials (~11 min). GC/MS of the product had M = 244 and M + 2 = 246, which indicated that the bromine substitution had occurred without loss of the trimethylsilyl moiety. ^{1}H NMR of the major product: ($CDCl_3$) δ 7.35 (1 H, d, J = 8.6 Hz), 6.90 (1 H, d, J = 3.1 Hz), 6.68 (1 H, dd, J = 3.1 Hz, J = 8.6 Hz), 0.36 (9 H, s).

o- and *p*-(Trimethylsilyl)anisole gave nearly quantitative yields of the corresponding bromo products. None of the longer retention species were seen by HPLC.

m-(Trimethylsilyl)anisole yielded primarily two compounds (2:1 ratio), which had longer retention times (28 and 31 min) than the starting material (~15 min) by HPLC. GC/MS indicated one major product with M = 258 and M + 2 = 260, which indicated that the bromine substitution occurred without loss of the trimethylsilyl moiety. ^{1}H NMR also indicated one major product: ($CDCl_3$) δ 7.41 (1 H, d, J = 8.6 Hz), 6.98 (1 H, d, J = 3.1 Hz), 6.73 (1 H, dd, J = 3.1 Hz, J = 8.6 Hz), 0.38 (9 H, s).

Bromination and Iodination of (Trimethylsilyl)phenyl Acetates. To a solution of (trimethylsilyl)phenyl acetate (0.12 mmol) in 1.0 mL of HOAc were added either 13 mg of NaBr (0.13 mmol) or 20 mg of NaI (0.13 mmol) and 17 mg of NCS (0.13 mmol). The reaction progress was followed by HPLC. Elevation of the reaction temperature to 60 °C in a dry bath/stirrer accelerated the reactions such that they were complete within 10 min for the brominations and 1 h for the iodinations. No degradation of the products or decrease in reaction yields were observed at the elevated temperature. Results are given in Table I.

Radiobromination and Radioiodination of (Trimethylsilyl)phenyl Acetates. Bromine-82. To a solution of 10 μL of trimethylsilylphenyl acetate dissolved in 500 μL of HOAc were added 2 mg of NCS and 25 of μL (~500 μCi) of an aqueous $NH_4{}^{82}Br$ solution (10 mg/mL). The reaction solution was then placed in a dry bath/stirrer at 60 °C. The reaction progress was followed by HPLC. All reactions were found to be complete within 10 min.

Bromine-77. To a vial containing 50 μL of HOAc was added 1 μL of *tert*-butyl hypochlorite at room temperature. To this solution were added 1 μL (~400 μCi) of a $Na^{77}Br$ solution (~0.02 M $NaHCO_3/NaCO_3$ in H_2O), and quickly thereafter 10 μL of (trimethylsilyl)phenyl acetate. The reaction mixture was placed in a dry bath/stirrer at 60 °C, and the reaction was followed by HPLC. All of the reactions were found to be complete within 10 min.

Iodine-131. To a vial containing 50 μL of HOAc was added 2 mg of NCS at room temperature. To this solution were added 5 μL (~160 μCi) of a $Na^{131}I$ solution (0.1 N NaOH) and quickly thereafter 10 μL of (trimethylsilyl)phenyl acetate. The reaction mixture was placed in a dry bath/stirrer at 60 °C, and the reaction was followed by HPLC. All of the reactions were complete within 2 h. Results of the radiohalogenations are given in Table I.

Acknowledgment. We thank Dr. T. Whaley for his helpful suggestions on this manuscript, Dr. C. Unkefer for his assistance in obtaining the proton spectra, and Drs. G. Bentley and J. Barnes and M. Ott for the bromine-77 used in this study. We gratefully acknowledge the financial support given by the U.S. Department of Energy.

Registry No. 1, 17881-95-7; 2, 17876-90-3; 7, 85153-08-8; 8, 18001-12-2; 9, 18001-11-1; **10a**, 1829-37-4; **10a** (^{82}Br), 85153-09-9; **10a** (^{77}Br), 85153-10-2; **10b**, 32865-61-5; **10b** (^{131}I), 85153-11-3; **11a**, 35065-86-2; **11a** (^{82}Br), 85153-12-4; **11a** (^{77}Br), 85153-13-5; **11b**, 42861-71-2; **11b** (^{131}I), 85153-14-6; **12a**, 1927-95-3; **12a** (^{82}Br), 85153-15-7; **12a** (^{77}Br), 85153-16-8; **12b**, 33527-94-5; **12b** (^{131}I), 85153-17-9; Me_3SiCl, 75-77-4; *o*-bromophenol, 95-56-7; *m*-bromophenol, 591-20-8; *p*-bromophenol, 106-41-2; (*p*-bromophenoxy)trimethylsilane, 17878-44-3; (*m*-bromophenoxy)trimethylsilane, 36971-28-5; (*o*-bromophenoxy)trimethylsilane, 36601-47-5; *p*-(trimethylsilyl)phenol, 13132-25-7; *o*-(trimethylsilyl)phenol, 15288-53-6; *o*-bromoanisole, 578-57-4; *m*-bromoanisole, 2398-37-0; *p*-bromoanisole, 104-92-7; *o*-(trimethylsilyl)anisole, 704-43-8; *p*-(trimethylsilyl)anisole, 877-68-9; 4-bromo-2-(trimethylsilyl)phenol, 67044-81-9.

(21) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.
(22) Benkeser, R. A.; Kryiak, H. R. *J. Am. Chem. Soc.* **1953**, *75*, 4528–4531.
(23) Eaborn, C. *J. Chem. Soc.* **1953**, 3148–3153.

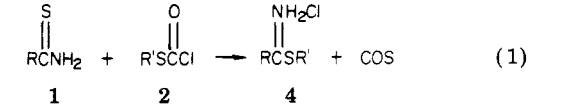
Mechanism of Thio Imino Ester Formation from the Reaction of Thioamides and Thiochloroformate Esters

David Anderson, Paul Zinke, and S. L. Razniak*

Department of Chemistry, East Texas State University, Commerce, Texas 75428

Received September 17, 1982

Previously we reported that thio imino esters can be prepared from thiochloroformate esters and thioamides according to the reaction:[1]



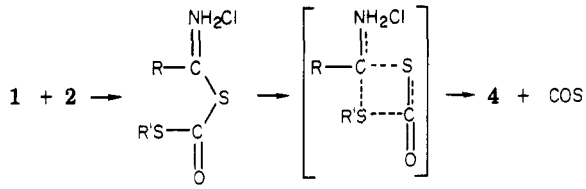
(1)

While further examples of this reaction were studied, an induction period and a steric effect on the yield of thio imino esters were observed.[2] Introduction of bulkier

(1) Razniak, S. L.; Flagg, E. M.; Siebenthall, F. M. *J. Org. Chem.* **1973**, *38*, 2242.

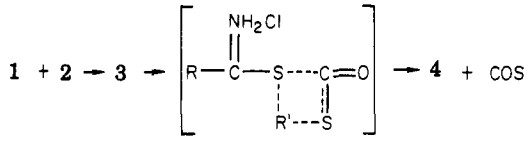
0022-3263/83/1948-1544$01.50/0

Scheme I

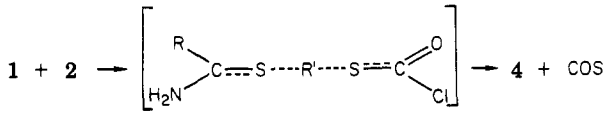


3

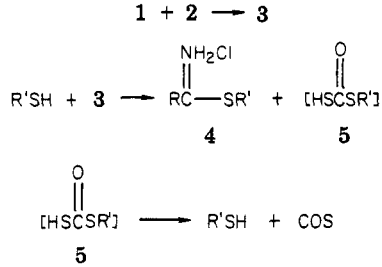
Scheme II



Scheme III



Scheme IV



substituents in the thioamide reactant or in the thiochloroformate ester decreased the yields of thio imino ester, the yield falling to 0.6% when 2-methylthiopropanamide was reacted with *S*-isobutyl thiochloroformate. These observations prompted us to investigate the mechanism of the reaction.

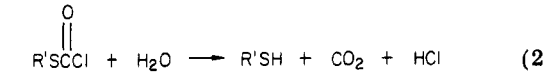
The four mechanisms for this reaction that were considered are summarized in Schemes I–IV. Mechanism I involves formation of the thio imino ester via cyclic collapse from an initially formed intermediate and is analogous to that proposed by Suydam et al. for the formation of imino esters from amides and chloroformates.[3] A cyclic mechanism was proposed by Wei and Tarbell for the decomposition of certain carboxylic thiocarbonic anhydrides that are structurally similar.[4] This mechanism differs from mechanism I with respect to the nucleophilic role of sulfur and site of nucleophilic attack.

Mechanism III involves the reaction proceeding via direct nucleophilic attack of the thioamide on the thiochloroformate ester. The observation that thioethanamide reacts with phenyl thiochloroformate to give phenyl thioethanimidate provides evidence against this mechanism because of the improbability of nucleophilic displacement occurring on the phenyl group under these reaction conditions.[2] However, in the case of aliphatic thiochloroformate esters, this S_N2 mechanism could not be a priori eliminated. The fourth mechanism considered is an ionic chain process in which attack of mercaptan on intermediate **3** forms the product and **5**, which in turn

Table I. Effect of Ethyl Thiochloroformate (A):1-Propanethiol (B) Ratios on Yields of Ethyl and *n*-Propyl Thioacetates (C and D, respectively)

molar ratios of A:B	% yield C	% yield D	molar ratios of C:D
2:1	60.6	39.4	1.5:1
1:2	29.5	70.5	0.4:1
1:10	9.2	90.8	0.1:1

regenerates the attacking mercaptan and carbonyl sulfide. The concerted formation of mercaptan and COS from the attack of mercaptan on **3** is an alternate possibility. The initial origin of R'SH is unspecified. One possible source is the reaction of the thiochloroformate ester with traces of moisture according to the reaction: Chain processes



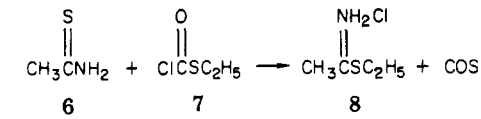
(2)

involving similar systems were proposed by Tarbell and co-workers in their studies on mixed anhydride decomposition.[5,6]

Mechanisms I and IV differ in the fate of the thioamide sulfur from mechanisms II and III. Mechanisms I and II involve concerted transition states leading directly to the observed products, while mechanisms III and IV involve a nonconcerted sequence of reactions leading to products. Labeling and nucleophilic competition studies were carried out to test each mechanism.

Results and Discussion

The system chosen for study was the reaction of thioethanamide with ethyl thiochloroformate.



The reaction of ^{35}S-labeled thioethanamide with ethyl thiochloroformate was carried out and the labeling of the COS produced determined. The carbonyl sulfide was assayed for activity as barium sulfate after conversion by the procedure of Andeeva.[7] The efficiency of the trapping

$$COS + 4H_2O_2 + BaCl_2 \rightarrow CO_2 + BaSO_4 + 2HCl + 3H_2O \quad (3)$$

procedure was established by generating known quantities of carbonyl sulfide by the reaction:

$$NH_4SCN + H_2O + H_2SO_4 \rightarrow COS + (NH_4)_2SO_4 \quad (4)$$

and subjecting it to the trapping procedure.[8,9] The recovered barium sulfate corresponded to 101.2% of the theoretical yield. The ethyl thioethanimidate hydrochloride, reaction residue, and barium sulfate were assayed for specific activity. The thio imino ester showed 1.9%, the reaction residue 3%, and the barium sulfate 95.2% of the original activity.

Competition studies were carried out by reacting ethyl thiochloroformate with a molar equivalent of thioethanamide and varying ratios of 1-propanethiol under conditions leading to thio imino ester formation. The reaction products were hydrolyzed with acetic acid buffer (pH 5) to convert the thio imino esters produced to the corresponding thiol esters, and the ester ratios were determined

(2) Flagg, E. M. Honors Thesis, East Texas State University, Commerce, TX, 1973.
(3) Suydam, F. H.; Greth, W. E.; Langerman, N. R. *J. Org. Chem.* **1969**, *34*, 292.
(4) Wei, L.; Tarbell, D. S. *J. Org. Chem.* **1968**, *33*, 1884.
(5) Chow, R. C. L.; Tarbell, D. S. *J. Org. Chem.* **1967**, *32*, 2188.
(6) Michejdd, C. J.; Tarbell, D. S. *J. Org. Chem.* **1964**, *29*, 1168.
(7) Andeeva, A. V. *Zavod. Lab.* **1938**, *7*, 279; *Chem. Abstr.* **1938**, *32*, 89843.
(8) Ferm, R. J. *Chem. Rev.* **1957**, *57*, 621.
(9) Stock, A.; Kuss, E. *Ber. Deutsch. Chem. Ges.* **1917**, *50*, 159.

by gas chromatography.[10] Authentic samples of *S*-ethyl thioethanoate and *S*-*n*-propyl thioethanoate were prepared by reported procedures.[11] In all cases *S*-*n*-propyl thioethanoate was found as a reaction product. The results of varying the 1-propanethiol ratios on the formation of *S*-ethyl thioethanoate and *S*-*n*-propyl thioethanoate are shown in Table I. Ethyl thioethanimidate was reacted with 1-propanethiol under reaction conditions for 1 h. Analysis after hydrolysis showed less than 0.4% of the products to be *S*-*n*-propyl thioacetate. This reaction was also followed by NMR observation of the quartet of ethyl thioethanimidate. No significant change was observable in the pattern until the reaction had proceeded for 7 h.

Preparation and Determination of Activity of ^{35}S-Labeled Thioethanamide (6). A 20.5-g (0.5 mol) sample of acetonitrile was mixed with 7.3 g (0.1 mol) of diethylamine and placed in a stainless steel pressure reactor. A 7.8 g (0.1 mol) sample of sodium sulfide, including approximately 5 mg of ^{35}S-labeled sodium sulfide (0.32 mCi), was placed in a three-necked, round-bottom flask fitted with a dropping funnel, a gas outlet tube, and a stopper. Thirty-five milliliters of concentrated sulfuric acid was added dropwise and the resulting hydrogen sulfide was trapped in the pressure reactor by use of a liquid nitrogen–acetone cold finger condenser. The reactor was sealed, a hydrogen sulfide cylinder was attached, and a pressure of 250 psi of hydrogen sulfide was maintained for 16 h while the temperature was held at 55 °C. The resulting thioethanamide crystals were filtered and recrystallized from ethanol and then from benzene to give 20.7 g of product melting at 114–116 °C (lit.[12] mp 115–116 °C): ^1H NMR (Me_2SO-d_6, Me_4Si), δ 9.2 (br s, 2 H, NH_2), 2.4 (s, 3 H, CH_3).

A 12.2-mg sample of the labeled thioethanamide was dissolved in 100 mL of chloroform. Three samples of 50 μL each were withdrawn and evaporated on separate planchets, mounted, and counted for 1 h. The background activity was 0.51 cpm. The activity of the thioethanamide was determined to be 9.6×10^4 cpm/g.

Trapping Procedure for Carbonyl Sulfide. An aqueous solution, 7.5% in calcium chloride and 1% in ammonium hydroxide, was prepared by adding to 1450 mL of water, 120 g of calcium chloride, and 50 mL of concentrated ammonium hydroxide. The solution was stirred overnight and then filtered to remove the insoluble matter. The solution was divided into two equal parts and each placed into 1-L suction flasks equipped with fritted glass bubblers. The traps were attached in series to the gas outlet tube of the thioacetamide–thiochloroformate reaction vessel. After completion of the major reaction, 100 mL of 10% hydrogen peroxide solution was added to each trap to oxidize the trapped COS to sulfate ion. An excess of barium chloride was added to precipitate the sulfate ions as barium sulfate. The solutions were stirred overnight to promote growth of larger crystals of $BaSO_4$, which were recovered by suction filtration. The IR spectrum agreed with the spectrum reported by Hunt.[13]

To establish the capacity of the trapping solutions, 3.8 g (0.05 mol) of ammonium thiocyanate was placed in a round-bottom flask fitted with a dropping funnel and gas inlet and outlet tubes. The gas outlet tube was attached to fritted glass bubblers placed in the 7.5% calcium chloride, 1% ammonium hydroxide trapping solution. Carrier gas flow was started, and concentrated sulfuric acid was added dropwise (30 min), generating carbonyl sulfide. The yield of $BaSO_4$ was 11.8 g (0.051 mol), 101.2% of theory.

Counting Procedure. Between 0.3 and 0.5 mg of the sample to be counted was placed on a planchet. The planchets were placed under a heat lamp, and chloroform was added and allowed to evaporate to form a thin sample film. The planchets were then mounted and counted. All samples were prepared and counted in triplicate. The counting period ranged from 30 min to 1 h. The background activity was determined to be 0.85 cpm.

Reaction of Ethyl Thiochloroformate (7) with ^{35}S-Labeled Thioethanamide (6). A 3.7-g (0.05 mol) sample of thioethanamide, 0.5 g containing the ^{35}S label, was placed into a 50-mL, three-neck, round-bottom flask fitted with a dropping funnel, a reflux condenser, and gas inlet and outlet tubes. Sufficient chloroform was added to cover the thioethanamide, and the carrier gas (nitrogen or argon) dried by H_2SO_4 was started. The effluent gas was bubbled through the trapping solution. The reaction mixture was heated to reflux and 6.9 g (0.052 mol) of ethyl thiochloroformate was added dropwise (20 min). The mixture was refluxed (1 h), transferred to an Erlenmeyer flask, and cooled. The resulting crystals were filtered (sintered glass), washed with cold chloroform, and stored in a vacuum desiccator. The melting point of the product was 142–143 °C (lit.[14] mp 143.5 °C).

The residual solution was evaporated, and the solid residue present was collected, dried, and stored. No attempt was made to analyze the residue.

The residue, $BaSO_4$, and solution residue were assayed for activity. The averages of multiple determinations are summarized below.

	activity cpm	% of total activity
1	9350	
3	180	1.9
rctn residue	280	3.0
$BaSO_4$	8900	95.2
total	9360	100.1

Ethyl Thioethanimidate Hydrochloride (8). This compound was prepared by the method previously reported.[1] The solid was recrystallized from chloroform: mp 139 °C [lit.[1,14] mp 139–141 °C, 143.5 °C]; NMR ($CDCl_3$) δ 3.5 (q, 2, CH_2), 2.7 (s, 3, CH_3C), 1.4 (t, 3, CH_2CH_3).

Competition Studies. In a 50-mL, three-neck, round-bottom flask fitted with a dropping funnel, a reflux condenser, a drying tube, and a thermometer were placed 7.5 g (0.1 mol) of thioacetamide and 5 mL of chloroform. The mixture was heated to reflux and 12.9 g (0.1 mol) of ethyl chlorothioformate was added dropwise (5 min), followed immediately by dropwise addition of 7.6 g (0.1 mol) of *n*-propyl mercaptan. The mixture was refluxed (25 min), immediately after which 2.0 mL of the reaction mixture was transferred to a 10-mL, single-neck, round-bottom flask and hydrolyzed with 5 mL of pH 5.0 acetate buffer (30 min). Samples of the chloroform layer were analyzed by gas chromatography and components were identified by comparison of retention times with those of authentic samples.

The reaction precipitate was filtered through a sintered glass filter and washed with cold chloroform. The semisolid product was hydrolyzed by the procedure given above

(10) Chaturuedi, R. K.; MacMahon, A. E.; Schmir, G. L. *J. Am. Chem. Soc.* **1967**, *89*, 6984.
(11) Wenzel, F. W., Jr.; Reid, E. E. *J. Am. Chem. Soc.* **1937**, *59*, 1089.
(12) Grasselli, J. E., Ed. "Atlas of Spectral Data and Physical Constants for Organic Compounds"; Chemical Rubber Co.: Cleveland, OH, 1973; p a275.
(13) Hunt, J. M.; Wisherd, M. P.; Bonham, L. C. *Anal. Chem.* **1950**, *22*, 1478.
(14) Hantzsch, A. *Ber. Deutsch. Chem. Ges.* **1931**, *64*, 665.

and gas chromatographic analysis of the hydrolyzate gave results identical with those of direct analysis of the solution.

Competition studies in which the ratio of mercaptan to chlorothioformate was varied were carried out by the procedure above. The molar ratios of mercaptan to chlorothioformate were 0.1:0.2, 0.2:0.1, and 0.5:0.005.

Exchange Study. In a 50-mL, single-neck, round-bottom flask fitted with a reflux condensor and a dropping funnel was placed 13.7 g (0.10 mol) of ethyl thioethanimidate hydrochloride in 5 mL of chloroform. The mixture was heated to reflux and 7.6 g of *n*-propyl mercaptan was added dropwise over a 5-min period. The mixture was refluxed for 1 h. After cooling, 2 mL of the solution was added to 5 mL of acetate buffer and the mixture was stirred for 30 min in a sealed round-bottom flask. The chloroform layer was sampled directly from the reaction flask and analyzed by gas chromatography. Components were identified by comparison of retention time with those of authentic samples. Less than 0.4% of the product was *S*-*n*-propyl thioethanoate and 99.5% was *S*-ethyl thioethanoate.

Conclusions

The determination that the sulfur of thioethanamide appears in carbonyl sulfide eliminated mechanisms II and III as being significant pathways for this reaction since both require the retention of the thioamide sulfur moiety in the thio imino ester product.

The almost total absence of *S*-*n*-propyl thioethanoate in the hydrolysis products from reaction of ethyl thioethanimidate with 1-propanethiol under reaction conditions that lead to thio imino ester formation precludes the possibility that the formation of *n*-propyl thioethanimidate in the competition reactions occurred subsequent to the formation of ethyl thioethanimidate. This is inconsistent with mechanism I in which a concerted cyclic collapse of the intermediate would not be diverted by the presence of other nucleophiles. In the system under study, mechanism IV would require ethanethiol to be the nucleophile sustaining the chain process. Ethanethiol and 1-propanethiol would be expected to have similar steric size and nucleophilicity. Therefore it would be expected to compete effectively with ethanethiol in the nucleophilic attack on intermediate III required by Scheme IV. As the concentration of 1-propanethiol is raised, the chain mechanism would predict that the principal thio imino ester produced be diverted from ethyl thioethanimidate to *n*-propyl thioethanimidate as the second mercaptan becomes the most abundant nucleophile. This is in accord with the results of the competition experiments in which *n*-propyl thioethanimidate, as evidenced by its hydrolysis product, became the dominant product. The ratio of *S*-ethyl to *S*-propyl thioethanoate produced parallels quite closely the ratio *S*-ethyl thiochloroformate to 1-propanethiol. The dominance of *n*-propyl thioethanimidate over ethyl thioethanimidate particularly at lower concentration of 1-propanethiol may be due to a greater nucleophilicity of 1-propanethiol over ethanethiol and/or the higher volatility of the latter, which would favor its escape from the reaction as it is formed.

We believe these labeling and competition studies are only consistent with an ionic chain process involving the formation of a reaction intermediate that undergoes nucleophilic attack to produce the observed products and regenerate the attacking nucleophile.

Acknowledgment. We gratefully acknowledge the support of the Office of Organized Research of East Texas State University. We also thank the Stauffer Chemical Co. for the donation of samples of ethyl thiochloroformate.

Registry No. 6, 62-55-5; 6 (^{35}S), 22456-76-4; 7, 2941-64-2; 8, 5426-05-1; COS, 463-58-1; $H_3CCH_2CH_2SH$, 107-03-9; acetonitrile, 75-05-8; hydrogen sulfide, 7783-06-4.

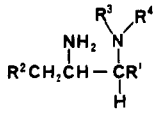
Amidopalladation of Tertiary Allylic Amines and of Terminal Olefins with Phthalimide and *N*-Methyltoluenesulfonamide

Kathlyn A. Parker* and Robert P. O'Fee

Department of Chemistry, Brown University, Providence, Rhode Island 02912

Received July 26, 1982

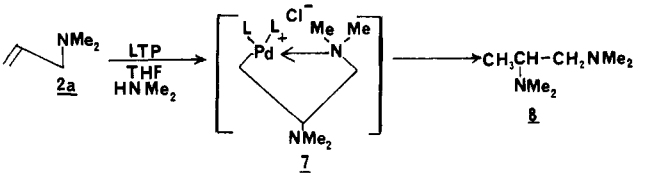
Our interest in the synthesis of quinonoid alkaloids such as naphthyridinomycin,[1] the saframycins,[2] and the reneiramycins[3] led us to consider methods for the synthesis of unsymmetrical 1,2-diamines. In particular, we wished to prepare substrates of general structure **1** in which one amino group is tertiary and the other is primary.



1

Application of the aminopalladation reaction to the double bond of an allylic amine appeared to be a potential solution to this problem. Oxypalladation[4] and carbopalladation[5] of allylic amines had been shown to be regiospecific (**2** → **3**); therefore, one might expect that aminopalladation also would proceed to the five-membered palladocycle. Further transformation could lead to a variety of functional group arrays (e.g., **4**,[6] **5**,[5] and **6**[7], Scheme I).

In fact, aminopalladation of allylic amine **2a** with lithium tetrachloropalladate (LTP) in tetrahydrofuran at 25 °C followed by hydrogenation gave diamine **8** in 60% yield. Presumably the reaction proceeds via the palladocycle **7**.



Difficulty was anticipated, however, in extending this aminopalladation to an addition in which a primary amine

(1) (a) Kluepfel, D.; Baker, H. A.; Piattoni, G.; Sehgal, S. N.; Sidorowicz, A.; Kingh, K.; Vezina, C. *J. Antibiot.* **1975**, *28*, 497. (b) Sygusch, J. *Ibid.*, **1975** errata, no. 3. (c) Sygusch, J.; Brisse, F.; Hanessian, S. *Acta Crystallogr., Sect. B* **1976**, *B32*, 1139.

(2) (a) Arai, T.; et al. *J. Antibiot.* **1977**, *30*, 1015. (b) Arai, T.; et al. *Tetrahedron Lett.* **1979**, 2355. (c) Arai, T.; et al. *Experientia* **1980**, *36*, 1025. (d) Arai, T.; et al. *J. Antibiot.* **1980**, *33*, 951. (e) Ishigura, K.; Sakiyama, S.; Takahashi, K.; Arai, T. *Biochemistry* **1978**, *17*, 2545.

(3) Frincke, J. M.; Faulkner, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 265.

(4) Cope, A. C.; Kliegman, J. M.; Friedrich, E. C. *J. Am. Chem. Soc.* **1967**, *89*, 287.

(5) Holton, R. A.; Kjonaas, R. A. *J. Am. Chem. Soc.*, *99*, **1977**, 4177.

(6) Åkermark, B.; Bäckvall, J. E.; Hegedus, L. S.; Zetterberg, K.; Sirala-Hansen, K.; Sjöberg, K. *J. Organomet. Chem.* **1974**, *72*, 127.

(7) (a) Bäckvall, J. E. *Tetrahedron Lett.* **1975**, 2225. (b) Bäckvall, J. E. *Tetrahedron Lett.* **1978**, 163. (c) Bäckvall, J. E.; Bjorkman, E. F. *J. Org. Chem.* **1980**, *45*, 2893. (d) Bäckvall, J. E. *J. Chem. Soc., Chem. Commun.* **1977**, 413. For the stereochemistry of aminopalladation, see: Akermark, B.; Bäckvall, J. E.; Siirala-Hansen, K.; Sjoberg, J.; Zetterberg, K. *Tetrahedron Lett.* **1974**, 1363.

0022-3263/83/1948-1547$01.50/0