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

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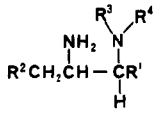
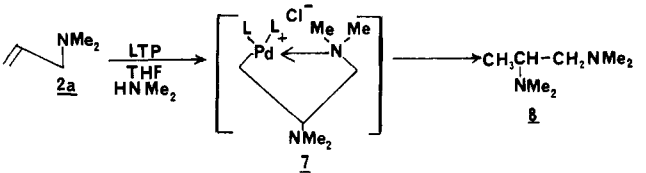
Our interest in the synthesis of quinonoid alkaloids such as naphthyridinomycin,[1] the saframycins,[2] and the reneiramycins[3] led us to consider methods for the synthesis of unsymmetrical 1,2-diamines. In particular, we wished to prepare substrates of general structure **1** in which one amino group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

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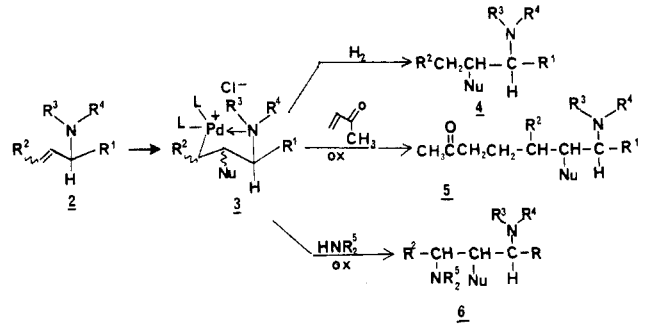
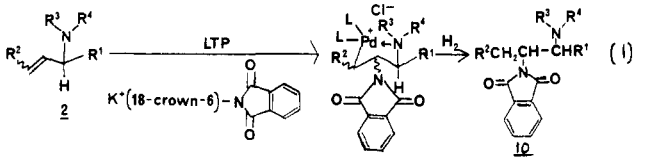
0022-3263/83/1948-1547$01.50/0

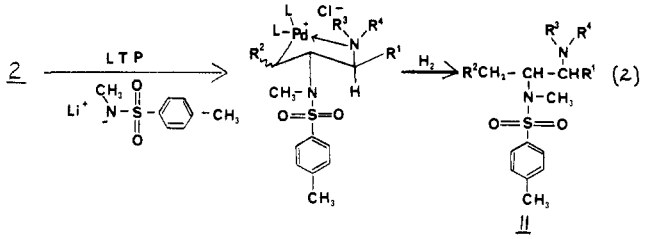
Scheme I



is the nucleophile. For simple terminal olefins, the additions of active methylene compounds[5] and of secondary amines[6] are high-yield processes (poorer yields are reported for additions of secondary amines to disubstituted olefins[6,7a-c]). The addition of primary amines to terminal olefins proceeds with unacceptably low yields; addition of ammonia has been reported to give only 5% of the desired amine.[6] We decided therefore to investigate the "amidopalladation" of tertiary allylic amines with nucleophiles which were synthetically equivalent to ammonia and primary amines.

The regiospecific additions of phthalimide (eq 1) and *N*-methyltoluenesulfonamide (eq 2) to tertiary allylic amines are discussed below.





Addition of Phthalimide to Tertiary Amines. Initial attempts to add phthalimide to allylic amine **2a** were conducted by adding potassium phthalimide to the potassium tetrachloropalladate (LTP) complex of **2a** in THF; in these early experiments no reaction was observed. We attributed this lack of reactivity to the fact that potassium phthalimide is insoluble in THF, and we therefore attempted to effect dissolution of the reagent by adding crown ether and acetonitrile to the THF solution. We found that the 18-crown-6/potassium phthalimide complex[8] was soluble in 1:1 THF/acetonitrile at temperatures slightly above the ambient. Furthermore, when the amine-LTP complex was treated with the crown ether complex of potassium phthalimide in THF/acetonitrile and the resulting mixture was stirred under hydrogen gas, the basic product **10a** was isolated in 39% yield.

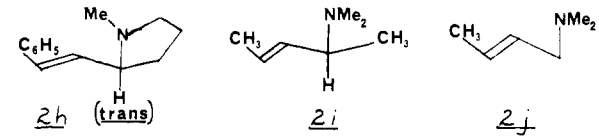
Alternative procedures were also successful. The use of the bis (acetonitrile)palladium(II) chloride complex of allylamine **2a** with the 18-crown-6/potassium phthalimide complex gave a quantitive yield of the substituted phthalimide **10a**. The use of the LTP complex of amine **2a** with the tetrabutylammonium salt of phthalimide (see Experimental Section) also resulted in a quantitative yield of the protected diamine **10a**.

Table I. Addition of Phthalimide to Tertiary Allylic Amines

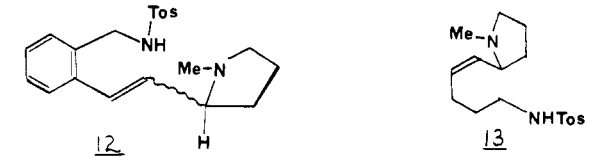
substrate	procedure	adduct	yield, %
2a ($R^1 = R^2 = H$; $R^3 = R^4 = CH_3$)	A[a]	**10a**	39
2a	B[b]	**10a**	99
2b ($R^1,R^4 = CH_2CH_2CH_2$; $R^2 = H$; $R^3 = CH_3$)	A	**10b**	95
2c ($R^1 = R^2 = H$; $R^3,R^4 = CH_2CH_2CH_2CH_2$)	A	**10c**	89
2d ($R^1 = R^2 = H$; $R^3 = CH_3$; $R^4 = n$-Bu)	A	**10d**	60
2e ($R^1 = R^2 = H$; $R^3 = CH_3$; $R^4 = CH_2C_6H_5$)	A	**10e**	63

[a] Procedure A: (1) LTP, potassium phthalimide, 18-crown-6, acetonitrile, THF; (2) H_2. [b] Procedure B: (1) LTP, tetrabutylammonium phthalimide, THF; (2) KBH_4.

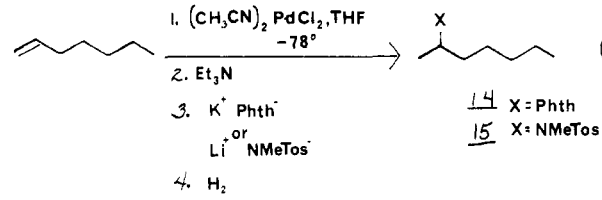
To test the generality of this reaction, we subjected a number of tertiary allylamines to the amidopalladation/hydrogenation sequence (Table I). In each of these cases, a substituted phthalimide was isolated in fair to excellent yield (these yields were not maximized). We were unable to isolate phthalimide adducts when amines **2h–j**, in which the double bond in the starting material is not terminal, were subjected to the same reaction conditions.



Addition of *N*-Alkyltoluenesulfonamide to Tertiary Allylic Amines. Addition of a primary amine equivalent to allylamines was also examined. The lithium salt of *N*-methyltoluenesulfonamide adds to the LTP complex of *N,N*-dimethylallylamine (**2a**) in THF to give, after reduction with KBH_4, the substituted toluenesulfonamide **11a** ($R^1 = R^2 = H$, $R^3 = R^4 = CH_3$) in 68% yield (eq 2, above). However, efforts to extend this reaction to cyclization to tosylamides **12** and **13** (in whch the olefin is nonterminal) have been unsuccessful to date.



Addition of Phthalimide and *N*-Methyltoluenesulfonamide to Isolated Terminal Double Bonds. We also tested our ammonia and primary amine equivalents in additions to isolated double bonds (eq 3). These reactions are capricious. However, modest yields of adducts may be obtained reproducibly if the nucleophile is added very slowly at −78 °C to a complex from the olefin, $(CH_3CN)_2PdCl_2$, and triethylamine[9] in THF.



(8) A procedure for the preparation of potassium 18-crown-6/potassium phthalimide is included in the Experimental Section. Subsequent to our preparation and use of this reagent in amidopalladation, Rasshofer and Vögtle reported its application as an improved phthalimide nucleophile. See: Rasshofer, N.; Vögtle, F. *Tetrahedron Lett.* **1978**, 1217.

Thus, 1-heptene was converted to phthalimide **14** in 37% yield and to toluenesulfonamide **15** in 32% yield (yields based on $PdCl_2$).

Experimental Section

General Methods. All reactions were carried out under a positive pressure of dry nitrogen or argon. Solvents were dried as follows: methylene cloride was distilled from barium oxide; ether, benzene, and pyridine were distilled from calcium hydride; tetrahydrofuran (THF) was distilled from sodium/benzophenone.

NMR spectra were recorded on a Varian A-60 or EM-360 spectrometer. Infrared spectra were obtained on a Perkin-Elmer 257 grating instrument or a Perkin-Elmer 681 spectrometer. Mass spectra were recorded at 50 eV on a Hitachi Perkin-Elmer mass spectrometer at the Regional Mass Spectroscopy Center at the University of Pennsylvania.

Reagents. Lithium tetrachloropalladate was prepared by stirring palladium(II) chloride and 2 equiv of lithium chloride in water with heating. The resulting dark red solution was cooled and filtered. The filtrate was evaporated to dryness, and the residual red-purple solid was pulverized and dried in a drying pistol. Bis(acetonitrile)palladium(II) chloride was prepared by stirring palladium(II) chloride overnight in refluxing acetonitrile under argon. The yellow precipitate was collected and dried at reduced pressure. The 18-crown-6 complex of potassium phthalimide[8] was prepared by stirring potassium phthalimide and 1 equiv of crown ether for 2 h in refluxing acetonitrile. The resulting solution was evaporated to dryness. The white residue was recrystallized from acetronitrile. A procedure for the preparation of tetrabutylammonium sulfinates[10] was modified for the preparation to tetrabutylammonium phthalimide. The product was a glass which eventually crystallized (mp 52–55 °C) on standing.

Procedure A: 2-(2-Phthalimidoethyl)-*N*-methylpyrrolidine (10b). To a solution of 290 mg (1.10 mmol) of lithium tetrachloropalladate in 5 mL of THF was added 85 mg (1.1 mmol) of *N*-methyl-2-vinylpyrrolidine in 5 mL of THF. Upon addition a yellow precipitate was observed to form and then to dissolve after a few seconds. (Care must be taken to avoid adding the amine too quickly!) After complete addition, the homogeneous red solution was stirred for 35 min and treated with a solution of 256 mg (1.5 mmol) of potassium phthalimide in 10 mL of THF/5 mL of acetonitrile containing sufficient 18-crown-6 to ensure solvation. Upon addition of the nucleophile, the reaction mixture became orange-red and slightly turbid. After being stirred overnight, the reaction mixture was stirred under 1 atm of hydrogen for 6 h. The granular palladium black was removed by filtration and the solution diluted with ether. The ethereal solution was washed with aqueous potassium hydroxide, water, and brine. The clear, colorless organic phase was dried and concentrated. Crystallization from hexane gave 265 mg (95%) of **10b**: mp 108–109 °C; NMR ($CDCl_3$) δ 7.80 (m, 4 H), 4.28 (br q, J = 6 Hz, 1 H), 3.00 (m, 3 H), 2.50 (s, 3 H), 1.78 (m, 4 H), 1.57 (d, J = 6 Hz, 3 H); IR ($CHCl_3$) 2940, 1790, 1740, 1640 cm^{-1}; high-resolution mass spectrum, calcd for $C_{15}H_{18}N_2O_2$ m/e 258.1367, found 258.1358.

Also from Procedure A: *N*-(2-Phthalimidopropyl)pyrrolidine (10c). Distillation at 120–123 °C (1 mm) afforded 89% of an orange oil: NMR ($CDCl_3$) δ 7.80 (m, J = 2 Hz, 4 H), 4.57 (m, 1 H), 3.48 (m, 2 H), 2.57 (m, 4 H), 1.68 (m, 4 H), 1.47 (d, J = 6 Hz, 3 H); IR (film) 2890, 1780, 1720, 1620 cm^{-1}. Anal. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.75; H, 7.02; N, 10.85. Found: C, 69.72; H, 7.17; N, 10.75.

1-(*N*-Methylbutylamino)-2-phthalimidopropane (10d). Distillation at 95 °C (0.75 mm) gave 60% of an orange oil: NMR ($CDCl_3$) δ 7.72 (m, 4 H), 4.50 (m, 1 H), 3.08 (m, 2 H), 2.55 (m, 2 H), 2.17 (s, 3 H), 1.42 (d, J = 6 Hz, 3 H), 1.17 (m, 7 H); IR (film) 3020, 1790, 1740, 1490 cm^{-1}; high-resolution mass spectrum, calcd for $C_{16}H_{22}N_2O_2$ m/e 274.1681, found 274.1687.

1-(*N*-Methylbenzylamino)-2-phthalimidopropane (10e). Distillation at 170 °C (0.65 mm) afforded 63% of a viscous, yellow oil: NMR ($CDCl_3$) δ 7.77 (m, 4 H), 7.20 (s, 5 H), 4.60 (m, 1 H), 3.62 and 3.32 (AB q, $J \approx$ 14 Hz, 2 H), 2.43 (m, 2 H), 2.20 (s, 3 H), 1.67 (d, J = 8 Hz, 3 H); IR (film) 3000, 1790, 1710 cm^{-1}; high resolution mass spectrum, calcd for $C_{19}H_{20}N_2O_2$ m/e 308.1524, found 308.1539.

Procedure B: 1-(Dimethylamino)-2-phthalimidopropane (10a). A solution of 0.234 mL (1.8 mmol) of *N,N*-dimethylallylamine in 10 mL of dry THF was added slowly with stirring to a solution of 470 mg (1.8 mmol) of lithium tetrachloropalladate in 25 mL of THF. The resulting orange-red solution was stirred at room temperature for 15 min. Then 776 mg (2.0 mmol) of tetra-*n*-butylammonium phthalimide in 30 mL of THF was added to the reaction mixture. The homogeneous solution was stirred for 6 h, and 97 mg (1.8 mmol) of potassium borohydride was added, followed by 2 mL of a 0.9 N solution of potassium hydroxide. The reaction mixture was stirred for 30 min. At this time the palladium black was removed by filtration, and the filtrate was passed through a short pad of Celite/Norit. The resulting clear solution was diluted with ether and washed with 10% KOH, water, and brine. After being dried ($MgSO_4$), the ethereal solution was concentrated to afford a light yellow crystalline solid. Recrystallization from $CHCl_3$/hexane gave 408 mg (99%) of analytically pure material: mp 98–99 °C; NMR ($CDCl_3$) δ 7.86 (m, J = 3 Hz, 4 H), 4.41 (m, 1 H); 3.10 (m, 2 H), 2.15 (s, 6 H), 1.42 (d, J = 6 Hz, 3 H); IR (film) 3030, 1785, 1710, 1580, 1400 cm^{-1}; mass spectrum, m/e 232 (M^+) and 58 (base peak). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.15; H, 6.92; N, 11.90.

2-Phthalimidoheptane (14). To 500 mg (2.0 mmol) of bis(acetonitrile)dichloropalladium in 150 mL of dry THF under argon was added 786 mg (8.0 mmol) of 1-heptene. The solution stirred until homogeneous (10 min). The amber-red reaction mixture was cooled to −80 °C and treated with 405 mg (4.0 mmol) of triethylamine in 2 mL of THF (precooled to −80 °C). After vigorous stirring of the reagents, 1.80 g (4.0 mmol) of the 18-crown-6 complex of potassium phthalimide was added while the reaction temperature remained below −60 °C. After 2 h at −60 °C, the reaction vessel was flushed with hydrogen and then maintained under a hydrogen atmosphere overnight. The palladium black was removed by filtration, and the filtrate was diluted with ether. The ethereal solution was washed with base, water, and brine and then finally dried. Concentration and subsequent distillation at 141 °C (1 mm) afforded (37%) of a clear, colorless oil: NMR ($CDCl_3$) δ 7.38 (m, 4 H), 4.35 (m, 1 H), 1.46 (d, J = 6 Hz, 3 H), 1.20 (br m, 11 H); IR (film) 3000, 1790, 1730, 1620 cm^{-1}; mass spectrum, m/e 245. Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.28; H, 7.92; N, 5.52.

2-(*N*-Methyl-*p*-toluenesulfonamido)heptane (15). To 500 mg (2.0 mmol) of bis(acetonitrile)dichloropalladium in 100 mL of dry THF (stirred under argon until homogeneous, 10 min) was added 393 mg (4.0 mmol) of 1-heptene (neat) over 10 min. The reaction mixture was then cooled to −80 °C; after 10 min, 405 mg (4.0 mmol) of triethylamine in 1 mL of THF (precooled to −80 °C) was added. The resulting amber solution was stirred at −80 °C for 15 min. Then, 467 mg (1.5 mmol) of lithium *N*-methyl-*p*-toluenesulfonamide was added slowly while the reaction temperature was maintained below −60 °C. After 90 min at −60 °C the cold bath was removed, and the reaction vessel was flushed with hydrogen. The solution was maintained under a hydrogen atmosphere overnight. Palladium black was removed by filtration, and the yellow filtrate was washed in 1 N sodium hydroxide, water, and brine. After the mixture was dried ($MgSO_4$), concentration afforded a greenish yellow oil which was chromatographed on silica gel to yield 182 mg (32%) of a yellow oil: bp 140 °C (0.75 mm); NMR ($CDCl_3$) δ 7.45 (m, 4 H), 2.61 (s, 3 H), 2.33 (br s, 4 H), 1.00 (m, 14 H); IR (film) 3039, 2980, 1610 cm^{-1}; mass spectrum, m/e 283. Anal. Calcd for $C_{15}H_{25}NSO_2$: C, 63.56; H, 8.89; N, 4.94. Found: C, 63.65; H, 9.05; N, 4.91.

1-(Dimethylamino)-2-(*N*-methyl-*p*-toluenesulfonamido)propane (11a). A 256-mg sample (3.0 mmol) of *N,N*-dimethylallylamine was added slowly with stirring to a solution of 785 mg (3.0 mmol) of LTP in 25 mL of THF. The reaction mixture was stirred for 15 min at room temperature. Then, 570 mg (3.0 mmol) of lithium *N*-methyl-*p*-toluenesulfonamide in 10 mL of THF was added, and the reaction mixture was stirred overnight. To this was added 162 mg (3.0 mmol) of potassium

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(10) Vennstra, G. E.; Zwaneburg, B. *Synthesis* **1975**, 519.

borohydride followed by 3.3 mL of 0.9 N KOH. After 30 min the palladium black was removed by filtration. The organic solution was extracted with 10% HCl, and the aqueous fractions were collected, neutralized, and extracted with ether. The ethereal solution was dried, concentrated, and distilled at 120–122 °C (4 mm) to give 550 mg (68%) of a yellow oil: NMR ($CDCl_3$) δ 7.35 (m, J = 8 Hz, 4 H), 4.20 (m, 1 H), 2.71 (s, 3 H), 2.45 (s, 3 H); 2.21 (br s, 8 H), 0.95 (d, J = 6 Hz, 3 H); IR (film) 2980, 1610, 1480, 1350 cm^{-1}; mass spectrum, m/e 270 (M^+). Anal. Calcd for $C_{13}H_{22}N_2O_2S$: C, 57.75; H, 8.20; N, 10.36; S, 11.86. Found: C, 57.76; H, 8.42; N, 10.30; S, 11.90.

Acknowledgment. We acknowledge helpful discussions with Professor Robert Holton (Virginia Polytechnic Institute) and Professor Louis Hegedus (Colorado State University). This work was supported by the National Institutes of Health (Grant No. AI-18665). K.A.P. is pleased to acknowledge additional support in the form of a Teacher-Scholar Award from the Camille and Henry Dreyfus Foundation.

Registry No. **2a**, 2155-94-4; **2b**, 85151-07-1; **2c**, 24420-11-9; **2d**, 24209-62-9; **2e**, 2520-97-0; **10a**, 3337-93-7; **10b**, 85151-08-2; **10c**, 85151-09-3; **10d**, 85151-10-6; **10e**, 85151-11-7; **11a**, 85151-12-8; **14**, 85151-13-9; **15**, 85151-14-0; LTP, 15525-45-8; $PdCl_2$, 7647-10-1; LiCl, 7447-41-8; $(CH_3CN)_2PdCl_2$, 14592-56-4; potassium phthalimide, 1074-82-4; tetra-*n*-butylammonium phthalimide, 85151-15-1; 1-heptene, 592-76-7.

Preparation of Methyl Ketones by the Sequential Treatment of Carboxylic Acids with Methyllithium and Chlorotrimethylsilane

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One of the major problems associated with the transformation of carboxylic acids 1 into the corresponding methyl ketones 2 using methyllithium has been the co-

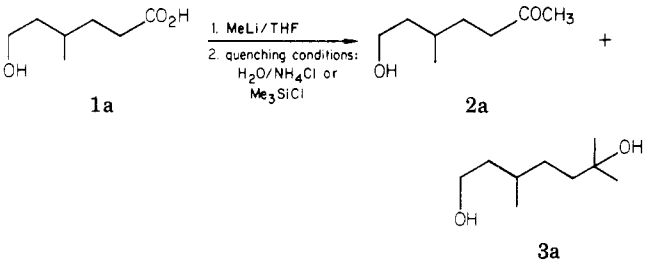
$$\underset{\mathbf{1}}{RCO_2H} \xrightarrow[2.\ H_3O^+]{1.\ MeLi} \underset{\mathbf{2}}{RCOCH_3} + \underset{\mathbf{3}}{RCOH(CH_3)_2}$$

production of unwanted tertiary alcohols **3**.[1] If addition of methyllithium to **1** is slow enough to insure complete conversion of the acid into the lithium carboxylate before carbonyl addition by a second equivalent of methyllithium occurs, then the formation of **3** is thought to result from the slow hydrolysis rate of methyllithium relative to the breakdown of **4** into methyl ketone, thus affording **3** during

$$\underset{\mathbf{4}}{RC(OLi)_2CH_3}$$

the workup procedure.[1] Quenching of the reaction medium by addition to dilute acid with rapid stirring has been one successful method of minimizing production of **3**.[2] The use of theoretical amounts of methyllithium,[3] preformed lithium carboxylates,[4] and THF as solvent to increase carboxylate solubility[5] has also been employed to avoid **3** formation. This last approach is especially useful when the carboxylic acid in question also contains hydroxy functionality.[6] Hydroxy acids necessitate the use of 1 equiv (at least) of methyllithium for each OH group present in the molecule as well.[7] Also, with hydroxy acids, recovery of starting material in addition to **3** can be a problem.[8]

We felt that it might be possible to subvert the production of **3** by using a somewhat different approach, namely, quenching the reaction mixture with a large excess of chlorotrimethylsilane (Me_3SiCl). The reaction of Me_3SiCl with any excess methyllithium should be extremely fast, thereby leaving no organometallic to react with ketone **2** in the subsequent aqueous workup step. To test the feasibility of the method, hydroxy acid **1a** was



	% 2a	% 3a
H_2O/NH_4Cl	63	37
Me_3SiCl	91	9

treated with 6.5 equiv of methyllithium at 0 °C. A portion of the resulting mixture was quenched by slow addition to saturated aqueous ammonium chloride with rapid stirring. GC analysis of the resulting mixture revealed a methyl ketone, **2a**, to tertiary alcohol, **3a**, ratio of 63:37. When the remainder of the reaction mixture was quenched with a large excess of Me_3SiCl (ca. 10 equiv) followed by aqueous workup using saturated aqueous ammonium chloride, the ratio of **2a** to **3a** was 91:9.

Encouraged by these preliminary findings, we have tested the method with a number of carboxylic acids and have found the results to be uniformly good. The results of the study are summarized in Table I and deserve some comment. In the cases we studied, the maximum amount of **3** formed was in the range of 10% (see Table I). The method gives excellent yields of pure **2** from hydroxy acids, phenolic acids, alkanoic acids, and aromatic acids. In no case was any trace of starting acid **1** observed upon workup. It is important to note that we made no attempt to minimize the quantities of either methyllithium or Me_3SiCl used. It was our intent to show that methyl ketones can be obtained even when a large excess of methyllithium is employed. It is to be expected that the amount of methyllithium used could be closer to the calculated stoichiometric value for the reagent.[3] This approach, which might well be important for large-scale reactions, would also reduce the amount of Me_3SiCl needed to ensure success. We have not explored the use of any solvent other than THF. One failure of the method was encountered

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(3) See, for instance: van Dorp, D. A.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1946**, *65*, 1607; and other references cited in ref 1.
(4) (a) House, H. O.; Bare, T. M. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, p 775. (b) Levine, R.; Karten, M. J.; Kadunce, W. M. *J. Org. Chem.* **1975**, *40*, 1770.
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