for the racemic β-lactam. The enantiomeric excess (ee) was determined to be ca. 14% through the use of the chiral shift reagent Eu(tfc)$_3$.[21,22] The shift reagent was added to an NMR sample until separation of the enantiotopic benzylic protons on C-4 of the β-lactam ring was observed. The relative areas under the peaks were then determined by integration.

(+)-1,4-Diphenyl-3-*N*-(benzoylamino)-3-methylazetidin-2-one (3b). The dianion from **1d** (0.993 g, 3 mmol) was allowed to react with **2a** (0.543 g, 3 mmol) to yield, after chromatography, 0.80 g (75%) of a white solid: mp 181–183 °C; $[\alpha]^{25}_D$ +0.57° (*c* 3.5, CH_2Cl_2). The spectral data was identical with that observed for the racemic β-lactam. The ee was observed to be ca. 4% by the method outlined above for **3a**.

(+)-*trans*-3-Methyl-1,3,4-triphenylazetidin-2-one (3c). The enolate generated from **1f** (1.44 g, 5 mmol) was allowed to react with **2a** (0.91 g, 5 mmol) to yield, after chromatography, 1.24 g (85%) of **3c** as a white solid: mp 167–169 °C; $[\alpha]^{25}_D$ +51.4° (*c* 3.5, CH_2Cl_2). Spectral data was identical with that observed for the racemic β-lactam. The ee was observed to be ca. 60% by the method outlined above for **3a**.

Attempted Resolution of Racemic 3c with Menthoxide. Lithium menthoxide was generated in 5 mL of THF from *n*-butyllithium (1.65 mL of a 1.57 N solution, 2 mequiv) and *l*-menthol (0.28 g, 1.8 mmol) at room temperature. To this stirred solution was added racemic **3c** (0.38 g, 1.2 mmol) as a THF solution (3 mL of THF) by using a syringe (upon addition of the β-lactam, the color changed from colorless to bright yellow). The reaction was stirred for 6 h at room temperature. It was worked up by being washed once with 10 mL of H_2O and once with 10 mL of saturated NaCl and then extracted with diethyl ether. The ethereal layer was dried ($MgSO_4$) and the solvent was removed in vacuo. After chromatography to remove the menthol, NMR and IR spectra confirmed that **3c** was the product, and polarimetry showed it to be racemic.

Control Experiment with Optically Active 3c. The above procedure was repeated with the exception that optically active **3c** ($[\alpha]^{25}_D$ +51.4° (*c* 3.5, CH_2Cl_2)) was used. After chromatography, NMR and IR spectra confirmed the presence of **3c**; $[\alpha]^{25}_D$ +49.1° (*c* 3.5, CH_2Cl_2).

(21) Tris[3-[(trifluoromethyl)hydroxymethylene]-*d*-camphorato]europium(III) derivative, available from Aldrich Chemical Co.
(22) This experiment was initially performed in these laboratories by Mr. David L. Turner.

Acknowledgment. We gratefully acknowledge financial support of this research by the National Institutes of Health (Grant No. GM 26268) and NIH Biomedical Research Funds administered by Texas A&M University.

Registry No. 1a, 774-40-3; **1b**, 74185-85-6; **1c**, 32619-69-5; **1d**, 74219-50-4; **1e**, 2510-99-8; **1f**, 32213-55-1; **1g**, 101-97-3; **1h**, 3289-28-9; **1i**, 97-62-1; **1j**, 1499-53-2; **2a**, 538-51-2; **2b**, 783-08-4; **2c**, 2362-79-0; **2d**, 2272-45-9; **2e**, 15485-32-2; **2f**, 889-37-2; **2g**, 3237-23-8; **2h**, 5918-68-3; **3a**, 74185-86-7; **3b**, 74185-87-8; *cis*-**3c**, 30358-30-6; *trans*-**3c**, 74185-88-9; **3d**, 16141-49-4; **3e**, 31492-21-4; **3f**, 5438-81-3; **3g**, 74185-89-0; **3h**, 74185-90-3; **3i**, 74185-91-4; **3j**, 74185-92-5; **3k**, 74185-93-6; **3l**, 69187-09-3; **3m**, 69187-10-6; **3n**, 34092-17-6.

Supplementary Material Available: Experimental procedures, spectral data, analytical data, and references for the β-lactams in Table I (4 pages). Ordering information is given on any current masthead page.

Syntheses of 1,2,4-Benzothiadiazine 1-Oxides and 1,2,4-Benzothiadiazines

Neville Finch,* Salvatore Ricca, Jr., and Lincoln H. Werner

Research Department, Pharmaceuticals Division, CIBA-GEIGY Corporation, Summit, New Jersey 07901

Ronald Rodebaugh

Analytical Research Services, CIBA-GEIGY Corporation, Ardsley, New York 10502

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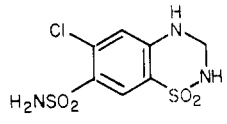
Reaction of ortho esters or dimethylformamide acetal with *o*-aminobenzenesulfinamides **9** gave 1,2,4-benzothiadiazine 1-oxides **6**. Reaction with 1 equiv of tributylphosphine provided the 1,2,4-benzothiadiazines **11**. Excess tributylphosphine caused rearrangement to the benzothiazoles **12**. A mechanism is proposed for this rearrangement via an intermediate such as **13**. The rearrangement of **13** on heating in benzene to an isomeric compound **16** provided additional support for this mechanism.

There is a wealth of literature on the 1,2,4-benzothiadiazine 1,1-dioxides[1] because of their utility as diuretics and antihypertensive agents, e.g., hydrochlorothiazide **1**[2] and diazoxide **2**.[3] However, there seems to be a dearth



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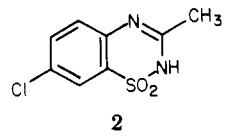
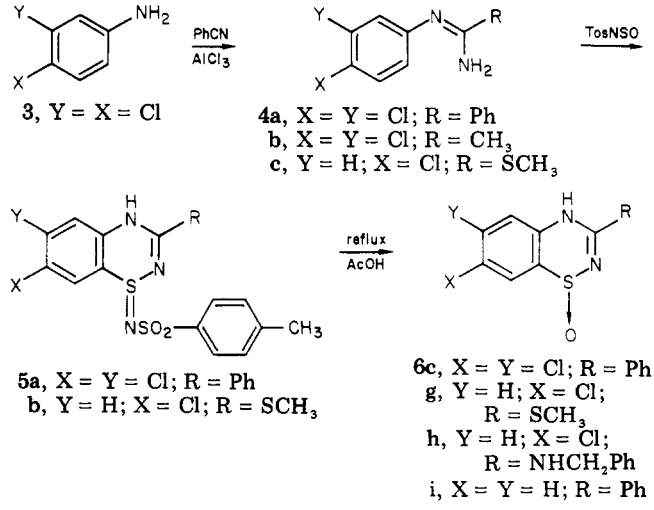


2

of work on the S^{II} and S^{IV} analogues, the 1,2,4-benzothiadiazines, and their *S*-oxides. Remarkably, there is only one paper to our knowledge describing a synthesis of 1,2,4-benzothiadiazine 1-oxides **6**[4] and two reports of the use of this synthesis.[5,11] A recent communication[6] described the formation of 7-chloro-3-phenyl-1,2,4-benzo-

Scheme I



3, Y = X = Cl

4a, X = Y = Cl; R = Ph
b, X = Y = Cl; R = CH_3
c, Y = H; X = Cl; R = SCH_3

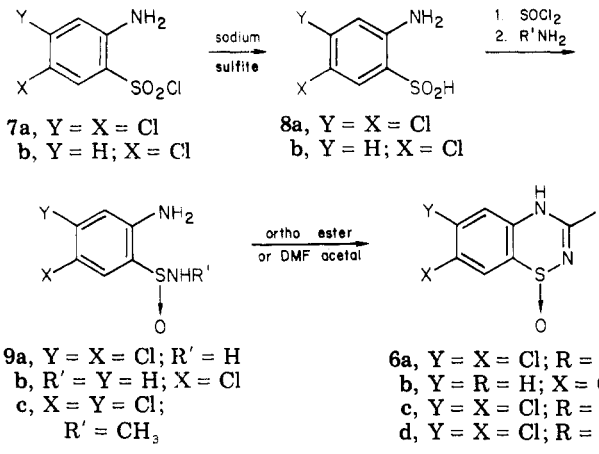
5a, X = Y = Cl; R = Ph
b, Y = H; X = Cl; R = SCH_3

6c, X = Y = Cl; R = Ph
g, Y = H; X = Cl; R = SCH_3
h, Y = H; X = Cl; R = $NHCH_2Ph$
i, X = Y = H; R = Ph

(1) Werner, L. H. In "Burger's Medicinal Chemistry", 4th ed.; Wolff, M. E., Ed; Wiley Interscience: New York, 1980; Part III, Chapter 40.
(2) Werner, L. H.; Halamandaris, A.; Ricca, Jr., S.; Dorfman, L.; deStevens, G. *J. Am. Chem. Soc.* **1960**, *82*, 1161.
(3) Topliss, J. G.; Konzelmann, L. M.; Shapiro, E. P.; Sperber, N.; Roth, F. E. *J. Med. Chem.* **1964**, *7*, 269.

0022-3263/80/1945-3416$01.00/0

Scheme II



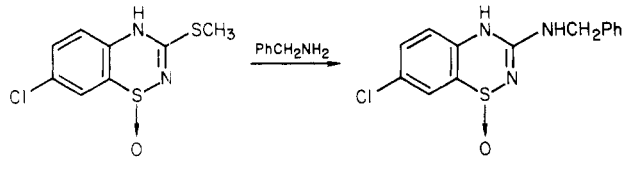
7a, Y = X = Cl
b, Y = H; X = Cl

8a, Y = X = Cl
b, Y = H; X = Cl

9a, Y = X = Cl; R' = H
b, R' = Y = H; X = Cl
c, X = Y = Cl; R' = CH_3

6a, Y = X = Cl; R = H
b, Y = R = H; X = Cl
c, Y = X = Cl; R = Ph
d, Y = X = Cl; R = CH_3

Scheme III



6g 6h

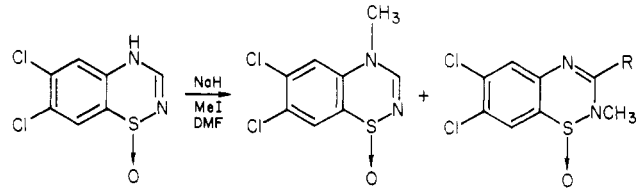
thiadiazine 1-oxide as a part of a structural proof.

The synthesis of Kresze[4] was successfully reproduced starting with *N*-phenylbenzamidine (Scheme I), but it failed with *N*-arylacetamidines. For the reasons outlined above, we were particularly interested in 1,2,4-benzothiadiazine 1-oxides **6** which were unsubstituted or had aliphatic substituents at the 3-position. We therefore developed an alternative synthesis which provided access to such compounds, e.g., compound **6d** (Scheme II). 3-Amino compounds were also described by Kresze and reported as being prepared by the standard procedure, but again no details were provided. In our hands they proved to be more accessible by displacement of methyl mercaptan from the 3-thiomethyl compound by the appropriate amine (Scheme III).

The alternative synthesis to the 1,2,4-benzothiadiazine 1-oxides **6**, which we have developed (Scheme II), starts from the 2-aminobenzenesulfonyl chlorides **7** which were utilized in 1,2,4-benzothiadiazine 1,1-dioxide syntheses. Reduction of the sulfonyl chlorides to the sulfinic acids **8** with sodium sulfite proceeded quantitatively.[7] The sulfinamides **9** were obtained via the sulfinyl chlorides and reaction with ammonia or amine. Conversion of the sulfinamides **9** to the 1,2,4-benzothiadiazine 1-oxides **6** could be accomplished by reaction with the appropriate ortho ester in the presence of *p*-toluenesulfonic acid or reaction with dimethylformamide dimethyl acetal.

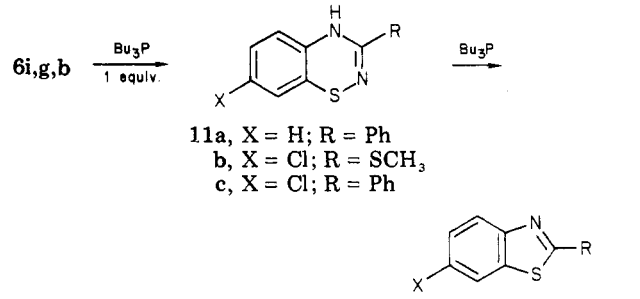
This synthesis permitted a specifically N-methylated compound to be prepared, i.e., compound **6e**. N-Methylation of the parent compound **6a** could then be studied (Scheme IV). A high yield of an approximately 1:2 mixture of two monomethylated products was obtained in which compound **6e** was the minor component. The mixture could be separated by preparative TLC. The

Scheme IV



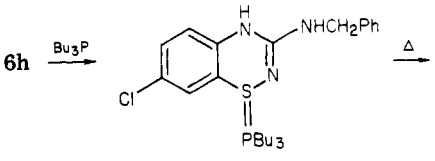
6a 10 6e, R = H
f, R = CH_3

Scheme V



11a, X = H; R = Ph
b, X = Cl; R = SCH_3
c, X = Cl; R = Ph

12a, X = H; R = Ph
b, X = Cl; R = N=PBu_3
c, X = Cl; R = H



13

12d (X = Cl; R = $NHCH_2Ph$) + Bu_3P=NH (**14**) and
12b + $PhCH_2NH_2$

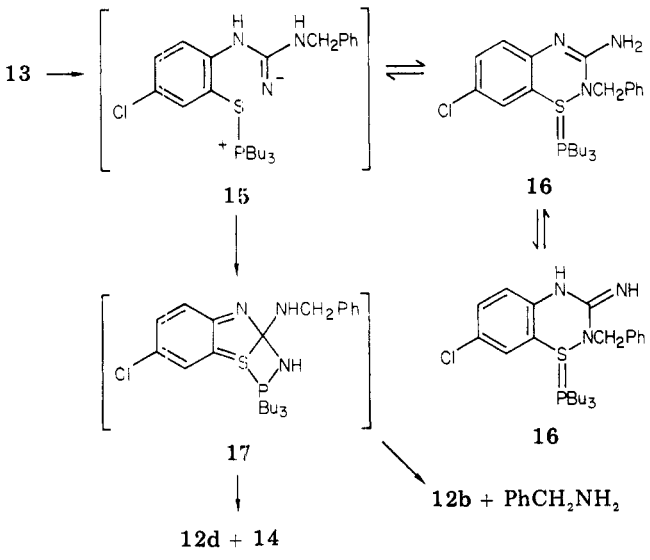
major component, compound **10**, was of some interest in that in the NMR spectrum in $CDCl_3$ the chemical shifts for the two aromatic protons were essentially identical with those of the starting material **6a** and different from those of the isomer **6e**. The finding has led us to favor the tautomeric structure analogous to compound **10** for the unsubstituted benzothiadiazines when they were in solution in aprotic solvents. Kresze favored the alternative tautomer analogous to compound **6e**. It may be predominant in protic solvents on the basis of UV spectral studies we carried out.

Finally we wished to provide a process for conversion of the benzothiadiazine 1-oxides **6** to the benzothiadiazines **11** (Scheme V). Attempts by Kresze[4] to reduce the benzothiadiazine 1-oxide **6** by using zinc/acetic acid or stannous chloride yielded benzothiazoles. Only with thionyl chloride did they achieve limited success. Reaction of compound **6i** with thionyl chloride effected deoxygenation, but chlorination of ring A also took place to yield **11c**.

Deoxygenation of the 1,2,4-benzothiadiazine 1-oxide **6i** occurred on brief reflux in benzene with 1 equiv of tributylphosphine, thereby providing the first synthesis of the ring-A-unsubstituted 1,2,4-benzothiadiazine **11a**. In the presence of excess tributylphosphine or if compound **11a** was subsequently reexposed to these reaction conditions, the product proved to be known 2-phenylbenzothiazole.[8] We presumed that nitrogen was being lost from the benzothiadiazine ring as tributylphosphinimine (**14**). Support for this view came from studying the effects of tributylphosphine on the thiomethyl compound **6g**

(4) Kresze, G.; Seyfried, C.; Treda, A. *Justus Liebigs Ann. Chem.* **1968**, *715*, 223–237.
(5) Markovskii, L. N.; Darmokhval, E. A. *Zh. Org. Khim.* **1973**, *9*, 644.
(6) Gilchrist, T. L.; Rees, C. V.; Vaughan, D. *J. Chem. Soc., Chem. Commun.* **1978**, 1049–1060.
(7) Muth, F. In "Methoden der Organischen Chemie (Houben-Weyl)", 4th ed.; Müller, E., Ed.; Georg Thieme Verlag: Stuttgart 1955; Vol. IX, pp 306–309.
(8) Bogert, M. T.; Abrahamson, E. J. *J. Am. Chem. Soc.* **1922**, *44*, 826.

Scheme VI



(Scheme V). One equivalent of tributylphosphine effected deoxygenation to the benzothiadiazine **11b**, but excess tributylphosphine yielded the benzothiazole **12b**, which retained the tributylphosphinimine moiety, expelling instead methyl mercaptan. In the cases where both pathways were possible by virtue of the nature of the leaving groups, mixtures of benzothiazoles resulted. Thus, compound **6b** yielded 6-chlorobenzothiazole (**12c**)[9] plus tributylphosphinimine (**14**) along with the benzothiazole **12b**, representing the product of the alternative pathway. A further insight into the mechanism was provided by the isolation of an intermediate **13** from the reaction of the 3-benzylamino compound **6h**. The structure of the intermediate **13** was assigned on the basis of the NMR spectrum. The marked downfield shift (>1 ppm) of the proton ortho to sulfur in compound **13** relative to the benzothiadiazine **11c** and the upfield shift of the proton para to sulfur suggest the presence of a polar peri S–P bond and an increased charge density on sulfur. Alternative structures involving pentacoordinate phosphorus or phosphorus bound to nitrogen do not adequately explain these chemical shift changes. Reflux of intermediate **13** in toluene under nitrogen transformed it cleanly into tributylphosphinimine (**14**),[10] equal amounts of the benzothiazoles **12d** and **12b**, and presumably benzylamine. A mechanism for this transformation is proposed (Scheme VI). Recently Rees[11] reported that the 1,2,4-benzothiadiazine **11a** on heating in benzene with triphenylphosphine yielded the benzothiazole **12a**. Triphenylphosphinimine was also identified via its *N*-tosyl derivative as a product of this reaction. Rees proposed, on the basis of the known reaction of trivalent phosphorus reagents with sulfenamides, that the initial attack of the triphenylphosphine was at the sulfur of the benzothiadiazine. Evidently the presence of a 3-benzylamino substituent rather than a 3-phenyl substituent stabilizes this initial adduct and permits isolation of an intermediate such as **13** in our case.

The ^{31}P NMR spectrum of the intermediate **13** in toluene was a single-line spectrum. When the solution was heated, a second line appeared at 1.75 ppm upfield. After 90 min, a 60:40 mixture of starting material and product resulted, and the appearance of a third species was just evident at 2.41 ppm upfield from the starting material. Neither of these materials was tributylphosphinimine, which was much further upfield (7.60 ppm). The relatively small changes in chemical shift suggested that the P–S environment was relatively little affected.[12]

On the basis of these ^{31}P NMR studies and a proton NMR study in C_6D_6 which showed a clean conversion of compound **13**, a preparative experiment was successfully carried out. The transformed material which was isomeric with **13** was isolated by preparative TLC. While the UV spectra of **13** and the transformation product differed in methanol, on addition of acid the UV spectra became very similar. This spectral similarity persisted if the solutions were then made basic. On the basis of TLC evidence, only a small amount of the intermediate **13** was transformed by this treatment. One may therefore conclude that the isomeric transformation product of **13** has the same chromophoric system. Structure **16** is therefore the most reasonable for this material. The tautomeric equilibrium for compound **16** seems to favor the endocyclic imine in protic media on the basis of the UV spectrum and the exocyclic imine in aprotic media on the basis of the NMR spectrum (Scheme VI). The obligatory intermediate for this transformation is therefore compound **15**, analogous to one of the intermediates proposed by Rees.[11] While the S–N bond cleavage is shown as being heterolytic, there is a possibility that it might occur homolytically. Racemization of optically active sulfinamides has been reported to occur via S–N bond homolysis.[13] The more speculative intermediate **17** is proposed rather than that favored by Rees[11] because of exclusive formation of tributylphosphine products bonded to NH rather than NCH_2Ph. It is clear, though, that additional studies are needed to precisely describe the transfer of the tributylphosphine moiety from sulfur to nitrogen.

Experimental Section

General Procedures. Melting points were determined in a Thomas-Hoover melting point apparatus and are uncorrected. NMR spectra were obtained on a Varian A60 spectrometer, IR spectra on a Perkin-Elmer 21 or 521 spectrophotometer, and mass spectra on an AEI MS902 spectrometer at 70 eV.

***N*-(3,4-Dichlorophenyl)benzamidine (4a).** 3,4-Dichloroaniline (**3**) (81 g, 0.5 mol) was well mixed with benzonitrile (51.5 g, 0.5 mol) in a beaker. With manual stirring, powdered anhydrous aluminum chloride (66.5 g, 0.5 mol) was added portionwise. The temperature of the mixture rose to approximately 100 °C. Addition of $AlCl_3$ was continued to maintain this temperature and took 45 min. The mixture was heated for 1 h in an oil bath following the addition to maintain an internal temperature of 100 °C. The mixture was then allowed to stand overnight at room temperature. The solid mass was crushed and slurried in water. The collected solids were then slurried in 50% NaOH. The resulting mixture was extracted with chloroform. The extracts were washed (water) and dried (Na_2SO_4), and the chloroform was removed in vacuo. The residue (61.2 g, 0.23 mol, 46%) crystallized. Further treatment of the insoluble material in the aqueous phase with additional 50% NaOH and chloroform extraction yielded additional material (64.2 g, 0.24 mol, 48%) which also crystallized on standing. A portion of this material (mp 105–109 °C) was recrystallized from ethyl acetate/hexane to give pure *N*-(3,4-dichlorophenyl)benzamidine (**4a**): mp 110–111 °C; NMR ($CDCl_3$) δ 7.96–7.58 (m, 2), 7.56–7.18 (m, 4), 7.03 (d, 1, J = 2.5 Hz), 6.77 (dd, 1, J = 8, 2.5 Hz), 4.95 (br s, 2, NH_2); IR (Nujol) 1610 (s), 1562 (s), 768 (m) cm^{-1}; mass spectrum, m/e 264 (M^+). Anal. Calcd for $C_{13}H_{10}Cl_2N_2$: C, 58.89; H, 3.80; N, 10.57. Found: C, 58.82; H, 3.84; N, 10.55.

(9) Takahashi, T.; Okada, T.; Ueda, Y., *Yakugaku Zasshi*, **1960**, *80*, 260–264.
(10) Birkhofer, L.; Kim, S. M. *Chem. Ber.* **1964**, *97*, 2100.
(11) Böhnisch, V. W.; Gilchrist, T. L.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2851–2854.
(12) We thank Dr. Steve Patt of Varian, Florham Park, NJ, for these spectra.
(13) Booms, R. E.; Cram, D. J. *J. Am. Chem. Soc.* **1972**, 5438–5446.

***N*-(6,7-Dichloro-3-phenyl-1,2,4-benzothiadiazin-1-ylidene)-*p*-toluenesulfonamide (5a).** Crude *N*-sulfinyl-*p*-toluenesulfonamide[4] (8.7 g, 0.040 mol) was dissolved with stirring in ethyl acetate (60 mL). *N*-(3,4-Dichlorophenyl)benzamidine (**4a**; 3.5 g, 0.13 mol) was added. The reddish amber solution became turbid on further stirring. It was allowed to stand overnight. The product **5a** (mp 202 °C dec) was collected, washed with ethyl acetate, and dried in vacuo: yield 5.7 g (0.012 mol, 94%); NMR (TFA) δ 11.43 (s,2), 8.20–7.10 (m, 11), 2.45 (s, 3); IR (Nujol) 1600 (s), 1530 (m), 1490 (s), 1308 (s), 1296 (s), 1285 (s), 1142 (s), 1084 (s), 944 (s) cm^{-1}; mass spectrum, *m/e* 463 (M^+). Anal. Calcd for $C_{20}H_{15}Cl_2N_3O_2S_2$: C, 51.72; H, 3.26; N, 9.05. Found: C, 51.82; H, 3.43; N, 9.22.

6,7-Dichloro-3-phenyl-1,2,4-benzothiadiazine 1-Oxide (6c) via Imine Hydrolysis. *N*-(6,7-Dichloro-1,2,4-benzothiadiazin-1-ylidine)-*p*-toluenesulfonamide (**5a**; 4 g, 8.6 mmol) was slurried in acetic acid (80 mL). The suspension was slowly heated to reflux in an oil bath during 90 min. After being refluxed for a few minutes, the reaction mixture was cooled. The suspended material collected, washed (water), and dried in vacuo. The residue **6c** (2.15 g, 6.9 mmol, 80%; mp 257 °C) was identical (mass, NMR, and IR spectra, TLC, and mixture melting point) with compound **6c** prepared via the ortho ester procedure described below.

***N*-[7-Chloro-3-(methylthio)-1,2,4-benzothiadiazin-1-ylidene]-*p*-toluenesulfonamide (5b).** *S*-Methyl-*p*-chlorophenylthiourea[14] (47.3 g, 0.236 mol) was dissolved in chloroform (50 mL), and a solution of *N*-sulfinyl-*p*-toluenesulfonamide[4] (128 g, 0.589 mol) in chloroform (130 mL) was added rapidly with stirring. The solution was refluxed, and SO_2 was evolved. The reaction mixture was allowed to stand overnight. The precipitate was collected, washed well with ethyl acetate, and dried to give **5b**: mp 190 °C; 63.4 g (0.158 mol, 67%); NMR (Me_2SO) δ 7.84–7.16 (m, 7), 2.37 (s, 3), 2.32 (s, 3); IR (Nujol) 1600 (m), 1548 (m), 1496 (s), 1310 (s), 1298 (s), 1188 (s), 1144 (s), 1084 (s), 934 (s) cm^{-1}. Anal. Calcd for $C_{15}H_{14}ClN_3O_2S_3$: C, 45.04; H, 3.53; N, 10.51. Found: C, 45.17; H, 3.61; N, 10.22.

2-Amino-4,5-dichlorobenzenesulfinic Acid (8a). 2-Amino-4,5-dichlorobenzenesulfonyl chloride (**7a**;[15] 104.2 g, 0.40 mol) was added portionwise during 2 h to a well-stirred solution of anhydrous sodium sulfite (100.8 g, 0.80 mol) in water (400 mL). The temperature of the reaction mixture was maintained below 40 °C by ice cooling and the pH around 9.5 (8–9.5) by dropwise addition of a 50% NaOH solution (36 mL). The reaction mixture was filtered through Filtercel. The filtrate was made strongly acidic (70% H_2SO_4) and cooled, and the precipitate of the sulfinic acid **8a** (100.4 g) was collected and dried in vacuo: mp 175 °C dec; NMR (Me_2SO) δ 7.68 (s, 3 exchangeable), 7.60 (s, 0.5), 7.47 (s, 0.5), 7.02 (s, 0.5), 6.98 (s, 0.5); mass spectrum, *m/e* 225 (M^+); TLC (silica gel GF; $CHCl_3$/MeOH/Py/2-propanol/H_2O, 50:20:5:10:20) single spot at 3.0 cm (sulfonic acid spotted on same plate at 4.0 cm). Anal. Calcd for $C_6H_5Cl_2NO_2S$: C, 31.87; H, 2.23; N, 6.20. Found: C, 31.78; H, 2.06; N, 6.16.

2-Amino-5-chlorobenzenesulfinic acid (8b). 2-Amino-5-chlorobenzenesulfonyl chloride (**7b**;[16] (10 g, 0.044 mol) was reduced by aqueous sodium sulfite in an analogous manner to give 2-amino-5-chlorobenzenesulfinic acid (**8b**): mp 171–173 °C dec; 8.4 g (0.044 mol, 100%); NMR (Me_2SO) δ 7.50 (s, 3, exchangeable), 7.37 (br s, 1.3), 7.20 (d, 0.7, J = 3 Hz), 6.88 (s, 0.7), 6.75 (s, 0.3); IR (Nujol) 1627 (m), 1614 (m), 1573 (m), 1055 (s), 1025 (s), 950 (s) cm^{-1}; TLC (silica gel GF; EtAc/MeOH/NH_4OH, 17:3:3) single spot at 5.0 cm. Anal. Calcd for $C_6H_6ClNO_2S$: C, 37.60; H, 3.16; N, 7.31. Found: C, 37.25; H, 3.05; N, 7.35.

2-Amino-4,5-dichlorobenzenesulfinamide (9a). 2-Amino-4,5-dichlorobenzenesulfinic acid (**8a**; 5.65 g, 0.025 mol) was slurried in dry (molecular sieves) 1,2-dimethoxyethane (75 mL). Thionyl chloride (4.5 g, 0.037 mol) was added dropwise. After 15 min the sulfinic acid dissolved. The reaction was stirred for 1 h. It was then added rapidly with stirring to liquid NH_3 (125 mL). The ammonia was allowed to evaporate overnight. The residue was partitioned between water and ethyl acetate. The ethyl acetate phase was washed (water) and dried ($MgSO_4$) and the solvent removed in vacuo. The residue (7.35 g, theory 5.6 g) solidified. The crude sulfinamide **9a** was used for subsequent reactions. A sample triturated with ether and dried in vacuo had the following: mp 158 °C dec; NMR (Me_2SO) δ 7.53 (s, 1), 6.97 (s, 1), 6.32 (s, 2, NH_2), 5.77 (s, 2, NH_2); TLC (silica gel GF; EtAc/MeOH/NH_4OH, 17:3:3) single spot at 10.5 cm (acid **8a** at 5.0 cm.) Anal. Calcd for $C_6H_6Cl_2N_2OS$: C, 32.01; H, 2.69; N, 12.45. Found: C, 32.43; H, 2.82; N, 12.36.

2-Amino-5-chlorobenzenesulfinamide (9b). 2-Amino-5-chlorobenzenesulfinic acid (**8b**) was reacted in 1,2-dimethoxyethane with thionyl chloride. The product was reacted with excess liquid ammonia as described above for the sulfinamide **9a**. The crude sulfinamide **9b** was obtained in quantitative yield from the sulfinic acid by this procedure. It was used as is for subsequent reactions: TLC (silica gel GF; EtAc/MeOH/NH_4OH, 17:3:3) single spot 11.0 cm (the acid **8b** ran at 3.0 cm).

6,7-Dichloro-3-phenyl-1,2,4-benzothiadiazine 1-Oxide (6c) via the Ortho Ester Synthesis. The crude sulfinamide **9a** (1 g, 4.4 mmol) was slurried in ethyl acetate (4 mL). Trimethyl orthobenzoate (3 mL, Aldrich Chem. Co.) and *p*-toluenesulfonic acid (100 mg) were added. The mixture was placed in a preheated oil bath (105–110 °C) for 90 min. A solution resulted, and the solvent was evaporated. The residue was redissolved in ethyl acetate. The solution was washed (water) and dried ($MgSO_4$), and the ethyl acetate was removed in vacuo. The residue (0.5 g) was refluxed briefly in ethanol (10 mL). It was collected, washed with ethanol, and dried in vacuo at 95 °C. The residue was 6,7-dichloro-3-phenyl-1,2,4-benzothiadiazine 1-oxide (**6c**): mp 262 °C dec; NMR (TFA) δ 8.17 (s, 1), 8.12 (s, 1), 8.05–7.55 (m, 5); IR (Nujol) 1594 (m), 1586 (m), 1534 (m) 1446 (s), 1032 (s), 942 (m), 888 (m), 688 (s) cm^{-1}; TLC (silica gel GF; EtAc/MeOH/NH_4OH, 75:15:10) single spot. Anal. Calcd for $C_{13}H_8Cl_2N_2OS$: C, 50.17; H, 2.59; N, 9.00. Found: C, 49.94; H, 2.56; N, 8.88.

6,7-Dichloro-1,2,4-benzothiadiazine 1-Oxide (6a). The crude sulfinamide **9a** (1 g, 4.4 mmol) slurried in ethyl acetate (4 mL) was reacted with triethyl orthoformate (3 mL) and *p*-toluenesulfonic acid (100 mg) and was worked up in an analogous manner as for compound **6c**. The product was **6a**: mp 238 °C dec; 900 mg (3.8 mmol, 87%); NMR (Me_2SO) δ 8.13 (s, 1), 8.10 (s, 1), 7.53 (s, 1); IR (Nujol) 1596 (m), 1584 (s), 1552 (m), 1450 (s), 1330 (s), 1020 (s), 760 cm^{-1}; TLC (silica gel GF; EtOAc/MeOH/NH_4OH, 17:3:3) single spot. Anal. Calcd for $C_7H_4Cl_2N_2OS$: C, 35.76; H, 1.71; N, 11.92. Found: C, 35.51; H, 1.70; N, 11.77.

7-Chloro-1,2,4-benzothiadiazine 1-Oxide (6b). The crude sulfinamide **9b** (18.7 g, 0.098 mol) was slurried in ethyl acetate (50 mL). Trimethyl ortho formate (50 mL) and *p*-toluenesulfonic acid (2 g) were added. The mixture was immersed in an oil bath at 105–110 °C for 1 h and cooled, and the solids were collected. The material collected was washed well with ethyl acetate and water. The material (mp 199–201 °C; 7.1 g, 0.035 mol, 36%) was recrystallized from ethyl acetate/ethanol to give the product **6b**: mp 220–222 °C; 6.4 g (0.032 mol, 32%); NMR (Me_2SO) δ 8.10 (s, 1), 7.88–7.27 (m, ABX, 3); IR (Nujol) 1594 (m), 1546 (m), 1496 (m), 1338 (s), 1027 (s), 824 (s) cm^{-1}; mass spectrum, *m/e* 200 (M^+). Anal. Calcd for $C_7H_5ClN_2OS$: C, 41.90; H, 2.51; N, 13.96. Found: C, 41.68; H, 2.74; N, 14.27.

6,7-Dichloro-3-methyl-1,2,4-benzothiadiazine 1-Oxide (6d). The crude sulfinamide **9a** (39.7 g, 0.176 mol) slurried in ethyl acetate (120 mL) was reacted with trimethyl orthoacetate (56 mL) and *p*-toluenesulfonic acid (4 g), and the mixture was worked up in an analogous manner as for compound **6c**. The product was **6d**: mp 275 °C dec; 9.5 g (0.038 mol, 22%); NMR (Me_2SO δ 8.07 (s, 1), 7.45 (s, 1), 2.33 (s, 3); IR 1622 (m), 1600 (m), 1570 (s), 1030 (s), 928 (m) cm^{-1}; TLC (silica gel GF; $CHCl_3$/MeOH, 9:1) single spot separable from the dioxide. Anal. Calcd for $C_8H_6Cl_2N_2OS$: C, 38.57; H, 2.43; N, 11.25. Found: C, 38.65; H, 2.52; N, 11.29.

2-Amino-4,5-dichloro-*N*-methylbenzenesulfinamide (9c). The sulfinamide **9c** was prepared via the crude sulfinyl chloride derived from the sulfinic acid **8a**, thionyl chloride, and excess methylamine in a manner analogous to that described for the sulfinamide **9a**. For 2-amino-4,5-dichloro-*N*-methylbenzenesulfinamide (**9c**): mp 147–148 °C; NMR (Me_2SO) δ 7.47 (s, 1), 6.98 (s, 1), 6.60–6.22 (br q, 1), 5.83 (br s, 1), 2.35 (d, 3, J = 6 Hz, J = 0 Hz after D_2O); IR (Nujol) 1620 (s), 1580 (m), 1540 (m), 1258

(14) Crowther, A. F.; Curd, F. H. S.; Rose, F. L. *J. Chem. Soc.* **1948**, 586–593.
(15) Heindel, N. D.; Hoko, C. C.; Birres, R. B.; Merkel, J. R. *J. Med. Chem.* **1972**, *15*, 118–120.
(16) Lanyi, G. Hungarian Patent Pat. 144772, 1969; *Chem. Abstr.* **1969**, *71*, 218862.

(m), 1064 (s), 1048 (s), 1032 (s), 926 (s) cm^{-1}; mass spectrum m/e 238 (M^+). Anal. Calcd for $C_7H_8Cl_2N_2OS$: C, 35.16; H, 3.37; N, 11.72. Found: C, 35.37; H, 3.48; N, 11.64.

6,7-Dichloro-2-methyl-1,2,4-benzothiadiazine 1-Oxide (6e). The sulfinamide **9c** (2.4 g, 0.010 mol) was slurried in ethyl acetate (20 mL) and dimethylformamide dimethyl acetal (3.6 g, 0.030 mol) added. The mixture was immersed in an oil bath at 110 °C for 45 min with stirring. The ethyl acetate was allowed to evaporate. The residue crystallized upon cooling of the mixture. The crystalline mass was triturated with ether. The crystals were collected, washed well with ether, and air-dried. They proved to be the benzothiadiazine 1-oxide **6e**: mp 188–190 °C; 0.4 g (1.36 mmol, 14%). This was recrystallized from aqueous methanol: mp 190–191 °C; NMR (Me_2SO δ 8.28 (s, 1), 7.95 (s, 1), 7.83 (s, 1), 3.68 (s, 3); IR (Nujol) 1590 (m), 1560 (s), 1342 (m), 1266 (s), 1120 (m), 1096 (s), 1074 (m), 914 (m) cm^{-1}; mass spectrum, m/e 248 (M^+). Anal. Calcd for $C_8H_6Cl_2N_2OS$: C, 38.57; H, 2.43; N, 11.25. Found: for C, 38.65; H, 2.62; N, 11.24.

6,7-Dichloro-2,3-dimethyl-1,2,4-benzothiadiazine 1-Oxide (6f). The sulfinamide **9c** (1.95 g, 8.15 mmol) slurried in ethyl acetate (8 mL) was reacted with trimethyl orthoacetate (5 mL) and *p*-toluenesulfonic acid (200 mg), and the mixture was worked up in an analogous manner as for compound **6c**. The product **6f** was more soluble and needed cooling and scratching to precipitate from the reaction mixture. The precipitate was collected, washed with ether, and air-dried. The product **6f** had the following: mp 128–129 °C; NMR (Me_2SO) δ 8.27 (s, 1), 7.73 (s, 1), 3.70 (s, 3), 2.52 (s, 3); IR (Nujol) 1600 (m), 1570 (s), 1536 (m), 1450 (s), 1384 (s), 1304 (s), 1282 (m), 1114 (s), 864 (m) cm^{-1}; mass spectrum, m/e 262 (M^+). Anal. Calcd for $C_9H_8Cl_2N_2OS$: C, 41.08; H, 3.06. Found: C, 41.07; H, 3.04.

Methylation of 6,7-Dichloro-1,2,4-benzothiadiazine 1-Oxide (6a). 6,7-Dichloro-1,2,4-benzothiadiazine 1-oxide (**6a**; 2.4 g, 0.01 mol) was slurried in dry (molecular sieves) DMF (12 mL) under N_2. A 57% NaH dispersion in mineral oil (420 mg, 0.01 mol) was added with stirring. Within 30 min a solution resulted. MeI (1.6 g, 0.011 mol) was added and the mixture stirred at room temperature for 4 h. A solid separated. This solid (1.7 g) was collected, washed, and dried. The filtrate was concentrated to dryness in vacuo to yield an oil (2.6 g). Trituration with ethanol yielded more solid material (0.48 g). The filtrate was diluted with water and extracted (ethyl acetate). The extracts were washed (water) and dried (Na_2SO_4), and the ethyl acetate was removed in vacuo. The solid residue (0.35 g) was combined with the other solids (2.53 g, 0.01 mol, 100%). This material was approximately a 1:2 mixture of the methylated isomer **6e** and **10**. Separation could be achieved by fractional crystallization from ethanol or by preparative TLC. A portion (1.35 g) of the material was chromatographed on preparative silica gel GF TLC plates eluted by $CHCl_3/Et_3N$. Narrow cuts were made of the principal bands, and these were eluted. The resulting material was crystallized from ethanol.

The faster moving material was the 2-methyl compound **6e**: 350 mg; mp 191–192 °C. It was identical (TLC, NMR, and IR) with the 6,7-dichloro-2-methyl-1,2,4-benzothiadiazine 1-oxide (**6e**) obtained from the dimethylformamide acetal reaction described above. The slower moving material was the 4-methyl compound **10**: 150 mg; mp 268–270 °C; NMR (Me_2SO) δ 8.12 (s, 1), 8.05 (s, 1), 7.78 (s, 1), 3.67 (s, 3); IR (Nujol) 1600 (m), 1568 (m), 1394 (m), 1058 (m), 1046 (s), 762 (m), 710 (m) cm^{-1}. Anal. Calcd for $C_8H_6Cl_2N_2OS$: C, 38.57; H, 2.43; N, 11.25. Found: C, 38.68; H, 2.58; N, 11.28.

7-Chloro-3-(methylthio)-1,2,4-benzothiadiazine 1-Oxide (6g). *N*-[7-Chloro-3-(methylthio)-1,2,4-benzothiadiazin-1-ylidene]-*p*-toluenesulfonamide (**5b**; 5 g, 0.125 mol) was heated to 100 °C in acetic acid (200 mL) with a Glass-col mantle. Heating was continued for 30 min following complete solution. The acetic acid was removed in vacuo and the residue triturated with ethyl acetate. The solids (2.4 g) were collected, washed well with ethanol, and dried. The resulting material was **6g**: 2.2 g (8.9 mmol, 71%); mp 217 °C dec; NMR (Me_2SO) δ 7.88 (d, 1, J = 2 Hz), 7.69 (dd, 1, J = 9, 2 Hz), 7.32 (d, 1, J = 9 Hz), 2.60 (s, 3); IR (Nujol) 1600 (s), 1540 (s), 1500 (s), 1184 (s), 1022 (s), 836 (s) cm^{-1}. Anal. Calcd for $C_8H_7ClN_2OS_2$: C, 38.94; H, 2.86; N, 11.36. Found: C, 39.32; H, 3.03; N, 11.05.

7-Chloro-3-(benzylamino)-1,2,4-benzothiadiazine 1-Oxide (6h). The 3-methylthio compound **6g** (1.85 g, 7.5 mmol) was slurried in water (35 mL), and benzylamine (2.4 g, 22.5 mmol) was added. The mixture was refluxed, and a solution resulted. On continued heating a precipitate developed, and after 2 h of reflux, heating was halted. The reaction mixture was allowed to stand overnight. It was made acidic (10 mL of 2 N HCl), and the solid was collected, washed (water), and dried. This material (1.7 g) was recrystallized from aqueous ethanol to give the 3-benzylamino compound **6h**: mp 246 °C dec; 1.15 g (3.76 mmol, 50%); NMR (Me_2SO) 7.61 (dd, 1, J = 9, 2 Hz), 7.43 (d, 1, J = 2 Hz), 7.32 (s, 5), 7.16 (d, 1, J = 9 Hz), 4.53 (d, 2, J = 6 Hz); IR (Nujol) 1646 (m), 1614 (m), 1580 (s), 1562 (m), 1496 (s), 1018 (s), 998 (s), 974 (m), 820 (m), 726 (s) cm^{-1}. Anal. Calcd for $C_{14}H_{12}ClN_3OS$: C, 54.99; H, 3.96; N, 13.74. Found: C, 54.52; H, 4.20; N, 13.70.

3-Phenyl-1,2,4-benzothiadiazine (11a). The benzothiadiazine 1-oxide[4] **6i** (1.15 g, 6.2 mmol) was slurried in benzene (30 mL) under N_2. Tributylphosphine (1.25 g, 6.2 mmol) was added. The mixture was brought to reflux rapidly by immersion in an oil bath at 105–110 °C. The refluxing was continued for a few minutes. A solution resulted. The solution was washed with water, dried (Na_2SO_4), and concentrated in vacuo. The residue (2.9 g) was chromatographed on preparative silica gel GF TLC plates developed with $CHCl_3$. The main fraction was eluted by methanol from the silica gel and was recrystallized from aqueous ethanol to give 3-phenyl-1,2,4-benzothiadiazine (**11a**): mp 120–121 °C; 1 g (4.4 mmol, 71%); NMR (Me_2SO) δ 9.25 (s, 1, NH), 7.83–7.25 (m, 5), 7.0–6.5 (m, 4); IR (Nujol) 1596 (m), 1568 (m), 1494 (m), 1416 (s), 1308 (m), 756 (s), 682 (s) cm^{-1}; mass spectrum, m/e 226 (M^+). Anal. Calcd for $C_{13}H_{10}N_2S$: C, 69.00; H, 4.45; N, 12.38. Found: C, 68.81; H, 4.49; N, 11.99.

2-Phenylbenzothiazole (12a). 3-Phenyl-1,2,4-benzothiadiazine (**11a**; 50 mg, 0.2 mmol) was refluxed under N_2 in benzene (2 mL) with tributylphosphine (0.1 mL). The progress of the reaction was monitored by TLC. (Silica gel GF developed by $CHCl_3$: compound **12a**, 8.0 cm; compound **11a**, 9.5 mm). After 70 min the reaction mixture was poured into water. The benzene layer was separated and dried (Na_2SO_4) and the solvent removed in vacuo. The residue proved to be 2-phenylbenzothiazole (**12a**, mp 117 °C) identical (IR, NMR, and mass spectra, TLC, and mixture melting, point) with material prepared by the literature procedure.[6]

7-Chloro-3-(methylthio)-1,2,4-benzothiadiazine (11b). The benzothiadiazine 1-oxide **6g** (950 mg, 3.85 mmol) was slurried in benzene (20 mL) under N_2. Tributylphosphine (780 mg, 3.85 mmol) was added, and the mixture was brought rapidly to reflux by immersion in an oil bath at 105–110 °C. At reflux a clear solution resulted. Heating was continued for approximately 2 min. The reaction mixture was poured into water. The benzene layer was separated, dried (Na_2SO_4), and concentrated to dryness in vacuo. The residue (1.5 g) was chromatographed on preparative silica gel GF TLC plates developed with $CHCl_3$. Two principal fractions were eluted with methanol. The slower moving fraction was an oil (1.19 g) consisting mainly of the phosphorane **12b**. The faster moving fraction crystallized; mp 150–157 °C dec. It was the desired benzothiodiazine **11b** (141 mg, 0.61 mmol, 16%). The analytical sample was obtained by recrystallization from aqueous ethanol: mp 168–169 °C: NMR (Me_2SO) δ 9.35 (s, 1 NH), 6.68 (dd, 1, J = 8.5, 2 Hz), 6.4 (d, 1, J = 2 Hz), 6.23 (d, 1, J = 8.5 Hz), 1.98 (s, 3); IR (Nujol) 1590 (m), 1550 (m), 1450 (s), 1144 (m), 802 (m) cm^{-1}; mass spectrum, m/e 230 (M^+). Anal. Calcd for $C_8H_7ClN_2S_2$: C, 41.64; H, 3.06; N, 12.14. Found: C, 42.17; H, 3.09; N, 12.26.

Reaction of 7-Chloro-3-(methylthio)-1,2,4-benzothiadiazine 1-Oxide (6g) with Excess Tributylphosphine. The benzothiadiazine 1-oxide **6g** (2 g, 8 mmol) was slurried in toluene (40 mL) under N_2. Tributylphosphine (3.2 g, 16 mmol) was added. The mixture was brought to rapid reflux by immersion in an oil bath at 120–125 °C. The mixture was refluxed for 5 min. A clear amber solution resulted. The toluene was removed in vacuo. The residue was dissolved in ethanol/water (1:1) on a steam bath. When the mixture cooled, the product **12b** separated (1.8 g, 4.7 mmol, 58%). It was recrystallized from aqueous ethanol: mp 108–109 °C; NMR (Me_2SO) δ 7.64 (br s, 1), 7.22 (br s, 2), 2.4–1.8 (m, ~6), 1.8–1.1 (m, ~12), 1.1–0.65 (br t, 9); IR (Nujol) 1584 (w), 1450 (br vs), 1217 (s), 956 (m), 806 (m) cm^{-1}; mass spectrum, m/e 384 (M^+). Anal. Calcd for $C_{19}H_{30}ClN_2PS$: C, 59.28; H, 7.86; N,

7.28. Found: C, 59.22; H, 8.07; N, 7.01.

Reaction of 7-Chloro-1,2,4-benzothiadiazine 1-Oxide (6b) with Tributylphosphine in Benzene. The benzothiadiazine 1-oxide **6b** (500 mg, 2.5 mmol) was slurried in benzene (10 mL) under N_2. Tributylphosphine (500 mg, 2.5 mmol) was added and the mixture refluxed for 24 h. The resulting solution was washed (water) and dried (Na_2SO_4), and the benzene was removed in vacuo. The residue (750 mg) was chromatographed on preparative silica gel GF plates developed with $CHCl_3$. The main fraction, eluted by methanol, crystallized [mp 43–44 °C (aqueous ethanol) (lit.[9] mp 43–44 °C)] and proved to be 6-chlorobenzothiazole (**12c**): NMR (Me_2SO) δ 9.4 (s, 1), 8.27 (d, 1, J = 2.5 Hz), 8.07 (d, 1, J = 8.5 Hz), 7.52 (dd, J = 8.5, 2.5 Hz); IR (Nujol) 1580 (m), 1088 (m), 872 (m), 850 (m), 838 (m), 826 (s), 800 (s), 750 (m) cm^{-1}; mass spectrum m/e 169 (M^+). Anal. Calcd for C_7H_4ClNS: C, 49.56; H, 2.38; N, 8.26. Found: C, 49.69; H, 2.61; N, 8.02.

In Toluene. The benzothiadiazine 1-oxide (**6b** (400 mg, 2 mol) was slurried in toluene under N_2. Tributylphosphine (809 mg, 4 mmol) was added. The mixture was refluxed for 20 min to form a solution. A sample was removed for GC analysis and was run on Chrom W with a 5% OV-17 stationary phase at 210–300 °C. The products were identified by comparison with authentic samples; the percentages were based on total volatiles injected. Unsilylated, the products were the phosphorane **12b** (1.13 min, 28%), the benzothiazole **12c** (2.77 min, 16%), $Bu_3P{=}O$ plus $Bu_3P{=}NH$ (**14**) (5.37 min, 46%), and starting material **6b** (23.76 min, 5%). Silylation permitted separation of $Bu_3P{=}O$ and $Bu_3P{=}NH$ as the N-silyl compound. The relative amounts of each were 10:3. Tributylphosphinimine (**14**) was prepared by the procedure of Birkhofer.[10]

Reaction of 7-Chloro-3-(benzylamino)-1,2,4-benzothiadiazine 1-Oxide (6h) with Tributylphosphine. A 4.6-g (0.15 mol) sample of **6h** was slurried in toluene (90 mL) under N_2. Tributylphosphine (9.1 g, 0.045 mol) was added. The mixture was immersed in an oil bath at 125–130 °C for 1 h. A slight exotherm was evident soon after refluxing commenced. An amber solution resulted. When the mixture cooled, a small amount (100 mg) of insoluble material was removed by filtration. The filtrate was concentrated in vacuo. The residue was triturated with hexane (3 × 50 mL). The residue was then crystallized with ethanol/water (1:1). The crystals of the phosphorane **13** (3.9 g, 0.0079 mol, 53%) had a melting point of 157–158 °C. An analytical sample was prepared by recrystallization from aqueous ethanol: mp 158–159 °C; NMR ($CDCl_3$) δ, 9.47 (br s, 1, NH), 7.72 (d, 1, J = 2.1 Hz), 6.84 (d, 1, J = 8.1 Hz), 6.61 (dd, 1, J = 8.1, 2.1 Hz), 6.22 (q, 1, NH), 4.49 (d, 2, J = 5.7 Hz), 2.07 (br m, 6), 1.48 (m, 12), 0.93 (t, 9); mass spectrum, m/e 491 (M^+); UV (MeOH) λ_{max} 250 nm (ϵ 22720), 286 (12380), 324 (4080); after being made acidic λ_{max} 272 nm (ϵ 13270), 294 (10740), 304 (10460); after acidic solution made basic λ_{max} 232 nm (ϵ 30710), 284 (18630). Anal. Calcd for $C_{26}H_{39}ClN_3PS$: C, 63.46; H, 7.99; N, 8.54. Found: C, 63.06; H, 8.14; N, 8.85.

Thermal Fragmentation of the Thiophosphorane 13. The thiophosphorane **13** (800 mg, 1.6 mmol) was refluxed in toluene (20 mL) under N_2 for 3 h. TLC on silica gel GF eluted by $CHCl_3$/ethyl acetate (4:1) showed by use of appropriate reference samples that the reaction was complete. Only a trace of the starting material **13** (at 2.00 cm) remained. The mixture consisted principally of the two benzothiazoles, **12d** (7.5 cm) and **12b** (10.0 cm), in approximately equal amounts. A trace of another material (at 11 cm), presumably tributylphosphinimine (**14**) was evident. This analysis was confirmed by GC on Chromosorb W (HP) with a 5% OV-17 stationary phase at 210–300 °C (20 °C/min). Tributylphosphinimine (**14**) could be positively identified (4.0-min retention time).

When the mixture was allowed to stand overnight, crystals of the 2-(benzylamino)-6-chlorothiazole (**12d**; 110 mg, 0.4 mmol, 25%) separated and were collected: mp 207–208 °C: NMR (Me_2SO) δ 8.58 (br s, 1, NH), 7.80 (m, 1), 7.53 (br s, 7), 4.62 (br s, 2); IR (Nujol) 1612 (s), 1564 (m), 1540 (m), 1346 (s), 812 (s) cm^{-1}; mass spectrum, m/e 274 (M^+). Anal. Calcd. for $C_{14}H_{11}ClN_2S$: C, 61.19; H, 4.04; N, 10.20. Found: C, 61.47; H, 4.11; N, 10.29.

The filtrate was concentrated to dryness. The residence (700 mg) was separated by preparative TLC (silica gel GF eluted by $CHCl_3$). The main fraction (130 mg, 21%) was characterized (NMR, IR, and mass spectra and C, H, and N analysis) and proved to be identical with the benzothiazole **12b** described above.

Isomerization of the Thiophosphorane 13. The thiophosphorane **13** (500 mg, 1.02 mmol) was refluxed in benzene (20 mL) for 17 h. By TLC (silica gel GF eluted by $CHCl_3$/ethyl acetate, 4:1). The thiophosphane **13** was almost completely transformed. The benzene was removed in vacuo. The residue was separated by preparative TLC. The main fraction was eluted (MeOH), redissolved in $CHCl_3$, filtered, and concentrated to dryness. The residue was the oily isomeric thiophosphorane **16**: 300 mg (60%); NMR ($CDCl_3$) δ 7.28 (br s, 7), 7.00 (dd, 1, J = 2, 8 Hz), 6.74 (d, 1, J = 8 Hz), 4.54 (s, 2), 2.50–0.70 (br t, 27); IR (film) 3420, 1570, 1532, 1438 cm^{-1}; UV (MeOH) λ_{max} 282 nm (ϵ 8570); after being made acidic λ_{max} 250 nm (sh, ϵ 12370), 294 (4860), 303 (4850); after acidic solution made basic λ_{max} 227 nm (ϵ 22990), 286 (14870); mass spectrum, m/e 491 (M^+). Anal. Calcd for $C_{26}H_{39}ClN_3PS$: C, 63.46; H, 7.99; N, 8.54. Found: C, 62.81; H, 7.95; N, 8.23.

The thiophosphorane **13** was dissolved in toluene. This sample in a Varian 200-MHz NMR instrument tuned to ^{31}P locked to C_6D_6 had a one-line spectrum at 36.271 ppm relative to H_3PO_4. On heating for 90–95 min at 60 °C, a 60:40 ratio of two peaks developed at 36.271 and 34.522 ppm relative to H_3PO_4. A tiny peak was evident at 33.859 ppm. Tributylphosphinimine in benzene had a one-line spectrum at 26.925 ppm.

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Registry No. 3, 95-76-1; **4a**, 23557-81-5; **5a**, 74063-11-9; **5b**, 74063-12-0; **6a**, 74063-13-1; **6b**, 74063-14-2; **6c**, 74063-15-3; **6d**, 74063-16-4; **6e**, 74063-17-5; **6f**, 74063-18-6; **6g**, 74063-19-7; **6h**, 74063-20-0; **6i**, 4826-05-5; **7a**, 36110-12-0; **7b**, 22737-08-2; **8a**, 74063-21-1; **8b**, 14687-99-1; **9a**, 74063-22-2; **9b**, 74063-23-3; **9c**, 74063-24-4; **10**, 74063-25-5; **11a**, 74063-26-6; **11b**, 74063-27-7; **12a**, 883-93-2; **12b**, 74063-28-8; **12c**, 2942-10-1; **12d**, 61249-37-4; **13**, 74063-29-9; **14**, 57831-27-3; **16** amine, 74063-30-2; **16** imine, 74063-31-3; benzonitrile, 100-47-0; N-sulfinyl-p-toluenesulfonamide, 4104-47-6; S-methyl-p-chlorophenylthiourea, 39536-21-5; trimethyl orthobenzoate, 707-07-3; triethyl orthoformate, 122-51-0; trimethyl orthoformate, 149-73-5; trimethyl orthoacetate, 1445-45-0; benzylamine, 100-46-9.