

Heteroaromatic N-Oxides. X.¹⁾ Synthesis and Reactions of Benzothiazole 3-Oxide

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Benzothiazole 3-oxide (II) was synthesized, starting from its 2-methyl derivative, *via* the corresponding aldoxime, carbonitrile, imido ester and carboxylic acid.

The reaction of the N-oxide II; deoxygenations, reactions with various nucleophilic agents (tosyl chloride, Ac_2O , $\text{C}_6\text{H}_5\text{MgBr}$, NaHSO_3 , $\text{NH}_2\text{NH}_2 \cdot \text{H}_2\text{O}$ and $\text{KCN} \cdot \text{BzCl}$) involving some 1,3-dipolarophiles (benzyne, $\text{C}_6\text{H}_5\text{NCO}$ and tetracyanoethylene), and quaternizations were investigated and compared with those of the corresponding imidazole N-oxide.

In the foregoing paper of this series,¹⁾ we reported that benzothiazole 3-oxide (II), unlike its 2-methyl analogue (I), could not be obtained by direct oxidation with permaleic acid. However, it became desirable to synthesize the N-oxide II in order to investigate its chemical reactivity, compared with that of the corresponding benzimidazole N-oxide (III) reported previously.³⁾

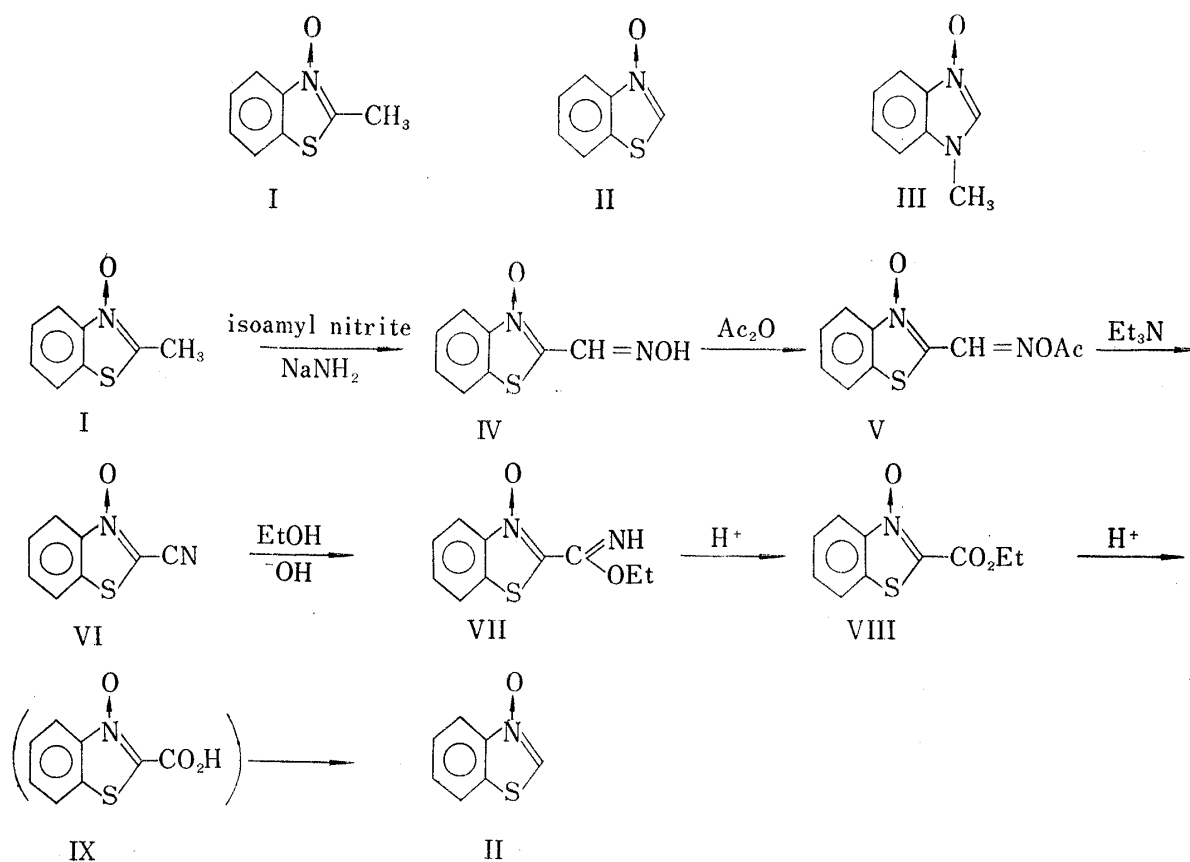


Chart 1

1) Part IX: S. Takahashi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **17**, 1598 (1969).

2) Location: *Fukushima-ku, Osaka*.

3) S. Takahashi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **12**, 783, 1290 (1964).

Synthesis of II has been accomplished by the conversion of I in a manner similar to that used for the synthesis of III from its 2-methyl derivative⁴): *via* aldoxime, carbonitrile, imido ester, and carboxylic acid (Chart 1).

Treatment of I with isoamyl nitrite in the presence of sodium amide gave 2-benzothiazole-carboxaldehyde oxime 3-oxide (IV). Reaction of IV with acetic anhydride gave the 2-acetoxyiminomethyl derivative (V) together with a small amount of the 2-cyano derivative (VI). The conversion of V into VI was effected by treatment with triethylamine. In the benzimidazole series,⁴) the corresponding oxime was dehydrated in one-step simply by treating with acetic anhydride, and the nitrile converted into the imido ester by heating its ethanolic solution;⁴) conversion of nitrile VI into ethyl 2-benzothiazolecarboimidate 3-oxide (VII), however, required also the addition of a catalytic amount of alkali. Hydrolysis of VII with hydrochloric acid under mild conditions gave ethyl 2-benzothiazolecarboxylate 3-oxide (VIII),

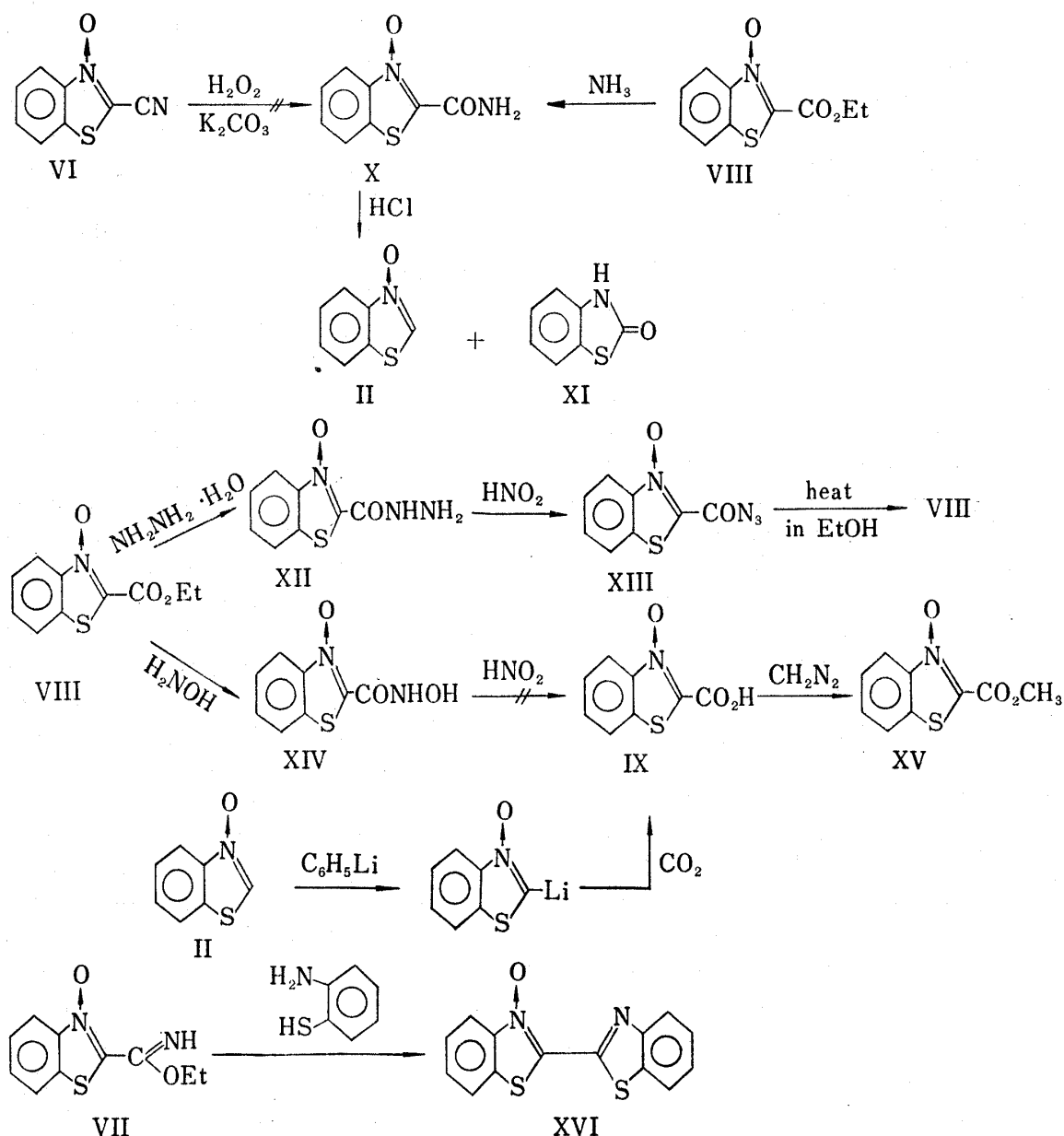


Chart 2

4) S. Takahashi and H. Kanō, *Chem. Pharm. Bull.* (Tokyo), **16**, 527 (1968).

which was then hydrolyzed to the desired product II by a further treatment of the acid under forced conditions.

Related to the synthetic procedure for II, some other derivatives of 2-benzothiazole-carboxylic acid were prepared. Treatment of VI with hydrogen peroxide in the presence of potassium carbonate did not give the expected 2-benzothiazolecarboxamide 3-oxide (X), yielding only an oxidative degradation product, orthanilic acid. Aminolysis of VIII gave X, which was converted into a mixture of II and 2-benzothiazolinone (XI) by treatment with hydrochloric acid. 2-Benzothiazolecarbohydrazide 3-oxide (XII), prepared from VIII and hydrazine hydrate, was treated with nitrous acid to give a crystalline product. Although an analytically pure sample of this product could not be obtained owing its instability, the structure assignment as 2-benzothiazolecarboxazide (XIII) followed from the method of preparation, IR bands at 2160 (ν_{N_3}) and 1685 cm^{-1} ($\nu_{C=O}$), and the conversion into VIII by refluxing in ethanol. Unlike the corresponding benzimidazole derivative,⁴⁾ 2-benzothiazole-hydroxamic acid 3-oxide (XIV) could not be converted into the 2-carboxylic acid IX by treating with nitrous acid; however, IX was prepared by successive treatments of II with phenyllithium and with carbon dioxide. Since the acid was liable to decarboxylation to II, it was converted immediately into its methyl ester (XV) for characterization. Reaction of the imido ester VII with *o*-aminothiophenol gave 2,2'-bibenzothiazole 3-oxide (XVI).

The N-oxide II was smoothly deoxygenated to benzothiazole (XVII) by hydrogenation over Raney nickel, but reduction was negligible with palladium on charcoal as a catalyst. Treatment of II with phosphorus trichloride also gave XVII, together with an almost equal amount of 2-chlorobenzothiazole (XVIII). The latter product probably arose from reaction of II with the phosphoryl chloride resulting from its initial reaction with phosphorus trichloride. Indeed, the reaction of II with phosphoryl chloride gave XVIII. Treatment of II with tosyl chloride also gave XVIII, accompanied by a small amount of XI. Reaction of II with acetic anhydride gave 2-acetoxybenzothiazole (XIX), which was hydrolyzed to XI during post-treatment. Heating II in acetonitrile solution gave 2,2'-bibenzothiazole 3-oxide, XVI, accompanied by a small amount of XI and several unidentified minor products.

Reaction of II with phenylmagnesium bromide in ether-benzene or in tetrahydrofuran gave 2-phenylbenzothiazole (XX), with pyridine N-oxide, this reaction in the latter solvent gave 1-hydroxy-2-phenyl-1,2-dihydropyridine.⁵⁾ Reaction of II with sodium hydrogen sulfite gave mainly the deoxygenated product XVII together with a small amount of 2-benzothiazole-sulfonic acid (XXI). Treatment of II with hydrazine hydrate at room temperature gave *o*-aminothiophenol in fairly good yield. Although the same ring-opening was observed with benzothiazole itself, the reaction with II seemed much faster. The Reissert reaction with II gave a mixture of XI and 3-(2-benzothiazolyl)-2-benzothiazolinone (XXII). It is noticeable that, with 1-methylbenzimidazole 3-oxide, the last three reactions mentioned above gave the corresponding 2-substituted derivatives ($-\text{SO}_3\text{H}$, $-\text{NHNH}_2$, and $-\text{CN}$) in good yields.⁴⁾

Reactions of II with the dipolarophiles such as benzyne and phenylisocyanate gave 2-(*o*-hydroxyphenyl)benzothiazole (XXIII) and a 1:3 mixture of 2-anilinobenzothiazole (XXIV) and 1,3-diphenyl-1-(2-benzothiazolyl)urea (XXV), respectively. The formation of XXIII and XXIV can be explained as occurring *via* a 1,3-dipolar cycloaddition intermediate, in a way similar to shown by the benzimidazole series.³⁾ The product XXV probably arose from reaction of XXIV with an excess of phenylisocyanate.⁶⁾ Reaction of II with tetracyanoethylene, which afforded 2-benzothiazolemalononitrile (XXVI), may also involve initial formation of a similar cycloadduct, as shown below. Reaction of the N-oxide II and tetracyanoethylene oxide gave the deoxygenated product, benzothiazole XVII in good yield. This reaction may

5) T. Kato and H. Yamanaka, *J. Org. Chem.*, **30**, 910 (1965).

6) The reaction of quinoxaline 1-oxide with phenylisocyanate was reported to give a similar type of urea derivative; C. Iijima, *Yakugaku Zasshi*, **87**, 164 (1967).

proceed as shown in Chart 4, although another expected product, dicyanoketone, was not detected.

Quaternization of II with methyl iodide failed, contrary to the case with the imidazole N-oxide III, giving only a mixture of XVII and the hemihydroiodide of II. These products could have arisen from the initially formed 3-methoxybenzothiazolium iodide undergoing cleavage by nucleophilic attack at the methoxy group by iodide ion. Alternatively, quaterni-

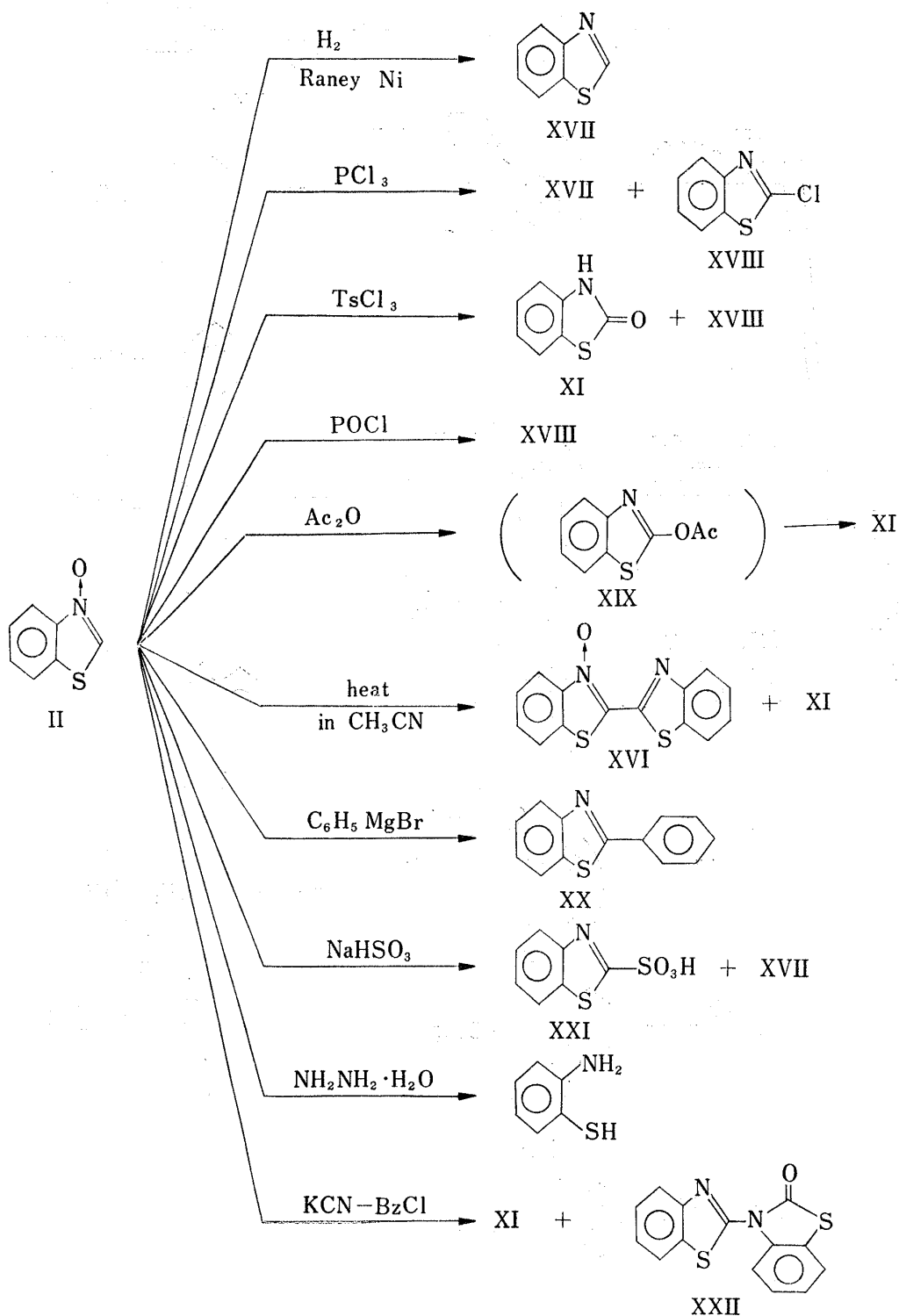


Chart 3

zation of II with acetic anhydride-perchloric acid, and with triethyloxonium fluoroborate, gave 3-acetoxybenzothiazolium perchlorate (XXVII) and 3-ethoxybenzothiazolium fluoroborate (XXVIII), respectively.

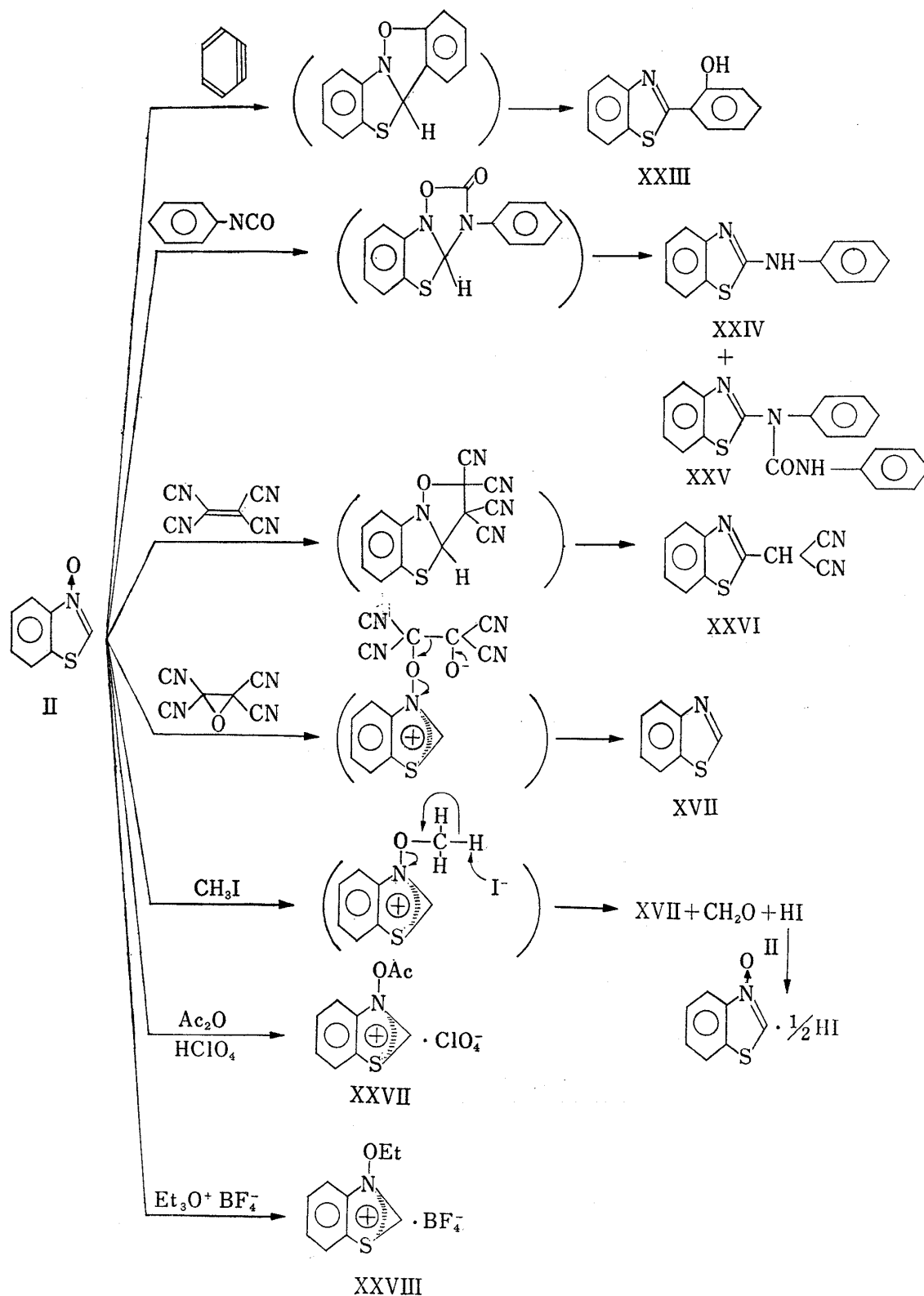


Chart 4

Experimental⁷⁾

2-Benzothiazolecarboxaldehyde Oxime 3-Oxide (IV)—To a suspension of 2-methylbenzothiazole 3-oxide (prepared from the dihydrate¹⁾ (20.0 g, 0.12 mole) by azeotropic dehydration with CHCl_3 in liq. NH_3 (ca. 360 ml) was added powdered NaNH_2 (7.00 g, 0.18 mole) and then added iso- $\text{C}_5\text{H}_{11}\text{ONO}$ (17.5 g, 0.15 mole) dropwise at ca. -70° . After stirring at the temperature for 0.5 hr, the reaction mixture was allowed to rise to its boiling point and the resulting solution was stirred for an additional 2 hr, then the excess NH_3 was removed. The residue was dissolved in H_2O (400 ml) and acidified with AcOH to give yellow crystals. Recrystallization from EtOH gave slightly yellow prisms, 19.5 g, 92%, mp 253° (decomp.). *Anal.* Calcd. for $\text{C}_8\text{H}_6\text{O}_2\text{N}_2\text{S}$: C, 49.47; H, 3.12; N, 14.43. Found: C, 49.67; H, 3.35; N, 14.47.

2-Acetoxyiminomethylbenzothiazole 3-Oxide (V)—A suspension of IV (10.0 g, 0.052 mole) and Ac_2O (6.3 ml, 0.067 mole) in AcOH (200 ml) was heated on a water-bath for 1.5 hr and the resulting solution was evaporated to give yellow scales (10.1 g), infrared spectrum of which showed it contained a small amount of the nitrile (VI). Recrystallization from acetone gave slightly yellow scales (8.0 g), mp $181\text{--}183^\circ$. *Anal.* Calcd. for $\text{C}_{10}\text{H}_8\text{O}_3\text{N}_2\text{S}$: C, 50.85; H, 3.41; N, 11.86. Found: C, 51.06; H, 3.45; N, 11.94.

2-Benzothiazolecarbonitrile 3-Oxide (VI)—A solution of V (3.0 g) and Et_3N (6.0 ml) in acetone (200 ml) was heated under reflux for 3 hr, and then evaporated. The residue was recrystallized from AcOEt to give colorless prisms (2.0 g), mp $151\text{--}152^\circ$. *Anal.* Calcd. for $\text{C}_8\text{H}_4\text{ON}_2\text{S}$: C, 54.55; H, 2.29; N, 15.91. Found: C, 54.51; H, 2.51; N, 16.17.

Ethyl 2-Benzothiazolecarboimidate 3-Oxide (VII)—To a solution of VI (6.30 g) in EtOH (60 ml) was added a solution of NaOH in EtOH (0.1%, 60 ml) with stirring at room temperature. After allowing to stand overnight at room temperature, the reaction mixture was evaporated and the residue was recrystallized from AcOEt to give colorless needles (7.2 g), mp $121\text{--}122^\circ$. *Anal.* Calcd. for $\text{C}_{10}\text{H}_{10}\text{O}_2\text{N}_2\text{S}$: C, 54.05; H, 4.54; N, 12.61. Found: C, 54.14; H, 4.66; N, 12.57.

A solution of VI (200 mg) in EtOH (20 ml) was heated under reflux for 4 hr, and evaporated. The residue was proved to be the starting material.

Ethyl 2-Benzothiazolecarboxylate 3-Oxide (VIII)—A suspension of VII (6.0 g) in 3N HCl (180 ml) was warmed at 50° for 0.5 hr and then evaporated. The residue was dissolved into a small amount of water, neutralized with NaHCO_3 and extracted with CH_2Cl_2 . Evaporation of the solvent gave colorless crystals (5.7 g), which were recrystallized from acetone to give colorless scales, mp $113\text{--}114^\circ$. *Anal.* Calcd. for $\text{C}_{10}\text{H}_9\text{O}_3\text{NS}$: C, 53.81; H, 4.06; N, 6.28. Found: C, 53.98; H, 4.07; N, 6.49.

Benzothiazole 3-Oxide (II)—A solution of VIII (10.0 g) in 3N HCl (300 ml) was heated on a water-bath for 1 hr and then evaporated. The residue was dissolved in a small amount of water, neutralized with NaHCO_3 , and extracted with CH_2Cl_2 . Evaporation of the solvent gave deep orange oil (7.1 g), which was chromatographed on Al_2O_3 (containing H_2O 3%) with $\text{CH}_2\text{Cl}_2\text{--MeOH}$ (5:1) to give slightly reddish brown tar. This tar was crystallized by addition of H_2O –acetone with scratching and recrystallized from AcOMe or ether to give colorless prisms (4.0 g), mp $45\text{--}48^\circ$. *Anal.* Calcd. for $\text{C}_7\text{H}_5\text{ONS}\cdot\text{H}_2\text{O}$: C, 49.71; H, 4.17; N, 8.28. Found: C, 50.21; H, 4.21; N, 7.89.

Reaction of VI with Hydrogen Peroxide—To a solution of VI (0.70 g) in acetone (20 ml) were added H_2O_2 (30%, 10.5 ml) and aq. K_2CO_3 solution (10%, 30 ml) with stirring at room temperature. After stirring for 2 hr and allowing to stand overnight, the solution was concentrated to give brown crystals (0.4 g), which were recrystallized from H_2O to give colorless scales and proved to be orthanilic acid.

2-Benzothiazolecarboxamide 3-Oxide (X)—A suspension of VIII (50 mg) in $\text{NH}_3\text{--EtOH}$ (satd. at 0° , 2.0 ml) was heated under reflux for 10 min. The resulting clear solution was cooled to give colorless scales (40 mg), mp $228\text{--}229^\circ$. *Anal.* Calcd. for $\text{C}_8\text{H}_6\text{O}_2\text{N}_2\text{S}$: C, 49.47; H, 3.12; N, 14.43. Found: C, 49.41; H, 3.16; N, 14.53.

Hydrolysis of X—A suspension of X (1.00 g) in 6N HCl 50 ml was heated under reflux for 2 hr, and the resulting solution was evaporated. The residue was neutralized with aq. NaHCO_3 solution and the insoluble product was collected by filtration (0.35 g), mp $135\text{--}137^\circ$, which was proved to be 2-benzothiazolinone⁸⁾ and the mother liquor was evaporated. The residue was extracted with CHCl_3 and evaporation of the CHCl_3 layer gave colorless crystals (0.46 g), mp $45\text{--}48^\circ$, which was recrystallized from AcOMe to give colorless prisms and proved to be II.

2-Benzothiazolecarbohydrazide 3-Oxide (XII)—A solution of VIII (1.00 g) and $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$ (80%, 0.25 ml) in EtOH (30 ml) was heated under reflux for 5 min, and the resulting clear solution was cooled

7) All melting points were taken on a Kofler hot stage and are uncorrected. Solvents were removed under reduced pressure using a rotary evaporator. Each identification was made comparison of the infrared spectrum with that of a sample prepared by an unequivocal route and if the sample had a melting point, it was also compared by mixed fusion. Infrared spectra were recorded with a JASCO Model IR-S Infrared Spectrophotometer.

8) M. Claasz, *Ber.*, **45**, 1015 (1912).

to give colorless crystals (0.90 g). Recrystallization from EtOH gave colorless needles, mp 207—208°. *Anal.* Calcd. for $C_8H_7O_2N_3S$: C, 45.94; H, 3.37; N, 20.09. Found: C, 45.82; H, 3.42; N, 19.89.

2-Benzothiazolecarboxazide 3-Oxide (XIII)—To a suspension of XII (1.0 g) in 1N HCl (30 ml) was added a solution of $NaNO_2$ in H_2O (ca. 20%) dropwise with stirring and cooling in an ice-water bath until starch-iodide paper turned blue (ca. 1.5 ml). After the addition, stirring was continued for further 15 min and the resulting pale yellow crystals were collected by filtration (0.9 g). Infrared spectrum of which showed absorption bands at 2160 and 1685 cm^{-1} but this compound was very unstable at room temperature and could not be submitted to elementary analysis.

Heating of XIII in Ethanol—A solution of XIII (0.50 g) in abs. EtOH (25 ml) was heated under reflux for 1 hr and then evaporated. The residue was recrystallized from EtOH to give colorless scales (0.35 g), mp 116—118°, and proved to be VIII.

2-Benzothiazolehydroxamic Acid 3-Oxide (XIV)—To a suspension of VIII (100 mg) in EtOH (5.0 ml) was added a solution of $NH_2OH \cdot HCl$ (50 mg) and $AcONa$ (60 mg) in H_2O (1.0 ml), and the resulting mixture was stirred for 2 hr, and then allowed to stand overnight at room temperature. The resulting solution was evaporated, EtOH (3.0 ml) was added to the residue and a crystalline product was collected by filtration (60 mg). Recrystallization from MeOH gave colorless prisms, mp 250° (decomp.). *Anal.* Calcd. for $C_8H_6O_3N_2S$: C, 45.72; H, 2.88; N, 13.33. Found: C, 45.63; H, 2.74; N, 13.41.

Attempted Synthesis of 2-Benzothiazolecarboxylic Acid 3-Oxide (IX) from XIV—To a suspension of XIV (100 mg) in 1N HCl (3.0 ml) was added a solution of $NaNO_2$ in H_2O (20%, 0.30 ml) dropwise with stirring in an ice-water bath. The starting material did not dissolved into the solution. After stirring 20 hr at room temperature, the precipitate was collected by filtration (95 mg), which was identified with the starting material.

Methyl 2-Benzothiazolecarboxylate 3-Oxide (XV)—To a solution of phenyllithium, prepared from Li (0.20 g) and bromobenzene (2.4 g) in ether (20 ml), was added ether (10 ml) and then a solution of II (prepared from the hydrate 0.50 g) in THF (20 ml) with stirring and cooling in a dry ice-acetone bath. After stirring and cooling were continued for additional 10 min, crushed dry ice (ca. 3 g) was added to the resulting solution, then the solution was evaporated. After being washed with ether (30 ml), the residue was suspended in H_2O (10 ml) and acidified with 6N HCl to give white crystalline mass (0.4 g), mp 30° (decomp.).

To a suspension of 2-benzothiazolecarboxylic acid 3-oxide obtained above in ether (10 ml) and MeOH (10 ml) was added CH_2N_2 -ether, prepared from N-nitroso-N-methylurethan (1.0 g). After standing for 1 hr at room temperature, the resulting solution was evaporated and the residue was recrystallized from MeOH to give colorless prisms (0.3 g), mp 148—150°. *Anal.* Calcd. for $C_9H_7O_3NS$: C, 51.68; H, 3.37; N, 6.70. Found: C, 51.72; H, 3.41; N, 6.77.

2,2'-Bibenzothiazole 3-Oxide (XVI)—A solution of VII (220 mg) and *o*-aminothiophenol·HCl (240 mg) in EtOH (5.0 ml) was heated under reflux for 2 hr, and evaporated. The residue was washed with H_2O and added EtOH to give a crystalline product (180 mg), which was recrystallized from acetone to give yellow prisms, mp 285—287°. *Anal.* Calcd. for $C_{14}H_8ON_2S_2$: C, 59.16; H, 2.84; N, 9.86. Found: C, 59.53; H, 2.79; N, 9.87.

Deoxygenation of II—A solution of $II \cdot H_2O$ (100 mg) in EtOH (10 ml) was shaken in H_2 atmosphere over Raney Ni (W-5, from 0.1 g alloy). After being absorbed calculated amount of H_2 , the catalyst was filtered off, and the filtrate was evaporated to give colorless oil (80 mg). Identification of this compound, XVII, was made by comparison of the retention time of gas-liquid chromatography with that of the authentic specimen (Apparatus: Varian Aerograph Model 1520-1B. Column: stainless steel 5' × 1/8" O.D., 5% SE-30 on chromosorb W (60—80 mesh). Temperature: injector 200°, column 125°, detector (FID) 200°. Carrier gas: N_2 20 ml/min. Retention time (adjusted): 1.82 min).

Attempted Deoxygenation of II over Palladium—A solution of $II \cdot H_2O$ (100 mg) in EtOH (10 ml) was shaken in H_2 atmosphere over palladium on charcoal (5% 20 mg). After 3 hr, during which time, very few amount of H_2 was absorbed, the catalyst was filtered off and the filtrate was evaporated to give colorless oil which solidified by addition of H_2O (0.1 ml). TLC (Al_2O_3 with CH_2Cl_2) showed that almost all the starting material was recovered and a small amount of II was deoxygenated.

Reaction of II with Phosphorus Trichloride—To a solution of II (prepared from the hydrate 150 mg) in $CHCl_3$ (3.0 ml) was added a solution of PCl_3 (130 mg) in $CHCl_3$ (2.0 ml) with stirring and cooling in an ice-water bath, and then the solution was allowed to stand at room temperature for 2 hr. The resulting turbid solution was shaken with aq. $NaHCO_3$ solution and the $CHCl_3$ layer was separated, concentrated and chromatographed on Al_2O_3 with CH_2Cl_2 to give XVII (40 mg) and 2-chlorobenzothiazole (65 mg). These compounds were identified with their authentic specimens by gas-liquid chromatography (carried out by the same conditions mentioned above. Retention time: XVII 1.82 min, XVIII 2.22 min).

Reaction of II with Tosyl Chloride—To a solution of II (prepared from the hydrate 300 mg) in $CHCl_3$ (3.0 ml) was added a solution of tosyl chloride (380 mg) in $CHCl_3$ (3.0 ml) with stirring and cooling in an ice-water bath, and then the resulting solution was heated under reflux for 3 hr. After neutralized with aq. $NaHCO_3$ solution, the organic layer was concentrated and chromatographed on Al_2O_3 with CH_2Cl_2 to give XVIII (204 mg) and XI (20 mg). The former was identified by gas-liquid chromatography and the latter was done by mixed melting point.

Reaction of II with Phosphoryl Chloride—To a solution of II (prepared from the hydrate 100 mg) in CHCl_3 (1.0 ml) was added a solution of POCl_3 (0.10 ml) in CHCl_3 (1.0 ml) dropwise with stirring and cooling in an ice-water bath. After the addition, the resulting solution was heated under reflux for 10 min, and then evaporated. The residue was neutralized with aq. NaHCO_3 solution and extracted with CH_2Cl_2 . Evaporation of the solvent gave colorless oil (75 mg), which was identified with an authentic specimen of XVIII by gas-liquid chromatography as mentioned above.

Reaction of II with Acetic Anhydride—A solution of II (prepared from the hydrate 120 mg) in Ac_2O (1.0 ml) was heated on a water bath for 5 min, and then evaporated. To the residue was added crushed ice, neutralized with NaHCO_3 and extracted with CH_2Cl_2 . The extract was chromatographed on Al_2O_3 (containing H_2O 3%) with CH_2Cl_2 to give colorless prisms (80 mg), mp 135–137°, which was proved to be XI and identified with an authentic specimen.⁹⁾

Heating of II in Acetonitrile—A solution of II (prepared from the hydrate 100 mg) in CH_3CN (3.0 ml) was heated under reflux for 4 hr, and then cooled. The resulting yellow crystalline product was collected by filtration (50 mg), which was recrystallized from acetone to give yellow prisms, mp 285–287° and identified with the sample XVI obtained above.

The filtrate was chromatographed on Al_2O_3 (containing H_2O 3%) with CH_2Cl_2 to give colorless prisms (10 mg), mp 135–137°, which was proved to be XI.⁸⁾

Reaction of II with Phenylmagnesium Bromide—A) In Tetrahydrofuran: To a solution of phenylmagnesium bromide in THF (prepared from Mg (240 mg), bromobenzene (1.60 g) in THF (5.0 ml) and I_2 (trace)) was added a solution of II (prepared from the hydrate 560 mg) in THF (5.0 ml) dropwise with stirring and cooling in an ice-water bath. After the addition, the solution was warmed to 40° for 0.5 hr, and then allowed to stand overnight at room temperature. To the resulting dark green solution was added H_2O (3 ml) dropwise with stirring and the solution was separated by decantation. The tarry residue was extracted with CH_2Cl_2 and the combined solution and extracts was concentrated, chromatographed on Al_2O_3 (containing H_2O 3%) with benzene to give 2-phenylbenzothiazole (60 mg) and many other unidentified products but 2-phenylbenzothiazole 3-oxide¹⁾ was not detected by TLC.

B) In Ether: To a solution of II (prepared from the hydrate 360 mg) in ether (100 ml) was added a solution of phenylmagnesium bromide in ether (prepared from Mg (240 mg), bromobenzene (1.60 g) in ether (10 ml)) dropwise with stirring at room temperature. After stirring for 3 hr and allowing to stand overnight, to the reaction mixture was added aq. NH_4Cl solution (satd. 10 ml) dropwise with stirring. The etherial layer was separated and the aqueous layer was extracted with CHCl_3 . The combined etherial layer and extracts was evaporated to give brown tar, which was chromatographed on Al_2O_3 (containing H_2O 3%) with benzene to give XX (100 mg) and several unidentified products but 2-phenylbenzothiazole 3-oxide¹⁾ was not detected by TLC.

Reaction of II with Sodium Hydrogen Sulfite—To a solution of $\text{II}\cdot\text{H}_2\text{O}$ (150 mg) in H_2O (3.0 ml) was added a solution of NaHSO_3 (130 mg) in H_2O (2.0 ml) dropwise with stirring at room temperature. About 10 min later, the solution became turbid. After stirring for 1 hr, the mixture was extracted with CH_2Cl_2 , and evaporation of the CH_2Cl_2 layer gave colorless oil (63 mg), which was proved to be XVII by gas-liquid chromatography (apparatus, conditions, and retention time were mentioned above). The aqueous layer was evaporated, and the residue was extracted with EtOH. The solvent was removed and to the extract was added 6N HCl (0.2 ml). The residue was dissolved into the solution and then white crystals precipitated again (20 mg), which were recrystallized from EtOH–AcOEt to give white crystals, mp >250°. *Anal.* Calcd. for $\text{C}_7\text{H}_5\text{O}_3\text{NS}_2$ (2-benzothiazolesulfonic acid): C, 39.08; H, 2.34; N, 6.51. Found: C, 39.11; H, 2.23; N, 6.28.

Reaction of II with Hydrazine Hydrate—To $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$ (100%, 2.0 ml) was added $\text{II}\cdot\text{H}_2\text{O}$ (200 mg) in small portions with stirring at room temperature. The reaction mixture foamed vigorously and brown tar separated, which dissolved into the solution again after a while. After standing overnight at room temperature, the solution was evaporated, H_2O was added to the residue and extracted with CHCl_3 . The CHCl_3 solution was evaporated to give yellow oil (100 mg) which was proved to be *o*-nitrothiophenol by the melting point of its picrate, mp 197° (decomp.).

Reaction of II with Potassium Cyanide-Benzoyl Chloride—To a solution of $\text{II}\cdot\text{H}_2\text{O}$ (0.20 g) and KCN (0.20 g) in H_2O (2.0 ml) was added benzoyl chlorid (0.20 ml) dropwise with stirring and cooling in an ice-water bath. After stirring and cooling were continued for 10 min, the resulting reddish brown solution was extracted with CH_2Cl_2 . The extract was chromatographed on Al_2O_3 (containing H_2O 3%) with benzene to give colorless scales (56 mg) and colorless prisms (25 mg). The former, mp 137–138°, was proved to be XI and the latter was recrystallized from ether to give colorless prisms, mp 148–150°. *Anal.* Calcd. for $\text{C}_{14}\text{H}_8\text{ON}_2\text{S}_2$ (3-(2-benzothiazolyl)-2-benzothiazolinone): C, 59.16; H, 2.84; N, 9.86. Found: C, 59.49; H, 2.94; N, 9.72. This compound was identified with an authentic specimen.⁹⁾

Reaction of II with Compzine—To a solution of II (prepared from the hydrate 0.50 g) in *tert*-BuOH (10 ml) was added benzenediazonium-2-carboxylate¹⁰⁾ (0.70 g) and the resulting suspension was stirred at

9) R.H. Campbell, S.T. Webster and J.J. D'Amico, U.S. Patent 3249621 (1964) [*C.A.*, **65**, 5463 (1966)].
10) M. Stiles, R.G. Miller and W. Burckhardt, *J. Am. Chem. Soc.*, **85**, 1792 (1963).

45° for 4 hr then allowed to stand overnight at room temperature. After evaporation, the residue was recrystallized from MeOH to give colorless thin prisms (0.40 g), mp 123—124°. *Anal.* Calcd. for C₁₃H₉ONS (2-(*o*-hydroxyphenyl)benzothiazole): C, 68.72; H, 3.99; N, 6.17. Found: C, 68.55; H, 4.01; N, 6.13.

Reaction of II with Phenyl Isocyanate—To a solution of II (prepared from the hydrate 187 mg) in CH₂Cl₂ (5.0 ml) was added a solution of phenyl isocyanate (140 mg) in CH₂Cl₂ (5.0 ml) and the resulting solution was heated under reflux for 1 hr. After evaporation, the residue was chromatographed on Al₂O₃ with CH₂Cl₂ to give colorless needles (120 mg) and then colorless prisms (50 mg).

The former was recrystallized from MeOH to give colorless needles, mp 139—140°, which was proved to be 1,3-diphenyl-1-(2-benzothiazolyl)urea. *Anal.* Calcd. for C₂₀H₁₅ON₃S: C, 69.55; H, 4.38; N, 12.17. Found: C, 69.63; H, 4.37; N, 12.42. This compound was identified with an authentic specimen prepared from 2-anilinobenzothiazole and phenyl isocyanate.

The latter was recrystallized from MeOH to give colorless prisms, mp 157—158°, which was proved to be 2-anilinobenzothiazole. *Anal.* Calcd. for C₁₃H₁₀N₂S: C, 69.01; H, 4.46; N, 12.38. Found: C, 68.83; H, 4.48; N, 12.64. This compound was identified with an authentic specimen prepared from 2-chlorobenzothiazole and aniline.

Reaction of II with Tetracyanoethylene—To a solution of II·H₂O (115 mg) in MeOH (1.0 ml) was added a solution of TCNE (100 mg) in MeOH (2.0 ml) with stirring at room temperature. A crystalline product precipitated from the resulting brown solution. After standing for 1 hr at room temperature, the reaction mixture was evaporated, acetone was added to the residue, and the crystalline product was collected (100 mg), which was recrystallized from MeOH to give colorless prisms, mp >250°. *Anal.* Calcd. for C₁₀H₅N₃S (2-benzothiazolemalononitrile): C, 60.30; H, 2.53; N, 21.10. Found: C, 59.97; H, 2.50; N, 21.17.

Reaction of II with Tetracyanoethylene Oxide—To a solution of II (prepared from the hydrate 100 mg) in CHCl₃ (5.0 ml) was added a solution of TCNEO (70 mg) in CHCl₃ (30 ml) at room temperature, and allowed to stand overnight at room temperature. The resulting yellow solution was concentrated and chromatographed on Al₂O₃ with benzene to give colorless oil (65 mg), which was proved to be XVII by gas-liquid chromatography (conditions were mentioned above).

Reaction of II with Methyl Iodide—To II (prepared from the hydrate 100 mg) was added CH₃I (1.0 ml). The N-oxide dissolved into the solution and a product precipitated immediately. After allowing to stand for 1 hr at room temperature, ether (5.0 ml) was added to the reaction mixture and the crystalline product was collected by filtration (70 mg), which was recrystallized from EtOH-AcOEt to give colorless prisms, mp 155° (decomp.). *Anal.* Calcd. for C₇H₅ONS·½HI·H₂O (benzothiazole 3-oxide hemihydroiodide): C, 35.97; H, 3.45; N, 5.99. Found: C, 36.30; H, 2.93; N, 5.66.

From the mother liquor, an oily product (20 mg) was obtained, which was proved to be XVII by gasliquid chromatography (conditions were mentioned above).

3-Acetoxybenzothiazolium Perchlorate (XXVII)—To a solution of II (prepared from the hydrate 100 mg) in AcOH (0.1 ml) was added Ac₂O (0.10 ml) with stirring and cooling in an ice-water bath. After allowing to stand for 5 min, to the solution was added a solution of HClO₄ (60%, 90 mg) in Ac₂O (0.30 ml) with stirring and cooling, and the solution was cooled for 1 hr. Addition of ether (5 ml) to this solution gave colorless oil, which solidified by scratching (140 mg). Recrystallization from CH₃CN-ether under 40° gave colorless prisms, mp 77—80°. *Anal.* Calcd. for C₉H₈O₆NSCl: C, 36.80; H, 2.72; N, 4.77. Found: C, 36.52; H, 2.96; N, 4.79.

3-Ethoxybenzothiazolium Fluoroborate (XXVIII)—A solution of II (prepared from the hydrate 100 mg) in CH₂Cl₂ (3.0 ml) was added a solution of triethyloxonium fluoroborate (ca. 0.1 g) in CH₂Cl₂ (5.0 ml) with stirring at room temperature. After allowing to stand at room temperature for 0.5 hr, the resulting slightly yellow solution was evaporated and the residue was crystallized by addition of ether, which was recrystallized from acetone-AcOEt to give colorless scales (120 mg), mp 122—124°. *Anal.* Calcd. for C₉H₁₀ONS·BF₄·½H₂O: C, 39.16; H, 4.02; N, 5.06. Found: C, 38.92; H, 4.04; N, 4.93.

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