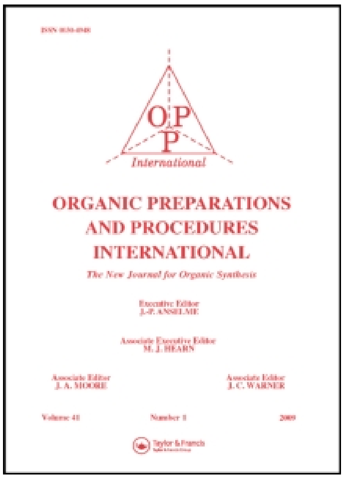

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SYNTHESIS OF 2-METHOXYDIBENZO [b,f] (1,4)-THIAZEPIN-11(10H)-ONE-5,5-DIOXIDE

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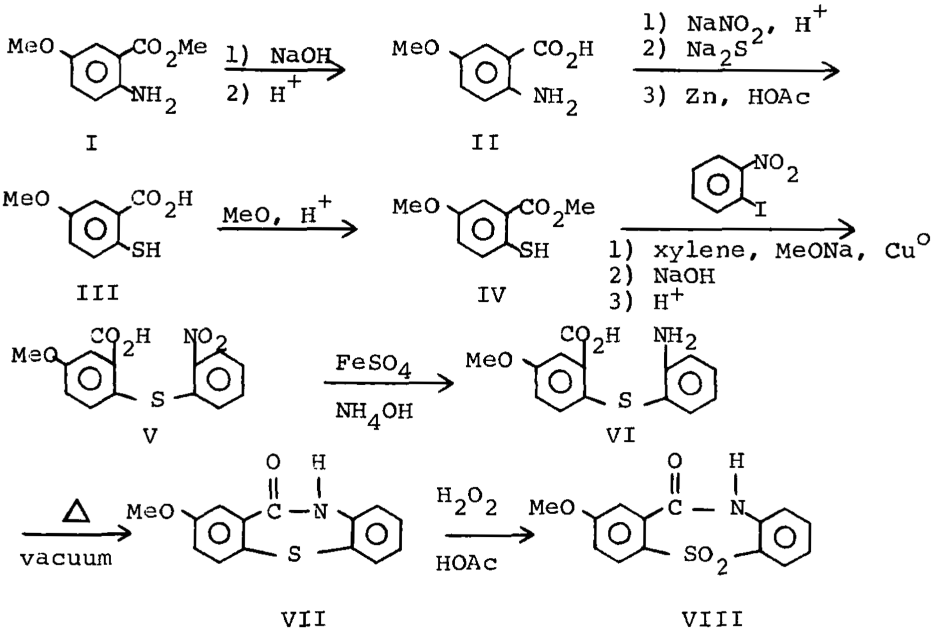
For use in another investigation, an unambiguous synthesis of the novel 2-methoxydibenzo [b,f] (1,4)-thiazepin-11(10H)-one-5,5-dioxide (VIII) was required. We now describe the preparation of VIII and several previously unknown compounds which resulted from the synthetic sequence as summarized by the equations.



EXPERIMENTAL[1]

Methyl 2-Amino-5-methoxybenzoate (I).- The required precursor of I, methyl 5-methoxy-2-nitrobenzoate, mp. 54-56° (EtOH-H_2O), lit.[2] mp. 55-57°, was obtained by the permanganate oxidation[3] of 3-methyl-4-nitroanisole, mp. 130-131°(H_2O), lit.[4] mp. 131-132°, followed by H_2SO_4 catalyzed esterification with methanol.

A solution of 5.0 g (0.0237 mole) of methyl 5-methoxy-2-nitrobenzoate in 100 ml of 95% ethanol was catalytically reduced (Parr apparatus) over 0.1 g of platinum oxide[5] at 40 psi and room temperature. The reaction mixture was shaken with hydrogen until three molecular equivalents were absorbed (about ten minutes). The filtered solution was evaporated *in vacuo* leaving an oil which was distilled under vacuum to give 4.20 g (98%) of desired I as a light yellow oil, bp. 114-115°/0.4 mm.

Anal. Calcd. for $C_9H_{11}NO_3$: C, 59.67; H, 6.08; N, 7.73. Found: C, 59.69; H, 6.08; N, 7.64.

5-Methoxyanthranilic Acid (II).- A mixture of 24.0 g (0.133 mole) of I, 150 ml of 20% aqueous sodium hydroxide and 125 ml of 95% ethanol was heated at reflux for 1 hr. The hot solution was filtered and the ethanol removed from the cooled filtrate by evaporation *in vacuo*. The remaining solution was carefully neutralized with 10% hydrochloric acid and the precipitate collected by suction filtration.

Recrystallization of this solid from water gave 20.0 g (90%) of II, mp. 149-151°, lit.[6] mp. 149-150.5°.

5-Methoxythiosalicylic Acid (III).- Sodium sulfide, 17.0 g (0.071 mole) and 5.0 g of powdered sulfur were added to 80 ml of boiling water. A solution of 30.0 g of sodium hydroxide in 75 ml of water was added to the stirred hot mixture and the resulting solution was cooled to 0° in an ice-salt bath and set aside for subsequent use.

In a 1-l beaker, placed in an ice-salt bath, was added 80 ml of water, 10.0 g (0.060 mole) of 5-methoxyanthranilic acid (II) and 15 ml of conc. hydrochloric acid and the mixture stirred while being cooled to 4°. To this cold, stirred solution was added cold aqueous sodium nitrite, 4.2 g (0.061 mole) in 30 ml of water from a separatory funnel whose tip was immersed below the surface of the reaction solution. During the addition, the temperature of the reaction mixture was not allowed to exceed 5°. The resulting solution was added over a 30 min period to the sulfide solution, prepared previously, while the temperature of the reaction mixture was maintained below 5°. The reaction mixture was then allowed to warm to room temperature and when the evolution of nitrogen ceased (1 hr), 50 ml of conc. hydrochloric acid was added. The resulting precipitate was collected by suction filtration, washed well with water and dissolved in boiling 10% aqueous sodium carbonate. This hot solution was filtered and the cooled filtrate acidified with conc. hydrochloric acid to give a solid which was collected, washed with water and air dried. This material was heated at reflux (6 hr) with 25.0 g of zinc dust in 300 ml of glacial acetic acid, followed by cooling and filtration, to afford a solid which was washed with water and then suspended in 200 ml of boiling water. The hot suspension was made alkaline with 50 ml of 33% aqueous sodium hydroxide and the resulting solution was boiled for 30 min. The solution was cooled, filtered and the filtrate acidified with conc. hydrochloric acid. The solid that separated was collected, washed with water and recrystallized from ethanol-water to afford 7.5 g (67%) of III, mp. 175-176°.

Anal. Calcd. for $C_8H_8O_3S$: C, 52.17; H, 4.35. Found: C, 52.33; H, 4.33.

Methyl 5-Methoxythiosalicylate (IV).- A mixture of 14.5 g (0.0788 mole) of III, 400 ml of methanol and 15 ml of conc. sulfuric acid was stirred at reflux for 8 hr. The methanol was removed by distillation and 400 ml of water was added to the remaining solution. The oil that separated was dissolved in ether and the ethereal solution washed with water and with 5% aqueous sodium bicarbonate before drying over anhydrous magnesium sulfate. Evaporation of the ether afforded an oil which was distilled *in vacuo* to give 13.2 g (84%) of IV, bp. 105-106°/0.3 mm.

Anal. Calcd. for $C_9H_{10}O_3S$: C, 54.54; H, 5.05; S, 16.16. Found: C, 54.73; H, 5.08; S, 15.95.

2-METHOXYDIBENZO[b,f](1,4)-THIAZEPIN-11(10H)-ONE-5,5-DIOXIDE

2-Carboxy-4-methoxy-2'-nitrodiphenyl Sulfide (V).- A mixture of 11.2 g (0.0565 mole) of IV, 14.0 g (0.0565 mole) of 1-iodo-2-nitrobenzene, 14.1 g (0.0565 mole) of sodium methoxide, 0.1 g of copper powder and 500 ml of xylene was refluxed for 24 hr and then steam distilled to remove the xylene. To the remaining solution was added 75 ml of 20% aqueous sodium hydroxide, 75 ml of 95% ethanol and the reaction mixture was refluxed for 30 min followed by filtration of the hot solution. Ethanol was distilled and the cooled solution acidified with 10% hydrochloric acid afforded a solid which was collected and air dried. Recrystallization of the solid from ethanol-water gave 11.7 g (68%) of V, mp. 185-187°.

Anal. Calcd. for $C_{14}H_{11}NO_5S$: C, 55.08; H, 3.61. Found: C, 54.97; H, 3.71.

2'-Amino-2-carboxy-4-methoxydiphenyl Sulfide (VI).- A solution of 13.8 g (0.045 mole) of V dissolved in 100 ml of ammonium hydroxide (1.23N) was added to a stirred boiling solution of 137.25 g (0.35 mole) of ferrous ammonium sulfate in 250 ml of water. The thick mixture was diluted with 50 ml of water and boiled for 5 min while adding 100 ml of conc. ammonium hydroxide. The cooled mixture was filtered and the filtrate concentrated to about 100 ml before careful acidification with glacial acetic acid. The precipitate was collected and recrystallized from acetic acid-water to afford 11.1 g (90%) of VI, mp. 150-151°.

Anal. Calcd. for $C_{14}H_{13}NO_3S$: C, 61.11; H, 4.73. Found: C, 61.33; H, 4.71.

2-Methoxydibenzo[b,f](1,4)-thiazepin-11(10H)-one (VII).- Compound VI, 1.0 g (0.00364 mole), was cyclized by heating for 5 hr at 138° under vacuum (0.3mm). Some phosphorus pentoxide, placed in a separate container, was included in the vacuum system during this cyclization procedure. Recrystallization from acetic acid-water afforded 0.7 g (75%) of VII, mp. 190-192°.

Anal. Calcd. for $C_{14}H_{11}NO_2S$: C, 65.37; H, 4.28. Found: C, 65.25; H, 4.33.

2-Methoxydibenzo[b,f] (1,4)-thiazepin-11(10H)-one-5,5-dioxide (VIII).- A mixture of 1.0 g (0.0039 mole) of VII, 25 ml of glacial acetic acid and 5 ml of 30% aqueous hydrogen peroxide was refluxed for 2 hr. The cooled solution was diluted with water and the collected precipitate was recrystallized from acetic acid-water to give 1.0 g (90%) of VIII, mp. 247-248°.

Anal. Calcd. for $C_{14}H_{11}NO_4S$: C, 58.13; H, 3.81: N, 4.84; S, 11.07.
Found: C, 57.95; H, 3.87; N, 4.77; S, 11.10.

REFERENCES

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1. Analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tennessee. All melting points are corrected. Boiling points are uncorrected.
2. T.P.C. Mulholland, J. Chem. Soc., 2702 (1958).
3. F. Ullman and M. Dootson, Ber., 51, 9 (1918).
4. B. Berinzaghi, A. Murazabal, R. Labriola and V. Deulofeu, J. Org. Chem., 10, 181 (1945).
5. R. Adams, V. Voorhees and R.L. Shriner, "Organic Syntheses", Coll. Vol. 1, 2nd ed., p. 463, John Wiley and Sons, Inc., New York, 1948.
6. M. Smith, E. Elesberg and M.L. Sherrill, J. Am. Chem. Soc., 68, 1301 (1946).

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