commercial grade and used directly except TMSO, which was dried over molecular sieves and distilled.

Melting points are by the capillary method and uncorrected. Those of CysA were obtained by inserting the capillary into the heating bath about 10 °C below the expected decomposition temperature. Elemental analysis are by Elek Microanalytical Laboratories, Torrance, Calif., and C. F. Geiger, Ontario, Calif.

Oxidation of L-Cystine. Iodine (1.5 g, 11.8 mg-atoms) was dissolved with stirring in a mixture of 24 g (99.9 mmol) of L-cystine and 150 mL of Me_2SO. Gradually, 18 mL (216 mmol) of concentrated hydrochloric acid was added. Stirring at room temperature was continued for 24 h by which time all L-cystine had dissolved and some dimethyl sulfide appeared as a second phase.[6]

The oxidation was also conducted by using 18 mL (160.2 mmol) of concentrated hydrobromic acid in place of the iodine and hydrochloric acid and heating for 6.75 h at 75 °C with distillation of dimethyl sulfide.

CysA–Me_2SO Compound. Acetone (375 mL) was gradually stirred into the mixture obtained by I_2–HCl catalyzed oxidation. After cooling in an ice bath for 2 h, the precipitate was filtered off, reslurried with an 8% solution of Me_2SO in acetone, again collected, and rinsed with acetone. Obtained was 46.5 g (94% yield) of CysA–Me_2SO compound. This sintered at 160 °C, then decomposed at about 180 °C. Recrystallization was accomplished by dissolving in Me_2SO and adding acetone but without change in the decomposition temperature, $[\alpha]^{25}_D$ +5.92° (11%, water). Other solvents such as ethyl acetate or chloroform could be used in place of acetone.

Anal. Calcd for $C_5H_{13}NO_6S_2$: C, 24.28; H, 5.30; N, 5.67; S, 25.93. Found: C, 24.64; H, 5.40; N, 5.45; S, 26.03. Calcd neut equiv, 247.3. Found, 248.3. Calcd % Me_2SO for $C_3H_7NO_5S{\cdot}C_2H_6OS$, 31.59. Found by reduction with 57% hydriodic acid,[7] 31.65.

Conversion of CysA–Me_2SO Compound to CysA. A. By Solvent Extraction. CysA–Me_2SO compound (10 g, 40.5 mmol) was mixed with 40 mL of methanol and repeatedly triturated over a 1.5-h period. CysA was filtered off and rinsed with fresh methanol. Obtained was 6.45 g (94% yield), mp 273–274 °C dec (lit.[8] mp 274 °C dec). Recrystallization from water gave CysA monohydrate, mp 272–274 °C dec (lit.[9] mp 278 °C dec), $[\alpha]^{25}_D$ +8.45° (7.4%, anhydrous basis, water) (lit.[10] +8.66°). Identification was confirmed by comparing the IR spectrum with that of authentic material.

Acetonitrile or ethanol could be used in place of methanol in this extraction.

B. By Vacuum Drying. CysA–Me_2SO compound (0.8838 g, 3.58 mmol) was heated for 9 h at 120 °C (10 mm). The residual CysA weighed 0.6022 g, mp 260–263 °C dec (lit.[8] mp 274 °C dec). Calcd wt loss for $C_3H_7NO_5S{\cdot}C_2H_6OS$, 31.59. Found, 31.86.

Direct Formation of CysA–Me_2SO Compound. On treating 1.10 g (5.90 mmol) of CysA monohydrate with 4 mL of Me_2SO, it dissolved slowly, and stirring and some heating were used to complete solution. Acetone (5 mL) was added to start precipitation. Later 2 mL more was added. After cooling in an ice bath, CysA–Me_2SO compound was filtered off and given a final rinse with acetone. Obtained was 1.37 g (94% yield) identical with that described above.

Other Cysteic Acid–Sulfoxide Compounds. About 2.9 mmol of the cysteic acid was treated with 2 mL of Me_2SO or 6–8 mL of TMSO. Solution occurred gradually and was usually completed with gentle heating. Precipitation was by addition of acetone. Yields were about 90%. Where possible, recrystallization was by dissolving in the same sulfoxide followed by addition of acetone. The appropriate cysteic acid was recovered by treating with methanol.

CysA–TMSO Compound. This darkened, then decomposed at 215–216 °C. Anal. Calcd for $C_7H_{15}NO_6S_2$: N, 5.13; S, 23.46. Found: N, 4.87; S, 23.61.

DL-Cysteic Acid–Me_2SO Compound. This showed partial melting at 161–165 °C followed by gradual decomposition. Anal. Calcd for $C_5H_{13}NO_6S_2$: N, 5.67; S, 25.93. Found: N, 5.82; S, 26.08.

DL-Homocysteic Acid–Me_2SO Compound. Addition of acetone resulted in formation of a syrup. This was extracted with fresh acetone until the extract would no longer rapidly decolorize added aqueous $KMnO_4$ solution. This syrup gradually crystallized. Its aqueous solution decolorized aqueous $KMnO_4$. Anal. Calcd for $C_6H_{15}NO_6S_2$: N, 5.36; S, 24.54. Found: N, 4.31; S, 20.75. Ratio: S to N, 2.1.

DL-Homocysteic Acid–TMSO Compound. A syrup was obtained as with Me_2SO. After exhaustive extraction with acetone, its aqueous solution continued to rapidly decolorize $KMnO_4$ solution.

Registry No.—L-Cysteic acid, 498-40-8; L-cystine, 56-89-3; Me_2SO, 67-68-5; cysA–Me_2SO compound, 60643-99-4; TMSO, 1600-44-8; cysA–TMSO compound, 60644-00-0; DL-cysteic acid, 3024-83-7; DL-cysteic acid–Me_2SO compound, 62337-55-7; DL-homocysteic acid, 504-33-6; DL-homocysteic acid–Me_2SO compound, 60644-01-1; DL-homocysteic acid–TMSO compound, 62337-56-8.

References and Notes

(1) O. G. Lowe, *J. Org. Chem.*, **41**, 2061 (1976).
(2) (a) D. Martin, A. Weise, and H.-J. Niclas, *Angew. Chem., Int. Ed. Engl.*, **6**, 318 (1967); (b) H. H. Szmant in "Dimethyl Sulfoxide", Vol. 1, S. W. Jacob et al., Ed., Marcel Dekker, New York, N.Y., 1971, pp 20–38 and 41–49.
(3) (a) D. Hadzi, *J. Chem. Soc.*, 5128 (1962); (b) J. A. Olabe, M. C. Giordano, and A. J. Arvia, *Electrochim. Acta*, **12**, 907 (1967); (c) M. A. Khuddus and D. Swern, *Tetrahedron Lett.*, 411 (1971).
(4) (a) H. Konishi, T. Ashida, and M. Kakudo. *Bull. Chem. Soc. Jpn.*, **41**, 2305 (1968); (b) W. A. Hendrickson and J. Karle, *Acta Crystallogr., Sect. B*, **27**, 427 (1971).
(5) (a) J. J. Lindberg and C. Majani, *Suom. Kemistil. B*, **37**, 21 (1964); (b) E. A. Tomic, *J. Appl. Polym. Sci.*, **11**, 2397 (1967); (c) A. V. Bailey, J. A. Harris, and E. L. Skau, *J. Chem. Eng. Data*, **13**, 265 (1968); (d) O. V. Nilov and V. F. Chesnokov, *Zh. Obshch. Khim.*, **43**, 2589 (1973); (e) H. Fujiwara, *J. Phys. Chem.*, **78**, 1662 (1974).
(6) In one experiment, the dimethyl sulfide was removed under vacuum, collected in a cold trap, and identified via the mercuric chloride derivative. See ref 1.
(7) Dimethyl Sulfoxide Technical Bulletin, Crown Zellerbach Corp., Aug 1966, p 21.
(8) K. Shinohara, *J. Biol. Chem.*, **96**, 285 (1932).
(9) H. T. Clarke, "Organic Syntheses", Collect. Vol. III, Wiley, New York, N.Y., 1955, p 266.
(10) E. Friedmann, *Beitr. Chem. Physiol. Pathol.*, **3**, 30 (1903).

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anhydro-2-Mercaptothiazolo[3,2-*f*]phenanthridinium Hydroxide, a Mesoionic Thiazole Ring System Containing Exocyclic Sulfur

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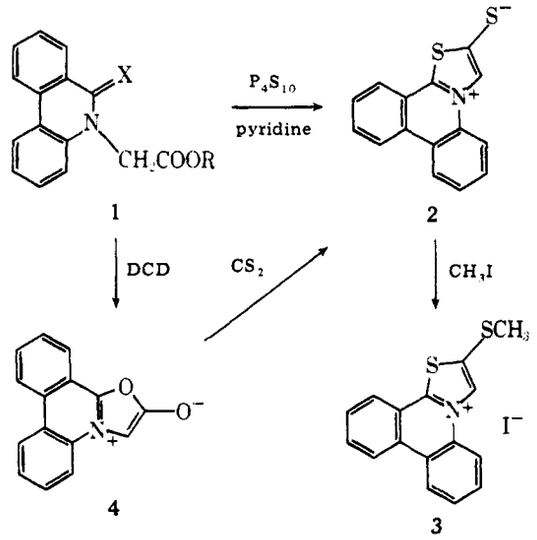
The synthesis of mesoionic ring systems with exocyclic sulfur atoms by a direct ring closure sequence is usually effective only in those systems with a nitrogen atom adjacent to the carbon bearing the sulfur, as in the 1,3,4-oxadiazole,[1] 1,3,4-thiadiazole,[1,2] and 1,2,4-triazole[3] ring systems. In these cases an isothiocyanate is presumed to be the reactive intermediate. Interconversion of mesoionic systems by the use of a reactive dipolarophile, such as the reaction of *anhydro*-2,4-diphenyl-5-hydroxy-3-methylxanthylium hydroxide with carbon disulfide to give *anhydro*-2,4-diphenyl-5-mercapto-3-methylthiazolium hydroxide,[4] requires an exceptionally reactive substrate and has only been successful in the above example, although the hydrolytic rearrangement of the *anhydro*-5-hydroxy-1,3,4-thiadiazolium hydroxide system to the corresponding *anhydro*-5-mercapto-1,3,4-oxadiazolium hydroxide system is well documented.[1] We now describe a direct approach that has been successful in the synthesis of the title ring system.

6-Oxo-5(6*H*)-phenanthridineacetic acid (**1**, R = H; X = O) when refluxed in pyridine for 1 h with an equimolar quantity of P_4S_{10} gave *anhydro*-2-mercaptothiazolo[3,2-*f*]phenanthridinium hydroxide (**2**), characterized further by the ready formation of 2-methylthiothiazolo[3,2-*f*]phenanthridinium iodide (**3**) on reaction with methyl iodide. Use of the methyl ester of **1** (R = CH_3; X = O) in toluene required 21.5 h of reflux for the formation of **2** whereas, if the reaction were run for shorter periods (45 min), no **2** was formed, the product isolated being the corresponding thioester **1** (R = CH_3; X = S). Confirmation of the structure of **2** was obtained by an alternative synthesis. Cyclization of **1** (R = H; X = O) with dicyclohex-

ylcarbodiimide gave the oxazolone 4 which was reacted in situ[5] with carbon disulfide to form 2. This mesoionic system did not undergo cycloaddition with dimethyl acetylenedicarboxylate.

Thionation of the amide carbonyl group is undoubtedly the initial step in the reaction. A longer reaction period converts the acid group into a thio acid which then undergoes a cyclodehydrative ring closure. This is an extremely attractive route



to mesoionic systems of this type but attempts to develop it as a general reaction sequence were unsuccessful under analogous conditions. *N*-Benzoyl-*N*-phenylglycine and its ethyl ester, as well as 2-oxo-1(2*H*)-pyridineacetic acid, gave multicomponent reaction mixtures.

Experimental Section[6]

***anhydro*-2-Mercaptothiazolo[3,2-*f*]phenanthridinium Hydroxide (2). A. By Ring Closure of 1 (R = H; X = O).** 6-Oxo-5(6*H*)-phenanthridineacetic acid[7] (0.5 g, 0.002 mol), P_4S_{10} (0.44 g, 0.002 mol), and pyridine (15 mL) were refluxed for 1 h, the initial light yellow reaction solution turning a deep red after 15 min. After the reaction mixture was poured onto ice, the orange precipitate obtained (0.3 g, 56%) crystallized from DMF or $CHCl_3$–CH_3OH as red plates: mp 298–300 °C dec; UV λ_{max} (C_2H_5OH) 232 nm sh (log ϵ 4.46), 237 (4.48), 252 sh (4.44), 257 (4.46), 263 (4.44), 303 sh (3.93), 310 (3.94), 321 (3.91), 334 sh (3.84), 349 (3.73), 361 (3.71), 392 sh (3.27); IR (Nujol) $\nu_{C=C/C=N}$ 1605, 1555, 1510 cm^{-1}; NMR (TFA) aromatic protons; M^+· *m/e* 267 (100).

Anal. Calcd for $C_{15}H_9NS_2$: C, 67.38; H, 3.39; N, 5.24; S, 23.99. Found: C, 67.16; H, 3.48; N, 5.34; S, 23.44.

B. By Ring Closure of 1 (R = CH_3; X = O). Methyl 6-oxo-5(6*H*)-phenanthridineacetate[7,8] (2.67 g, 0.01 mol), P_4S_{10} (2.45 g, 0.011 mol), and toluene (50 mL) when refluxed for 21.5 h resulted in the formation of a suspension which, after treatment with a solution of $CHCl_3$ (50 mL) and 5% NaOH (50 mL), gave an orange product (2.7 g). Recrystallization gave a product identical[9] with that obtained above.

C. From 1 (R = H; X = O) and DCD/CS_2. The acid 1 (R = H; X = O) (0.64 g, 0.025 mol) and *N*,*N*′-dicyclohexylcarbodiimide (0.60 g, 0.029 mol) were refluxed in CS_2 (30 mL) for 24 h. After cooling, the suspended red product was collected and this product triturated with hot EtOH to remove *N*,*N*-dicyclohexylurea. The orange-red prisms remaining, 0.27 g (40%), mp ca. 300 °C dec, were identical[9] with the product obtained above.

2-Methylthiothiazolo[3,2-*f*]phenanthridinium Iodide[10] (3). A suspension of 2 (0.13 g) in CH_3OH (20 mL) and excess methyl iodide was heated under reflux until a clear yellow solution resulted. The solvent was evaporated and the residue triturated with anhydrous ether resulting in an orange-yellow product (0.18 g) which crystallized from ethanol (Norit) as yellow needles: mp 250–255 °C dec; UV λ_{max} (CH_3OH) 230 nm (log ϵ 4.47), 250 (4.44), 267 (4.62), 293 sh (4.08), 370 (4.14); NMR (Me_2SO-d_6) δ 2.92 (s, 3, SCH_3), 7.67–9.12 (m, 8, aromatic), 9.55 (s, 1, C_5H).

Anal. Calcd for $C_{16}H_{12}NIS_2$: C, 46.95; H, 2.96; N, 3.42. Found: C, 46.90; H, 2.92; N, 3.64.

Methyl 6-Thio-5(6*H*)-phenanthridineacetate (1, R = CH_3; X = S). A mixture of 1 (R = CH_3; X = O), P_4S_{10} (0.566 g, 0.926 mol), and toluene (15 mL) was refluxed for 45 min. After cooling, 5% NaOH (10 mL) and $CHCl_3$ (20 mL) were added and the mixture was stirred for 1.5 h and then filtered. The filtrate was washed with H_2O and saturated NaCl solution, dried ($MgSO_4$), and evaporated. The residue (0.495 g) was chromatographed on silica gel (150 g) using 15% EtOAc–cyclohexane, the product (80 mg, 11%) being collected in 300 mL after a small forerun of eluate. It crystallized from ether as colorless needles: mp 184–185 °C; UV λ_{max} (C_2H_5OH) 245.5 nm (log ϵ 4.61), 250 (4.59), 266 (4.21), 291 (3.92), 308 (3.71), 321 (3.70), 355 sh (3.99), 369 (4.12), 387 (3.99); IR (Nujol) ν_{CO} 1740 cm^{-1}; M^+· *m/e* 283 (100).

Anal. Calcd for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62; N, 4.94; S, 11.31. Found: C, 67.99; H, 4.88; N, 4.96; S, 11.22.

Registry No.—1 (R = H; X = O), 37046-34-7; 1 (R = Me; X = O), 62416-28-8; 1 (R = Me; X = S), 62416-29-9; **2**, 62416-30-2; **3**, 62416-31-3; methyl iodide, 74-88-4.

References and Notes

(1) A. R. McCarthy, W. D. Ollis, and C. A. Ramsden, *J. Chem. Soc., Perkin Trans. 1*, 627 (1974), and earlier references cited therein.
(2) K. T. Potts and C. Sapino, *Chem. Commun.*, 672 (1968).
(3) K. T. Potts, S. K. Roy, and D. P. Jones, *J. Heterocycl. Chem.*, **2**, 105 (1965); *J. Org. Chem.*, **32**, 2245 (1967); K. T. Potts, S. K. Roy, S. W. Schneller, and R. M. Huseby, *ibid.*, **33**, 2559 (1968).
(4) R. Huisgen, E. Funke, F. C. Schaefer, H. Gotthardt, and E. Brunn, *Tetrahedron Lett.*, 1809 (1967).
(5) Several examples of this in situ use of oxazolones have appeared in the literature; e.g., see K. T. Potts and D. McKeough, *J. Am. Chem. Soc.*, **96**, 4268, 4276 (1974); K. T. Potts, J. Baum, E. Houghton, D. N. Roy, and U. P. Singh, *J. Org. Chem.*, **39**, 3619 (1974); F. M. Hershenson, *ibid.*, **37**, 3111 (1972).
(6) Evaporations were carried out under reduced pressure on the steam bath and melting points were determined in capillaries. Spectral characterizations were carried out with the following instrumentation: NMR, Varian A-60A spectrometer; IR, Perkin-Elmer Model 421 spectrophotometer; UV, Cary Model 14 spectrophotometer.
(7) R. F. Cookson, J. W. James, R. E. Rodway, and R. G. Simmonds, *J. Heterocycl. Chem.*, **9**, 475 (1972).
(8) R. M. Acheson and A. O. Plunkett, *J. Chem. Soc.*, 3758 (1962).
(9) Criteria used were superimposable IR spectra and nondepression of mixture melting point.
(10) We thank Dr. J. Baum for this experiment.

A Regiospecific Synthesis of Haematommic Acid

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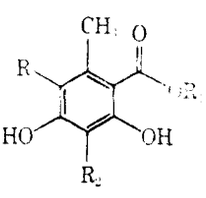
Haematommic acid (**1a**), a common fragment of many depsidones and depsides,[1] has previously been synthesized by two different routes both of which suffer from either experimental difficulties or hazards. St. Pfau[2] first reported the synthesis of **1a** by the reaction of ethyl orsellinate (**1b**) with zinc cyanide and hydrogen chloride in diethyl ether. This reaction yielded a 40/60 mixture of ethyl haematommate (**1c**)



	R_1	R_2	R_3
1a	H	CHO	H
b	Et	H	H
c	Et	CHO	H
d	Et	H	CHO
e	$C_6H_5CH_2$	H	H
f	$C_6H_5CH_2$	CHO	H