[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

Studies in the Thiapyran Series. The Preparation, Properties and Reactions of 1,4-Thiapyrone-1-dioxide

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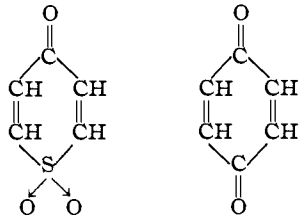
A comparison of the structural formulas of 1,4-thiapyrone-1-dioxide (I) and *p*-benzoquinone (II) suggests that these two compounds might possess



I II

many chemical and pharmacological properties in common. Several investigators[2] have demonstrated the similarity in the behavior of α,β-unsaturated sulfones and α,β-unsaturated ketones in addition reactions involving both symmetrical and unsymmetrical reagents, and Kohler and Larsen[3] have shown that the addition reactions of α-phenylsulfonyl-β-benzoylethylene with unsymmetrical reagents are similar to those of β-benzoylacrylic esters, the mode of addition being controlled by the conjugated system —C=C—C=O. Although these and other investigations[4] have provided evidence for the temporary expansion of the valence shell of sulfur to accommodate ten electrons, the characteristic enolization of the initial 1,4-addition products of quinones to yield stable hydroquinones as the final products would not be expected to have a counterpart in the thiapyrone dioxide series.

The preparation of 1,4-thiapyrone-1-dioxide has been described by Arndt and Bekir,[5] who obtained a very small amount of the compound as the final product of a five-step synthesis starting with ethyl β-thiodipropionate.[6] In order to prepare the relatively large amounts of I required in the present work, we have re-investigated each step in the original procedure and by applying various modifications have succeeded in obtaining a greatly improved over-all yield of the desired product.

(1) American Chemical Society Postdoctoral Fellow, 1946–1948.

(2) (a) Kohler and Potter, THIS JOURNAL, **57**, 1316 (1935); (b) Alexander and McCombie, *J. Chem. Soc.*, 1913 (1931); (c) Kretov, *J. Russ. Phys.-Chem. Soc.*, **62**, 1 (1930); *C. A.*, **24**, 4257 (1930).

(3) Kohler and Larsen, THIS JOURNAL, **57**, 1448 (1935).

(4) (a) Rothstein, *J. Chem. Soc.*, 309 (1937); 1550, 1553, 1558 (1940); (b) Fehnel and Carmack, "The Ultraviolet Absorption Spectra of Organic Sulfur Compounds," presented before the Division of Organic Chemistry of the American Chemical Society at the Chicago meeting, April, 1948.

(5) Arndt and Bekir, *Ber.*, **63**, 2393 (1930).

(6) The earlier steps in this synthesis were first carried out by (a) Bennett and Scorah, *J. Chem. Soc.*, 194 (1927); (b) Bennett and Waddington, *ibid.*, 2829 (1929).

1,4-Thiapyrone-1-dioxide, like its carbonyl analog, *p*-benzoquinone, is a sternutator, stains the skin yellow, and is decomposed by aqueous alkali with the formation of a deep red color. The ultraviolet absorption spectra of *p*-benzoquinone, 1,4-thiapyrone-1-dioxide, and 2,3-dihydro-1,4-thiapyrone-1-dioxide are compared in Fig. 1.

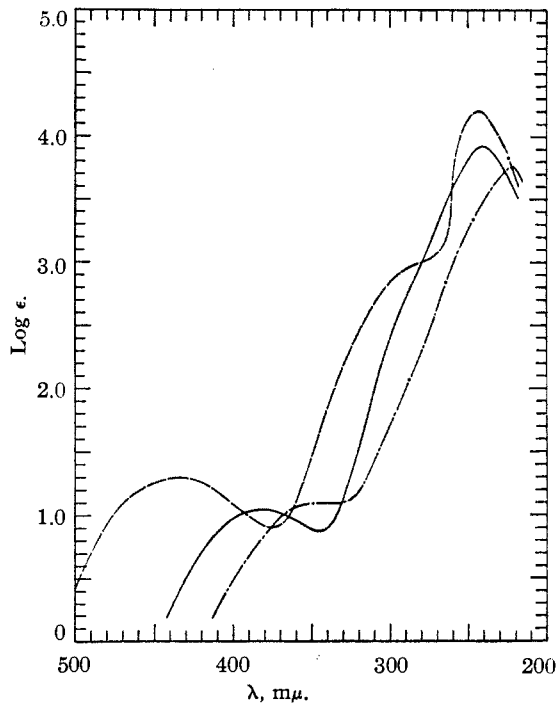
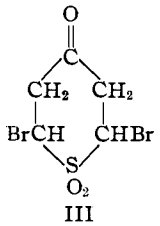


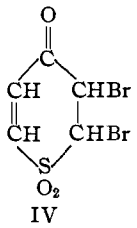
Fig. 1.—Absorption spectra of 1,4-thiapyrone-1-dioxide, ——; 2,3-dihydro-1,4-thiapyrone-1-dioxide, —·—·—; *p*-benzoquinone, — — —.

On treatment with zinc and acetic acid, 1,4-thiapyrone-1-dioxide is smoothly reduced to the corresponding saturated heterocycle, tetrahydro-1,4-thiapyrone-1-dioxide. Two molecules of hydrogen bromide may be added to I in the presence of a large excess of the reagent in acetic acid solution, but the reaction appears to be reversible and the dibromo compound readily loses hydrogen bromide on warming in aqueous or acetic acid solution. This rather unstable addition product (m. p. 130–133° dec.) has quite different properties from the stable isomer, 3,5-dibromotetrahydro-1,4-thiapyrone-1-dioxide (m. p. 220–222° dec.) obtained by bromination of tetrahydrothiapyrone dioxide,[5] and has been assigned structure III on the basis of Kohler and Larsen's observations[3] regarding the mode of addition of unsymmetrical addenda to unsaturated ketosulfones.

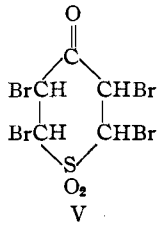


III

The addition of either one or two molecules of bromine to I proceeds readily at room temperature, giving as the initial products the dibromide IV and the tetrabromide V. The isolation of

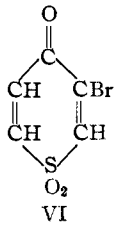


IV

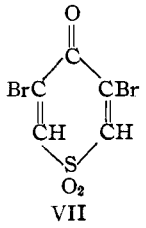


V

these compounds proved to be rather difficult, since, like the corresponding quinone bromides,[7] they readily lose hydrogen bromide on warming and are gradually converted into the mono- and dibromothiapyrone dioxides, VI and VII. The structures assigned to the latter compounds, which



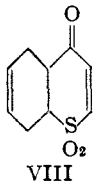
VI



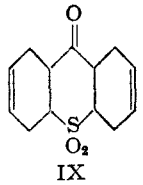
VII

are the only isolable products of bromination when no special precautions are taken to prevent the dehydrobromination of the initial adducts, follow from a consideration of the relative ease of dehydrobromination of the 3,5- and 2,6-dibromotetrahydrothiapyrone dioxides.

The stepwise addition of butadiene to I occurs slowly at room temperature and more rapidly at elevated temperatures, yielding mono- and di-adducts (VIII and IX) analogous to the products obtained in a similar manner from *p*-benzoquinone.[8]

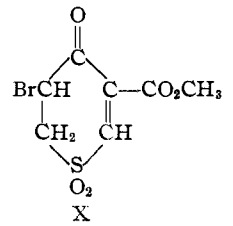


VIII

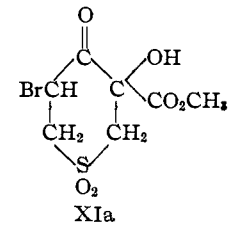


IX

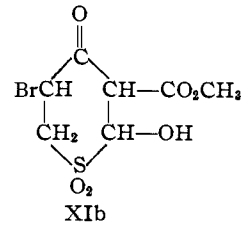
3,5-Dibromo-3-carbomethoxytetrahydro-1,4-thiapyrone-1-dioxide, prepared in the course of this investigation by the bromination of 3-carbomethoxytetrahydro - 1,4 - thiapyrone - 1 - dioxide, was found to lose one molecule of hydrogen bromide so readily that a good yield of a monobromocarbomethoxydihydrothiapyrone dioxide



X



XIa



XIb

was obtained merely by refluxing the dibromo compound with aqueous acetic acid. The product is undoubtedly the 2,3-dihydro compound X. In one similar experiment, however, the product isolated appeared, on the basis of the analytical data, to be a bromohydroxycarbomethoxytetrahydrothiapyrone dioxide. Either structure XIa or XIb might be assigned to this compound, depending on whether the bromine atom was replaced directly by a hydroxyl group or, as is more probable, hydrogen bromide was first split out to give X, which then added a molecule of water, the hydroxyl becoming attached to the carbon *beta* to the carbonyl function. All attempts to repeat the preparation of this compound, starting with either the dibromo derivative or with X, were unsuccessful, and its structure was not further investigated.

Experimental[9]

Improved Preparation of 1,4-Thiapyrone-1-dioxide (I).—A mixture of 289 g. (1.4 moles) of methyl β-thiodipropionate,[10] 2.8 moles of alcohol-free sodium methoxide (freshly prepared from 64.3 g. of sodium), and 1 liter of anhydrous ether was stirred and refluxed for three hours. The mixture was cooled quickly to room temperature and poured into an ice-cold solution of 178 ml. of acetic acid in 1 liter of water. After vigorous agitation, the layers were separated and the aqueous layer was extracted repeatedly with small portions of ether until the extracts no longer gave a violet color with ferric chloride solution. The extracts were added to the original ether layer, and the combined solution was washed with aqueous sodium bicarbonate and dried over anhydrous magnesium sulfate. After removal of the ether, the residual oil was distilled under diminished pressure to yield 158.8 g. (65%) of **3-carbomethoxytetrahydro-1,4-thiapyrone** as a colorless oil, b. p. 120–125° at 5 mm. The analytical sample was obtained by redistillation of a small portion of this material; b. p. 120° at 5 mm., $n^{20}D$ 1.5234.

Anal. Calcd. for $C_7H_{10}O_3S$: C, 48.26; H, 5.79. Found: C, 48.31; H, 5.79.

Hydrolysis and decarboxylation of the cyclic ketoester was accomplished in a single step by treatment with 10%

(7) Nef, *J. prakt. Chem.*, [2] **42**, 161 (1890).

(8) Diene additions of quinones have been studied by Diels, *et al.*, *Ber.*, **62B**, 2337 (1929), and by Alder and Stein, *Ann.*, **501**, 247 (1933).

(9) Microanalyses were performed by Miss Sarah H. Miles. All melting points are corrected.

(10) Gershbein and Hurd, THIS JOURNAL, **69**, 241 (1947).

sulfuric acid according to the method of Bennett and Scorah.[6a] A reflux period of two hours sufficed to complete the reaction in the case of the methyl ester. Evaporation of the dried ether extract afforded colorless crystals of crude tetrahydro-1,4-thiapyrone melting at 58–62° (reported[6a] m. p., 65–66°); yield, 84%.

To a solution of 56.0 g. (0.48 mole) of tetrahydrothiapyrone in 500 ml. of glacial acetic acid, 114 ml. (1.00 mole) of 30% hydrogen peroxide was added in small portions while the mixture was cooled under the tap to moderate the reaction. After the strongly exothermic reaction had subsided, 400 ml. of the solvent was distilled from the mixture and the residue was cooled to crystallize out the major portion of the product as almost colorless needles melting at 164–167° (reported[6b] m. p., 170°). A further small quantity of crude product was obtained by evaporation of the filtrate to dryness on the steam-bath and recrystallization of the residue from acetic acid; total yield of tetrahydro-1,4-thiapyrone-1-dioxide, 54.7 g. (77%).

A warm solution of 38.3 g. (0.26 mole) of the crude dioxide in 450 ml. of glacial acetic acid was shaken with 83.2 g. (0.52 mole) of bromine for several minutes and was then cooled to room temperature and filtered. 3,5-Dibromotetrahydro-1,4-thiapyrone-1-dioxide was thus obtained as colorless needles, m. p. 220–222° dec. (reported[5] m. p., 220° dec.); yield, 71.9 g. (91%).

Attempts to dehydrobrominate this material by treatment with pyridine according to the original method of Arndt and Bekir[5] led to the formation of considerable tarry material and only small amounts of the desired product. Almost quantitative yields of pure product were obtained, however, when the dibromo compound was treated briefly with sodium acetate in refluxing acetone. In a typical experiment, a suspension of 12.2 g. (0.04 mole) of the dibromo compound in 150 ml. of hot acetone was added gradually over a fifteen-minute period to a mechanically stirred, refluxing suspension of 27.2 g. (0.20 mole) of powdered sodium acetate trihydrate in 150 ml. of acetone. Stirring and refluxing were continued for another ten minutes, and the dark red mixture was cooled and filtered. Concentrated hydrochloric acid was added dropwise to the filtrate until the color of the solution changed from red to yellow, and the mixture was refiltered to remove the precipitate of sodium chloride. The clear yellow filtrate was evaporated to dryness on the steam-bath, leaving a yellow-brown crystalline residue which was recrystallized from glacial acetic acid (Norit) to yield 3.9 g. of yellow crystals, m. p. 173–174° (reported[5] m. p., 174°). The mother liquor was worked up to provide a second crop of crystals, which was recrystallized and added to the original product to give a combined yield of 1,4-thiapyrone-1-dioxide (I) of 5.5 g. (96%). This compound is readily soluble in water, ethanol, and acetone; slightly soluble in cold acetic acid; and insoluble in hydrocarbon solvents. It sublimes as long yellow needles at temperatures somewhat below its melting point. Purified samples appear to be entirely stable when stored in contact with air.

The **oxime** was obtained as colorless needles which, after recrystallization from water, decomposed violently without melting at 196°.

Anal. Calcd. for $C_5H_5NO_3S$: C, 37.72; H, 3.17. Found: C, 37.77; H, 2.93.

The **semicarbazone** was obtained as a pale yellow microcrystalline powder, m. p. 237–239° dec., after recrystallization from water (Norit).

Anal. Calcd. for $C_6H_7N_3O_3S$: C, 35.81; H, 3.51. Found: C, 35.67, 35.86; H, 3.76, 3.35.

Reduction of 1,4-Thiapyrone-1-dioxide.—A mixture of 1.00 g. of I, 2.0 g. of zinc dust, and 15 ml. of glacial acetic acid was refluxed for one hour, after which the yellow color of the solution had disappeared. The unreacted zinc was filtered off, and the filtrate was saturated with hydrogen sulfide and refiltered. Evaporation of the clear filtrate to dryness on the steam-bath afforded 0.89 g. (87%) of almost colorless crystals which melted at 167–169° after recrystallization from acetic acid and exhibited no melting-point depression when mixed with authentic tetrahydro-1,4-thiapyrone-1-dioxide.

2,6-Dibromotetrahydro-1,4-thiapyrone-1-dioxide (III).—One gram of I was dissolved in 6 ml. of glacial acetic acid saturated with dry hydrogen bromide, and more hydrogen bromide was passed into the solution until precipitation was complete. The crystalline precipitate was collected and dried at room temperature to yield 0.9 g. of 2,6-dibromotetrahydro-1,4-thiapyrone-1-dioxide as brownish needles, m. p. 126–131° dec. Although this material appeared to be only slightly soluble in cold acetic acid, all attempts to recrystallize it from this solvent resulted in the formation of yellow solutions from which only negligible amounts of the dibromo compound could be recovered on cooling; m. p. 130–133° dec.

Anal. Calcd. for $C_5H_6Br_2O_3S$: C, 19.62; H, 1.99. Found: C, 20.06; H, 1.99.

When a sample of this compound was boiled with water for a few seconds, and was then cooled, acidified with dilute nitric acid, and treated with aqueous silver nitrate, a copious precipitate of silver bromide formed at once.

3-Bromo-1,4-thiapyrone-1-dioxide (VI).—To a solution of 1.00 g. (0.007 mole) of I in 25 ml. of glacial acetic acid there was added 1.11 g. (0.007 mole) of bromine, and the mixture was allowed to stand for four hours at 5°. After removal of the solvent by evaporation *in vacuo* at room temperature, the dark-colored, semicrystalline residue was recrystallized from methanol (Norit) to yield 0.50 g. (32%) of pale yellow crystals, m. p. 173–174° dec. with previous sintering. Another recrystallization from methanol gave the pure compound melting at 189–190° dec., when immersed in a bath at 185° and heated rapidly; considerable decomposition occurred above 150° when the compound was heated slowly from room temperature.

Anal. Calcd. for $C_5H_3BrO_3S$: C, 26.92; H, 1.36. Found: C, 26.96; H, 1.29.

3,5-Dibromo-1,4-thiapyrone-1-dioxide (VII).—A mixture of 1.44 g. (0.01 mole) of I, 3.20 g. (0.02 mole) of bromine, and 30 ml. of glacial acetic acid was allowed to stand at 5° until all the solid had dissolved and the color of the solution had faded to pale yellow. The mixture was poured into 60 ml. of ice-water and the resultant yellow precipitate was collected, washed with water, and dried; m. p. 157–161°; yield, 1.87 g. (62%). Recrystallization from methanol (Norit) gave pale yellow needles, m. p. 160–162°.

Anal. Calcd. for $C_5H_2Br_2O_3S$: C, 19.88; H, 0.67. Found: C, 19.79; H, 0.67.

2,3-Dibromo-2,3-dihydro-1,4-thiapyrone-1-dioxide (IV).—A solution of 1.44 g. (0.01 mole) of I in 50 ml. of hot chloroform was cooled to precipitate the thiapyrone dioxide as a microcrystalline suspension. A solution of 1.60 g. (0.01 mole) of bromine in 10 ml. of chloroform was added to this suspension in small portions over a thirty-minute period with vigorous agitation after each addition. The solvent was removed by evaporation under reduced pressure at room temperature, leaving a dark-colored sirup which slowly solidified on standing for several days. This product was digested with a little hot benzene, care being taken not to prolong the period of heating any longer than absolutely necessary, and the benzene extract was cooled to precipitate 0.6 g. of colorless powder, m. p. 133–135° dec. Cautious recrystallization of this material from benzene gave the dibromide as colorless crystals, m. p. 138–139° dec.

Anal. Calcd. for $C_5H_4Br_2O_3S$: C, 19.75; H, 1.33. Found: C, 20.74; H, 1.25.

This compound lost hydrogen bromide so readily that further purification could not be effected by repeated recrystallization. Analytical and melting-point data obtained for the same sample on different dates also indicate that the compound gradually undergoes dehydrobromination on standing at room temperature.

2,3,5,6-Tetrabromotetrahydro-1,4-thiapyrone-1-dioxide (V).—A mixture of 1.44 g. (0.01 mole) of I, 3.20 g. (0.02

mole) of bromine, and 65 ml. of chloroform was allowed to stand for one hour at room temperature with occasional agitation, and the solvent was then removed by evaporation under reduced pressure. The dark-colored residue was heated for a few minutes with a little acetic acid and the suspension was cooled and filtered. The insoluble portion was washed with a little cold acetic acid and dried *in vacuo* to yield 0.4 g. of colorless powder, m. p. 195–198° dec. with previous sintering and blackening. This compound dissolved slowly in hot acetic acid, water, and methanol with the production of a yellow color.

Anal. Calcd. for $C_5H_4Br_4O_3S$: C, 12.95; H, 0.87. Found: C, 13.20; H, 0.85.

The acetic acid filtrate from the isolation of the tetrabromide was evaporated and the residue was worked up with methanol to yield 1.6 g. of pale yellow needles. After repeated recrystallization from methanol, this material melted at 158–160° and failed to depress the melting point of the 3,5-dibromo-1,4-thiapyrone-1-dioxide described above.

3-Bromotetrahydro-1,4-thiapyrone-1-dioxide.—To a microcrystalline suspension obtained by cooling a hot solution of 7.40 g. (0.05 mole) of tetrahydro-1,4-thiapyrone-1-dioxide in 100 ml. of glacial acetic acid, 8.00 g. (0.05 mole) of bromine was added dropwise over a twenty-minute period. The mixture was agitated vigorously after each addition, and after all the bromine had been added the precipitate was filtered off and dried *in vacuo* over potassium hydroxide to yield 8.39 g. (74%) of colorless silky needles, m. p. 176–179°. Recrystallization from acetic acid raised the melting point to 182–183°.

Anal. Calcd. for $C_5H_7BrO_3S$: Br, 35.19. Found: Br, 35.66.

2,3-Dihydro-1,4-thiapyrone-1-dioxide.—3-Bromotetrahydro-1,4-thiapyrone-1-dioxide (6.81 g., 0.03 mole) was dehydrobrominated by treatment with sodium acetate trihydrate (9.5 g., 0.07 mole) in boiling acetone (100 ml.) exactly as in the case of the 3,5-dibromo compound. The first crystallization of the crude product from acetic acid (Norit) afforded 3.41 g. (78%) of very pale yellow needles, m. p. 144–146°. Several further recrystallizations from this solvent raised the melting point to 147–148°. This compound gave a deep red color on treatment with aqueous alkali.

Anal. Calcd. for $C_5H_6O_3S$: C, 41.07; H, 4.14. Found: C, 41.11; H, 4.11.

The **oxime** was obtained as colorless needles which melted at 178–179°, dec., after recrystallization from water.

Anal. Calcd. for $C_5H_7NO_3S$: C, 37.24; H, 4.38. Found: C, 37.01; H, 4.53.

$\Delta^{2,7}$-Octahydrothiaxanthone-5-dioxide (IX).—Twenty-five milliliters of purified dioxane[11] was saturated with butadiene (*ca.* 3.8 g., 0.070 mole) at room temperature, 2.0 g. (0.014 mole) of I was added, and the mixture was heated in an autoclave at 140–150° for four hours. On cooling, most of the product crystallized out of the solution in a nearly pure condition; yield, 2.5 g. (72%) of almost colorless plates, m. p. 228–234°, dec., when immersed in a bath previously heated to above 200°. Recrystallization from acetic acid afforded colorless needles, m. p. 235–236°, dec. This compound gave no color on treatment with aqueous sodium hydroxide.

Anal. Calcd. for $C_{13}H_{16}O_3S$: C, 61.88; H, 6.39. Found: C, 61.78; H, 6.21.

Δ^6-Tetrahydro-1,4-benzothiapyrone-1-dioxide (VIII).—A mixture of 2.00 g. (0.014 mole) of I, 3.8 g. (0.070 mole) of butadiene, and 25 ml. of purified dioxane was heated in an autoclave at 100° for four hours, after which the solvent was distilled off and the semicrystalline residue was extracted repeatedly with boiling water. On cooling, the combined aqueous extracts deposited 1.10 g. (40%) of colorless needles, m. p. 146–156°. After several recrystallizations from ethanol, this compound melted at 157–159° and gave a deep yellow color with aqueous sodium hydroxide.

Anal. Calcd. for $C_9H_{10}O_3S$: C, 54.54; H, 5.09. Found: C, 54.57; H, 4.85.

A small amount (*ca.* 0.3 g.) of the di-addition product was isolated from the water-insoluble residue by extraction with hot acetic acid. On dilution with several volumes of water, the acetic acid extract slowly deposited a white solid which melted at 229–231° dec. after recrystallization from acetic acid and which failed to depress the melting point of the di-adduct described above.

In an experiment in which a suspension of I in an ethanol solution of butadiene was allowed to stand at room temperature for seven days, a small amount of crystalline material melting at 153–156° was isolated and identified as the mono-adduct by the method of mixed melting points.

3-Carbomethoxytetrahydro-1,4-thiapyrone-1-dioxide.—Oxidation of 1.74 g. (0.01 mole) of 3-carbomethoxytetrahydro-1,4-thiapyrone with 2.5 ml. (0.022 mole) of 30% hydrogen peroxide in 12 ml. of glacial acetic acid afforded 1.35 g. (65%) of colorless crystals melting at 115–116° after recrystallization from water. This compound gave a blood-red color with ferric chloride solution.

Anal. Calcd. for $C_7H_{10}O_5S$: C, 40.75; H, 4.89. Found: C, 40.84; H, 5.01.

3,5-Dibromo-3-carbomethoxytetrahydro-1,4-thiapyrone-1-dioxide.—Bromine (2.72 g., 0.017 mole) was added to a suspension of 1.75 g. (0.0085 mole) of the above ketoester in 10 ml. of glacial acetic acid, and the mixture was agitated until all the solid had dissolved. The clear red solution was placed in a vacuum desiccator over potassium hydroxide and allowed to stand for two weeks. At the end of this time all of the solvent had evaporated and 2.90 g. (94%) of a pale yellow crystalline solid, m. p. 155–165° dec., remained. After repeated recrystallization from ethyl acetate, the pure product was obtained as colorless needles melting at 182–183° dec.

Anal. Calcd. for $C_7H_8Br_2O_5S$: C, 23.10; H, 2.22. Found: C, 23.26, 23.27; H, 2.38, 2.24.

3-Bromo-5-carbomethoxy-2,3-dihydro-1,4-thiapyrone-1-dioxide (X).—A solution of 2.00 g. of the above dibromo compound in 50 ml. of 50% aqueous acetic acid was refluxed for ten minutes, and the crystalline precipitate obtained on cooling was recrystallized from ethyl acetate to yield 1.10 g. (71%) of colorless plates, m. p. 156–157° with previous sintering. This compound gave a positive Beilstein test for halogen.

Anal. Calcd. for $C_7H_7BrO_5S$: C, 29.70; H, 2.49. Found: C, 29.50; H, 2.29.

5-Bromo-3(or 2?)-hydroxy-3-carbomethoxytetrahydro-1,4-thiapyrone-1-dioxide (XI).—In one experiment in which 3,5-dibromo-3-carbomethoxytetrahydro-1,4-thiapyrone-1-dioxide was heated briefly with aqueous acetic acid as above, a colorless crystalline compound melting at 175–177°, dec., after recrystallization from ethyl acetate was obtained. Subsequent attempts to repeat

TABLE I

ULTRAVIOLET ABSORPTION DATA

Compound	$\lambda_{max.}$,[a] mμ	Log ε
1,4-Thiapyrone-1-dioxide	380	1.04
	240	3.93
2,3-Dihydro-1,4-thiapyrone-1-dioxide	(340)	1.10
	221	3.74
p-Benzoquinone[b]	433	1.31
	(275)	3.03
	243	4.21

[a] The wave lengths in parentheses refer to prominent inflection points. [b] *Cf.* Anderson and Yanko, THIS JOURNAL, **56**, 782 (1934); Light, *Z. physik. Chem.*, **122**, 414 (1926); Hartley and Leonard, *J. Chem. Soc.*, **95**, 34 (1909).

(11) Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Company, New York, N. Y., 1941, p. 369.

the preparation of this compound afforded only the dihydro compound X or unchanged starting material.

Anal. Calcd. for $C_7H_9BrO_6S$: C, 27.92; H, 3.01. Found: C, 27.86, 28.10, 27.88; H, 3.21, 3.12, 3.25.

Ultraviolet Absorption Spectra.—The spectra were determined in purified dioxane with a Beckman Quartz Spectrophotometer, Model DU, using an approximately constant spectral band width of *ca.* 1 mμ. *p*-Benzoquinone (Eastman practical grade) was purified by recrystallization from water and subsequent sublimation at 100°; m. p. 114–115°. 1,4-Thiapyrone-1-dioxide and 2,3-dihydro-1,4-thiapyrone-1-dioxide were both recrystallized from acetic acid and then sublimed *in vacuo* at temperatures slightly below their melting points; the sublimed samples melted at 174–175° and 147–148°, respectively. The wave lengths and extinction coefficients at the absorption maxima are summarized in Table I.

Summary

An improved procedure for the synthesis of 1,4-thiapyrone-1-dioxide, a sulfonyl analog of *p*-benzoquinone, has been described, and the addition reactions of this compound with hydrogen, hydrogen bromide, bromine and butadiene have been investigated. A number of new thiapyrone derivatives have been prepared and characterized. The ultraviolet absorption spectra of 1,4-thiapyrone-1-dioxide and 2,3-dihydro-1,4-thiapyrone-1-dioxide have been determined and compared with the spectrum of *p*-benzoquinone.

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[A CONTRIBUTION OF THE CHEMICAL LABORATORY OF CLARK UNIVERSITY]

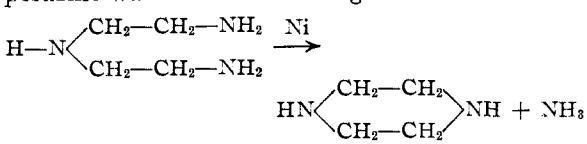
Preparation of Piperazine[1]

BY WILLIAM B. MARTIN AND ARTHUR E. MARTELL

The formation of secondary amines from primary amines by catalytic deamination has been mentioned by Adkins in the case of the formation of dibenzylamine from benzylamine. Also, C. W. Hoerr, *et al.*,[2] have recently prepared secondary aliphatic amines by the same method.

Kyrides[3] has described the preparation of piperazine from ethylenediamine and diethylenetriamine by the same method. The reaction was carried out without solvent at high temperatures (about 235°) in an autoclave. No yields were reported. This reaction has been subjected to considerable investigation in this Laboratory, and it seemed desirable at this time to report on the investigation to supplement the disclosures of the Kyrides patent.

Diethylenetriamine was heated with Raney nickel under various experimental conditions. The results of these experiments are tabulated below. In all cases ammonia was evolved and piperazine was formed according to the reaction



A temperature of about 150° or somewhat higher was found to be most suitable for the reaction. When a low-boiling solvent such as xylene or toluene was used at atmospheric pressure, the reaction proceeded very slowly and little piperazine was obtained. The reaction seemed to be endothermic, and an increase of the rate of heating at atmospheric pressure merely resulted in a more rapid evolution of ammonia. After the reaction had proceeded for a while the temperature would gradually rise to the reflux point of the solvent.

Allowing the ammonia to escape from the reaction mixture does not tend to improve the yield of piperazine. The yields are in general somewhat higher when the reaction is carried out in an autoclave. This may have been due in part to the loss of piperazine through volatilization in the escaping ammonia, since the vapor pressure of piperazine, even at room temperature, is fairly high. At any rate, the reaction does not approach a state of equilibrium. In all cases in which the ammonia was not allowed to escape, very little unreacted diethylenetriamine was isolated. As a further test, piperazine was treated with several molar proportions of alcoholic ammonia in an autoclave at 150° for ten hours in the presence of Raney nickel catalyst. No diethylenetriamine or ethylenediamine was obtained, and substantially all the piperazine was recovered by fractional distillation.

In all the reactions attempted some high-boiling fractions and viscous high molecular weight residues were obtained. These were evidently mixtures of higher "polyalkylene polyamines" which probably resulted from linear deamination of diethylenetriamine to form tetraethylenepentamine and higher homologs. The use of solvent is important in cutting down intermolecular condensation and in improving the yield of piperazine. This was also found to be the case by Pollard, *et al.*,[4] in the preparation of piperazine by the catalytic dehydration of hydroxyethylethylenediamine. In general, the use of a solvent decreased the formation of high boiling tarry residues. Of the solvents employed, moderately high boiling hydrocarbons gave the best results.

Similar results were obtained when the experi-

(1) Adkins, "Reactions of Hydrogen," The University of Wisconsin Press, Madison, Wis., 1937, p. 55.

(2) C. W. Hoerr, *et al.*, *J. Org Chem.*, **9**, 201–210 (1944).

(3) Kyrides, U. S. Patent 2,267,686, December 23, 1941.

(4) Pollard, *et al.*, U. S. Patent 2,400,022, May 7, 1946.