A second decomposition mixture was dissolved in benzene, *m*-tolyl *m*-trifluoromethylbenzenesulfonate was added to an aliquot as an internal standard, and analysis by GLC on 5% SE-30 on Chromosorb W (Table I) showed successive peaks for *m*-trifluoromethylphenol and *m*-trifluoromethylphenyl *m*-trifluoromethylbenzenesulfonate. When absolute ethanol was added before GLC analysis, a new peak for ethyl *m*-trifluoromethylbenzenesulfonate appeared between the other two peaks and the peak for *m*-trifluoromethylphenol approximately doubled in area.

A second aliquot of the benzene solution of the reaction mixture was concentrated, methylene chloride was added, and the solution was extracted twice with water and once with 5% aqueous potassium hydroxide. The aqueous alkaline extract and the two water washes were combined and evaporated to dryness in a rotary evaporator. A portion of this residue was dissolved in 10 ml of water and adjusted to pH 6 with hydrochloric acid. This solution was cooled in an ice bath and added to a cold solution of *S*-benzylthiouronium chloride (5.0 g) in water (30 ml). The tan precipitate which formed was collected, dried, and recrystallized from hot 25% ethanol to give *S*-benzylthiouronium 2-hydroxy-4-trifluoromethylbenzenesulfonate (mp 193–194°). The mother liquor from the tan precipitate yielded *S*-benzylthiouronium *m*-trifluoromethylbenzenesulfonate (mp 133–134°). These salts were identified by melting point and ir spectra.

A new reaction mixture was prepared and concentrated, methylene chloride was added, and the methylene chloride solution was extracted twice with water and once with 5% aqueous potassium hydroxide. The combined aqueous layers were evaporated to dryness using a rotary evaporator. The solid residue was dissolved in a minimum amount of water (less than 10 ml), the solution was adjusted to pH 6 with hydrochloric acid, and a cold solution of *S*-benzylthiouronium chloride (3.0 g) in water (15 ml) was added. The precipitate which formed from this minimum amount of solution was collected by filtration, dried, and analyzed by ir using the base line technique to determine the relative amounts of the two component sulfuric acid salts.

Acknowledgment. We wish to express our thanks to Dr. Robert L. Waller for providing some of the kinetic data.

Registry No.—1, 35673-10-0; 5, 55400-69-6; *m*-trifluorobenzenesulfonyl chloride, 777-44-6; phenol, 108-95-2; *o*-ethylphenol, 90-00-6; *m*-ethylphenol, 620-17-7; *p*-ethylphenol, 123-07-9; *o*-cumenol, 88-69-6; *m*-cumenol, 618-45-1; *p*-cumenol, 99-89-8; *m*-trifluoromethyphenol, 98-17-9; ethanol, 64-17-5; *S*-benzylthiouronium chloride, 538-28-3; *S*-benzylthiouronium 2-hydroxy-4-trifluoromethylbenzenesulfonate, 55400-70-9; *S*-benzylthiouronium *m*-trifluoromethylbenzenesulfonate, 2342-60-1; benzene, 71-43-2; cumene, 98-82-8; ethylbenzene, 100-41-4.

References and Notes

(1) (a) Presented at the International Conference on the Mechanisms of Reactions in Solution at the University of Kent at Canterbury, July 1970. Taken in part from the Ph.D thesis of P. K. T., 1970. (b) For the previous paper of this series see R. L. Dannley, R. V. Hoffman, P. K. Tornstrom, R. L. Waller, and R. Srivastava, *J. Org. Chem.*, **39**, 2543 (1974). (c) NDEA Fellow, 1966–1969. This work supported in part by National Science Foundation Grant GP-19018.
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Preparation and Hydrolysis of Aminocyclopropyl and Aminocyclobutyl Sulfones[1]

Ronald H. Rynbrandt* and Fred E. Dutton

Diabetes and Atherosclerosis Research, The Upjohn Company, Kalamazoo, Michigan 49001

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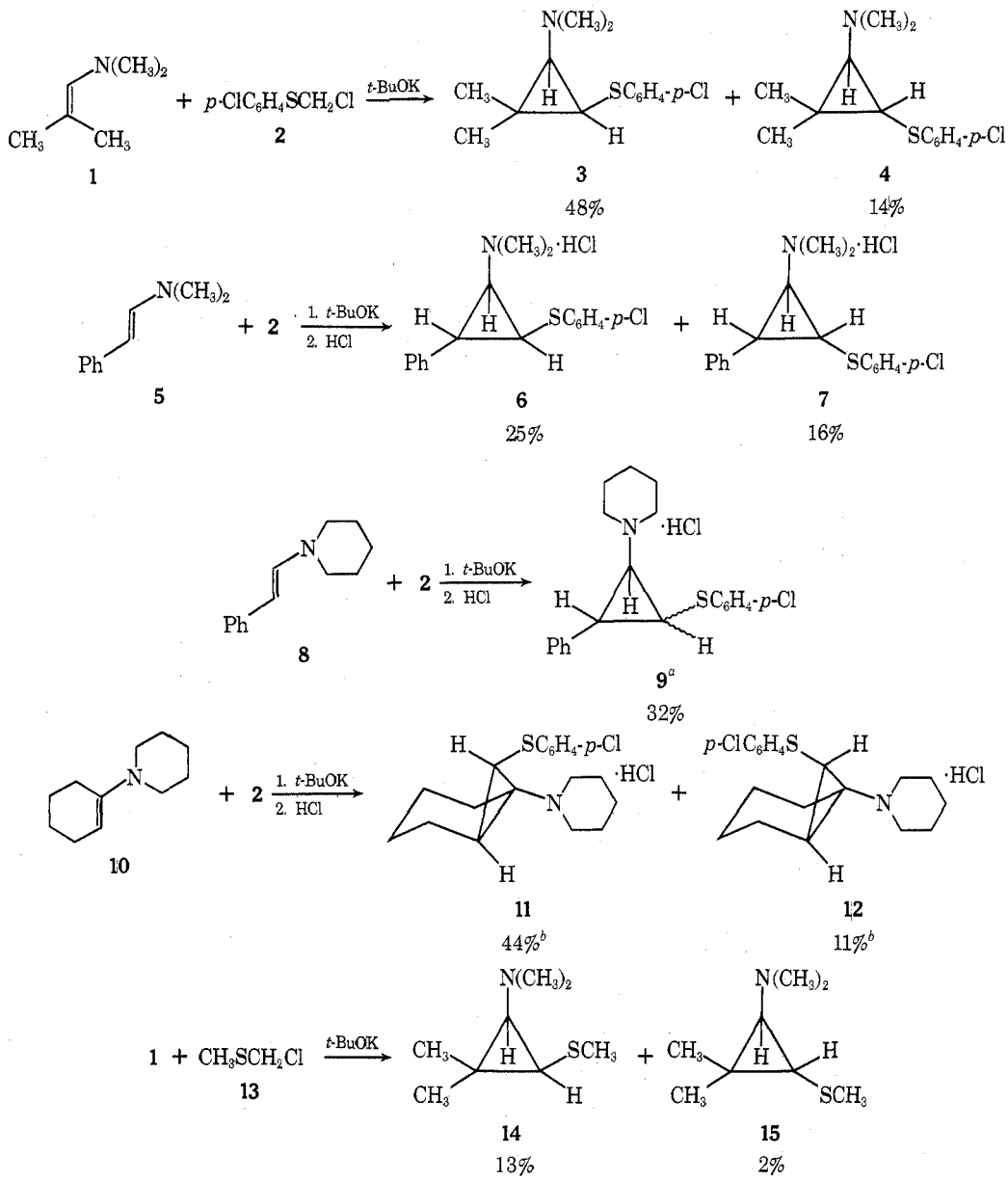
This report describes (1) the synthesis of aminocyclopropyl sulfides and their aqueous potassium permanganate oxidation to afford ring-opened sulfone acids and ketones; (2) the synthesis and facile hydrolysis of an aminocyclopropyl sulfone to afford a ring-opened aldehyde; and (3) the synthesis and hydrolysis of aminocyclobutyl sulfones to afford ring-opened aldehydes. It is proposed that these ring-opening reactions occur via zwitterionic intermediates.

There has been recent interest in the ring opening of cyclopropanes via zwitterionic intermediates.[1b-6] Ring-opening reactions of cyclopropylamines have also received recent attention.[1b,3,5-9] However, all of these systems require elevated temperatures and/or acidic or basic conditions. In contrast, we have found that aminocyclopropyl sulfones undergo a facile hydrolytic ring opening at room temperature. This report describes (1) the synthesis of aminocyclopropyl sulfides and their aqueous potassium permanganate oxidation to afford ring-opened products; (2) the synthesis and facile hydrolysis of an aminocyclopropyl sulfone; and (3) the synthesis and hydrolysis of aminocyclobutyl sulfones. We propose that these ring-opening reactions occur via zwitterionic intermediates, and discuss the factors influencing zwitterion formation.

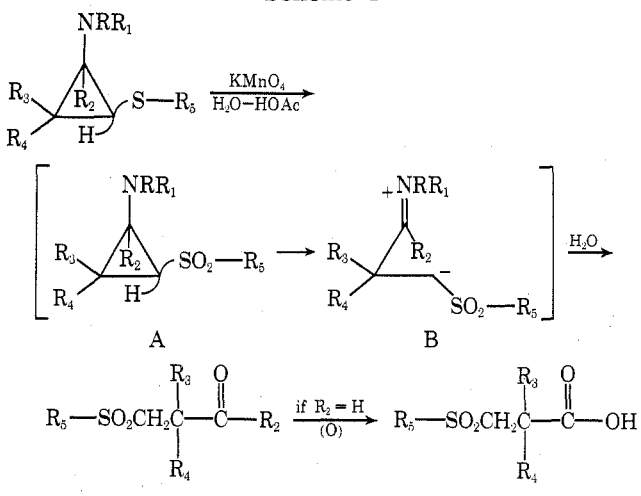
Preparation and Aqueous Potassium Permanganate Oxidation of Aminocyclopropyl Sulfides. The reaction of thiocarbenes (or carbenoids[10]), generated from chloromethyl sulfides and potassium *tert*-butoxide in ether, with enamines afforded the aminocyclopropyl sulfides shown in Table I. The yields ranged from poor to good, the lowest being observed with chloromethyl methyl sulfide. Rationale for the configurational assignments and an explanation for the observed stereoselectivities have been presented.[1a] Oxidation of the aminocyclopropyl sulfides **3**, **9**, and **11** + **12** with potassium permanganate in aqueous acetic acid at 25–30° afforded ring-opened sulfone acids and/or ketones in good yields. The products and yields are summarized in Table II. Structural proof for the products has been previously described.[1b] These conversions can be best

Table I
Conversion of Enamines to Aminocyclopropyl Sulfides

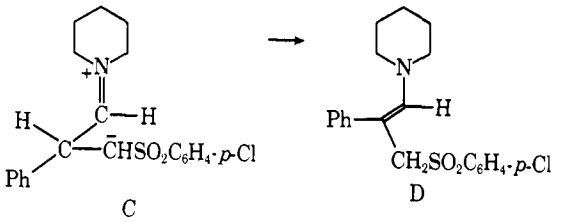


[a] Stereochemistry unassigned. [b] Isomer ratio based on ^{1}H NMR; quantitative separation not accomplished.

Scheme I

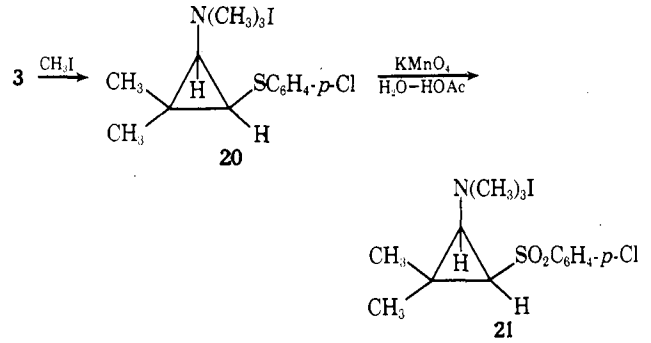


rationalized by initial formation of an aminocyclopropyl sulfone intermediate (A) which subsequently opened to a zwitterionic intermediate (B). Reaction of the zwitterion with water would afford the ring-opened aldehyde or ketone. In the cases where R_2 = H, the aldehyde would then be oxidized to the acid. This mechanistic sequence is summarized in Scheme I. The reaction of **9** to afford **18** as the major product deserves special consideration. The oxidative decarboxylation of **17** into **18** is not the major pathway for the formation of **18**, since treatment of **17** under identical reaction conditions afforded only a 14% yield of **18** with a 60% recovery of **17**. The formation of the major portion of **18** can be rationalized by the oxidative cleavage of the enamine intermediate D. Acid **17** presumably arose from intermediate C in a manner analogous to the formation of **16**. Presumably a major driving force for these ring-opening reactions is the formation of well-stabilized zwitterionic intermediates. Evidence for zwitterion involvement was ob-



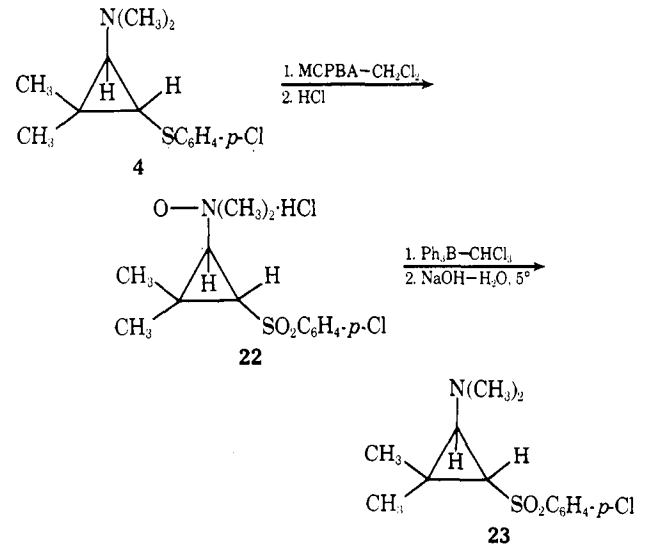
C D

tained when the quaternary ammonium salt **20**, a compound in which the electron pair of the nitrogen atom is not available for zwitterion stabilization, was submitted to similar oxidizing conditions (see Experimental Section). The product obtained (63% yield) was the unopened sulfone **21**.



20 **21**

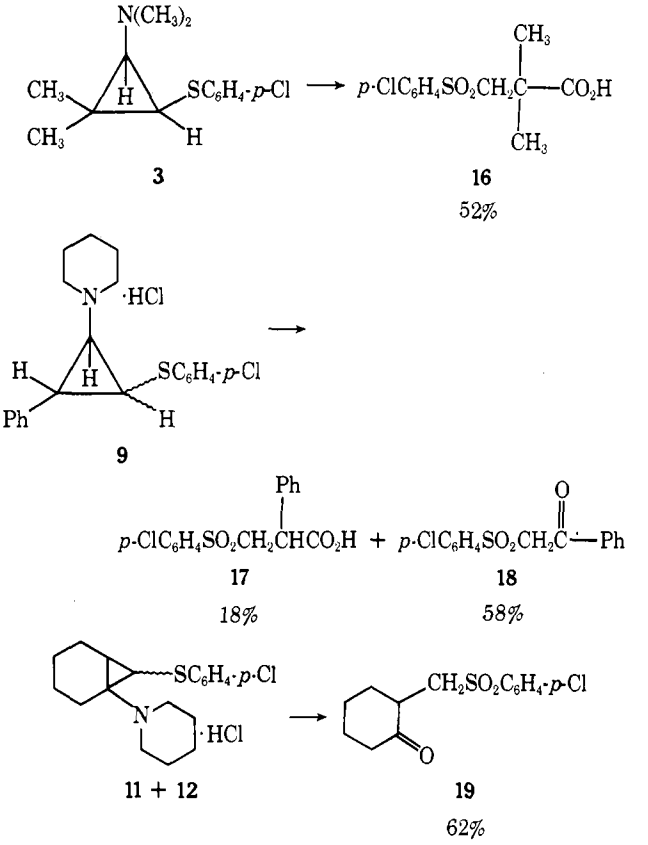
Preparation and Hydrolysis of Aminocyclopropyl Sulfones. With the presumption that aminocyclopropyl sulfones were a relatively unstable class of compounds, we set out to prepare examples of this class of compounds utilizing the mildest conditions we could envisage. Oxidation of *trans*-2-[(*p*-chlorophenyl)thio]-*N*,*N*,3,3-tetramethylcyclopropylamine (**4**) with 2 equiv of *m*-chloroperoxybenzoic acid (MCPBA) in chloroform at 5° afforded a complex, inseparable mixture of products. However, treatment with 4.5 equiv of MCPBA at −60° with slow warming to room temperature afforded a 75% yield of the amine oxide sulfone **22** (isolated as the hydrochloride). Amine oxides have



4 **22** **23**

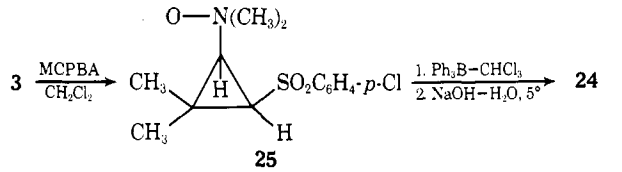
been used to oxidize triarylboranes to the corresponding boric esters.[11] This suggested that a triarylborane, such as the commercially available triphenylborane,[12] could be used to reduce amine oxides to the corresponding amines under nonhydrolytic conditions. Indeed, treatment of **22** with triphenylborane in chloroform at room temperature followed by treatment with cold, aqueous sodium hydroxide solution afforded a 79% yield of *trans*-2-[(*p*-chlorophenyl)sulfonyl]-*N*,*N*,3,3-tetramethylcyclopropylamine (**23**). This compound was extremely sensitive to atmospheric moisture and under controlled conditions (aqueous methanol at 25° for 10 min) rapidly hydrolyzed to the ring-opened aldehyde **24** (84% yield). The identity of **24** was

Table II
Oxidation of Aminocyclopropyl Sulfides with Potassium Permanganate in Aqueous Acetic Acid



confirmed by comparison with an authentic sample prepared by the MCPBA oxidation of 3-[(*p*-chlorophenyl)-thio]-2,2-dimethylpropionaldehyde.[13] This facile hydrolysis of **23** is in accord with our proposal that aminocyclopropyl sulfones are intermediates in the aqueous potassium permanganate oxidation of aminocyclopropyl sulfides.

An analogous preparation of the corresponding *cis* aminocyclopropyl sulfone was attempted. Oxidation of **3** under conditions similar to those used for the trans isomer afforded the amine oxide **25** (83% yield). Reduction of **25** with triphenylborane using a cold sodium hydroxide solution work-up afforded an 86% yield of the ring-opened aldehyde **24**. An investigation of the ^{1}H NMR spectrum of the reduction mixture before the aqueous work-up suggested that the desired cis aminocyclopropyl sulfone was present. Previous experience with aqueous sensitive compounds had shown that the chromatographic absorbent that had caused

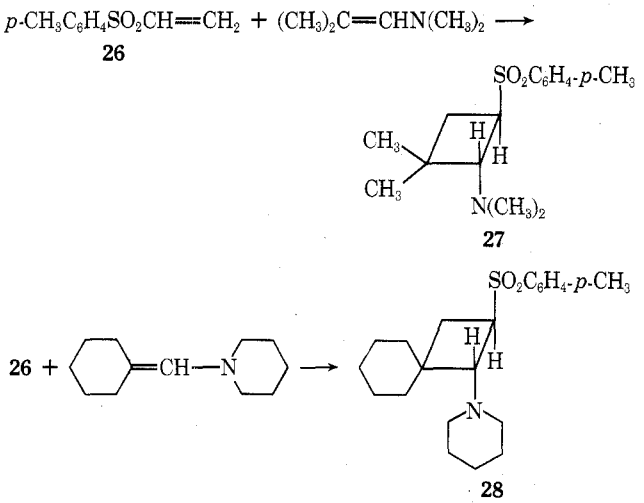


25

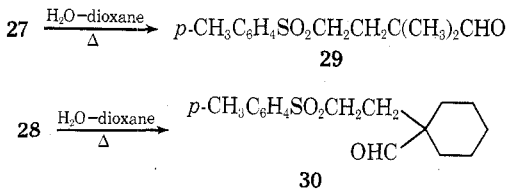
the least hydrolysis was acetylated cellulose. The crude reduction mixture was submitted to column chromatography using Woelm acetyl cellulose as the absorbent and eluted with *n*-hexane; the only identifiable product was the trans aminocyclopropyl sulfone **23** (42% yield). Thus the cis aminocyclopropyl sulfone which presumably formed on reduction of **25** isomerized to the trans isomer **24.** This isomerization and the hydrolysis of **23** can be best rationalized by the intermediacy of a zwitterion of type B.

Preparation and Hydrolysis of Aminocyclobutyl Sulfones. The next higher homologs, aminocyclobutyl sulfones, are known, stable compounds.[14] Brannock did cleave *N,N*,2,2-tetramethyl-4-(methylsulfonyl)cyclobutylamine by quaternization of the amino group followed by hydrolysis with aqueous base.[14] He attributed this cleavage to the dealdolization of a hydroxycyclobutyl sulfone intermediate.

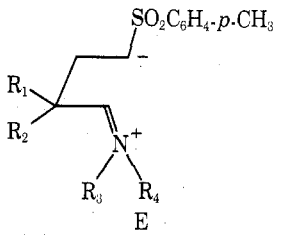
Compounds *trans-N,N*,2,2-tetramethyl-4-(*p*-tolylsulfonyl)cyclobutylamine (**27**) and *trans*-1-[2-(*p*-tolylsulfonyl)spiro[3.5]non-1-yl]piperidine (**28**) were prepared by treatment of *p*-tolyl vinyl sulfone (**26**) with the appropriate enamine in refluxing benzene. The gross structures of **27** and **28** were assigned on the basis of ir, ^{1}H NMR, mass spectra, elemental analyses, and chemical analogy.[14]



The assignment of cis or trans stereochemistry on the basis of vicinal coupling constants cannot be made with any assurance.[15,16] The assignment of a trans relationship between the amino and sulfonyl functions is based upon the commonly accepted mechanism of 1,2-cycloaddition reactions of enamines, i.e., a zwitterionic intermediate with free rotation leading to the thermodynamically more stable product.[15,17,18] When aqueous dioxane solutions of **27** and **28** were heated at reflux, the aldehydic sulfones 2,2-dimethyl-4-(*p*-tolylsulfonyl)butyraldehyde (**29**) and 1-[2-(*p*-tolylsulfonyl)ethyl]cyclohexanecarboxaldehyde (**30**) were obtained in 83 and 74% yields, respectively. The formation



of **29** and **30** can be best rationalized by formation of a zwitterionic intermediate (E), analogous to the cyclopropyl homolog, which subsequently reacts with water to form the aldehydic sulfones. The conditions required (ca. 100°, 17–18 hr) for these conversions are considerably more vigorous than those (25°, 10 min) required for the analogous aminocyclopropyl sulfone **23.** This suggests that ring strain



E

is a major driving force in the formation of such zwitterionic intermediates. The reaction sequence, **26** → **29** or **30,** represents a convenient preparation of α,α-dialkyl-γ-sulfone aldehydes.

Experimental Section

All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Ir spectra were obtained on a Perkin-Elmer Model 421 recording spectrometer in Nujol mulls, the ^{1}H NMR spectra were recorded on a Varian A-60A spectrometer, and the mass spectra were determined on an Atlas CH-4 spectrometer.

Preparation of Aminocyclopropyl Sulfides. The following procedure for the preparation of *cis*- and *trans*-2-[(*p*-chlorophenyl)thio]-*N,N*,3,3-tetramethylcyclopropylamine (**3** and **4**) is representative. Chloromethyl *p*-chlorophenyl sulfide (50.0 g, 0.259 mol) in anhydrous ether (650 ml) was added dropwise over a 2-hr period to a stirred mixture of potassium *tert*-butoxide (34.8 g, 0.311 mol) and *N,N*,2-trimethylpropenylamine (77.0 g, 0.777 mol) in anhydrous ether (350 ml). The temperature was maintained at 25 ± 2° by means of a cooling bath. After stirring for an additional 2.5 hr at room temperature, the reaction mixture was diluted with water (400 ml) and the layers were separated. The ether layer was washed with water (200 ml) and extracted with 1 *N* HCl solution (3 × 500 ml). The combined HCl extracts were washed with ether (2 × 200 ml) and made strongly alkaline with 6 *N* NaOH solution. The resulting milky suspension was extracted with ether (3 × 500 ml) and the combined extracts were dried (Na_2SO_4). The solvent was removed in vacuo to afford 51.3 g (77% yield) of crude product. Chromatographic separation on silica gel (elution with 10% EtOAc in benzene) afforded 31.8 g (48% yield) of **3,** mp 59–61° (EtOH–H_2O), and 9.4 g (14% yield) of **4,** bp 100–104° (0.09 mm), respectively. The analytical and spectral data are summarized in Table III.

Oxidation of *cis*-2-[(*p*-Chlorophenyl)thio]-*N,N*,3,3-tetramethylcyclopropylamine (3) with Potassium Permanganate in H_2O–HOAc. Potassium permanganate (15.0 g, 0.094 mol) in 50% aqueous acetic acid (600 ml) was added dropwise to a stirred, cooled (20–25°) solution of **3** (10.0 g, 0.039 mol) in 50% aqueous acetic acid (200 ml). After stirring for an additional 2 hr at 20–25°, the reaction mixture was diluted with water (1200 ml) and then digested on a steam bath for 2 hr to precipitate the finely divided manganese dioxide. After standing at room temperature for 2 hr, the precipitate was removed by filtration through Celite and the solvent of the filtrate was removed in vacuo. The residue was partitioned between chloroform (250 ml) and water (100 ml). The organic layer was separated, washed with saturated $NaHCO_3$ solution (3 × 100 ml) and water (100 ml), and dried (Na_2SO_4). The solvent was removed in vacuo and the residue was recrystallized from ether–petroleum ether to afford 5.6 g (52% yield) of 2,2-dimethyl-3-[(*p*-chlorophenyl)sulfonyl]propionic acid (**16**): mp 134–135.5°;[1b] ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 6 H), 3.47 (s, 2 H), 7.63 (q, 4 H), 12.2 (s, 1 H); mass spectrum *m/e* 276, 278 (M^+).

Anal. Calcd for $C_{11}H_{13}ClSO_4$: C, 47.74; H, 4.73; Cl, 12.81; S, 11.59. Found: C, 47.96; H, 4.72; Cl, 12.84; S, 11.43.

Oxidation of 1-[2-(*p*-Chlorophenylthio)-3-phenylcyclopropyl]piperidine Hydrochloride (9) with Potassium Permanganate in H_2O–HOAc. Oxidation of **9** (2.00 g, 5.26 mmol) with potassium permanganate (2.34 g, 14.8 mmol) in a manner analogous to the oxidation of **3** afforded 1.9 g of product mixture which was partitioned between chloroform (100 ml) and water (100 ml). The organic phase was separated and extracted with saturated Na_2CO_3 solution (2 × 50 ml). The organic phase was dried (Na_2SO_4) and the solvent was removed in vacuo. The residue was recrystallized from ethanol to afford 0.90 g (58% yield) of α-(*p*-chlorophenylsulfonyl)acetophenone (**18**): mp 133–134° (lit.[20] mp 134.5°); ^{1}H NMR ($CDCl_3$) δ 4.73 (s, 2 H), 7.3–8.0 (m, 9 H); mass spectrum *m/e* 294, 296 (M^+).

Anal. Calcd for $C_{14}H_{11}ClO_3S$: C, 57.04; H, 3.76; Cl, 12.03; S, 10.88. Found: C, 57.33; H, 4.01; Cl, 11.96; S, 10.65.

Table III
Aminocyclopropyl Sulfides

Compd	Mp or bp (mm), °C	Recrystn solvent	^{1}H NMR, δ (CDCl$_3$)	Formula[a]
3	59–61	EtOH–H_2O	1.19 (s, 6 H), 1.69 (d, 1 H, J = 7 Hz), 1.96 (d, 1 H, J = 7 Hz), 2.27 (s, 6 H), 7.20 (s, 4 H)	$C_{13}H_{18}ClNS$
4	100–104 (0.09)		1.08 (s, 3 H), 1.33 (s, 3 H), 1.44 (d, 1 H, J = 3.5 Hz), 1.91 (d, 1 H, J = 3.5 Hz), 2.20 (s, 6 H)	$C_{13}H_{18}ClNS$
6	141.5–142.5	$CHCl_3$–Et_2O	2.90 (t, 1 H, J = 6.5 Hz), 3.0–3.25 (br, 7 H), 3.93 (d of d, 1 H, J = 5.0 and 6.5 Hz), 7.0–7.6 (br m, 9 H)	$C_{17}H_{19}Cl_2NS$
7	160–160.5	$CHCl_3$–Et_2O	2.75–3.10 (br, 6 H), 3.30–3.55 (br, 1 H), 3.55–3.90 (m, 2 H), 7.13 (s, 4 H), 7.22 (s, 5 H)	$C_{17}H_{19}Cl_2NS$
9	155.5–156 dec	$CHCl_3$–Et_2O	1.20–2.30 (br m, 7 H), 2.7–4.0 (br m, 7 H), 7.17 (s, 4 H), 7.25 (s, 5 H)	$C_{20}H_{23}Cl_2NS$
11	175.5–176	EtOH–Et_2O	0.9–3.7 (br, imposed d at 2.31, J = 5.5 Hz, 20 H), 7.30 (s, 4 H)	$C_{18}H_{25}Cl_2NS$
12	215.5–216	EtOH–Et_2O	1.1–3.6 (br, 19 H), 3.82 (d, 1 H, J = 10 Hz), 7.28 (s, 4 H)	$C_{18}H_{25}Cl_2NS$
14	65–68 (13)		1.08 (s, 3 H), 1.24 (s, 3 H), 1.44 (d, 1 H, J = 7.5 Hz), 1.59 (d, 1 H, J = 7.5 Hz), 2.09 (s, 3 H), 2.22 (s, 6 H)	$C_8H_{17}NS$
15	58–60 (13)		1.09 (s, 3 H), 1.22 (s, 3 H), 1.30 (d, 1 H, J = 3.5 Hz), 1.62 (d, 1 H, J = 3.5 Hz), 2.03 (s, 3 H), 2.21 (s, 6 H)	$C_8H_{17}NS$

[a] The compounds described in this table gave satisfactory analyses (within ± 0.4% of theoretical value) for C, H, N, and S (and Cl where applicable) except 7. Calcd for 7: S, 9.42. Found: S, 9.97.

The above sodium carbonate extracts were combined and acidified with 6 *N* hydrochloric acid. The resulting milky suspension was extracted with chloroform (2 × 50 ml) and the combined extracts were dried (Na_2SO_4). The solvent was removed in vacuo and the residue was recrystallized from benzene–petroleum ether to afford 0.30 g (18% yield) of 2-phenyl-3-(*p*-3-chlorophenylsulfonyl)propionic acid (**17**): mp 145–147°;[1b] ^{1}H NMR ($CDCl_3$) δ 3.2–4.2 (m, 3 H), 7.22 (s, 5 H), 7.55 (q, 4 H); mass spectrum *m/e* 324, 326 (M^+).

Anal. Calcd for $C_{15}H_{13}ClO_4S$: C, 55.47; H, 4.03; Cl, 10.92; S, 9.87. Found: C, 55.42; H, 3.98; Cl, 10.91; S, 9.98.

Oxidation of *endo*- and *exo*-1-[7-[(*p*-Chlorophenyl)thio]-6-norcaryl]piperidine Hydrochloride (11 and 12) with Potassium Permanganate in H_2O–HOAc. Oxidation of a mixture of **11** and **12**[19] (2.00 g, 5.6 mmol) with potassium permanganate (1.68 g, 10.6 mmol) in a manner analogous to the oxidation of **3** afforded 0.99 g (62% yield) of 2-[[(*p*-chlorophenyl)sulfonyl]methyl]cyclohexanone (**19**): mp 65–66° (hexane);[1b] ^{1}H NMR ($CDCl_3$)[21] δ 1.2–2.7 (br m, 8 H), 2.86 (d of d, J = −14 and 7 Hz, 1 H) 3.05 (m, 1 H), 3.91 (d of d, J = −14 and 3 Hz, 1 H), 7.70 (q, 4 H); mass spectrum *m/e* 286, 288 (M^+).

Anal. Calcd for $C_{13}H_{15}ClO_3S$: C, 54.45; H, 5.24; Cl, 12.39; S, 11.17. Found: C, 54.57; H, 5.42; Cl, 12.65; S, 11.41.

***cis*-*N,N,N*-Trimethyl-*N*-[[1,1-dimethyl-2-(*p*-chlorophenyl)thio]cyclopropyl]ammonium Iodide (20).** A mixture of **3** (10.0 g, 0.039 mol), methyl iodide (40 ml, 0.65 mol), and 2-butanone (100 ml) was heated at reflux for 45 hr. The reaction mixture was cooled slightly, ether was added to the cloud point, and the mixture was further cooled to afford 12.8 g (82% yield) of **20**: mp 96–98°; ^{1}H NMR ($CDCl_3$) δ 1.49 (s, 3 H), 1.62 (s, 3 H), 2.73 (d, J = 8.5 Hz, 1 H), 3.65 (s, 9 H), 4.18 (d, J = 8.5 Hz, 1 H), 7.35 (s, 4 H).

Anal. Calcd for $C_{14}H_{21}ClINS$: C, 42.27; H, 5.32; N, 3.52; S, 8.06; I, 31.91. Found: C. 42.02; H, 5.55; N, 3.50; S, 8.14, I, 31.77.

***cis*-*N,N,N*-Trimethyl-*N*-[[1,1-dimethyl-2-(*p*-chlorophenyl)sulfonyl]cyclopropyl]ammonium Iodide (21).** A solution of potassium permanganate (23.9 g, 0.151 mol) in 50% aqueous acetic acid (500 ml) was added over a 15-min period to a stirred, cooled (20–25°) solution of **20** (10.0 g, 0.0251 mmol) in 50% aqueous acetic acid (200 ml). After stirring for an additional 2 hr at 20–25°, the reaction mixture was heated on a steam bath for 3 hr. The precipitate was removed by filtration through Celite and the filtrate was treated with sodium bisulfite solution until colorless and no longer gave a positive starch–iodide test. A solution of potassium iodide (4.16 g, 0.0251 mol) in water (25 ml) was added and the solvent was removed in vacuo to afford a white semisolid. Residual water and acetic acid were removed azeotropically with chloroform to afford a dry powder which was vigorously stirred with boiling chloroform (2 l.). The hot solution was filtered and the solvent of the filtrate was removed in vacuo. The residue was recrystallized from absolute ethanol to afford 6.82 g (63% yield) of **21**: mp 183–184° dec; ^{1}H NMR (Me_2SO-d_6) δ 1.02 (s, 3 H), 1.62 (s, 3 H), 3.21 (d, J = 9 Hz, 1 H), 3.40 (s, 9 H), 3.64 (d, J = 9 Hz, 1 H), 7.72 (q, 4 H).

Anal. Calcd for $C_{14}H_{21}ClINO_2S$: C, 39.12; H, 4.93; N, 3.26; Cl, 8.25; S, 7.46. Found: C, 39.35; H, 5.10; N, 3.00; Cl, 8.74; S, 7.73.

***trans*-2-[(*p*-Chlorophenyl)sulfonyl]-*N,N*,3,3-tetramethylcyclopropylamine *N*-Oxide Hydrochloride (22).** A solution of *m*-chloroperoxybenzoic acid (25.10 g, 0.123 mol) in methylene chloride (300 ml) was added dropwise to a stirred solution of **4** (7.00 g, 0.0274 mol) in methylene chloride (300 ml) maintained at −60 to −70°. The mixture was stirred for an additional 1 hr at −60 to −70° and then at ambient temperature for 18 hr. The mixture was poured onto a column of grade I basic alumina (1 kg) and eluted with 10% methanol in chloroform. Concentration of the appropriate fractions gave 7.92 g of oil which could not be made to crystallize. Treatment with anhydrous HCl in chloroform afforded 6.26 g (75% yield) of **22** (hygroscopic): mp 153.5–155.5°; ^{1}H NMR ($CDCl_3$) δ 1.48 and 1.53 (2 s, 6 H), 3.68 (d, J = 5.0 Hz, 1 H), 3.83 (s, 6 H), 4.44 (d, J = 5.0 Hz, 1 H), 7.72 (q, 4 H).

Anal. Calcd for $C_{13}H_{19}Cl_2NO_3S$: C, 45.88; H, 5.63; N, 4.12; Cl, 20.84. Found: C, 45.69; H, 5.58; N, 3.94; Cl, 21.01.

***trans*-2-[(*p*-Chlorophenyl)sulfonyl]-*N,N*,3,3-tetramethylcyclopropylamine (23).** A solution of triphenylborane[12] (3.35 g, 15.5 mmol) in chloroform (60 ml) was added dropwise to a stirred solution of **22** (4.72 g, 15.5 mmol) in chloroform (80 ml) under nitrogen, producing a slightly exothermic reaction. After stirring at ambient temperature for 4 hr the reaction mixture was washed briefly with cold 1 *N* sodium hydroxide solution and immediately dried (Na_2SO_4). The solvent was removed in vacuo and the residue was recrystallized from *n*-pentane to afford 2.52 g (57% yield) of **23** (hygroscopic): mp 81–85°; NMR ($CDCl_3$) δ 1.23 (s, 3 H), 1.42 (s, 3 H), 2.07 (d, J = 4.0 Hz, 1 H), 2.15 (s, 6 H), 2.35 (d, J = 4.0 Hz, 1 H), 7.67 (q, 4 H).

Anal. Calcd for $C_{13}H_{18}ClNO_2S$: C, 54.25; H, 6.30; N, 4.87; Cl, 12.32; S, 11.14. Found: C, 54.15; H, 6.27; N, 4.14; Cl, 12.59; S, 11.17.

Hydrolysis of 23. A mixture of **23** (0.10 g, 0.35 mmol), methanol (1 ml), and water (1 ml) was allowed to stand at 20–25° for 10 min. The reaction mixture was diluted with water (100 ml) and extracted with methylene chloride (4 × 75 ml). The combined extracts were washed with water (50 ml) and dried (Na_2SO_4). The solvent was removed in vacuo and the residue was recrystallized from hexane to afford 0.76 g (84% yield) of 3-[(*p*-chlorophenyl)sulfonyl]-2,-2-dimethylpropionaldehyde (**24**), mp 68–70°. The ir and ^1H NMR spectra were identical with those of an authentic sample prepared below.

3-[(*p*-Chlorophenyl)thio]-2,2-dimethylpropionaldehyde. 3-[(*p*-Chlorophenyl)thio]-2,2-dimethylpropionic acid[1b] (28.3 g, 0.115 mol) was converted into the acid chloride with thionyl chloride (86% yield), bp 119–122° (0.2 mm). Lithium tri-*tert*-butoxyaluminum hydride (25.2 g, 0.0992 mol) in tetrahydrofuran (25 ml) was added dropwise to a stirred, cooled (−60 to − 70°) solution of the above acid chloride (26.1 g, 0.0992 mol) in THF (100 ml). The reaction mixture was stirred for an additional 1 hr at −60 to −70° and then allowed to warm to room temperature over a 1-hr period. The solvent was removed in vacuo. Water (500 ml) was added and the slurry was filtered. The solid was slurried with ethanol (1 l.) and filtered. The solvent of the filtrate was removed in vacuo and the residue was subjected to absorption chromatography on silica gel (eluted with methylene chloride). From the appropriate fractions there was obtained 12.0 g (53% yield) of 3-[(*p*-chlorophenyl)thio]-2,2-dimethylpropionaldehyde: bp 115–117° (2 mm); ^1H NMR ($CDCl_3$) δ 1.11 (s, 6 H), 3.02 (s, 2 H), 7.15 (s, 4 H) 9.67 (s, 1 H); mass spectrum *m/e* 228, 230 (M^+).

Anal. Calcd for $C_{11}H_{13}ClOS$: C, 57.76; H, 5.73; Cl, 15.50; S, 14.02. Found: C, 57.71; H, 5.59; Cl, 15.68; S, 13.68.

3-[(*p*-Chlorophenyl)sulfonyl]-2,2-dimethylpropionaldehyde (24). *m*-Chloroperoxybenzoic acid (17.75 g, 0.087 mol) in methylene chloride (400 ml) was added dropwise to a stirred solution of 3-[(*p*-chlorophenyl)thio]-2,2-dimethylpripionaldehyde (10.0 g, 0.0436 mol) in methylene chloride (350 ml) at ambient temperature. After stirring overnight, the reaction mixture was poured into a solution of saturated sodium carbonate (800 ml), containing sodium bisulfite (2 g), and shaken. The organic phase was separated and dried (Na_2SO_4). The solvent was removed in vacuo and the residue was recrystallized from hexane to afford 7.0 g (61% yield) of **24:** mp 68–70°; ^1H NMR ($CDCl_3$) δ 1.33 (s, 6 H), 3.35 (s, 2 H), 7.71 (q, 4 H), 9.52 (s, 1 H); mass spectrum *m/e* 260, 262 (M^+).

Anal. Calcd for $C_{11}H_{13}ClO_3S$: C, 50.67; H, 5.02; Cl, 13.60; S, 12.30. Found: C, 50.83; H, 5.09; Cl, 13.83; S, 12.50.

***cis*-2-[(*p*-Chlorophenyl)sulfonyl]-*N,N*,3,3-tetramethylcyclopropylamine *N*-Oxide (25).** A solution of *m*-chloroperoxybenzoic acid (22.4 g, 0.11 mol) in chloroform (300 ml) was added dropwise to a stirred solution of **3** (10.0 g, 0.0367 mol) in chloroform (300 ml) maintained at −60 to −70°. After the addition was completed, the mixture was stirred at ambient temperature for 20 hr and poured onto a column of grade I basic alumina (1 kg) and eluted with 10% methanol in chloroform. Concentration of the appropriate fractions afforded crude **25** which was recrystallized from chloroform–hexane to afford 9.23 g (83% yield) of **25** (hygroscopic): mp 176° dec; ^1H NMR ($CDCl_3$) δ 1.14 (s, 3 H), 1.89 (s, 3 H), 2.44 (d, J = 8.0 Hz, 1 H), 3.18 (d, J = 8.0 Hz, 1 H), 3.30 (s, 3 H), 3.43 (s, 3 H), 7.70 (q, 4 H).

Anal. Calcd for $C_{18}H_{18}ClNO_3S$: C, 51.39; H, 5.97; N, 4.61; Cl, 11.67; S, 10.56. Found: C, 51.63; H, 5.94; N, 4.72; Cl, 11.85; S, 10.53.

Reaction of 25 with Triphenylborane. A. Aqueous Work-up. Reaction of triphenylborane (0.36 g, 1.64 mmol) with **25** (0.50 g, 1.64 mmol) under the same conditions used for the preparation of **23** afforded 0.37 g (86% yield) of **24,** mp 68–70°. The ir and ^1H NMR spectra were identical with those of an authentic sample prepared above.

B. Chromatographic Work-up. All of the operations were conducted under a nitrogen atmosphere. A solution of triphenylborane[12] (0.36 g, 1.64 mmol) in chloroform (20 ml) was added dropwise to a stirred solution of **25** (0.50 g, 1.64 mmol) in chloroform (20 ml). After stirring at ambient temperature for 6 hr the bulk of the solvent was removed and the residue was subjected to absorption chromatography. The absorbant was Woelm acetyl cellulose (40 g) which had been soaked in benzene for 20 hr, slurry pressure packed into a glass column, and washed thoroughly with *n*-hexane. The column was eluted with *n*-hexane. Concentration of the appropriate fractions gave 0.22 g (47% yield) of **23,** mp 82–84°. The ir and ^1H NMR spectra were identical with those of **23** prepared above.

***trans*-*N,N*,2,2-Tetramethyl-4-(*p*-tolylsulfonyl)cyclobutylamine (27).** A solution of *N,N*,2-trimethylpropenylamine (5.0 g, 0.050 mol) and **26** (9.1 g, 0.050 mol) in benzene (75 ml) was heated at reflux for 20 hr. The solvent was removed on a rotary evaporator and the residue was dissolved in ether (200 ml) and extracted with cold 10% HCl solution (3 × 100 ml). The combined extracts were washed with ether (2 × 50 ml) and then made basic with Na_2CO_3 solution. The oily suspension was extracted with ether (3 × 100 ml) and the combined extracts were dried (Na_2SO_4). The solvent was removed and the residue was recrystallized from hexane to afford 10 g (71% yield) of **27:** mp 73–74°; ^1H NMR ($CDCl_3$) δ 7.54 (q, 4 H), 3.58 (m, 1 H), 2.88 (d, J = 8 Hz, 1 H), 2.42 (s, 3 H), 2.21 (s, 6 H), 1.66 (m, 2 H), 1.15 (s, 3 H), 1.09 (s, 3 H); mass spectrum *m/e* 281 (M^+).

Anal. Calcd for $C_{15}H_{23}NO_2S$: C, 64.06; H, 8.19; N, 4.98; S, 11.39. Found: C, 63.81; H, 8.24; N, 4.87; S, 11.60.

***trans*-1-[2-(*p*-Tolylsulfonyl)spiro[3.5]non-1-yl]piperidine (28).** A solution of 1-(cyclohexylidenemethyl)piperidine[14] (8.9 g, 0.050 mol) and **26** (9.1 g, 0.050 mol) in benzene (100 ml) was heated at reflux for 18 hr. The solvent was removed and the residue was worked up as in the preparation of **27.** Recrystallization from hexane afforded 12 g (67% yield) of **28:** mp 119.5–121°; NMR ($CDCl_3$) δ 7.53 (q, 4 H), 3.60 (m, 1 H), 2.94 (d, J = 8 Hz, 1 H), 2.70–2.10 (broad m, 7 H), 1.87–0.90 (broad m, 18 H); mass spectrum *m/e* 361 (M^+).

Anal. Calcd for $C_{21}H_{31}NO_2S$: C, 69.77; H, 8.64; N, 3.88; S, 8.86. Found: C, 69.57; H, 8.70; N, 3.84; S, 8.98.

2,2-Dimethyl-4-(*p*-tolylsulfonyl)butyraldehyde (29). A solution of **27** (7.74 g, 0.027 mol) in water (100 ml) and dioxane (100 ml) was heated at reflux for 15 hr. The solvent was removed on a rotary evaporator and the residue was dissolved in methylene chloride (250 ml) and washed with water (50 ml). The solution was dried (Na_2SO_4) and the solvent was removed. The residue was recrystallized from hexane–cyclohexane to afford 5.71 g (83% yield) of **29:** mp 89–91°; NMR ($CDCl_3$) δ 9.06 (s, 1 H), 7.57 (q, 4 H), 3.20–2.84 (m, 2 H), 2.44 (s, 3 H), 2.03–1.66 (m, 2 H), 1.05 (s, 6 H); mass spectrum *m/e* 255 ($M^+ + 1$).

Anal. Calcd for $C_{13}H_{18}O_3S$: C, 61.42; H, 7.09; S, 12.60. Found: C, 61.36; H, 7.14; S, 12.82.

1-[2-(*p*-Tolylsulfonyl)ethyl]cyclohexanecarboxaldehyde (30). A solution of **28** (2.0 g, 0.0055 mol) in water (20 ml) and dioxane (20 ml) was heated at reflux for 17 hr. The reaction mixture was worked up as in the preparation of **29.** Recrystallization from hexane afforded 1.2 g (74% yield) of **30:** mp 58–59.5°; NMR ($CDCl_3$) δ 9.01 (s, 1 H), 7.50 (q, 4 H), 3.12–2.78 (m, 2 H), 2.42 (s, 3 H), 2.05–1.04 (broad m, 12 H); mass spectrum *m/e* 294 (M^+).

Anal. Calcd for $C_{16}H_{22}O_3S$: C, 65.26; H, 7.55. Found: C, 65.26; H, 7.53.

Registry No.—1, 6906-32-7; **2,** 7205-90-5; **3,** 37608-38-1; **4,** 37608-39-2; **5,** 14846-39-0; **6,** 51348-75-5; **7,** 51348-76-6; **8,** 55606-20-7; **9,** 51275-72-0; **10,** 2981-10-4; **11,** 37608-43-8; **12,** 37608-44-9; **13,** 2373-51-5; **14,** 37608-46-1; **15,** 37608-47-2; **16,** 36603-36-8; **17,** 36603-44-8; **18,** 36603-45-9; **19,** 55606-21-8; **20,** 51275-73-1; **21,** 55606-22-9; **22,** 55606-23-0; **23,** 55606-24-1; **24,** 55606-25-2; **25,** 55606-26-3; **26,** 5535-52-4; **27,** 55606-27-4; **28,** 55606-28-5; **29,** 55606-29-6; **30,** 55606-30-9; potassium permanganate, 7722-64-7; methyl iodide, 74-88-4; *m*-chloroperoxybenzoic acid, 937-14-4; triphenylborane, 960-71-4; 3-[(*p*-chlorophenyl)thio]-2,2-dimethylpropionyl chloride, 55606-31-0; 3-[(*p*-chlorophenyl)thio]-2,2-dimethylpropionaldehyde, 55606-32-1; 1-(cyclohexylidenemethyl)piperidine, 6604-81-5.

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Hydrogen and Alkyl Transfer in the Rearrangements of 2-Alkenyl-1,2-dihydroquinolines[1]

John J. Eisch* and David R. Comfort

Departments of Chemistry, The State University of New York at Binghamton, Binghamton, New York 13901, and The Catholic University of America, Washington, D.C. 20017

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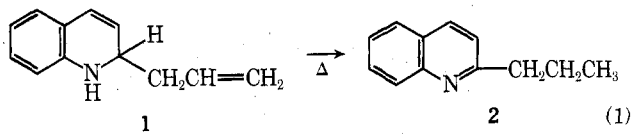
The addition of vinyl- or allylmagnesium chloride to quinoline yielded, at 25° and upon hydrolysis, the corresponding 2-alkenyl-1,2-dihydroquinoline. Heating the Grignard adduct with quinoline directly or heating the isolated dihydroquinoline caused isomerization to the corresponding 2-*n*-alkylquinoline or its magnesium salt, respectively. When the respective adducts were prepared from 2-deuterioquinoline and the subsequent isomerizations carried out, the resulting 2-*n*-alkylquinolines were found to be deuterated exclusively at the β position of the side chain. The coisomerization of 2-allyl-1,2-dihydroquinoline and 2-allyl-2,4-dideuterio-1,2-dihydroquinoline led to the production of much monodeuterated 2-*n*-propylquinoline, which indicates that such hydrogen transfer is largely, if not exclusively, intermolecular. 1,2-Dihydroquinolines and their N-metallic salts were found to undergo rather facile 1,2 elimination of RH or RM. In fact, 2-allyl-2-methyl-1,2-dihydroquinoline, as its *N*-magnesium chloride salt, was found to revert to quinaldine and allylmagnesium chloride. These components then recombined at higher temperatures to yield 4-allyl-2-methyl-1,4-dihydroquinoline as its *N*-magnesium salt. The foregoing findings point to two distinct pathways for intermolecular hydrogen transfer: (a) in the Grignard isomerization, a sequence involving MgHCl elimination, allyl–propenyl group isomerization, and 1,4 readdition of MgHCl; and (b) in the dihydro isomerization, elimination of RH in a free-radical initiation step, followed by concerted six-center hydrogen transfers and base-promoted allyl–propenyl group isomerization.

Hydrogen-transfer reactions of certain dihydropyridines have received much attention, since their conversion into pyridine derivatives is fundamental to the coenzymatic activity of dihydronicotinamide–adenine dinucleotide.[2] A special instance of this hydrogen transfer is that of isomerization, first observed in the rearrangement of 2-allyl-1,2-dihydroquinoline into 2-*n*-propylquinoline[3] (eq 1). Subse-



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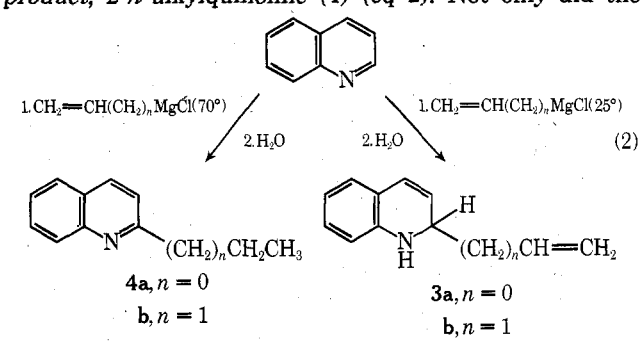
quently, isomerizing hydrogen transfers have been noted with similar derivatives, such as 4-allyl-1,4-dihydropyridines[4,5] and 2-phenylethynyl-1,2-dihydropyridine.[6]

In these isomerizations the dihydropyridinoid derivative acts, in a formal sense, both as a hydrogen donor and acceptor. As a consequence, a detailed study of the nature and scope of these rearrangements appeared to offer a unique opportunity for gaining a better understanding of hydrogen-transfer processes in these heterocycles.

The present report describes the preparation and rearrangement behavior of certain 2-alkenyl-1,2-dihydroquinolines, that bear a deuterium atom or a methyl group at C_2 and in which the alkenyl group is vinyl, allyl, and phenyl. The thermal and photochemical reactivity of these derivatives was examined in order to obtain information on (a) the nature of any intermediates; (b) the fate of any deuterium undergoing transfer; (c) the inter- or intramolecularity of the rearrangement; and (d) the nature of the reaction mechanism.

Results

The reaction of vinyl- or allylmagnesium chloride with quinoline yields the simple 1,2 adduct (**3**) at 25°, but prolonged heating favors the formation of the rearrangement product, 2-*n*-alkylquinoline (**4**) (eq 2). Not only did the



(2)

Grignard adducts themselves, namely the 2-alkenyl-1,2-dihydro-1-quinolylmagnesium chlorides, undergo rearrangement, but also the isolated, pure dihydro compounds, **3a** and **3b**, were found to isomerize into **4a** and **4b**, respectively, in 50–80% yields when heated under a nitrogen atmosphere above 130°. In addition, the irradiation at 254 nm of **3b** dissolved in benzene also caused isomerization into 2-*n*-propylquinoline (**4b**, 20% after 24 hr), but much deallylation with the formation of quinoline (60%) accompanied this process.

The fate of the NH and C_2H groups in **3** during the isomerization was studied by synthesizing C_2-deuterated analogs of **3a** and **3b** from 2-deuterioquinoline and the appropriate Grignard reagents (eq 2). Thermal rearrangement of