[Chem. Pharm. Bull. 27(9)1982—1994(1979)]

UDC 547.789.6'546.21.04 : 547.869.2.04

Studies on Benzothiazoline Derivatives. IV.[1] Synthesis and Novel Ring Expansion Reaction of Benzothiazoline Sulfoxides[2]

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(Received October 17, 1978)

The oxidation of 3-acylbenzothiazolines (IV) with *m*-chloroperbenzoic acid gave 3-acylbenzothiazoline sulfoxides (V) and sulfone (VI) in high yield. The stereochemistry of the compounds V is discussed on the basis of nuclear magnetic resonance spectroscopic studies.

Reaction of the compound V with refluxing acetic anhydride resulted in the formation of novel ring expansion products, 4-acylbenzothiazine derivatives. A mechanism involving the sulfenic anhydride as an intermediate is proposed for this ring expansion.

Keywords——ring expansion reaction; ring transformation; benzothiazoline sulfoxide; benzothiazoline sulfone; benzothiazine derivative; aromatic solvent induced shifts; tetrahydrophenothiazine derivative; sulfenic anhydride intermediate

The ring transformation of thiazoline derivatives, as represented by the rearrangement of penicillin sulfoxides to cephalosporins, has been extensively studied during the past 10 years. In the previous paper, we reported an interesting ring transformation of 2,2-disubstituted benzothiazolines to 3-oxo-2,3-dihydro-4H-1,4-benzothiazines or benzothiazoles in the reaction with haloacyl halides or acid anhydrides.[1]

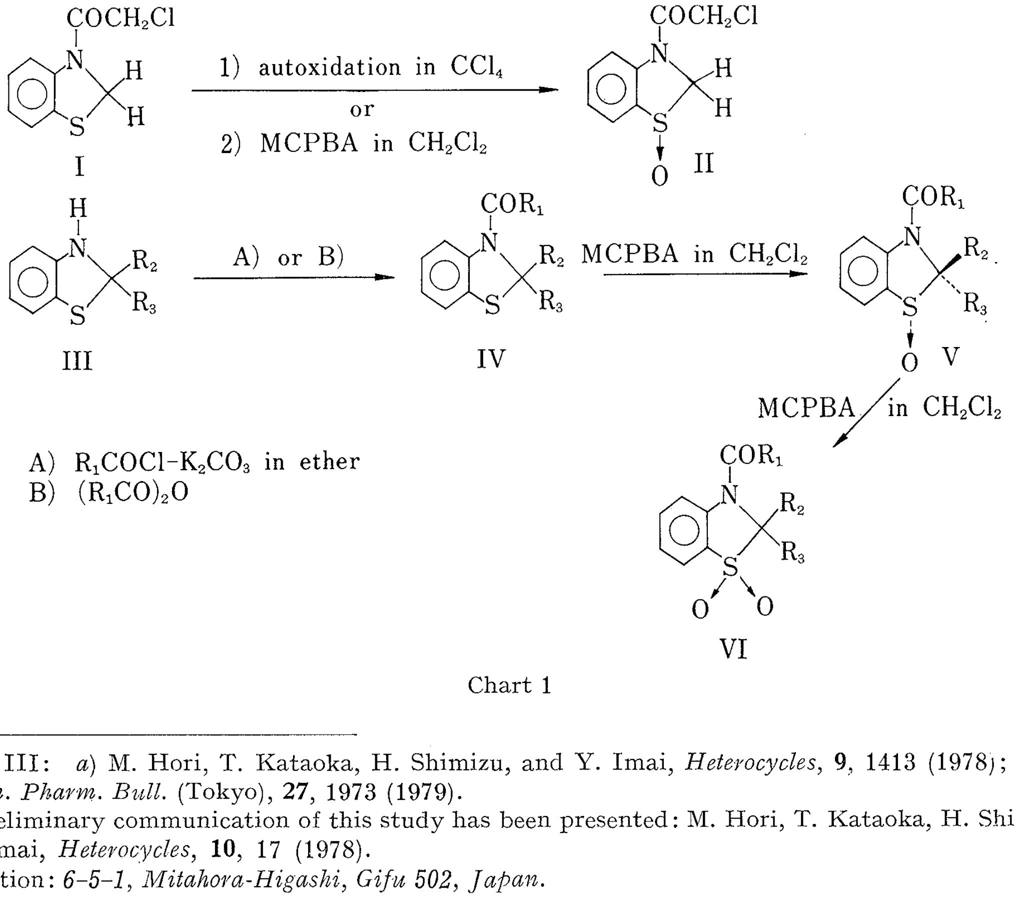

Chart 1

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[1] Part III: *a*) M. Hori, T. Kataoka, H. Shimizu, and Y. Imai, *Heterocycles*, **9**, 1413 (1978); *b*) *Idem*, *Chem. Pharm. Bull.* (Tokyo), **27**, 1973 (1979).

[2] A preliminary communication of this study has been presented: M. Hori, T. Kataoka, H. Shimizu, and Y. Imai, *Heterocycles*, **10**, 17 (1978).

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Table I. Properties of 3-Acylbenzothiazolines (IV)

Compd. No.	R_1	R_2	R_3	Method	Reaction time (hr)	Yield (%)	Appearance	mp or bp (°C) (Recryst. solvent)	Formula	Analysis (%) Calcd. (Found)		
										C	H	N
IVa[a]	CH_3	CH_3	CH_3	A	24	96	Colorless oil	118—120 [1 mmHg]	$C_{11}H_{13}NOS$	63.73 (63.57	6.31 6.13	6.74 6.56)
IVb[a]	CH_3	CH_3	C_6H_5	B	4	82	Colorless prisms	117—118 (Pet. ether)	$C_{16}H_{15}NOS$	71.33 (71.06	5.61 5.68	5.20 4.97)
IVc	CH_3	C_2H_5	C_2H_5	B[b]	4	62	Colorless columns	90.5—91 (Pet. ether)	$C_{13}H_{17}NOS$	66.35 (66.36	7.28 7.33	5.95 5.84)
IVd	CH_3	CH_3	$CH_2CO_2C_2H_5$	B	2	78	Colorless oil	180 [2 mmHg]	$C_{14}H_{17}NO_3S$	60.19 (60.41	6.13 6.16	5.01 5.09)
IVe	CH_3	$-(CH_2)_5-$		B[b]	2	83	Colorless oil	150 [0.1 mmHg]	$C_{14}H_{17}NOS$	67.98 (67.97	6.93 6.89	5.66 5.46)
IVf	CH_3	$-\underset{\substack{\vert \\ CH_3}}{C}H(CH_2)_4-$		B[b]	4	28	Colorless columns	126—128 (EtOH)	$C_{15}H_{19}NOS$	68.93 (68.87	7.33 7.29	5.36 5.20)
IVg	CH_3	CH_3	H	A	5	76	Colorless oil	114—116 [0.01 mmHg]	$C_{10}H_{11}NOS$	62.15 (61.86	5.74 5.62	7.25 7.18)
IVh	CH_3	C_2H_5	H	A	11	82	Colorless oil	144—146 [0.5 mmHg]	$C_{11}H_{13}NOS$	63.73 (63.69	6.32 6.31	6.76 6.81)
IVi	CH_3	C_6H_5	H	A	3	87	Colorless columns	93—94 (*n*-Hexane)	$C_{15}H_{13}NOS$	70.56 (70.38	5.13 5.28	5.49 5.23)
IVj	C_6H_5	CH_3	H	A	3.5	94	Colorless needles	87—88.5 (*n*-Hexane)	$C_{15}H_{13}NOS$	70.56 (70.41	5.13 5.13	5.49 5.55)

[a] These compounds have already been reported in the previous paper.[1]

[b] When the reaction time was prolonged, interesting but unidentified products appeared, which were separated from IV by means of column chromatography on silica gel using ether–pet. ether (1:3) or benzene as an eluent. Studies are now in progress on this interesting reaction and the results will be published shortly.

Table II. Spectral Data for 3-Acylbenzothiazolines (IV)

Compd. No.	IR ν cm^{-1} (C=O)	NMR δ ($CDCl_3$)	
		$COCH_3$ (3H, s)	Aromatic and other protons
IVa	1670	2.37	1.95 (6H, s, C_2–2CH_3), 6.95—7.30(4H, m, ArH)
IVb	1650	2.35	2.08 (3H, s, C_2–CH_3), 7.00—7.85 (9H, m, ArH)
IVc	1660	2.46	1.00 (6H, t, J=7 Hz, 2$CH_2C\underline{H}_3$), 1.50—2.45 (2H, m, $C\underline{H}_2CH_3$), 2.50—3.15 (2H, m, $C\underline{H}_2CH_3$), 6.95—7.40 (4H, m, ArH)
IVd	1730 1670	2.43	1.23 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 2.07 (3H, s, C_2–CH_3), 3.39 (2H, ABq, J=16.5 Hz, $\Delta\nu$=7.2 Hz, C_2–CH_2–), 4.13 (2H, q, J=7.5 Hz, $C\underline{H}_2CH_3$), 6.88—7.30 (4H, m, ArH)
IVe	1670	2.40	1.10—3.20 (10H, m, cyclohexane H), 6.90—7.50 (4H, m, ArH)
IVf	1650	2.43	0.92 (3H, d, J=7 Hz, CH_3), 1.60 (8H, m, cyclohexane H), 3.07 (1H, m, $C\underline{H}CH_3$), 6.90—7.33 (4H, m, ArH)
IVg	1650	2.35	1.56 (3H, d, J=8 Hz, CH_3), 5.95 (1H, br. s, C_2–H), 6.95—7.40 (4H, m, ArH)
IVh	1660	2.36	0.96 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.85 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 5.48—6.00 (1H, br. s, C_2–H), 6.80—7.80 (4H, m, ArH)
IVi	1670	2.25	6.80 (1H, br. s, C_2–H), 7.00—7.50 (8H, m, ArH), 7.50—8.50 (1H, m, ArH)
IVj	1630	—	1.63 (3H, d, J=6 Hz, CH_3), 5.96 (1H, q, J=6 Hz, C_2–H), 6.50—7.65 (9H, m, ArH)

TABLE III. Properties of 3-Acylbenzothiazoline 1-Oxides (V)

Compd. No.	R_1	R_2	R_3	Reaction time (hr)	Yield (%)	Appearance	mp or bp (°C) (Recryst. solvent)	Formula	Analysis (%) Calcd. (Found) C	H	N
Va	CH_3	CH_3	CH_3	24	86	Colorless columns	120 (EtOH–*n*-hexane)	$C_{11}H_{13}NO_2S$	59.17 (59.38	5.87 5.93	6.27 6.10)
Vb	CH_3	C_6H_5	CH_3	20	99	Colorless columns	160—161 (EtOH–*n*-hexane)	$C_{16}H_{15}NO_2S$	67.34 (67.56	5.30 5.35	4.91 5.00)
Vc	CH_3	C_2H_5	C_2H_5	20	75	Colorless plates	98.5—99 (Ether–pet. ether)	$C_{13}H_{17}NO_2S$	62.12 (62.37	6.82 6.84	5.57 5.57)
cis-Vd[a]	CH_3	CH_3	$CH_2CO_2C_2H_5$	20	50.3	Colorless prisms	111—112 (EtOH–*n*-hexane)	$C_{14}H_{17}NO_4S$	56.93 (57.08	5.80 5.70	4.74 4.67)
trans-Vd[a]	CH_3	$CH_2CO_2C_2H_5$	CH_3	20	38.4	Colorless oil	*b*)	$C_{14}H_{17}NO_2S$		*b*)	
Ve	CH_3	$-(CH_2)_5-$		20	86	Colorless needles	143—144 (CH_2Cl_2–ether)	$C_{14}H_{17}NO_2S$	63.85 (63.88	6.51 6.47	5.32 5.19)
Vf	CH_3	$-\underset{CH_3}{CH}(CH_2)_4-$		24	85	Colorless plates	144—146 (CH_2Cl_2–ether)	$C_{15}H_{19}NO_2S$	64.95 (64.90	6.90 6.85	5.05 4.87)
cis-Vg[c]	CH_3	H	CH_3	18	~3	Colorless columns	143—144 (Ether)	$C_{10}H_{11}NO_2S$	57.39 (57.24	5.30 5.39	6.69 6.44)
trans-Vg[c]	CH_3	CH_3	H	18	83	Colorless prisms	116—117 (Benzene–ether)	$C_{10}H_{11}NO_2S$	57.39 (57.38	5.30 5.28	6.69 6.70)
Vh	CH_3	C_2H_5	H	16	84	Colorless oil	176—178 [0.1 mmHg]	$C_{11}H_{13}NO_2S$	59.17 (58.89	5.87 5.98	6.27 6.25)
Vi	CH_3	C_6H_5	H	24	93	Colorless needles	169—170 (EtOH)	$C_{15}H_{13}NO_2S$	66.40 (66.50	4.83 4.83	5.16 5.02)
Vj	C_6H_5	CH_3	H	16	72	Colorless prisms	151—152 (EtOH–*n*-hexane)	$C_{15}H_{13}NO_2S$	66.40 (66.18	4.83 4.79	5.16 5.02)

a) The separation of these two isomers was carried out by column chromatography on silica gel using ether as an eluent to give *cis*-Vd from the first fraction and *trans*-Vd from the second fraction.

b) This compound was not analyzed because it decomposed on distillation, but the structure was unambiguously established by the spectral data.

c) The separation of these two isomers was performed by preparative TLC on silica gel using ethyl acetate as a developing solvent to give *cis*-Vg from the less polar zone (higher *Rf* value) and *trans*-Vg from the more polar zone (lower *Rf* value).

Table IV. Spectral Data for 3-Acylbenzothiazoline 1-Oxides (V)

Compd. No.	IR ν cm^{-1}		NMR δ ($CDCl_3$)	
	(C=O)	(S–O)	$COCH_3$ (3H, s)	Aromatic and other protons
Va	1670	1040	2.52	1.48 (3H, s, CH_3), 2.03 (3H, s, CH_3), 7.15—7.80 (3H, m, ArH), 7.85—8.10 (1H, m, ArH)
Vb	1660	1060	2.34	2.42 (3H, s, CH_3), 7.00—8.10 (9H, m, ArH)
Vc	1680	1040	2.55	0.90 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 1.16 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 1.50—2.40 (2H, m, $C\underline{H}_2CH_3$), 2.70—3.20 (2H, m, $C\underline{H}_2CH_3$), 7.25—7.70 (3H, m. ArH), 7.80—8.10 (1H, m, ArH)
cis-Vd	1730 1670	1040	2.55	1.30 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 1.62 (3H, s, CH_3), 3.65 (2H, ABq, $J=18$ Hz, $\Delta\nu=40$ Hz, $CH_2CO_2^-$), 4.24 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 7.10—7.70 (3H, m, ArH), 7.85—8.15 (1H, m, ArH)
trans-Vd	1730 1680	1060	2.52	1.20 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 2.06 (3H, s, CH_3), 2.97 (2H, s, $CH_2CO_2^-$), 4.05 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 7.15—8.15 (3H, m, ArH), 7.85—8.15 (1H, m, ArH)
Ve	1660	1050	2.51	1.15—2.40 (10H, m, cyclohexane H), 7.10—7.80 (3H, m, ArH), 7.80—8.10 (1H, m, ArH)
Vf	1675	1040	2.55	0.41 (3H, d, $J=7.5$ Hz, CH_3), 1.80 (8H, m, cyclohexane H), 3.00 (1H, m, $C\underline{H}CH_3$), 7.13—8.05 (4H, m, ArH)
cis-Vg	1665	1040	2.41	1.65 (3H, d, $J=7$ Hz, CH_3), 5.62 (1H, q, $J=7$ Hz, C_2-H), 7.25—7.90 (4H, m, ArH)
trans-Vg	1660	1040	2.46	1.43 (3H, d, $J=8$ Hz, CH_3), 5.43 (1H, q, $J=8$ Hz, C_2-H), 7.15—8.35 (4H, m, ArH)
Vh	1670	1040	2.45	1.12 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 1.40—2.00 (2H, q, $J=7.5$ Hz, $C\underline{H}_2CH_3$), 5.08—5.50 (1H, br.s, C_2-H), 7.16—8.30 (4H, m, ArH)
Vi	1670	1040	2.27	6.36 (1H, br. s, C_2-H), 7.05—8.00 (8H, m, ArH), 8.30—8.90 (1H, m, ArH)
Vj	1655	1040	—	1.42 (3H, d, $J=7$ Hz, CH_3), 5.54 (1H, q, $J=7$ Hz, C_2-H), 7.08—7.82 (8H, m, ArH), 7.82—8.05 (1H, m, ArH)

The present paper describes the synthesis and structures of benzothiazoline sulfoxides and sulfones[4] and a novel ring expansion reaction of benzothiazoline sulfoxides to benzothiazines.

Synthesis of 3-Acylbenzothiazoline 1-Oxides and 1,1-Dioxides

N-Alkyl substituted benzothiazolines are very sensitive to oxygen, and undergo autoxidation to yield ring opening products or give unidentified complex mixtures on oxidation with peracid.[5]

We have now found that stirring N-acylated benzothiazoline (I) in CCl_4 at 40—45° for 1 week yielded the corresponding sulfoxide (II) in 27% yield. This suggested the possibility of synthesizing N-acylated benzothiazoline sulfoxides or sulfones by oxidation using oxidizing agents such as peracid. In fact, when I was treated with 1 eq. of *m*-chloroperbenzoic acid (MCPBA) in CH_2Cl_2, II was obtained in high yield. We have successfully synthesized 3-acylbenzothiazoline sulfoxides (V) and sulfones (VI) by MCPBA oxidation of the corresponding 3-acylbenzothiazolines (IV) in CH_2Cl_2. The latter compounds were conveniently prepared by acylation of benzothiazolines (III) with acyl halides in the presence of K_2CO_3 (method

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4) The only previous report is: H. Breuer and E. Schulze, U.S. Patent 3720683 (1973) [*C.A.*, **79**, 18693*u* (1973)].

5) M. Hori, T. Kataoka, H. Shimizu, Y. Imai, and H. Fujimura, *Yakugaku Zasshi*, **95**, 634 (1975).

A) or with acid anhydride (method B) as shown in Chart 1. Acetylation of benzothiazoline-2-spirocyclohexane (IIIe) by method A was unsuccessful, but proceeded well by method B. On treatment with 2 eq. of MCPBA, 3-acetylbenzothiazoline-2-spirocyclohexane (IVe) and 3-acetylbenzothiazoline-2-spiro(2-methylcyclohexane) (IVf), which have sterically hindered substituents at the 2-position, underwent degradation reactions and failed to give the corresponding sulfones. The above results are summarized in Tables I—VI.

The 3-acylbenzothiazoline 1-oxides (Vb, Vd, Vf, Vg, Vh, Vi and Vj) are expected to have two configurational isomers due to the stereochemical relationship between the sulfoxide moiety and 2-substituents. However, studies of the nuclear magnetic resonance (NMR) spectra of Vf, Vh, Vi or Vj indicated the presence of essentially only one isomer, whose configuration is probably *trans* (*i. e.* sulfoxide relative to sterically hindered substituent). This

Table V. Properties of 3-Acylbenzothiazoline 1,1-Dioxides (VI)

Compd. No.	R_1	R_2	R_3	Reaction Time (hr)	Yield (%)	Appearance	mp or bp (°C) (Recryst. solvent)	Formula	Analysis (%) Calcd. (Found)		
									C	H	N
VIa	CH_3	CH_3	CH_3	9	96	Colorless needles	134 (EtOH–*n*-Hexane)	$C_{11}H_{13}NO_3S$	55.21 (55.13	5.48 5.51	5.85 5.73)
VIc	CH_3	C_2H_5	C_2H_5	20	88	Colorless prisms	46—47 (Ether–pet. ether)	$C_{13}H_{17}NO_3S$	58.40 (58.45	6.41 6.36	5.24 5.08)
VId	CH_3	CH_3	$CH_2CO_2C_2H_5$	20	54	Colorless needles	67.5—68.5 (Ether–pet. ether)	$C_{14}H_{17}NO_3S$	54.01 (54.16	5.50 5.50	4.50 4.28)
VIg	CH_3	H	CH_3	24	93	Colorless needles	133—133.5 (EtOH–*n*-hexane)	$C_{10}H_{11}NO_3S$	53.32 (53.35	4.92 4.85	6.22 6.23)
VIh	CH_3	C_2H_5	H	24	92	Colorless oil	158—160 [0.1 mmHg]	$C_{11}H_{13}NO_3S$	55.21 (55.30	5.48 5.51	5.85 5.75)
VIi	CH_3	C_6H_5	H	18	78	Colorless columns	135—136 (EtOH–*n*-hexane)	$C_{15}H_{13}NO_3S$	62.70 (62.49	4.56 4.53	4.87 4.76)
VIj	C_6H_5	CH_3	H	16	87	Colorless needles	112—113 (Ether–*n*-hexane)	$C_{15}H_{13}NO_3S$	62.70 (62.43	4.56 4.66	4.87 4.64)

Table VI. Spectral Data for 3-Acylbenzothiazoline 1 1-Dioxides (VI)

Compd. No.	IR ν cm^{-1}		NMR δ ($CDCl_3$)	
	(C=O)	(SO_2)	$COCH_3$ (3H, s)	Aromatic and other protons
VIa	1660	1320 1150	2.49	1.81 (6H, s, C_2-$2CH_3$), 7.20—8.00 (4H, m, ArH)
VIc	1680	1310 1120	2.43	0.92 (6H, t, $J=7.5$ Hz, $2CH_2C\underline{H}_3$), 1.90—2.70 (4H, m, $2C\underline{H}_2CH_3$), 7.10—7.90 (4H, m, ArH)
VId	1740 1680	1330 1140	2.53	1.23 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 1.92 (3H, s, CH_3), 3.23 (2H, ABq, $J=16$ Hz, $\Delta\nu=12$ Hz, CH_2CO_2–), 4.12 (2H, q, $J=7.5$ Hz, $C\underline{H}_2CH_3$), 7.18—7.95 (4H, m, ArH)
VIg	1680	1320 1160	2.45	1.65 (3H, d, $J=8$ Hz, CH_3), 5.22 (1H, q, $J=8$ Hz, C_2–H), 7.20—8.25 (4H, m, ArH)
VIh	1680	1330 1150	2.45	1.06 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 2.00 (2H, q, $J=7.5$ Hz, $C\underline{H}_2CH_3$) 5.23 (1H, t, $J=6.5$ Hz, C_2–H), 7.30—8.20 (4H, m, ArH)
VIi	1690	1320 1155	2.20	6.00 (1H, s, C_2–H), 7.10—8.00 (8H, m, ArH), 8.45—8.75 (1H, m, ArH)
VIj	1655	1330 1160	—	1.68 (3H, d, $J=7$ Hz, CH_3), 5.30 (1H, q, $J=7$ Hz, C_2–H), 6.85—7.68 (8H, m, ArH), 7.68—7.91 (1H, m, ArH)

configuration seems reasonable in view of that of 2,2-disubstituted 1,3-dithiolane 1-oxides.[6] On the other hand, the NMR spectra of crude Vd suggested the presence of *cis* and *trans* isomers (sulfoxide to ethoxycarbonylmethyl group) as a 5 : 4 mixture, which was successfully separated by column chromatography on silica gel using ether as an eluent. The structural assignments of *cis*-Vd and *trans*-Vd were based on NMR chemical shifts. In chloroform, the minor isomer has its methyl resonance at lower field (δ: 2.05) than the major isomer (δ: 1.62), and its methylene resonance at higher field (δ: 2.95 *vs.* 3.65 (AB quartet center)). On the basis of the known deshielding effect of a proximate sulfinyl oxygen, it is assigned the *trans* structure (*trans*-Vd). Therefore, the major isomer is assigned the *cis* structure (*cis*-Vd). Both *cis*-Vd and *trans*-Vd gave the same sulfone (VId), mp 68—69°, in good yield on MCPBA oxidation.

cis- and *trans*-3-Acetyl-2-methylbenzothiazoline 1-oxides (*cis*-Vg and *trans*-Vg) were also successfully separated by preparative thin–layer chromatography (TLC) on silica gel using ethyl acetate as the developing solvent. The structural assignments of *cis*-Vg and *trans*-Vg were based on their chromatographic retention times and NMR spectroscopy results, including aromatic solvent-induced shifts (ASIS) together with the NMR chemical shift studies discussed above (see Table IV). These methods were widely used by Johnson *et al.*,[7] Anderson *et al.*,[8] and Whitney *et al.*[9] in the configurational assignments of *cis–trans* stereoisomers of cyclic sulfoxides having a methyl group at a neighboring carbon atom. The minor isomer has the larger *Rf* value on TLC, suggesting that in this isomer the sulfoxide oxygen is more sterically hindered and therefore of *cis* configuration (*cis*-Vg). The major isomer with the smaller *Rf* value is consequently assigned the *trans* configuration (*trans*-Vg). This assignment is strongly supported by the ASIS studies, which indicated a larger shielding relative to an inert solvent (chloroform), of the C-methyl group in the *trans* isomer, while a larger shielding occurs for the methine proton in the *cis* isomer. This is indeed observed (see Table VII) using the assignment given above (C-methyl: $\Delta_{trans}/\Delta_{cis}=1.57$, methine: $\Delta_{trans}/\Delta_{cis}=5.14$).

TABLE VII. Solvent Effects in the NMR Spectra of 3-Acetyl-2-methylbenzothiazoline 1-Oxide (Vg)

Compd. No.	Solvent	δ CH$_3$	δ H	$\Delta^{CH_3}_{CDCl_3-C_6D_6}$	$\Delta^{H}_{CDCl_3-C_6D_6}$	$\Delta^{CH_3}_{trans}/\Delta^{CH_3}_{cis}$	$\Delta^{H}_{trans}/\Delta^{H}_{cis}$
cis-Vg	CDCl$_3$	1.65	5.62	+0.42	+1.08	1.57	5.14
	C$_6$D$_6$	1.23	4.54				
trans-Vg	CDCl$_3$	1.43	5.43	+0.66	+0.21		
	C$_6$D$_6$	0.77	5.22				

The ratio of the isomers obtained may reflect the likelihood that MCPBA oxidation takes place by approach to the 3-acetylbenzothiazolines from the least hindered side.

A Novel Ring Expansion Reaction of 3-Acetylbenzothiazoline 1-Oxides

On refluxing 2-alkyl substituted 3-acetylbenzothiazoline sulfoxides in acetic anhydride, a novel ring expansion reaction occurred to give 4-acetylbenzothiazines.[10]

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6) C.H. Chen, *Tetrahedron Lett.*, **1976**, 25.

7) J.J. Rigau, C.C. Bacon, and C.R. Johnson, *J. Org. Chem.*, **35**, 3655 (1970).

8) K.K. Anderson, R.L. Caret, and I.K. Nielson, *J. Am. Chem. Soc.*, **96**, 8026 (1974).

9) T.A. Whitney and W.H. Pirkle, *Tetrahedron Lett.*, **1974**, 2299.

10) The synthesis of 4*H*-1,4-benzothiazines by the reaction of 2,2-dialkyl substituted benzothiazolines with sulfuryl chloride at 0° was recently reported by Prota *et al.* (F. Chioccara, G. Prota, R.A. Nicolaus, and E. Novellino, *Synthesis*, **1977**, 876).

Thus, 3-acetyl-2,2-dimethylbenzothiazoline 1-oxide (Va) was refluxed in acetic anhydride to give two products VII and VIII in yields of 31.5% and 48.6%, respectively. The structures of these compounds were confirmed by elementary analyses and spectral data. Compound VII was isomerized to VIII quantitatively on heating at 150° for 3 hr. The reaction of Ve with acetic anhydride gave IX and X in 72.1 and 13.8% yields, respectively. On heating, compound IX was not isomerized to X, but decomposed. Similarly, Vf afforded XI and XII in yields of 22.5% and 39.1%, respectively. In this case, ring expansion in the direction of the carbon atom carrying the methyl group did not occur. In the reaction of *cis*-Vd, which may be able to ring-expand in two directions, the isolated product was XIII (37.4% yield), indicating expansion only in the direction of the ethoxycarbonylmethyl group. The *exo*-methylene compound XIII′ was not observed. This is not unexpected if one considers that XIII′ is much less stable compared with XIII, having an α,β-conjugated ester system.

The reaction of Vb with acetic anhydride was more complex and unexpected products, XV, XVI[11] and XVII, were obtained in yields of 7%, 10% and 15%, respectively, in

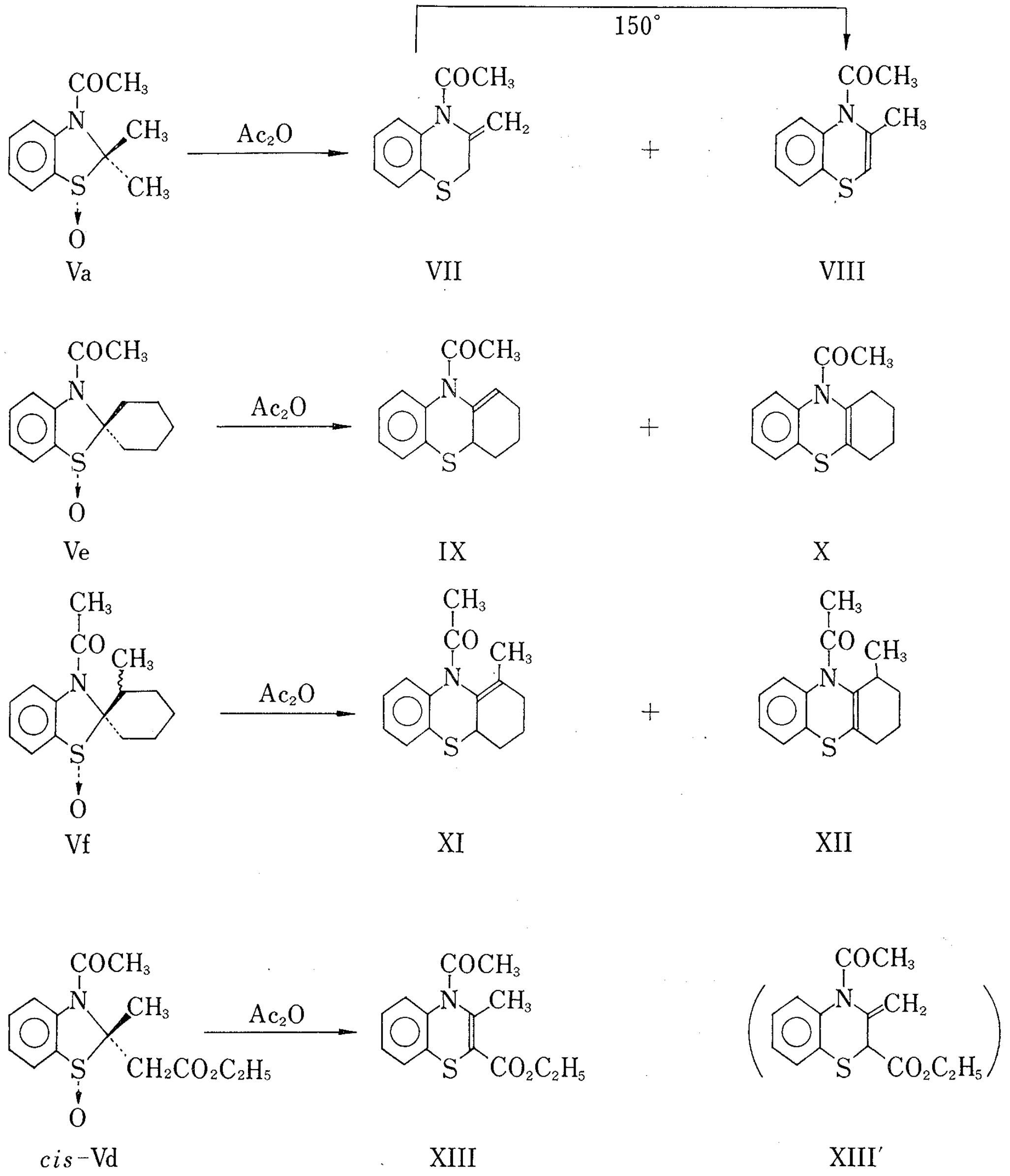

Chart 2

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[11] M. Wilhelm and P. Schmidt, *J. Heterocycl. Chem.*, 6, 635 (1969).

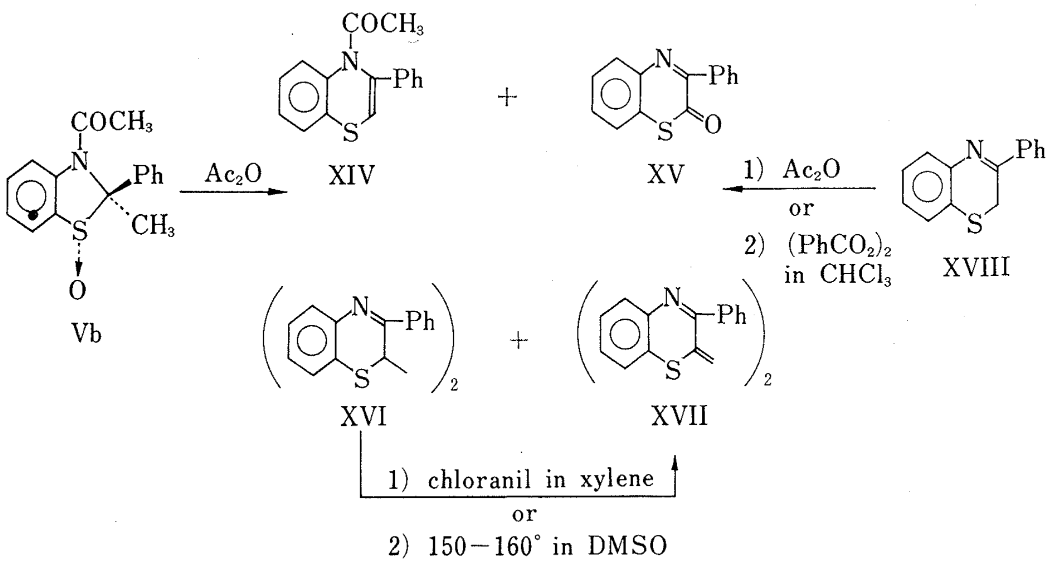

Chart 3

addition to the expected product XIV (37.8%). The formation of XV, XVI and XVII probably involves autoxidation of initially formed 3-phenyl-2*H*-1,4-benzothiazine (XVIII) (for the formation of this compound, see Chart 6) under the reaction conditions used. This view is supported by the results of the following experiments. Refluxing XVIII[11] in acetic anhydride gave XIV, XV, XVI and XVII in 18, 25.2, 28.4 and 11.3% yields, respectively. Stirring XVIII in chloroform in the presence of benzoyl peroxide at room temperature for 3 days afforded XV, XVI and XVII in yields of 37.1%, 13.1% and 13.2%, respectively. Finally, on treatment with chloranil in refluxing xylene or on heating at 150—160° in dimethyl sulfoxide (DMSO), XVI was converted into XVII in high yield.

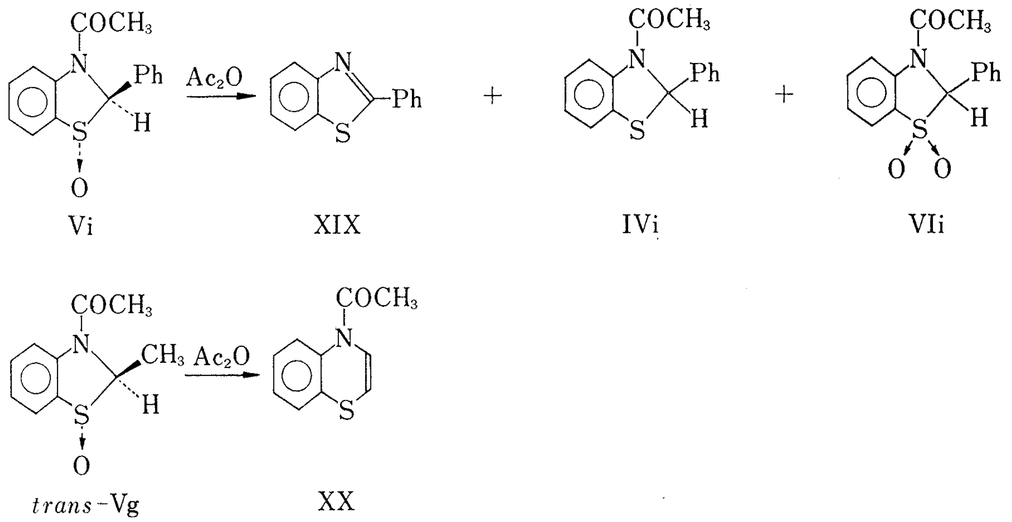

Chart 4

Next, we examined the reaction of 2-monosubstituted benzothiazoline sulfoxides with acetic anhydride. Vi gave XIX[12] in 57.1% yield together with IVi and VIi. On the other hand, *trans*-Vg gave only a ring expansion product XX in 39.3% yield (Chart 4). Compound XX was identical (mixed mp, infrared (IR) and NMR spectra) with a sample synthesized unambiguously by the route depicted in Chart 5. Oxidation of XXI[13] with MCPBA in CH_2Cl_2

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12) H. Lankelma and P.X. Sharnoff, *J. Am. Chem. Soc.*, **53**, 2654 (1931); M.T. Bogert and A. Stull, *ibid.*, **47**, 3078 (1925).

13) R.N. Prasad and K. Tietje, *Can. J. Chem.*, **44**, 1247 (1966).

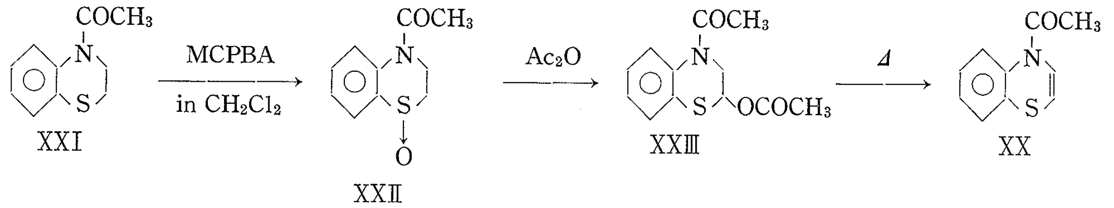

Chart 5

gave the corresponding sulfoxide XXII, which was subjected to the Pummerer rearrangement in acetic anhydride to yield an isolable acetate XXIII. On heating at 250° for 5 hr in the absence of a solvent, compound XXIII was deacetylated to give XX in 41% yield. The formation of XX from *trans*-Vg is rather unusual because sulfoxides having at least one proton at the α-position usually give the products of a normal Pummerer-type rearrangement upon treatment with acetic anhydride.[14] To our knowledge, this is the first example of an α-monosubstituted cyclic sulfoxide undergoing ring expansion in the reaction with acetic anhydride.

Two possible mechanisms (path a and path b) for the ring expansion reaction of benzothiazoline sulfoxides to benzothiazines can be considered, as shown in Chart 6. Path a involves initial acetylation of oxygen of the sulfoxide, forming an intermediate XXIV, followed by S–C_2 cleavage with β-hydrogen abstraction to give the sulfenic anhydride XXVI as an intermediate, which then leads to the immonium ion XXVII by recyclization with the loss of

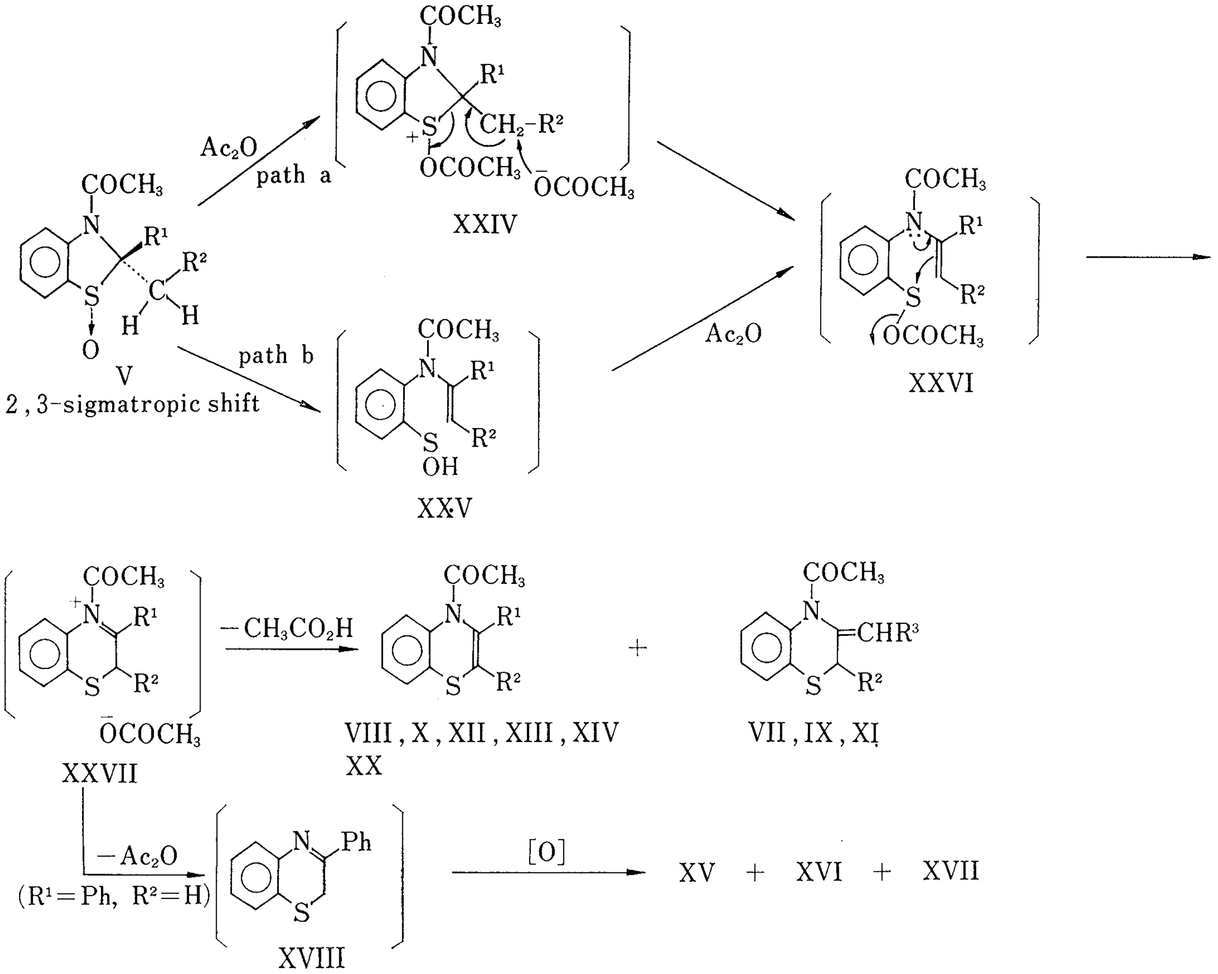

Chart 6

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[14] R.B. Morin, D.O. Spry, and R.A. Mueller, *Tetrahedron Lett.*, **1969**, 849.

acetate ion. Collapse of the immonium ion XXVII leads to XV, XVI and XVII by way of XVIII, and VIII, X, XII, XIII, XIV and XX by deacetylation in the *endo*-direction as well as VII, IX and XI by deacetylation in the *exo*-direction. On the other hand, path b 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 XXV which is acetylated by acetic anhydride to give the intermediate XXVI. The latter mechanism is more generally accepted in similar reaction, as seen in the transformation of penicillin sulfoxides to cephalosporins (Morin rearrangement[15]), in which the sulfenic acid intermediates have been isolated.[16] The present ring expansion of Vb, Vd or Vf can also be explained quite reasonably by the path b mechanism. The ring expansion of *trans*-Vg might be explained by assuming that *trans*-Vg probably epimerized to the *cis* form before ring opening under the reaction conditions used.

Finally, we propose a normal Pummerer-type rearrangement mechanism for the formation of XIX from Vi, as shown in Chart 7.

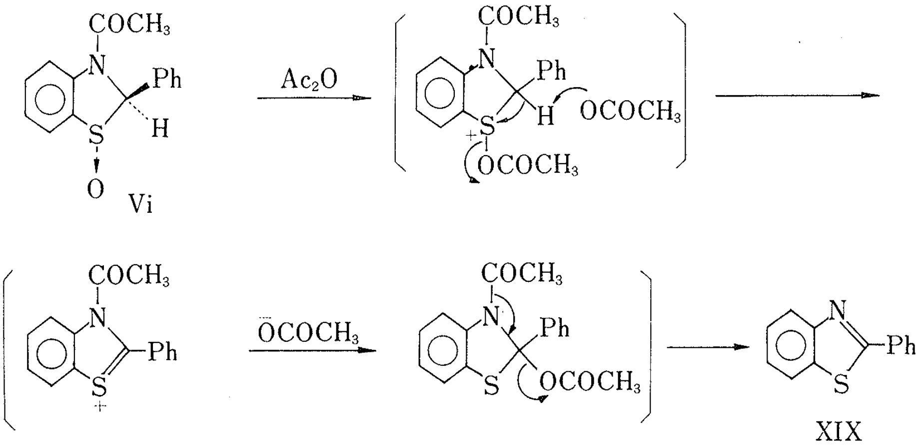

Chart 7

The novel ring expansion reaction of benzothiazoline sulfoxides described in the present paper may prove to be widely applicable for the preparation of 1,4-benzothiazines.

Experimental

Melting points were taken on a Yanagimoto micromelting point apparatus and are uncorrected. IR spectra were determined on a JASCO IRA-1 machine. NMR spectra were determined on a Hitachi R-20B spectrometer; chemical shifts are given in parts per million relative to tetramethylsilane as an internal standard. Mass spectra (MS) were taken on a Hitachi RMU-6E spectrometer at an ionizing voltage of 70 eV. Ultraviolet (UV) spectra were measured with a Hitachi 200-10 spectrometr.

The following benzothiazolines were synthesized by the methods reported in the literature. 2,2-Dimethylbenzothiazoline (IIIa), 2-methyl-2-phenylbenzothiazoline (IIIb), 2,2-diethylbenzothiazoline (IIIc), benzothiazoline-2-spirocyclohexane (IIIe),[17] 2-methylbenzothiazoline (IIIg), 2-ethylbenzothiazoline (IIIh)[18] and 2-phenylbenzothiazoline (IIIi).[19]

2-Ethoxycarbonylmethyl-2-methylbenzothiazoline (IIId)——Ethyl acetoacetate (11.44 g, 88 mmol) was added to a solution of *o*-aminobenzenethiol (10 g, 80 mmol) in xylene (150 ml), and the mixture was refluxed for 4 hr with stirring. Xylene was evaporated and the residue was chromatographed on silica gel using benzene as an eluent to give an oil which was purified by vacuum distillation to afford 6.17 g (32.5%) of pale

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15) E.H. Flynm, "Cephalosporins and Penicillins," Academic Fress, Inc., New York, 1972, p.183. P.G. Sammes, *Chem. Revs.*, **76**, 113 (1976).

16) T.S. Chou, J.R. Burgtoff, A.L. Ellis, S.R. Lammert, and S.P. Kukolja, *J. Am. Chem. Soc.*, **96**, 1609 (1974).

17) R.C. Elderfield and E.C. McClenachan, *J. Am. Chem. Soc.*, **82**, 1982 (1960).

18) H. Larive, A.J. Chambonnet, and J. Metzger, *Bull. Chim. France*, **1963**, 1675 [*C.A.*, **60**, 2735*b* (1964)].

19) S. Tagami, C. Tabuchi, K. Morimoto, and D. Shiho, *Yakugaku Zasshi*, **94**, 929 (1974).

yellow oil, bp 140° (0.15 mmHg) (lit.[20] 190—192° (15 mmHg)). *Anal.* Calcd. for $C_2H_{15}NO_2S$: C, 60.76; H, 6.33; N, 5.91. Found: C, 60.86; H, 6.15; N, 5.84. NMR ($CDCl_3$) δ: 1.25 (3H, t, J=7 Hz, $C\underline{H}_2CH_3$), 1.85 (3H, s, C_2–CH_3), 3.00 (2H, ABq, J=15 Hz, δAB=26 Hz, –CH_2CO_2–), 4.20 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 5.00—5.20 (1H, br.s, NH), 6.50—7.20 (4H, m, ArH).

Benzothiazoline-2-spiro(2-methylcyclohexane) (IIIf)——2-Methylcyclohexanone (2.24 g, 20 mmol) was added to a solution of *o*-aminobenzenethiol (2.5 g, 20 mmol) in EtOH (50 ml), and the mixture was refluxed for 4 hr with stirring under a nitrogen atmosphere. The solvent was evaporated off *in vacuo* and the resulting oil was vacuum-distilled to give 3.8 g (86%) of yellow oil, bp 162—168° (4.5 mmHg). *Anal.* Calcd. for $C_{13}H_{17}NS$: C, 71.18; H, 7.81; N, 6.39. Found: C, 71.04; H, 7.72; N, 6.46. IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3350 (NH). NMR ($CDCl_3$) δ: 1.05 (3H, d, J=6 Hz, CH_3), 1.60 (8H, m, cyclohexane H), 2.37 (1H, m, $C\underline{H}$–CH_3), 3.93 (1H, br.s, NH), 6.45—7.12 (4H, m, ArH).

3-Chloroacetylbenzothiazoline 1-Oxide (II)——a) Autoxidation of 3-Chloroacetylbenzothiazoline (I)[1]: A mixture of I (1.28 g, 6 mmol) and CCl_4 (20 ml) was stirred at 40—45° for one week. The resulting solid was filtered off and recrystallized from EtOH–*n*-hexane to afford 0.345 g (25%) of II as colorless needles, mp 176—178°. *Anal.* Calcd. for $C_9H_8ClNO_2S$: C, 47.06; H, 3.51; N, 6.10. Found: C, 47.14; H, 3.51; N, 6.09. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1670 (CO), 1040 (SO). NMR (CF_3CO_2H) δ: 4.63 (2H, s, $COCH_2Cl$), 5.48 (2H, ABq, J=14.5 Hz, δAB=39.2 Hz, C_2-2H), 7.35—8.80 (4H, m, ArH). MS *m/e*: 229 (M^+), 136 (base).

b) Oxidation of I with MCPBA: MCPBA (85%; 0.231 g, 0.93 mmol) was added portionwise with stirring to an ice-cold solution of I (0.2 g, 0.93 mmol) in CH_2Cl_2 (10 ml). After stirring for 24 hr at room temperature, the reaction mixture was neutralized by the addition of saturated $NaHCO_3$ solution and the organic layer was separated, washed with water, dried over $MgSO_4$ and evaporated down under reduced pressure. Ether was added to the residual oil to form a solid which was recrystallized from EtOH to give 0.212 g (99%) of II. This compound was identical with the sulfoxide obtained above in all respects.

Preparation of 3-Acetylbenzothiazolines (IVa, IVc, IVd and IVg). General Procedure (Method A)——A solution of acetyl chloride (1.6 g, 20 mmol) in dry ether (10 ml) was added slowly to a suspension of benzothiazolines (IIIa, IIIc, IIId and IIIg) (0.5 mmol) and K_2CO_3 (4.2 g, 30 mmol) in dry ether (50 ml). The mixture was refluxed for 3—24 hr with stirring, then excess K_2CO_3 was filtered off and the filtrate was evaporated to dryness under reduced pressure. The residual oil was vacuum-distilled. IVd solidified after distillation, and was recrystallized from *n*-hexane to obtain an analytical sample. Analytical and spectral data are listed in Tables I and II.

Preparation of 3-Acetylbenzothiazolines (IVb, IVe, IVf, IVh and IVi). General Procedure (Method B)——A mixture of benzothiazolines (IIIb, IIIe, IIIf, IIIh and IIIi) (26 mmol) and acetic anhydride (25 ml) was refluxed for 2—4 hr with stirring. Acetic anhydride was evaporated off *in vacuo* and the residue was washed with aqueous $NaHCO_3$ solution, then extracted with CH_2Cl_2. The extract was washed with water, dried over $MgSO_4$ and evaporated down. The residue was purified by vacuum distillation or recrystallization from the appropriate solvent. The results are listed in Tables I and II.

3-Benzoyl-2-methylbenzothiazoline (IVj)——A solution of benzoyl chloride (2.81 g, 20 mmol) in dry ether (10 ml) was added slowly to a stirred mixture of K_2CO_3 (8.5 g, 60 mmol) and 2-methylbenzothiazoline (IIIg) (1.51 g, 10 mmol) in dry ether (30 ml), and the mixture was refluxed for 3.5 hr. After cooling, K_2CO_3 was removed by filtration and the filtrate was washed with aqueous $NaHCO_3$ and dried over $MgSO_4$. The solvent was removed by distillation and the residual oil was purified by vacuum distillation. Analytical and spectral data are listed in Tables I and II.

General Procedure for the Preparation of 3-Acylbenzothiazoline 1-Oxides (Va—Vi)——MCPBA (10 mmol) was added portionwise to a stirred, ice-cooled solution of 3-acylbenzothiazolines (IVa—IVi) (10 mmol) in CH_2Cl_2 (50 ml), and the mixture was stirred for 24 hr at room temperature. The reaction mixture was washed with aqueous $NaHCO_3$ solution, dried over $MgSO_4$ and evaporated down *in vacuo*. The residue was vacuum-distilled or recrystallized from an appropriate solvent. The results are listed in Tables III and IV.

General Procedure for the Preparation of 3-Acylbenzothiazoline 1,1-Dioxides (VI)——A mixture of 3-acylbenzothiazoline 1-oxides (V) (2 mmol) and MCPBA (3 mmol) in CH_2Cl_2 (30 ml) was stirred for 9—24 hr at room temperature. The reaction mixture was washed with aqueous $NaHCO_3$ then the CH_2Cl_2 layer was separated, washed with water and dried over $MgSO_4$. The solvent was evaporated off under reduced pressure and the residue was purified by vacuum distillation or recrystallization. Analytical and spectral data are listed in Tables V and VI.

Reaction of 3-Acetyl-2,2-dimethylbenzothiazoline 1-Oxide (Va) with Acetic Anhydride——A mixture of Va (0.558 g, 2.5 mmol) and acetic anhydride (35 ml) was refluxed for 1 hr with stirring. Acetic anhydride was evaporated off under reduced pressure then aqueous $NaHCO_3$ was added to the residue, and stirred for 30 min. The mixture was extracted with CH_2Cl_2 and the extract was washed with water, dried over $MgSO_4$ and evaporated down *in vacuo* to give a crude oil. Separation of the oil by preparative TLC on silica gel using ether–pet. ether (4: 7) as a developing solvent afforded 0.161 g (32%) of 4-acetyl-3-methylene-2,3-4*H*-1,4-benzothiazine (VII) and 0.25 g (49%) of 4-acetyl-3-methyl-4*H*-1,4-benzothiazine (VIII). VII: Colorless

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[20] A.I. Kiprianov and V.A. Portnyagina, *Zhur. Obshchei. Khim.*, **25**, 2257 (1955) [*C.A.*, **62**, 9378*f* (1956)].

plates from ether–*n*-hexane, mp 93—94°. *Anal.* Calcd. for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82. Found: C, 64.51; H, 5.28; N, 6.79. IR ν_{max}^{KBr} cm^{-1}: 1660 (CO), 925 (=CH_2). NMR ($CDCl_3$) δ: 2.20 (3H, s, $COCH_3$), 3.89 (2H, br.s, C_2–H), 5.33 (1H, s, $=C\langle^{H}_{\underline{H}}$), 5.42 (1H, br.s, $=C\langle^{\underline{H}}_{H}$), 7.00—7.90 (4H, m, ArH). UV λ_{max}^{EtOH} nm (ε): 300 (1100), 290 (1500), 255 (9700), 229 (17000), 205 (16000). MS *m/e*: 205 (M$^+$), 163 (base). VIII: Colorless oil, bp 120° (0.3 mmHg). *Anal.* Calcd. for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82. Found: C, 64.49; H, 5.41; N, 6.61. IR ν_{max}^{neat} cm^{-1}: 1670 (CO). NMR ($CDCl_3$) δ: 2.11 (3H, s, $COCH_3$), 2.25 (3H, d, $J=1$ Hz, C_3–CH_3), 6.28 (1H, q, $J=1$ Hz, C_2–H), 7.10—7.50 (4H, m, ArH).

Thermal Isomerization of VII to VIII——Compound VII (0.205 g, 1 mmol) was heated in the absence of a solvent at 150° for 3 hr. The oily reaction mixture obtained was vacuum-distilled to provide 0.191 g (94%) of VIII. This compound was identified with the sample obtained above by comparison of the IR and NMR spectra.

Reaction of 3-Acetylbenzothiazoline-2-spirocyclohexane 1-Oxide (Ve) with Acetic Anhydride——A mixture of Ve (1 g, 38 mmol) and acetic anhydride (25 ml) was refluxed for 1 hr, and worked up as described for Va to give a crude oil. Separation of the oil by preparative TLC on silica gel using ether–pet. ether (1 : 1) as a developing solvent yielded 0.487 g (72.1%) of 10-acetyl-2,3,4,4a-tetrahydrophenothiazine (IX) and 0.128 g (13.75%) of 10-acetyl-1,2,3,4-tetrahydrophenothiazine (X) IX: Colorless prisms from EtOH–*n*-hexane, mp 100—101°. *Anal.* Calcd. for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71. Found: C, 68.46; H, 6.13; N, 5.13. IR ν_{max}^{KBr} cm^{-1}: 1660 (CO). NMR ($CDCl_3$) δ: 1.50—2.50 (6H, m, C_2–2H, C_3–2H, C_4–2H), 2.17 (3H, s, $COCH_3$), 4.25 (1H, m, C_{4a}–H), 6.00 (1H, d.t, $J=2$ and 4 Hz, C_1–H), 7.00—7.70 (4H, m, ArH). UV λ_{max}^{EtOH} nm (ε): 300 (1050), 290 (1410), 255 (1400), 230 (18200), 215 (12800). MS *m/e*: 245 (M$^+$), 203 (base). X: Colorless prisms from EtOH–*n*-hexane, mp 146—147°. *Anal.* Calcd. for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71. Found: C, 68.66; H, 6.19; N, 5.67. IR ν_{max}^{KBr} cm^{-1}: 1660 (CO). NMR ($CDCl_3$) δ: 1.50—2.00 (4H, m, C_2–2H, C_3–2H), 2.08 (3H, s, $COCH_3$), 2.15—2.70 (4H, m, C_1–2H, C_4–2H), 7.00—7.80 (4H, m, ArH). UV λ_{max}^{EtOH} nm (ε): 253.5 (8520), 212.5 (13870). MS *m/e*: 245 (M$^+$), 202 (base).

Reaction of 3-Acetylbenzothiazoline-2-spiro (2-methylcyclohexane)1-Oxide (Vf) with Acetic Anhydride——A mixture of Vf (0.555 g, 2 mmol) and acetic anhydride (10 ml) was refluxed for 2 hr and worked up as usual. The resulting oil was subjected to preparative TLC on silica gel using ether–pet. ether (1 : 3) to yield 0.117 g (22.5%) of 10-acetyl-1-methyl-2,3,4,4a-tetrahydrophenothiazine (XI) and 0.203 g (39.1%) of 10-acetyl-1-methyl-1,2,3,4-tetrahydrophenothiazine (XII). XI: Colorless columns from *n*-hexane, mp 117—118°. *Anal.* Calcd. for $C_{15}H_{17}NOS$: C, 69.46; H, 6.61; N, 5.40. Found: C, 69.64; H, 6.71; N, 5.41. IR ν_{max}^{KBr} cm^{-1}: 1650 (CO). NMR ($CDCl_3$) δ: 1.75 (3H, s, CH_3), 1.92 (6H, m, $3CH_2$), 2.15 (3H, s, $COCH_3$), 4.34 (1H, m, C_{4a}–H), 7.05—7.70 (4H, m, ArH). UV λ_{max}^{EtOH} nm (ε): 233 (10220), 255 (4570), 292 (774), 302 (540). XII: Colorless columns from EtOH, mp 147°. *Anal.* Calcd. for $C_{15}H_{17}NOS$: C, 69.46; H, 6.61; N, 5.40. Found: C, 69.36; H, 6.53; N, 5.46. IR ν_{max}^{KBr} cm^{-1}: 1650 (CO). NMR ($CDCl_3$) δ: 1.20 (3H, d, $J=7.5$ Hz, CH_3), 1.88 (4H, m, $2CH_2$), 2.11 (3H, s, $COCH_3$), 2.37 (2H, m, CH_2), 3.21 (1H, m, $C\underline{H}$–CH_3), 7.30—7.70 (4H, br.s, ArH). UV λ_{max}^{EtOH} nm (ε): 255 (4300).

Reaction of 3-Acetyl-2-ethoxycarbonylmethyl-2-methylbenzothiazoline 1-Oxide (*cis*-Vd) with Acetic Anhydride——A mixture of *cis*-Vd (0.72 g, 2.44 mmol) and acetic anhydride (30 ml) was refluxed for 3 hr. The reaction mixture was worked up as usual to give a crude oil which was subjected to preparative TLC on silica gel using ether–pet. ether (1 : 1) as a solvent to afford 0.253 g (37.4%) of 4-acetyl-2-ethoxycarbonyl-3-methyl-4*H*-1,4-benzothiazine (XIII) as colorless prisms, mp 64—64.5° after recrystallization from pet. ether. *Anal.* Calcd. for $C_{14}H_{15}NO_3S$: C, 60.63; H, 5.45; N, 5.05. Found: C, 60.86; H, 5.46; N, 5.04. IR ν_{max}^{KBr} cm^{-1}: 1690 (CO), 1680 (CO). NMR ($CDCl_3$) δ: 1.36 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 2.15 (3H, s, C_3–CH_3), 2.63 (3H, s, $COCH_3$), 4.34 (2H, q, $J=7$ Hz, $C\underline{H}_2CH_3$), 7.10—7.70 (4H, m, ArH).

Reaction of 3-Acetyl-2-methyl-2-phenylbenzothiazoline 1-Oxide (Vb) with Acetic Anhydride——A mixture of Vb (0.068 g, 2.4 mmol) and acetic anhydride (20 ml) was refluxed for 2 hr and worked up as usual to give a crude oil which was separated by preparative TLC on silica gel using ether–pet. ether (1 : 4) as a solvent to give the following four compounds. 4-Acetyl-3-phenyl-4*H*-1,4-benzothiazine (XIV): yield: 0.242 g (37.8 %), bp 196° (0.5 mmHg). *Anal.* Calcd. for $C_{16}H_{13}NOS$: C, 71.88; H, 4.90; N, 5.24. Found: C, 71.87; H, 4.95; N, 4.85. IR ν_{max}^{KBr} cm^{-1}: 1680 (CO). NMR ($CDCl_3$) δ: 1.95 (3H, s, $COCH_3$), 6.85 (1H, s, C_2–H), 7.00—8.20 (9H, m, ArH). 2-Oxo-3-phenyl-2*H*-1,4-benzothiazine (XV): yield: 0.035 g (7%), yellow needles from *n*-hexane, mp 100—101°. *Anal.* Calcd. for $C_{14}H_9NOS$: C, 70.27; H, 3.79; N, 5.85. Found: C, 70.41; H, 3.67; N, 5.72. IR ν_{max}^{KBr} cm^{-1}: 1610 (CO). NMR ($CDCl_3$) δ: 7.20—7.80 (5H, m, ArH), 7.80—8.35 (4H, m, ArH). MS *m/e*: 239 (M$^+$), 211 (base). 2-(3-Phenyl-2*H*-1,4-benzothiazin-2-yl)-3-phenyl-2*H*-1,4-benzothiazine (XVI): yield: 0.098 g (18%), light yellow prisms, mp 234° (lit.[11] 234—235°). *Anal.* Calcd. for $C_{28}H_{20}N_2S_2$: C, 75.00; H, 4.50; N, 6.25. Found: C, 75.21; H, 4.68; N, 6.05. IR ν_{max}^{KBr} cm^{-1}: 1590, 1560, 1540. NMR ($CDCl_3$) δ: 4.16 (2H, s, C_2–H, $C_{2'}$–H), 6.85—7.85 (18H, m, ArH). MS *m/e*: 448 (M$^+$), 224 (base). The identity of this compound was confirmed by comparison of the mp, and IR and NMR spectra with those of the authentic compound. $\Delta^{2,2'}$-Bi-(3-phenyl-2*H*-1,4-benzothiazine) (XVII): yield: 0.07 g (15%), red needles from EtOH–*n*-hexane, mp 264°. *Anal.* Calcd. for $C_{28}H_{18}N_2S_2$: C, 75.30; H, 4.06; N, 6.27. Found: C, 75.35; H, 4.16; N, 5.99. IR ν_{max}^{KBr} cm^{-1}: 1540, 1450. NMR ($CDCl_3$) δ: 6.85—8.15 (m, ArH). MS *m/e*: 446 (M$^+$, base).

Reaction of 3-Phenyl-2*H*-1,4-benzothiazine (XVIII)[11] with Acetic Anhydride——A solution of XVIII

(0.5 g, 2.22 mmol) in acetic anhydride was refluxed for 3 hr with stirring. After removing excess acetic anhydride by evaporation *in vacuo*, saturated $NaHCO_3$ solution was added to the residue and the mixture was stirred for 30 min at room temperature. The mixture was extracted with $CHCl_3$ and the extract was washed with water, then dried over $MgSO_4$. The solvent was evaporated off to give a crude oil which was separated by preparative TLC on silica gel using ether–pet. ether as a solvent to yield XIV (0.107 g, 18%), XV (0.133 g, 25.2%), XVI (0.141 g, 28.4%) and XVII (0.056 g, 11.3%). These compounds were identical with the corresponding compounds obtained from the above reaction on the basis of their mp, and IR and NMR spectra.

Oxidation of XVIII with Benzoyl Peroxide——A solution of benzoyl peroxide (0.1 g, 0.41 mmol) in $CHCl_3$ (10 ml) was added to a solution of XVIII (0.5 g, 2.22 mmol) in $CHCl_3$ (30 ml), and the mixture was stirred for 72 hr at room temperature. The reaction mixture was washed with aqueous $NaHCO_3$ solution, then with water, and the $CHCl_3$ layer was separated, dried over $MgSO_4$ and evaporated to dryness. The residual oil was separated by preparative TLC on silica gel using ether–pet. ether (1: 4) as a solvent to yield XV (0.197 g, 37.1%), XVI (0.065 g, 13.1%) and XVII (0.065 g, 13.2%). The spectra of these compounds were in accord with those of authentic samples.

Reaction of XVI with Chloranil——A solution of XVI (0.448 g) and chloranil (0.492 g) in xylene (20 ml) was refluxed for 24 hr with stirring. Xylene was removed by vacuum distillation to leave a crude oil which was purified by column chromatography (silica gel) using pet. ether as an eluent. The resulting solids were recrystallized from EtOH-*n*-hexane to give XVII (0.38 g, 85.2%) as red needles. This compound was identical with an authentic sample on the basis of the mp, and IR and NMR spectra.

Oxidation of XVI in DMSO——A solution of XVI (0.448 g, 1 mmol) in DMSO (20 ml) was stirred for 24 hr at 150—160°. The solvent was removed under reduced pressure and the residue was column-chromatographed on silica gel using pet. ether as an eluent to afford crystals. Recrystallization from EtOH-*n*-hexane gave XVII (0.348 g, 78%) as red needles.

Reaction of 3-Acetyl-2-phenylbenzothiazoline 1-Oxide (Vi) with Acetic Anhydride——A solution of Vi (0.516 g, 1.9 mmol) in acetic anhydride (20 ml) was refluxed for 2 hr with stirring and worked up as usual. The resulting oil was separated by preparative TLC on silica gel using benzene to give 0.229 g (57%) of 2-phenylbenzothiazole (XIX) as colorless prisms, mp 112°, 0.142 g (29%) of 3-acetyl-2-phenylbenzothiazoline (IVi) and 0.068 g (8%) of 3-acetyl-2-phenylbenzothiazoline 1,1-dioxide (VIi). These three compounds were identified by comparison of mp, *Rf* value in TLC, and IR and NMR spectra with those of authentic samples.

Reaction of *trans*-3-Acetyl-2-methylbenzothiazoline 1-Oxide (*trans*-Vg) with Acetic Anhydride——A solution of *trans*-Vg (1.672 g, 8 mmol) in acetic anhydride (20 ml) was refluxed for 5 hr with stirring and the reaction mixture was worked up as usual. The resulting oil was purified by preparative TLC on silica gel using ether–pet. ether (3: 1) to give 0.6 g (39.3%) of 4-acetyl-4*H*-1,4-benzothiazine (XX). Recrystallization from *n*-hexane gave colorless prisms, mp 92—93.5°. *Anal.* Calcd. for $C_{10}H_9NOS$: C, 62.80; H, 4.74; N, 7.32. Found: C, 62.65; H, 4.80; N, 7.31. IR ν_{max}^{KBr} cm^{-1}: 1670 (CO). NMR ($CDCl_3$) δ: 2.30 (3H, s, $COCH_3$), 6.13 (1H, d, $J=6.5$ Hz, C_2-H), 6.90 (1H, br.s, $J=6.5$ Hz, C_3-H), 7.15—7.65 (4H, m, ArH). UV λ_{max}^{EtOH} nm (ε): 290 (3910), 265 (9540), 238 (10600), 212.5 (7670). MS *m/e*: 191 (M^+), 149 (base).

4-Acetyl-2,3-dihydro-4*H*-1,4-benzothiazine 1-Oxide (XXII)——MCPBA (1.052 g, 5.18 mmol) was added slowly to an ice-cooled solution of 4-acetyl-2,3-dihydro-4*H*-1,4-benzothiazine (XXI)[14] (1 g, 5.18 mmol) in CH_2Cl_2 (40 ml) with stirring, and stirring was continued for 16 hr at room temperature. The reaction mixture was washed with aqueous $NaHCO_3$, then water and the separated CH_2Cl_2 layer was dried over $MgSO_4$. The solvent was evaporated off and the residue was subjected to column chromatography on silica gel using $CHCl_3$ as an eluent to give a yellow oil (1.031 g, 95.2%). IR ν_{max}^{neat} cm^{-1}: 1660 (CO), 1040 (SO). NMR ($CDCl_3$) δ: 2.28 (3H, s, $COCH_3$), 2.80—4.30 (3H, m, C_2-H, C_3-2H), 4.26—4.80 (1H, m, C_2-H), 7.30—8.00 (4H, m, ArH). This compound could not be analyzed because it decomposed on vacuum distillation, but the structure was unambiguously established by the IR and NMR spectra.

2-Acetoxy-4-acetyl-2,3-dihydro-4*H*-1,4-benzothiazine (XXIII)——A solution of XXII (1.031 g, 4.93 mmol) in acetic anhydride (30 ml) was refluxed for 12 hr with stirring. Acetic anhydride was evaporated off under reduced pressure, then aqueous $NaHCO_3$ was added to the residue and stirred for 30 min at room temperature. The mixture was extracted with CH_2Cl_2 and the extract was evaporated to dryness after drying over $MgSO_4$. The residue was subjected to vacuum distillation to give a colorless oil (0.982 g, 79%), bp 160° (0.05 mmHg). *Anal.* Calcd. for $C_{12}H_{13}NO_3S$: C, 57.35; H, 5.21; N, 5.57. Found: C, 57.12; H, 5.21; N, 5.46. IR ν_{max}^{neat} cm^{-1}: 1740 (CO), 1660 (CO). NMR ($CDCl_3$) δ: 2.10 (3H, s, $OCOCH_3$), 2.28 (3H, s, $NCOCH_3$), 3.65 (1H, d.d, $J=3.5$, 14 Hz, C_3-H), 4.68 (1H, d.d, $J=5$, 14 Hz, C_3-H), 6.38 (1H, d.d, $J=3.5$, 5 Hz, C_2-H), 7.00—7.45 (4H, m, ArH).

4-Acetyl-4*H*-1,4-benzothiazine (XX)——Compound XXIII (0.259 g, 1.03 mmol) was heated at 250° in the absence of a solvent for 5 hr. The reaction mixture was purified by preparative TLC on silica gel using ether–pet. ether as a solvent, and the resulting crystals were recrystallized from *n*-hexane to afford colorless prisms (0.08 g, 41%), mp 92.5—93°. *Anal.* Calcd. for $C_{10}H_9NOS$: C, 62.80; H, 4.74; N, 7.32. Found: C, 62.54; H, 4.74; N, 7.28. IR ν_{max}^{KBr} cm^{-1}: 1670 (CO). NMR ($CDCl_3$) δ: 2.30 (3H, s, $COCH_3$), 6.13 (1H, d, $J=6.5$ Hz, C_2-H), 6.90 (1H, br.d, $J=6.5$ Hz, C_3-H), 7.15—7.65 (4H, m, ArH).