Alkylations of Heterocyclic Ambident Anions. IV. Alkylation of 5-Carbethoxy- and 5-Nitro-2-pyridone Salts[1]

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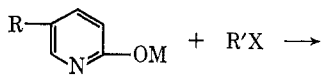
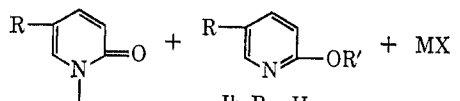
Electron-withdrawing groups on the 5 position of 2-pyridone caused increased N-alkylation. The effect was more pronounced with silver salts than with sodium salts. Only small solvent or cation effects were observed for alkali metal salts. Silver salts gave more O-alkylation than did alkali metal salts but were subject to a solvent effect. Alkylations of silver salts under heterogeneous conditions were slow and gave only O-alkylation.

The conclusion that alkali metal salts of 2-pyridone are predominantly alkylated at nitrogen and that silver salts give increased amounts of oxygen-alkylated product is based on preparative experiments from several laboratories where detailed product analyses were not attempted.[2] Data to evaluate the effect of substituents on alkylations are also limited. However, available evidence indicates that substituents on the 5 position (*para* to the hydroxy group) do not effect product distribution.[2]

In recent studies it was observed that heterogeneity of the reaction medium was probably a determining factor for the site of alkylation of 2-pyridone[3] and 2-pyrimidones.[4] The present paper reports on a study where the cation and solvent were varied in alkylations of salts of 2-hydroxypyridine (I), 2-hydroxy-5-carbethoxypyridine (II), and 2-hydroxy-5-nitropyridine (III)[5] with halides and tosylates.



I, R = H
II, R = CO_2Et
III, R = NO_2



Ia, R = H
IIa, R = CO_2Et
IIIa, R = NO_2

Ib, R = H
IIb, R = CO_2Et
IIIb, R = NO_2

Results and Discussion

Effect of Alkylating Agents.—The data from alkylations of the sodium salts of the 2-hydroxypyridines I, II, and III in dimethylformamide at ambient temperatures are summarized in Table I. The increase in ether formation, when the alkylating agent was changed from methyl to ethyl to isopropyl halide had been observed previously in alkylations of 2-hydroxypyridine[3] and 2-hydroxypyrimidine,[4] and demonstrates that nitrogen alkylation has a greater steric requirement than does oxygen alkylation. In addition, as the group at the 5 position of the ring was varied from hydrogen to carbethoxy to nitro, alkylation at nitrogen increased. This relatively small but real effect of substituents was observed in alkylations with ethyl and isopropyl halides, where unsubstituted 2-hydroxypyridine (I) gave significant amounts of O-alkylation product.

TABLE I

EFFECTS OF ALKYLATING AGENTS ON THE ALKYLATION OF SODIUM SALTS IN DIMETHYLFORMAMIDE AT ROOM TEMPERATURE[a]

Substrate	Alkyl halide[b]	% yield[c]	Product distribution N	O	P[d]
I	MeI[e]	93	95	5	
	EtI[e]	87	69	31	
	i-PrI[e]	90	30	61	9
	$PhCH_2I$[e]	99	98	2	
II	MeI	68	100		
	EtI	73	78	22	
	i-PrI	84	42	51	7
	$PhCH_2I$	84	98	2	
III	MeI	100	99	1	
	EtI	100	89	11	
	EtOTs	90	78	22	
	i-PrI	82	54	46	
	i-PrOTs	71	47	53	
	$PhCH_2I$	85	96	4	

[a] Alkylations were completed in 24 hr. The analyses were done after 5 days. No O–N isomerization was observed. [b] Reactions were conducted with 200% excess alkyl halides. In benzylation, only 50% excess halide was used. [c] Determined by quantitative vapor phase chromatography. [d] Regenerated hydroxypyridine from elimination reaction. [e] Reference 3.

Several reactions of the sodium salt of III with alkyl halides were studied at elevated temperature (64°). No change in the products ratio was observed in methylations and ethylations. When isopropylation was carried out at 64°, a decrease in yield of ether was observed accompanied by the regeneration of III, indicative of dehydrohalogenation.

Effect of Cation.—Similar N- to O-product ratios were obtained from alkylations of sodium, potassium, or lithium salts. The rates of alkylation of lithium salts were slower than those of sodium and potassium salts. No change in product distribution was observed when the leaving group was varied from chloride to bromide to iodide. Generally, a higher yield was obtained when the alkyl bromide was used.

In dimethylformamide the silver salts of 2-hydroxypyridines or the free acid with silver carbonate gave more O-alkylation when compared with sodium salts. In the alkylations of the silver salt I in dimethylform-

(1) This investigation was supported by Public Health Service Research Grant No. CA-02857 and Grant No. CA-10746 from the National Cancer Institute.

(2) For a recent review of pyridine alkylations, see H. Meislich, "Pyridine and Its Derivatives," Part II, E. Klingsberg, Ed., Interscience Publishers, New York, N. Y., 1962, pp 631–640.

(3) G. C. Hopkins, J. P. Jonak, H. J. Minnemeyer, and H. Tieckelmann, *J. Org. Chem.*, **32**, 4040 (1967).

(4) G. C. Hopkins, J. P. Jonak, H. Tieckelmann, and H. J. Minnemeyer, *ibid.*, **31**, 3969 (1966).

(5) The term hydroxypyridine is simply a nomenclature convenience and does not refer to the predominant tautomeric form.

amide, 2-pyridone was regenerated in quantity and, therefore, it was difficult to compare with silver salts of II and III in this solvent. However, the effect of substituents was generally in the same direction as that observed for alkylations of sodium salts but was more pronounced. N-ethylation of sodium salts increased from 69 to 79 to 89% as the hydroxypyridine was varied from I to II to III, but with the corresponding silver salts, N-ethylation increased from 21 to 66 to 91% (Table II).

TABLE II

EFFECTS OF ALKYLATING AGENTS ON THE ALKYLATION OF SILVER SALTS IN DIMETHYLFORMAMIDE AT ROOM TEMPERATURE[a]

Substrate	Alkyl halide[b]	% yield	Product distribution N	O	P[c]
I	MeI[d]	81	73	12	14
	EtI	76	21	40	39
	i-PrBr[d]	No alkylation. Only 2-pyridone was formed.			
	$PhCH_2Br$[d]	85	54	46	
II	MeI	73	96	4	
	EtI	85	66	34	
	i-PrI	94	20	75	5
	$PhCH_2I$	78	89	11	
III	MeI	62	88	12	
	EtI	52	91	9	
	i-PrI	49	36	64	
	$PhCH_2I$	46	96	4	
	MeI[e]	100	88	12	
	EtI[e]	100	83	17	
	i-PrI[e]	100	38	62	

[a] The analyses were performed after 5 days. [b] A 200% excess of alkyl halides was used. In benzylations, a 50% excess of halide was used. [c] Regenerated 2-hydroxypyridines. [d] Reference 3. [e] Silver carbonate and 2-hydroxy-5-nitropyridine were used in place of the isolated salt.

The silver salts were not soluble in dimethylformamide. All of the reaction mixtures were heterogeneous in the beginning but became homogeneous as the reactions proceeded despite the low solubility product of silver iodide in dimethylformamide (3.65×10^{-17} $mol^2/l.^2$).[6]

When the alkylating agent was varied from a 5% to a 200% excess (in DMF) yields from methylations and ethylation of I, II, and III improved with excess alkylating agent. When an excess of isopropyl halide was used with silver salts, a large quantity of 2-pyridone was regenerated. In contrast, when sodium salts were used the yield was increased slightly with an excess of isopropyl halide.

Solvent Effects.—Solvent effects on product distribution in alkylations of sodium salts were small. However, rates of reactions were solvent dependent.

Alkylations of sodium salts of I, II, and III with methyl iodide resulted in greater than 95% nitrogen alkylation in all solvents used (dimethyl sulfoxide, acetonitrile, dimethylformamide, ethyl alcohol, acetone, diglyme, and ethyl acetate). With ethyl iodide, N-alkylation of II varied from 78 to 94%. This relatively small solvent effect is consistent with a reaction which proceeds through a transition state which gives both the O- and the N-alkylated product.[7]

Reactions in dimethylformamide, dimethyl sulfoxide, methanol, or ethanol were homogeneous and proceeded at reasonable rates. Generally, the solubility of sodium salts decreased as the dielectric constant decreased. Reactions did not occur with suspensions in nonpolar solvents such as benzene, *n*-hexane, and tetrahydrofuran.

Contrary to the observations with alkali metal salts, the site of alkylation of silver salts was strongly solvent dependent (Table III). The silver salt of II gave 96% N-methylation in dimethylformamide and only 2% when hexane was used. In all alkylations of silver salts the reaction mixtures were heterogeneous in the early stages of the reaction.

TABLE III

SOLVENT EFFECTS ON ALKYLATION OF THE SILVER SALTS AT ROOM TEMPERATURE[a,b]

Substrate	Alkyl halide	Solvent	% yield	Product distribution N	O	P[c]
I	EtI	DMF	76	21	40	39
		Ether[d]	93	1	96	3
II	MeI	DMF	73	96	4	
		$DMF-H_2O$	69	68	32	
		MeOH	85	20	80	
		Ether	100	8	92	
		Benzene	93	5	95	
		Hexane	87	2	98	
II	EtI	MeCN	97	5	92	3
		DMF	85	66	34	
		$DMF-H_2O$	70	12	70	18
		MeOH	79	16	84	
		Acetone	100	8	92	
		Ether	62		100	
		Benzene	100		100	
		Hexane	97	2	98	
III	EtI	DMF	52	91	9	
		MeOH	31	53	47	
		Benzene	71	12	88	
		Hexane	62	10	90	

[a] For reactions in DMF, the analyses were performed after 5 days. For reactions in other solvents the reaction time was 10 days. [b] Alkylating agent was used in 200% excess. [c] 2-hydroxypyridine derivatives. [d] Reference 3.

When hexane, benzene, and ether were used as solvent, the pyridone silver salts and the products were essentially all in the solid phase throughout the reaction and almost exclusive O-alkylation was observed. The rate of alkylation was very slow. When 200% excess of alkyl halide was used, only 10% products were obtained after 12 hr at ambient temperatures. After 10 days, the yield was more than 95% O-alkylated products for all alkyl halides used.

When dimethylformamide was used as the solvent in a methylation of the silver salt of II, only 4% of the product was the methyl ether, but, when a 1:1 ratio (by volume) of dimethylformamide and water was used, the ether product increased to 32%. Similar results were obtained in ethylations and isopropylations. Alkylation of the silver salt of II in acetonitrile (ϵ 38.8)

(6) H. Chateau and M. C. Moncet, *J. Chim. Phys.*, **60**, 1060 (1963).

(7) K. B. Brower, R. L. Ernst, and J. S. Chen, *J. Phys. Chem.*, **68**, 3814 (1964).

gave much more ether than alkylations in dimethylformamide (ϵ 36).

Silver salts form soluble complexes in dimethylformamide. In one experiment the ethylation of silver salts of II in this solvent was followed from start to completion (Table IV). After an induction period, the reaction rate increased dramatically and the solution became homogeneous after 6 hr. The N-ethyl-2-pyridone to 2-ethoxypyridine product ratio was the same throughout the reaction. In another experiment the reaction was stopped when it was approximately one-half completed. The precipitate was filtered and washed with fresh dimethylformamide and benzene to give silver iodide in much less than theoretical yield (20%). The silver salt of II was not detected in the precipitate.

TABLE IV

REACTION OF THE ETHYL IODIDE WITH THE SILVER SALT OF II IN DIMETHYLFORMAMIDE AT ROOM TEMPERATURE

Time, min	% completion	Product distribution N	O
30	4.7		
60	21.5	70	30
80	46	69	31
100	74	68	32
400[a]	77	68	32

[a] The mixture was homogeneous after 400 min.

These observations have demonstrated that alkylations of silver salts in dimethylformamide were homogeneous reactions which gave both the N- and O-alkylated products and that generally the product distribution in homogeneous reactions is solvent dependent. In contrast, reactions of the silver salt in hexane and benzene were heterogeneous and gave exclusive O-alkylation.

Experimental Section

Materials.—All solvents and alkylating agents were reagent grade and usually stored over Linde Molecular Sieves. Additional purification, when necessary, was carried out by standard methods. The salts of 2-hydroxypyridine and its derivatives were obtained according to the method reported.[3] 2-Hydroxypyridine-5-carboxylic acid and 2-hydroxy-5-nitropyridine were obtained from Aldrich Company. Potassium and silver salts of 2-hydroxy-5-nitropyridine, 1-methyl-, 1-ethyl-, 1-isopropyl-, and 1-benzyl-5-nitro-2-pyridone, and 1-methyl-5-carbethoxy-2-pyridone are prepared according to the known procedure.[8,9]

Vapor Phase Chromatography.—The reaction mixtures were analyzed on a F & M Model 720 gas chromatograph. For derivatives of 2-hydroxypyridine, a 2-ft stainless steel column packed with 10% XF-1150 on silanized Chromosorb W was used. The helium flow was 90 ml/min and the temperature was programmed at 15°/min from 100 to 240°. For the derivatives of 2-hydroxy-5-nitropyridine and 2-hydroxy-5-carbethoxypyridine, a 2-ft stainless steel column packed with 10% silicon gum rubber (SE-30) on silanized Chromosorb W was used. The helium flow was 110 ml/min and the temperature was programmed at 15°/min from 110 to 260°. All quantitative analysis data were obtained by comparison with a calibration plot of weighed sample *vs.* peak area.

Alkylation Procedures.—Hydroxypyridine or the salt (0.50–1.00 mmol) was weighed in a small glass vial and usually 2 ml of solvent was added. A suitable amount of alkyl halide was added below the surface with a 100-μl. syringe. The reaction mixture, in a stoppered glass vial, was placed on a shaker. After an appropriate reaction period, 10–40-μl. samples were taken and subjected to vpc analysis.

2-Hydroxy-5-carbethoxypyridine.—Rath[9] reported that, by bubbling hydrogen chloride into the solution of 2-hydroxypyridine-5-carboxylic acid and ethanol, the corresponding ethyl ester could be obtained in 65% yield. In the present preparation, sulfuric acid was used. The product was isolated in 78% yield. After recrystallization from ethyl acetate, the melting point was 151.0–151.5° (lit.[9] 150°).

Sodium Salt of 2-Hydroxy-5-carbethoxypyridine.—Freshly cut sodium (2.3 g, 0.1 g-atom) dissolved in 100 ml of ethanol was added to the solution of II (16.7 g, 0.1 mol) suspended in 100 ml of absolute ethanol. After stirring at room temperature overnight, the solvent was removed under reduced pressure and anhydrous ether was added in large excess. After filtration, the sodium salt was obtained as white crystals, yield 18 g (95%). Titrated by standardized hydrochloric acid, the purity of this salt was 99.9%.

Potassium Salt of 2-Hydroxy-5-carbethoxypyridine.—This compound was prepared by the method which was used for the sodium salt with the exception that potassium hydroxide was used in place of freshly cut sodium. After the work-up procedure, the potassium salt which was analyzed for two molecules of water of crystallization was obtained, yield 16 g (99%). The anhydrous potassium salt was obtained after heating the salt at 50–55° at reduced pressure.

Silver Salt of 2-Hydroxy-5-carbethoxypyridine.—Silver nitrate (25.5 g, 0.15 mol) in 50 ml of water was added to II (16.7 g, 0.1 mol) suspended in 120 ml of water. After the reaction mixture stood in the dark overnight, it was neutralized with 50% ammonium hydroxide (about 15 ml). The white precipitate was centrifuged, was washed with water, ethanol, and ether, and was dried under vacuum, yield 22.2 g (81%). By using Volhard titration method[10] with ferric alum as indicator, it was found that this salt was at least 99% pure.

2-Methoxy-5-carbethoxypyridine.—Silver carbonate (11.9 g, 0.04 mol) and II (6.7 g, 0.04 mol) reacted with methyl iodide (20.5 g, 0.14 mol) for 36 hr in 60 ml of benzene at room temperature in the dark. The reaction mixture was cooled and filtered. The filtrate was washed with 30 ml of 10% sodium bicarbonate solution and then washed twice with 30 ml of water. The benzene solution was dried over magnesium sulfate, filtered, and evaporated under reduced pressure. After steam distillation, the distillate was extracted with 30 ml of chloroform three times. The chloroform was then removed under reduced pressure and a pale yellow color liquid was obtained, yield 3.9 g (51%). The analytical sample was collected from gas chromatography.

Anal. Calcd for $C_9H_{11}NO_3$: C, 59.65; H, 6.13; N, 7.73. Found: C, 59.69; H, 6.31; N, 7.55.

2-Ethoxy- and 2-Isopropyloxy-5-carbethoxypyridine.—The method used for these preparations was the same as that used for the 2-methoxy derivative. 2-Ethoxy derivative was isolated in 70% yield, bp 125–129° (0.7 mm).

Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.51; H, 6.85; N, 7.18. Found: C, 61.87; H, 7.09; N, 7.33.

2-Isopropyloxy-5-carbethoxypyridine was isolated in 77% yield.

Anal. Calcd for $C_{11}H_{15}NO_3$: C, 61.13; H, 7.24; N, 6.69. Found: C, 63.06; H, 7.47; N, 6.94.

2-Benzyloxy-5-carbethoxypyridine.—The procedure used for the preparation of the 2-methoxy derivative was used here with the exception that the isolated silver salt of II was used in place of silver carbonate. The product was isolated in 75% yield before recrystallization. After recrystallization from ligroin (bp 63–75°), the melting point was 50–51°.

Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.01; H, 5.89; N, 5.45. Found: C, 70.31; H, 5.92; N, 5.46.

1-Ethyl-5-carbethoxy-2-pyridone.—Potassium hydroxide (3 g, .054 mol) in 40 ml of absolute ethanol was added slowly to the solution of II (8 g, 0.048 mol) in 100 ml of absolute ethanol. Ethyl iodide (10 g, 0.064 mol) was then added. After refluxing the reaction mixture for 2.5 hr, the solvent was removed under reduced pressure and the residue was extracted with large amounts of ether. After removing ether at reduced pressure and by steam distillation, the residue was extracted with 30 ml of chloroform three times. The chloroform layer was washed with 50 ml of 25% ammonium hydroxide to remove unreacted II and then washed twice with 100 ml of water. After drying over

(8) C. Rath, *Justus Liebigs Ann. Chem.*, **484**, 52 (1930).
(9) A. Bing and C. Rath, *ibid.*, **487**, 127 (1931).
(10) R. A. Day and A. L. Underwood, "Quantitative Analysis," Prentice-Hall, Inc., Englewood Cliffs, New Jersey. 1958, pp 102–106.

magnesium sulfate the solvent was evaporated, yield 5.5 g (59%), bp 130° (0.7 mm).

Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.51; H, 6.85; N, 7.18. Found: C, 61.44; H, 6.80; N, 7.08.

1-Isopropyl- and 1-Benzyl-5-carbethoxy-2-pyridones.—The procedure used for the preparation of 1-ethyl-5-carbethoxy-2-pyridone was used with the exception that the potassium salt of II was used. For 1-isopropyl-5-carbethoxy-2-pyridone, after recrystallization from ligroin (bp 63–75°), the yield was 37%, mp 91–92°.

Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.16; H, 7.24; N, 6.69. Found: C, 63.35; H, 7.47; N, 6.48.

For **1-benzyl-5-carbethoxy-2-pyridone**, the yield was 47%, mp 60.0–60.5°.

Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.01; H, 5.89; N, 5.45. Found: C, 70.03; H, 5.89; N, 5.60.

Sodium Salt of 2-Hydroxy-5-nitropyridine.—The procedure used for the preparation of sodium salt of II was employed. The yield was 86%.

2-Methoxy-5-nitropyridine.—A cold solution of freshly cut sodium (1.45 g, 0.063 mol) in 50 ml of methanol was added slowly to the solution of 2-chloro-5-nitropyridine (10 g, 0.063 mol) in 150 ml of methanol with stirring and continued cooling. After warming to room temperature, the reaction mixture was allowed to stand overnight with stirring. Solvent was removed *in vacuo* and the residue was extracted with 50 ml of chloroform three times. The chloroform was then washed with two 25-ml portions of water and the solvent was removed under reduced pressure. The product was recrystallized from ethanol, yield 9.4 g (90%), mp 108.0–108.5° (lit.[8] 108–109°).

2-Ethoxy- and 2-Benzyloxy-5-nitropyridine.—These compounds were prepared by the method used for 2-methoxy-5-nitropyridine. The 2-ethoxy-5-nitropyridine was obtained in 98% yield, mp 90–91° (lit.[8] 91–92°). 2-Benzyloxy-5-nitropyridine was obtained in 95% yield, mp 107–108° (lit.[8] 107.0–107.5°).

2-Isopropyloxy-5-nitropyridine.—Isopropyl iodide (15.3 g, 0.09 mol) was added to the solution of the sodium salt of III (9.2 g, 0.057 mol) in 50 ml of absolute ethanol. The reaction mixture was refluxed until the color of the solution changed to dark brown (about 4 hr). The solvent was removed *in vacuo* and, after steam distillation, the distillate was extracted three times with 30 ml of chloroform. After the chloroform was removed under reduced pressure, the product was recrystallized from ethanol and water, yield 2 g (19%), mp 51.5–52.5°.

Anal. Calcd for $C_8H_{10}N_2O_3$: C, 52.74; H, 5.53; N, 15.38. Found: C, 52.40; H, 5.76; N, 15.28.

Registry No.—2-Ethoxy-5-carbethoxypyridine, 24903-80-8; 2-benzyloxy-5-carbethoxypyridine, 24903-81-9; 1-ethyl-5-carbethoxy-2-pyridone, 24903-82-0; 1-isopropyl-5-carbethoxy-2-pyridone, 24903-83-1; 1-benzyl-5-carbethoxy-2-pyridone, 24903-84-2; 2-isopropyloxy-5-nitropyridine, 24903-85-3.

Thietanes. Syntheses, Configurations, and Conformations of 2,4-Diphenylthietanes and Their Oxides

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cis- and *trans*-2,4-diphenylthietane (IV and V), their 1-oxides (VI and VII, respectively), and their 1,1-dioxides (VIII and IX, respectively) have been synthesized. Configurations were assigned primarily from the nmr data. The angles of pucker of *cis*-2,4-diphenylthietane *trans*-1-oxide (VI) and of 3-chlorothietane (X) were calculated from their nmr spectra and were in excellent agreement with the angles of pucker of these compounds determined from X-ray crystal analysis (for VI) and from dipole moment data (for X). Pyrolysis of *cis*- or *trans*-2,4-diphenylthietane 1,1-dioxide (VIII or IX) yielded a mixture of *cis*- and *trans*-1,2-diphenylcyclopropanes.

Because of the unusual stereochemistry observed in the formation and decomposition of the intermediate thiirane 1,1-dioxide in the Ramberg–Bäcklund reaction,[1] some years age we decided to investigate the formation and decomposition, both thermal and catalytic, of substituted thietanes, their monoxides, and dioxides. In this paper, we describe the syntheses and the determinations of configurations and conformations of the 2,4-diphenylthietanes, their monoxides, and dioxides.[2] In subsequent papers we shall report the rearrangement of either *cis*- or *trans*-2,4-diphenylthietane 1,1-dioxide on treatment with ethylmagnesium bromide to *trans*-1,2-diphenylcyclopropanesulfinic acid,[3] the conversion of either *cis*- or *trans*-2,4-diphenylthietane 1-oxide on treatment with potassium *t*-butoxide to *cis*-1,2-diphenylcyclopropanesulfinic acid and *cis*-1,2-diphenylcyclopropanethiol, the rearrangement of 2,4-diphenylthietane 1,1-dioxides with magnesium *t*-butoxide to 3,5-diphenyl-1,2-oxathiolane 2-oxides,[4] and the conversion of *trans*-2,4-diphenylthietane with potassium *t*-butoxide to 2,3,5-triphenylthiophene and 1,2,4,5-tetraphenylbenzene (low yield).

Synthesis.[5]—The thietanes were synthesized by the sequence of reactions depicted in Scheme I. Ethanethiolic acid was added to benzalacetophenone to give 1,3-diphenyl-3-acetylthio-1-propanone (I) in excellent yield (68–99.5%). Compound I was reduced to 1,3-diphenyl-3-hydroxy-1-propanethiol (II) (97.7% yield) with lithium aluminum hydride in tetrahydrofuran, and II was converted without extensive purification to 1,3-diphenyl-3-chloro-1-propanethiol (III) (90.8% yield) with concentrated hydrochloric acid. Compound III was converted to a mixture of *cis*- and *trans*-2,4-diphenylthietanes (IV and V) (mp 40–85°, 95% yield) with aqueous sodium hydroxide. Fractional crystallization of this mixture from ether and/or petroleum ether gave *trans*-2,4-diphenylthietane (V) (12–15% yield) and a sharp-melting complex of approximately equal amounts of the *cis*- and *trans*-2,4-

(1) F. G. Bordwell and E. Doomes, Abstracts, 157th National Meeting of the American Chemical Society, Minneapolis, Minn., April 1969, No. ORGN 55; F. G. Bordwell, B. B. Jarvis, and P. W. Corfield, *J. Amer. Chem. Soc.*, **90**, 5298 (1968); L. A. Paquette, *Accounts Chem. Res.*, **1**, 209 (1968).

(2) A preliminary account of this work has been published: R. M. Dodson and G. Klose, *Chem. Ind.* (London), 450 (1963).

(3) R. M. Dodson and G. Klose, *ibid.*, 1203 (1963).

(4) R. M. Dodson, P. D. Hammen, and R. A. Davis, *Chem. Commun.*, 9 (1968); correction, *ibid.*, 535 (1968).

(5) (a) The syntheses of thietanes have recently been reviewed: M. Sander, *Chem. Rev.*, **66**, 341 (1966). (b) For more recent methods and references to more recent methods, see L. A. Paquette and M. Rosen, *J. Amer. Chem. Soc.*, **89**, 4102 (1967); *J. Org. Chem.*, **33**, 3027 (1968); L. A. Paquette, M. Rosen, and H. Stucki, *ibid.*, **33**, 3020 (1968); D. C. Dittmer and E. S. Whitman, *ibid.*, **34**, 2004 (1969); A. Ohno, Y. Ohnishi, and G. Tsuchihashi, *Tetrahedron Lett.*, 161, 283 (1969).