[Chem. Pharm. Bull.]
[32(7)2571—2590(1984)]

Non-stereospecific Ring Expansion Reactions of Benzothiazoline Sulfoxides¹⁾

HIROSHI SHIMIZU, NORIHIRO UEDA, TADASHI KATAOKA,
and MIKIO HORI*

Gifu College of Pharmacy, 6-1, Mitahora-higashi
5-chome, Gifu 502, Japan

(Received October 24, 1983)

The stereochemistry of novel ring expansions of benzothiazoline sulfoxides to benzothiazines by reaction with acetic anhydride was examined. Reaction of *trans*-3-acetyl-2-ethyl-2-methylbenzothiazoline 1-oxide with acetic anhydride afforded 4-acetyl-3-ethylidene-2,3-dihydro-4*H*-1,4-benzothiazine and 4-acetyl-3-ethyl-4*H*-1,4-benzothiazine, which are the products expanded in the direction of the substituent *cis* to the sulfoxide moiety, and 4-acetyl-2-methyl-3-methylidene-2,3-dihydro-4*H*-1,4-benzothiazine and 4-acetyl-2,3-dimethyl-4*H*-1,4-benzothiazine, which are the products expanded in the opposite direction (*trans*). Similar results were also obtained from the reaction of the sulfoxides, *trans*-4-acetyl-2-benzyl-2-methylbenzothiazoline 1-oxide, and *cis*- and *trans*-3-acetyl-2-ethoxycarbonylmethyl-2-methylbenzothiazoline 1-oxides, with acetic anhydride. Thus, it was confirmed that this ring expansion is non-stereospecific and quite different from the similar ring transformation of penicillin sulfoxides to cephalosporins. The major factor in this non-stereospecificity was found to be an easy cleavage of the C₂-S bond of the benzothiazoline ring due to electronic effects of the nitrogen atom at the β -position to the sulfur atom in comparison with the ring expansions of related six-membered benzothiazine sulfoxides and thiochroman sulfoxides.

Keywords—ring expansion; benzothiazine sulfoxide; 1,3-benzothiazine; 1,4-benzothiazine; stereospecificity; acetic anhydride

In our earlier papers,²⁾ we reported a novel ring expansion of benzothiazoline sulfoxides **1** to benzothiazines **7**, **8**. We also discussed in those papers several possible mechanisms (paths a, b and c in Chart 1) for the ring expansion, but could not decide which is correct because of lack of any evidence at that stage. Path a begins with a 2,3-sigmatropic rearrangement of hydrogen of the 2-alkyl group, whose configuration relative to the sulfoxide should be *cis*, and gives a sulfenic acid intermediate **2**, which is then acetylated by acetic anhydride to give the second intermediate **4**. The sulfenic anhydride intermediate **4** leads to the immonium ion **5** by recyclization with the loss of acetate ion. Collapse of the immonium ion **5** leads to **7** by deacetylation in the *exo*-direction as well as **8** by deacetylation in the *endo*-direction. This mechanism is stereospecific and is generally accepted for the similar reaction, as seen in the transformation of penicillin sulfoxides to cephalosporins (Morin rearrangement).³⁾ Path b involves initial acetylation of oxygen of the sulfoxide with acetic anhydride, forming an intermediate **3**, followed by S-C₂ bond cleavage with β -hydrogen abstraction to give the sulfenic anhydride **4**. In path c, direct S-C₂ bond cleavage of the intermediate **3** occurs due to the participation of the lone electron pairs on the nitrogen atom at the 3-position to form an intermediate **6** which leads to the intermediate **4**. In the intermediate **3**, the stereochemistry of the sulfoxide may be lost by pyramidal inversion on the sulfonium center, and the intermediate **6** apparently loses the stereochemistry of the sulfoxide because of direct ring opening. If path b or c is the dominant mechanism in the above ring expansion, the products expanded in the direction of the substituent *trans* to the sulfoxide might also be produced, indicating that the reaction is non-stereospecific. This is quite different from the case of the

Chart 1

path a mechanism.

In order to elucidate the mechanism involved in the formation of benzothiazines, we examined in detail the reaction of some benzothiazoline sulfoxides having two different substituents at the C_2 -position with acetic anhydride, and obtained unambiguous experimental evidence supporting path c. We also carried out the reaction of related cyclic sulfoxides, 1,4- and 1,3-benzothiazine sulfoxides, with acetic anhydride to elucidate the factors affecting the non-stereospecificity in the ring expansions of benzothiazoline sulfoxides.

Results and Discussion

Ring Expansions of 2,2-Disubstituted 3-Acetylbenzothiazoline 1-Oxides

The required new benzothiazoline 1-oxides, 9 and 14 were synthesized by the conventional method reported in our previous paper^{2b)} and the separation of the *cis* and *trans* isomers was carried out by fractional crystallization or column chromatography. The determination of the configuration of the sulfoxides was done mainly by proton nuclear magnetic resonance ($^1\text{H-NMR}$) spectral analysis according to the previous paper^{2b)} (experimental section). The results of the reaction of 3-acetylbenzothiazoline 1-oxides with acetic anhydride are summarized in Table I. Refluxing *trans*-3-acetyl-2-ethyl-2-methylbenzothiazoline 1-oxide (9) in acetic anhydride for 1.5 h produced four benzothiazines, 10 (29%),

TABLE I. Reactions of 3-Acetylbenzothiazoline 1-Oxides with Acid Anhydride

Sulfoxides	Reaction conditions	Products (Yields (%))
9	Reflux Ac ₂ O	10 (28.7)	11 (15)	12 (25.3)	13 (6.9)
14	Reflux Ac ₂ O	15 (34.6)	16 (5.2)	17 (22.9)	18 (8.7)
19	Reflux Ac ₂ O	20 (41.9)	21 (42)	22 (3)
23	Reflux Ac ₂ O	20 (25.8), 21 (23), 22 (17)
24	Reflux Ac ₂ O	25 (39.3)
26	0—25°C (CF ₃ CO) ₂ O	27 (32)
28	0—25°C (CF ₃ CO) ₂ O	29 (38)			
19	0—25°C (CF ₃ CO) ₂ O	21 (25.8), 22 (15.8)			

11 (15%), 12 (25%) and 13 (7%). From the reaction of *trans*-3-acetyl-2-benzyl-2-methylbenzothiazoline 1-oxide (14), similar results were obtained, affording four ring-expanded products, 15 (35%), 16 (5%), 17 (23%) and 18 (9%). Compounds 10, 11, 15 and 16 are the products expanded in the direction of the substituents (methyl groups of 9 and 10) *cis* to the sulfoxide moiety. On the other hand, compounds 12, 13, 17 and 18 are the products expanded in the direction of the substituents (ethyl group of 9, benzyl group of 14) *trans* to the sulfoxide oxygen. The ratio of the products ring-expanded in the two directions is *ca.* 4:3 in both sulfoxides 9 and 14. These results indicate that the ring expansions proceeded equally

with either the *cis*- or the *trans*-sulfoxide, and the reactions are non-stereospecific. Non-stereospecificity of the ring expansion was also observed in the case of *trans*-3-acetyl-2-ethoxycarbonylmethyl-2-methylbenzothiazoline 1-oxide (**23**), as shown in Table I. Although the *cis*-sulfoxide **19** gave the products **20** and **21** expanded in the direction of the *cis*-ethoxycarbonylmethyl group in a total yield of 84%, together with the product **22** expanded in the opposite direction in only 3% yield, the *trans*-sulfoxide **23** gave **20** and **21** (total yield of 49%), which are the products expanded in the *trans* direction, and 17% yield of **22** expanded in the *cis* direction. This result shows that the ring expansion proceeds in the direction of the substituent having more acidic protons if the acidity of protons in the two substituents is very different. *trans*-3-Acetyl-2-methylbenzothiazoline 1-oxide (**24**) also afforded a ring-expanded product **25** in 39% yield.

Next, in order to examine the epimerization of the sulfoxides under the reaction conditions used, we tried to observe other isomers of the sulfoxides in the course of the reaction by thin-layer chromatography and $^1\text{H-NMR}$ spectral analysis. No isomer was observed in the cases of the sulfoxides **14** and **24** under these reaction conditions. In the case of the sulfoxides **19** and **23**, it was quite difficult to observe the isomers under reflux conditions since they reacted completely within *ca.* 10 min. Therefore, these sulfoxides were heated at 80°C in acetic anhydride, and after half of the sulfoxides had reacted we checked the isomerization. However, no isomer was observed in either case.

We tried the ring expansion of the sulfoxides with trifluoroacetic anhydride at 0–25°C, where thermally induced epimerization or reaction of the sulfoxides may not occur. Treatment of 3-acetyl-2,2-dimethyl- (**26**) or *trans*-3-acetyl-2-methyl-2-phenylbenzothiazoline 1-oxide (**28**) with trifluoroacetic anhydride at 0–25°C caused ring expansion to afford the benzothiazine **27** or **29** in 32 or 38% yield, respectively (Table I). Moreover, stirring of **19** in trifluoroacetic anhydride yielded two ring-expansion products, **21** and **22**, in yields of 26 and 16%, respectively. These results indicate that acid anhydrides act as strong initiators of the ring opening of the benzothiazoline ring.

Based on the above results, it became apparent that the ring expansion of ben-

Chart 2

zothiazoline sulfoxides to benzothiazines is non-stereospecific and therefore proceeded through path b or c in Chart 1.

Ring transformation of penicillin sulfoxides to cephalosporins can be regarded as a ring expansion of the thiazoline skeleton, and it is quite well-known that the reaction is stereospecific.³⁾ Morin *et al.*⁴⁾ reported that a similar ring transformation also occurred in 2,2-dimethyl-1-thiochroman 1-oxide (**30**), as shown in Chart 2. We next examined the stereospecificity of this ring transformation of thiochroman sulfoxide using 2-benzyl-2-methyl-1-thiochroman 1-oxide (**31**) and 1-benzyl-1-methyl-2-thiochroman 2-oxide (**38**). The *trans*-sulfoxide **31** was prepared as a sole stereoisomer by addition of benzyl bromide to the anion of *cis*-2-methyl-1-thiochroman 1-oxide⁴⁾ (generated by treatment with lithium diisopropylamide in THF) (Chart 3). The *trans*-sulfoxide **38** was synthesized by *m*-chloroperbenzoic acid (MCPBA) oxidation of the 2-thiochroman **37** prepared through four steps starting from 2-thianaphthylum perchlorate⁵⁾ as shown in Chart 3.

On heating under reflux in xylene in the presence of *p*-toluenesulfonic acid, both the sulfoxides **31** and **38** gave the products expanded only in the direction of the methyl group *cis* to the sulfoxide moiety, namely, **32** (27.1%) and **33** (20.4%) from **31**, and **39** (43.2%) and **40** (51.7%) from **38**; these results indicate that the ring expansion in these systems is stereospecific (Chart 3). The structures of the products **32**, **33**, **39** and **40** were determined on the basis of the spectral data in comparison with those of the analogous benzothiepine derivatives reported by Morin *et al.*⁴⁾ Upon refluxing in acetic anhydride for 45 min, the sulfoxide **38** underwent a normal Pummerer-type rearrangement to give **36** in 43% yield with no ring-expansion product.

Ring Expansion of Benzothiazine Sulfoxides

As described above, acid anhydride-induced ring expansion of benzothiazoline sulfoxides

i) LDA-PhCH₂Br, ii) *p*-TsOH-xylene, iii) MeMgI, iv) SO₂Cl₂-HClO₄,
v) PhCH₂MgCl, vi) 10% Pd-C(H₂), vii) MCPBA

Chart 3

is non-stereospecific, and it may be regarded as a characteristic reaction of the benzothiazoline skeleton. It seems reasonable to consider that this non-stereospecificity may result from easy cleavage⁶⁾ of the C₂-S bond in the thiazoline ring due to the participation of the lone electron pairs on the nitrogen atom at the 3-position of benzothiazoline 1-oxide (path c). To confirm this hypothesis, the ring expansions of related cyclic sulfoxides containing a nitrogen atom should be examined, and the following two kinds of benzothiazine sulfoxides were selected: i) 1,4-benzothiazine 1-oxides, in which direct electronic effects of the nitrogen atom on the cleavage of the C₂-S bond leading to ring expansion are blocked, since one methylene linkage is introduced between the sulfur and nitrogen atoms, ii) 1,3-benzothiazine 1-oxides which have nitrogen and sulfur atoms in the same relative positions (1 and 3) as those in the benzothiazoline ring. Moreover, these six-membered ring structures are useful to examine whether the non-stereospecificity is attributed to five-membered ring structure.

A. Ring Expansion of 1,4-Benzothiazine 1-Oxides

Syntheses of several 1,4-benzothiazine 1-oxides required for the studies were achieved by the route shown in Chart 4. Treatment of *o*-aminobenzenethiol with α -bromopropionic acid or α -bromophenylacetic acid in xylene afforded the 3-oxo-1,4-benzothiazine **41** or **42** in 83 or 53% yield, respectively, and the product was methylated to give **43** or **44** in the yield of 89.4 or 99%, respectively. Compound **41** was led to **45** by treatment with benzyl bromide after stirring with lithium diisopropylamide. Compounds **41**, **43**, **44** and **45** were reduced with lithium aluminum hydride in THF to the 1,4-benzothiazines **46**, **47**, **48** and **49** in high yields, and these products were acetylated with acetic anhydride to afford the *N*-acetyl-1,4-benzothiazines **50**, **51**, **52** and **53**. The *N*-acetyl-1,4-benzothiazines were oxidized with 1 eq of MCPBA to yield the corresponding sulfoxides **54**, **55**, **56** and **57**.

The sulfoxides synthesized as above are expected to have two configurational isomers.

i) R-CHCO₂H (R=Me, Ph), ii) LDA-THF, iii) MeI or PhCH₂Br,
 iv) LiAlH₄-THF, v) Ac₂O, vi) MCPBA

Chart 4

TABLE II. Aromatic Solvent-Induced Shifts (ASIS) in the ^1H -NMR Signals of 1,3- and 1,4-Benzothiazine 1-Oxide Derivatives

Sulfoxides	<i>trans</i> or <i>cis</i> (Me to S-O)	ppm of Me in the solvent		ASIS ($\delta_{\text{CDCl}_3} - \delta_{\text{C}_6\text{D}_6}$)	$\Delta_{\text{trans}}/\Delta_{\text{cis}}$
		CDCl_3	C_6D_6		
54	<i>trans</i> (54b)	1.51	1.04	0.47	1.18
	<i>cis</i> (54a)	1.34	0.94	0.40	
55	<i>trans</i>	1.30	0.95	0.35	1.30
	<i>cis</i>	1.25	0.98	0.27	
56	<i>trans</i> (56b)	1.86	1.50	0.36	1.33
	<i>cis</i> (56a)	1.68	1.36	0.27	
71	<i>trans</i> ^{a)}				
	<i>cis</i> (62a)	2.18	1.73	0.45	
72	<i>trans</i> (63b)	1.79	1.27	0.52	1.11
	<i>cis</i> (63a)	1.70	1.23	0.47	

a) Not obtained.

^1H -NMR spectral analysis or TLC indicated the presence of two isomers in **54**, **56** and **57**. Except in the case of **56**, the separation of the isomers by PLC on silica gel was unsuccessful. The configurational assignments of *cis-trans* stereoisomers were performed by ^1H -NMR spectral analysis, especially of the aromatic solvent-induced shifts (ASIS) in benzene of the signals of the 2-methyl group adjacent to the sulfoxide. ASIS studies have been widely used⁷⁾ in configurational assignments of *cis-trans* stereoisomers of cyclic sulfoxides having a methyl group at a neighboring carbon atom, and show a large shielding relative to an inert solvent (chloroform) of the C-methyl group *trans* to the oxygen. Our results are summarized in Table II. This assignment was also in good accordance with the retention times on TLC, in which the isomer more sterically hindered at the sulfoxide oxygen has the shorter retention time.⁷⁾

Refluxing of *trans*-4-acetyl-2-methyl-2-phenyl-2,3-dihydro-4*H*-1,4-benzothiazine 1-oxide (**56a** having the methyl group *cis* to the sulfoxide oxygen) in acetic anhydride for 1.5 h afforded a ring-expansion product **59** in 26% yield together with 4-acetyl-2-acetoxymethyl-2-phenyl-2,3-dihydro-4*H*-1,4-benzothiazine (**60**) in 52% yield. On the other hand, the *cis*-sulfoxide (**56b** having the methyl group *trans* to the sulfoxide oxygen) was unaffected under the same reaction conditions. This stereospecific reaction can be explained only in terms of a mechanism involving the sulfenic acid **58** as a first intermediate formed by thermal 2,3-sigmatropic rearrangement of **56a**, similar to the mechanism proposed for the ring transformation of penicillin sulfoxides, as shown in Chart 5. The *cis*-sulfoxide **56b** was epimerized in small amounts to the *trans*-isomer **56a** on refluxing in xylene for 7 h or in acetic anhydride for 1.5 h, which suggested the possibility of the ring expansion of the *cis*-sulfoxide on prolonged heating. This was confirmed by the finding that when refluxed for 6 h in acetic anhydride **56b** also gave **60** and **59** in 20.7 and 13.5% yields, respectively. Treatment of **59** with *p*-toluenesulfonic acid in refluxing benzene for 30 min yielded **61** with the loss of acetic acid. However, addition of a few drops of concentrated sulfuric acid caused the ring expansion of **60** to give **61**, possibly *via* the episulfonium ion intermediate **62**. On refluxing in xylene in the presence of *p*-toluenesulfonic acid, **56a** gave a complex mixture containing a small amount of **61**, which was identified by ^1H -NMR spectral analysis. The structure of **61** was determined mainly on the basis of ^1H -NMR spectral data. One of the C_2 -protons of **61** is coupled to the C_4 -proton with an allylic coupling constant of $J=2.3$ Hz, while the other C_2 -proton is not

Chart 5

coupled to the C_4 -proton. It was reported⁸⁾ that an allylic coupling constant takes the maximum value when the dihedral angle between the C-H bond and double bond is 90° and the minimum value when the angle is 0° or 180° . Inspection of a Dreiding model of **61** shows that the dihedral angle of one of the C_2 -protons and the C_4 -proton is approximately 90° and that of the other C_2 -proton and the C_4 -proton is nearly 0° , and thus the J value (2.3 Hz) seems consistent with the expected value for this structure. Further, the Dreiding model excluded the isomeric benzothiazepine structure having a double bond between positions 2 and 3, for which the dihedral angle between each of the C_2 -protons and the C_4 -proton is nearly 45° . Treatment of 4-acetyl-2,2-dimethyl-2,3-dihydro-4*H*-1,4-benzothiazine 1-oxide (**55**) with refluxing acetic anhydride afforded **63** in 66.6% yield. On refluxing in acetic

anhydride, both **54a** and **54b** were converted into **65** and **66** by normal Pummerer-type rearrangement *via* the intermediate **64**. These results are quite different from those in the case of 3-acetyl-2-methylbenzothiazoline 1-oxide (**24**).

B. Ring Expansion of 1,3-Benzothiazine 1-Oxides⁹⁾

1,3-Benzothiazine 1-oxides were synthesized as shown in Chart 6. Reaction of thioalicylamide¹⁰⁾ with acetophenone or ethyl methyl ketone in the presence of *p*-toluenesulfonic acid afforded 4-oxo-1,3-benzothiazine **67** or **68** in 72.4 or 98.5% yield, respectively. Compounds **67** and **68** were methylated with dimethyl sulfate to give the *N*-methyl-4-oxo-1,3-benzothiazines **69** and **70** in 54 and 91% yields, respectively; these products were easily led to the corresponding sulfoxides **71** and **72** by oxidation with MCPBA. In the synthesis of **69**, compound **74** was isolated as a by-product in 11% yield, presumably by the base-catalyzed β -elimination of the sulfonium ion **73** which might be formed *in situ* by methylation of **69** with excess dimethyl sulfate as shown in Chart 6.

¹H-NMR spectra showed only one isomer in **71**, but two isomers in **72**. The stereostructures were determined by ASIS studies as for 1,4-benzothiazine 1-oxides. The results are given in Table II together with the results for 1,4-benzothiazine 1-oxides.

trans-2,3-Dimethyl-2-phenyl-4-oxo-2,3-dihydro-1,3-benzothiazine 1-oxide (**71**) was refluxed in acetic anhydride for 2 h to give ring-expanded products, 4-methyl-3-phenyl-5-oxo-4,5-dihydro-1,4-benzothiazepine (**75**, 32%) and 2-acetyl-4-methyl-3-phenyl-5-oxo-4,5-dihydro-1,4-benzothiazepine (**76**, 39.6%) together with a reductive product (**69**, 5.3%) as shown in Chart 7. Unfortunately, the reaction of the corresponding *cis*-sulfoxide could not be carried out since we could not synthesize the *cis*-sulfoxide by the oxidation of **69** with MCPBA as described above. Therefore, we investigated the reaction of *trans*-2-ethyl-2,3-dimethyl-4-oxo-2,3-dihydro-1,3-benzothiazine 1-oxide (**72a**) having two different alkyl groups at the 2-position with acetic anhydride to obtain four ring-expanded products, 3-ethyl-4-methyl-5-oxo-4,5-dihydro-1,4-benzothiazepine (**77**, 10.3%), 3-ethylidene-4-methyl-5-oxo-2,3,4,5-tetrahydro-1,4-benzothiazepine (**78**, 25%), 2-acetoxyethylidene-3-ethylidene-4-methyl-5-oxo-

i) MeCOR-*p*-TsOH, ii) NaH-DMF, iii) Me₂SO₄, iv) MCPBA

Chart 6

Chart 7

2,3,4,5-tetrahydro-1,4-benzothiazepine (**79**, 23.4%) and 2,4-dimethyl-3-methylene-5-oxo-2,3,4,5-tetrahydro-1,4-benzothiazepine (**80**, 10.3%) (Chart 7). Compounds **77**, **78** and **79** are the products expanded in the direction of the methyl group *cis* to the sulfoxide, while compound **80** is the product expanded in the opposite direction (ethyl group *trans* to the sulfoxide). On the other hand, when the sulfoxide **72a** was refluxed in benzene in the presence of a catalytic amount of *p*-toluenesulfonic acid, two ring-expanded products, **77** and 2,3,4-trimethyl-5-oxo-4,5-dihydro-1,4-benzothiazepine (**81**), were obtained in yields of 15 and 20.7%, respectively. These results show that the ring expansion occurred non-stereospecifically. However, it was found that the sulfoxide was easily epimerized to a mixture of *cis*- and *trans*-sulfoxides in the ratio of 1 : 1 when refluxed in acetic anhydride for 30 min or in xylene for 25 min. This observation indicates that the loss of stereospecificity may be attributed to epimerization of the sulfoxide before the ring opening.

It has been established that penicillin sulfoxide is in thermal equilibrium with the sulfenic acid, partly based on the evidence that on refluxing a solution of penicillin sulfoxide in benzene containing deuterium oxide, deuterium is incorporated into the 2-methyl group.¹¹⁾ This technique was applied to the sulfoxide **72a**. When a solution of **72a** in xylene containing deuterium oxide was refluxed for 3 h, no deuterium incorporation was observed in the recovered **72a** by ^1H -NMR and mass spectroscopy. This result shows that the sulfoxide **72a** is

Chart 8

not in thermal equilibrium with the corresponding sulfenic acid. Therefore, it is reasonable to consider that the ring expansion reaction of **72a** proceeded *via* the mechanism involving the acetoxysulfonium ion intermediate **82**, followed by ring opening just as in the case of benzothiazoline sulfoxides, as shown in Chart 8. Compound **76** may result from acetylation of the intermediate **83**, followed by addition of the sulfenyl group to the substituted double bond. Compound **79** may be produced *via* the intermediate **84** formed by enol acetylation of the 2-acetylated benzothiazepine (R = Et) corresponding to **76**.

In conclusion, it was clarified that the ring expansion of benzothiazoline sulfoxides to benzothiazines is a non-stereospecific reaction, in which acetic anhydride acts as a strong initiator. The non-stereospecificity arises from the easy cleavage of the C₂-S bond of the thiazoline ring due to the electronic effects of the nitrogen atom at the β -position (path c), on the basis of the results obtained with related cyclic sulfoxides, 1,3- and 1,4-benzothiazine sulfoxides. Ring expansion of 1,4-benzothiazine sulfoxides is stereospecific, and hence the reaction begins with 2,3-sigmatropic rearrangement of the sulfoxides by a mechanism similar to that proposed for the ring expansion of penicillin sulfoxides.

Experimental

Melting points were determined with a Yanagimoto micro melting point apparatus, and are uncorrected. Infrared (IR) absorption spectra were determined on a JASCO IRA-1 infrared spectrometer. ¹H-NMR spectra were taken on a Hitachi R-20B spectrometer, and chemical shifts are given in the δ (ppm) scale with tetramethylsilane as the internal standard (s, singlet; d, doublet; t, triplet; m, multiplet). Mass spectra (MS) were recorded on a JEOL JMSD-300 spectrometer with a JMA 2000 on-line system at 70 eV. Thin-layer chromatography (TLC) was performed on pre-coated Kieselgel 60 F₂₅₄ plates (Merck).

2-Ethyl-2-methylbenzothiazoline—A solution of 2-aminobenzenethiol (12.5 g), ethyl methyl ketone (7.2 g) and *p*-toluenesulfonic acid (0.6 g) in benzene (250 ml) was refluxed with stirring for 10 h while the water formed was continuously separated. After cooling, the solvent was removed *in vacuo* and the residue was distilled to give 15.9 g (89%) of 2-ethyl-2-methylbenzothiazoline as a pale yellow oil, bp 105–106 °C (1 mmHg). IR (neat): 3340 cm⁻¹ (NH).

¹H-NMR (CDCl₃) δ: 1.01 (3H, t, *J* = 7 Hz, CH₂CH₃), 1.64 (3H, s, CH₃), 1.88 (2H, q, *J* = 7 Hz, CH₂CH₃), 3.76 (1H, brs, NH), 6.48–7.10 (4H, m, ArH). MS *m/e*: 179 (M⁺). Anal. Calcd for C₁₀H₁₃NS: C, 67.00; H, 7.31; N, 7.81. Found: C, 67.21; H, 7.20; N, 7.90.

3-Acetyl-2-ethyl-2-methylbenzothiazoline—A solution of 2-ethyl-2-methylbenzothiazoline (10 g) in acetic anhydride (30 ml) was heated at 100–110 °C with stirring for 4 h. Acetic anhydride was evaporated off under reduced pressure and the residue was washed with an aqueous NaHCO₃ solution, then extracted with dichloromethane. The extract was washed with water, dried over MgSO₄ and evaporated down. The residue was distilled to give 11.5 g (93%) of 3-acetyl-2-ethyl-2-methylbenzothiazoline as a pale yellow oil, bp 131–133 °C (1 mmHg). IR (neat): 1670 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 0.98 (3H, t, *J* = 7 Hz, CH₂CH₃), 1.95 (3H, s, CH₃), 1.67–2.83 (2H, m, CH₂CH₃), 2.38 (3H, s, COCH₃), 6.90–7.23 (4H, m, ArH). MS *m/e*: 221 (M⁺). Anal. Calcd for C₁₂H₁₅NOS: C, 65.12; H, 6.83; N, 6.33. Found: C, 64.52; H, 6.66; N, 6.24.

trans-3-Acetyl-2-ethyl-2-methylbenzothiazoline 1-Oxide (9)—MCPBA (0.92 g) was added portionwise to a stirred, ice-cooled solution of 3-acetyl-2-ethyl-2-methylbenzothiazoline (1 g) in dichloromethane (40 ml) and the mixture was stirred at room temperature for 20 h. The reaction mixture was washed with an aqueous NaHCO₃ solution, dried over MgSO₄ and evaporated down *in vacuo* to give 1.05 g of 3-acetyl-2-ethyl-2-methylbenzothiazoline 1-oxide as a mixture of *cis* and *trans* isomers (*ca.* 1:5 by ¹H-NMR spectral analysis). Attempts to separate the mixture by using column chromatography or preparative thin-layer chromatography (PLC) were unsuccessful, so the separation was performed by fractional recrystallization from benzene–hexane to give pure *cis*-sulfoxide as colorless needles and *trans*-sulfoxide as colorless prisms. *cis*-3-Acetyl-2-ethyl-2-methylbenzothiazoline 1-oxide: mp 100–102 °C. IR (KBr): 1670 (CO), 1045 cm⁻¹ (SO). ¹H-NMR (CDCl₃) δ: 1.20 (3H, t, *J* = 7.5 Hz, CH₂CH₃), 1.46 (3H, s, CH₃), 2.10–3.10 (2H, m, CH₂CH₃), 2.52 (3H, s, COCH₃), 7.08–7.73 (3H, m, ArH), 7.80–8.00 (1H, m, ArH). Anal. Calcd for C₁₂H₁₅NO₂S: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.77; H, 6.33; N, 5.83. The ¹H-NMR spectrum in C₆D₆ showed the 2-methyl signal at δ 1.20. The ASIS (δ_{CDCl₃}–δ_{C₆D₆}) value was 0.26. **9**: mp 116–118 °C. IR (KBr): 1665 (CO), 1050 cm⁻¹ (SO). ¹H-NMR (CDCl₃) δ: 0.94 (3H, t, *J* = 7.5 Hz, CH₂CH₃), 1.59–2.20 (2H, m, CH₂CH₃), 1.98 (3H, s, CH₃), 2.50 (3H, s, COCH₃), 7.10–7.70 (3H, m, ArH), 7.80–8.00 (1H, m, ArH). Anal. Calcd for C₁₂H₁₅NO₂S: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.68; H, 6.31; N, 5.72. The ¹H-NMR spectrum of **9** in C₆D₆ showed the 2-methyl signal at δ 1.88. The ASIS value was 0.10.

trans-3-Acetyl-2-methyl-2-benzylbenzothiazoline 1-Oxide (14)—A solution of MCPBA (85%, 1.47 g) in dichloromethane (60 ml) was added to an ice-cold solution of 3-acetyl-2-methyl-2-benzylbenzothiazoline¹²⁾ (2.05 g) in dichloromethane (40 ml), and the mixture was stirred at 0 °C for 18 h. Work-up as described for **9** gave a crude oil which was subjected to column chromatography on silica gel using chloroform as a solvent to give 57 mg of *cis*-3-acetyl-2-methyl-2-benzylbenzothiazoline 1-oxide, 758 mg of the *trans*-sulfoxide **14** and 828 mg of a mixture of *cis*- and *trans*-sulfoxide. The *cis*-sulfoxide was recrystallized from ether to form colorless needles, mp 115–116 °C. IR (KBr): 1680 (CO), 1045 cm⁻¹ (SO). ¹H-NMR (CDCl₃) δ: 1.40 (3H, s, CH₃), 2.53 (3H, s, COCH₃), 3.85 (2H, ABq, *J* = 15 Hz, CH₂), 7.05–7.95 (9H, m, ArH). Anal. Calcd for C₁₇H₁₇NO₂S: C, 68.14; H, 5.66; N, 4.61. Found: C, 68.20; H, 5.72; N, 4.68. The *trans*-sulfoxide **14** was recrystallized from ether to afford colorless prisms, mp 101–102 °C. IR (KBr): 1683 (CO), 1060 cm⁻¹ (SO). ¹H-NMR (CDCl₃) δ: 2.03 (3H, s, CH₃), 2.38 (3H, s, COCH₃), 3.16 (2H, s, CH₂), 6.80–7.90 (9H, m, ArH). Anal. Calcd for C₁₇H₁₇NO₂S: C, 68.46; H, 5.78; N, 4.69. Found: C, 68.20; H, 5.72; N, 4.68.

Reaction of 9 with Acetic Anhydride—A mixture of **9** (0.6 g) and acetic anhydride (25 ml) was refluxed with stirring for 1.5 h. Acetic anhydride was evaporated off under reduced pressure, then an aqueous NaHCO₃ solution was added to the residue, and the whole was stirred for 30 min. The mixture was extracted with dichloromethane and the extract was washed with water, then dried over MgSO₄. Removal of the solvent afforded a crude oil, which was separated by preparative TLC on silica gel using ethyl acetate–hexane (1:2). The first fraction gave 38 mg (6.8%) of 3-acetyl-2-ethyl-2-methylbenzothiazoline, which was identical with an authentic sample. The second fraction afforded 83 mg (15%) of 4-acetyl-3-ethyl-4*H*-1,4-benzothiazine (**11**) as a colorless oil, bp 150 °C (bath temp., 1.5 mmHg). IR (neat): 1670 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.08 (3H, t, *J* = 7 Hz, CH₂CH₃), 2.10 (3H, s, COCH₃), 2.68 (2H, br q, *J* = 7 Hz, CH₂CH₃), 6.31 (1H, t, *J* = 1 Hz, C₂–H), 7.08–7.48 (4H, m, ArH). MS *m/e*: 219 (M⁺). Anal. Calcd for C₁₂H₁₃NOS: C, 65.72; H, 5.98; N, 6.39. Found: C, 65.47; H, 5.94; N, 6.30. The third fraction was a mixture and was further purified by preparative TLC on silica gel using ethyl acetate–hexane (1:1) to afford 38 mg (6.9%) of 4-acetyl-2,3-dimethyl-4*H*-1,4-benzothiazine (**13**), which was recrystallized from ether–pet. ether to yield colorless prisms, mp 103–104 °C. IR (KBr) 1665 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 2.05 (3H, q, *J* = 1 Hz, CH₃), 2.10 (3H, s, COCH₃), 2.15 (3H, q, *J* = 1 Hz, CH₃), 7.00–7.48 (4H, m, ArH). MS *m/e*: 219 (M⁺). Anal. Calcd for C₁₂H₁₃NOS: C, 65.72; H, 5.98; N, 6.39. Found: C, 65.77; H, 5.97; N, 6.40. The fourth fraction gave 140 mg (25.3%) of 4-acetyl-2-methyl-3-methylene-2,3-dihydro-4*H*-1,4-benzothiazine (**12**), which was purified by microdistillation to give a colorless oil, bp 158 °C (bath temp., 1.5 mmHg). IR (neat): 1680 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.56 (3H, d, *J* = 7.5 Hz, CH₃), 2.23 (3H, s, COCH₃), 4.23 (1H, br q, *J* = 7.5 Hz, C₂–H), 5.28 (1H, d, *J* = 1 Hz, =CH₂), 5.40 (1H, q, *J* = 1 Hz, =CH₂), 6.98–7.65 (4H, m, ArH). MS *m/e*: 219 (M⁺). Anal. Calcd for C₁₂H₁₃NOS: C, 65.72; H, 5.98; N, 6.39. Found: C, 65.53; H, 6.02; N, 6.30. An oil from the last fraction was distilled in a microdistillation apparatus to give 159 mg (28.7%) of 4-acetyl-3-ethylidene-2,3-dihydro-4*H*-1,4-benzothiazine (**10**) as a colorless oil, bp 156 °C (bath temp., 1.5 mmHg). IR (neat): 1670 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.77 (3H, dt, *J* = 1, 7.5 Hz, CH₃), 2.17 (3H, s, COCH₃),

3.89 (2H, m, C₂-H), 5.78 (1H, tq, $J = 1, 7.5$ Hz, CH), 6.97–7.56 (4H, m, ArH). MS m/e : 219 (M^+). Anal. Calcd for C₁₂H₁₃NOS: C, 65.72; H, 5.98; N, 6.39. Found: C, 65.34; H, 5.96; N, 6.36.

Reaction of 14 with Acetic Anhydride—A mixture of **14** (0.6 g) and acetic anhydride (25 ml) was refluxed with stirring for 1.5 h, and worked up as described above to give a crude oil. The oil was subjected to preparative TLC on silica gel using ethyl acetate–hexane (1:3). The first fraction gave 31.6 mg (5.3%) of 3-acetyl-2-benzyl-2-methylbenzothiazoline. The second fraction afforded 30.9 mg (5.2%) of 4-acetyl-3-benzyl-4*H*-1,4-benzothiazine (**16**), mp 114–115 °C (lit.¹²) mp 113–114 °C). ¹H-NMR (CDCl₃) δ : 2.05 (3H, s, COCH₃), 4.03 (2H, d, $J = 1$ Hz, CH₂), 6.30 (1H, t, $J = 1$ Hz, =CH–), 6.70–7.60 (9H, m, ArH). The third fraction gave 52 mg (8.7%) of 4-acetyl-3-methyl-2-phenyl-4*H*-1,4-benzothiazine (**18**) as colorless prisms after recrystallization from ethanol, mp 136.5–137.5 °C (lit.¹²) mp 133–134 °C). IR (KBr): 1670 cm^{–1} (CO). ¹H-NMR (CDCl₃) δ : 2.15 (3H, s, CH₃), 2.20 (3H, s, COCH₃), 7.10–7.60 (9H, m, ArH). Anal. Calcd for C₁₇H₁₅NOS: C, 72.82; H, 5.38; N, 4.89. Found: C, 72.57; H, 5.38; N, 4.98. The fourth fraction gave 137.4 mg (22.9%) of 4-acetyl-3-methylene-2-phenyl-2,3-dihydro-4*H*-1,4-benzothiazine (**17**), which was recrystallized from ethanol to form colorless prisms, mp 136–137 °C. IR (KBr): 1670 cm^{–1} (CO). ¹H-NMR (CDCl₃) δ : 1.60 (3H, s, COCH₃), 5.25 (3H, m, =CH₂ and –CHPh), 6.90–7.60 (9H, m, ArH). Anal. Calcd for C₁₇H₁₅NOS: C, 72.84; H, 5.40; N, 4.98. Found: C, 72.57; H, 5.38; N, 4.98. The last fraction provided 207.6 mg (34.6%) of 4-acetyl-3-benzylidene-2,3-dihydro-4*H*-1,4-benzothiazine (**15**) as colorless plates after recrystallization from ethanol, mp 113–114 °C. IR (KBr): 1670 cm^{–1} (CO). ¹H-NMR (CDCl₃) δ : 2.25 (3H, s, COCH₃), 4.10 (2H, s, CH₂), 6.75 (1H, s, CH), 7.10–7.70 (9H, m, ArH). Anal. Calcd for C₁₇H₁₅NOS: C, 72.60; H, 5.40; N, 4.93. Found: C, 72.57; H, 5.38; N, 4.98.

Reaction of *cis*-3-Acetyl-2-ethoxycarbonylmethyl-2-methylbenzothiazoline 1-Oxide (19) with Acetic Anhydride—A mixture of **19**^{2b} (0.6 g) and acetic anhydride (25 ml) was refluxed with stirring for 1.5 h and worked up as usual to yield a crude oil, which was subjected to preparative TLC on silica gel using hexane–ethyl acetate (2:1). The first fraction gave 17 mg (3%) of 4-acetyl-3-ethoxycarbonylmethyl-4*H*-1,4-benzothiazine (**22**) as a pale yellow oil, bp 150 °C (bath temp., 1.5 mmHg). IR (neat): 1735 (CO), 1670 cm^{–1} (CO). ¹H-NMR (CDCl₃) δ : 1.28 (3H, t, $J = 7.5$ Hz, CH₂CH₃), 2.14 (3H, s, COCH₃), 4.18 (2H, q, $J = 7.5$ Hz, CH₂CH₃), 4.37 (2H, d, $J = 1.5$ Hz, CH₂CO₂Et), 6.28 (1H, t, $J = 1.5$ Hz, –CH=), 6.97–7.55 (4H, m, ArH). MS m/e : 277 (M^+). Anal. Calcd for C₁₄H₁₅NO₃S: C, 60.63; H, 5.45; N, 5.05. Found: C, 60.24; H, 5.52; N, 5.05. The second fraction gave 237 mg (42%) of 4-acetyl-2-ethoxycarbonyl-3-methyl-4*H*-1,4-benzothiazine (**21**) as colorless prisms after recrystallization from pet. ether, mp 64–64.5 °C. IR (KBr) 1690, 1680 cm^{–1} (CO). ¹H-NMR (CDCl₃) δ : 1.36 (3H, t, $J = 7$ Hz, CH₂CH₃), 2.15 (3H, s, C₃–CH₃), 2.63 (3H, s, COCH₃), 4.34 (2H, q, $J = 7$ Hz, CH₂CH₃), 7.10–7.70 (4H, m, ArH). Anal. Calcd for C₁₄H₁₅NO₃S: C, 60.63; H, 5.45; N, 5.05. Found: C, 60.86; H, 5.46; N, 5.04. The third fraction gave 236 mg (42%) of an oil, which was a mixture (1:2) of **21** and 4-acetyl-2-ethoxycarbonyl-3-methylene-2,3-dihydro-4*H*-1,4-benzothiazine (**20**). A pure sample of **20** could not be obtained, because **20** was gradually converted to **21** during the separation from **21** on silica gel.¹³ However, the structure of **20** was elucidated on the basis of the ¹H-NMR spectrum: ¹H-NMR (CDCl₃) δ : 1.24 (3H, t, $J = 7.5$ Hz, CH₂CH₃), 2.24 (3H, s, COCH₃), 4.16 (2H, q, $J = 7.5$ Hz, CH₂CH₃), 4.75 (1H, s, CH), 5.45 (1H, s, =CH), 5.54 (1H, s, =CH₂).

Reaction of *trans*-3-Acetyl-2-ethoxycarbonylmethyl-2-methylbenzothiazoline 1-Oxide (23) with Acetic Anhydride—A solution of **23**^{2b} (0.516 g) in acetic anhydride (20 ml) was refluxed with stirring for 1.5 h and worked up as described for the reaction of **19** with acetic anhydride to afford 125 mg (25.8%) of **20**, 110 mg (23%) of **21**, 81 mg (17%) of **22** and 11 mg (2.3%) of 3-acetyl-2-ethoxycarbonylmethyl-2-methylbenzothiazoline.

Reaction of *trans*-3-Acetyl-2-methylbenzothiazoline 1-Oxide (24) with Acetic Anhydride—A solution of **24**^{2b} (0.84 g) in acetic anhydride (15 ml) was refluxed with stirring for 3 h and the reaction mixture was worked up as usual. The oily mixture was separated by preparative TLC on silica gel using hexane–ethyl acetate (1:2) as a solvent to afford 0.31 g (39.3%) of 4-acetyl-4*H*-1,4-benzothiazine (**25**). Recrystallization from hexane gave colorless prisms, mp 92–93 °C. IR (KBr): 1670 cm^{–1} (CO). ¹H-NMR (CDCl₃) δ : 2.30 (3H, s, COCH₃), 6.13 (1H, d, $J = 6.5$ Hz, C₂-H), 6.90 (1H, br s, $J = 6.5$ Hz, C₃-H), 7.15–7.65 (4H, m, ArH). Anal. Calcd for C₁₀H₉NOS: C, 62.80; H, 4.74; N, 7.32. Found: C, 62.65; H, 4.80; N, 7.31.

Reaction of 3-Acetyl-2,2-dimethylbenzothiazoline 1-Oxide (26) with Acetic Anhydride at 80–90 °C—A solution of **26**^{2b} (0.5 g) in acetic anhydride (20 ml) was heated at 80–90 °C in an oil bath for 25 h. Work-up as usual afforded 18 mg (3.9%) of 3-acetyl-2,2-dimethylbenzothiazoline, 158 mg (34.4%) of 4-acetyl-3-methyl-4*H*-1,4-benzothiazine (**27**) and 25 mg (5.4%) of 4-acetyl-3-methylene-2,3-dihydro-4*H*-1,4-benzothiazine.^{2b}

Reaction of 26 with Trifluoroacetic Anhydride—A solution of trifluoroacetic anhydride (2 g) in dry dichloromethane (5 ml) was added to a stirred solution of **26** (0.5 g) in dry dichloromethane (15 ml) at 0 °C. The mixture was stirred for 24 h, then aqueous NaHCO₃ solution was added to hydrolyze the excess trifluoroacetic anhydride. The organic layer was washed with water, dried over MgSO₄, and concentrated to dryness. The residual oil was purified by preparative TLC on silica gel using hexane–ethyl acetate (2:1) to give 148 mg (32%) of **27**.

Reaction of *trans*-3-Acetyl-2-methyl-2-phenylbenzothiazoline 1-Oxide (28) with Trifluoroacetic Anhydride—Trifluoroacetic anhydride (4 ml) was added to a solution of **28**^{2b} (0.4 g) in dry dichloromethane (15 ml) at 0 °C, and the mixture was stirred for 1 h at the same temperature, then for 2 h at room temperature. Work-up as above afforded a crude oil which was purified by preparative TLC on silica gel using hexane–ethyl acetate (3:1) to give 144 mg (38%)

of 4-acetyl-3-phenyl-4*H*-1,4-benzothiazine (29).^{2b)}

Reaction of 19 with Trifluoroacetic Anhydride—A solution of trifluoroacetic anhydride (1.42 g) in dichloromethane (3.5 ml) was added to a stirred solution of 19 (0.5 g) in dry dichloromethane (10 ml) at 0°C. The mixture was stirred for 2 h at 0°C, then work-up as above gave an oil, which was separated by preparative TLC on silica gel using hexane–ethyl acetate (2:1) to yield 121 mg (25.8%) of 21 and 74 mg (15.8%) of 22.

trans-2-Benzyl-2-methyl-1-thiochroman 1-Oxide (31)—An ether solution of *n*-butyllithium (1.1 N, 5.1 ml) was added to a stirred solution of diisopropylamine (0.8 ml) in dry tetrahydrofuran (7 ml). After 30 min at room temperature, the lithium diisopropylamide solution was cooled to –76°C in a dry ice–acetone bath, then *cis*-2-methyl-1-thiochroman 1-oxide⁴⁾ (1 g) was added, and the mixture was stirred for 1 h. To this orange-red solution was added a solution of benzyl bromide (0.85 ml) in dry tetrahydrofuran (3.5 ml), which had been pre-cooled to –76°C. After 30 min at –76°C and 1 h at room temperature, an aqueous NH₄Cl solution was added to the mixture and the whole was extracted with ether. The organic layer was washed with water, dried over MgSO₄ and evaporated. The residual oil was passed through silica gel with a mixture of ethyl acetate–hexane (2:1) to afford 1.35 g (90%) of 31, a single isomer, as a colorless oil which could not be crystallized and could not be distilled because of thermal decomposition. The structure was confirmed on the basis of the spectral data: IR (neat): 1015 cm^{–1} (SO). ¹H-NMR (CDCl₃) δ: 1.20 (3H, s, CH₃), 1.80–2.02 (2H, m, C₃–H), 2.83–2.95 (2H, m, C₄–H), 3.00 (2H, s, CH₂Ph), 7.05–7.58 (8H, m, ArH) 7.65–7.88 (1H, m, ArH). MS *m/e*: 270 (M⁺), 254 (M⁺ – O).

Ring Expansion of 31—A mixture of 31 (0.5 g) and *p*-toluenesulfonic acid (9.25 mg) in dry xylene was refluxed for 45 min. The reaction mixture was washed with an aqueous NaHCO₃ solution and water, and dried over MgSO₄. The solvent was evaporated off and the residue was subjected to preparative TLC on silica gel with chloroform–hexane (1:4) to give 0.13 g (27.1%) of 3-benzylidene-2,3,4,5-tetrahydro-1-benzothiepin (32) and 96 mg (20.4%) of 3-benzyl-2,5-dihydro-1-benzothiepin (33). Compound 32: colorless oil. ¹H-NMR (CDCl₃) δ: 2.30–2.63 (2H, m, C₄–H), 2.98–3.25 (2H, m, C₅–H), 3.45 (2H, s, C₂–H), 6.33 (1H, s, olefinic H), 6.93–7.63 (9H, m, ArH). MS *m/e*: 252 (M⁺). Compound 33: colorless oil. ¹H-NMR (CDCl₃) δ: 2.38–2.68 (1H, m, C₂–H), 2.90–3.18 (1H, m, C₂–H), 3.28 (2H, br s, CH₂Ph), 3.60 (2H, br d, *J* = 6 Hz, C₅–H), 5.68 (1H, br t, *J* = 6 Hz, C₄–H). MS *m/e*: 252 (M⁺). Compound 32 was converted to the corresponding sulfone by oxidation with MCPBA in 46% yield: colorless prisms (ether–hexane), mp 133–134°C. IR (KBr): 1140, 1310 cm^{–1} (SO₂). ¹H-NMR (CDCl₃) δ: 2.48–2.73 (2H, m, C₄–H), 3.23–3.48 (2H, m, C₅–H), 4.09 (2H, s, C₂–H), 6.78 (1H, s, olefinic H), 7.13–8.18 (9H, m, ArH). MS *m/e*: 284 (M⁺). Anal. Calcd for C₁₇H₁₆O₂S: C, 71.80; H, 5.67. Found: C, 72.03; H, 5.74.

1-Methyl-2-thiochromene (34)—2-Thianaphthylm perchlorate⁵⁾ (11.9 g) was added portionwise with stirring to an ethereal solution of methylmagnesium iodide [prepared from Mg (2.3 g) and methyl iodide (13.2 g) in ether by the usual method] at room temperature. The reaction mixture was hydrolyzed with an ice-cooled NH₄Cl solution and extracted with ether. The extract was dried over MgSO₄, and removal of the solvent afforded 6.1 g (77.9%) of 34 as an oil, which was distilled to give a pale yellow oil, bp 110°C (5 mmHg). ¹H-NMR (CDCl₃) δ: 1.48 (3H, d, *J* = 7 Hz, CH₃), 3.95 (1H, qd, *J* = 7, 1.5 Hz, C₁–H), 6.32 (1H, dd, *J* = 10, 1.5 Hz, C₃–H), 6.72 (1H, d, *J* = 10 Hz, C₄–H), 7.00–7.35 (4H, m, ArH). Anal. Calcd for C₁₀H₁₀S: C, 74.00; H, 6.21. Found: C, 74.12; H, 6.31.

1-Methyl-2-thianaphthylm Perchlorate (35)—An ice-cooled, stirred solution of SO₂Cl₂ (2.5 g) in absolute ether (30 ml) was slowly added to a solution of 34 (3 g) in absolute ether (30 ml) at –20°C and the mixture was stirred for 30 min. Then absolute ether (60 ml) was added, followed by ice-cooled 70% perchloric acid (30 ml), and the whole was stirred for 30 min. The precipitate was filtered and washed with acetic acid and absolute ether, then dried. The crystals were recrystallized from acetic acid to give 3.54 g (73.4%) of 35 as a pale green powder, mp 148–150°C (dec.). IR (KBr): 1090–1150 cm^{–1} (ClO₄[–]). ¹H-NMR (CF₃CO₂H) δ: 3.71 (3H, s, CH₃), 8.20–9.23 (6H, m, ArH). Anal. Calcd for C₁₀H₉ClO₄S: C, 46.07; H, 3.49. Found: C, 46.13; H, 3.40.

1-Benzyl-1-methyl-2-thiochromene (36)—Compound 35 (4.61 g) was slowly added with stirring to an ethereal solution of benzylmagnesium chloride [prepared from Mg (1.3 g) and benzyl chloride (6.72 g) in absolute ether] and the mixture was worked up as usual. The resulting oil was passed through silica gel using pet. ether as a solvent to give 3.84 g (86.1%) of 36, which was purified by distillation, bp 110–120°C (5 mmHg). ¹H-NMR (CDCl₃) δ: 1.65 (3H, s, CH₃), 3.03 (2H, ABq, *J* = 13.5 Hz, CH₂), 6.41 (1H, d, *J* = 10.5 Hz, C₃–H), 6.60–7.23 (10H, m, ArH and C₄–H). Anal. Calcd for C₁₇H₁₆S: C, 80.91; H, 6.39. Found: C, 81.14; H, 6.38.

1-Benzyl-1-methyl-2-thiochroman (37)—The chromene 36 (1.55 g) in ethanol (90 mg) was stirred at room temperature under hydrogen (40 atm) over 10% palladium carbon (1.13 g) for 3.5 h. The mixture was filtered, the filtrate was evaporated down, and the residue was purified by distillation to afford 1.32 g (83.9%) of 37 as a colorless oil, bp 140°C (5 mmHg). ¹H-NMR (CDCl₃) δ: 1.60 (3H, s, CH₃), 2.35–3.05 (4H, m, –CH₂–CH₂–), 3.16 (2H, ABq, *J* = 13.5 Hz, CH₂Ph), 6.75–7.25 (9H, m, ArH). Anal. Calcd for C₁₇H₁₈S: C, 80.27; H, 7.13. Found: C, 80.26; H, 7.28.

trans-1-Benzyl-1-methyl-2-thiochroman 2-Oxide (38)—MCPBA (2 g) was added to a solution of 37 (2.52 g) in dichloromethane (100 ml) with cooling in an ice-bath, and the mixture was stirred overnight. The reaction mixture was washed with a saturated NaHCO₃ solution and extracted with dichloromethane. The extract was washed with water and dried over MgSO₄. Removal of the solvent gave a solid residue, which was recrystallized from benzene–hexane to afford 1.88 g (70.4%) of 38 as colorless prisms, mp 94–95°C. IR (KBr): 1040 cm^{–1} (SO). ¹H-NMR (CDCl₃) δ: 1.68 (3H, s, CH₃), 2.25–3.75 (4H, m, –CH₂–CH₂–), 3.07 (2H, br, CH₂Ph), 6.63–7.25 (9H, m, ArH). MS

m/e: 270 (M^+). *Anal.* Calcd for $C_{17}H_{18}OS$: C, 75.52; H, 6.71. Found: C, 75.29; H, 6.79.

Ring Expansion of 38—A mixture of **38** (0.3 g) and *p*-toluenesulfonic acid (5.5 mg) in dry xylene (10 ml) was heated under reflux with stirring for 45 min. After cooling, the reaction mixture was washed with an aqueous $NaHCO_3$ solution. The organic layer was separated, washed with water and dried over $MgSO_4$. Evaporation of the solvent afforded an oil, which was subjected to preparative TLC on silica gel using benzene–hexane (1:1) to give 121 mg (43.2%) of 1,2,4,5-tetrahydro-1-benzylidene-3-benzothiepin (**39**) as colorless needles (benzene–hexane) and 144.8 mg (51.7%) of 4,5-dihydro-1-benzyl-3-benzothiepin (**40**) as an oil. **39**: mp 154–155 °C. 1H -NMR ($CDCl_3$) δ : 2.70–3.50 (4H, m, $-CH_2CH_2-$), 3.45 (2H, s, CH_2), 6.66 (1H, s, $=CH-$), 6.77–7.33 (9H, m, ArH). MS *m/e*: 252 (M^+). *Anal.* Calcd for $C_{17}H_{16}S$: C, 80.91; H, 6.39. Found: C, 81.17; H, 6.43. **40**: 1H -NMR ($CDCl_3$) δ : 2.50–3.40 (4H, m, $-CH_2CH_2-$), 3.70 (2H, s, CH_2Ph), 6.55 (1H, s, $=CH-$), 6.85–7.58 (9H, m, ArH). MS *m/e*: 252 (M^+). Product **40** was an oil, so the structure was further confirmed by leading it to the corresponding crystalline sulfone by MCPBA oxidation as follows. MCPBA (247.5 mg) was added to a solution of **40** (145 mg) in dichloromethane (5 ml) and the mixture was stirred for 2 h, then washed with an aqueous $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$ and evaporated. The residual solid was recrystallized from benzene–hexane to give 140.1 mg (85.9%) of 4,5-dihydro-1-benzyl-3-benzothiepin 3,3-dioxide as colorless needles, mp 159–161 °C, IR (KBr): 1120, 1300 cm^{-1} (SO_2). 1H -NMR ($CDCl_3$) δ : 3.21 (4H, s, $-CH_2CH_2-$), 3.97 (2H, s, CH_2Ph), 6.94 (1H, s, $=CH-$), 7.15–7.76 (9H, m, ArH). MS *m/e*: 284 (M^+). *Anal.* Calcd for $C_{17}H_{16}O_2S$: C, 71.80; H, 5.67. Found: C, 71.83; H, 5.61.

Reaction of 38 with Acetic Anhydride—The sulfoxide **38** (307.8 mg) in acetic anhydride (10 ml) was heated under reflux with stirring for 45 min. After evaporation of the acetic anhydride under reduced pressure, the residual oil was dissolved in dichloromethane and washed with an aqueous $NaHCO_3$ solution and water. The organic layer was separated, dried over $MgSO_4$ and evaporated. The residual oil was separated by preparative TLC using benzene–hexane (1:2) to isolate 123.1 mg (42.8%) of **36** as a colorless oil, which was identical with an authentic sample.

2-Methyl-3-oxo-2,3-dihydro-4H-1,4-benzothiazine (41)—A mixture of *o*-aminobenzenethiol (5 g) and α -bromopropionic acid (4.17 g) was heated under a nitrogen atmosphere at 120–125 °C. After cooling, the reaction mixture was dissolved in dichloromethane and washed with an aqueous $NaHCO_3$ solution and water. The organic layer was dried over $MgSO_4$ and evaporated to give 4 g (83%) of **41** as colorless columns after recrystallization from ethanol, mp 130–131 °C. IR (KBr): 3180 (NH), 1660 cm^{-1} (CO). 1H -NMR ($CDCl_3$) δ : 1.48 (3H, d, $J=7$ Hz, CH_3), 3.55 (1H, d, $J=7$ Hz, C_2-H), 6.75–7.38 (4H, m, ArH), 9.88 (1H, br s, NH). MS *m/e*: 179 (M^+). *Anal.* Calcd for C_9H_9NOS : C, 60.31; H, 5.06; N, 7.81. Found: C, 60.56; H, 5.06; N, 7.99.

2-Phenyl-3-oxo-2,3-dihydro-4H-1,4-benzothiazine (42)—A solution of *o*-aminobenzenethiol (5 g) and α -bromophenylacetic acid (5.9 g) in dry xylene (40 ml) was heated under reflux for 40 min under a nitrogen atmosphere. The precipitated crystals were dissolved in chloroform and the solution was washed with an aqueous $NaHCO_3$ solution and water, then dried over $MgSO_4$. Removal of the solvent afforded 3.52 g (53%) of **42**, which was recrystallized from ethanol to form colorless needles, mp 206–207 °C (lit.¹⁴) 208–209 °C. IR (KBr): 3200 (NH), 1670 cm^{-1} (CO). 1H -NMR ($DMSO-d_6$) δ : 4.92 (1H, s, CH), 6.70–7.70 (9H, m, ArH), 10.85 (1H, br s, NH). *Anal.* Calcd for $C_{14}H_{11}NOS$: C, 69.68; H, 4.59; N, 5.80. Found: C, 69.63; H, 4.60; N, 5.55.

2,2-Dimethyl-3-oxo-2,3-dihydro-4H-1,4-benzothiazine (43)—A solution of *n*-butyllithium in ether (1.1 N, 62.5 ml) was added to a stirred solution of diisopropylamine (5.75 g) in dry tetrahydrofuran (70 ml) at 0 °C under a nitrogen atmosphere. After 30 min at room temperature, the lithium diisopropylamide solution was again cooled to 0 °C and **41** (5 g) was added. To the orange dianion solution thus generated, a solution of methyl iodide (3.98 g) in dry tetrahydrofuran (40 ml) was added. The reaction mixture was stirred at 0 °C for 2 h and at room temperature for 2 h, then acidified by adding dilute acetic acid and extracted with ether. The ether layer was washed with an aqueous $NaHCO_3$ solution and water, and dried over $MgSO_4$. Evaporation of the ether left a gummy oil, which was crystallized by adding ether to give 4.82 g (89.4%) of **43** as colorless needles after recrystallization from ethanol, mp 155–156 °C. IR (KBr): 1660 cm^{-1} (amide). 1H -NMR ($CDCl_3$) δ : 1.49 (6H, s, $2CH_3$), 6.80–7.35 (4H, m, ArH), 9.60 (1H, br s, NH). MS *m/e*: 193 (M^+). *Anal.* Calcd for $C_{10}H_{11}NOS$: C, 62.15; H, 5.74; N, 7.25. Found: C, 61.93; H, 5.69; N, 7.19.

2-Methyl-2-phenyl-3-oxo-2,3-dihydro-4H-1,4-benzothiazine (44)—Compound **44** was prepared in 92% yield from **42** by the same method as described for the preparation of **43**, colorless prisms (benzene–hexane), mp 180–181 °C. IR (KBr): 1670 cm^{-1} (CO). 1H -NMR ($CDCl_3$) δ : 1.82 (3H, s, CH_3), 6.69–7.61 (9H, m, ArH), 9.60–9.90 (1H, br s, NH). MS *m/e*: 255 (M^+). *Anal.* Calcd for $C_{15}H_{13}NOS$: C, 70.56; H, 5.13; N, 5.49. Found: C, 70.80; H, 4.88; N, 5.40.

2-Benzyl-2-methyl-3-oxo-2,3-dihydro-4H-1,4-benzothiazine (45)—Compound **45** was prepared in 89.4% yield by benzylation of **41** with benzyl bromide instead of methyl iodide by the same method as described for **43**; colorless prisms (ethanol–hexane), mp 145–147 °C. IR (KBr): 3180 (NH), 1660 cm^{-1} (CO). 1H -NMR ($CDCl_3$) δ : 1.45 (3H, s, CH_3), 2.95 (2H, s, CH_2Ph), 6.75–7.55 (9H, m, ArH). MS *m/e*: 269 (M^+). *Anal.* Calcd for $C_{16}H_{15}NOS$: C, 71.34; H, 5.61; N, 5.20. Found: C, 71.56; H, 5.60; N, 4.92.

2-Methyl-2,3-dihydro-4H-1,4-benzothiazine (46)—A solution of **43** (4 g) in dry tetrahydrofuran (65 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (1.45 g) in dry tetrahydrofuran (50 ml), and the mixture was refluxed for 8 h. After cooling, the reaction mixture was treated with ethyl acetate and water to destroy excess $LiAlH_4$,

and extracted with ether. The ether layer was washed with water, dried over MgSO_4 , then evaporated to give 3.48 g (94.3%) of **46** as a yellow oil after distillation, bp 133–135 °C (2 mmHg). IR (neat): 3400 cm^{-1} (NH). $^1\text{H-NMR}$ (CDCl_3) δ : 1.30 (3H, d, $J=7$ Hz, CH_3), 3.13–4.20 (4H, m, $\text{C}_2\text{-H}$, $\text{C}_3\text{-H}$ and NH), 6.34–7.20 (4H, m, ArH). MS m/e : 165 (M^+). Anal. Calcd for $\text{C}_9\text{H}_{11}\text{NS}$: C, 65.41; H, 6.71; N, 8.48. Found: C, 64.79; H, 6.69; N, 8.44.

2,2-Dimethyl-2,3-dihydro-4H-1,4-benzothiazine (47)—A solution of **43** (3 g) in dry tetrahydrofuran (40 ml) was added to a stirred suspension of LiAlH_4 (1.2 g) in dry tetrahydrofuran (40 ml) and the reaction mixture was refluxed for 8 h. Work-up as above gave 2.4 g (86.3%) of **47** as a yellow oil, bp 125–130 °C (bath temp., 2 mmHg). IR (neat): 3400 cm^{-1} (NH). $^1\text{H-NMR}$ (CDCl_3) δ : 1.38 (6H, s, 2CH_2), 3.18 (2H, s, CH_2), 3.88 (1H, br s, NH), 6.38–7.03 (4H, m, ArH). MS m/e : 179 (M^+). Anal. Calcd for $\text{C}_{10}\text{H}_{13}\text{NS}$: C, 67.00; H, 7.31; N, 7.81. Found: C, 66.89; H, 7.50; N, 7.76.

2-Methyl-2-phenyl-2,3-dihydro-4H-1,4-benzothiazine (48)—Reduction of **44** (3.5 g) with LiAlH_4 (0.89 g) in tetrahydrofuran (70 ml) as described above gave 2.61 g (79%) of **48** as colorless prisms after recrystallization from ether–hexane, mp 67–69 °C. IR (KBr): 3410 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3) δ : 1.70 (3H, s, CH_3), 3.50 (2H, ABq, $J=11$ Hz, CH_2), 3.45–3.90 (1H, br s, NH), 6.35–7.63 (9H, m, ArH). MS m/e : 241 (M^+). Anal. Calcd for $\text{C}_{15}\text{H}_{15}\text{NS}$: C, 74.65; H, 6.26; N, 5.80. Found: C, 74.59; H, 6.25; N, 5.84.

2-Benzyl-2-methyl-2,3-dihydro-4H-1,4-benzothiazine (49)—Reduction of **45** (2.5 g) with LiAlH_4 (0.6 g) in tetrahydrofuran (40 ml) as described above afforded 2.3 g (97%) of **49** as an oil, bp 152 °C (1 mmHg). IR (neat): 3400 cm^{-1} (NH). $^1\text{H-NMR}$ (CDCl_3) δ : 1.23 (3H, s, CH_3), 2.91 (2H, s, CH_2Ph), 3.14 (2H, s, $-\text{CH}_2-$), 3.69 (1H, br s, NH), 6.33–7.43 (4H, m, ArH), 7.19 (5H, br s, ArH). MS m/e : 255 (M^+). Anal. Calcd for $\text{C}_{16}\text{H}_{17}\text{NS}$: C, 75.25; H, 6.71; N, 5.48. Found: C, 75.41; H, 6.84; N, 5.44.

4-Acetyl-2-methyl-2,3-dihydro-4H-1,4-benzothiazine (50)—A solution of **46** (3.2 g) in acetic anhydride (30 ml) was heated with stirring at 100–110 °C for 2 h. Excess acetic anhydride was evaporated off under a vacuum and the residual oil was dissolved in chloroform. The chloroform layer was washed with an aqueous NaHCO_3 solution and water, and dried over MgSO_4 . Removal of the solvent gave 3.7 g (92.3%) of **50**, which was distilled to give a colorless oil, bp 121–125 °C (bath temp., 2 mmHg). IR (neat): 1660 cm^{-1} (CO). $^1\text{H-NMR}$ (CDCl_3) δ : 1.38 (3H, d, $J=6$ Hz, CH_3), 2.18 (3H, s, COCH_3), 3.03 (1H, ABq, $J=12.5$ Hz, $\text{C}_3\text{-H}$), 3.38–3.90 (1H, m, $\text{C}_2\text{-H}$), 4.48 (1H, ABq, $J=12.5$ Hz, $\text{C}_3\text{-H}$), 6.79–7.45 (4H, m, ArH). MS m/e : 207 (M^+). Anal. Calcd for $\text{C}_{11}\text{H}_{13}\text{NOS}$: C, 63.74; H, 6.32; N, 6.76. Found: C, 63.58; H, 6.33; N, 6.64.

4-Acetyl-2,2-dimethyl-2,3-dihydro-4H-1,4-benzothiazine (51)—A solution of **47** (2.3 g) in acetic anhydride (20 ml) was heated at 100 °C for 2.5 h and worked up as above to yield 2.78 g (97.9%) of **51** as colorless prisms after recrystallization from hexane, mp 76–77 °C. IR (KBr): 1660 cm^{-1} (CO). $^1\text{H-NMR}$ (CDCl_3) δ : 1.46 (6H, s, 2CH_3), 2.26 (3H, s, COCH_3), 3.86 (2H, s, CH_2), 7.10 (4H, br s, ArH). MS m/e : 221 (M^+). Anal. Calcd for $\text{C}_{12}\text{H}_{15}\text{NOS}$: C, 65.12; H, 6.38; N, 6.33. Found: C, 64.90; H, 6.90; N, 6.11.

4-Acetyl-2-methyl-2-phenyl-2,3-dihydro-4H-1,4-benzothiazine (52)—A solution of **48** (2.3 g) in acetic anhydride (15 ml) was heated at 100 °C for 2.5 h, and worked up as above to give a brown crude oil, which was extracted with hot hexane. The hexane extract was concentrated to afford 2.26 g (84%) of **52**, which was recrystallized from ethanol–hexane to form colorless prisms, mp 87–88 °C. IR (KBr): 1660 cm^{-1} (CO). $^1\text{H-NMR}$ (CDCl_3) δ : 1.88 (3H, s, CH_3), 2.07 (3H, s, COCH_3), 4.12 (2H, ABq, $J=13$ Hz, CH_2), 6.94–7.69 (9H, m, ArH). MS m/e : 283 (M^+). Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{NOS}$: C, 72.05; H, 6.05; N, 4.94. Found: C, 72.17; H, 6.25; N, 4.93.

4-Acetyl-2-benzyl-2-methyl-2,3-dihydro-4H-1,4-benzothiazine (53)—A solution of **49** (2.3 g) in acetic anhydride (12 ml) was heated at 100–110 °C for 2 h with stirring, and worked up as usual to give **53** as a colorless oil in quantitative yield, bp 165 °C (1 mmHg). IR (neat): 1660 cm^{-1} (CO). $^1\text{H-NMR}$ (CDCl_3) δ : 1.34 (3H, s, CH_3), 2.19 (3H, s, COCH_3), 2.93 (2H, s, CH_2Ph), 3.88 (2H, ABq, $J=13.5$ Hz, CH_2), 6.78–6.63 (4H, m, ArH), 7.23 (5H, m, ArH). MS m/e : 297 (M^+). Anal. Calcd for $\text{C}_{18}\text{H}_{19}\text{NOS}$: C, 72.69; H, 6.44; N, 4.71. Found: C, 72.61; H, 6.63; N, 4.91.

4-Acetyl-2-methyl-2,3-dihydro-4H-1,4-benzothiazine 1-Oxide (54)—MCPBA (85% purity, 1.96 g) was added to a stirred solution of **50** (2 g) in dichloromethane (50 ml) at -10 °C and the mixture was stirred for 5 h. Work-up as usual yielded 1.96 g (91%) of **54** as an oil. The oil was an inseparable mixture of *cis*- and *trans*-isomeric sulfoxides. The ratio of *cis*- and *trans*-sulfoxides was *ca.* 1:3 on the basis of the integration of the 2-methyl group signal in the $^1\text{H-NMR}$ spectrum: *trans*-sulfoxide (**54a**): $^1\text{H-NMR}$ (CDCl_3) δ : 1.34 (3H, d, $J=7$ Hz, CH_3), 2.25 (3H, s, COCH_3). *cis*-sulfoxide (**54b**): $^1\text{H-NMR}$ (CDCl_3) δ : 1.51 (3H, d, $J=7$ Hz, CH_3), 2.23 (3H, s, COCH_3). The mass spectrum of the *cis*- and *trans*-mixture showed a molecular ion peak at m/e 223.

4-Acetyl-2,2-dimethyl-2,3-dihydro-4H-1,4-benzothiazine 1-Oxide (55)—MCPBA (85%, 1.84 g) was added to a stirred solution of **51** (2 g) in dichloromethane (60 ml) at 0 °C, and the mixture was stirred for 3 h. Work-up as usual afforded 1.98 g (93%) of **55** as an oil, IR (neat): 1670 (CO), 1045 cm^{-1} (SO). $^1\text{H-NMR}$ (CDCl_3) δ : 1.25 (3H, s, CH_3), 1.30 (3H, s, CH_3), 2.30 (3H, s, COCH_3), 3.41 (1H, d, $J=14$ Hz, $\text{C}_3\text{-H}$), 4.33 (1H, d, $J=14$ Hz, $\text{C}_3\text{-H}$), 7.43–7.65 (3H, m, ArH), 7.73–7.90 (1H, m, ArH). MS m/e : 237 (M^+). High-resolution MS m/e : 237.0802 (Calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_2\text{S}$, 237.0804). $^1\text{H-NMR}$ (C_6D_6) δ : 0.95 (3H, s, CH_3), 0.98 (3H, s, CH_3), 1.88 (3H, s, COCH_3), 3.28 (1H, d, $J=14$ Hz, $\text{C}_3\text{-H}$), 4.08 (1H, d, $J=14$ Hz, $\text{C}_3\text{-H}$), 6.78–7.24 (3H, m, ArH), 7.58–7.82 (1H, m, ArH).

4-Acetyl-2-methyl-2-phenyl-2,3-dihydro-4H-1,4-benzothiazine 1-Oxide (56)—MCPBA (85%, 1.43 g) was added to a stirred solution of **52** (2 g) in dichloromethane (60 ml) at 0 °C. The mixture was stirred for 5 h at 0 °C and 13 h at room temperature, then work-up as usual afforded a crude oil, to which ether was added to form crystals of *trans*-4-

acetyl-2-methyl-2-phenyl-2,3-dihydro-4*H*-1,4-benzothiazine 1-oxide (**56a**), 1.4 g (66.3%).

The crystals were recrystallized from benzene–hexane to give colorless prisms, mp 141–142 °C. IR (KBr): 1660 (CO), 1050 cm⁻¹ (SO). ¹H-NMR (CDCl₃) δ: 1.63 (3H, s, CH₃), 2.15 (3H, s, COCH₃), 3.81 (1H, d, *J* = 14.5 Hz, CH₂), 4.87 (1H, d, *J* = 14.5 Hz, CH₂), 7.08–7.78 (9H, m, ArH). MS *m/e*: 299 (M⁺). Anal. Calcd for C₁₇H₁₇NO₂S: C, 68.20; H, 5.72; N, 4.68. Found: C, 68.36; H, 5.70; N, 4.60. The filtrate was further subjected to preparative TLC on silica gel using hexane–ethyl acetate (2:1) to give 145 mg (6.9%) of **56a** and 447 mg (21%) of the *cis*-sulfoxide (**56b**). The sulfoxide **56b** was recrystallized from dichloromethane–hexane to form colorless prisms, mp 133–134 °C. IR (KBr): 1660 (CO), 1050 cm⁻¹ (SO). ¹H-NMR (CDCl₃) δ: 1.86 (3H, s, CH₃), 2.29 (3H, s, COCH₃), 4.32 (2H, ABq, *J* = 14.5 Hz, CH₂), 6.92–7.54 (9H, m, ArH). MS *m/e*: 299 (M⁺). Anal. Calcd for C₁₇H₁₇NO₂S: C, 68.36; H, 5.70; N, 4.60. Found: C, 68.09; H, 5.57; N, 4.70.

4-Acetyl-2-benzyl-2-methyl-2,3-dihydro-4*H*-1,4-benzothiazine 1-Oxide (57)—MCPBA (85%, 1.43 g) was added to a stirred solution of **53** (2.1 g) in dichloromethane (50 ml) cooled to 0 °C. The mixture was stirred for 5.5 h at 0 °C, then work-up as usual gave 1.9 g (86%) of **57** as an oil, which was an inseparable mixture of *cis*- and *trans*-sulfoxides in a ratio of *ca.* 1:1 as determined by integration of the singlet signals at δ 1.05 and 1.08 attributable to the methyl group of the two isomers, respectively. The mass spectrum of the mixture showed a molecular ion peak at *m/e* 313.

2-Methyl-2-phenyl-4-oxo-2,3-dihydro-1,3-benzothiazine (67)—A mixture of thiosalicylamide¹⁰ (3 g), acetophenone (2.5 g) and *p*-toluenesulfonic acid (0.3 g) in dry xylene (50 ml) was refluxed with stirring for 10 h while the water formed was continuously separated. After cooling, the precipitate was collected by filtration and dissolved in chloroform. The chloroform solution was washed with an aqueous NaHCO₃ solution and water. The organic layer was dried over MgSO₄ and evaporated under reduced pressure to give 3.17 g of **67**. The above xylene filtrate was washed with an aqueous NaHCO₃ solution and water, and dried over MgSO₄. Evaporation of the solvent gave a further 0.45 g of **67**. The total yield of **67** was 3.62 g (72.4%). Recrystallization from ethanol–dichloromethane gave colorless prisms, mp 206–207 °C. IR (KBr): 1650 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 2.00 (3H, s, CH₃), 6.95–7.71 (8H, m, ArH), 7.90 (1H, br s, NH), 7.96–8.14 (1H, m, ArH). MS *m/e*: 255 (M⁺). Anal. Calcd for C₁₅H₁₃NOS: C, 70.56; H, 5.13; N, 5.49. Found: C, 70.50; H, 5.07; N, 5.36.

2-Ethyl-2-methyl-4-oxo-2,3-dihydro-1,3-benzothiazine (68)—A mixture of thiosalicylamide (0.5 g), methyl ethyl ketone (10 ml) and *p*-toluenesulfonic acid (0.3 g) in dry xylene (15 ml) was heated under reflux for 50 h and worked up as described for **67** to give 0.67 g (98.5%) of **68**, which was recrystallized from hexane to form colorless prisms, mp 123–125 °C. IR (KBr): 1655 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.02 (3H, t, *J* = 8 Hz, CH₂CH₃), 1.15 (3H, s, CH₃), 1.97 (1H, q, *J* = 8 Hz, CH₂CH₃), 7.06–7.55 (3H, m, ArH), 7.90 (1H, br s, NH), 8.04–8.22 (1H, m, ArH). MS *m/e*: 207 (M⁺). Anal. Calcd for C₁₁H₁₃NOS: C, 63.74; H, 6.32; N, 6.76. Found: C, 64.01; H, 6.44; N, 6.59.

2,3-Dimethyl-2-phenyl-4-oxo-2,3-dihydro-1,3-benzothiazine (69)—A solution of **67** (1 g) in dry dimethylformamide (20 ml) was added to a stirred suspension of sodium hydride (50% in oil, 0.2 g) in dry dimethylformamide (10 ml). The mixture was stirred for 1 h at room temperature, then a mixture of dimethyl sulfate (0.51 g) and dry dimethylformamide (4 ml) was added. The whole was stirred for 10 min at room temperature and then at 100 °C for 1 h. After cooling, the reaction mixture was made basic with 1*N* sodium hydroxide solution and extracted with dichloromethane. The extract was washed with water, dried over MgSO₄, then evaporated under reduced pressure. The residue was subjected to preparative TLC on silica gel with hexane–ethyl acetate (3:1). The first fraction afforded 648 mg (53.8%) of **69** as colorless prisms after recrystallization from hexane, mp 125–126 °C. IR (KBr): 1640 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 2.06 (3H, s, CH₃), 3.10 (3H, s, NCH₃), 6.96–7.60 (8H, m, ArH). MS *m/e*: 269 (M⁺). Anal. Calcd for C₁₆H₁₅NOS: C, 71.34; H, 5.61; N, 5.20. Found: C, 71.10; H, 5.61; N, 5.13. The second fraction gave 119 mg (10.7%) of *o*-methylthio[*N*-methyl-*N*-(1-phenylvinyl)]benzamide (**74**) as colorless prisms after recrystallization from hexane, mp 93–94 °C. IR (KBr): 1640 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 2.40 (3H, s, SCH₃), 3.28 (3H, s, NCH₃), 5.22 (1H, s, olefinic H), 5.30 (1H, s, olefinic H), 6.80–7.46 (9H, m, ArH). MS *m/e*: 283 (M⁺). Anal. Calcd for C₁₇H₁₇NOS: C, 72.05; H, 6.05; N, 4.94. Found: C, 72.08; H, 6.12; N, 4.97.

2-Ethyl-2,3-dimethyl-4-oxo-2,3-dihydro-1,3-benzothiazine (70)—Compound **70** was prepared by methylation of **68** (0.56 g) with dimethyl sulfate (0.5 g) by the same method as described for **67** in the yield of 0.544 g (90.7%), colorless prisms (hexane), mp 55–56 °C. IR (KBr): 1640 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 0.95 (3H, t, *J* = 7 Hz, CH₂CH₃), 1.66 (3H, s, CH₃), 1.92 (2H, q, *J* = 7 Hz, CH₂CH₃), 3.16 (3H, s, NCH₃), 7.04–7.55 (3H, m, ArH), 8.02–8.20 (1H, m, ArH). MS *m/e*: 221 (M⁺). Anal. Calcd for C₁₂H₁₅NOS: C, 65.12; H, 6.83; N, 6.33. Found: C, 65.12; H, 6.93; N, 6.35.

***trans*-2,3-Dimethyl-2-phenyl-4-oxo-2,3-dihydro-1,3-benzothiazine 1-Oxide (71)**—MCPBA (85%, 0.291 g) was added to a stirred solution of **69** (0.385 g) in dichloromethane (15 ml) at –10––15 °C. The reaction mixture was stirred for 3 h at –10 °C, then worked up as usual to give 0.498 g (87.4%) of **71**, which was recrystallized from benzene–hexane to form colorless prisms, mp 169–170 °C. IR (KBr): 1640 (CO), 1060 cm⁻¹ (SO). ¹H-NMR (CDCl₃) δ: 2.18 (3H, s, CH₃), 3.33 (3H, s, NCH₃), 7.23 (5H, s, ArH), 7.40–7.80 (3H, m, ArH), 8.08–8.28 (1H, m, ArH). ¹H-NMR (C₆D₆) δ: 1.73 (3H, s, CH₃), 2.97 (3H, s, NCH₃), 6.60–7.28 (8H, m, ArH), 8.19–8.34 (1H, m, ArH). MS *m/e*: 285 (M⁺). Anal. Calcd for C₁₆H₁₅NO₂S: C, 67.34; H, 5.30; N, 4.91. Found: C, 67.39; H, 5.28; N, 4.79.

2-Ethyl-2,3-dimethyl-4-oxo-2,3-dihydro-1,3-benzothiazine 1-Oxide (72)—MCPBA (85%, 0.443 g) was added to a stirred solution of **70** (0.482 g) in dichloromethane (30 ml) at 0 °C and the mixture was stirred for 1.5 h. Work-up as

usual gave a mixture of *cis*- and *trans*-sulfoxides (**72**), which were separated by preparative TLC on silica gel with hexane-ethyl acetate (1 : 2). *trans*-sulfoxide (**72a**): yield, 387 mg (74.4%), colorless prisms (hexane-dichloromethane), mp 109–111 °C. IR (KBr): 1640 (CO), 1050 cm⁻¹ (SO). ¹H-NMR (CDCl₃) δ: 1.07 (3H, t, *J* = 7 Hz, CH₂CH₃), 1.61–2.02 (2H, m, CH₂CH₃), 1.70 (3H, s, CH₃), 3.23 (3H, s, NCH₃), 7.57–7.83 (3H, m, ArH), 8.07–8.34 (1H, m, ArH). ¹H-NMR (C₆D₆) δ: 0.69 (3H, t, *J* = 7 Hz, CH₂CH₃), 1.03–1.86 (2H, m, CH₂CH₃), 1.70 (3H, s, CH₃), 6.95–7.23 (2H, m, ArH), 7.40–7.77 (1H, m, ArH), 8.03–8.36 (1H, m, ArH). MS *m/e*: 237 (M⁺). Anal. Calcd for C₁₂H₁₅NO₂S: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.60; H, 6.27; N, 5.90. *cis*-sulfoxide (**72b**): yield, 89 mg (17.1%), colorless prisms (benzene-hexane), mp 92–93 °C. IR (KBr): 1640 (CO), 1060 cm⁻¹ (SO). ¹H-NMR (CDCl₃) δ: 0.98 (3H, t, *J* = 7 Hz, CH₂CH₃), 1.57–2.07 (2H, m, CH₂CH₃), 1.79 (3H, s, CH₃), 3.23 (3H, s, NCH₃), 7.43–7.83 (3H, m, ArH), 7.95–8.18 (1H, m, ArH). ¹H-NMR (C₆D₆) δ: 0.48 (3H, t, *J* = 7 Hz, CH₂CH₃), 1.27 (3H, s, CH₃), 1.45–1.85 (2H, m, CH₂CH₃), 2.78 (3H, s, NCH₃), 6.84–7.23 (2H, m, ArH), 7.55–7.77 (1H, m, ArH), 8.02–8.17 (1H, m, ArH). MS *m/e*: 237 (M⁺). Anal. Calcd for C₁₂H₁₅NO₂S: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.67; H, 6.45; N, 5.84.

Reaction of 54 with Acetic Anhydride—A mixture of **54** (0.406 g) and acetic anhydride (20 ml) was heated under reflux for 1 h and 40 min. Work-up as usual afforded a crude oil, which was purified by preparative TLC on silica gel using hexane-ethyl acetate (2 : 1) to give an oil as the major isolable compound. The oil was found to be a 1 : 1 mixture of two compounds by ¹H-NMR spectroscopic analysis. The NMR spectrum showed a series of signals assignable to 4-acetyl-2-methyl-4*H*-1,4-benzothiazine (**65**), including a doublet signal (*J* = 1.6 Hz) due to the methyl group at δ 2.05, a singlet signal due to the acetyl group at δ 2.25 and a quartet signal (*J* = 1.6 Hz) due to the C₃-olefinic proton coupled with the methyl group at δ 6.63, and another series of signals assignable to 4-acetyl-2-methylene-2,3-dihydro-4*H*-1,4-benzothiazine (**66**), including a singlet signal due to the acetyl group at δ 2.26, a broad singlet signal due to the C₃-methylene at δ 4.39, a triplet signal (*J* = 1 Hz) due to one of the *exo*-methylene protons at δ 5.13 and another triplet signal (*J* = 1 Hz) due to the other *exo*-methylene proton at δ 5.25. The separation of these two compounds was tried by further preparative TLC using hexane-ethyl acetate (2 : 1) to afford 48 mg of **65** as the sole compound isolated. The other compound **66** was assumed to be decomposed during the chromatographic work-up. **65**: colorless oil, bp 125–127 °C (bath temp., 2 mmHg). IR (neat): 1660 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 2.05 (3H, d, *J* = 1.6 Hz, CH₃), 2.25 (3H, s, COCH₃), 6.63 (1H, q, *J* = 1.6 Hz, CH), 7.05–7.60 (4H, m, ArH). MS *m/e*: 205 (M⁺), 162 (base). High-resolution MS *m/e*: 205.0533 (Calcd for C₁₁H₁₁NOS, 205.0535).

Reaction of 55 with Acetic Anhydride—A solution of **55** (0.5 g) in acetic anhydride (1 ml) was heated under reflux for 4 h, and worked up as usual to leave a crude oil, which was subjected to preparative TLC on silica gel with hexane-ethyl acetate (1 : 1). The first fraction afforded 392 mg (66.6%) of 4-acetyl-2-acetoxymethyl-2-methyl-2,3-dihydro-4*H*-1,4-benzothiazine (**63**) as colorless needles from hexane-ether, mp 103–104 °C. IR (KBr): 1740 (ester), 1655 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.50 (3H, s, CH₃), 2.10 (3H, s, OCOCH₃), 2.23 (3H, s, COCH₃), 3.55 (1H, d, *J* = 14 Hz, C₃-H), 4.10 (2H, ABq, *J* = 11.6 Hz, CH₂O-), 4.28 (1H, d, *J* = 14 Hz, C₃-H), 7.02–7.21 (4H, m, ArH). MS *m/e*: 279 (M⁺). Anal. Calcd for C₁₄H₁₇NO₃S: C, 60.19; H, 6.13; N, 5.01. Found: C, 60.08; H, 6.23; N, 4.91. The second fraction gave 40 mg of unidentified product as colorless columns from hexane-ether; the mass spectrum showed a molecular ion peak at *m/e* 279.

Reaction of 56a with Acetic Anhydride—A solution of **56a** (0.3 g) in acetic anhydride (10 ml) was heated under reflux for 1.5 h. The crude oil obtained by the usual work-up was subjected to preparative TLC on silica gel with hexane-ethyl acetate (1 : 1). The first fraction gave 175 mg (51.5%) of 4-acetyl-2-acetoxymethyl-2-phenyl-2,3-dihydro-4*H*-1,4-benzothiazine (**60**) as an oil, bp 182–183 °C (1 mmHg). IR (neat) 1750 (ester), 1660 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.97 (3H, s, CH₃), 2.15 (3H, s, CH₃), 3.62 (1H, d, *J* = 13 Hz, CH₂), 4.54 (2H, ABq, *J* = 11.5 Hz, CH₂), 4.99 (1H, d, *J* = 13 Hz, CH₂), 6.96–7.62 (9H, m, ArH). MS *m/e*: 341 (M⁺). Anal. Calcd for C₁₉H₁₉NO₃S: C, 66.84; H, 5.61; N, 4.10. Found: C, 66.56; H, 5.65; N, 4.10. The second fraction was concentrated to give 88 mg (25.9%) of 5-acetyl-3-acetoxy-3-phenyl-2,3,4,5-tetrahydro-1,5-benzothiazepine (**59**), which was recrystallized from ether to form colorless needles, mp 160–161.5 °C. IR (KBr): 1742 (ester), 1660 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.82 (3H, s, OCOCH₃), 2.13 (3H, s, COCH₃), 2.69 (1H, d, *J* = 15 Hz, C₂-H), 3.12 (1H, d, *J* = 15 Hz, C₄-H), 4.09 (1H, dd, *J* = 15, 2 Hz, C₄-H), 5.33 (1H, dd, *J* = 15, 2 Hz, C₂-H), 7.00–7.80 (9H, m, ArH). MS *m/e*: 341 (M⁺), 281 (M⁺ - CH₃CO₂H). Anal. Calcd for C₁₉H₁₉NO₃S: C, 66.84; H, 5.61; N, 4.10. Found: C, 66.65; H, 5.57; N, 4.07.

Reaction of 56b with Acetic Anhydride—A solution of **56b** (0.25 g) in acetic anhydride (10 ml) was heated under reflux for 1.5 h. At this stage, it was found that **56b** was almost completely unchanged, and therefore the mixture was further refluxed for 4.5 h. Work-up as for **56a** gave 60 mg (20.7%) of **60** and 39 mg (13.5%) of **59**.

5-Acetyl-3-phenyl-2,5-dihydro-1,5-benzothiazepine (61)—Method A: A mixture of **60** (100 mg) and a few drops of conc H₂SO₄ in dry benzene (10 ml) was heated under reflux for 30 min. The reaction mixture was neutralized by adding an aqueous NaHCO₃ solution, then washed with water and dried over MgSO₄. The solvent was evaporated off and the residue was purified by preparative TLC on silica gel with hexane-ethyl acetate (4 : 1) to afford 46 mg (56%) of **61** as an oil. IR (neat): 1660 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.90 (3H, s, COCH₃), 3.78 (1H, dd, *J* = 17, 2.3 Hz, C₂-H), 5.52 (1H, d, *J* = 17 Hz, C₂-H), 6.05 (1H, d, *J* = 2.3 Hz, C₄-H), 7.10–7.67 (9H, m, ArH). High-resolution MS *m/e*: 281.0890 (Calcd for C₁₇H₁₅NOS, 281.0888).

Method B: A mixture of **59** (50 mg) and a catalytic amount of *p*-toluenesulfonic acid in dry benzene (5 ml) was refluxed for 30 min and worked up as above to give 38 mg (92%) of **61**.

Reaction of 71 with Acetic Anhydride—A solution of **71** (0.34 g) in acetic anhydride (15 ml) was heated under reflux for 2 h and worked up as usual. The resulting oil was subjected to preparative TLC on silica gel with hexane–ethyl acetate (2:1). The first fraction gave 102 mg (32%) of 4-methyl-3-phenyl-5-oxo-4,5-dihydro-1,4-benzothiazepine (**75**) as an orange oil, bp 170–173 °C (bath temp., 1 mmHg). IR (neat): 1630 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 3.14 (3H, s, NCH₃), 6.55 (1H, s, olefinic H), 7.05–7.93 (9H, m, ArH). MS *m/e*: 267 (M⁺). Anal. Calcd for C₁₆H₁₃NOS: C, 71.88; H, 4.90; N, 5.24. Found: C, 72.16; H, 4.96; N, 5.07. The second fraction afforded 17 mg (5.3%) of **69**. The third fraction gave 140 mg (39.6%) of 2-acetyl-4-methyl-3-phenyl-5-oxo-4,5-dihydro-1,4-benzothiazepine (**76**) as orange columns after recrystallization from ethanol, mp 168–169 °C. IR (KBr): 1660 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 2.00 (3H, s, CH₃), 3.10 (3H, s, NCH₃), 7.13–7.99 (9H, m, ArH). MS *m/e*: 309 (M⁺). Anal. Calcd for C₁₈H₁₅NO₂S: C, 69.88; H, 4.89; N, 4.53. Found: C, 70.08; H, 4.84; N, 4.40. From the last fraction, 37 mg of **71** was recovered.

Reaction of 72a with Acetic Anhydride—A solution of **72a** (0.327 g) in acetic anhydride (15 ml) was refluxed with stirring for 2.5 h and worked up as usual. The residual oil was subjected to preparative TLC on silica gel with hexane–ethyl acetate (1:1). The first fraction afforded 31 mg (10.3%) of 3-ethyl-4-methyl-5-oxo-4,5-dihydro-1,4-benzothiazepine (**77**) as an oil, bp 119–122 °C (bath temp., 1 mmHg). IR (neat): 1630 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 0.93 (3H, t, *J* = 7.5 Hz, CH₂CH₃), 2.34 (2H, br q, *J* = 7.5 Hz, CH₂CH₃), 3.27 (3H, s, NCH₃), 6.25 (1H, br s, olefinic H), 7.27–7.44 (3H, m, ArH), 7.60–7.82 (1H, m, ArH). MS *m/e*: 219 (M⁺). High-resolution MS *m/e*: 219.0665 (Calcd for C₁₂H₁₃NOS, 219.0670). The second fraction was further purified by preparative TLC (hexane–ethyl acetate (2:1)) to give 31 mg (10.3%) of 2,4-dimethyl-3-methylene-5-oxo-2,3,4,5-tetrahydro-1,4-benzothiazepine (**80**) as an oil, IR (neat): 1650 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.51 (3H, d, *J* = 7 Hz, CH₃), 3.34 (3H, s, NCH₃), 4.28 (1H, br q, *J* = 7 Hz, C₂–H), 5.00 (2H, br s, CH₂), 7.19–7.75 (4H, m, ArH). MS *m/e*: 219 (M⁺). High-resolution MS *m/e*: 219.0724 (Calcd for C₁₂H₁₃NOS, 219.0718). The third fraction was also further purified by preparative TLC on silica gel with hexane–ethyl acetate (2:1) to give 75 mg (25%) of 3-ethylidene-4-methyl-5-oxo-2,3,4,5-tetrahydro-1,4-benzothiazepine (**78**) as pale yellow prisms after recrystallization from hexane–dichloromethane, mp 72–74 °C. IR (KBr): 1635 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.45 (3H, d, *J* = 7 Hz, CH₃), 3.20 (3H, s, NCH₃), 5.56 (1H, q, *J* = 7 Hz, olefinic H), 3.87 (2H, br s, CH₂), 7.19–7.74 (4H, m, ArH). MS *m/e*: 219 (M⁺). Anal. Calcd for C₁₂H₁₃NOS: C, 65.72; H, 5.98; N, 6.39. Found: C, 65.67; H, 5.94; N, 6.11. The last fraction gave 98 mg (23.4%) of 2-(1-acetoxyethylidene)-3-ethylidene-4-methyl-5-oxo-2,3,4,5-tetrahydro-1,4-benzothiazepine (**79**) as colorless leaflets after recrystallization from hexane–dichloromethane, mp 96–97 °C. IR (KBr): 1775 (ester), 1660 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.78 (3H, d, *J* = 7 Hz, CH₃), 2.00 (3H, s, CH₃), 2.30 (3H, s, CH₃), 3.06 (3H, s, NCH₃), 6.18 (1H, q, *J* = 7 Hz, CH), 7.30–7.40 (3H, m, ArH), 7.55–7.79 (1H, m, ArH). MS *m/e*: 303 (M⁺). Anal. Calcd for C₁₆H₁₇NO₃S: C, 63.35; H, 5.65; N, 4.62. Found: C, 63.60; H, 5.62; N, 4.65.

Thermal Reaction of 72a in the Presence of *p*-Toluenesulfonic Acid—A mixture of **72a** (83 mg) and *p*-toluenesulfonic acid (16.6 mg) in dry benzene (7 ml) was refluxed for 1 h under a nitrogen atmosphere. The solvent was evaporated off and the residual mixture was purified by preparative TLC on silica gel using ethyl acetate–hexane (2:3). The first fraction gave 11.5 mg (15%) of **77**. The second fraction afforded 15.9 mg (20.7%) of 2,3,4-trimethyl-5-oxo-4,5-dihydro-1,4-benzothiazepine (**81**) as colorless crystals after recrystallization from hexane–dichloromethane, mp 105–106 °C. IR (KBr): 1620 cm⁻¹ (CO). ¹H-NMR (CDCl₃) δ: 1.91 (3H, q, *J* = 0.5 Hz, CH₃), 2.06 (3H, q, *J* = 0.5 Hz, CH₃), 3.24 (3H, s, NCH₃), 7.26–7.45 (3H, m, ArH), 7.62–7.85 (1H, m, ArH). MS *m/e*: 219 (M⁺). Anal. Calcd for C₁₂H₁₃NOS: C, 65.72; H, 5.98; N, 6.39. Found: C, 65.65; H, 6.00; N, 6.41.

References and Notes

- 1) Preliminary communication of part of this work: M. Hori, T. Kataoka, H. Shimizu, and N. Ueda, *Tetrahedron Lett.*, **1981**, 1701.
- 2) a) M. Hori, T. Kataoka, H. Shimizu, and Y. Imai, *Heterocycles*, **10**, 17 (1978); b) *Idem*, *Chem. Pharm. Bull.*, **27**, 1982 (1979).
- 3) E. H. Flynn, "Cephalosporins and Penicillins," Academic Press, Inc., New York, p. 183; P. G. Sammes, *Chem. Rev.*, **76**, 113 (1976).
- 4) R. B. Morin, D. O. Spry, and R. A. Mueller, *Tetrahedron Lett.*, **1969**, 849.
- 5) A. Lüttringhaus and N. Engelhard, *Chem. Ber.*, **93**, 1525 (1960); C. C. Price, M. Hori, T. Parasaran, and M. Polk, *J. Am. Chem. Soc.*, **85**, 2278 (1963).
- 6) Cf. M. Hori, T. Kataoka, H. Shimizu, and Y. Imai, *Chem. Pharm. Bull.*, **25**, 1482 (1977); Treatment of **28** with methyl iodide–silver perchlorate gave acetophenone in quantitative yield; acetophenone may be formed via a sulfonium ion intermediate (unpublished data).
- 7) K. K. Anderson, R. L. Caret, and I. K. Nielson, *J. Am. Chem. Soc.*, **96**, 8026 (1974); J. J. Rigau, C. C. Bacon, and C. R. Johnson, *J. Org. Chem.*, **35**, 3655 (1970).
- 8) M. Karplus, *J. Am. Chem. Soc.*, **82**, 4431 (1960); D. J. Collins, J. J. Hobbs, and S. Sternhell, *Aust. J. Chem.*, **16**, 1030 (1963); E. W. Garbisch, Jr., *J. Org. Chem.*, **27**, 4249 (1962); *idem*, *J. Am. Chem. Soc.*, **86**, 5561 (1964).
- 9) Morin *et al.* have reported the ring expansion of 2,2,3-trimethyl-4-oxo-2,3-dihydro-1,3-benzothiazine 1-oxide

with acetic anhydride-sodium acetate. However, the stereospecificity of the reaction could not be clarified since they used the 2,2-dimethyl substituted benzothiazine sulfoxide (R. B. Morin and D. O. Spry, *J. Chem. Soc., Chem. Commun.*, **1970**, 335).

- 10) A. Reissert and E. Manns, *Chem. Ber.*, **61**, 1308 (1928).
- 11) R. D. G. Cooper, *J. Am. Chem. Soc.*, **92**, 5010 (1970).
- 12) F. Chioccare, G. Prota, R. A. Nicolaus, and E. Novellino, *Synthesis*, **1977**, 876.
- 13) In our previous paper^{2b)} we reported that compound **20** was not obtained in a similar reaction. It is now considered that **20** was converted into **21** during separation and work-up, because in that work, we used non-polar solvents (ether-pet. ether mixture) as the developing solvent for chromatography, and a long time was required for the separation.
- 14) A. Takamizawa, H. Sato, and Y. Sato, *Chem. Pharm. Bull.*, **20**, 892 (1972).