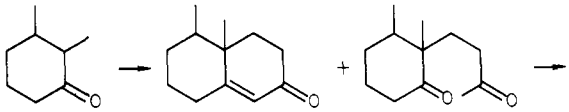
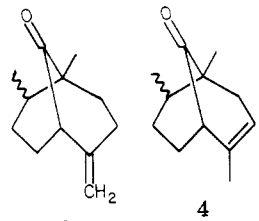
at 0–5 °C, a mixture of octalones and diketones (eq 1) was



1 + 2 (1)

isolated. The structure of the mixture was inferred from the singlet absorptions due to the vinyl proton (δ 5.75) and the methyl proton (δ 2.10) in the NMR spectrum as well as the characteristic carbonyl absorptions at 1675 and 1710 cm^{-1} in the IR spectrum. Base-catalyzed cyclization[8] of the mixture of octalones and diketones with sodium methoxide in methanol at 45–50 °C afforded a 33% yield of 1 and 2 in a ratio ≥9:1 as determined by ^{13}C NMR analysis.[9] A mixture (~5%) of the bicyclic ketones 3 and 4 were also isolated, after chromatography, in a 2:1 ratio as determined by ^{13}C NMR analysis.



3 4

When 2,3-dimethylcyclohexanone and methyl vinyl ketone were refluxed in the presence of sulfuric acid in benzene for 20 h, the octalones 1 and 2 (~25%) were obtained in a ratio of ≥9:1, and the bicyclo[3.3.1]nonenones 3 and 4 (5–7%) were also isolated as minor components of the reaction mixture.

Experimental Section

***cis*-5,10-Dimethyl-1(9)-octal-2-one (1).** A mixture of 2,3-dimethylcyclohexanone (19.0 g, 0.15 mol) and methyl vinyl ketone (10.5 g, 12.1 mL, 0.15 mol) in 100 mL of benzene was cooled to 0 °C (ice–salt bath). Concentrated sulfuric acid (3.0 mL) was added dropwise via a syringe, and the reaction mixture was stirred at 0 °C for 2 h. After 2 h, methyl vinyl ketone (6.1 mL, 0.075 mol) and 1.0 mL of concentrated sulfuric acid (dropwise addition) were added, and the reaction mixture was stirred at 0 °C for an additional 2.5 h. A final addition of methyl vinyl ketone (6.1 mL, 0.075 mol) was added, and the reaction mixture was stirred overnight at 0 °C.

The reaction mixture was poured into 400 mL of ether, and the polymeric residue was washed with two 200-mL portions of ether. The organic solutions were combined and washed with 200 mL of a 1 N sodium hydroxide solution and 400 mL of brine. The aqueous solution was rewashed with two 400-mL portions of ether; and the organic solutions were combined, dried ($MgSO_4$), and concentrated in vacuo to afford an oil. Distillation afforded 6.8 g (36%) of recovered 2,3-dimethylcyclohexanone [bp 60–65 °C (15 mm)] and 12.2 g of a mixture of octalones and diketones: bp 85–95 °C (0.03 mm); NMR (CCl_4) δ 5.75 (s), 1.15 (s), 2.10 (s); IR (neat) 1675, 1710 cm^{-1}. Cyclization of the mixture with sodium methoxide in methanol by following the procedure of Marshall and Schaeffer[8] and subsequent distillation and chromatography on silica gel (elution with hexanes and ether–hexane solutions) afforded 8.7 g (33%) of 1 and 2 in a ratio ≥9:1 as determined by ^{13}C NMR[9] analysis (the spectral properties of the mixture of 1 and 2 were identical with those reported[10] previously for 1 and 2) and approximately 5% of the bicyclo[3.3.1]nonenones 3 and 4 in a 2:1 ratio: ^{13}C NMR (90 M Hz, proton decoupled, $CDCl_3$) 217.82, 217.23, 217.03 and 216.37 (carbonyls), 134.16 and 133.78 (endocyclic quarternary carbon), 123.03 and 122.74 (endocyclic tertary carbon), 110.75 and 110.19 ppm (exocyclic methylene); IR (neat) 1720 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O$: C, 80.84; H, 10.18. Found: C, 80.71; H, 10.20.

Acknowledgment. We thank Dr. L. Jaques and Mr. A. F. Johnson, Jr., of the A. H. Robins Pharmaceutical Co. for recording the ^{13}C NMR spectra, the Research Administration Fund (SMU) for partial support of this work, and Mr. R. J. Chambers for technical assistance.

Registry No. 1, 43209-93-4; 2, 43209-94-5; 3, 78019-73-5; 4, 78019-74-6; 2,3-dimethylcyclohexanone, 13395-76-1; methyl vinyl ketone, 78-94-4.

(8) J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964).
(9) G. I. Birnbaum, A. Stoessl, S. H. Grover, and J. B. Stothers, *Can. J. Chem.*, **52**, 993 (1974).
(10) We thank Professor R. K. Boeckman, Jr., for providing a sample of a mixture of 1 and 2.

α-Oxoketene Dithioacetal Chemistry. 2. Conjugate Reductions with Electrophilic Reducing Agents

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Regiospecific hydride reductions of α,β-unsaturated carbonyl compounds continue to play an important role in organic synthesis. In recent years an increased number of reports have appeared describing the regiospecific reduction of various β-heteroatom enones.[2] These reductions have increased in popularity by virtue of the ease of preparation of the β-heteroatom enones and their subsequent conversion to those functionalities routinely used by organic chemists in synthesis. As with the hydride reductions of simple unsaturated carbonyl systems, reductions of these functionalized enones are not always straightforward, and many times complex mixtures of reduction products arise. There are, however, a number of specific and synthetically useful β-heteroatom enone reductions that give either 1,2 hydride reduction and thus allylic alcohols (or the products of dehydration) as products[2a-c] or 1,4 hydride reduction and thus β-functionalized carbonyl compounds as products.[2c-f,h,i]

α-Oxoketene dithioacetals are highly functionalized three-carbon units whose utility in synthesis has steadily been increasing.[3] As part of a program to explore the chemistry of these compounds, we were intrigued with the possibility of selectively controlling, by hydride delivery, the various oxidation levels at each of the three carbon atoms in the α-oxoketene dithioacetal system. Our earliest

(1) Taken in part from the Senior Independent Project of D.M.S., Kalamazoo College, Kalamazoo, MI, 1981.
(2) (a) W. F. Gannon and H. O. House, *Org. Synth.*, **40**, 14 (1960); (b) M. Stiles and A. L. Longroy, *J. Org. Chem.*, **32**, 1095 (1967); (c) O. Dann and G. Voltz, *Justus Liebigs Ann. Chem.*, **685**, 167 (1965); (d) A. D. Harmon and C. R. Hutchinson, *Tetrahedron Lett.*, 1293 (1973); (e) C. Kashima, Y. Yamamoto, and Y. Tsuda, *J. Org. Chem.*, **40**, 526 (1975); (f) J. Froberg, G. Magnusson, and S. Thoren, *Tetrahedron Lett.*, 1621 (1975); (g) G. Stork and R. L. Danheiser, *J. Org. Chem.*, **38**, 1775 (1973); (h) H. Minato, *J. Chem. Soc C*, 1575 (1967); (i) R. F. Borch, M. D. Bernstein, and H. D. Durst, *J. Am. Chem. Soc.*, **93**, 2897 (1971).
(3) For the use of α-oxoketene dithioacetals in synthesis see: E. J. Corey and R. H. K. Chen, *Tetrahedron Lett.*, 3817 (1973); I. Shahak and Y. Sasson, *ibid.*, 4207 (1973); J. Maignan and J. Vialle, *Bull. Soc. Chim. Fr.*, 2388 (1973); S. M. S. Chanhan and H. Junijappa, *Synthesis*, 880 (1974); 798 (1975); R. R. Rastogi, H. Ila, and H. Junijappa, *J. Chem. Soc., Chem. Commun.*, 645 (1975); A. Kumar, H. Ila, and H. Junijappa, *ibid.*, 593 (1976); M. Watanabi, K. Matsuno, T. Kinoshita, and S. Furukawa, *Heterocycles*, **6**, 1781 (1977); M. Augustin, G. Jahreis, and W.-D. Rudorf, *Synthesis*, 472 (1977); W.-D. Rudorf, A. Schierhorn, and M. Augustin, *Tetrahedron*, **35**, 551 (1979); A. Kakeli, S. Ito, K. Nakaniski, and M. Kitagawa, *Chem. Lett.*, 297 (1979); T. Nishio, M. Sugawara, and Y. Omoto, *J. Heterocycl. Chem.*, **16**, 815 (1978); M. Augustin and C. H. Groth, *J. Prakt. Chem.*, **321**, 205, 215 (1979).

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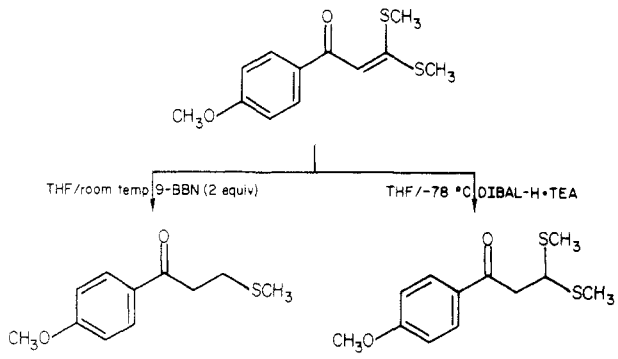
Scheme I



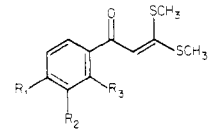
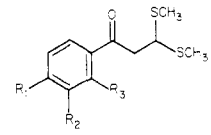
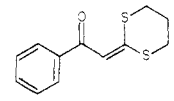
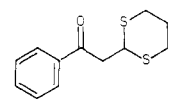
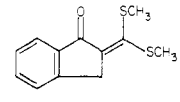
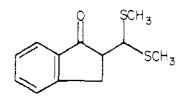
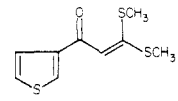
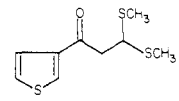
9 (83%) 2 (83%)

attempts at regiospecific reductions of these systems,[4] reported herein, was with aryl-α-oxoketene dithioacetals because of a related interest in functionalized C_6–C_3 units.

We have found that diisobutylaluminum hydride (DIBAL-H), 9-borabicyclo[3.3.1]nonane (9-BBN), and 1,3,2-benzodioxaborole (catecholborane) reduce aryl-α-oxoketene dithioacetals in a conjugate manner to give β-functionalized carbonyl compounds in good yield. Although DIBAL-H[5] and 9-BBN[6] are generally regarded as the reagents of choice for regiospecific 1,2-reductions of α,β-unsaturated carbonyl compounds, there have been a few isolated examples where DIBAL-H has afforded products of conjugate reduction.[7,8] Interestingly, the substrates involved in such cases were β-heteroatom enone systems. Conjugate reduction of an α,β-unsaturated ketone or aldehyde by 9-BBN, to our knowledge, has not previously been reported.

DIBAL-H reduction of α-oxoketene dithioacetal 1 at −78 °C in tetrahydrofuran followed by a mild acid ($NH_4^+Cl^-$ and then 2 N HCl) workup afforded the saturated ketone 2 in 75% isolated yield. While not interfering with the isolation of 2 (column chromatography), there was evidence of side products being formed in the reaction that reflected a competing 1,2-reduction process. Since electrophilic reducing agents are thought to form donor–acceptor complexes with solvents (such as THF), as well as with the reduction substrate,[9] we thought the use of a stronger complexing agent (Lewis base) such as triethylamine[10] might suppress the tendency for 1,2-reduction. This was based on our feeling that the 1,2-reduction process was occurring via a low concentration of a DIBAL–substrate complex. Reduction of 1 with DIBAL-H·TEA (see Experimental Section) afforded 2 (Scheme I) in 83% yield

Table I. Reductions with Diisobutylaluminum Hydride–Triethylamine

substrate	product	yield, %
		
1a, $R_1 = OCH_3$; $R_2 = R_3 = H$	**2a**	83
b, $R_1 = R_2 = R_3 = H$	**b**	77
c, $R_1 = R_3 = H$; $R_2 = OCH_3$	**c**	79
d, $R_1 = R_2 = R_3 = OCH_3$	**d**	65
		63 (69)[a]
3	**4**	
		66
5	**6**	
		72
7	**8**	

[a] Yield obtained from reduction with DIBAL.

with only trace amounts of any side products. The use of the DIBAL-H·TEA complex not only resulted in higher yields when compared to the results with DIBAL alone but also gave extremely clean and rapid reactions.

The DIBAL-H·TEA reductions required 1.4 equiv of the reducing agent for maximum yields. If less than 1.4 equiv was used, substantial amounts of starting material was isolated from the reaction. Several unsuccessful attempts were made to observe the aluminum enolate intermediate thought to be involved in this reduction by both ^1H and ^{13}C NMR. While solutions of the enolate appeared stable for hours at −78 °C, at 0 °C and above decomposition took place and made interpretation of the spectra impossible. Evidence for the enolate was obtained, however, by quenching the reaction with a 20% DCl/D_2O solution which afforded the expected α-deuterio ketone. Representative examples of the DIBAL-H·TEA reduction are given in Table I.

DIBAL-H was not the only electrophilic reducing agent that delivered hydride in a conjugate manner. Reduction of 1 with 9-BBN (1 equiv) gave the β-methylthio ketone 9 in 53% yield along with unreacted starting material. A second reduction using 2 equiv of 9-BBN gave 9 in 83% yield. To probe this reduction a little further, we reduced 1 with catecholborane, a much less electrophilic reducing agent.[11] The reduction (1 equiv of catecholborane) resulted in the formation of a mixture of 2 (56%) and 9 (10%). The 9-BBN reduction, and to a lesser extent the catecholborane reduction, both apparently involve a very reactive intermediate that can quite effectively complete for hydride during the course of the reaction. At present the nature of this intermediate is only speculative.

In conclusion, we have demonstrated that reduction of α-oxoketene dithioacetals with certain electrophilic reducing agents proceeds in a conjugate manner and in synthetically useful yields. The products of these reduc-

(4) We have recently shown that LAH reduction of α-oxoketene dithioacetals proceeds in a regio- and stereospecific manner with respect to C-1 and C-2 to give β-hydroxy dithioacetals. R. B. Gammill, P. M. Gold, and S. A. Miszak, *J. Am. Chem. Soc.*, **102**, 3094 (1980).

(5) For leading references on the reduction of α,β-unsaturated ketones with DIBAL see: (a) E. Winterfeldt, *Synthesis*, 617 (1975); (b) C. F. Lane, *Aldrichimica Acta*, **9**, 31 (1976). For leading references on the reduction of α,β-unsaturated ketones with 9-BBN see ref 5b and references therein.

(6) For references to conjugate reduction of α,β-unsaturated ketones see: W. R. Jackson and A. Zurgiyah, *J. Chem. Soc.*, 5280 (1965); E. L. Ashby, J. J. Lin, and R. Kovar, *J. Org. Chem.*, **41**, 2194 (1976); M. F. Semmelhack and R. D. Stauffer, *ibid.*, **40**, 3619 (1975); J. M. Fortunato and B. Ganum, *ibid.*, 41, 2194 (1976); E. J. Corey, K. B. Becker, and R. K. Varma, *J. Am. Chem. Soc.*, **94**, 8616 (1972); E. J. Corey, S. M. Albonico, U. Koelliker, T. K. Schaaf, and R. K. Varma, *ibid.*, **93**, 1491 (1971); H. C. Brown and H. M. Hess, *J. Org. Chem.*, **34**, 2206 (1969);

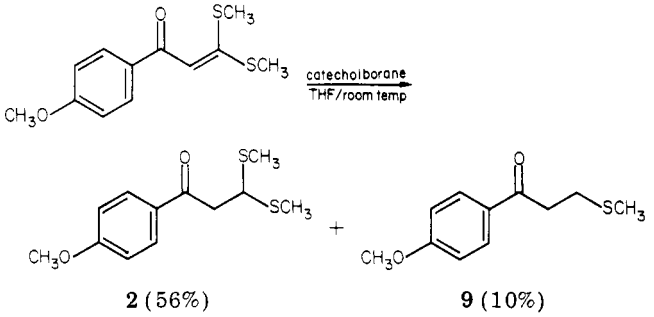
(7) E. Winterfeldt, *Synthesis*, 617 (1975), ref 123.

(8) H. Rischke, J. D. Wilcock, and E. Winterfeldt, *Chem. Ber.*, **106**, 3106 (1973).

(9) See ref 5a.

(10) P. Binger, *Angew. Chem., Int. Ed. Engl.*, **2**, 686 (1963), and references therein.

(11) C. F. Lane and G. W. Kabalka, *Tetrahedron*, **32**, 981 (1976).



tions are β-functionalized carbonyl systems in which the oxidation level of the β-carbon can be adjusted by the choice of the reducing agent used.

The mechanistic details of these reductions and the chemistry of intermediates involved is presently under study.

Experimental Section

Mass spectra, infrared spectra, ultraviolet spectra and combustion analysis were obtained by the Physical and Analytical Chemistry Department of the Upjohn Co. ^{1}H NMR spectra were obtained at 60 MHz in chloroform-*d* solutions containing tetramethylsilane as an internal standard. Infrared spectra were obtained on a Perkin-Elmer 197 spectrophotometer as mulls or neat liquids. Combustion analyses were also obtained from Micro-Analysis, Inc. Thin-layer chromatography was conducted by using Merck glass plates (catalog No. 5760, 0.25-mm thickness) precoated with silica gel 60 F-254. The TLC plates were visualized by UV light or iodine. Column chromatography (25% EtOAc/Skellysolve B) was conducted at medium pressure by utilizing silica gel 60 (E. Merck, 230–400 mesh). All solvents for chromatography were reagent grade and distilled in glass (Burdick and Jackson). All reductions described herein were conducted under an atmosphere of nitrogen with freshly distilled tetrahydrofuran (from $LiAlH_4$) in flamed glassware. All compounds were isolated by medium-pressure chromatography in 25% EtOAc/Skellysolve B. The diisobutylaluminum hydride, 9-borabicyclo[3.3.1]nonane, and 1,3,2-benzodioxaborole were all purchased from The Aldrich Chemical Co.

General Experimental Procedure for DIBAL·TEA Reductions. Preparation of the DIBAL·TEA Complex. To a fresh bottle of diisobutylaluminum hydride (1.0 M, in hexane, Aldrich) was added 108 mL of triethylamine at room temperature under nitrogen. This resulted in a 0.86 M solution in diisobutylaluminum hydride. This bottle was stored at 0 °C and used for all reductions reported below. An alternate method that does not involve using an entire bottle of the reducing agent is given in the example below.

3,3-Bis(methylthio)-1-(4-methoxyphenyl)-1-propanone (2a). Diisobutylaluminum hydride (1.0 M solution in hexane, 14 cm^3, 14 mmol) was added to tetrahydrofuran (10 mL) under nitrogen at −78 °C. To that solution was added triethylamine (2.0 mL, 14 mmol). The resulting mixture was then stirred for 30 min. In a separate reaction vessel under an atmosphere of nitrogen was added 3,3-bis(methylthio)-1-(4-methoxyphenyl)-2-propen-1-one (2.54 g, 10 mmol) followed by tetrahydrofuran (50 mL). That solution was cooled to −78 °C. The DIBAL·TEA solution was removed from the flask via syringe and added to the unsaturated ketone 1 rapidly. After the mixture was stirred for 15 min, the reaction was quenched by the addition of a saturated $NH_4^+Cl^-$ solution (8 mL). After the mixture warmed to room temperature, ether (100 mL) was added to the reaction and then washed with 2 N HCl (5 × 100 mL). The aqueous washes were then back-extracted with ether (3 × 100 mL). The combined ether extracts were dried ($MgSO_4$), and the solvent was removed in vacuo to give 2.53 g of an orange oil. Chromatography over silica gel with 25% EtOAc/hexane as eluant gave 2.05 g (80%) of **2a**: mp 56–57 °C; IR ($CHCl_3$) 1680, 1600, 1575, 1510, 1255, 1220, 1175, 1165, 1020, 985, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.9 (d, 2 H, aromatic, J = 9 Hz), 6.9 (d, 2 H, aromatic, J = 9 Hz), 4.3 (t, 1 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 3.8 (s, 3 H, OCH_3), 3.31 (d, 2 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 2.1 (s, 6 H, 2 SCH_3); mass spectrum, *m/e* (relative intensity) 256 (18), 241 (4), 209 (20), 136 (31), 135 (100), 107 (18), 92 (30), 77 (33), 74 (11), 64 (12), 63 (7). Anal. Calcd for $C_{12}H_{16}O_2S_2$: C, 56.25; H, 6.25; S, 25.00. Found: C, 56.12; H, 6.30; S, 25.29. An 83% yield was obtained when the DIBAL·H·TEA solution described above was used.

3,3-Bis(methylthio)-1-phenyl-1-propanone (2b): oil; IR ($CHCl_3$) 1680, 1600, 1565, 1510, 1255, 1220, 1175, 1165, 1020, 985, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.1–7.8 (m, 2 H, aromatic), 7.6–7.3 (m, 3 H, aromatic), 4.35 (t, 1 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 3.38 (d, 2 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 2.1 (s, 6 H, 2 SCH_3); mass spectrum, *m/e* (relative intensity) 226 (26), 180 (8), 179 (50), 163 (10), 131 (24), 106 (13), 105 (100), 103 (9), 77 (55), 51 (16). Anal. Calcd for $C_{11}H_{14}OS_2$: C, 58.40; H, 6.19; S, 28.31. Found: C, 58.63; H, 6.35; S, 28.45.

3,3-Bis(methylthio)-1-(3-methoxyphenyl)-1-propanone (2c): oil; IR 1695, 1605, 1585, 1490, 1345, 1250, 1200, 1050, 990, 875, 785, 685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.6–7.1 (m, 4 H, aromatic), 4.30 (t, 1 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 3.87 (s, 3 H, OCH_3), 3.40 (d, 2 H, $CH_2CH(SCH_3)_2$), 2.18 (s, 6 H, 2 SCH_3); mass spectrum, *m/e* (relative intensity) 256 (5), 209 (15), 136 (8), 135 (100), 107 (21), 92 (15), 77 (18). Anal. Calcd for $C_{12}H_{16}O_2S_2$: C, 56.23; H, 6.29; S, 24.98. Found: C, 56.50; H, 6.15; S, 24.81.

3,3-Bis(methylthio)-1-(2,3,4-trimethoxyphenyl)-1-propanone (2d): oil; IR 1675, 1590, 1495, 1465, 1410, 1290, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.53 (d, 1 H, J = 9 Hz, aromatic), 6.75 (d, 1 H, J = 9 Hz, aromatic), 4.35 (t, 1 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 3.98 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.45 (d, 2 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 2.15 (s, 6 H, 2 SCH_3); mass spectrum, *m/e* (relative intensity) 316 (5), 301 (4), 269 (1), 196 (11), 195 (100), 152 (5), 151 (4), 137 (2), 109 (2). Anal. Calcd for $C_{14}H_{20}O_4S_2$: C, 53.15; H, 6.37; S, 20.24. Found: C, 53.29; H, 6.32; S, 20.17.

1-Phenyl-2-(1,3-dithian-2-yl)ethanone (4): mp 59–61 °C; IR 1695, 1595, 1580, 1220, 1170, 760, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.1–7.9 (m, 2 H, aromatic), 7.6–7.2 (m, 3 H, aromatic), 4.68 (t, 1 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 3.35 (d, 2 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 2.8 (m, 4 H, aliphatic), 2.0 (m, 2 H, aliphatic); mass spectrum, *m/e* (relative intensity) 239 (12), 238 (81), 196 (12), 133 (53), 119 (34), 106 (10), 105 (100), 77 (47), 51 (11). Anal. Calcd for $C_{12}H_{14}OS_2$: C, 60.49; H, 5.92; S, 26.87. Found: C, 60.30; H, 5.85; S, 27.09.

2-[Bis(methylthio)methylene]-2,3-dihydro-1*H*-indan-1-one (6): mp 45–47 °C; IR 1705, 1605, 1590, 1290, 1280, 765 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.90–7.15 (m, 4 H, aromatic), 4.37 (m, 1 H), 3.26 (m, 3 H), 2.25 (s, 3 H, SCH_3), 2.15 (s, 3 H, SCH_3); mass spectrum, *m/e* (relative intensity) 238 (12), 192 (14), 191 (87), 147 (29), 145 (18), 144 (18), 143 (30), 116 (23), 115 (100), 89 (17), 61 (20). Anal. Calcd for $C_{12}H_{14}OS_2$: C, 60.50; H, 5.88; S, 26.89. Found: C, 60.56; H, 5.75; S, 26.94.

3,3-Bis(methylthio)-1-(3-thienyl)-1-propanone (8): mp 40–42 °C; IR 3100, 1675, 1510, 1415, 1250, 1230, 790 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.12 (m, 1 H, aromatic), 7.5 (m, 2 H, aromatic), 4.40 (t, 1 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 3.32 (d, 2 H, $CH_2CH(SCH_3)_2$, J = 7.5 Hz), 2.20 (s, 6 H, 2 SCH_3); mass spectrum, *m/e* (relative intensity) 232 (4), 186 (2), 185 (17), 113 (3), 112 (4), 111 (100), 83 (5). Anal. Calcd for $C_9H_{12}OS_3$: C, 46.51; H, 5.20; S, 41.39. Found: C, 46.62; H, 5.26; S, 41.55.

3-(Methylthio)-1-(4-methoxyphenyl)-1-propanone (9). To a tetrahydrofuran solution (100 mL) of 9-BBN (4.88 g, 40 mmol; room temperature) was added 3,3-bis(methylthio)-1-(4-methoxyphenyl)-2-propen-1-one (1; 5.08 g, 20 mmol) in tetrahydrofuran (25 mL) rapidly. The reaction was stirred for 3.5 h and then quenched by the addition of a 1% KOH solution (25 mL). The reaction was then poured into a separatory funnel and washed with 1% KOH (2 × 75 mL), 5% HCl (3 × 75 mL), and brine (2 × 75 mL). After the mixture was dried ($MgSO_4$) and the solvent removed in vacuo, 5.20 g of a brown oil was isolated. Chromatography (250 g of silica gel packed in 25% EtOAc/hexane) afforded 3.50 g (83%) of **9**: mp 29–30.5 °C; IR 1670, 1605, 1575, 1520, 1260, 1025, 840, 825, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.91 (d, 2 H, J = 9 Hz, aromatic), 6.93 (d, 2 H, J = 9 Hz, aromatic), 3.81 (s, 3 H, OCH_3), 3.4–2.7 (m, 4 H, aliphatic), 2.1 (s, 3 H, SCH_3); mass spectrum, *m/e* (relative intensity) 210 (20), 182 (26), 164 (11), 163 (90), 136 (9), 135 (100), 107 (26), 92 (19), 77 (27), 55 (17). Anal. Calcd for $C_{11}H_{14}O_2S$: C, 62.85; H, 6.66; S, 15.23. Found: C, 63.09; H, 6.60; S, 15.71.

Reduction of 1 with Catecholborane. To a tetrahydrofuran solution (10 mL) of catecholborane (240 mg, 2 mmol) was added a tetrahydrofuran solution (5 mL) of 1 (508 mg, 2 mmol) under nitrogen at 0 °C. The reaction was stirred at 0 °C for 3 h and then diluted with a saturated K_2CO_3 solution (10 mL). The reaction mixture was extracted with ether (3 × 25 mL), the ether extracts were combined and dried ($MgSO_4$), and the solvent was removed in vacuo to give 480 mg of a dark brown oil. Chromatography (25% EtOAc/Skelly B) afforded 330 mg of a 7:1 mixture (determined by NMR) of **2** (56%) and **9** (10%): R_f 0.52 for **2** in 25% EtOAc/Skelly B; R_f 0.49 for **9** in 25% EtOAc/Skelly B.

Registry No. **1a**, 33868-76-7; **1b**, 13636-88-9; **1c**, 56944-71-9; **1d**, 78018-43-6; **2a**, 78018-44-7; **2b**, 19063-71-9; **2c**, 78018-45-8; **2d**, 78018-46-9; **3**, 19607-10-4; **4**, 78018-47-0; **5**, 61402-25-3; **6**, 78018-48-1; **7**, 78018-49-2; **8**, 78018-50-5; **9**, 78018-51-6; DIBAL·TEA complex, 78019-42-8.

Ultrasound in Heterogeneous Organic Reactions. An Improved Procedure for the Synthesis of Thioamides

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Thioamides are an interesting class of organic compounds which have been utilized in a variety of synthetic transformations,[1] including several methods for the selective reduction of amides to amines.[2] A thioamide is normally prepared by refluxing the corresponding amide with excess P_4S_{10} in various solvents.[1] Since the reaction is heterogeneous in nature, it usually requires a large excess of P_4S_{10} and it must be carried out for prolonged times. An alternative procedure for the conversion of amides to thioamides utilizing the dimer of *p*-methoxyphenylthionophosphine sulfide in toluene at 100 °C has recently been reported.[3] Both of these procedures suffer, however, from the high temperatures and prolonged reaction times necessary in order to carry out the transformation.

We now report that the rate of conversion of amides to thioamides is dramatically increased by irradiation of the reaction mixture in the water bath of an ultrasonic laboratory cleaner.[4] Typically, a solution of the amide in dry THF (0.1 M) is treated with 1–1.5 equiv of P_4S_{10} and irradiated in an ultrasonic laboratory cleaner bath at 30–40 °C for 1–2 h with efficient stirring. When no more starting material is detected by thin-layer chromatography, the reaction is worked up and the residue is purified by flash chromatography[5] with methylene chloride followed by crystallization. The thioamides are obtained in good to excellent yields by this procedure.

The advantage of this procedure over previous thioamidation methods include the shorter reaction times (1–2 h), the lower reaction temperatures (30–40 °C), and the elimination of the requirement for large excesses of P_4S_{10}. This procedure should prove to be particularly useful for the preparation of thioamides in systems containing other sensitive functionality.

We are currently examining the acceleration of a number of other heterogeneous reaction by the use of ultrasonic irradiation,[4] and we will report our results in due course.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Proton magnetic resonance spectra were obtained on a Varian EM-360L spectrometer and chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane as an internal standard. A Bransonic 12 bath sonicator (80 W) was used to generate ultrasonic irradiation.

The THF used in these experiments was distilled from sodium benzophenone ketyl, the P_4S_{10} was from a freshly open bottle (MCB Reagent), and the starting amides were either commercially available or prepared by standard methods.

General Procedure for Preparation of Thioamides. The amide (2.00 mmol) was dissolved in anhydrous THF (20 mL) in a 50-mL round-bottomed flask equipped with a magnetic stirring bar. The flask was placed in the water bath of the ultrasonic apparatus which contained a submerged, air-driven magnetic stirrer. To the reaction solution was added P_4S_{10} (445 mg, 1.0 mmol), the magnetic stirrer was started, and the reaction mixture was irradiated with ultrasound for 20–30 min. Within the first 15 min a nearly homogeneous solution was obtained, followed shortly by the formation of a white, phosphorous-containing precipitate. An additional portion of P_4S_{10} (445 mg, 1.0 mmol) was added to the mixture and sonication with efficient stirring was continued for an additional 30 to 90 min. If TLC indicated the presence of unreacted amide, another portion of P_4S_{10} (1.0 mmol) was added and irradiation was continued for 30 min. The final bath temperature never exceeded 40 °C. The heterogeneous mixture was cooled to ambient temperature and filtered. The solid byproduct was washed with several small portions of methylene chloride, the filtrates were combined, and solvents were removed in vacuo, giving a residue which was purified by flash chromatography[5] on silica gel 60 (40–63 μm) with methylene chloride to provide the thioamides which crystallized on standing.

***N*-Benzyl-2-thiopiperidone.**[2] Reaction of *N*-benzyl-2-piperidone by the above procedure afforded 315 mg (77%) of the thioamide: mp 25 °C; NMR ($CDCl_3$) δ 7.33 (s, 5 H), 5.27 (s, 2 H), 2.85–3.45 (m, 4 H), 1.50–1.90 (m, 4 H).

***N*,*N*-Dimethylthiobenzamide.** Reaction of *N*,*N*-dimethylbenzamide by the above procedure afforded 256 mg (78%) of the thioamide: mp 68–69 °C (lit.[6] mp 67 °C); NMR ($CDCl_3$) δ 7.35 (s, 5 H), 3.51 (s, 3 H), 3.07 (s, 3 H).

***N*,*N*-Dimethylthiophenylacetamide.** Reaction of *N*,*N*-dimethylphenylacetamide by the above procedure afforded 300 mg (84%) of the thioamide: mp 80–81 °C (lit.[6] mp 81 °C); NMR ($CDCl_3$) δ 7.34 (s, 5 H), 4.28 (s, 2 H), 3.45 (s, 3 H), 3.17 (s, 3 H).

***N*-Methylthiophenylacetamide.** Reaction of *N*-methylphenylacetamide by the above procedure afforded 304 mg (92%) of the thioamide: mp 61–63 °C (lit.[6] mp 63 °C); NMR ($CDCl_3$) δ 7.32 (s, 5 H), 4.06 (s, 2 H), 3.40 (d, 3 H).

***N*-Methylthioacetanilide.** Reaction of *N*-methylacetanilide by the above procedure afforded 351 mg (97%) of the thioamide: mp 57.5–58.5 °C (lit.[7] mp 59 °C); NMR ($CDCl_3$) δ 7.10–7.70 (m, 5 H), 3.72 (s, 3 H), 2.37 (s, 3 H).

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Registry No. *N*-Benzyl-2-thiopiperidone, 17642-89-6; *N*,*N*-dimethylthiobenzamide, 15482-60-7; *N*,*N*-dimethylthiophenylacet-

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(1) (a) Reid, E. E. "Organic Chemistry of Bivalent Sulfur"; Chemical Publishing Co.: New York, 1962; Vol. IV. (b) Walter, W.; Voss, J. In "The Chemistry of Amides"; Zabicky, J., Ed.; J. Wiley & Sons: New York, 1970; pp 383–475. (c) Hurd, R. N.; DeLaMeter, G. *Chem. Rev.* **1961**, *61*, 45. (d) Petrov, K. A.; Andreev, L. N. *Russ. Chem. Rev.* **1971**, *40*, 505.

(2) Raucher, S.; Klein, P. *Tetrahedron Lett.* **1980**, 4081 and references cited therein.

(3) Scheibye, S.; Pedersen, B. S.; Lawesson, S. O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 229.

(4) For other applications of ultrasound as a tool for organic synthesis, see: (a) Sjoberg, K. *Tetrahedron Lett.* **1966**, 6383; (b) Luche, J.-L.; Damiano, J.-C. *J. Am. Chem. Soc.* **1980**, *102*, 7926 and references cited therein. For a discussion of the factors which may be responsible for the acceleration of the rate of chemical reactions by ultrasonic irradiation, see: (c) Ensminger, D. "Ultrasonics"; Marcel Dekker: New York, 1973; Chapter 11; (d) El'Piner, I. "Ultrasound-Physical, Chemical, and Biological Effects"; Consultants Bureau: New York, 1964.

(5) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(6) Kinder, K. *Justus Liebigs Ann. Chem.* **1923**, *431*, 187.

(7) Wallach, O. *Chem. Ber.* **1880**, *13*, 527.

0022-3263/81/1946-3558$01.25/0