the National Institutes of Health (CA-04536), for which the authors are grateful.

**Registry No.**—I, 6906-32-7; II, 2403-57-8; III, 2403-55-6; IV, 23297-04-3; *cis*-**1**, 50640-23-8; *trans*-**1**, 50640-24-9; *cis*-**2**, 50640-25-0; *trans*-**2**, 50640-26-1; *cis*-**3**, 50640-27-2; *trans*-**3**, 50640-28-3; *cis*-**4**, 50640-29-4; *trans*-**4**, 50640-30-7; *cis*-**5**, 50640-31-8; *trans*-**5**, 50640-32-9; *trans*-**6**, 50640-33-0; *cis*-**7**, 41959-68-6; *trans*-**7**, 41959-69-7; *cis*-**8**, 50640-34-1; *trans*-**8**, 50640-35-2; *cis*-**9**, 50640-36-3; *trans*-**9**, 50640-37-4; *cis*-**10**, 50640-38-5; *trans*-**10**, 31752-27-9; *cis*-**11**, 50640-39-6; *trans*-**11**, 50640-40-9; *cis*-**12**, 50640-41-0; *trans*-**12**, 50640-42-1; *cis*-**13**, 50640-43-2; *trans*-**13**, 50640-44-3; *cis*-**14**, 50640-45-4; *trans*-**14**, 50640-46-5; *cis*-**15**, 50640-47-6; *trans*-**15** picrate, 50640-49-8; *trans*-**16**, 50640-50-1; *cis*-**17**, 50640-51-2; *trans*-**17**, 50640-52-3; *cis*-**18**, 50640-53-4; *trans*-**18**, 50640-54-5; *cis*-**19**, 50640-55-6; *trans*-**19**, 50640-56-7; *cis*-**20**, 50640-57-8; *trans*-**20**, 50640-58-9; *cis*-**21**, 50640-59-0; *trans*-**21**, 50640-60-3; *cis*-**22**, 50640-61-4; *trans*-**22**, 50640-62-5; *cis*-**23**, 50640-63-6; *trans*-**23**, 50640-64-7; *trans*-**24**, 50640-65-8; *trans*-**25**, 50640-66-9; *trans*-**26**, 50640-67-0; *trans*-**27**, 50640-68-1; *cis*-**28**, 50640-69-2; *trans*-**28**, 50640-70-5; 2,4,4-trimethylthietan-3-one 1,1-dioxide, 31686-74-5.

## References and Notes


(1) (a) T. J. Wallace, *Quart. Rev., Chem. Soc.*, **20**, 67 (1966); (b) G. Opitz, *Angew. Chem., Int. Ed. Engl.*, **6**, 107 (1967); (c) W. E. Truce and L. K. Liu, *Mech. React. Sulfur Compounds*, **4**, 145 (1969); (d) T. Nagai and N. Tokura, *Int. J. Sulfur Chem. B*, **7**, 207 (1972).

(2) (a) L. A. Paquette, *J. Org. Chem.*, **29**, 2854 (1964); (b) L. A. Paquette, J. P. Freeman, and R. W. Houser, *ibid.*, **34**, 2901 (1969); (c) G. Pagani and S. Maiorana, *Chim. Ind. (Milan)*, **53**, 261 (1971); (d) C. T. Goralski, *J. Org. Chem.*, **37**, 2080 (1972).

(3) In a few reactions with I small amounts (6% or less) of *N,N*-dimethylsulfonamides were obtained.

(4) (a) Opitz, *et al.*, *Justus Liebigs Ann. Chem.*, **684**, 98 (1965); (b) L. A. Paquette and M. Rosen, *J. Amer. Chem. Soc.*, **89**, 4102 (1967); (c) A. M. Hamid and S. Trippett, *J. Chem. Soc. C*, 1612 (1968); (d) L. A. Paquette, *J. Org. Chem.*, **34**, 2896 (1969); (e) K. Nagarajan and S. R. Mehta, *ibid.*, **35**, 4248 (1970); (f) O. Tsuge, S. Iwanami, and S. Hagio, *Bull. Chem. Soc. Jap.*, **45**, 237 (1972).

(5) A concerted process has been proposed to account for the asymmetric synthesis obtained in the reaction of sulfene with optically active enamines: L. A. Paquette, J. P. Freeman, and S. Maiorana, *Tetrahedron*, **27**, 2599 (1971).

(6) R. Gompper, *Angew. Chem., Int. Ed. Engl.*, **8**, 312 (1969).

(7) For a discussion on carbanion stabilization by halogen atoms see K. J. Klabunde and D. J. Burton, *J. Amer. Chem. Soc.*, **94**, 5985 (1972), and references cited therein.

(8) R. B. Woodman and R. Hoffman, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970, pp 68–69.

(9) (a) N. D. Epiotis, *J. Amer. Chem. Soc.*, **94**, 1924 (1972); (b) N. D. Epiotis, private communication.

(10) B. Evans, *et al.*, *J. Chem. Soc.*, 1159 (1927), report the synthesis of this compound but later work by M. S. Kharash, *J. Org. Chem.*, **3**, 180 (1938), indicated that the earlier report was erroneous and all attempts by Kharash to prepare this compound were unsuccessful.

(11) W. E. Truce and C.-I. M. Lin, *J. Amer. Chem. Soc.*, **95**, 4426 (1973).

(12) This compound has been obtained in solution contaminated with the corresponding acid, and isolated as an anilide: W. E. Truce and J. Woodman, unpublished results.

(13) L. A. Paquette, M. Rosen, and H. Stucki, *J. Org. Chem.*, **33**, 3020 (1968).

(14) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); *J. Amer. Chem. Soc.*, **85**, 2870 (1963).

(15) G. D. Andreetti, L. Cavalco, and P. Sgarabotto, *Gazz. Chim. Ital.*, **101**, 440 (1971).

(16) V. Z. El-Hewehi, *J. Prakt. Chem.*, **23**, 38 (1964).

(17) Pyong Nae Son, Ph.D. Thesis, Purdue University, 1966.

(18) A. Lanson and R. B. Tinkler, *J. Chem. Soc. C*, 654 (1969).

(19) V. Z. El-Hewehi and D. Hempel, *J. Prakt. Chem.*, **21**, 286 (1963).

(20) M. P. Sammes, C. M. Wylie, and J. G. Hoggert, *J. Chem. Soc. C*, 2151 (1971).

(21) Prepared by J. Woodman according to the method of W. E. Truce and C. W. Vriesen, *J. Amer. Chem. Soc.*, **75**, 2525 (1953).

(22) J. R. Norell, Ph.D. Thesis, Purdue University, 1963.

(23) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. I, Wiley, New York, N. Y., 1967, p 1198.

(24) W. A White and H. Weingarten, *J. Org. Chem.*, **32**, 213 (1966).

(25) D. P. Roelofsen and H. Van Bekkum, *Recl. Trav. Chim. Pays-Bas*, **91**, 605 (1972).

(26) T. Klingler, Ph.D. Thesis, Purdue University.

(27) G. Opitz, H. Schempp, and H. Adolph, *Justus Liebigs Ann. Chem.*, **684**, 92 (1965).

(28) Note added in Proof. P. D. Buttero and S. Maiorana, *J. Chem. Soc., Perkin Trans.*, **1**, 2540 (1973).


# Preparation of 3,4-Dimethylenepyrrolidine and 1-Alkyl-3,4-dimethylenepyrrolidines by the Thermal Elimination of Sulfur Dioxide

Raphael M. Ottenbrite* and Peter V. Alston

*Department of Chemistry and Pharmaceutical Chemistry, Virginia Commonwealth University, Richmond, Virginia 23284*

*Received October 9, 1973*

The reaction of 3,4-bis(bromomethyl)-2,5-dihydrothiophene 1,1-dioxide with primary alkylamines gives 5-alkyl-1,3,4,6-tetrahydrothieno[3,4-*c*]pyrrole 2,2-dioxides as well as 1,4-HBr elimination products. These bicyclic thienopyrroles were thermally decomposed, eliminating sulfur dioxide, to give 3,4-dimethylenepyrrolidine and the corresponding *N*-alkyl-3,4-dimethylenepyrrolidines, which have been characterized spectrally and analytically.

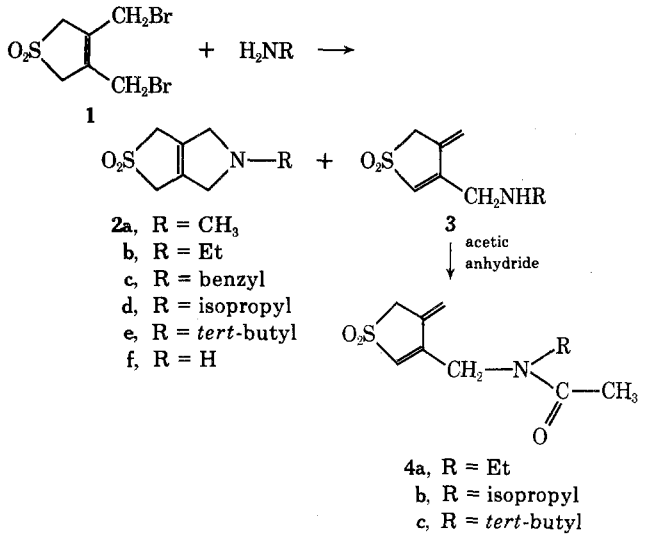
The preparation of 1-substituted 3,4-dimethylenepyrrolidines and their sulfone precursors has recently been of considerable interest.[1-5] These compounds have specific utility as reactants in the Diels–Alder reaction,[6] as monomers in polymerization reactions, and for their medicinal applications. The synthetic utilization of sulfur dioxide as a protecting agent for the synthesis of 1-aryl-3,4-dimethylenepyrrolidines has been demonstrated.[2,4] This report describes the extension of this method to the preparation of the novel secondary amine, 3,4-dimethylenepyrrolidine as well as 1-alkyl-3,4-dimethylenepyrrolidines.

In the nucleophilic reaction of primary amines with 3,4-bis(bromomethyl)-2,5-dihydrothiophene 1,1-dioxide, it has been proposed[2,4] that a competing reaction was a 1,4-HBr elimination due to the acidic character of the sulfolene protons. We found no evidence for this type of elimination in our earlier study[2] of this reaction with monosubstituted anilines. However, this elimination appears to be more facile with primary alkylamines, and subsequently we were able to isolate for the first time the 1,4-HBr elimination product for a series of such amines from this reaction.

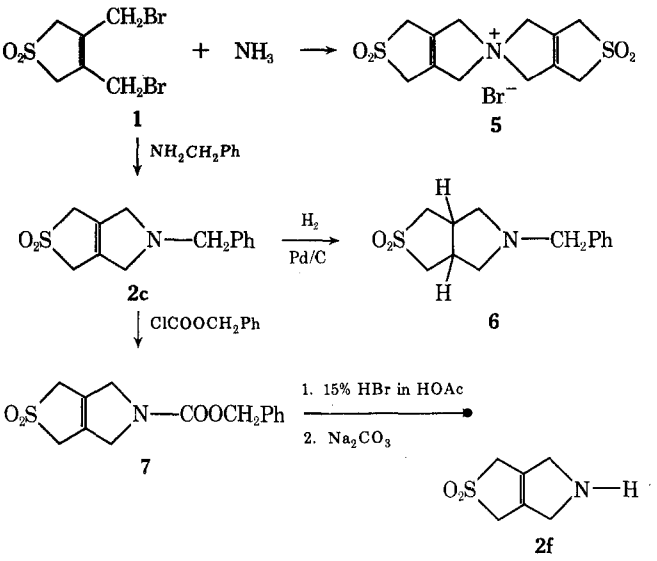
## Results and Discussion

The reaction of alkylamines with **1** was carried out as previously described[1] and the bicyclic compounds (**2**) were isolated in moderate yields (21–40%) (Scheme I). The 1,4-HBr elimination products (**3**) were observed in the reaction mixtures for all cases by nmr. We were not able to isolate these compounds (**3**)[7] directly from the reaction

**Scheme I**




**Scheme II**




mixtures; consequently, their acetylated derivatives (**4**) were isolated by the method of McElvain.[8] These acetylated derivatives were characterized in the cases of **4a–4c**. The amount of 1,4-HBr elimination product formed appears to be sensitive to the reaction conditions. Under our usual reaction conditions[1] (3:1 molar ratio of amine to **1** in acetonitrile), considerable amounts of both **2** and **3** were obtained in all cases. However, we found that an almost quantitative yield (determined by nmr) of the elimination product was obtained when the reactions were carried out in MeOH with a 3.5:1 molar ratio of amine to **1**.

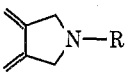
An initial attempt to prepare 1,3,4,6-tetrahydrothieno-[3,4-*c*]pyrrole 2,2-dioxide (**2f**) involved reacting **1** with ammonia (Scheme II). Using a method similar to Bobbitt, *et al.*,[9] the dibromo sulfone (**1**) was added to an ammonia–acetonitrile solution (50:1 molar ratio of ammonia to **1**), but only an intractable oil was obtained. When a 10:1 molar ratio of ammonia to **1** in acetonitrile was used, the 5,5-spirobis(1,3,4,6-tetrahydrothieno[3,4-*c*]pyrrolidinium 2,2-dioxo) bromide (**5**) was obtained in 70% yield. Similarly, lower concentrations of ammonia also gave the spiro product.

Indirect approaches to the synthesis of **2f** were next employed (Scheme II). The first attempt involved catalytic cleavage of the benzyl group in **2c**, similar to the procedure of Mattocks and Hartung.[10] It was found, however, that reduction of the tetrasubstituted double bond took place more readily than the cleavage of the benzyl group. This gave compound **6** in good yield (70%). Since catalytic cleavage of the benzyl group proved ineffective in this case, the benzyl group was replaced by a carbobenzyloxy group[11] by treating **2c** with benzylchloroformate to yield compound **7**. Cleavage of the carbobenzyloxy group was accomplished by treating **7** with 15% HBr in glacial acetic acid to give the amine hydrobromide salt which was neutralized with sodium carbonate to give the sulfone precursor **2f**.

Thermal decomposition (120°) of these masked exocyclic dienes (**2a–2f**) under reduced pressure (0.1 mm) led to the elimination of sulfur dioxide and recovery of the exocyclic dienes (**8a–8f**) as well as some polymeric material[12] (Scheme III). These dienes were liquids (~room temperature) and polymerized readily upon standing to give white, brittle, water-soluble polymers (**9**). The dienes (**8a–8f**) were characterized by their nmr spectra (Table I). Picrate derivatives (**10a** and **10b**) of **8f** and **8a** gave sharp melting points. The exocyclic dienes (**8a**, **8c**, **8d**) reacted readily with methyl iodide (Scheme III) to give their corresponding pyrrolidinium iodide salts (**11a–11c**) in good yields (55–67%).

In conclusion, primary alkylamines react with the dibromo sulfone (**1**) to give the corresponding pyrroline compounds (**2**) in lower yields (21–40%) than the previously

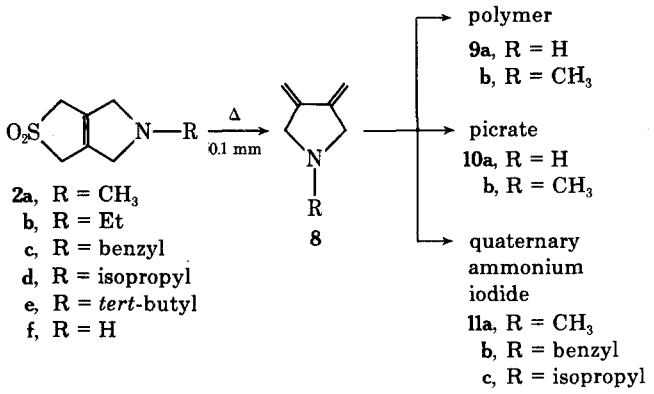
**Table I**
**3,4-Dimethylenepyrrolidines (8)**




| | | Nmr spectra[a] | | | |
|---|---|---|---|---|---|
| Compd | Yield, % | Endo vinyl hydrogens | Exo vinyl hydrogens | Methylene hydrogens adjacent to N | R |
| **8f** | 40 | 5.54 (t, $J$ = 2 Hz) | 5.12 (m) | 3.72 (t, $J$ = 2 Hz) | 5.95 (bs, N–H) |
| **8a**[b] | 65 | 5.32 (t, $J$ = 2 Hz) | 4.85 (m) | 3.24 (t, $J$ = 2 Hz) | 2.34 (s, $CH_3$) |
| **8b** | 56 | 5.43 (t, $J$ = 2 Hz) | 5.00 (m) | 3.54 (t, $J$ = 2 Hz) | 2.71 (q, $J$ = 7 Hz, $-CH_2CH_3$), 1.18 (t, $J$ = 7 Hz, $-CH_2CH_3$) |
| **8c** | 67 | 5.43 (t, $J$ = 2 Hz) | 4.97 (m) | 3.44 (t, $J$ = 2 Hz) | 7.35 (s, $-CH_2C_6H_5$), 3.66 (s, $-CH_2C_6H_5$) |
| **8d** | 55 | 5.44 (t, $J$ = 2 Hz) | 5.00 (m) | 3.57 (t, $J$ = 2 Hz) | 2.86 [h, $J$ = 7 Hz, $-CHC(CH_3)_2$], 1.17 [d, $J$ = 7 Hz, $-CHC(CH_3)_2$] |
| **8e** | 60 | 5.46 (t, $J$ = 2 Hz) | 5.00 (m) | 3.62 (t, $J$ = 2 Hz) | 1.18 [s, $-C(CH_3)_3$] |

[a] Determined with $CDCl_3$ solution except **8f** for which DMSO-$d_6$ was used. Chemical shifts ($\delta$) are relative to TMS ($\delta$ = 0.0). Signals are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; h, heptet; m, multiplet. [b] This compound has been characterized by Gaoni.[5] Our nmr spectrum for this compound is in agreement with Gaoni except for the chemical shift ($\delta$) of the exo vinyl hydrogens which he assigned a value of 4.39.

**Scheme III**




studied[2] monosubstituted anilines (50–83%). This is caused by a 1,4-HBr elimination reaction which competes with the nucleophilic cyclization process. Furthermore, it is difficult to prevent substantial polymerization of 1-alkyl-3,4-dimethylenepyrrolidines under our conditions for the thermal elimination of sulfur dioxide from **2**. Consequently, the use of sulfur dioxide as a protecting agent for the preparation of 1-alkyl-3,4-dimethylenepyrrolidines is not as advantageous as it is with their aryl counterparts.[2] This method, however, is presently the only available procedure for the preparation of 3,4-dimethylenepyrrolidine itself.

## Experimental Section

Melting points were obtained in a Thomas-Hoover melting point apparatus and are uncorrected. Nmr spectra were recorded on a Varian A-60 and a Perkin-Elmer R-24. Chemical shifts ($\delta$) are relative to TMS ($\delta$ = 0.0). Nmr signals are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; h, heptet; bs, broad singlet. Ir spectra (potassium bromide pellets) were recorded on a Perkin-Elmer 337, and elemental analysis were carried out on a Perkin-Elmer 240. Uv spectra were recorded on a Beckman DK-2. All the compounds in Table I were prepared by essentially the same procedure given below for 3,4-dimethylenepyrrolidine.

**5-*tert*-Butyl-1,3,4,6-tetrahydrothieno[3,4-*c*]pyrrole 2,2-Dioxide (2e).** A solution of the dibromo sulfone (1) (3.04 g, 10 mmol) and 35 mmol of *tert*-butylamine in 200 ml of acetonitrile was stirred at rm temperature for 1 hr. The reaction mixture was filtered to remove the *tert*-butylamine hydrobromide which precipitated and the filtrate was evaporated to dryness. The residue was dissolved in methanol and neutralized with sodium carbonate. The methanol was removed under reduced pressure and the resultant residue was triturated with 150 ml of ether. The ethereal extracts were reduced in volume to 20 ml, and petroleum ether was added to make the solution cloudy. The petroleum ether–ether solution was allowed to stand in a freezer overnight, and 0.45 g (21%) of the bicyclic product was obtained: mp 100–102°; ir max 1322, 1262, 1180, 1115 $cm^{-1}$; nmr ($CDCl_3$) $\delta$ 3.77 and 3.66 (fused singlets, 8 H), 1.14 (s, 9 H).

*Anal.* Calcd for $C_{10}H_{17}NO_2S$: C, 55.78; H, 7.96; N, 6.51. Found: C, 55.80; H, 8.02; N, 6.33.

**Acetylated Derivative of 4-(*N*-*tert*-Butylaminomethyl)-2-hydro-3-methylenethiophene 1,1-Dioxide (4c).** The petroleum ether–ether solution from the procedure of **2e** was evaporated to dryness, and the resulting oil was stirred with 3 ml of acetic anhydride for 4 hr. The reaction mixture was diluted with 20 ml of 3 *N* HCl and extracted with methylene chloride. The methylene chloride was removed under vacuum to give an oil. Crystallization from ether gave 0.35 g (14%) of **4c**: mp 194–196° dec; ir max 1636, 1392, 1290, 1222, 1115 $cm^{-1}$; nmr ($CDCl_3$) $\delta$ 6.63 (m, 1 H), 5.47 (m, 2 H), 4.28 (m, 2 H), 4.06 (m, 2 H), 2.03 (m, 3 H), 1.45 (s, 9 H).

*Anal.* Calcd for $C_{12}H_{19}NO_3S$: C, 56.02; H, 7.44, N, 5.44. Found: C, 55.46; H, 7.57, N, 5.33.

**5-Isopropyl-1,3,4,6-tetrahydrothieno[3,4-*c*]pyrrole 2,2-Dioxide (2d).** Procedure same as for **2e**: yield 41%; mp 118–120° dec; ir max 2778, 1295, 1262, 1172, 1103, 1094 $cm^{-1}$; nmr ($CDCl_3$) $\delta$ 3.79 and 3.62 (fused singlets, 8 H), 2.79 (h, $J$ = 7 Hz, 1 H), 1.11 (d, $J$ = 7 Hz, 6 H).

*Anal.* Calcd for $C_9H_{15}NO_2S$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.78; H, 7.50; N, 6.90.

**Acetylated Derivative of 4-(*N*-Isopropylaminomethyl)-2-hydro-3-methylenethiophene 1,1-Dioxide (4b).** Procedure same as for **4c**: yield 22%; mp 155–156°; ir max 1626, 1440, 1404, 1280, 1224, 1187, 1110 $cm^{-1}$; uv $\lambda_{max}$ ($CH_3OH$) 233 m$\mu$ ($\epsilon$ 19,450); nmr ($CDCl_3$) $\delta$ 6.50 (m, 1 H), 5.70–5.3 (m, 2 H), 4.45–3.8 (m, 5 H), 2.4–1.8 (m, 3 H), 1.15 (d, $J$ = 7 Hz, 6 H).

*Anal.* Calcd for $C_{11}H_{17}NO_3S$: C, 54.31; H, 7.04; N, 5.76. Found: C, 53.95; H, 7.21; N, 5.69.

**Acetylated Derivative of 4-(*N*-Ethylaminomethyl)-2-hydro-3-methylenethiophene 1,1-Dioxide (4a).** Procedure same as for **4c**: yield 15%; mp 125–126°; ir max 1646, 1633, 1441, 1397, 1273, 1220, 1105 $cm^{-1}$; nmr ($CDCl_3$) $\delta$ 6.46 (m, 1 H), 5.7–5.3 (m, 2 H), 4.35 (m, 2 H), 4.00 (m, 2 H), 3.37 (q, $J$ = 7 Hz, 2 H), 2.3–2.00 (m, 3 H), 1.19 (t, $J$ = 7 Hz, 3 H).

*Anal.* Calcd for $C_{10}H_{15}NO_3S$: C, 52.40; H, 6.60; N, 6.11. Found: C, 52.28; H, 6.55; N, 5.95.

**5,5′-Spirobis(1,3,4,6-tetrahydrothieno[3,4-*c*]pyrrolidinium 2,2-dioxo) Bromide (5).** Ammonia (1.02 g, 60 mmol) was dissolved in 100 ml of acetonitrile and added to a solution of 3.04 g (10 mmol) of **1** in 200 ml of acetonitrile. The reaction mixture was allowed to stand for 1 hr during which time the spiro compound and ammonium bromide precipitated. The precipitate was washed with 100 ml of hot methanol to yield 1.33 g (70%) of the spiro compound as a residue; no melting point up to 300°; ir max 1318, 1281, 1269, 1181, 1114, 1093 $cm^{-1}$; nmr ($D_2O$) $\delta$ 4.73 (m, 8 H), 4.12 (m, 8 H); mol wt[13] 371, 375 (actual 382).

*Anal.* Calcd for $C_{12}H_{16}NS_2O_4Br$: C, 37.90; H, 4.22; N, 3.70. Found: C, 38.10; H, 4.40; N, 4.00.

**5-Benzyl-1,3,3a,4,6,6a-hexahydrothieno[3,4-*c*]pyrrole 2,2-Dioxide (6).** A 3.0-g solution of compound **2c** in 50 ml of glacial acetic acid was hydrogenated over 2.0 g of 10% Pd/C and 0.5 g of platinum oxide at 47 psi of hydrogen pressure for 24 hr. The acetic acid solution was filtered to remove the catalyst and evaporated to dryness. The residue remaining was diluted with $H_2O$ and neutralized with sodium carbonate. The $H_2O$ solution was evaporated and its residue triturated with 200 ml of ether. From this ether extract, 2.1 g (70%) of product was obtained; mp 94–96°; ir max 1320, 1283, 1241, 1217, 1140, 1129, 1095, 737 $cm^{-1}$; nmr ($CDCl_3$) $\delta$ 7.31 (s, 5 H), 3.63 (s, 2 H), 3.4 to 2.5 (m, 10 H).

*Anal.* Calcd for $C_{13}H_{17}NSO_2$: C, 62.20; H, 6.82; N, 5.52. Found: C, 61.90; H, 6.84; N, 5.36.

**5-Carbobenzyloxy-1,3,4,6-tetrahydrothieno[3,4-*c*]pyrrole 2,2-Dioxide (7).** A solution of 1.2 g of **2c** in 5 ml of benzyl chloroformate was allowed to stand for 10 hr at room temperature. The reaction mixture was diluted with ether, and the product was collected by filtration. Recrystallization in acetone–ether yielded 1.13 g (80%) of **7**: mp 134° dec; ir max 1750 (broad), 1730, 1445, 1410 (broad), 1332, 1300, 1173, 1030, 945, 756, 695 $cm^{-1}$; nmr (acetone-$d_6$) $\delta$ 7.35 (s, 5 H), 5.11 (s, 2 H), 4.27 (s, 4 H), 3.88 (s, 4 H).

*Anal.* Calcd for $C_{14}H_{15}NSO_4$: C, 57.34; H, 5.16; N, 4.78. Found: C, 57.55; H, 5.35; H, 4.48.

**1,3,4,6-Tetrahydrothieno[3,4-*c*]pyrrole 2,2-Dioxide (2f).** To 1.0 g of compound **7** dissolved in 10 ml of glacial acetic acid was added 10 ml of 30% HBr in glacial acetic acid. The reaction mixture was allowed to stir for 3 hr and then diluted with 100 ml of ether. The amine hydrobromide salt (70%) precipitated and was collected by filtration. The amine hydrobromide salt was dissolved in $H_2O$ and neutralized with $Na_2CO_3$. The free amine (64%) was extracted from the water solution with methylene chloride: mp 116° dec; ir max 3360, 1414, 1280 (broad), 1173, 1119, 1093, 753 $cm^{-1}$; nmr ($CDCl_3$) $\delta$ 3.83 (s, 8 H), 1.86 (s, 1 H); nmr ($CF_3COOH$) $\delta$ 4.57 (s, 4 H), 4.17 (s, 4 H).

*Anal.* Calcd for $C_6H_9NSO_2$: C, 45.28; H, 5.70; N, 8.80. Found: C, 45.37; H, 5.51; N, 8.53.

**3,4-Dimethylenepyrrolidine (8f).** The sulfone precursor (**2f**) was thermally decomposed at 120° under vacuum (0.1 mm). The exocyclic diene was trapped in a flask cooled to Dry Ice–acetone temperatures with some polymerization occurring. The reaction flask was connected to the cooled flask by a U-tube wrapped with heating tape to prevent appreciable sublimation: yield 40%; nmr ($D_2O$) $\delta$ 5.70 (t, $J$ = 2 Hz, 2 H), 5.22 (m, 2 H), 4.08 (t, $J$ = 2 Hz, 4 H).

**Polymer (9a) of 3,4-Dimethylenepyrrolidine.** Compound **8f** (liquid) polymerized readily upon standing at room temperature to give a water-soluble polymer: nmr ($D_2O$) $\delta$ 4.05 (bs, 4 H), 2.31 (bs, 4 H).

**Picrate (10a) of 3,4-Dimethylenepyrrolidine.** The exocyclic diene (**8f**) (~0.09 g) was dissolved in 2 ml of MeOH and added to

2 ml of MeOH saturated with picric acid. The solution was filter to remove polymeric material which had precipitated and then allowed to stand for 2 hr at room temperature. Ether (50 ml) was added to the solution, which was then left in a freezer for 36 hr. During this time, 0.065 g (20%) of orange picrate crystals precipitated: mp 118–119°; nmr (acetone-$d_6$) $\delta$ 8.6 (s, 2 H), 5.79 (m, 2 H), 5.28 (m, 2 H), 5.07 and 4.37 (m, 4 H) (N–H not observed).

*Anal.* Calcd for $C_{12}H_{12}N_4O_7$: C, 44.44; H, 3.70; N, 17.24. Found: C, 44.69; H, 3.64; N, 17.24.

**Polymer (9b) of 1-Methyl-3,4-dimethylenepyrrolidine.** Compound **8a** (liquid) polymerized readily upon standing at room temperature to give a water-soluble polymer: nmr ($D_2O$) $\delta$ 4.14 (bs, 4 H), 3.0 (bs, 3 H), 2.34 (bs, 4 H).

**Picrate (10b) of 1-Methyl-3,4-dimethylenepyrrolidine.** To a solution of the exocyclic diene **8a** (~0.25 g) in 5 ml of methanol was added 5 ml of methanol saturated with picric acid. The solution was allowed to stand for 3 hr at room temperature after which time 60 ml of ether was added. The solution was left in a freezer for 48 hr and during this time 0.52 g (67%) of yellow picrate crystals precipitated: mp 101–103°; nmr (acetone-$d_6$) $\delta$ 8.67 (s, 2 H), 5.74 (m, 2 H), 5.29 (m, 2 H), 4.37 (m, 4 H), 3.18 (s, 3 H) (N–H not observed).

*Anal.* Calcd for $C_{13}H_{14}N_4O_7$: C, 46.15; H, 4.14; N, 16.56. Found: C, 46.06; H, 4.09; N, 16.36.

**1,1-Dimethyl-3,4-dimethylenepyrrolidinium Iodide (11a).** Compound **2a** (0.6 g) was decomposed by the same procedure used for the preparation of **8f**. The 1-methyl-3,4-dimethylenepyrrolidine recovered was dissolved in 3 ml of methylene chloride. To this solution was added 3 ml of methyl iodide. The reaction was allowed to stand overnight and 0.52 g (65%) of **11a** was collected by filtration: mp 179° dec; ir max 916 $cm^{-1}$; nmr (DMSO-$d_6$) $\delta$ 5.78 (m, 2 H), 5.33 (m, 2 H), 4.31 (m, 4 H), 3.12 (s, 6 H).

*Anal.* Calcd for $C_8H_{14}NI$: C, 38.24; H, 5.60; N, 5.58. Found: C, 37.94; H, 5.54; N, 5.52.

**1-Methyl-1-benzyl-3,4-dimethylenepyrrolidinium Iodide (11b).** Procedure same as for **11a**: yield 67%; mp 146–147° dec; ir max 907, 750, 696 $cm^{-1}$; nmr (DMSO-$d_6$) $\delta$ 7.42 (s, 5 H), 5.72 (m, 2 H), 5.26 (m, 2 H), 4.7–3.8 (m, 6 H), 2.8 (s, 3 H).

*Anal.* Calcd for $C_{14}H_{18}NI$: C, 51.36; H, 5.50; N, 4.28. Found: C, 51.16; H, 5.40; N, 4.10.

**1-Methyl-1-isopropyl-3,4-dimethylenepyrrolidinium Iodide (11c).** Procedure same as for **11a**: yield 55%; mp 250–252° dec; ir max 1429, 913 $cm^{-1}$; nmr (DMSO-$d_6$) $\delta$ 5.81 (m, 2 H), 5.30 (m, 2 H), 4.38 (m, 4 H), 3.84 (h, $J$ = 7 Hz, 1 H), 2.75 (s, 3 H), 2.03 (d, $J$ = 7 Hz, 6 H).

*Anal.* Calcd for $C_{10}H_{18}NI$: C, 43.02; H, 6.50; N, 5.01. Found: C, 43.33; H, 6.43; N, 4.91.

**Acknowledgment.** The authors wish to thank Texaco Incorporated for their fellowship support of P. V. Alston, and the National Science Foundation for their financial support through Grant No. GP 26616.

**Registry No.**—**1**, 18214-57-8; **2a**, 35105-72-7; **2b**, 35105-73-8; **2c**, 35105-74-9; **2d**, 50586-20-4; **2e**, 50586-21-5; **2f**, 50586-22-6; **4a**, 50586-23-7; **4b**, 50586-24-8; **4c**, 50586-25-9; **5**, 50586-26-0; **6**, 50586-27-1; **7**, 50586-28-2; **8a**, 50521-42-1; **8b**, 50586-29-3; **8c**, 505086-30-6; **8d**, 50586-31-7; **8e**, 50586-32-8; **8f**, 50586-16-8; **9a**, 50586-17-9; **9b**, 50678-88-1; **10a**, 50586-33-9; **10b**, 50586-34-0; **11a**, 50586-35-1; **11b**, 50586-36-2; **11c**, 50586-37-3; *tert*-butylamine, 75-64-9; isopropylamine, 75-31-0.

## References and Notes

(1) R. M. Ottenbrite and P. V. Alston, *J. Org. Chem.*, **37**, 3360 (1972).
(2) R. M. Ottenbrite and P. V. Alston, *J. Heterocycl. Chem.*, **10**, 785 (1973).
(3) P. V. Alston and R. M. Ottenbrite, "Synthesis of Some 1-Substituted-3,4-Dimethylenepyrrolidines," presented at the Virginia Academy of Science Annual Meeting, College of William and Mary, Williamsburg, Va, May 3, 1973.
(4) H. W. Gschwend and H. Haider, *J. Org. Chem.*, **37**, 59 (1972).
(5) Y. Gaoni, *Tetrahedron Lett.*, 2361 (1973).
(6) R. M. Ottenbrite and P. V. Alston, "Sigma Effects on the Diels–Alder Reaction," presented at 56th Conference of the Chemical Institute of Canada, Montreal, June 5, 1973.
(7) Analogous type dienes are known to polymerize readily: J. D. Park and R. J. McMurtry, *J. Org. Chem.*, **32**, 2397 (1967).
(8) S. M. McElvain, "The Characterization of Organic Compounds," Macmillan, New York, N. Y., 1964, p 174.
(9) J. M. Bobbitt, L. H. Amundson, and R. I. Steiner, *J. Org. Chem.*, **25**, 2232 (1968).
(10) A. M. Mattocks and W. H. Hartung, *J. Amer. Chem. Soc.*, **68**, 2108 (1946).
(11) H. L. Yale and F. A. Sowinski (to E. R. Squibb and Sons, Inc.), U. S. Patent 3,528,459, June 28, 1966.
(12) In the thermal decomposition of **2d** and **2e**, some rearranged product[2] (~5%) was observed by nmr; however, this compound did not interfere with further reactions of the intermediate exocyclic dienes (**8d** and **8e**).
(13) Determined by the Mohr method: D. A. Skoog and D. M. West, "Analytical Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1965, p 218.

# Synthesis of 1,3,4,5,6,7,8,8a-Octahydro-2-methyl-4a-phenylisoquinolin-6-ols. Novel Fragments of the Morphine Molecule

Neville Finch,* Louis Blanchard, R. T. Puckett, and L. H. Werner

*Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation, Summit, New Jersey 07901*

*Received August 13, 1973*

Renewed efforts were made to gain access to the long neglected morphine fragment **2d**, *trans*-1,3,4,5,6,7,8,8a-octahydro-2-methyl-4a-phenylisoquinolin-6-ol. Previous efforts by McElvain involved an unsuccessful attempt at the conjugate addition of phenylmagnesium bromide to the enone **17**, 1,3,4,7,8,8a-hexahydro-2-methylisoquinolin-6-one. Our first attempt involved intramolecular alkylation of the ketal **8b**, which was not successful. Use of diphenylcopper lithium, however, enabled us to achieve conjugate addition to the enone **17**, giving stereospecifically the cis ketone **18**, 1,3,4,7,8,8a-hexahydro-2-methyl-4a-phenylisoquinolin-6-one, whose structure was confirmed by X-ray analysis of the methobromide. The stereochemistry of reduction and methyllithium addition to this ketone **18** is discussed.

In the search for new structural types possessing analgetic activity the pentacyclic structure of morphine (1) has been subjected to many modifications. One of these, compound **2a**, represents an interesting target type, which has been subjected to only one additional study since compound **2a** was reported.[1]

A study by McElvain described an unsuccessful attempt to gain access to this type by a synthetic approach which was quite similar to our successful route.[2]

The reason for this apparent neglect of otherwise attractive target compounds such as **2a–d** while other modifications have been extensively explored[3] is perhaps the syn-