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Refluxing the oxime (**1**) of 2-methyl-2*H*-1,2-benzothiazin-4(3*H*)one 1,1-dioxide with trifluoroacetic acid or with boron trifluoride in acetic acid gives the corresponding *N*-acyl derivative (**2** or **3**) of 4-amino-2-methyl-2*H*-1,2-benzothiazin-3(4*H*)one 1,1-dioxide. This transformation appears to be related to the acid catalyzed conversion of α-tetralone oxime to α-naphthylamine.

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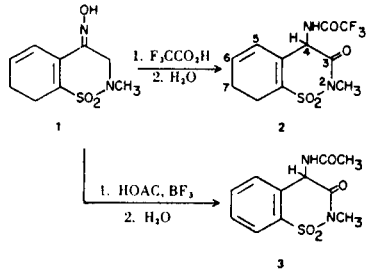
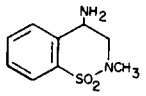
Semmler-Wolff Aromatization (3,4) is an alternative to Beckmann Rearrangement which often takes place with α,β-unsaturated cyclic ketoximes. The acid catalyzed conversion of α-tetralone oxime to α-naphthylamine (5) is a typical example for which Bhatt (6) has proposed a mechanism. We wish to report what appears to be a related reaction in the 1,2-benzothiazine series.



Refluxing the oxime **1** with excess trifluoroacetic acid followed by dilution of the reaction mixture with water resulted in precipitation of a product which was shown to have structure **2**. This substance was characterized by a strong NH band at 3350 and strong carbonyl bands at 1740 and 1706 cm^{-1}. Its weak absorption (λ max 267 (ε 1,100) and 274 (ε 1,040) mμ) in the ultraviolet was similar to that observed earlier with **4** (7). The methyl and



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amide protons were represented in the nmr spectrum (DMSO) by a singlet at 3.17 and an exchangeable doublet (J = 8 cps) at 10.53 ppm, respectively. Acidic character of the tertiary hydrogen (C_4-H) was indicated by its appearance as an exchangeable doublet (J = 8 cps) at 6.07 ppm.

The analogous product **3** was obtained when a mixture of boron trifluoride and acetic acid was used in place of the trifluoroacetic acid. In this case, the carbonyl bands were found at 1708 and 1690 cm^{-1} while in the nmr spectrum (DMSO) the NH and C_4-H protons appeared as exchangeable doublets (J-8 cps) at 8.93 and 6.17 ppm, respectively.

The formation of *N*-methylsaccharin **5** on oxidation of **2** with aqueous acidic permanganate gave evidence for the attachment of a carbon atom to the benzene ring. Acid hydrolysis of **3** gave an amino acid hydrochloride which appeared to be **6**, though the results of elemental analyses were somewhat outside the usually acceptable limits. The infrared spectrum showed the carbonyl band at 1700 cm^{-1}. Heating this substance above its melting point resulted in gas evolution with the formation of an amine hydrochloride which no longer showed the carbonyl absorption. Conversion to the free base gave a crystalline compound analyzing correctly for **7**.

Refluxing **2** with pyrrolidine gave rise to the amphoteric substance **8** which was also converted to **5** on permanganate oxidation. The nmr spectrum (deuteriochloroform) showed the tertiary hydrogen as a non-exchangeable broadened singlet at 5.72 ppm. Evidence for the primary amino function of **8** was given by a Van Slyke nitrogen determination as well as by conversion to **9** by refluxing with ethyl formate. Alkylation of **9** with methyl iodide in aqueous-ethanolic sodium hydroxide gave **10** which no longer had acidic properties. The tertiary hydrogen of both **9** and **10** appeared in the nmr spectrum (deuteriochloroform) as a non-exchangeable doublet (J = 8 cps) at 6.76 ppm which became a singlet when the NH was exchanged with deuterium.

The transformation of **1** to **2** can be envisioned as taking place through a path such as that depicted in chart 2. According to this scheme, the oxime ester tautomer

Chart 1

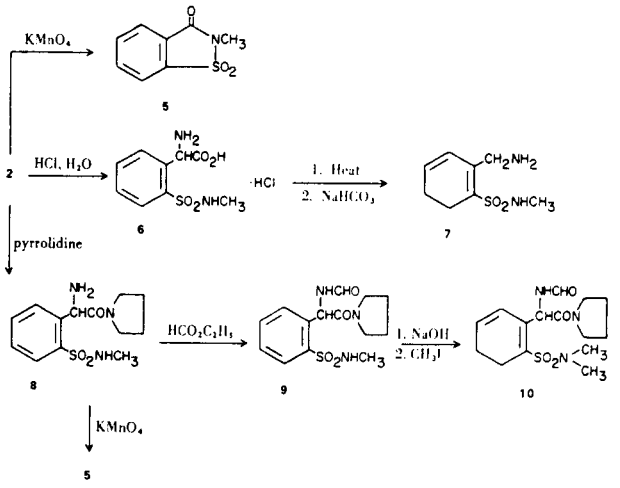
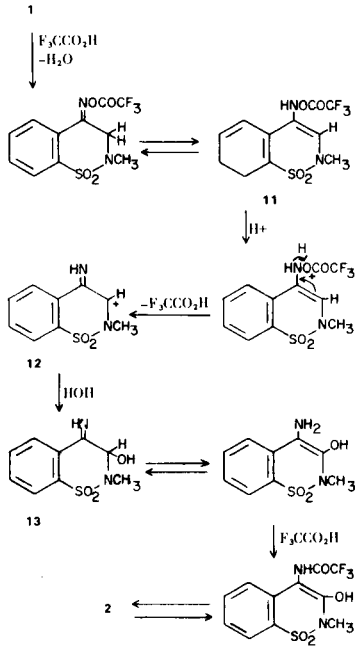


Chart 2



11 undergoes acid catalyzed conversion to **12** in a manner analogous to that postulated by Bhatt (6) for the initial stages in the mechanism of the Semmler-Wolff aromatization of α-tetralone oxime. In the case of **12**, aromatization is precluded by the presence of the *N*-methyl sulfonamide group so that reaction with water can take place to give **13**. Final formation of **2** would then involve straightforward tautomerization and acylation steps.

EXPERIMENTAL (8)

4-Trifluoroacetamido-2-methyl-2*H*-1,2-benzothiazin-3(4*H*)one 1,1-Dioxide (**2**).

A solution of 15 g. of 2-methyl 2*H*-1,2-benzothiazin-4(3*H*)one 1,1-dioxide oxime (**1**) in 200 ml. of trifluoroacetic acid was refluxed for one hour and then poured into 1200 ml. of ice-water. The resulting precipitate was collected and dissolved in ether. The ether solution was washed with water, dried over sodium sulfate, and distilled to dryness to give 16.5 g. of residue, m.p. 165-169°. Recrystallization from isopropyl ether gave 10.8 g. of product, m.p. 169-170°.

Anal. Calcd. for $C_{11}H_9F_3N_2O_4S$: C, 41.00; H, 2.82; F, 17.69; N, 8.69; S, 9.95. Found: C, 41.23; H, 3.04; F, 18.07; N, 8.44; S, 10.16.

4-Acetamido-2-methyl-2*H*-1,2-benzothiazin-3(4*H*)one 1,1-Dioxide (**3**).

A mixture of 12 g. of 2-methyl-2H-1,2-benzothiazin-4(3*H*)one oxime (**1**), 150 ml. of glacial acetic acid, and 90 ml. of boron trifluoride etherate was refluxed for three hours, poured into 800 ml. of ice-water, and extracted with dichloromethane. Evaporation of the washed organic layer gave a residue which was triturated with a small amount of cold ether and then crystallized from a mixture of dichloromethane and isopropyl alcohol to give 6.2 g. of product m.p. 191-192. Another recrystallization raised the m.p. to 192-193°.

Anal. Calcd. for $C_{11}H_{12}N_2O_4S$: C, 49.25; H, 4.51; N, 10.44. Found: C, 49.50; H, 4.64; N, 10.62.

α-Amino-α-carboxy-*N*-methyl-*o*-toluenesulfonamide Hydrochloride (**6**).

A mixture of 2.0 g. of 4-trifluoroacetamide-2-methyl-2*H*-1,2-benzothiazin-3(4*H*)one 1,1-dioxide (**2**), 50 ml. of 10% aqueous hydrochloric acid, and 50 ml. of methanol was refluxed for 40 hours. The methanol was distilled off, 50 ml. of water was added, and the solution was washed with dichloromethane. The aqueous layer was taken to dryness, the residue was triturated with several portions of ether and was then refluxed with 30 ml. of acetonitrile. On cooling, there was obtained 780 mg. of white crystals which sintered at 138° and melted with evolution of gas at 160°. Recrystallization from acetonitrile gave 450 mg. of material having the same melting characteristics. A sample was dried *in vacuo* at 80° for 20 hours.

Anal. Calcd. for $C_9H_{13}ClN_2O_4S$: C, 38.51; H, 4.67; N, 9.98; S, 11.42. Found: C, 38.11; H, 5.18; N, 10.07; S, 11.04.

α-Amino-*N*-methyl-*o*-toluenesulfonamide (**7**).

A 325 mg. portion of α-amino-α-carboxy-*N*-methyl-*o*-toluenesulfonamide hydrochloride (**6**) was heated *in vacuo* at 140° for 20 hours during which time the material fused. The solid, obtained on cooling, was devoid of carbonyl absorption. It was dissolved in water and the solution was made alkaline with sodium bicarbonate and extracted with dichloromethane. Evaporation of the dichloromethane followed by recrystallization of the residue from bezene gave 60 mg. of product, m.p. 110-112° (sinters at 104°).

Anal. Calcd. for $C_8H_{12}N_2O_2S$: C, 47.98; H, 6.04; N, 13.99; S, 16.01. Found: C, 48.08; H, 6.14; N, 14.26; S, 16.07.

α-Amino-*N*-methyl-α-(1-pyrrolidinylcarbonyl)-*o*-toluenesulfonamide (**8**).

A solution of 8 g. of 4-trifluoroacetamide-2-methyl-2*H*-1,2-benzothiazin-3(4*H*)one 1,1-dioxide (**2**) in 50 ml. of pyrrolidine was refluxed for 15 minutes and then most of the excess pyrrolidine was evaporated. The residue was triturated with several portions of petroleum ether (30-60°), dissolved in 150 ml. of dichloromethane and 300 ml. of isopropyl ether was added. Concentration by distillation at atmospheric pressure gave 5.3 g. of a first crop of crystals, m.p. 144-145° and 1.2 g. of a second crop, m.p. 142-144°. Recrystallization of the first crop from dichloromethane-isopropyl ether gave 4.8 g. of product, m.p. 144.5-145.5°.

Anal. Calcd. for $C_{13}H_{19}N_3O_3S$: C, 52.51; H, 6.44; N (Dumas), 14.13; N (Van Slyke), 4.71; S, 10.78. Found: C, 52.75; H, 6.34; S, 10.80; N (Dumas), 14.06; N (Van Slyke), 5.82; S, 10.80.

α-Formamide-*N*-methyl-α-(1-pyrrolidinylcarbonyl)-*o*-toluenesulfonamide (**9**).

A mixture of 3.0 g. of α-amino-*N*-methyl-α-(1-pyrrolidinylcarbonyl)-*o*-toluenesulfonamide (**8**) and 100 ml. of ethyl formate was refluxed for 18 hours. Most of the excess ethyl formate was removed by distillation *in vacuo* and the residue was partitioned between ether and 0.5 *N* hydrochloric acid. Evaporation of the ether layer gave 2.2 g. of white solid, m.p. 196-198°. Recrystallization from dichloromethane-benzene gave 1.5 g. of product, m.p. 198-200°.

Anal. Calcd. for $C_{14}H_{19}N_3O_4S$: C, 51.68; H, 5.89; N, 12.91; S, 9.85. Found: C, 51.91; H, 5.96; N, 12.90; S, 9.75.

α-Formamide-*N*,*N*-dimethyl-α-(1-pyrrolidinylcarbonyl)-*o*-toluenesulfonamide (**10**).

To a solution of 650 mg. of α-formamide-*N*-methyl-α-(1-

pyrrolidinylcarbonyl)-*o*-toluenesulfonamide (**9**) in a mixture of 25 ml. of ethanol and 2.0 ml. of 1.0 *N* sodium hydroxide was added 1.4 g. of methyl iodide followed by 10 ml. of water. The solution was allowed to stand at room temperature for 20 hours, diluted with 200 ml. of water, and extracted with dichloromethane. The residue, obtained on evaporation of the dichloromethane, was crystallized from acetonitrile to give 405 mg. of product, m.p. 185-186°.

Anal. Calcd. for $C_{15}H_{21}N_3O_4S$: C, 53.08; H, 6.24; N, 12.38; S, 9.45. Found: C, 53.04; H, 6.28; N, 12.14; S, 9.42.

Permanganate Oxidation of 4-Trifluoroacetamido-2-methyl-2*H*-1,2-benzothiazin-3(4*H*)one 1,1-Dioxide.

A mixture of 644 mg. of 4-trifluoroacetamide-2-methyl-2*H*-1,2-benzothiazin-3(4*H*)one 1,1-dioxide (**2**), 1.5 g. of potassium permanganate, and 50 ml. of 10% sulfuric acid was refluxed with stirring for one hour, cooled to room temperature, and decolorized by the addition of sodium bisulfite. The resulting white precipiate was collected and dissolved in dichloromethane. Evaporation of the dried solution gave 155 mg. of white crystals, m.p. 130-131°. Recrystallization from ethanol gave pure *N*-methylsaccharin, m.p. 131-132°, identified by comparison with an authentic sample.

Permanganate Oxidation of α-Amino-*N*-methyl-α-(1-pyrrolidinylcarbonyl)-*o*-toluenesulfonamide.

A solution of 600 mg. of α-amino-*N*-methyl-α-(1-pyrrolidinylcarbonyl)-*o*-toluenesulfonamide and 1.2 g. of potassium permanganate in 30 ml. of 10% sulfuric acid was heated on a steam bath at 90° for 30 minutes, cooled to room temperature, and decolorized by the addition of sodium bisulfite. The resulting precipitate was collected and dissolved in dichloromethane. Evaporation of the dried solution gave 145 mg. of white crystals, m.p. 130-131°. Recrystallization from ethanol gave pure *N*-methylsaccharin, m.p. 131-132°, identified by comparison with an authentic sample.

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(8) Melting points were determined using the Thomas-Hoover capillary melting point apparatus which was calibrated against known standards. The ultraviolet and infrared spectra were obtained, respectively, with a Beckman DKI spectrophotometer and a Baird Model 455 double-beam instrument. The former were determined as solutions in 95% ethanol and the latter as Nujol mulls. Nmr spectra were determined in either deuterated DMSO or deuteriochloroform, using the Varian A-60 spectrometer with TMS as an internal standard. The drying agent used throughout was sodium sulfate.