

Frank T. Coppo and Maged M. Fawzi*

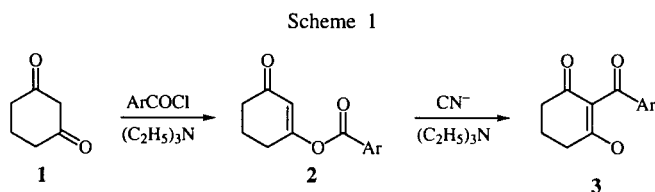
E. I. DuPont de Nemours Agricultural Products, Stine-Haskell Research Center, P.O. Box 30,
Newark, Delaware 19714

Received December 23, 1997

The reaction of 2-chloro-4-(methylsulfonyl)benzoyl chloride (**5**) with 1-methyl-1*H*-2,1-benzothiazin-4-(3*H*)-one 2,2-dioxide (**4**) gave the *O*-benzoyl compound, 1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 2-chloro-4-(methylsulfonyl)benzoate (**6**), which rearranged to give the *C*-benzoyl isomer, [2-chloro-4-(methylsulfonyl)phenyl] (4-hydroxy-1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-3-yl)methanone (**7**). The *O*-cinnamoyl compound **13** that resulted from the addition of 2,4-dichlorocinnamoyl chloride (**11**) to compound **4** rearranged to give the *C*-cinnamoyl compound, 3-(2,4-dichlorophenyl)-1-(4-hydroxy-1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-3-yl)-2-propen-1-one (**15**). On the other hand, 1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 3-phenyl-2-propenoate (**19**) (from cinnamoyl chloride (**17**) and compound **4**) rearranged to give 2,3-dihydro-6-methyl-2-phenyl-4*H*,6*H*-pyrano[3,2-*c*][2,1]benzothiazin-4-one 5,5-dioxide (**21**), an example of a hitherto unknown ring system. Additional examples of this novel heterocycle were prepared from 1-methyl-7-(trifluoromethyl)-1*H*-pyrido[2,3-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (**23**) and 1-methyl-1*H*-thieno[3,2-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (**8**).

J. Heterocyclic Chem., **35**, 983 (1998).

Recently, several 2-benzoyl 1,3-cyclohexanediones **3** have been patented as herbicides [1]. The compounds were prepared from 1,3-cyclohexanedione (**1**) and the benzoyl chlorides. The initial step in the synthesis is the formation of the *O*-benzoyl compounds **2** which readily rearrange to the *C*-benzoyl isomers **3** in the presence of cyanide ion or acetone cyanohydrin and a base [2] (Scheme 1).

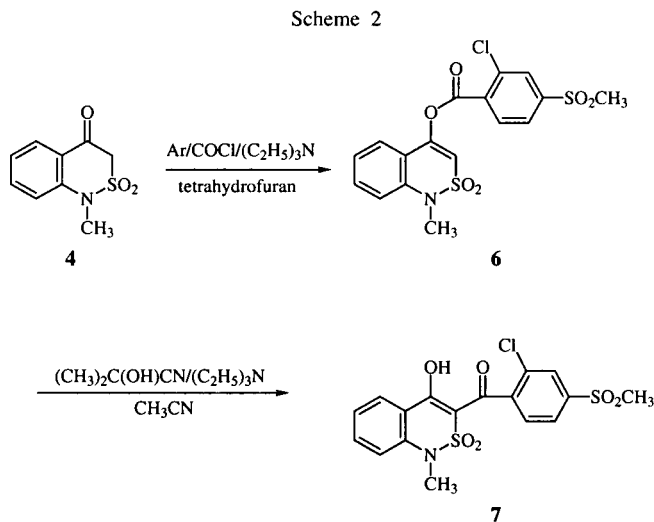


During the course of our work on the reactions of the methylene group of 1-methyl-1*H*-2,1-benzothiazin-4(3*H*)-one 2,2-dioxide (**4**), we investigated the reaction of acid chlorides with compound **4**.

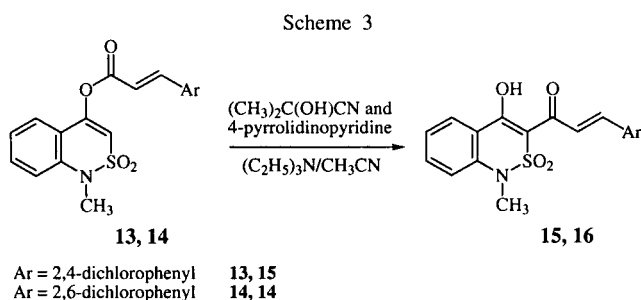
As in the case of 1,3-cyclohexanedione (**1**), we observed that the addition of 2-chloro-4-(methylsulfonyl)benzoyl chloride (**5**) to 1-methyl-1*H*-2,1-benzothiazin-4(3*H*)-one 2,2-dioxide (**4**) and triethylamine in tetrahydrofuran led to the formation of the *O*-benzoyl compound, 1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 2-chloro-4-(methylsulfonyl)benzoate (**6**) which rearranged in the presence of acetone cyanohydrin and triethylamine in acetonitrile to give the *C*-benzoyl isomer, [2-chloro-4-(methylsulfonyl)phenyl] (4-hydroxy-1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-3-yl)methanone (**7**) (Scheme 2). Similarly, 1-methyl-1*H*-thieno[3,2-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (**8**)

reacted with compound **5** to give the *O*-benzoyl compound 1-methyl-2,2-dioxido-1*H*-thieno[3,2-*c*][1,2]thiazin-4-yl 2-chloro-4-(methylsulfonyl)benzoate (**9**). The latter compound rearranged to give [2-chloro-4-(methylsulfonyl)phenyl] (4-hydroxy-2,2-dioxido-1-methyl-1*H*-thieno[3,2-*c*][1,2]thiazin-3-yl)methanone (**10**).

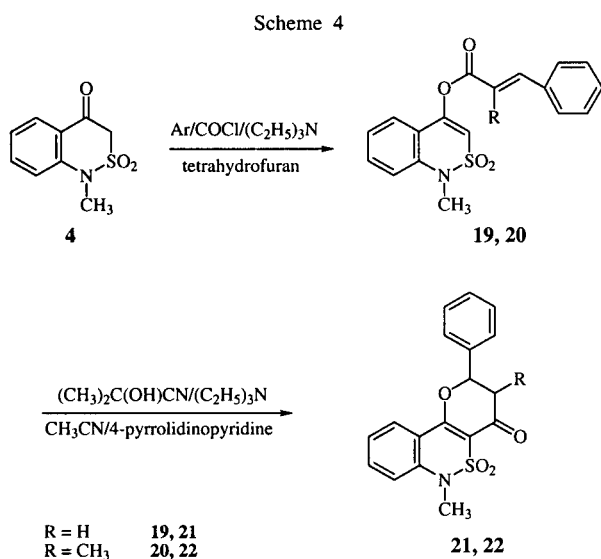
The reaction of 2,4-dichlorocinnamoyl chloride (**11**) and 2,6-dichlorocinnamoyl chloride (**12**) with compound **4** in the presence of triethylamine in tetrahydrofuran gave the *O*-cinnamoyl compounds, 1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 3-(2,4-dichlorophenyl)-2-propenoate (**13**) and 1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 3-(2,6-dichlorophenyl)-2-propenoate (**14**). Compounds **13** and **14** readily rearranged to give the *C*-cinnamoyl compounds, 3-(2,4-dichlorophenyl)-1-(4-hydroxy-1-methyl-2,2-dioxido-



1*H*-2,1-benzothiazin-3-yl)-2-propen-1-one (**15**) and 3-(2,6-dichlorophenyl)-1-(4-hydroxy-1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-3-yl)-2-propen-1-one (**16**) (Scheme 3).



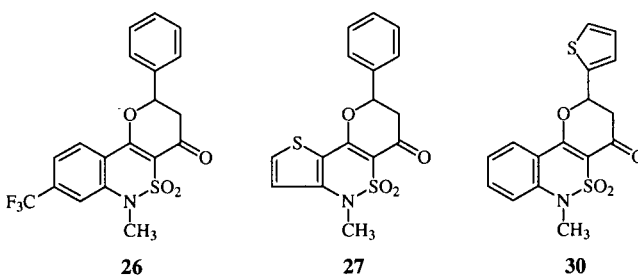
In addition, we reacted cinnamoyl chloride (**17**) and α -methylcinnamoyl chloride (**18**) with compound **4** and isolated the expected enol esters, 1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 3-phenyl-2-propenoate (**19**) and 1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 2-methyl-3-phenyl-2-propenoate (**20**). Surprisingly, rearrangement of the esters **19** and **20** in the presence of acetone cyanohydrin, triethylamine and 4-pyrrolidinopyridine in acetonitrile gave 2,3-dihydro-6-methyl-2-phenyl-4*H*,6*H*-pyrano[3,2-*c*][2,1]benzothiazin-4-one 5,5-dioxide (**21**) and 2,3-dihydro-3,6-dimethyl-2-phenyl-4*H*,6*H*-pyrano[3,2-*c*][2,1]benzothiazin-4-one 5,5-dioxide (**22**), examples of a novel heterocyclic system (Scheme 4).



In order to prepare additional examples of the tricyclic heterocycle, we reacted 1-methyl-7-(trifluoromethyl)-1*H*-pyrido[2,3-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (**23**) [3] and 1-methyl-1*H*-thieno[3,2-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (**8**) [4] with cinnamoyl chloride to give

1-methyl-2,2-dioxido-7-(trifluoromethyl)-1*H*-pyrido[2,3-*c*][1,2]thiazin-4-yl 3-phenyl-2-propenoate (**24**) and 1-methyl-2,2-dioxido-1*H*-thieno[3,2-*c*][1,2]thiazin-4-yl 3-phenyl-2-propenoate (**25**). Rearrangement of compounds **24** and **25** gave 2,3-dihydro-6-methyl-2-phenyl-8-(trifluoromethyl)pyrano[2,3-*e*]pyrido[2,3-*c*][1,2]thiazin-4(6*H*)-one 5,5-dioxide (**26**) and 2,3-dihydro-6-methyl-2-phenylpyrano[2,3-*e*]thieno[3,2-*c*][1,2]thiazin-4(6*H*)-one 5,5-dioxide (**27**).

In addition, we synthesized 1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 3-(2-thienyl)-2-propenoate (**28**) [from compound **4** and 3-(2-thienyl)acryloyl chloride (**29**)] and rearranged it to 2,3-dihydro-6-methyl-2-(2-thienyl)-4*H*,6*H*-pyrano[3,2-*c*][2,1]benzothiazin-4-one 5,5-dioxide (**30**).

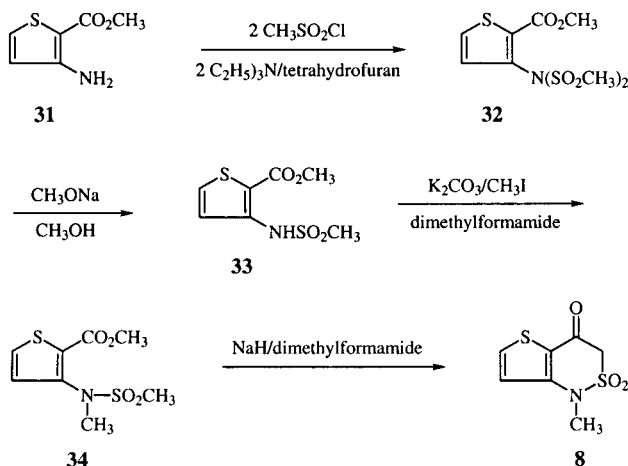


The 1-methyl-1*H*-thieno[3,2-*c*]-1,2-thiazin-4(3*H*)-one 2,2-dioxide (**8**) used in this work was synthesized by the addition of two equivalents of methanesulfonyl chloride to methyl 3-amino-2-thiophenecarboxylate (**31**) to give methyl 3-[bis(methylsulfonyl)amino]-2-thiophenecarboxylate (**32**). Removal of one of the methanesulfonyl groups produced methyl 3-[(methylsulfonyl)amino]-2-thiophenecarboxylate (**33**). The alkylation of sulfonamide **33** with methyl iodide gave methyl 3-[methyl(methylsulfonyl)amino]-2-thiophenecarboxylate (**34**). Treatment of the latter compound with sodium hydride led to the formation of 1-methyl-1*H*-thieno[3,2-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (**8**). The method of preparation is outlined in Scheme 5.

EXPERIMENTAL

Melting points were determined with a Thomas Hoover capillary melting point apparatus and are reported uncorrected. The ¹H nmr spectra were recorded using a Varian Unity Plus 300 or Varian VXR 400. Chemical shift values are reported in parts per million on the δ scale. The nmr spin multiplicities are indicated by the symbols: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Elemental analyses were performed by Quantitative Technologies Inc., Whitehouse, New Jersey, U.S.A. The 1-methyl-1*H*-2,1-benzothiazin-4(3*H*)-one 2,2-dioxide (**4**) used in this project was prepared by the literature method [5] and the 2-chloro-4-(methanesulfonyl)benzoic acid (**5**) is a known compound [6]. We used a dispersion of sodium hydride in mineral oil (60%).

Scheme 5



Methyl 3-[Bis(methylsulfonyl)amino]-2-thiophenecarboxylate (32).

Under a nitrogen atmosphere, methanesulfonyl chloride (37.0 g, 0.32 mole) was added dropwise over twenty minutes to a cold (-5°) and stirred solution of methyl 3-amino-2-thiophenecarboxylate (31) (25.0 g, 0.16 mole) and triethylamine (33.0 g, 0.32 mole) in 300 ml of tetrahydrofuran. The temperature was kept below 10° during the addition. When the addition was complete, the reaction mixture was stirred at ambient temperature overnight, and then diluted with water/ice (approximately 800 ml). The precipitated solid was removed by filtration, washed with water, dried and crystallized from acetonitrile, yield 41.0 g (82%), mp $165\text{--}167^\circ$; ^1H nmr (deuteriochloroform): 3.45 (s, 6H), 3.91 (s, 3H), 7.10 (d, $J = 5.3$ Hz, 1H), 7.55 (d, $J = 5.3$ Hz, 1H).

Anal. Calcd. for $\text{C}_8\text{H}_{11}\text{NO}_6\text{S}_3$: C, 30.66; H, 3.54; N, 4.47. Found: C, 30.96; H, 3.48; N, 4.29.

Methyl 3-[(Methylsulfonyl)amino]-2-thiophenecarboxylate (33).

Under a nitrogen atmosphere, methyl 3-bis(methylsulfonyl)amino-2-thiophenecarboxylate (32) (40 g, 0.128 mole) was added at ambient temperature to a stirred solution of sodium methoxide (14.8 g, 0.27 mole) in 300 ml of methanol. The resulting suspension was stirred at room temperature for 24 hours, most of the methanol was removed under vacuum and 4 *N* hydrochloric acid was added until the reaction mixture was acidic. The solid product was removed by filtration, washed with water and crystallized from tetrahydrofuran, yield 26.0 g (86%), mp $136\text{--}137^\circ$; ^1H nmr (deuteriochloroform): 3.07 (s, 3H), 3.90 (s, 3H), 7.39 (d, $J = 5.4$ Hz, 1H), 7.51 (d, $J = 5.4$ Hz, 1H), 9.40 (s, 1H).

Anal. Calcd. for $\text{C}_7\text{H}_9\text{NO}_4\text{S}_2$: C, 35.73; H, 3.86; N, 5.95. Found: C, 35.73; H, 3.86; N, 5.85.

Methyl 3-[Methyl(methylsulfonyl)amino]-2-thiophenecarboxylate (34).

Under a nitrogen atmosphere, methyl iodide (17.1 g, 0.12 mole) was added to a stirred solution of methyl 3-[(methylsulfonyl)amino]-2-thiophenecarboxylate (33) (25.9 g, 0.11 mole) in 100 ml of dimethylformamide in the presence of potassium carbonate (31.0 g, 0.22 mole). The reaction mixture was stirred at

room temperature overnight, and then water (approximately 300 ml) was added. The precipitated solid was removed by filtration, washed with water, dried and crystallized from acetonitrile, yield 25.2 g (92%), mp $146\text{--}147^\circ$; ^1H nmr (deuteriochloroform): 2.98 (s, 3H), 3.33 (s, 3H), 3.89 (s, 3H), 7.16 (d, $J = 5.25$ Hz, 1H), 7.46 (d, $J = 5.25$ Hz, 1H).

Anal. Calcd. for $\text{C}_7\text{H}_{11}\text{NO}_4\text{S}_2$: C, 38.54; H, 4.45; N, 5.62. Found: C, 38.76; H, 4.32; N, 5.52.

1-Methyl-1*H*-thieno[3,2-*c*][1,2]thiazin-4(3*H*)-one 2,2-Dioxide (8).

Under a nitrogen atmosphere, sodium hydride (3.0 g, 0.075 mole) was added in three portions to a cold (0°) stirred suspension of methyl 3-[methyl(methylsulfonyl)amino]-2-thiophenecarboxylate (34) (9.1 g, 0.037 mole) in 50 ml of dimethylformamide. The reaction mixture was stirred at ambient temperature for 3 hours. A few milliliters of methanol were added to quench the excess sodium hydride used and then the reaction mixture was acidified with 1*N* hydrochloric acid. The solid product was removed by filtration, washed with water, dried and crystallized from ethyl acetate, yield 5.1 g (65%), mp $144\text{--}145^\circ$; ^1H nmr (deuteriochloroform): 3.44 (s, 3H), 4.25 (s, 2H), 6.91 (d, $J = 5.3$ Hz, 1H), 7.83 (d, $J = 5.3$ Hz, 1H).

Anal. Calcd. for $\text{C}_7\text{H}_7\text{NO}_3\text{S}_2$: C, 38.70; H, 3.25; N, 6.45. Found: C, 38.58; H, 3.35; N, 6.21.

General Procedure for the Preparation of the *O*-Benzoates and *O*-Cinnamates, (Enol Esters). Compounds 6, 9, 13, 14, 19, 20, 24, 25 and 28.

Under a nitrogen atmosphere, the acid chloride (0.007 mole) was added to a cold (*ca.* 5°) solution of 4, 8 or 23 (0.007 mole) and triethylamine (1.2 ml) in tetrahydrofuran (25–50 ml). The reaction mixture was stirred at ambient temperature overnight, and then diluted with ice/water (approximately 150 ml). The solid product was removed by filtration, washed with water and crystallized from a suitable solvent. In several instances (compounds 14, 19, 24 and 25), the products were isolated from the aqueous media by extraction with ethyl acetate. The ethyl acetate extracts were combined, washed with water and dried over magnesium sulfate. Removal of the magnesium sulfate by filtration and concentration of the filtrates gave the crude products. The crude products crystallized when triturated with the crystallization solvent. Data for the compounds synthesized are given below:

1-Methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 2-Chloro-4-(methylsulfonyl)benzoate (6).

This compound was prepared from 1-methyl-1*H*-2,1-benzothiazin-4(3*H*)-one 2,2-dioxide (4) and 2-chloro-4-(methylsulfonyl)benzoyl chloride (5), and crystallized from acetonitrile, yield 85%, mp $153\text{--}154^\circ$; ^1H nmr (deuteriochloroform): 3.14 (s, 3H), 3.56 (s, 3H), 7.18 (s, 1H), 7.21–7.29 (m, 2H), 7.60 (dt, $J = 1.5, 7.9$ Hz, 1H), 7.70 (dd, $J = 1.5, 7.9$ Hz, 1H), 8.01 (dd, $J = 1.8, 8.3$ Hz, 1H), 8.15 (d, $J = 1.5, 1\text{H}$), 8.21 (d, $J = 8.3, 1\text{H}$).

Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{ClNO}_6\text{S}_2$: C, 47.72; H, 3.30; N, 3.27. Found: C, 47.87; H, 3.42; N, 3.03.

1-Methyl-2,2-dioxido-1*H*-thieno[3,2-*c*][1,2]thiazin-4-yl 2-Chloro-4-(methylsulfonyl)benzoate (9).

This compound was prepared from 1-methyl-1*H*-thieno[3,2-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (8) and 2-chloro-4-(methylsulfonyl)benzoyl chloride (5), and crystallized from acetonitrile,

yield 73%, mp 188-189°; ¹H nmr (deuteriochloroform): 3.14 (s, 3H), 3.58 (s, 3H), 6.99 (d, J = 5.3, 1H), 7.03 (s, 1H), 7.60 (d, J = 5.3, 1H), 7.99 (dd, J = 1.7, 8.0 Hz, 1H), 8.14 (d, J = 1.7, 1H), 8.17 (d, J = 8.0, 1H).

Anal. Calcd. for C₁₅H₁₂ClNO₆S₃: C, 41.52; H, 2.79; N, 3.23. Found: C, 41.31; H, 2.82; N, 2.97.

1-Methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 3-(2,4-Dichlorophenyl)-2-propenoate (**13**).

This compound was prepared from 1-methyl-1*H*-2,1-benzothiazine-4(3*H*)-one 2,2-dioxide (**4**) and 2,4-dichlorocinnamoyl chloride (**11**), and crystallized from ethyl acetate, yield 67%, mp 193-194°; ¹H nmr (dimethyl-d₆ sulfoxide): 3.46 (s, 3H), 7.14 (d, J = 15.9 Hz, 1H), 7.31 (dt, J = 1.0, 7.6 Hz, 1H), 7.48 (d, J = 8.5, 1H), 7.59 (dd, J = 2.3, 8.3 Hz, 1H), 7.64 (s, 1H), 7.67-7.73 (m, 2H), 7.82 (d, J = 2.0 Hz, 1H), 8.10 (d, J = 15.9, 1H), 8.15 (d, J = 8.5 Hz, 1H).

Anal. Calcd. for C₁₈H₁₃Cl₂NO₄S: C, 52.69; H, 3.19; N, 3.41. Found: C, 52.51; H, 3.18; N, 3.26.

1-Methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 3-(2,6-Dichlorophenyl)-2-propenoate (**14**).

This compound was prepared from 1-methyl-1*H*-2,1-benzothiazine-4(3*H*)-one 2,2-dioxide (**4**) and 2,6-dichlorocinnamoyl chloride (**12**), and crystallized from 1-chlorobutane, yield 70%, mp 141-142°; ¹H nmr (deuteriochloroform): 3.54 (s, 3H), 6.87 (d, J = 16.3 Hz, 1H), 7.15 (s, 1H), 7.23-7.29 (m, 3H), 7.42 (d, J = 8.0 Hz, 2H), 7.58 (dt, J = 1.5, 7.8 Hz, 1H), 7.74 (dd, J = 1.5, 8.3 Hz, 1H), 8.09 (d, J = 16.3 Hz, 1H).

Anal. Calcd. for C₁₈H₁₃Cl₂NO₄S: C, 52.69; H, 3.19; N, 3.41. Found: C, 52.63; H, 3.18; N, 3.33.

1-Methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 3-Phenyl-2-propenoate (**19**).

This compound was prepared from 1-methyl-1*H*-2,1-benzothiazine-4(3*H*)-one 2,2-dioxide (**4**) and cinnamoyl chloride (**17**), and crystallized from 1-chlorobutane, yield 64%, mp 119-120°; ¹H nmr (deuteriochloroform): 3.53 (s, 3H), 6.64 (d, J = 15.9 Hz, 1H), 7.08 (s, 1H), 7.10-7.64 (m, 8H), 7.72 (dd, J = 1.5, 8.3 Hz, 1H), 7.93 (d, J = 15.9 Hz, 1H).

Anal. Calcd. for C₁₈H₁₅NO₄S: C, 63.33; H, 4.43; N, 4.10. Found: C, 63.02; H, 4.60; N, 3.81.

1-Methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 2-Methyl-3-phenyl-2-propenoate (**20**).

This compound was prepared from 1-methyl-1*H*-2,1-benzothiazine-4(3*H*)-one 2,2-dioxide (**4**) and α-methylcinnamoyl chloride (**18**), and crystallized from acetonitrile, yield 44%, mp 145-146°; ¹H nmr (deuteriochloroform): 2.27 (d, J = 1.5 Hz, 3H), 3.54 (s, 3H), 7.04 (s, 1H), 7.2-7.6 (m, 8H), 7.70 (dd, J = 1.5, 8.3 Hz, 1H), 7.97 (m, 1H).

Anal. Calcd. for C₁₉H₁₇NO₄S: C, 64.21; H, 4.82; N, 3.94. Found: C, 64.50; H, 4.66; N, 4.04.

1-Methyl-2,2-dioxido-7-(trifluoromethyl)-1*H*-pyrido[2,3-*c*][1,2]thiazin-4-yl 3-Phenyl-2-propenoate (**24**).

This compound was prepared from 1-methyl-7-(trifluoromethyl)-1*H*-pyrido[2,3-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (**23**) and cinnamoyl chloride (**17**), and crystallized from acetonitrile, yield 70%, mp 218-219°; ¹H nmr (deuteriochloroform): 3.69 (s, 3H), 6.64 (d, J = 16.0 Hz, 1H), 7.29 (s, 1H), 7.44-7.52 (m,

4H), 7.62 (d, J = 7.8 Hz, 1H), 7.63 (d, J = 7.3, 1H), 7.96 (d, J = 16.0 Hz, 1H), 8.18 (d, J = 7.8 Hz, 1H).

Anal. Calcd. for C₁₈H₁₃F₃N₂O₄S: C, 52.68; H, 3.19; N, 6.83. Found: C, 52.63; H, 3.25; N, 6.69.

1-Methyl-2,2-dioxido-1*H*-thieno[3,2-*c*][1,2]thiazin-4-yl 3-Phenyl-2-propenoate (**25**).

This compound was prepared from 1-methyl-1*H*-thieno[3,2-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (**8**) and cinnamoyl chloride (**17**), and crystallized from acetonitrile, yield 28%, mp 158-159°; ¹H nmr (deuteriochloroform): 3.55 (s, 3H), 6.57 (d, J = 16.0 Hz, 1H), 6.96 (s, 1H), 6.96 (d, J = 5.3, 1H), 7.44-7.48 (m, 3H), 7.56 (d, J = 5.3 Hz, 1H), 7.60-7.63 (m, 2H), 7.90 (d, J = 16.0 Hz, 1H).

Anal. Calcd. for C₁₆H₁₃NO₄S₂: C, 55.32; H, 3.77; N, 4.03. Found: C, 55.33; H, 3.75; N, 3.98.

1-Methyl-2,2-dioxido-1*H*-2,1-benzothiazin-4-yl 3-(2-Thienyl)-2-propenoate (**28**).

This compound was prepared from 1-methyl-1*H*-2,1-benzothiazine-4(3*H*)-one 2,2-dioxide (**4**) and 3-(2-thienyl)acryloyl chloride (**29**), and crystallized from acetonitrile, yield 53%, mp 164-165°; ¹H nmr (deuteriochloroform): 3.53 (s, 3H), 6.42 (d, J = 15.6 Hz, 1H), 7.07 (s, 1H), 7.11-7.64 (m, 6H), 7.72 (dd, J = 1.5, 8.3 Hz, 1H), 8.02 (d, J = 15.6 Hz, 1H).

Anal. Calcd. for C₁₆H₁₃NO₄S₂: C, 55.32; H, 3.77; N, 4.03. Found: C, 54.96; H, 3.50; N, 3.92.

General Procedure for the Rearrangement. The Preparation of the C-Benzoyl compounds **7**, **10**, the C-Cinnamoyl Compounds **15**, **16** and the Pyrano Compounds **21**, **22**, **26**, **27**, **30**.

Under a nitrogen atmosphere, acetone cyanohydrin (2-3 drops) and 4-pyrrolidinopyridine (2 drops of a 5% solution in tetrahydrofuran) were added at room temperature to a stirred suspension of the enol ester (0.8-1.6 g) and triethylamine (2.5 equivalents) in acetonitrile (10-20 ml). Within less than one hour, clear solutions were obtained. The reaction mixtures were stirred for an additional 3-5 hours, and then diluted with 1*N* hydrochloric acid (approximately 100 ml). Solid products were removed by filtration. In several instances the products were isolated by extraction with ethyl acetate and purified by column chromatography on silica gel eluting with ethyl acetate/hexane (2:1). The products from the chromatography were crystallized from a suitable solvent. Compounds **10**, **16**, **21**, **22**, **26**, **27** and **30** were isolated by extraction. Data for the compounds synthesized are listed below.

[2-Chloro-4-(methylsulfonyl)phenyl]-(4-hydroxy-1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-3-yl)methanone (**7**).

This compound was prepared from compound **6**, and crystallized from tetrahydrofuran, yield 68%, mp 230-231°; ¹H nmr (acetone-d₆): 3.30 (s, 3H), 3.43 (s, 3H), 7.48 (dt, J = 1.0, 7.5 Hz, 1H), 7.53 (d, J = 8.3 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.90 (m, 1H), 8.07 (d, J = 1.8, 8.0 Hz, 1H), 8.10 (d, J = 1.5, 1H), 8.25 (dd, J = 1.5, 8.0 Hz, 1H), 16.2 (br s, 1H).

Anal. Calcd. for C₁₇H₁₄ClNO₆S₂: C, 47.72; H, 3.30; N, 3.27. Found: C, 48.01; H, 3.34; N, 3.54.

[2-Chloro-4-(methylsulfonyl)phenyl]-(4-hydroxy-2,2-dioxido-1-methyl-1*H*-thieno[3,2-*c*]thiazin-3-yl)methanone (**10**).

This compound was prepared from compound **9**, yield 30%, mp 228-229°; ¹H nmr (acetone-d₆): 3.29 (s, 3H), 3.50 (s, 3H),

7.33 (d, *J* = 5.4, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 8.05 (dd, *J* = 1.7, 7.9 Hz, 1H), 8.08 (d, *J* = 1.7, 1H), 8.40 (d, *J* = 5.4 Hz, 1H).

Anal. Calcd. for C₁₅H₁₂ClNO₆S₃: C, 41.52; H, 2.79; N, 3.23. Found: C, 41.49; H, 2.77; N, 3.05.

3-(2,4-Dichlorophenyl)-1-(4-hydroxy-1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-3-yl)-2-propen-1-one (**15**).

This compound was prepared from compound **13**, and crystallized from acetonitrile, yield 17%, mp 219-220°; ¹H nmr (dimethyl-d₆ sulfoxide): 3.41 (s, 3H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 8.3, 1H), 7.58 (dd, *J* = 1.5, 8.3 Hz, 1H), 7.79-7.89 (m, 4H), 8.09 (d, *J* = 15.6 Hz, 1H), 8.10 (dd, *J* = 1.5, 8.0 Hz, 1H).

Anal. Calcd. for C₁₈H₁₃Cl₂NO₄S: C, 52.69; H, 3.19; N, 3.41. Found: C, 52.46; H, 3.05; N, 3.31.

3-(2,6-Dichlorophenyl)-1-(4-hydroxy-1-methyl-2,2-dioxido-1*H*-2,1-benzothiazin-3-yl)-2-propen-1-one (**16**).

This compound was prepared from compound **14**, and crystallized from ethyl acetate, yield 40%, mp 181-182°; ¹H nmr (dimethyl-d₆ sulfoxide): 3.41 (s, 3H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.46-7.51 (m, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.83 (dt, *J* = 1.5, 7.8 Hz, 1H), 7.97 (d, *J* = 15.9 Hz, 1H), 8.03 (d, *J* = 15.9 Hz, 1H), 8.12 (dd, *J* = 1.5, 7.8 Hz, 1H).

Anal. Calcd. for C₁₈H₁₃Cl₂NO₄S: C, 52.69; H, 3.19; N, 3.41. Found: C, 52.59; H, 3.35; N, 3.39.

2,3-Dihydro-6-methyl-2-phenyl-4*H*,6*H*-pyrano[3,2-*c*][2,1]benzothiazin-4-one 5,5-Dioxide (**21**).

This compound was prepared from compound **19**, and crystallized from ethyl acetate, yield 31%, mp 154-155°; ¹H nmr (deuteriochloroform): 3.09 (dd, *J* = 1.9, 16.0 Hz, 1H), 3.25 (dd, *J* = 7.5, 16.0 Hz, 1H), 3.48 (s, 3H), 4.59 (dd, *J* = 1.9, 17.5 Hz, 1H), 7.22-7.36 (m, 7H), 7.6 (m, 1H), 7.98 (dd, *J* = 1.5, 8.1 Hz, 1H).

Anal. Calcd. for C₁₈H₁₅NO₄S: C, 63.33; H, 4.43; N, 4.10. Found: C, 63.18; H, 4.61; N, 3.97.

2,3-Dihydro-3,6-dimethyl-2-phenyl-4*H*,6*H*-pyrano[3,2-*c*][2,1]-benzothiazin-4-one 5,5-Dioxide (**22**).

This compound was prepared from compound **20**, and crystallized from 1-chlorobutane, yield 27%, mp 144-145°; ¹H nmr (deuteriochloroform): 1.50 (d, *J* = 7.3 Hz, 3H), 3.19 (dq, *J* = 2.1, 7.3 Hz, 1H), 3.48 (s, 3H), 4.20 (d, *J* = 2.1 Hz, 1H), 7.22-7.36 (m, 7H), 7.60 (m, 1H), 7.98 (dd, *J* = 1.5, 8.0 Hz, 1H).

Anal. Calcd. for C₁₉H₁₇NO₄S: C, 64.21; H, 4.82; N, 3.94. Found: C, 64.10; H, 4.97; N, 3.88.

2,3-Dihydro-6-methyl-2-phenyl-8-(trifluoromethyl)pyrano[2,3-*e*]pyrido[2,3-*c*][1,2]thiazin-4(6*H*)-one 5,5-Dioxide (**26**).

This compound was prepared from compound **24**, and crystallized from 1-chlorobutane, yield 56%, mp 202-203°; ¹H nmr (deuteriochloroform): 3.15 (dd, *J* = 1.9, 16.0 Hz, 1H), 3.28 (dd, *J* = 7.5, 16.0 Hz, 1H), 3.65 (s, 3H), 4.65 (dd, *J* = 1.9, 7.5 Hz, 1H), 7.25-7.41 (m, 5H), 7.58 (d, *J* = 8.1 Hz, 1H), 8.41 (d, *J* = 8.1 Hz, 1H).

Anal. Calcd. for C₁₈H₁₃F₃N₂O₄S: C, 52.68; H, 3.19; N, 6.83. Found: C, 52.51; H, 3.33; N, 6.61.

2,3-Dihydro-6-methyl-2-phenylpyrano[2,3-*e*]thieno[3,2-*c*][1,2]thiazin-4(6*H*)-one 5,5-Dioxide (**27**).

This compound was prepared from compound **25**, and crystallized from ethyl acetate, yield 28%, mp 188-189°; ¹H nmr (deuteriochloroform): 3.08 (dd, *J* = 1.8, 16.0 Hz, 1H), 3.26 (dd, *J* = 7.5, 16.0 Hz, 1H), 3.50 (s, 3H), 4.53 (dd, *J* = 1.8, 7.5 Hz, 1H), 6.97 (d, *J* = 5.5 Hz, 1H), 7.27-7.37 (m, 5H), 7.60 (d, *J* = 5.5 Hz, 1H).

Anal. Calcd. for C₁₆H₁₃NO₄S₂: C, 55.32; H, 3.77; N, 4.03. Found: C, 55.16; H, 3.87; N, 3.74.

2,3-Dihydro-6-methyl-2-(2-thienyl)-4*H*,6*H*-pyrano[3,2-*c*][2,1]-benzothiazin-4-one 5,5-Dioxide (**30**).

This compound was prepared from compound **28**, yield 40%, mp 164-165°; ¹H nmr (deuteriochloroform): 3.24 (d, *J* = 4.8 Hz, 2H), 3.51 (s, 3H), 4.84 (t, *J* = 4.8 Hz, 1H), 6.94 (dd, *J* = 3.5, 5.1 Hz, 1H), 7.20 (td, *J* = 1.0, 3.5 Hz, 1H), 7.23-7.32 (m, 3H), 7.60 (m, 1H), 7.95 (dd, *J* = 1.5, 8.0 Hz, 1H).

Anal. Calcd. for C₁₆H₁₃NO₄S₂: C, 55.32; H, 3.77; N, 4.03. Found: C, 55.30; H, 3.78; N, 3.88.

Acknowledgment.

We thank Mrs. G. L. Blankenship and Mr. J. C. Groce, Jr. for recording the nmr spectra. In addition, we wish to thank Mrs. B. W. Dotts and Mrs. C. D. Smith for their help with the nomenclature.

REFERENCES AND NOTES

- [1a] C. G. Carter, D. L. Lee, W. J. Michaely and G. W. Kraatz, U.S. Patent 4,946,981 (issued August 7, 1990); [b] T. Morita, T. Oono, T. Shimozono, K. Hirayama, H. Ishikawa, H. Yoshizawa and M. Yoshihara, Japan Kokai Tokkyo Koho, JP 06,271,498 [94,271,498] (September 27, 1994), *Chem. Abstr.*, **122**, 290445 (1995); [c] T. Morita, T. Oono, T. Shimozono, K. Hirayama, H. Ishikawa, H. Yoshizawa and M. Yoshihara, Japan Kokai Tokkyo Koho, JP 07 69,963 [95,69,963] (March 14, 1995); *Chem. Abstr.*, **123**, 111591 (1995); [d] I. Nasuno, M. Shibata, M. Sakamoto and K. Koike, PCT Int. Appl. WO 94 08,988 (April 28, 1994); *Chem. Abstr.*, **121**, 10852 (1994).
- [2a] C. G. Knudsen, European Patent Appl. EP 249,150 (December 16, 1987); *Chem. Abstr.*, **109**, 6219 (1988); [b] J. Kast, W. Von Deyn, C. Nuebling, H. Walter, M. Gerber and K. Westphalen, European Patent Appl. EP 666,254 (August 9, 1995); *Chem. Abstr.*, **124**, 8285 (1996).
- [3] F. T. Coppo and M. M. Fawzi, a manuscript describing the preparation of 1-methyl-7-(trifluoromethyl)-1*H*-pyrido[2,3-*c*][1,2]-thiazin-4(3*H*)-one 2,2-dioxide (**23**) was submitted to the *J. Heterocyclic Chem.*
- [4] We did not find any literature references pertaining to 1-methyl 1*H*-thieno[3,2-*c*][1,2]thiazin-4(3*H*)-one 2,2-dioxide (**8**). Currently, the compound can be purchased from Maybridge Chemical Company, Ltd.
- [5] J. G. Lombardino, *J. Heterocyclic Chem.*, **9**, 315 (1972).
- [6a] R. W. Brown, *J. Org. Chem.*, **56**, 4974 (1991); [b] B. F. Cain, R. N. Seelye and G. J. Atwell, *J. Med. Chem.*, **17**, 922 (1974).