spectrum (80 eV), *m/e* (relative intensity) 149 (33), 134 (3), 121 (16), 120 (15), 106 (30), 105 (35), 91 (56), 88 (100), 77 (22), 73 (18), 57 (52), 55 (36), 44 (27), 43 (74), 42 (45), 41 (76), and 39 (60).

Isopropyl Dimethyldithiocarbamate.[12]—Isopropylmagnesium bromide (0.20 mol) was treated with 24.14 g (0.10 mol) of tetramethylthiuram disulfide. After addition of aqueous NH_4Cl, the ether solution was filtered, dried ($MgSO_4$), and evaporated to give 12.3 g (75%) of a light brown oil, which distilled to give the colorless dithiocarbamate: bp 67–69° (0.08 mm) (lit.[13] 126° (12 mm)); uv max (95% EtOH) 223 mμ (ε 12,830), 248 (11,620), and 277 (13,220); ir ($CHCl_3$) 2975, 2940, 2880, 1500, 1380, 1265, 1153, 1065, 990, 880, 753, and 580 cm^{-1}; nmr ($CDCl_3$) δ 1.45 (d, 6, J = 7.5 Hz), 4.05 (septet, 1, J = 7.5 Hz) and 3.57 (s, 6); mass spectrum (80 eV), *m/e* (relative intensity) 163 (52), 121 (31), 120 (11), 88 (100), 73 (13), 44 (15), 43 (18), and 41 (22).

***t*-Butyl Dimethyldithiocarbamate.**—*t*-Butylmagnesium chloride (0.21 mol) was treated with 17.11 g (0.07 mol) of tetramethylthiuram disulfide. After hydrolysis the mass was filtered and the precipitate was washed with ether. The ether was dried ($MgSO_4$) and evaporated giving 13.5 g of a crude black oil, which was distilled giving 8.2 g (71%) of the yellow dithiocarbamate, bp 60–64° (0.08 mm). When the product was cooled in a Dry Ice–acetone bath, colorless crystals formed. It slowly decomposed to tetramethylthiuram disulfide at room temperature. Therefore a good analysis could not be obtained: uv max (95% EtOH) 222 mμ (ε 8600), 250 (8450), and 280 (9550); ir ($CHCl_3$) 2975, 2930, 2865, 1500, 1460, 1375, 1260, 1160, 1140, 1060, 995, 870, 595, and 570 cm^{-1}; nmr ($CDCl_3$) δ 1.65 (s, 9), and 3.40 (s, 6); mass spectrum (80 eV), *m/e* (relative intensity) 166 (12), 121 (27), 88 (95), 73 (18), 57 (56), 44 (31), 42 (50), 41 (100), and 39 (58). *Anal.* Calcd for $C_7H_{15}NS_2$: C, 47.35; H, 8.53; N, 7.96; S, 36.16. Found: C, 48.13; H, 8.64; N, 8.09; S, 35.28.

(12) M. J. Janssen, A. Balasubramanian, and C. N. R. Rao, *J. Sci. Ind. Res.*, **20B**, 349 (1961).

(13) C. W. Pluijgers, "Direct and Systematic Antifungal Action of Dithiocarbamate Acid Derivatives," Thesis, Utrecht, 1959.

Phenyl Dimethyldithiocarbamate.[4]—Phenylmagnesium bromide (0.20 mol) was treated with 0.10 mol of tetramethylthiuram disulfide. After hydrolysis the ether was separated, washed, dried ($MgSO_4$), and evaporated to give a semisolid red oil. Crystallization from cyclohexane gave 5.2 g (26%) of the dithiocarbamate: mp 94–95°; uv max (95% EtOH) 215 mμ (ε 19,600), 243 (12,700), 248 (12,400), and 270 (9200); ir ($CHCl_3$) 2990, 2940, 1510, 1480, 1450, 1390, 1260, 1150, 990, 870, 690, 570, and 510 cm^{-1}; nmr ($CDCl_3$) δ 3.45 (s, 6) and 7.41 (s, 5); mass spectrum (80 eV), *m/e* (relative intensity) 197 (49), 109 (7), 88 (100), 77 (10), 73 (18), and 42 (11). *Anal.* Calcd for $C_9H_{11}NS_2$: C, 54.78; H, 5.57; N, 7.10; S, 32.51. Found: C, 54.77; H, 5.69; N, 7.06, S, 32.61.

***trans*-Styryl Dimethyldithiocarbamate.**—To *trans*-styrylmagnesium bromide from 0.30 mol of *trans*-β-bromostyrene was added 0.10 mol of tetramethylthiuram disulfide. After the usual work-up the ether solution was evaporated to a semisolid, which was crystallized from benzene–hexane to give 11.0 g (51%) of the dithiocarbamate. An analytical sample was obtained from further recrystallization: mp 93–94°; uv max (95% EtOH) 217 mμ (ε 18,950), 275 (25,100), and 302 (17,420); ir ($CHCl_3$) 2990, 2940, 2860, 1610, 1550, 1450, 1390, 1260, 1155, 990, 950, 880, 690, 590, and 570 cm^{-1}; nmr ($CDCl_3$) δ 3.45 (s, 6), 6.75 (d, 1, J = 16 Hz), 7.37 (m, 5), and 7.50 (d, 1, J = 16 Hz); mass spectrum (80 eV), *m/e* (relative intensity), 223 (20), 88 (100), 73 (4), and 42 (3). *Anal.* Calcd for $C_{11}H_{13}NS_2$: C, 59.15; H, 5.86; N, 6.27; S, 28.72. Found: C, 59.26; H, 6.00; N, 6.36; S, 28.15.

Registry No.—Methyl dimethyldithiocarbamate, 3735-92-0; ethyl dimethyldithiocarbamate, 617-38-9; isopropyl dimethyldithiocarbamate, 23885-26-9; *t*-butyl dimethyldithiocarbamate, 23885-27-0; phenyl dimethyldithiocarbamate, 16906-70-0; *trans*-styryl dimethyldithiocarbamate, 23846-99-3; TMTD, 137-26-8.

Acknowledgment.—The author wishes to thank Professor Glenn A. Berchtold for his helpful advice.

Isolation of an Unstable Intermediate in the Reaction of Tetramethyl-3-thio-1,3-cyclobutanedione with Diazomethane

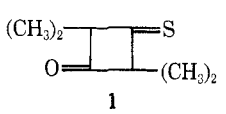
C. E. DIEBERT

Research Laboratories, Tennessee Eastman Company, Division of Eastman Kodak Company, Kingsport, Tennessee 37662

Received November 6, 1969

The reaction of tetramethyl-3-thio-1,3-cyclobutanedione (**1**) with diazomethane gave 4,4,6,6-tetramethyl-1-thiaspiro[2.3]hexan-5-one (**9**). An unstable intermediate isolated from this reaction was tentatively assigned the structure of 3,4-diaza-6,6,8,8-tetramethyl-7-oxo-1-thiaspiro[4.3]oct-3-ene (**8a**) on the basis of infrared and nmr spectra. The thiirane ring of **9** was found to be surprisingly unreactive toward nucleophilic and electrophilic reagents, although it could be desulfurized with triphenylphosphine to give 2,2,4,4-tetramethyl-3-methylenecyclobutanone (**17**) or with Raney nickel to yield 2,2,3,4,4-pentamethylcyclobutanone as the major product. Reduction of **9** with lithium aluminum hydride or sodium borohydride gave a mixture of isomeric alcohols **12**, leaving the thiirane ring unattacked.

The synthesis of tetramethyl-3-thio-1,3-cyclobutanedione (**1**) was recently reported.[1,2] This compound is



1

one of the few stable aliphatic thio ketones known. It has no tendency to polymerize or dimerize, in contrast to most aliphatic thio ketones.[3,4] The ready availability of **1** allowed studies of the chemistry of an aliphatic thione group without the complications of dimerization, enolization, etc. This account will be limited primarily to a discussion of the reaction of the thione group with diazomethane and to a discussion of the chemistry of the resulting products.

The first report of the reaction between a diazoalkane and a thio ketone was that of Staudinger and Siegwart,[5] who investigated the reaction between diphenyldiazomethane and various diaryl thio ketones (Scheme I). The reaction resulted in the formation of tetrasubstituted thiiranes, which lost sulfur upon heating to give the corresponding ethylenes. Staudinger and Siegwart postulated the formation of an unstable Δ^2-1,2,3-

(1) E. U. Elam and H. E. Davis, *J. Org. Chem.*, **32**, 1562 (1967).

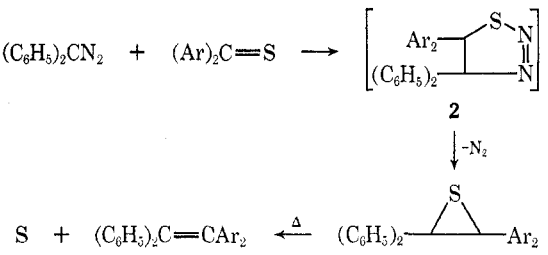
(2) R. D. Lipscomb (to E. I. du Pont de Nemours and Co., Inc.), U. S. Patent 3,297,765 (Jan 10, 1967).

(3) R. Mayer, J. Morgenstern, and I. Fabian, *Angew. Chem.*, **76**, 157 (1964).

(4) E. Campaigne in "The Chemistry of the Carbonyl Group," S. Patai, Ed., Interscience Publishers, Inc., New York, N. Y., 1966, p 917.

(5) H. Staudinger and J. Siegwart, *Helv. Chim. Acta*, **3**, 833 (1920).

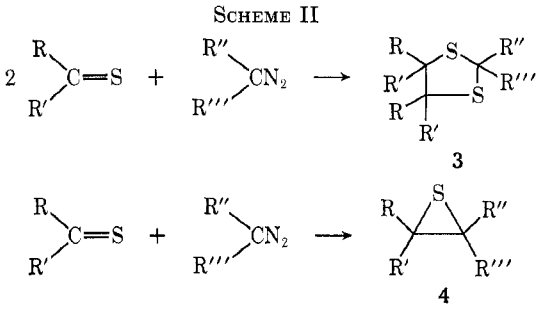
SCHEME I



thiadiazoline intermediate 2, but they were not able to isolate it or provide any evidence for its existence.

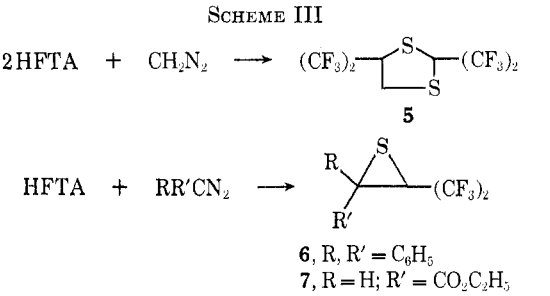
Since 1930 Schönberg and coworkers have described, in an extensive series of papers, similar reactions between diazoalkanes and various diaryl thio ketones.[6] They isolated either a 1,3-dithiolane **3** or a thiirane **4** but they never found both in the same reaction (Scheme II).

SCHEME II



The reactions of hexafluorothioacetone (HFTA) with diazomethane, diphenyldiazomethane, and ethyl diazoacetate have been reported.[7] HFTA with diazomethane yields the unsymmetrical product, 2,2,5,5-tetrakis(trifluoromethyl)-1,3-dithiolane (**5**). With diphenyldiazomethane or ethyl diazoacetate, HFTA gives the normal thiirane derivative (**6** or **7**, Scheme III).

SCHEME III



Results and Discussion

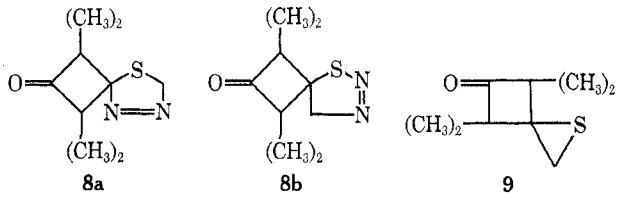
Reaction of Tetramethyl-3-thio-1,3-cyclobutanedione (1) with Diazomethane.—When an ether solution of the monothione **1** was treated with an ether solution of diazomethane, the initial red color disappeared as the diazomethane was added and no nitrogen was evolved. When the ether was removed at 0° or below, a white solid A was obtained; this solid spontaneously lost nitrogen when allowed to warm to room temperature or when refluxed in ether–pentane to give a new white solid **9**.

(6) A. Schönberg, B. Konig, and E. Singer, *Chem. Ber.*, **100**, 767 (1967), and references therein.

(7) W. J. Middleton and W. H. Sharkey, *J. Org. Chem.*, **30**, 1384 (1965).

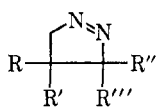
The spectral data obtained from **9** established its structure as that of 4,4,6,6-tetramethyl-1-thiaspiro-[2.3]hexan-5-one.[8]

The infrared spectrum of A displayed strong bands at 1780 (cyclobutanone carbonyl) and at 1565 cm^{-1} (–N=N–). No absorption due to the RN_2^+ group was observed in the region of 2100 cm^{-1}. The nmr spectrum showed absorptions at 1.17 and 1.25 (each singlets with combined area of 12, CH_3) and at 5.70 ppm (singlet with area of 2, CH_2). From the spectral data, it appears that there are two reasonable structures for A: a Δ^3-1,3,4-thiadiazoline (**8a**) or a Δ^2-1,2,3-thiadiazoline (**8b**). These are the products from the two possible modes of addition of diazomethane to the



thiocarbonyl group. Although the infrared spectrum is compatible with both structures, the nmr spectrum suggests that **8a** is the more probable structure on the basis of the low field position of the methylene protons. No nmr data were found for the chemical shift of a methylene group in a Δ^2-1,2,3-thiadiazoline or a Δ^3-1,3,4-thiadiazoline.

The most nearly analogous compounds for which nmr data were found were 1-pyrazolines (**10a–10d**), which were prepared by the reaction of diazomethane with electron-deficient olefins.[9,10] In these compounds the methylene protons showed a chemical shift in the range of δ 4.20–4.81 ppm. On this basis, A was assigned



10a–10d

10a, R and R′ = CH_3; R″ = CN; R‴ = CO_2CH_3
b, R and R′ = CH_3CH_2; R″ = CN; R‴ = CO_2CH_3
c, R = CH_3; R′ = CH_3CH_2; R″ = CN; R‴ = CO_2CH_3
d, R and R′ = CH_3; R″ and R‴ = CN

the structure of 3,4-diaza-6,6,8,8-tetramethyl-7-oxo-1-thiaspiro[4.3]oct-3-ene (**8a**)[11] to account for the downfield shift of the methylene protons (~1 ppm) relative to the 1-pyrazolines. Structure **8a** is assumed to be correct for the unstable intermediate in discussions in the text, although it is recognized that structure **8b** cannot be discarded since the nmr evidence is not entirely definitive.

Thermal Decomposition of the Thiadiazoline 8a.—The rate of decomposition of **8a** in carbon tetrachloride at 49 ± 2° was followed by integrating the areas of the

(8) The photochemistry of 4,4,6,6-tetramethyl-1-thiaspiro[2.3]hexan-5-one was described in a recent communication: J. G. Pacifici and C. E. Diebert, *J. Amer. Chem. Soc.*, **91**, 4595 (1969).

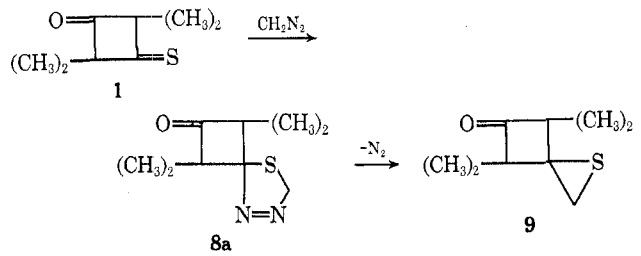
(9) J. Bus, H. Steinberg, and Th. J. de Boer, *Monatsh. Chem.*, **44**, 675 (1967).

(10) D. E. McGreer, R. S. McDaniel, and M. J. Vinjé, *Can. J. Chem.*, **43**, 1389 (1965).

(11) During the preparation of this paper, an isolable intermediate was reported in the reaction of hexafluorothioacetone with bis(trifluoromethyl)-diazomethane. The intermediate was shown to have a structure analogous to **8a** on the basis of its ^{19}F nmr spectrum: W. J. Middleton, *J. Org. Chem.*, **34**, 3201 (1969).

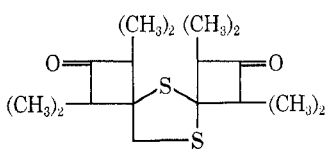
two different methylene resonances as the decomposition proceeded. The decomposition followed first-order kinetics, with $k = 5.2(10^{-4})$ sec^{-1}. The only product found from the decomposition was the thiirane **9**. The reaction sequence is shown in Scheme IV.

SCHEME IV



This report appears to be the first to describe the actual isolation and spectral characterization of an intermediate in the reaction of unsubstituted diazoalkanes with a thio ketone.[11]

Decomposition of the Thiadiazoline 8a in Excess Monothione 1.—When **8a** was decomposed in the presence of excess monothione **1**, a new product was obtained in addition to the thiirane **9**. This new compound showed infrared absorption at 1765 cm^{-1} (cyclobutanone carbonyl). A high-resolution mass spectrum of the compound gave the molecular weight as 326.1371. The molecular weight calculated for the molecular formula $C_{17}H_{26}O_2S_2$ is 326.1374. Therefore, the compound was an adduct containing two molecules of monothione **1** and one methylene group. The nmr spectrum of the compound in deuteriochloroform displayed four singlets at δ 1.28, 1.38, 1.43, and 3.18 ppm in the area ratio of 6:3:3:1. Addition of a small amount of benzene to the deuteriochloroform solution caused the singlet at δ 1.28 ppm to split into two singlets; no other new peaks were observed. On the basis of the spectral data, this compound was assigned structure **11**, which is analogous to the HFTA–diazomethane adduct **5**.



Reactions of Thiirane 9.—The reactions of **9** which were investigated are summarized in Scheme V.

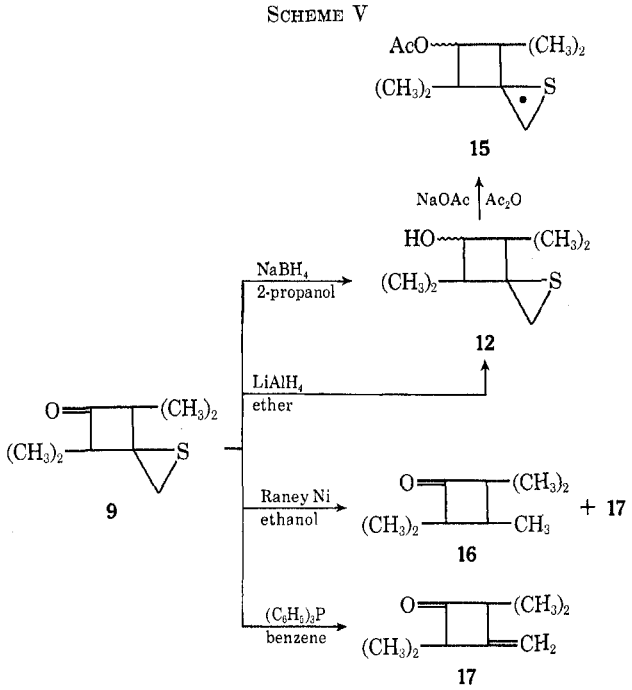
Ring-opening reactions of thiiranes with both electrophilic and nucleophilic reagents are usually facile.[12,13] Polymerization of the thiirane is often an important competing reaction. Surprisingly, **9** failed to react with copper bronze in refluxing xylene for 3.5 hr, with morpholine at 100° for 24 hr, with acetyl chloride at reflux for 3.5 hr, or with 0.1 *N* sodium methoxide in methanol at reflux for 1.5 hr.

Reduction of **9** with sodium borohydride or lithium aluminum hydride gave a mixture of *cis*- and *trans*-4,4,6,6-tetramethyl-1-thiaspiro[2.3]hexan-5-ols (**12**).

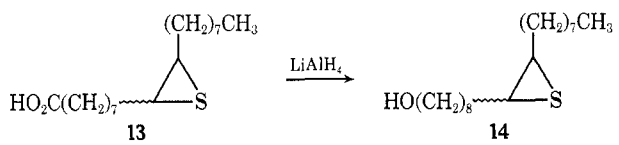
(12) M. Sander, *Chem. Rev.*, **66**, 297 (1966).

(13) D. D. Reynolds and D. L. Fields in "The Chemistry of Heterocyclic Compounds," A. Weissberger, Ed., Vol. 19, Part 1, Interscience Publishers, Inc., New York, N. Y., 1964, p 602.

SCHEME V



There was no evidence for reduction of the thiirane ring. These reactions further demonstrate the unreactive nature of the thiirane ring in episulfide **9**, since reduction of thiiranes with lithium aluminum hydride usually gives mercaptans resulting from attack of the hydride at the least substituted carbon of the thiirane ring.[14,15] However, the *cis* and *trans* thiiranes **13** are known to react with lithium aluminum hydride to yield the *cis* and *trans* alcohols **14** without opening of the thiirane ring.[16]



The mixture of alcohols **12** reacted with acetic anhydride in the presence of sodium acetate to give a mixture of *cis* and *trans* acetates **15**. No ring-opened product from this reaction was found.

Thiirane **9** was desulfurized with Raney nickel in ethyl alcohol to give 2,2,3,4,4-pentamethylcyclobutanone (**16**) and 2,2,4,4-tetramethyl-3-methylenecyclobutanone (**17**).

When **9** was heated with triphenylphosphine in refluxing benzene, it reacted slowly to give only one product, 2,2,4,4-tetramethyl-3-methylenecyclobutanone (**17**). The physical constants of **16** and **17** were in good agreement with reported values, thus providing further confirmation of the structure of **9**.

Owing to the proximity of the methylene and carbonyl groups, it was thought that the ultraviolet spectrum of **17**[17] should display 1,3-π interaction similar to that postulated for the homologous compound, 3-methy-

(14) F. G. Bordwell, H. M. Andersen, and B. M. Pitt, *J. Amer. Chem. Soc.*, **76**, 1082 (1954).

(15) R. L. Jacobs and R. D. Schuetz, *J. Org. Chem.*, **26**, 3472 (1961).

(16) J. F. McGhie, W. A. Ross, F. J. Julietti, B. E. Grimwood, G. Usher, and N. M. Waldron, *Chem. Ind.* (London), 1980 (1962).

(17) The synthesis of **17** was reported by D. P. Hamon, *J. Amer. Chem. Soc.*, **90**, 4513 (1968), and its ultraviolet spectrum was recorded. This author did not discuss its ultraviolet spectrum.

lenecyclobutanone.[18,19] Thus, the ultraviolet spectrum of **17** was examined. The methylenecyclobutanone **17** showed the following absorptions in the ultraviolet: λ_{max}^{hexane} 211 nm (ϵ 1800), 313 (22). The pentamethylcyclobutanone[20] **16** showed the following absorption: λ_{max}^{hexane} 311 nm (ϵ 23), none in the 200-nm region. The bands at ~310 nm in **16** and **17** can be attributed to an $n\rightarrow\pi^*$ absorption of the carbonyl group. The band at 211 nm in **17** is at a longer wavelength than would be expected for the $\pi\rightarrow\pi^*$ absorption of a nonconjugated ethylene group and presumably is not due to a $\pi\rightarrow\pi^*$ absorption of the carbonyl group, since **16** shows no absorption in the 200-nm region. Thus, it appears that the 211-nm absorption in **17** is most reasonably attributed to a $\pi\rightarrow\pi^*$ charge-transfer band resulting from overlap of the π orbitals of the ketone and double bond.[19,21]

Experimental Section[22]

Materials.—Diazomethane was generated from N,N'-dimethyl-N,N'-dinitrosoterephthalamide (Aldrich Chemical Co.).[23] The tetramethyl-3-thio-1,3-cyclobutanedione[1] used in these studies was ≥95% pure by glpc.

4,4,6,6-Tetramethyl-1-thiaspiro[2.3]hexan-5-one (9).—Tetramethyl-3-thio-1,3-cyclobutanedione (15.6 g, 0.1 mol) was dissolved in *ca.* 100 ml of dry ether and cooled to 0° while the solution was stirred by means of a magnetic stirrer. Diazomethane was generated and slowly distilled into the ether solution until the initial deep red color of the solution had changed to a faint yellow. No nitrogen was evolved during addition of the diazomethane. The ether was then removed below 20° by means of a rotary evaporator. The residual mixture of solid and oil began to evolve nitrogen upon warming to room temperature. The mixture was dissolved in boiling pentane and filtered to remove traces of suspended matter. During the filtration, evolution of gas was vigorous. The pentane filtrate was cooled in Dry Ice and filtered to yield 11.4 g (67%) of a white solid, mp 77.5–81°. Recrystallization of the solid from pentane yielded an analytical sample of **9**, mp 80–82°.

The following spectral data were obtained on **9**: ir (KBr) 2960, 1785, 1445, 1375, 1360, 1005, 815, and 665 cm^{-1}; nmr ($CDCl_3$) δ 2.55 (singlet, area 2, CH_2), 1.18 and 1.12 ppm (both singlets with combined area of 12, CH_3); uv λ_{max}^{hexane} 209 nm (ϵ 610), 225 (190), 265 (62), and 313 (21). The mass spectrum of **9** showed the mass of the parent ion to be 170.

Anal. Calcd for $C_9H_{14}OS$: C, 63.48; H, 8.29; S, 18.83. Found: C, 63.36; H, 8.36; S, 18.50.

Isolation of the Unstable Intermediate 8a.—An aliquot of the cold ether solution of intermediate **8a**, prepared as described above, was transferred to a Schlenk tube, and the ether was pumped off while the solution was maintained at 0° or below. After the ether was completely removed, a white solid remained. The sample was stored at −60°, the Schlenk tube was opened under nitrogen, and the sample was dissolved in carbon tetrachloride. The temperature of the nmr probe was adjusted to 49 ± 2°, and a nmr spectrum was obtained on the freshly prepared sample. The intermediate showed absorptions at δ 5.70 (singlet, area 2, CH_2) and 1.25 and 1.17 ppm (both singlets with combined area of 12, CH_3). As the decomposition of **8a** proceeded, new absorptions at δ 2.55 (singlet), 1.18 (singlet), and 1.12 ppm (singlet) appeared. No absorption due to other decomposition products was observed. The rate of decomposition of **8a** was obtained by integrating the areas of the methylene proton signals at δ 5.70 and 2.55 ppm. The decomposition was found to obey first-order kinetics, with $k = 5.2(10^{-4})$ sec^{-1}.

The infrared spectrum (CCl_4) of **8a** displayed strong absorption at 2930, 1780, 1565, 1450, 1375, 1360, and 1025 cm^{-1}.

Decomposition of the Intermediate 8a in the Presence of Excess Monothione 1.—Monothione **1** (1.56 g, 10 mmol) was dissolved in 10 ml of anhydrous ether, the solution was cooled to 0°, and diazomethane (25 ml of 0.33 *M* solution, 8.3 mmol) was added dropwise. After the addition of diazomethane was completed, the ether was removed by means of rotary evaporator to give a red, semisolid product. About 5 ml of hexane was added to the reaction product, and the solution was warmed on a steam bath. The solution was cooled and then filtered to yield 0.50 g (31% based on **1**) of the 2:1 adduct **11**, mp 162–164°. Glpc analysis of the filtrate showed the presence of unchanged monothione **1** as well as thiirane **9**.

The following spectral data were obtained on **11**: ir (KBr) 2960, 1765, 1450, 1372, 1352, and 1020 cm^{-1}; nmr ($CDCl_3$) δ 3.18 (singlet, area 2, CH_2), 1.43 (singlet, area 6, CH_3), 1.38 (singlet, area 6, CH_3), and 1.28 ppm (singlet, area 12, CH_3); nmr ($CDCl_3$–benzene) δ 2.88 (singlet area 2, CH_2) and 1.33, 1.28, 1.23, and 1.08 ppm (all singlets, combined area 24, CH_3). A high-resolution mass spectrum of **11** gave the mass of the parent ion as 326.1371; the calculated mass for the molecular formula $C_{17}H_{26}O_2S_2$ is 326.1374.

4,4,6,6-Tetramethyl-1-thiaspiro[2.3]hexan-5-ol (12). A. From Reduction with Sodium Borohydride.—Thiirane **9** (1.70 g, 10 mmol) was dissolved in 15 ml of dry 2-propanol. Sodium borohydride (0.76 g, 20 mmol) dissolved in 10 ml of dry 2-propanol was added dropwise to the stirred reaction mixture. The mixture was stirred at room temperature for 17 hr, and excess borohydride was then destroyed by addition of 2% hydrochloric acid. The aqueous solution (pH 2) was saturated with sodium chloride, 20 ml of ether was added, and the ether phase was then washed with two 20-ml portions of saturated sodium chloride solution. The organic phase was separated, dried over anhydrous sodium sulfate, filtered, and evaporated to give 1.7 g (99%) of a mixture of *cis* and *trans* alcohols **12**, mp 45–53°. The alcohol mixture was recrystallized from 30–60° petroleum ether to give an analytical sample, mp 57–59°.

The infrared spectrum (CCl_4) showed absorption at 3600, 3450, 2940, 1465, 1375, 1365, and 1075 cm^{-1}. The nmr spectrum ($CDCl_3$) indicated that the sample was a 30:70 mixture of isomeric alcohols. The major isomer showed absorption at δ 3.76 (–O–C(H)–), 2.44 (CH_2), 2.14 (OH), 1.13 (CH_3), and 0.98 ppm (CH_3); the other isomer showed corresponding absorption at δ 3.88, 2.38, 2.14, 1.10, and 1.01 ppm. All absorptions were singlets. Since suitable model compounds were not available, assignment of absorptions to the appropriate isomer was not possible. The ultraviolet spectrum of the mixture of isomers showed absorption at λ_{max}^{hexane} 208 nm (ϵ 730) and 261 (44). The mass spectrum of the mixture showed the mass of the parent ion to be 172.

Anal. Calcd for $C_9H_{16}OS$: C, 62.74; H, 9.36; S, 18.61. Found: C, 62.87; H, 9.02; S, 18.61.

B. From Reduction with Lithium Aluminum Hydride.—Lithium aluminum hydride (0.40 g, 10 mmol) was suspended in 20 ml of anhydrous ether. Thiirane **9** (1.70 g, 10 mmol) was dissolved in 15 ml of ether and added dropwise to the stirred suspension. The mixture was then refluxed for 2 hr. The reaction mixture was cooled to *ca.* 5°, and water (0.4 ml), 15% sodium hydroxide (0.4 ml), and water (1.2 ml) were added successively. The resulting fine, granular precipitate was collected on a filter and washed with a small amount of ether. The ether filtrate was then dried over anhydrous sodium sulfate. The ether solution was filtered, and the filtrate was then evaporated to give 1.4 g (82%) of **12**, mp 55–58°.

The infrared and nmr spectra of the mixture of alcohols were identical with the spectra reported under A. The nmr spectrum indicated the sample to be a 25:75 mixture.

(18) F. F. Caserio and J. D. Roberts, *J. Amer. Chem. Soc.*, **80**, 5837 (1958).
(19) P. Dowd and K. Sachdev, *ibid.*, **89**, 714 (1967).
(20) J-M. Conia and J. Gore, *Bull. Soc. Chim. Fr.*, 1968 (1964).
(21) S. Winstein, L. de Vries, and R. Orloski, *J. Amer. Chem. Soc.*, **83**, 2020 (1961).
(22) Melting points were obtained with a Thomas–Hoover capillary melting point apparatus and are uncorrected. The nmr spectra were obtained with a Varian A-60 spectrometer equipped with a variable-temperature probe and a Varian HA-100 spectrometer. Chemical shifts are expressed in δ values (parts per million) from tetramethylsilane as internal standard; coupling constants are expressed in cycles per seconds. Mass spectra were obtained with a Consolidated Electrodynamics Corp. Model 21-110B mass spectrometer operated at an ionizing voltage of 70 eV. Infrared spectra were obtained with a Perkin-Elmer Infracord and a Perkin-Elmer Model 421 spectrophotometer. Ultraviolet spectra were obtained with a Cary Model 14-MS and a Perkin-Elmer Hitachi Model 123 spectrophotometer. Glpc analyses were done with an F & M Model 810 chromatograph using a 20% silicone QF-1 on Chromosorb P (1/8 in. × 6 ft) column. Elemental analyses were performed by the Analytical Services Laboratory of Tennessee Eastman Research Laboratories.
(23) J. A. Moore and D. E. Reed, *Org. Syn.*, **41**, 16 (1961).

2,2,4,4-Tetramethyl-3-methylenecyclobutanone (17).—A mixture of 9 (1.70 g, 10 mmol) and triphenylphosphine (2.62 g, 10 mmol) in 20 ml of dry benzene was refluxed for 38 hr. The reaction mixture was periodically examined by glpc. The reaction was found to be about 50% complete after 3 hr and about 90% complete after 38 hr. The reaction proceeded cleanly to give only triphenylphosphine sulfide and **17**; no other products were found by glpc.

Samples of **17** (mp 42.5–44°) were collected from an analytical chromatograph in capillary tubes. The following spectral data[24] were obtained: ir (CCl_4) 3050, 2940, 1790, 1675, 1460, 1000, and 890 cm^{-1}; uv λ_{max}^{hexane} 211 nm (ϵ 1800) and 313 (22); nmr (CCl_4) δ 5.03 (singlet) and 1.22 ppm (singlet) with area ratio 1:6. The mass spectrum showed the mass of the parent ion to be 138.

A 2,4-dinitrophenylhydrazone of **17** was prepared, mp 145–147°; uv $\lambda_{max}^{abs\ EtOH}$ 212 nm (ϵ 6510), 230 (6360), and 355 (10,300).

Anal. Calcd for $C_{15}H_{18}N_4O_4$: C, 56.60; H, 5.70; N, 17.60. Found: C, 56.81; H, 5.73; N, 17.58.

4,4,6,6-Tetramethyl-1-thiaspiro[2.3]hexan-5-yl Acetate (15).—The mixture of *cis* and *trans* alcohols **12** (0.5 g, 2.9 mmol) was heated with 0.5 g of sodium acetate and 5 ml of acetic anhydride on a steam bath for 2 hr. The solution was then poured into 30 ml of cold water. The mixture was allowed to stand, with occasional stirring, for 30 min. The aqueous mixture was extracted with three 20-ml portions of ether, and the combined ether extracts were washed with cold 15% sodium carbonate. The ether layer was dried over anhydrous sodium sulfate, filtered, and evaporated to give 0.54 g (87%) of a white solid. The mixture of *cis* and *trans* acetates was recrystallized from 30–60° petroleum ether, mp 35–37.5°.

The following spectral data were obtained for **15**: ir (KBr) 2960, 1740, 1460, 1450, 1365, 1230, and 1050 cm^{-1}; the nmr ($CDCl_3$) of the major isomer showed absorption at δ 4.60 (AcOCH), 2.46 (CH_2), 2.10 (CH_3CO_2), 1.12 (CH_3), and 1.07 ppm (CH_3); the minor isomer displayed corresponding absorptions at δ 4.74, 2.40, 2.10, 1.18, and 0.98 ppm. All peaks in the nmr spectrum were singlets, and the spectrum showed that the sample was a 30:70 mixture. A high-resolution mass spectrum of the mixture gave the measured mass of the parent ion as 214.1032, which corresponds to the molecular formula $C_{11}H_{18}O_2S$ (calcd for $C_{11}H_{18}O_2S$: 214.1027).

Reaction of Thiirane 9 with Raney Nickel.—Thiirane **9** (1.0 g, 5.9 mmol) was dissolved in 25 ml of ethyl alcohol and Raney nickel catalyst (~10 g) was added. The reaction mixture became warm. The mixture was refluxed under nitrogen for 3 hr and then filtered through Celite filter aid.

The filtrate was examined by glpc. A major product and a minor product were found. These two products were collected from the analytical glpc in capillary tubes. The minor product was shown to have structure **17** by comparison of its infrared spectrum with that of an authentic sample.

The major product, 2,2,3,4,4-pentamethylcyclobutanone (**16**), was isolated as a colorlessl iquid. The following spectral data were obtained for **16**: ir (neat) 2950, 1785, 1580, 1380, 1 365, and 1040 cm^{-1}; nmr ($CDCl_3$) δ 1.97 (quartet, $CHCH_3$, J = 7 cps), 1.17 (singlet, CH_3), 1.06 (singlet, CH_3), and 1.03 ppm (doublet, $CHCH_3$, J = 7 cps) [lit.[25] nmr (CCl_4) δ 1.91, 1.15, 1.06, and 1.06 ppm]; uv λ_{max}^{hexane} 311 nm (ϵ 23), [lit.[20] uv λ_{max}^{hexane} 311 nmr (ϵ 22)]. The mass spectrum of **16** showed the mass of the parent ion to be 140.

A 2,4-dinitrophenylhydrazone of **16** was prepared, mp 144–145° (lit.[20] mp 145°).

Registry No.—**8a**, 23604-61-7; **9**, 23604-62-8; **11**, 23604-63-9; *cis*-**12**, 23601-92-5; *trans*-**12**, 23601-93-6; *cis*-**15**, 23601-94-7; *trans*-**15**, 23601-95-8; **17**, 20019-11-8; 2,4-dinitrophenylhydrazone of **17**, 23604-65-1.

Acknowledgment.—The author is grateful to Dr. V. W. Goodlett and Mr. H. D. Kinder, Research Laboratories, Tennessee Eastman Co., for helpful discussions of the nmr spectra.

(24) The spectral data agree favorably with those reported by Hamon.[17]

(25) B. Braillon, J. Salaun, J. Gore, and J-M. Conia, *Bull. Soc. Chim. Fr.* 1981 (1964).

The Facilitation of Sodium Borohydride Reduction of Esters of Phenols and of Acidic Alcohols

SHO TAKAHASHI[1] AND LOUIS A. COHEN

National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland 20014

Received June 6, 1969

The reduction of esters (RCOOR') by sodium borohydride is facilitated by use of R' groups more electronegative than methyl, rate enhancements of at least 300-fold having been demonstrated. The rates of reduction of substituted phenyl esters correlate linearly with the pK_a values of the corresponding phenols (ρ = 2.6), a separate correlation being obtained for alcohols. In 1,2-dimethoxyethane as solvent, esters of acidic alcohols are 10–50 times as reactive toward borohydride as are those of phenols of comparable pK_a, the difference being ascribed to conformational or steric obstruction by the aromatic ring; furthermore, reduction is significantly faster in media containing water. By use of an appropriate alcohol for esterification, carboxyl groups can be reduced selectively to primary alcohols in the presence of functional groups which are reactive toward more powerful reducing agents.

Esters of simple carboxylic acids are normally resistant to reduction by sodium borohydride.[2] However, reduction can sometimes be effected by activation of the reagent, *e.g.*, by its conversion, *in situ*, into lithium or magnesium borohydride,[3] or to a more reactive alkoxyborohydride.[4]

In connection with studies on the selective modification of proteins,[5] we encountered the problem of effecting the specific reduction of esters under the mildest possible conditions. Since lithium borohydride[6a] and diborane[5,6b] are known to reduce amides as well as esters, and since the solubility and stability properties of proteins restrict the use of the methods cited above, an alternative mode of reduction was sought.

In a number of instances, sodium borohydride has been effective in reducing esters of carboxylic acids con-

(1) Associate in the Visiting Program, National Institutes of Health, 1967–1969.

(2) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, Chapter 2.

(3) H. C. Brown, E. J. Mead, and B. C. Subba Rao, *J. Amer. Chem. Soc.*, **77**, 6209 (1955).

(4) (a) H. C. Brown and E. J. Mead, *ibid.*, **75**, 6263 (1953); (b) H. C. Brown, E. J. Mead, and C. J. Shoaf, *ibid.*, **78**, 3616 (1956); (c) M. S. Brown and H. Rapoport, *J. Org. Chem.*, **28**, 3261 (1963).

(5) See, *e.g.*, S. Takahashi and L. A. Cohen, *Biochemistry*, **8**, 864 (1969).

(6) (a) A. C. Chinbnall and M. W. Rees, *Biochem. J.*, **68**, 105 (1958); (b) O. Yonemitsu, T. Hamada, and Y. Kanaoka, *Tetrahedron Lett.*, 3575 (1968).