N-(2-Mercaptoethyl)alanine (3).—A partial solution of **2** (1.00 g, 3.37 mmoles) in water (70 ml) was shaken with hydrogen at 50 psi and 30% palladium on charcoal (0.50 g) in a Parr apparatus for a total of 48 hr, more catalyst (0.50 g) being added after the first 24 hr. The catalyst was removed by filtration through a Celite pad under nitrogen and rinsed with water (50 ml). The dark filtrate and washings were combined and evaporated to dryness *in vacuo* and the residue was extracted with methanol (100 ml) at 40°. The extract was treated with charcoal and filtered under nitrogen; the filtrate was evaporated to dryness *in vacuo* leaving **2** as a white solid, which was dried *in vacuo* over P_2O_5: yield 680 mg (68%); mp 212°; infrared absorption (KBr) at 3190–1820 (NH_2^+), 1620 (s, NH_2^+), and 1560 cm^{-1} (s, CO_2^-).

Anal. Calcd for $C_5H_{11}NO_2S$: C, 40.24; H, 7.43; N, 9.39; SH, 22.17. Found: C, 40.00; H, 7.39; N, 9.20; SH, 22.0.

Diethyl N,N'-(Dithiodiethylene)bisalaninate (4).—Ethanol (100 ml) was saturated with hydrogen chloride at room temperature and added to a suspension of **2** (10.0 g, 33.7 mmoles) in ethanol (100 ml). The solid rapidly disssolved, and the solution was heated under reflux for 2 hr. Benzene (40 ml) was added to the solution, which was slowly distilled until 130 ml of distillate was collected. The remaining solution was evaporated to dryness *in vacuo* at 60° leaving a viscous syrup, which was triturated thoroughly in ethanol (10 ml) saturated at 0° with ammonia. The white suspension was diluted with ether (200 ml) and filtered from ammonium chloride, which was washed with ether (two 30-ml portions). The filtrate and washings were combined and evaporated to dryness at 60° *in vacuo* (0.1 mm), and the residue was re-extracted with ether (100 ml). The filtered ether solution was evaporated to dryness at 60° (0.1 mm) and the residue was kept at this temperature and pressure for several hours leaving **4** as a colorless, clear oil: yield 5.18 g (44%); $n^{25}D$ 1.4942; infrared absorption (film) at 3320 (w, NH), 2975 (m), 2930, 2905, and 2840 (CH), 1730 (s, C=O), and 1175 cm^{-1} (ms, COC).

Anal. Calcd for $C_{14}H_{28}N_2O_4S_2$: C, 47.70; H, 7.97; N, 7.95; S, 18.19. Found: C, 47.84; H, 7.97; N, 7.87; S, 18.2.

2,2'-[Dithiobis(ethylenimino)]bispropionamide (5a).—A solution of **4** (3.78 g, 10.7 mmoles) in methanol (80 ml) was saturated with ammonia at 0° and heated in a stainless steel pressure vessel (glass liner) at 90° overnight. The resultant solution was evaporated to dryness *in vacuo* and the residue was dissolved in hot ethanol (15 ml), treated with charcoal, and filtered. Refrigeration of the filtrate produced **5a** as white crystals, which were washed with cold ethanol (10 ml) and dried *in vacuo* over P_2O_5: yield 2.51 g (80%); mp 125–127°; infrared absorption (KBr) at 3265 (s, sharp, NH), 3300 and 3125 (NH_2), 2977, 2910, and 2830 (CH), 1690 (s, amide I), and 1660 cm^{-1} (s, amide II).

Anal. Calcd for $C_{10}H_{22}N_4O_2S_2$: C, 40.79; H, 7.53; N, 19.03; S, 21.78. Found: C, 41.05; H, 7.56; N, 18.83; S, 21.9.

2,2'-[Dithiobis(ethylenimino)]bis(N-methylpropionamide) (5b).—A solution of **4** (7.05 g, 20.0 mmoles) and methylamine (53.0 g, 1.73 moles) in methanol (90 ml) was heated in a stainless steel pressure vessel (glass liner) at 90° for 16 hr. The reaction mixture was evaporated on a rotary evaporator to an oil, which was dissolved in ethyl acetate (20 ml), charcoaled, and filtered. Evaporation of the filtrate at 60° (0.2 mm) left **5b** as a viscous oil: yield 6.38 g (99%); $n^{27.4}D$ 1.5380; infrared absorption (film) at 3300 (m, broad, NH), 2960, 2920, and 2830 (CH), 1650 (s, amide I), and 1530 cm^{-1} (m, amide II).

Anal. Calcd for $C_{12}H_{26}N_4O_2S_2$: C, 44.69; H, 8.13; N, 17.37; S, 19.89. Found: C, 44.79; H, 8.12; N, 17.35; S, 19.8.

2-(2-Mercaptoethylamino)propionamide (6a) Hydrochloride.—A sample of **5a** (3.00 g, 10.2 mmoles), which had been recrystallized three times from ethanol, was suspended in ethanol (100 ml) and hydrogenated in a Parr apparatus at 50 psi in the presence of 30% palladium on charcoal (0.50 g). After 16 hr, additional catalyst (0.50 g) was added, and the hydrogenation was continued for 24 hr. The resulting mixture was filtered under N_2, and the filtrate was evaporated at 35° on a rotary evaporator to about 15 ml. Addition of 6.35 *N* hydrogen chloride in ethanol (3.47 ml, 22.0 mmoles) and ether (100 ml) caused the separation of an oil, which crystallized when the mixture was cooled. The **6a** hydrochloride was collected under N_2 and dried *in vacuo* over P_2O_5: yield 2.97 g (79%); mp 121–123°; infrared absorption (KBr) at 3500–2200 (NH_2^+), 1680 (s, amide I), and 1610 cm^{-1} (w, amide II).

Anal. Calcd for $C_5H_{12}N_2OS\cdot HCl$: C, 32.51; H, 7.09; N, 15.17; S, 17.36; SH, 17.90. Found: C, 32.74; H, 6.94; N, 14.92; S, 17.51; SH, 17.5.

2-(2-Mercaptoethylamino)-N-methylpropionamide (6b) Hydrochloride.—A solution of **5b** (3.20 g, 9.92 mmoles) in ethanol (100 ml) was hydrogenated at 50 psi in the presence of 30% palladium on charcoal (0.50 g) in a Parr apparatus for a total of about 40 hr, additional catalyst (0.50 g) being added after about 16 hr. The resulting mixture was filtered under N_2, and the filtrate was evaporated at 35° on a rotary evaporator to about 15 ml. Addition of 9.50 *N* hydrogen chloride in ethanol (2.30 ml, 21.8 mmoles) and ether (100 ml) caused the separation of an oil. The supernatant ether layer was removed by decantation, and the oily product was dried *in vacuo* over P_2O_5 to give pure **6b** as a resinous solid: yield 3.55 g (90%); melting point indefinite; infrared absorption (KBr) at 3150–2250 (NH_2^+), 1675 (s, amide I), and 1565 cm^{-1} (m, amide II).

Anal. Calcd for $C_6H_{14}N_2OS\cdot HCl$: C, 36.26; H, 7.61; N, 14.10; S, 16.14; SH, 16.64. Found: C, 36.07; H, 7.46; N, 13.90; S, 16.07; SH, 16.53.

Ethyl 2-Methyl-2-thiazolidinecarboxylate (7).—A mixture of 2-aminoethanethiol hydrochloride[11] (17.8 g, 0.157 mole), xylene (187 ml), chloroform (125 ml), acetic acid (39 ml), ethyl pyruvate (18.2 g, 0.157 mole), and sodium acetate (12.9 g, 0.157 mole) was refluxed under N_2 for 3 hr. A portion of the solvent (50 ml) was removed by distillation at atmospheric pressure; the remainder was removed *in vacuo* (water aspirator) at 100° (oil bath). The residue was stirred with benzene (100 ml) and the filtered solution was evaporated *in vacuo* (rotary evaporator). The residual oil was fractionated *in vacuo* by means of a short Vigreux column. The desired ester distilled at 56° (0.4 mm) [lit.[5] bp 87° (0.4 mm)]: yield 22.2 g (81%); infrared absorption (film) at 3310 (w, sharp, NH), 2980 (m), 2935, and 2880 (CH), 1730 (s, C=O), and 1175 cm^{-1} (s, COC).

Anal. Calcd for $C_7H_{13}NO_2S$: C, 47.97; H, 7.48; N, 7.99. Found: C, 48.11; H, 7.60; N, 7.86.

2-Methyl-2-thiazolidinecarboxamide (8).—A solution of **7** (5.00 g, 28.5 mmoles) in methanol (30 ml) was saturated with ammonia at 0°, heated in a stainless steel pressure vessel (glass liner) at 85° for 21 hr, and evaporated to dryness *in vacuo*. Crystallization of the residual crude **8** from 1:2 methanol–benzene (24 ml) gave white crystals, which were dried *in vacuo* over P_2O_5: yield 2.95 g (71%); mp 143°; infrared absorption (KBr) at 3500–3010 (NH, NH_2, with sharp bands at 3430, 3305, and 3180), 2990, 2975, 2940, and 2875 (CH), 1670 (s, amide I), and 1570 cm^{-1} (wm, amide II).

Anal. Calcd for $C_5H_{10}N_2OS$: C, 41.07; H, 6.89; N, 19.16. Found: C, 41.19; H, 6.94; N, 18.92.

Registry No.—**1**, 13084-13-4; **2**, 13084-14-5; **3**, 13084-15-6; **4**, 13084-16-7; **5a**, 13084-17-8; **5b**, 13084-18-9; **6a** hydrochloride, 13084-19-0; **6b** hydrochloride, 13084-20-3; **7**, 13084-21-4; **8**, 13084-22-5.

Acknowledgment.—The authors are indebted to Mrs. Anne Gallagher Laseter for exploratory work on the synthesis of **3** and to Dr. W. C. Coburn, Jr., for interpretation of infrared spectra.

(11) Evans Chemetics, Inc., New York, N. Y.

Ring Contraction in the Clemmensen Reduction of a Cyclic β-Triketone

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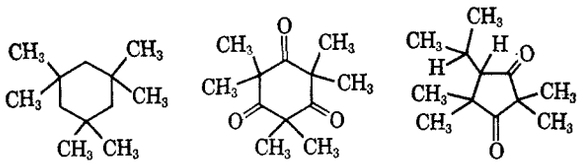
Relative to our work in nmr studies of conformational isomerization in six-membered rings containing *gem*-dimethyl groups,[1,2] we have attempted to synthe-

(1) R. W. Murray, P. R. Story, and M. L. Kaplan, *J. Am. Chem. Soc.*, **88**, 526 (1966).

(2) R. W. Murray and M. L. Kaplan, *Tetrahedron*, **23**, 1575 (1967).

size 1,1,3,3,5,5-hexamethylcyclohexane (I). This molecule is of particular theoretical interest since models indicate that the boat conformation may be the form of lowest energy.



I II III

Only one report of the synthesis of I has appeared.[3] This preparation involved five steps with an over-all yield of less than 3%. Furthermore, a conclusive proof of structure was lacking.

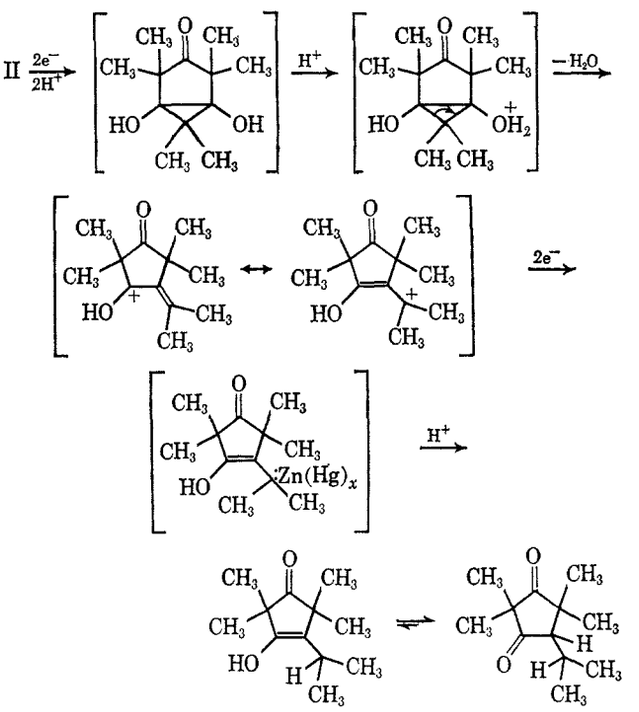
A more direct approach to I was attempted by reducing 1,1,3,3,5,5-hexamethylcyclohexanetrione (II) with amalgamated zinc and hydrochloric acid using the method of Martin.[4] Instead of the desired saturated hydrocarbon (I) a new compound, 2,2,4,4-tetramethyl-5-isopropylcyclopentane-1,3-dione (III), was isolated in good yield.

The structure of III has been established principally by elemental analysis and infrared and nmr spectroscopy. Compound III analyzed for $C_{12}H_{20}O_2$. The infrared spectrum of III has a carbonyl absorption at 1745 cm^{-1} characteristic of five-membered ring ketones.[5] The nmr spectrum[6] of III consists of a doublet at τ 7.53 (J = 7.0 cps), a complex multiplet at 8.05, a singlet at 8.66, and multiplet at 8.88. The integrated areas are 0.9, 1.0, 2.9, and 15.0, respectively. The doublet at τ 7.53 is assigned to the methine proton attached to the ring. Proof that this proton is adjacent to a carbonyl group was arrived at through use of a deuterium-exchange reaction. When III was stirred three times with basic D_2O and then extracted, the doublet at τ 7.53 disappeared apparently leaving the remainder of the spectrum undisturbed. The multiplet at τ 8.05 would be expected to become more simple but, because of its small size and complexity, no significant change could be observed.

A more detailed examination of the multiplet at τ 8.88 is permitted by taking advantage of the variation of chemical shift in mixed solvents. In pure carbon tetrachloride, the expanded high-field multiplet appears as a doublet followed by three absorption lines of varying intensity. As increasing amounts of benzene are added and spectra taken, it becomes evident from the relative changes of position that the multiplet is composed of two doublets each of area 3 (J = 6.0 cps) and three singlets each with a relative intensity of 3. The presence of an isopropyl group in compound III accounts for the two doublets in the τ 8.88 multiplet and for the complex multiplet at 8.05 with a relative area of 1. This nonequivalence of the isopropylmethyl groups is expected in molecules which have an asymmetric center,[7] and the coupling constant J = 6.0 cps is consistent[7] with the vicinal coupling in the isopropyl group. The singlet at τ 8.66 and the low-field singlet of the multiplet at 8.88 are assigned to the *gem*-dimethyl protons flanked by the two carbonyl groups. The remaining two singlets of the τ 8.88 multiplet are assigned to the second *gem*-dimethyl group on the ring.

Recently it has been demonstrated that the Clemmensen reduction of 1,3-diketones results in rearranged products and that this appears to be a general reaction.[8] No report of the Clemmensen reduction of β-triketones has appeared. The mechanism proposed by Staschewski[9] for β-diketone rearrangement will account for our results (see Scheme I). It is interesting to note that subsequent attempts to reduce III by the Clemmensen method did not succeed and III was recovered unchanged.

SCHEME I



Experimental Section[10]

Reduction of 1,1,3,3,5,5-Hexamethylcyclohexanetrione (II).—Mossy zinc (120 g) was amalgamated by 5-min shaking with 12 g of mercuric chloride, 200 ml of water, and 6 ml of concentrated hydrochloric acid in a 1-l., round-bottom flask. The solution was then decanted and in the following order were added 75 ml of water, 175 ml of concentrated hydrochloric acid, 100 ml of toluene, and II (21 g, 0.1 mole, Frinton). The mixture was refluxed for 25 hr. Three 75-ml portions of concentrated hydrochloric acid were added periodically to the refluxing solution. After the reaction cooled, the layers were separated and the aqueous layer was extracted three times with ether. The ether and toluene were combined and dried over Na_2SO_4. The solution was filtered and concentrated by distillation on a spinning-band column at atmospheric pressure. Upon lowering the pressure to 8 mm, essentially all the product distilled at 89° to give 10 g (51%) of a semisolid material. A gas chromatographic analysis (20 ft × 3/8 in., 20% Dow 710, 190°, flow rate 200 cc/min) of this product showed it to be composed of four components, three of them being very minor. The major fraction was (retention

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(5) D. H. Whiffen and H. W. Thompson, *J. Chem. Soc.*, 1005 (1946).

(6) Nmr spectra were taken on a Varian A-60 spectrometer and are reported as τ values relative to external TMS.

(7) F. A. Bovey, *Chem. Eng. News*, **43** (32), 98 (1965).

(8) N. J. Cusack and B. R. Davis, *J. Org. Chem.*, **30**, 2062 (1965).

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(10) Melting points were taken on a Kofler hot-stage microscope and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer Infracord spectrophotometer. Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Ind. 46226.

time 32 min) collected. It was a white, crystalline solid, mp 30°. The infrared carbonyl absorptions occurred at 1745 (s) and at 1780 cm^{-1} (w). The nmr spectrum in $CHCl_3$ consisted of a doublet at τ 7.53, multiplet at 8.05, singlet at 8.66, and multiplet at 8.88. The integrated areas are 0.9, 1.0, 2.9, and 15.0, respectively.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27; O, 16.30. Found: C, 73.55; H, 10.31; O, 16.50.

Registry No.—III, 13016-41-6.

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Intramolecular Hydrogen Bonding in *o*-Methylmercapto Derivatives of N-Methylaniline and N-Methyl-4-aminoazobenzene[1]

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The recent report of Szmant and Rigau[3] on the intramolecular hydrogen bonding in *cis*-2-phenylmercaptoindanol prompted us to report our observations on the strong hydrogen bonding present in derivatives of 2-methylmercaptoaniline. This came to our attention during the isolation of 3-methylmercapto-N-methyl-4-aminoazobenzene (**1**) from cold, alkaline digests of livers from rats fed the hepatocarcinogen, N,N-dimethyl-4-aminoazobenzene (**2**).[4] At the time when the identity of **1** was still unknown to us, we were struck by the disparity between its behavior on alumina chromatography (similar to that of tertiary aminoazo dyes) and its chemical behavior (as a secondary amine). Upon chromatography on carboxymethylcellulose in citric acid–ethanol, it proved to be considerably less basic than **2**.[4] Lithium aluminum hydride reduction of the N-acetyl or N-benzoyl derivative of **1** cleaved the amide linkage, regenerating **1**.[4] Similar treatment of the N-acetyl derivative of 3-methyl-N-methyl-4-aminoazobenzene (**3**) yielded the expected N-ethyl derivative.

The infrared spectra of **1** also indicated hydrogen bonding of the N hydrogen to the *ortho* substituent, as shown in Table I. The appropriate frequencies for **3** are shown for comparison. A similar contrast in the effects of the different *ortho* substituents is found in the spectra of the parent amines, 2-methylmercapto-N-methylaniline and N-methyl-*o*-toluidine. In the spectrum of **3**, the area of the peak at 3344 is twice that of the peak at 3442 cm^{-1}, which is at the same frequency as the single peak shown by neat N-methyl-*o*-toluidine. These data permit the interpretation that the higher frequency band in the KBr medium may be ascribed to intermolecular hydrogen bonding between dye molecules, while the lower frequency, more intense band is due to the much more likely hydrogen bonding of dye molecules to the KBr matrix.

TABLE I

EFFECTS OF AN *o*-MeS GROUP ON SPECTRA AND pK_a VALUES OF AROMATIC AMINES

Compd	N–H stretching frequency, cm^{-1}	pK_a
1	3386[a,b]	2.03[e]
3	3344, 3442,[a] 3468[b]	2.94[e]
2-MeS-N-Me-aniline	3386[c,d]	3.71[f]
N-Me-*o*-toluidine	3442,[c] 3460[d]	4.58[f]

[a] KBr pellet. [b] CCl_4 solution, 2 mg/ml. [c] Pure liquid. [d] CCl_4 solution, 0.2% (v/v). [e] 23°, 1% ethanol in 0.1 *M* HCl–KCl buffers. [f] 23°, 1% ethanol in 0.05 *M* citrate buffers.

The previous qualitative observation of the weakly basic character of **1** was confirmed by determination of its pK_a value, which is shown in Table I. Whether this base-weakening effect is actually due to hydrogen bonding is uncertain. The difference in pK_a values between those for 2-methylmercapto-N-methylaniline and N-methyl-*o*-toluidine is only slightly greater than the difference of the pK_a values reported for 4-methylmercaptoaniline and *p*-toluidine[5] and thus appears to be due in large part to inductive and resonance effects.

The *o*-methylmercapto group confers a high specificity on reactions of 1,4-phenylenediamine. 3-Methylmercapto-4-aminoazobenzene could be synthesized readily by condensation of nitrosobenzene and 2-methylmercapto-1,4-phenylenediamine in acetic acid–ethanol. The unhindered amino group was preferred to the hydrogen-bonded amino group by a ratio of 21:1. Similarly, condensation of nitrosobenzene with 2-methylmercapto-5-methyl-1,4-phenylenediamine favored compound **4** over compound **5** by a ratio of 11:1 (Chart I).

The evidence cited makes it clear that, if favored by a rigid configuration, sulfide sulfur can serve effectively as an electron donor in hydrogen bonding to amines.

Experimental Section

Infrared spectra were taken on a Beckman IR-10 spectrophotometer, set on the slow scanning speed (100 cm^{-1}/min, uncertainty in reading 3 cm^{-1}). The pK_a values were determined by the method of Sawicki and Ray.[6] The melting points were estimated to ±1° from the slopes of the melting curves obtained with the Accumelt apparatus (American Instrument Co.).

N-Methyl-2-methylmercaptoaniline.—2-Methylmercaptoaniline (Aldrich, 21.7 g, 0.156 mole) was dissolved in a mixture of 100 ml of 90% formic acid and 500 ml of benzene and the mixture was refluxed on a steam bath until no more water and formic acid could be collected in a water trap. The remaining solvent was removed under vacuum, and the residual oil was shaken with 250 ml of 5% Na_2CO_3 and drawn off. The carbonate solution was washed with 50 ml of ether, the ether was added to the oil, and the combined organic material was dried over Na_2SO_4. The ether was removed under vacuum and the residue was dried further by dissolving it in benzene and boiling off the solvent at atmospheric pressure until a clear distillate was obtained. The remaining solvent was removed under vacuum to give 25 g of crude N-formyl-2-methylmercaptoaniline (96% yield, single N–H band in infrared spectrum). This product was dissolved in 200 ml of ether and added over a 45-min period to a mixture of 11.4 g (0.3 mole) of $LiAlH_4$ in 500 ml of anhydrous ether. The mixture was stirred for another hour, and then refluxed for another

(1) This work was supported by Program-Project Grant CA-07175 of the National Cancer Institute, U. S. Public Health Service, and by a grant from the Jane Coffin Childs Memorial Fund for Medical Research.

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