mercurio)acetate (3) was prepared according to the literature procedure.[9]

Synthesis of Compounds 4 and 5. Palladium chloride (0.89 g, 5 mmol) and lithium chloride (0.42 g, 10 mmol) were dissolved in 50 mL of dry THF. The solution was cooled to 0 °C, and ethyl (acetoxymercurio)acetate (3) (1.73 g, 5 mmol), norbornene (0.94 g, 10 mmol), and 1-octen-3-one (6.3 g, 50 mmol) were added. The reaction was stirred at 0 °C for 1 h and was then allowed to warm up to room temperature. After being stirred for 4 days, the reaction mixture was diluted with ether, filtered, washed with saturated ammonium chloride solution, and dried over Na_2SO_4. After removal of the solvent, the excess 1-octen-3-one was distilled under reduced pressure. Gas chromatographic–mass spectral analysis of the reaction mixture showed that the desired product 4 was obtained along with compound 5 in a ratio of ~4:1 in a total yield of 70%. The mixture was separated by column chromatography using 4:1 hexane/ethyl acetate as the eluant.

The desired product 4 was isolated in 40% yield: ^{1}H NMR ($CDCl_3$) δ 0.91 (3 H, t, J = 7 Hz, CH_3), 1.16–2.52 (23 H, m), 4.06 (q) and 4.07 (q) (2 H, J = 7.2 Hz, OCH_2, diastereomeric ester hydrogens), 6.05 (1 H, d, J = 14.5 Hz, C=CHC=O), 6.59 (1 H, dd, J = 10.7 and 14 Hz, CH=CC=O); ^{13}C NMR ($CDCl_3$) δ 200.1, 172.8, 146.8, 130.5, 60.2, 49.1, 43.4, 42.7, 41.6, 40.3, 36.5, 33.5, 31.4, 29.5, 28.7, 23.9, 22.4, 14.1, 13.8; IR (neat) 2960 (CH), 1745 (ester C=O), 1680 (enone C=O), 1610 (C=C) cm^{-1}; MS (70 eV), m/z 306 (M^+), 278 ($M^+ - CH_2{=}CH_2$), 261 ($M^+ - OCH_2CH_3$), 260 ($M^+ - CH_3CH_2OH$), 207 ($M^+ - COC_5H_{11}$), 162 (207 - OCH_2CH_3); MS, m/z 306.22065 (calcd for $C_{19}H_{30}O_3$, 306.21950).

Compound 5: MS (70 eV), m/z 400 (M^+), 372, 344, 327, 286, 215, 205, 147, 133, 119, 99, 91, 79, 67, 54, 43.

Synthesis of Compounds 6 and 7. A general literature procedure was employed.[11] The enone 4 (0.27 g, 0.89 mmol) and $CeCl_3{\cdot}7H_2O$ (0.33 g, 0.89 mmol) were dissolved in methanol (2.25 mL). Sodium borohydride (0.034 g, 0.89 mmol) was added, and the reaction mixture was stirred for 5 min. It was then diluted with ether and water, and the ether layer was separated. The aqueous layer was extracted with ether, dried over Na_2SO_4, and evaporated to give 0.247 g (90% yield) of crude hydroxy ester 6, which was immediately reduced further.

The hydroxy ester 6 was reduced to hydroxy aldehyde 7 by using i-Bu_2AlH and a procedure identical with that described later for the synthesis of compound 10: 60% overall yield from compound 4; ^{1}H NMR ($CDCl_3$) δ 0.81–2.4 (24 H, m), 3.90 (1 H, m, C*H*OH), 5.2–5.4 (2 H, m, vinyl), 9.57 (1 H, s, CHO); ^{13}C NMR ($CDCl_3$) δ 202.5, 138.5, 128.4, 68.4, 49.2, 46.4, 43.2, 42.7, 41.7, 41.3, 41.2, 33.4, 32.4, 29.6, 28.2, 27.9, 23.8, 23.7, 22.5, 14.0 (extra peaks due to diastereomers); IR (neat) 3400–3200 (OH), 2960 (CH), 1720 (C=O) cm^{-1}; MS, m/z 246.19826 [calcd for $C_{17}H_{26}O$ (M^+ - 18), 246.1983].

Synthesis of Compound 8. Hydroxy aldehyde 7 was subjected to the Wittig reaction as described later for the synthesis of compound 11, and the desired acid 8 was obtained in 62% yield: ^{1}H NMR ($CDCl_3$) δ 0.89–2.42 (31 H, m), 3.7–3.8 (1 H, m, C*H*OH), 5.20–5.52 (4 H, m, vinyl); ^{13}C NMR ($CDCl_3$) δ 177.5, 133.2, 131.9, 128.3, 127.6, 73.2, 49.8, 49.2, 47.3, 47.2, 43.3, 42.6, 39.8, 37.3, 33.1, 31.9, 29.8, 29.3, 25.3, 24.4, 22.7, 14.1; IR (neat) 3500–2700 (CO_2H, OH), 1710 (C=O) cm^{-1}; MS, m/z 330.25643 [calcd for $C_{22}H_{34}O_2$ (M^+ - 18), 330.25588].

Synthesis of Hydroxy Ester 9. A general literature procedure was followed.[12] Compound 4 (0.22 g, 0.72 mmol) was taken up in 37 mL of dry THF and cooled to -78 °C. To this was added 3.77 mL (15.75 equiv) of 3.0 M MeMgBr in diethyl ether. The reaction as stirred at -78 °C for 4 h. The reaction was then quenched with 10 mL of saturated ammonium chloride solution and allowed to warm up to room temperature. After an additional 25 mL of saturated ammonium chloride solution was added, the reaction mixture was extracted with ether. The ether layer was washed with saturated sodium chloride solution and dried over Na_2SO_4 and the solvent removed under vacuum. Column chromatography of the resulting residue using 1:1 hexane/ethyl acetate as the eluant yielded 137 mg (59% yield) of compound 9: ^{1}H NMR ($CDCl_3$) δ 0.79–2.4 (28 H, m), 4.05 (2 H, q, J = 7 Hz, OCH_2), 5.3–5.4 (2 H, m, vinyl); ^{13}C NMR ($CDCl_3$) δ 173.7, 138.0, 128.2, 72.7, 60.2, 49.2, 43.3, 43.3, 42.8, 42.8, 37.0, 33.4, 32.4, 29.8, 29.0, 28.2, 27.6, 23.9, 23.7, 22.7, 14.3, 14.1 (extra peaks due to diastereomers); IR (neat) 3800–3150 (OH), 2880 (C=CH), 1730 (C=O), 1640 (C=C) cm^{-1}; MS, m/z 304.23916 [calcd for $C_{20}H_{30}O_2$ (M^+ - H_2O), 304.2402].

Synthesis of Hydroxy Aldehyde 10. Ester 9 (137 mg, 0.425 mmol) was taken up in 28 mL of methylene chloride and cooled to -78 °C. This solution was treated with 1.4 mL of 1 M i-Bu_2AlH in methylene chloride (3.3 equiv) and stirred for 3 h at -78 °C. The reaction mixture was then quenched with 1 mL of methanol and treated with 3 mL of saturated ammonium chloride solution. The reaction mixture was then warmed to room temperature, diluted with ether, washed with saturated ammonium chloride solution, and dried over Na_2SO_4 and the solvent removed under vacuum. Flash column chromatography of the resulting residue yielded 106 mg (90% yield) of the desired hydroxy aldehyde 10: ^{1}H NMR ($CDCl_3$) δ 0.75–2.4 (26 H, m), 5.32–5.34 (2 H, m, vinyl), 9.57 (1 H, m, CHO); ^{13}C NMR ($CDCl_3$) δ 202.8, 138.4, 128.4, 72.7, 49.2, 49.1, 46.4, 43.2, 42.9, 41.7, 41.3, 41.2, 33.4, 32.3, 29.7, 29.0, 28.2, 27.8, 23.7, 22.6, 14.0 (extra peaks due to diastereomers); IR (neat) 3500–3300 (OH), 2960 (CH), 1720 (C=O) cm^{-1}; MS, m/z 260.2142 [calcd for $C_{18}H_{28}O$ (M^+ - 18), 260.2140].

Synthesis of Compound 11. A general literature procedure for this Wittig reaction was employed.[13] (4-Carboxybutyl)triphenylphosphonium bromide (0.70 g, 1.58 mmol) was suspended in 6 mL of THF under a nitrogen atmosphere. Potassium *tert*-butoxide (0.36 g, 3.2 mmol) was added, and the orange-colored mixture was stirred for 15 min at room temperature. Then hydroxy aldehyde 10 (0.11 g, 0.395 mmol) in 3.8 mL of THF was added, and the reaction mixture was stirred at room temperature for 3 h. Sulfuric acid (40 mL of 2 N) and water were added, and the product was extracted with ether, washed with 2 N sulfuric acid and water, and dried over $MgSO_4$. The residue obtained after evaporation of the solvent was chromatographed by using 1:1 hexane/ethyl acetate plus a few drops of acetic acid to yield 77 mg (54% yield) of compound 11: ^{1}H NMR ($CDCl_3$) δ 0.80–2.24 (34 H, m), 5.2–5.4 (4 H, m, vinyl); ^{13}C NMR ($CDCl_3$) δ 178.2, 133.0, 131.6, 128.5, 127.6, 76.6, 49.7, 47.6, 43.5, 40.1, 35.5, 33.5, 33.1, 32.4, 31.9, 30.0, 29.8, 29.3, 26.8, 26.6, 24.9, 24.7, 22.7, 14.1 (extra peaks due to diastereomers); IR (neat) 3500–3200 (OH, CO_2H), 1720 (C=O) cm^{-1}; MS, m/z 344.27101 [calcd for $C_{23}H_{36}O_2$ (M^+ - 18), 344.27154].

Acknowledgment. We gratefully acknowledge the National Institutes of Health and the American Heart Association, Iowa Affiliate, for financial support, and Johnson Matthey Inc. and Englehard Industries for generous loans of palladium chloride.

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Synthesis of 4-Phenyl-5*H*-pyrido[3,4-*b*][1,4]benzothiazin-3-(2*H*)-ones (4-Phenylazaphenothiazines) via Activated Dimethylformamide Reagents

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Received October 14, 1986

We previously reported on the synthesis and biological activity of a series of oxopyridobenzothiazine-4-carbonitriles (azaphenothiazines).[1] These compounds were synthesized by a novel α-pyridone annulation reaction,

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0022-3263/87/1952-1366$01.50/0

which we had also utilized to prepare a variety of bicyclic[2] and tricyclic systems.[3] The unique biological properties and therapeutic potential of these azaphenothiazines prompted us to pursue analogues where the carbonitrile group was replaced by other functionality.

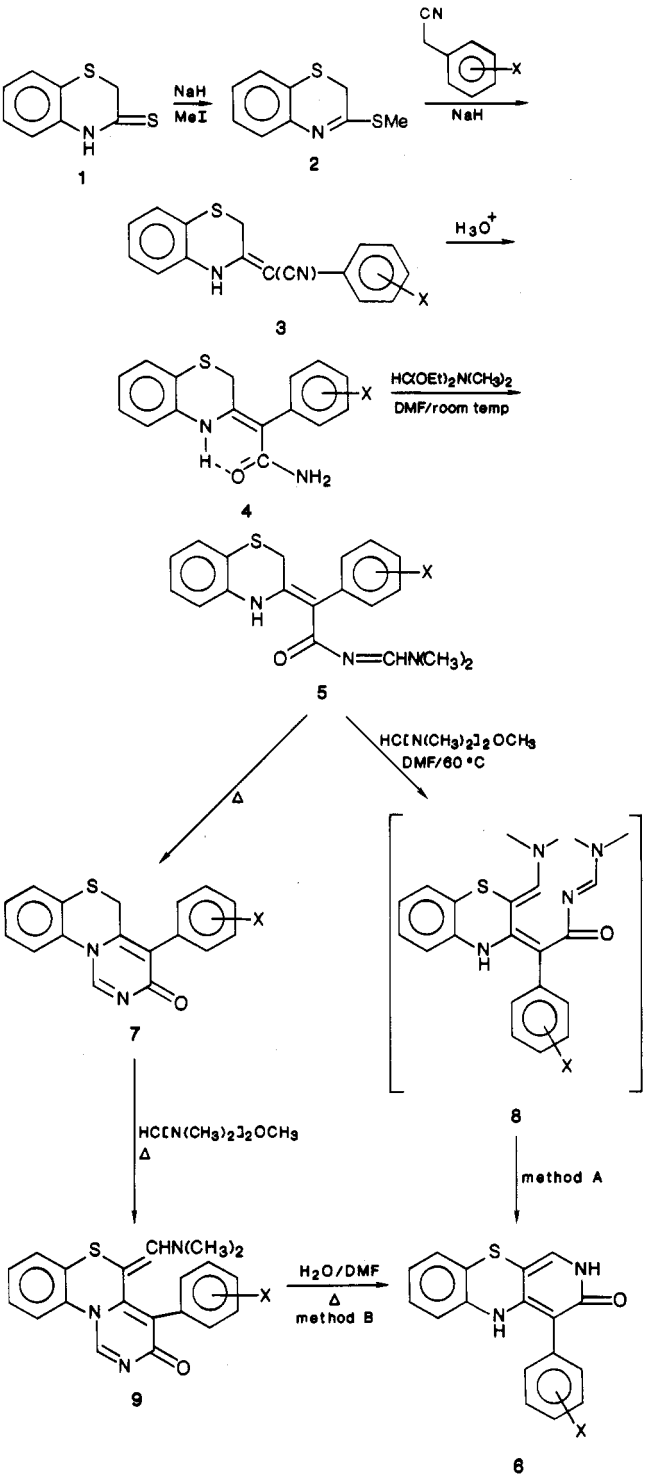
In the course of this work, we attempted to prepare, by the previously developed route, azaphenothiazines wherein a phenyl group was present instead of the carbonitrile. Thus, lactim ether **2**, prepared from thiolactam **1** as previously described,[1] was treated with the anion of various phenylacetonitriles to afford adducts **3**, usually as a mixture of *E*/*Z* isomers (Scheme I).[4] These isomeric carbonitriles were hydrated to the corresponding carboxamido compounds, which appear as a single geometric isomer by NMR spectroscopy as we observed in the case of the cyanoacetamide adducts.[1] These amides were readily converted to the (*N*,*N*-dimethylamino)methylene adducts (acylamidines) **5** by using dimethylformamide diethyl acetal. However, thermal cyclization of these acylamidines in DMF failed to produce the desired annulated α-pyridones **6**. Instead, the annulated pyrimidones **7**, characterized by a methylene resonance at about 3.3 ppm and a pyrimidone ring-proton resonance at about 8.8 ppm, were formed, apparently due to the increased nucleophilicity of the thiazine nitrogen in this system. Replacement of the strongly electronegative nitrile with a less electronegative phenyl group is responsible for the increased nucleophilicity of this heteroatom.[5]

We had hoped to circumvent this problem by treatment of **5** with the more reactive bis(dimethylamino)methoxymethane reagent to produce **8** at temperatures below those that cause **5** to cyclize to **7**. The enamino compound **8** would then be converted to **6** by the previously described hydrolysis/cyclization sequence.[1] However, exposure of **5** (X = H, *p*-Cl, *o*-Cl, *o*-F, *m*-CF_3) to this aminal ester reagent at 60–80 °C in DMF directly afforded the desired α-pyridones **6** as bright yellow solids characterized by a pyridone ring-proton resonance at about 7.2 ppm.

We envision this unexpected transformation as proceeding through formation of the bisadduct **8**, which then cyclizes to **6**. This cyclization can proceed via a direct interaction of the enamine moiety with the lone pair of electrons on the acylamidine nitrogen of **8**. Alternatively, the dimethylamine present in the reaction mixture may add to the acylamidine of **8** to again trigger a favorable 6-*Endo-Trig* cyclization.[6] Elimination of dimethylamine would provide the pyridone nucleus containing a highly labile bis(dimethylamino)methyl group on the pyridone nitrogen. Nucleolysis with water, alcohol, or dimethylamine yields the observed N-unsubstituted pyridones **6**. We favor the latter mechanism since we had previously isolated an analogue of bisadduct **8** where a cyano group was present instead of the phenyl substituent.[1] In this case temperatures above those of the cyclization process described herein but in the absence of the nucleophilic amine failed to provide the α-pyridone cyclization product. Moreover, when compound **8** with cyano instead of phenyl was treated with diethylamine in DMF at ca. 85 °C, the corresponding α-pyridone was produced.[7] This route (method A) was utilized to prepare the annulated pyridones possessing an unsubstituted phenyl as well as those with a *p*-Cl, *o*-Cl, *o*-F, or *m*-CF_3 substituent.[8]

In several instances, however, this method was unsuc-

Scheme I[a]



[a] Method A, X = H, 4-Cl, 2-Cl, 2-F, 3-CF_3; method B, X = 4-Cl, 4-F, 4-OCH_3.

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(3) Chorvat, R. J.; Desai, B. N. *J. Heterocycl. Chem.* **1980**, *17*, 1313.
(4) These mixtures (ca. 1:1) of double-bond isomers were generally converted to the corresponding carboxamido compounds without separation. In one case (X = *o*-F), the individual isomers were isolated. Each yielded the same amide upon hydration.
(5) For a discussion of the effect of various substituents on the pK_a of amines, see: Perrin, D. D.; Dempsey, B.; Serjeant, E. P. *pK_a Predictions for Organic Acids and Bases*; Chapman and Hall: New York, 1981; Chapter 4.
(6) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.
(7) Chorvat, R. J., unpublished results.
(8) This mechanism casts some doubt on whether the cyclization mechanism proposed in our earlier work is exclusively a hydrolysis (of the acylamidine)/cyclization process. In the presence of aqueous ammonium hydroxide solution, cyclization of **8** (CN instead of phenyl) can be proceeding by both hydrolysis/cyclization and ammonia-mediated cyclization through addition to the acylamidine moiety.[1]

cessful in producing certain substituted-phenyl α-pyridones. When adducts **5** with either a *p*-F or *p*-OCH_3 substituent on the phenyl ring were treated with bis(dimethylamino)methoxymethane at about 50 °C, the pyrimidone adduct **9** was the main product. In these cases even this moderately elevated temperature initially caused cyclization of **4** to the pyrimidone **7**, which then underwent condensation at the carbon adjacent to the sulfur atom to provide the tricyclic enamine **9**.

Annulated pyrimidones had previously been reported to be precursors of α-pyridones.[9] In this series, we also found that the annulated pyrimidones **7** could be converted to the pyridones **6** in an analogous manner. Thus, treatment of **7** with bis(dimethylamino)methoxymethane afforded enamino adduct **9**. Hydrolysis of **9** in aqueous DMF at elevated temperatures yielded pyridones **6** in high yield (method B). In this system the pyrimidone nucleus is susceptible to hydration and cleavage yielding an formamidocarbonyl intermediate. This, in turn, undergoes cyclization with the (dimethylamino)methylene moiety to afford, upon loss of the formyl group, the isolated product **6**. In addition to phenyl pyridones with a *p*-F or a *p*-OCH_3 substituent, the *p*-Cl phenyl compound was also prepared in this manner.

In summary, the DMF acetal or bis(dimethylamino)-methoxymethane-mediated cyclization of the described α-substituted acrylamide derivatives of benzothiazines is highly dependent on the nature of the α-substituent. A strong electron-withdrawing substituent such as a cyano group directs thermal ring closure of intermediate acylamidines to annulated α-pyridones (azaphenothiazines) via an enamine cyclization. Less electron demanding α-substituents (phenyl groups) produce systems where enhanced nucleophilicity of the phenothiazine nitrogen causes an alternate thermal cyclization process to dominate. In these cases, the tricyclic annulated α-pyridones were produced either through a direct cyclization of the intermediate acylamidine **8** (method A) or through a tricyclic pyrimidone, which undergoes enamine functionalization to **9** followed by rearrangement via hydrolytic cleavage of the pyrimidone ring and subsequent cyclization (method B).

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were recorded on Varian T-60, Varian FT-80, or GE QE-300 spectrometers with Me_4Si as an internal standard. UV spectra were obtained on a Beckman DK-2A instrument by the group of A. J. Damascus. Compounds were subjected to elemental analysis by the group of E. Zielinski.

2*H*-1,4-Benzothiazine-3(4*H*)-thione (1) was prepared according to the procedure of Prasad.[10]

3-(Methylthio)-2*H*-1,4-benzothiazine (2) was prepared as previously described.[1]

(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)phenylacetonitriles 3. The preparation of the 4-chlorophenylacetonitrile adduct is representative. To 12.0 g (0.25 mol) of a 50% NaH/mineral oil dispersion, previously washed twice with Skelly B to remove the oil, suspended in 300 mL of DMF at room temperature in a nitrogen atmosphere was added 32 g (0.21 mol) of 4-chlorophenylacetonitrile in portions over a 15–20-min period. The solution was then stirred for 30 min before the thiolactim ether (**2**) solution, prepared from 30 g (0.166 mol) of thiolactam 1/300 mL of THF/15 mL of MeI, was added dropwise. After addition, the reaction mixture was stirred at room temperature for 1–2 h, neutralized with glacial HOAc, and diluted with ca. 2 volumes of H_2O, which caused formation of precipitate, which was collected, affording 31.2 g (63%) of adduct. This material, consisting of a mixture of *E*/*Z* isomers, was generally suitable for the subsequent reaction. Recrystallization of the crude solid from methanol provided **3** (X = 4-Cl): mp 137–139 °C; NMR (Me_2SO-d_6) δ 3.65/3.85 (2 H, s, CH_2's of *Z*/*E* isomers, ca. 2.5:1 ratio); 9.62/10.07 (1 H, br s, NH's of respective isomers, ca. 2.5:1 ratio). Anal. Calcd for $C_{16}H_{11}ClN_2S$: C, 64.32; H, 3.71; N, 9.38. Found: C, 64.30; H, 3.47; N, 9.22.

(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)phenylacetonitrile (3, X = H): recrystallized from MeOH (40%); mp 133–135 °C; NMR (Me_2SO-d_6) δ 3.84 (2 H, s, CH_2), 9.45 (1 H, br s, NH) (*Z* isomer).

Anal. Calcd for $C_{16}H_{12}N_2S \cdot {}^1/_2H_2O$: C, 70.30; H, 4.79; N, 10.25. Found: C, 70.81; H, 4.20; N, 10.01.

(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)(2-fluorophenyl)-acetonitriles 3 (X = 2-F). Without separation of isomers the yield was 61%. Chromatography of the crude product consisting of about a 2:1 mixture of double-bond isomers using ethyl acetate/toluene (1:50) on silica gel initially afforded the *Z* isomer, which was recrystallized from MeOH: mp 158–160 °C; NMR ($CDCl_3$) δ 3.42 (2 H, apparent d, CH_2).

Anal. Calcd for $C_{16}H_{11}FN_2S$: C, 68.07; H, 3.93; N, 9.92. Found: C, 67.85; H, 3.86; N, 9.89.

Subsequent fractions gave the *E* isomer, which was recrystallized from MeOH: mp 138–140 °C; NMR ($CDCl_3$) δ 3.83 (2 H, s, CH_2).

Anal. Calcd for $C_{16}H_{11}FN_2S$: C, 68.07; H, 3.93; N, 9.92. Found: C, 68.27; H, 3.85; N, 10.03.

(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)(2-chlorophenyl)-acetonitrile (3, X = 2-Cl): recrystallized from MeOH (49%); mp 155–158 °C; NMR (Me_2SO-d_6) δ 3.27/3.87 (2 H, s, CH_2's of *Z*/*E* isomers, ca. 1:4 ratio), 9.17/9.92 (1 H, br s, NH's, ca. 4:1 ratio).

Anal. Calcd for $C_{16}H_{11}ClN_2S$: C, 64.32; H, 3.71; N, 9.38. Found: C, 64.07; H, 3.68; N, 9.30.

(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)[3-(trifluoromethyl)phenyl]acetonitrile (3, X = 3-CF_3): recrystallized from MeOH (63%); mp 142–145 °C; NMR δ (Me_2SO-d_6) 3.66/3.87 (2 H, s, CH_2's of *Z*/*E* isomers, ca. 1:3 ratio), 9.70/10.04 (1 H, br s, NH's, ca. 3:1 ratio).

Anal. Calcd for $C_{17}H_{11}F_3N_3S$: C, 61.44; H, 3.14; N, 8.45. Found: C, 61.38; H, 3.38; N, 8.41.

(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)(4-fluorophenyl)-acetonitrile (3, X = 4-F): recrystallized from MeOH (55%); mp 120–122 °C; NMR ($CDCl_3$) δ 3.75 (2 H, s, CH_2 of *E* isomer).

Anal. Calcd for $C_{16}H_{11}FN_2S$: C, 68.07; H, 3.93; N, 9.92. Found: C, 68.08; H, 3.94; N, 9.76.

(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)(4-methoxyphenyl)acetonitrile (3, X = 4-OCH_3): recrystallized from MeOH (64%); mp 151–153 °C; NMR (Me_2SO-d_6) δ 3.56/3.81 (2 H, s, CH_2's of *Z*/*E* isomers, ca. 3:4 ratio), 3.76/3.78 (3 H, s, OCH_3's of respective isomers), 9.27/9.84 (1 H, br s, NH's of respective isomers).

Anal. Calcd for $C_{17}H_{14}N_2OS$: C, 69.36; H, 4.79; N, 9.52. Found: C, 69.42; H, 4.76; N, 9.45.

2-(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)-2-phenylacetamides 4. The synthesis of the 4-chlorophenylacetamide adduct is representative with the exception of the *p*-methoxyphenyl analogue (vide infra). A 2.0-g (0.0067 mol) portion of *p*-chlorophenylacetonitrile adduct was stirred in 12 mL of concentrated H_2SO_4 containing 1 mL of H_2O for 2.5 h at room temperature. After cooling of the solution in an ice bath, addition of H_2O caused formation of a precipitate, which was collected and dried. Recrystallization from MeOH afforded 1.8 g (85%) of amide **4** (X = 4-Cl): mp 188–191 °C; NMR (Me_2SO-d_6) δ 3.25 (2 H, s, CH_2); UV (MeOH) max 340 nm (ε 21 300), 275 (17 600).

Anal. Calcd for $C_{16}H_{13}ClN_2OS$: C, 60.66; H, 4.14; N, 8.84. Found: C, 60.41; H, 4.18; N, 9.12.

2-(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)-2-phenylacetamide (4, X = H): recrystallized from MeOH (76%); mp 149–151 °C; NMR (Me_2SO-d_6) δ 3.24 (2 H, s, CH_2); UV (MeOH) max 339 nm (ε 15 400), 275.5 (12 200).

Anal. Calcd for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N, 9.92. Found: C, 68.07; H, 5.04; N, 9.78.

2-(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)-2-(2-fluorophenyl)acetamide (4, X = 2-F): recrystallized from MeOH (85%); mp 156–158 °C; NMR ($CDCl_3$) δ 3.20 (2 H, s, CH_2); UV

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(MeOH) max 338 nm (ε 22 600), 276 (19 600).

Anal. Calcd for $C_{16}H_{13}FN_2OS$: C, 63.98; H, 4.36; N, 9.33. Found: C, 63.88; H, 4.31; N, 9.24.

2-(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)-2-(2-chlorophenyl)acetamide (4, X = 2-Cl): recrystallized from MeOH (68%); mp 167–169 °C; NMR (Me_2SO-d_6) δ 3.02 (1 H, d, J = 15 Hz, HCH_a), 3.18 (1 H, d, J = 15 Hz, HCH_b); UV (MeOH) max 338.5 nm (ε 21 800), 275 (18 400).

Anal. Calcd for $C_{16}H_{13}ClN_2OS$: C, 60.66; H, 4.14; N, 8.84. Found: C, 60.55; H, 4.15; N, 8.75.

2-(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)-2-[3-(trifluoromethyl)phenyl]acetamide (4, X = 3-CF_3): recrystallized from MeOH (88%); mp 167–168 °C; NMR (Me_2SO-d_6) δ 3.25 (2 H, s, CH_2); UV (MeOH) max 338.5 nm (ε 22 400), 275 (18 800).

Anal. Calcd for $C_{17}H_{13}F_3N_2OS$: C, 58.28; H, 3.74; N, 8.00. Found: C, 58.49; H, 3.88; N, 7.98.

2-(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)-2-(4-fluorophenyl)acetamide (4, X = 4-F): recrystallized from MeOH (75%); mp 190–192 °C; NMR (Me_2SO-d_6) δ 3.28 (2 H, s, CH_2); UV (MeOH) max 338 nm (ε 19 900), 275 (15 500).

Anal. Calcd for $C_{16}H_{13}FN_2OS$: C, 63.98; H, 4.36; N, 9.33. Found: C, 63.94; H, 4.38; N, 9.23.

2-(2*H*-1,4-Benzothiazin-3(4*H*)-ylidene)-2-(4-methoxyphenyl)acetamide. A 5.0-g (0.016 mol) portion of the methoxyphenyl nitrile precursor was dissolved into 50 mL of a 3:1 mixture of H_2SO_4/HOAc, and the solution was stirred at ambient temperature for 5 h. The mixture was then cautiously poured into H_2O, and the aqueous solution was extracted three times with ethyl acetate. The combined extracts were washed with water and dried over $MgSO_4$. Solvent removal in vacuo from the filtered solution afforded an oil, which was triturated with ether to give 3.1 g (58%) of crystalline product: recrystallized from MeOH; mp 183–184 °C; NMR (Me_2SO-d_6) δ 3.22 (2 H, s, CH_2), 3.78 (3 H, s, OCH_3); UV (MeOH) max 275 nm (ε 14 600), 223 (19 100).

Anal. Calcd for $C_{17}H_{16}N_2O_2S$: C, 65.36; H, 5.20; N, 8.97. Found: C, 65.32; H, 5.16; N, 8.98.

4-Phenyl-5*H*-pyrido[3,4-*b*][1,4]benzothiazin-3(2*H*)-ones 6. Method A. The preparation of the 4-chlorophenyl derivative is representative. To 35 g (0.11 mol) of amide in 300 mL of DMF in a nitrogen atmosphere at room temperature was added 20 g (0.14 mol) of dimethylformamide diethyl acetal, and the reaction mixture was stirred at ambient temperature for 2 h. To this solution was then added 42 g (0.27 mol) of bis(dimethylamino)-methoxymethane (practical grade, 85%), and the reaction mixture was heated in a nitrogen atmosphere at 50–60 °C for 6 h. The cooled solution was then slowly added to 400 mL of H_2O with vigorous stirring, and the oil that separated eventually solidified and was collected. Trituration with a 200-mL portion of MeOH at room temperature followed by trituration with a 500-mL portion of boiling MeOH gave, after the bright yellow collected solid was washed with ethyl acetate and ether, 23.2 g (64%) of pyridone 6 (X = 4-Cl): recrystallized from DMF/H_2O; mp >300 °C; NMR (Me_2SO-d_6) δ 7.17 (1 H, s, pyridone H) ; UV (MeOH) max 290 nm (ε 13 400), 255.5 (27 600), 234.5 (22 100).

Anal. Calcd for $C_{17}H_{11}ClN_2OS$: C, 62.48; H, 3.39; N, 8.57. Found: C, 62.35; H, 3.43; N, 8.70.

4-Phenyl-5*H*-pyrido[3,4-*b*][1,4]benzothiazin-3(2*H*)-one (6, X = H): recrystallized from MeOH (42%); mp 266–271 °C; NMR (Me_2SO-d_6) δ 7.19 (1 H, s, pyridone H); UV (MeOH) max 293 nm (ε 9800), 257.5 (22 600), 233 (18 200).

Anal. Calcd for $C_{17}H_{12}N_2OS$: C, 69.84; H, 4.14; N, 9.58. Found: C, 70.16; H, 4.13; N, 9.80.

4-(2-Fluorophenyl)-5*H*-pyrido[3,4-*b*][1,4]benzothiazin-3(2*H*)-one (6, X = 2-F): recrystallized from DMF/H_2O (49%); mp >300 °C; NMR (Me_2SO-d_6) δ 7.21 (1 H, s, pyridone H); UV (MeOH) max 291 nm (ε 12 200), 255.5 (26 400), 233 (20 600).

Anal. Calcd for $C_{17}H_{11}FN_2OS$: C, 65.79; H, 3.57; N, 9.03. Found: C, 65.84; H, 3.65; N, 8.86.

4-(2-Chlorophenyl)-5*H*-pyrido[3,4-*b*][1,4]benzothiazin-3(2*H*)-one (6, X = 2-Cl): triturated with MeOH (37%); mp >300 °C; NMR (Me_2SO-d_6) δ 7.20 (1 H, s, pyridone H); UV (MeOH) max 290 nm (ε 13 400), 255.5 (27 600), 234.5 (22 100).

Anal. Calcd for $C_{17}H_{11}ClN_2OS$: C, 62.48; H, 3.39; N, 8.57. Found: C, 62.18; H, 3.54; N, 8.38.

4-[3-(Trifluoromethyl)phenyl]-5*H*-pyrido[3,4-*b*][1,4]-benzothiazin-3(2*H*)-one (6, X = 3-CF_3): triturated with MeOH (28%); mp 268–270 °C; NMR (Me_2SO-d_6) δ 7.21 (1 H, s, pyridone H); UV (MeOH) max 294 nm (ε 11 500), 257 (26 300), 235 (21 600).

Anal. Calcd for $C_{18}H_{11}F_3N_2OS$: C, 60.00; H, 3.08; N, 7.77. Found: C, 60.20; H, 3.06; N, 7.87.

4-Phenyl-5*H*-pyrido[3,4-*b*][1,4]benzothiazin-3(2*H*)-ones 6. Method B. The preparation of the 4-fluorophenyl derivative 6 (X = 4-F) via tricyclic pyrimidone precursor 7 (X = 4-F) is representative. To 0.23 g (0.000 77 mol) of amide 4 in 5 mL of DMF in a nitrogen atmosphere was added 0.22 g (0.0015 mol) of dimethylformamide diethyl acetal, and the reaction mixture was heated at 95 °C for $2^1/_2$ h. After cooling, the solution was diluted with water and the solid that formed was collected, affording 0.17 g (73%) of pale yellow product: recrystallized from DMF/H_2O; mp 255–258 °C; NMR (Me_2SO-d_6) δ 3.82 (2 H, s, CH_2), 8.86 (1 H, s, pyrimidone H); UV (MeOH) max 282 nm (ε 15 200), 262 (17 500), 223 (17 000).

Anal. Calcd for $C_{17}H_{11}FN_2OS$: C, 65.79; H, 3.57; N, 9.03. Found: C, 65.66; H, 3.54; N, 9.04.

Conversion of Pyrimidones 7 to Pyridones 6. The preparation of the 4-fluorophenyl derivative is representative. To 1.3 g (0.0042 mol) of pyrimidone 7 (X = 4-F) in 40 mL of DMF was added 2.5 g (0.0169 mol) of bis(dimethylamino)methoxymethane, and the reaction mixture was stirred at 55–60 °C in a nitrogen atmosphere overnight. The cooled reaction mixture was then diluted with 20 mL of H_2O, and the now-heterogeneous mixture was refluxed for 6 h. After cooling, the fluffy, pale yellow needles were collected, washed with ethyl acetate, and dried, affording 0.74 g (57%) of product: mp >300 °C; NMR (Me_2SO-d_6) δ 7.17 (1 H, s, pyridone H); UV (MeOH) max 282 nm (ε 15 200), 262 (17 500), 223.5 (17 000).

Anal. Calcd for $C_{17}H_{11}FN_2OS$: C, 65.79; H, 3.57; N, 9.03. Found: C, 65.72; H, 3.54; N, 9.21.

(4-Chlorophenyl)pyrimidone 7 (X = 4-Cl): recrystallized from DMF/H_2O (59%); mp 291–294 °C; NMR (Me_2SO-d_6) δ 3.79 (2 H, s, CH_2), 8.82 (1 H, s, pyrimidone H); UV (MeOH) max 286 nm (ε 15 800), 262 (19 400), 226 (20 000).

Anal. Calcd for $C_{17}H_{11}ClN_2OS$: C, 62.48; H, 3.39; N, 8.57. Found: C, 62.12; H, 3.66; N, 8.66.

(4-Methoxyphenyl)pyrimidone 7 (X = 4-OCH_3): recrystallized from DMF/H_2O (66%); mp 249–251 °C; NMR (Me_2SO-d_6) δ 3.78 (2 H, s, CH_2, and 3 H, s, OCH_3), 8.77 (1 H, s, pyrimidone H); UV (MeOH) max 257.5 nm (ε 13 900), 223.5 (13 700).

Anal. Calcd for $C_{18}H_{14}N_2O_2S$: C, 67.06; H, 4.38; N, 8.69. Found: C, 66.50; H, 4.42; N, 8.76.

(4-Chlorophenyl)pyridone 6 (X = 4-Cl): recrystallized from DMF/H_2O (82%); mp >300 °C; NMR (Me_2SO-d_6) δ 7.17 (1 H, s, pyridone H); UV (MeOH) max 257 nm (ε 27 400), 236 (21 600).

Anal. Calcd for $C_{17}H_{11}ClN_2OS$: C, 62.48; H, 3.39; N, 8.57. Found: C, 62.26; H, 3.30; N, 8.60.

(4-Methoxyphenyl)pyridone 6 (X = 4-OCH_3): recrystallized from DMF/H_2O (55%); mp >300 °C; NMR (Me_2SO-d_6) δ 3.82 (3 H, s, OCH_3), 7.16 (1 H, s, pyridone H); UV (MeOH) max 258 nm (ε 16 000), 228.5 (13 900).

Anal. Calcd for $C_{18}H_{14}N_2O_2S$: C, 67.06; H, 4.38; N, 8.69. Found: C, 66.77; H, 4.24; N, 8.72.

Acknowledgment. We thank Patricia Finnegan of our Physical Methodology Department for assistance with spectral interpretation and Patti Topp for typing the manuscript.