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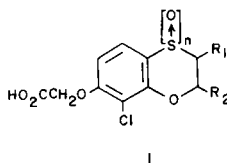
Somerville, New Jersey 08876

Received November 1, 1982

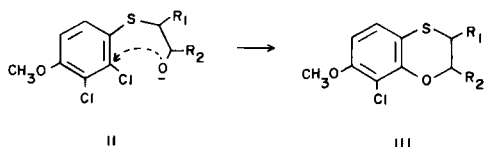
Several (dihydrobenzoxathiinyloxy)acetic acids have been prepared as potential antihypertensive agents. The dihydrobenzoxathiin ring system was constructed *via* an intramolecular alkoxide displacement reaction.

J. Heterocyclic Chem., **20**, 867 (1983).

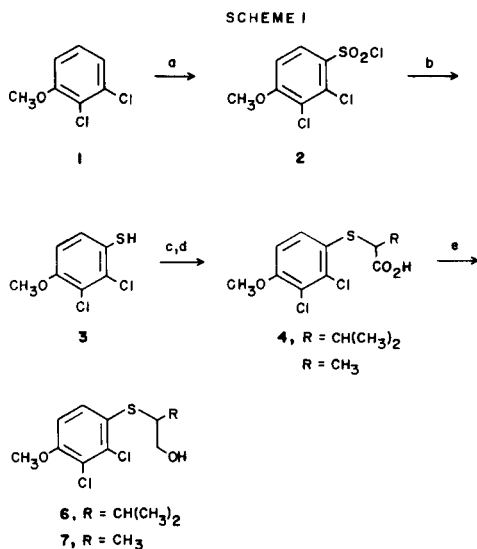
In the context of our cardiovascular research program, we have undertaken the synthesis of several (dihydrobenzoxathiinyloxy)acetic acids **I** as potential antihypertensive agents with diuretic properties [1-3].



Our novel approach to the dihydrobenzoxathiin nucleus **III** was devised from an intramolecular alkoxide **II** induced chloride displacement. [4].

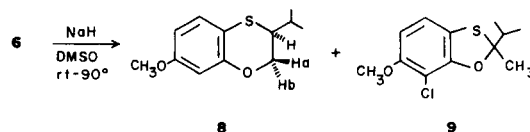


The synthesis of the precursor (β -arylthio)alcohols is outlined in Scheme I. Chlorosulfonation of 2,3-dichloroanisole (**1**) and reduction of the resultant sulfonyl chloride **2** with zinc and sulfuric acid provided thiophenol **3** in 73% yield. Condensation of **3** with α -bromoalkanoic acids gave α -arylthioalkanoic acids **4** and **5**. Borane reduction of these acids yielded alcohols **6** and **7**, respectively.



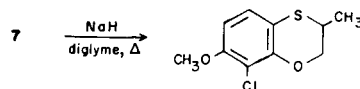
Reagents: a. chlorosulfonic acid; b. zinc, 25% aq. H₂SO₄; c. sodium hydride, DMF; d. α -bromoisovaleric acid (R = CH(CH₃)₂) or α -bromopropionic acid (R = CH₃); e. BH₃/THF.

Initial attempts at cyclization of the β -arylthio-3-methylbutanol **6** using dimethyl sodium in dimethylsulfoxide resulted in a 27:73 mixture of two isomeric compounds. Chromatographic separation and analysis by gc-ms confirmed their isomeric nature with the expected molecular weight of 258. The nmr spectra data established their structural assignments as dihydrobenzoxathiin **8** and benzoxathiole **9**.



Characteristically, the proton nmr of **8** contains a multiplet at 1.91 as expected for the isopropyl methine proton, a multiplet at 3.14 for the methine proton α to sulfur, a doublet of doublets at 4.21 (J = 7, 11 Hz) assigned to the diastereotopic proton H_a and a doublet of doublets at 4.66 ppm (J = 3, 11 Hz), for H_b. The proton spectrum of **9** is quite distinguishable with a three proton singlet at 1.80 and a one proton multiplet at 2.30 ppm. These downfield shifted signals are indicative of the sterically crowded situation of the methyl and methine groups attached at the quaternary carbon of the oxathiole ring. In addition, ¹³C-nmr, with CW-off resonance decoupling, was supportive [5]. Compound **9** has additional methyl and quaternary carbon signals and lacks a methylene and methine signal when compared to compound **8**.

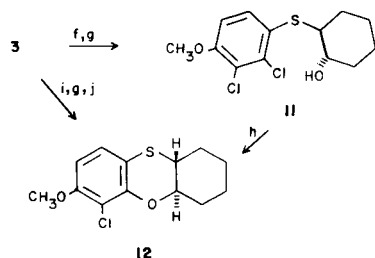
Being aware of this isomeric complication, we sought to modify the reaction conditions. When diglyme was employed as a solvent, a clean cyclization of (β -arylthio)propanol **7** to the corresponding 2,3-dihydro-3-methyl-1,4-benzoxathiin **10** resulted in 63% yield.



In the interest of generating a cyclic disubstituted analog, thiophenol **3** was alkylated with cyclohexene-oxide to give *trans*-(β -arylthio)cyclohexanol **11**. Cyclization

under the above conditions provided *trans*-hexahydrophenoxathiin **12** in 74% yield. Similarly, a one pot procedure using 1,2-dimethoxyethane as a solvent resulted in an 82% overall yield of **12**.

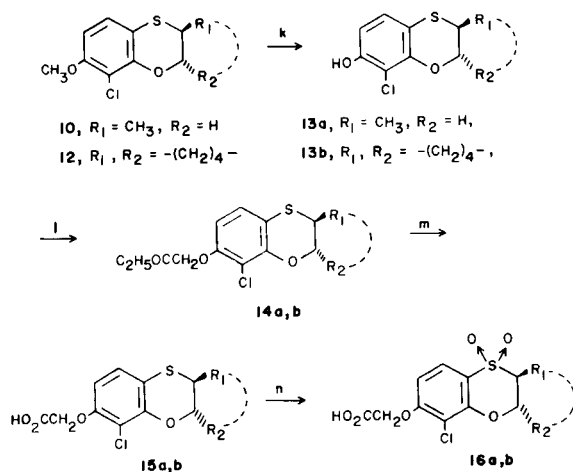
SCHEME II



Reagents: f. NaH, DMF, r.t.; g. cyclohexene oxide; h. NaH, diglyme, Δ ; i. NaH, DME, r.t.; j. DME, Δ .

Conversion of anisoles **10** and **12** to their corresponding oxyacetic acid derivatives is outlined in Scheme III. Demethylation was accomplished with molten pyridine hydrochloride to give phenols **13**. Condensation with ethyl bromoacetate using potassium carbonate in 2-butanone or dimethylformamide provided ethyl (aryloxy)acetates **14**. Alkaline hydrolysis in refluxing aqueous ethanol yielded the targeted (dihydrobenzoxathiinyloxy)acetic acids **15**. Oxidation with 30% hydrogen peroxide in refluxing glacial acetic acid resulted in sulfone derivatives **16**.

SCHEME III



Reagents: k. pyridine-HCl, 180°; l. K₂CO₃, ethyl bromoacetate; m. NaOH, aq. ethanol, Δ ; n. H₂O₂, HOAc, Δ .

Compounds **10-16** were less active than several reference standards in cardiovascular primary screening.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 727 or a Pye Unicam SP3-200 spectrophotometer. Nuclear magnetic resonance spectra were taken at 60 MHz on either a JEOL C-60HL or a JEOL FX-60 spectrometer, and chemical shifts are

given relative to internal tetramethylsilane. Mass spectra were obtained from a Finnigan Model 4000 spectrometer interfaced to a Finnigan 9610 gas chromatograph and equipped with an INCOS data system. Elemental analysis was performed by Micro-Tech Laboratories, Skokie, Illinois. Thin layer chromatograms were run on silica gel PF-254 plates, preparative thick layer chromatography was run on P254 silica gel plates (20 × 20 cm), and column chromatography was performed using silica gel 60 (E. Merck, AG) or absorption alumina (Fisher Scientific).

2,3-Dichloro-4-methoxybenzenesulfonyl Chloride (**2**).

Chlorosulfonic acid (10 ml, 152 mmoles) was added slowly to 2,3-dichloroanisole (**1**) (5.31 g, 30 mmoles) over a 30 minute period. The mildly exothermic reaction became a yellow solution on completion of addition and was subsequently stirred at room temperature for one hour. After quenching the reaction with 200 g crushed ice, the resultant solid was collected, air-dried and recrystallized from ether-pentane to give 6.9 g (83%) of off-white prisms, mp 93-95°; ir (chloroform): 1180, 1390 cm⁻¹ (SO₂Cl); nmr (deuteriochloroform): δ 4.10 (s, 3, OCH₃), 7.60 (q, 2, aromatic H).

Anal. Calcd. for C₇H₅Cl₃O₃S: C, 30.51; H, 1.83. Found: C, 30.74; H, 1.78.

2,3-Dichloro-4-methoxythiophenol (**3**).

A mixture of **2** (9.37 g, 30 mmoles), 72 g of crushed ice, 13 ml of concentrated sulfuric acid and zinc dust (12 g, 0.18 g-atom) was warmed to reflux and maintained there for 16 hours. The mixture was cooled, diluted with dichloromethane and stirred at room temperature for two hours. The excess zinc was removed by filtration and the organic extract was washed with water and aqueous sodium bicarbonate, and dried (magnesium sulfate). Concentration (rotovaporator) gave a white solid which was recrystallized from ether-pentane to give 5.5 g (88%) of colorless needles, mp 81.5-83°; nmr (deuteriochloroform): δ 3.90 (m, 4, OCH₃, SH), 7.05 (q, 2, aromatic H).

Anal. Calcd. for C₇H₆Cl₂OS: C, 40.21; H, 2.89; S, 15.34. Found: C, 40.20; H, 2.86; S, 15.44.

α -(2,3-Dichloro-4-methoxyphenylthio)isovaleric Acid (**4**).

A solution of **3** (12.3 g, 59 mmoles) in 100 ml of anhydrous dimethylformamide was added to sodium hydride (99%, 3.13 g, 130 mmoles) with efficient stirring. After stirring for ten minutes, a solution of α -bromoisovaleric acid (9.6 g, 53 mmoles) in 85 ml of anhydrous dimethylformamide was added gradually. The reaction was stirred at room temperature for three hours, diluted with 500 ml water and filtered. The filtrate was acidified with 3N hydrochloric acid and the precipitate was collected, washed with water and air-dried. Recrystallization from acetone-pentane gave 13.1 g (81%) of a white crystalline solid, mp 176.5-178.5°; ir (potassium bromide): 1690 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 1.05 (m, 6, CH₃), 2.07 (m, 1, CH), 3.55 (d, 1, SCH), 3.90 (s, 3, OCH₃), 7.38 (q, 2, aromatic H); ms: M⁺ m/e 308.

Anal. Calcd. for C₁₂H₁₀Cl₂O₃S: C, 46.62; H, 4.57. Found: C, 46.80; H, 4.59.

α -(2,3-Dichloro-4-methoxy)phenylthio]propionic Acid (**5**).

Using the above described method with **3** (6.5 g, 31 mmoles), sodium hydride (99%, 1.7 g, 71 mmoles) in 50 ml dimethylformamide and α -bromopropionic acid (5.2 g, 34 mmoles) in 10 ml dimethylformamide, 6.8 g (78%) of colorless prisms were obtained on recrystallization from acetone-hexane, mp 119-120°; ir (chloroform): 1710 cm⁻¹; nmr (deuteriochloroform + DMSO-d₆): δ 1.48 (d, 3, CH₃), 3.31 (q, 1, SCH), 3.95 (s, 3, OCH₃), 7.23 (q, 2, aromatic H).

Anal. Calcd. for C₁₀H₁₀Cl₂O₃S: C, 42.72; H, 3.59; S, 11.40. Found: C, 42.71; H, 3.53; S, 11.36.

2-[(2,3-Dichloro-4-methoxy)phenylthio]-3-methylbutanol (**6**).

To a solution of **4** (7.7 g, 25 mmoles) in 170 ml of anhydrous tetrahydrofuran under nitrogen was added 0.94 N borane/THF (43 ml, 40 mmoles) and the resulting mixture was refluxed for one hour. After cooling, the reaction was quenched with 1N hydrochloric acid and extracted with ether. The organic extract was washed with saturated sodium bi-

carbonate, water and brine and dried (magnesium sulfate). Concentration (rotovaporator) gave 8.0 g of a colorless oil. Preparative thick layer chromatography of 0.2 g of this oil using dichloromethane gave 0.18 g (97%) of a colorless oil; ir (chloroform): 3450 cm^{-1} (OH); nmr (deuteriochloroform): δ 1.10 (d, 6, CH_3), 1.70-2.50 (m, 2, CH, OH), 3.07 (q, 1, CH), 3.68 (m, 2, OCH_2), 3.93 (s, 3, OCH_3), 7.20 (q, 2, aromatic H); ms: M^+ m/e 294.

Anal. Calcd. for $\text{C}_{12}\text{H}_{16}\text{Cl}_2\text{O}_2\text{S}$: C, 48.83; H, 5.46. Found: C, 48.95; H, 5.66.

2-[(2,3-Dichloro-4-methoxy)phenylthio]propanol (7).

Using the above procedure with **5** (13.5 g, 48 mmoles) and 1.0M borane/THF (72 ml, 72 mmoles), a workup gave 13.0 g white solid that was recrystallized from ether-hexane to give 9.5 g (74%) of white crystals, mp 67-69°; ir (chloroform): 3400 cm^{-1} (OH); nmr (deuteriochloroform): δ 1.32 (d, 3, CH_3), 2.15 (m, 1, OH), 3.20-3.70 (m, 3, SCH, OCH_2), 3.90 (s, 3, OCH_3), 7.11 (q, 2, aromatic H); ms: M^+ m/e 266.

Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{Cl}_2\text{O}_2\text{S}$: C, 44.95; H, 4.53. Found: C, 44.81; H, 4.42.

8-Chloro-2,3-dihydro-3-isopropyl-7-methoxy-1,4-benzoxathiin (8).

To a mixture of sodium hydride (37 mg, 1.5 mmoles) in 2 ml of anhydrous dimethylsulfoxide under nitrogen was added a solution of **6** (200 mg, 0.7 mmole) in 3 ml of dimethylsulfoxide. The reaction was stirred at room temperature for 30 minutes and at 90° for one hour. The cooled mixture was diluted with water and extracted with ether. The organic extract was washed with brine and dried (magnesium sulfate). Concentration (rotovaporator) gave 137 mg of an oil. Preparative layer chromatography using 1:1 ether:pentane gave 101 mg of a colorless oil. Gcms analysis of this material revealed this oil to be a 27:73 mixture of isomers **8** and **9**, respectively, with M^+ m/e 258. A second preparative layer chromatography of 57 mg of this oil using 1:4 dichloromethane:carbon tetrachloride yielded a lower R_f component, 21 mg (12%) of a white solid, mp 74-77°; nmr (deuteriochloroform): δ 1.10 (d, 6, CH_3), 1.91 (m, 1, CH), 3.14 (m, 1, SCH), 3.88 (s, 3, OCH_3), 4.21 (dd, 1, J = 7, 11 Hz, H_a), 4.66 (dd, 1, J = 3, 11 Hz, H_b), 6.75 (q, 2, aromatic H); ms: M^+ m/e 258.

Anal. Calcd. for $\text{C}_{12}\text{H}_{15}\text{ClO}_2\text{S}$: C, 55.71; H, 5.84. Found: C, 55.48; H, 5.77.

7-Chloro-2-isopropyl-6-methoxy-2-methyl-1,3-benzoxathiole (9).

As a result of the experimental procedure described above for **8**, the second preparative layer chromatography yielded a higher R_f component, 26 mg (15%) of a colorless oil, nmr (deuteriochloroform): δ 1.05 (d, 6, CH-(CH_3)₂), 1.80 (s, 3, C-CH₃), 2.30 (m, 1, CH), 3.85 (s, 3, OCH_3), 6.66 (q, 2, aromatic H); ms: M^+ m/e 258.

Anal. Calcd. for $\text{C}_{12}\text{H}_{15}\text{ClO}_2\text{S}$: C, 55.71; H, 5.84. Found: C, 55.96; H, 5.80.

8-Chloro-2,3-dihydro-7-methoxy-3-methyl-1,4-benzoxathiin (10).

To sodium hydride, from washing 50% oil dispersion (1.62 g, 34 mmoles) with hexane, in 10 ml of anhydrous diglyme was added a solution of **7** (7.2 g, 27 mmoles) in 70 ml of diglyme. The resulting mixture was refluxed for one hour. After cooling, the reaction mixture was quenched with ice water and extracted with ether. The organic extract was washed with water, dried (magnesium sulfate) and concentrated (rotovaporator) to give 5.0 g off-white solid. Recrystallization from ether/hexane yielded 3.9 g (63%) of off-white crystals, mp 104-106°; nmr (deuteriochloroform): δ 1.40 (d, 3, CH_3), 3.44 (m, 1, SCH), 3.92 (s, 3, OCH_3), 3.96-4.72 (m, 2, OCH_2), 6.80 (q, 2, aromatic H); ms: M^+ m/e 230.

Anal. Calcd. for $\text{C}_{10}\text{H}_{11}\text{ClO}_2\text{S}$: C, 52.06; H, 4.81. Found: C, 51.70; H, 4.84.

trans-2-[(2,3-Dichloro-4-methoxy)phenylthio]cyclohexanol (11).

A solution of **3** (6.3 g, 30 mmoles) in 35 ml of anhydrous dimethylformamide was added to sodium hydride, from washing 50% oil dispersion (1.7 g, 35 mmoles) with hexane, with efficient stirring and ice bath cooling. After 30 minutes, a solution of cyclohexene oxide (3.2 g, 33 mmoles) in 15 ml of dimethylformamide was added dropwise and the resulting

mixture stirred at room temperature overnight. The reaction mixture was diluted with water and extracted with ether. The organic extract was washed with water, dried (magnesium sulfate) and concentrated (rotovaporator) to give 8.5 g of brown semi-solid. Column chromatography on silica gel (100 g) with 1:4 hexane:dichloromethane yielded 4.9 g (52%) of a light tan solid, mp 65-67°; ir (chloroform): 3550 cm^{-1} (OH); nmr (deuteriochloroform): δ 1.00-2.40 (m, 8, CH_2), 2.58-3.08 (m, 2, SCH, OH), 3.35 (m, 1, OCH), 3.95 (s, 3, OCH_3), 7.22 (q, 2, aromatic H); ms: M^+ m/e 306.

Anal. Calcd. for $\text{C}_{13}\text{H}_{16}\text{Cl}_2\text{O}_2\text{S}$: C, 50.82; H, 5.25. Found: C, 50.79; H, 5.21.

trans-4-Chloro-3-methoxy-5a,6,7,8,9,9a-hexahydrophenoxathiin (12).

To sodium hydride, from washing 50% oil dispersion (1.9 g, 39 mmoles) with hexane, was added **3** (6.3 g, 30 mmoles) in 80 ml of anhydrous diglyme with ice bath cooling. After the resulting mixture was stirred at room temperature for 30 minutes, a solution of cyclohexene oxide (3.1 g, 32 mmoles) in 10 ml of diglyme was added. After stirring at room temperature for three hours, the reaction mixture was refluxed for 30 minutes. After cooling and diluting with water, the mixture was extracted with ether. The organic extract was washed with water, dried (magnesium sulfate) and concentrated (rotovaporator) to an off-white solid. Trituration with hexane gave 6.0 g (74%) of a white solid, mp 130-132°; nmr (deuteriochloroform): δ 1.10-2.05 (m, 8, CH_2), 3.10 (m, 1, SCH), 3.60-4.10 (m, 4, OCH, OCH_2), 6.75 (q, 2, aromatic H); ms: m^+ m/e 270.

Anal. Calcd. for $\text{C}_{13}\text{H}_{15}\text{ClO}_2\text{S}$: C, 57.66; H, 5.58. Found: C, 57.71; H, 5.68.

On a larger scale (0.12 mole), it was found that this preparation can be performed in dimethoxyethane at reflux overnight to give **12** in 82% yield.

8-Chloro-2,3-dihydro-7-hydroxy-3-methyl-1,4-benzoxathiin (13a).

A mixture of **10** (26.7 g, 0.12 mole) and pyridine hydrochloride (540 g, 4.7 mmoles) was heated at 180° for six hours. The mixture was cooled, diluted with water and extracted with ether. The organic extract was washed with 5% hydrochloric acid and water, and dried (magnesium sulfate). Concentration (rotovaporator) gave a brown oil that was chromatographed by preparative hplc using 65% dichloromethane:hexane yielding 17.4 g (67%) of a pale yellow solid, mp 61-63°; ir (chloroform): 3500 cm^{-1} (OH); nmr (deuteriochloroform): δ 1.38 (d, 3, CH_3), 3.45 (m, 1, SCH), 3.80-4.75 (m, 2, OCH_2), 5.60 (s, 1, OH), 6.85 (q, 2, aromatic H); ms: (MH)⁺ m/e 217.

Anal. Calcd. for $\text{C}_9\text{H}_9\text{ClO}_2\text{S}$: C, 49.88; H, 4.19. Found: C, 49.94; H, 4.20.

trans-4-Chloro-3-hydroxy-5a,6,7,8,9,9a-hexahydrophenoxathiin (13b).

Using the procedure described above with **12** (5.7 g, 21 mmoles) and pyridine hydrochloride (97 g, 840 mmoles), workup yielded 5.2 g brown residue. Recrystallization from dichloromethane:hexane gave 2.2 g (41%) of pale yellow crystals, mp 89-91°; ir (chloroform): 3500 cm^{-1} (OH); nmr (deuteriochloroform): δ 1.15-2.60 (m, 8, CH_2), 3.10 (m, 1, SCH), 3.86 (m, 1, OCH), 5.54 (s, 1, OH), 6.78 (q, 2, aromatic H); ms: M^+ m/e 256.

Anal. Calcd. for $\text{C}_{12}\text{H}_{13}\text{ClO}_2\text{S}$: C, 56.13; H, 5.10. Found: C, 56.42; H, 5.44.

Ethyl [(8-Chloro-2,3-dihydro-3-methyl-1,4-benzoxathiin-7-yl)oxy]acetate (14a).

A mixture of **13a** (16.3 g, 76 mmoles), ethyl bromoacetate (11 ml, 99 mmoles), anhydrous potassium carbonate (17.8 g, 129 mmoles) and 250 ml of 2-butanone was refluxed with stirring for three hours. The resulting mixture was filtered and the filtrate concentrated (rotovaporator) to give a yellow solid. Recrystallization from acetone:hexane yielded 19 g (83%) of a white solid, mp 102-104°; ir (potassium bromide): 1760 cm^{-1} (C=O); nmr (DMSO- d_6): δ 1.05-1.52 (m, 6, CH_3), 3.57 (m, 1, SCH), 3.90-4.82 (m, 4, OCH_2), 4.97 (s, 2, $\text{OCH}_2\text{C}=\text{O}$), 6.95 (q, 2, aromatic H); ms: M^+ m/e 302.

Anal. Calcd. for $\text{C}_{13}\text{H}_{15}\text{ClO}_4\text{S}$: C, 51.57; H, 4.99. Found: C, 51.74; H, 4.94.

Ethyl [(*trans*-4-Chloro-5a,6,7,8,9,9a-hexahydrophenoxathiin-3-yl)oxy]acetate (**14b**).

A mixture of **13b** (4.5 g, 18 mmoles), ethyl bromoacetate (3.7 g, 22 mmoles), potassium carbonate (4.0 g, 29 mmoles) and 35 ml of dimethylformamide was warmed at 60° for two hours. The product was precipitated from ice water, collected, dried and recrystallized from acetone:hexane to yield 3.6 g (60%) of a pale yellow solid, mp 114-117°; ir (potassium bromide): 1755 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 0.90-2.40 (m, 11, CH₂, CH₃), 3.13 (m, 1, SCH), 3.50-4.40 (m, 3, OCH, OCH₂), 4.85 (s, 2, OCH₂C=O), 6.80 (m, 2, aromatic H); ms: M⁺ m/e 342.

Anal. Calcd. for C₁₆H₁₉ClO₄S: C, 56.05; H, 5.59. Found: C, 55.60; H, 5.50.

[(8-Chloro-2,3-dihydro-3-methyl-1,4-benzoxathiin-7-yl)oxy]acetic Acid (**15a**).

A mixture of **14a** (16.0 g, 53 mmoles), 200 ml ethanol and 200 ml 20% sodium hydroxide was refluxed for two hours. The cooled mixture was concentrated to ca. 200 ml, diluted with water, acidified with concentrated hydrochloric acid and extracted with ether. The organic extract was dried (magnesium sulfate) and concentrated (rotovaporator) to give 14 g of an off-white solid. Recrystallization from acetone-hexane gave 10.0 g (69%) of a white solid, mp 186-188°; ir (potassium bromide): 1740 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 1.41 (d, 3, CH₃), 3.45 (m, 1, SCH), 3.84-4.65 (m, 2, OCH₂), 4.70 (s, 2, OCH₂C=O), 6.74 (q, 2, aromatic H), 12.65 (broad, 1, OH); ms: M⁺ m/e 275.

Anal. Calcd. for C₁₁H₁₁ClO₄S: C, 48.09; H, 4.04. Found: C, 47.89; H, 4.00.

[(*trans*-4-Chloro-5a,6,7,8,9,9a-hexahydrophenoxathiin-3-yl)oxy]acetic Acid (**15b**).

Using the above procedure with **14b** (24.0 g, 70 mmoles), workup and recrystallization from acetone-hexane gave 16 g (73%) of a pink solid, mp 206.5-209°; ir (potassium bromide): 1740 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 1.00-2.50 (m, 8, CH₂), 3.14 (m, 1, SCH), 3.82 (m, 1, OCH), 4.77 (s, 2, OCH₂C=O), 6.81 (q, 2, aromatic H), 12.74 (broad, 1, OH); ms: M⁺ m/e 314.

Anal. Calcd. for C₁₄H₁₅ClO₄S: C, 53.41; H, 4.80; Cl, 11.26. Found: C, 53.43; H, 4.93; Cl, 11.32.

[(8-Chloro-2,3-dihydro-3-methyl-1,4-benzoxathiin-7-yl)oxy]acetic Acid 4,4-Dioxide (**16a**).

Hydrogen peroxide (30%, 5 ml, 44 mmoles) was added dropwise to a solution of **15a** (3.0 g, 11 mmoles) in 20 ml glacial acetic acid and the resulting mixture was refluxed for five hours. After cooling, the reaction mixture was diluted with ethyl acetate, washed with water and dried (magnesium sulfate). Concentration (rotovaporator) gave 3.1 g of crude white solid that was recrystallized from acetone-hexane to yield 2.3 g (69%) of a white solid, mp 207-210°; ir (potassium bromide): 1740 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 1.42 (d, 3, CH₃), 3.92 (m, 1, SCH), 4.45-5.10 (m, 4, OCH₂), 7.37 (q, 2, aromatic H), 12.60 (broad, 1, OH); ms: (MH)⁺ m/e 307.

Anal. Calcd. for C₁₁H₁₁ClO₆S: C, 43.07; H, 3.62. Found: C, 43.15; H, 3.54.

[(*trans*-4-Chloro-5a,6,7,8,9,9a-hexahydrophenoxathiin-3-yl)oxy]acetic Acid 10,10-Dioxide (**16b**).

Using the above method with **15b** (5.5 g, 18 mmoles), hydrogen peroxide (7.8 ml, 69 mmoles) and 30 ml glacial acetic acid, workup and recrystallization from ethanol gave 3.9 g (64%) of white crystals, mp 240-242°; ir (potassium bromide): 1730 cm⁻¹ (C=O); nmr (DMSO-d₆): δ 1.10-2.40 (m, 8, CH₂), 3.88 (m, 1, SCH), 4.35-5.18 (m, 3, OCH, OCH₂), 7.38 (q, 2, aromatic H), 12.65 (broad, 1, OH); ms: M⁺ m/e 346.

Anal. Calcd. for C₁₄H₁₅ClO₈S: C, 48.49; H, 4.36. Found: C, 48.76; H, 4.42.

Acknowledgement.

The authors wish to express their appreciation to Marc N. Agnew, Peter Kranack and Anastasia Rizwaniuk for spectral data and June Baird-Strupczewski for literature search information. We also gratefully acknowledge Rose Marie Boysen for assistance in the preparation of this manuscript.

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- [2] Tolmesoxide, 5-methyl-4-methylsulfinyl veratrole, has significant antihypertensive properties: J. G. Collier, R. E. Lorge and B. F. Robinson, *Br. J. Clin. Pharmacol.*, **5** 35 (1978); D. C. Doxey, *ibid.*, **63**, 111 (1978).
- [3] A report, "Novel Antihypertensive Agents with Diuretic Properties. [(6,7-Dichloro[b]thien-5-yl)oxy]acetic Acids and 1,1-Dioxides", has been presented: S. R. Caldwell, H. H. Ong, J. A. Profitt, J. J. Tegeler, J. M. Kitzen, J. Wilker, 182nd American Chemical Society National Meeting, Med. Chem. Div., August 23-28, 1981, Abstract No. 9.
- [4] For other methods of preparing dihydrobenzoxathiins see: W. E. Parham, J. D. Jones, *J. Am. Chem. Soc.*, **76**, 1068 (1954); J. H. Verheijen, H. Kloosterziel, *Synthesis*, 451 (1975).
- [5] The cmr spectra of **8** indicates 3 methyl (20.0, 20.1, 77.0), one methylene (69.4), 4 methine (30.1, 45.6, 105.5, 125.0) and 4 quaternary carbons (111.6, 111.8, 148.2, 153.4 ppm). The cmr spectra of **9** contains 4 methyl (18.0, 18.2, 26.1, 56.6), 3 methine (39.1, 104.9, 118.9) and 5 quaternary carbons (106.0, 107.2, 118.9, 153.1, 153.8 ppm). Exact carbon assignments are not possible with currently available data.