1,2-Benzothiazines VII (1). The Boron Trifluoride Catalyzed Rearrangement of the Epoxide Derived from 3-Benzylidene-2-methyl-2*H*-1,2-benzothiazin-4(3*H*)one 1,1-Dioxide

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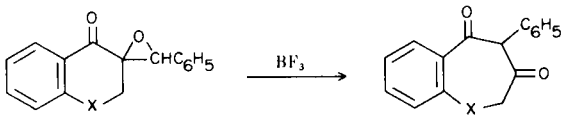
House and Wasson (2) have shown that the boron trifluoride catalyzed rearrangement of 2-benzalcycloalkanone epoxides proceeds *via* benzoyl migration to give ring expanded β-diketones. Extrapolation of this reaction (3,4,5) to the epoxide **1a** derived from α-tetralone (3,4) as well as its heterocyclic analogs 1b-d (5) has been demonstrated to yield the expected products of structure **2**. We now wish to report the results of our attempt to carry out the same type of rearrangement in the 1,2-benzothiazine series.



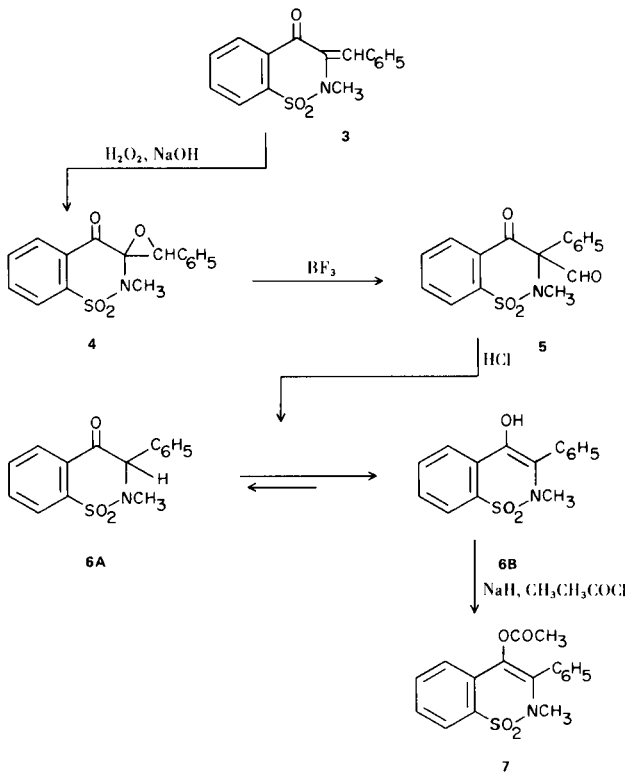
1 **2**

(a) X = CH_2
(b) X = O
(c) X = S
(d) X = SO_2

The reaction of **3** (6) with hydrogen peroxide and sodium hydroxide in tetrahydrofuran gave rise to the epoxide **4**, whose infrared spectrum (mull) showed a carbonyl band at 1695 cm^{-1}. Treatment of **4** with boron trifluoride etherate in dichloromethane did not give the ring expanded diketone which would have been analogous to **2**. Instead, there was obtained a non-acidic keto-aldehyde **5** having the original 1,2-benzothiazine skeleton. This substance (7) was characterized by aldehyde and ketone bands at 1730 and 1690 cm^{-1}, respectively, and the structural assignment was compatible with the nmr spectrum which showed the characteristic aldehyde proton at 10.1 ppm.

Refluxing **5** with hydrochloric acid in aqueous methanol resulted in decarbonylation to give **6**. The infrared spectrum when taken as a Nujol mull showed the presence of a strong hydroxy band at 3350 cm^{-1}, a weak olefinic band at 1595 cm^{-1}, and the complete absence of carbonyl absorption. In chloroform solution there was observed a weak carbonyl band at 1710 cm^{-1} and the hydroxy band

CHART I



at 3550 cm^{-1} was still very strong. Thus, it became apparent that this substance exists predominantly in the enol form **6B**. Further evidence for this structural assignment was given by the nmr spectrum which showed the OH as a broad exchangeable signal at 5.67 ppm. Reaction of **6** with sodium hydride and acetyl chloride in tetrahydrofuran resulted in conversion to the acetyl derivative **7**.

The observed melting point of **6** depended considerably on the rate of heating, thus suggesting that a chemical change occurred during melting. A sample, which was heated *in vacuo* at 140° for three hours, melted and then resolidified on cooling. The mull spectrum of this material now showed a moderate sized carbonyl band at 1700

cm^{-1} as well as the hydroxy band at 3380 cm^{-1}. Thus, it appeared that some of the **6B** had been converted to the keto form **6A** on melting. However, when this fused material was recrystallized from benzene, only the original enol **6B** could be isolated.

The formation of **5** rather than an analog of **2** is apparently the result of boron trifluoride catalyzed phenyl migration in epoxide **4**. This preference for phenyl migration as opposed to benzoyl migration has been reported for sulfuric acid catalyzed rearrangement of 3-benzylideneoxindole epoxide (4) and the boron trifluoride catalyzed rearrangement of the epoxides derived from benzalacenaphthenone (4), methyleneanthrone (3), and benzalanthrone (3).

EXPERIMENTAL

Melting points were determined in open capillaries with a Thomas-Hoover Capillary Melting Point Apparatus which was calibrated against known standards. The ultraviolet and infrared spectra were determined with a Beckman DK-1 spectrophotometer and a Baird Model 455 spectrophotometer, respectively. The nmr spectra were measured in deuteriochloroform using a Varian A-60 spectrometer with tetramethylsilane as an internal standard.

3-Benzyl-3, α-epoxy-2-methyl-2*H*-1,2-benzothiazin-4(3*H*)one 1,1-Dioxide (**4**).

To a solution of 18 g. (0.06 mole) of 3-benzylidene-2-methyl-2*H*-1,2-benzothiazin-4(3*H*)one 1,1-dioxide (3) in 300 ml. of tetrahydrofuran was added 90 ml. of 30% aqueous hydrogen peroxide. To the stirred solution was slowly added 60 ml. of 1.0 *N* sodium hydroxide, the temperature being maintained at 0 to +5° during the addition. After stirring at this temperature for 30 minutes, the reaction mixture was poured into 3000 ml. of ice water and the resulting precipitate was collected and dissolved in dichloromethane. This solution was washed with water, dried over sodium sulfate, and evaporated to give a gummy residue. Trituration with petroleum ether (30-60°) gave 15.5 g. of white crystals, m.p. 120-123° dec., which was of sufficient purity for use in the subsequent step. A portion was recrystallized from ethanol to give an analytical sample, m.p. 126-128° dec. The material appeared to decompose on standing.

Anal. Calcd. for $C_{16}H_{13}NO_4S$: C, 60.94; H, 4.16; N, 4.44; S, 10.17. Found: C, 60.92; H, 4.08; N, 4.24; S, 10.18.

3-Formyl-2-methyl-3-phenyl-2*H*-1,2-benzothiazin-4(3*H*)one 1,1-Dioxide (**5**).

A solution of 37.8 g. (0.12 mole) of 3-benzyl-3-α-epoxy-2-methyl-2*H*-1,2-benzothiazin-4(3*H*)one 1,1-dioxide (4) in 1500 ml. of dichloromethane was cooled to -5° and 300 ml. of boron trifluoride etherate was added. The resulting solution was allowed to stand at a temperature of 0 to -5° for 30 minutes and then poured into ice water. The layers were separated and the organic layer was successively washed with water, 1.0 *N* sodium hydroxide and water. It was then dried over sodium sulfate and evaporated to a residue which was triturated with 50 ml. of hot ether to give 23.5 g. of crystals, m.p. 147-148° (gas evolution). Recrystallization of a portion from a large volume of ether gave an analytical sample, m.p. 148-149° (gas evolution).

Anal. Calcd. for $C_{16}H_{13}NO_4S$: C, 60.94; H, 4.16; N, 4.44; S, 10.17. Found: C, 61.05; H, 4.13; N, 4.38; S, 10.32.

4-Hydroxy-2-methyl-3-phenyl-2*H*-1,2-benzothiazine 1,1-Dioxide (**6**).

A mixture of 15.7 g. (0.05 mole) of 3-formyl-2-methyl-3-phenyl-2*H*-1,2-benzothiazin-4(3*H*)one 1,1-dioxide (**5**), 200 ml. of methanol, and 30 ml. of 10% aqueous hydrochloric acid was refluxed for 20 minutes. The solution was filtered while hot and concentrated to a volume of 75 ml. On standing at room temperature there was obtained 12.9 g. of white crystals. The melting characteristics were dependent on the rate of heating. Samples immersed in the melting point bath at 125° with the temperature rising at the rate of 1° per minute started to decompose at 132° and melted completely at 148°. Samples kept at 132° for 30 minutes melted completely. Recrystallization from methanol gave 11.0 g. of product having the same melting characteristics; uv λ max (ethanol): 324 nm (ε, 15,000); λ max (0.05 *N* sodium hydroxide in ethanol): 236 nm (infl, ε, 11,000), 274 nm (ε, 5,700), 377 nm (ε, 11,400).

Anal. Calcd. for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87; S, 11.16. Found: C, 62.84; H, 4.58; N, 4.91; S, 11.22.

4-Acetoxy-2-methyl-3-phenyl-2*H*-1,2-benzothiazine 1,1-Dioxide (**7**).

To a suspension of 0.017 mole of sodium hydride (55% mineral oil dispersion) in 50 ml. of tetrahydrofuran, was added a solution of 5.0 g. (0.017 mole) of 4-hydroxy-2-methyl-3-phenyl-2*H*-1,2-benzothiazine 1,1-dioxide (6) in 50 ml. of tetrahydrofuran, the temperature being maintained at -20°. The mixture was stirred at this temperature for 2 hours and a solution of 1.36 g. (0.017 mole) of acetyl chloride in 5 ml. of tetrahydrofuran was added dropwise and stirring was continued at -20° for 2 hours. It was poured into 800 ml. of cold 1% hydrochloric acid and extracted wtih dichloromethane. The organic layer was washed successively with cold 0.1 *N* sodium hydroxide and water, dried over sodium sulfate, and evaporated. The residue was recrystallized from methanol-dichloromethane to give 4.5 g. of product, m.p. 174-175°; ν max (Nujol) 1780 cm^{-1}; λ max (ethanol) 290 nm (ε 14,000).

Anal. Calcd. for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59; N, 4.25; S, 9.73. Found: C, 62.26; H, 4.62; N, 4.54; S, 9.85.

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(7) These bands refer to the spectrum taken as a Nujol mull. In chloroform the corresponding bands were at 1745 and 1695 cm^{-1}.