2- or 4-Thiazolylmethyl Cyclopropanecarboxylates: Their Synthesis and Insecticidal Activities^{†,††}

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From a consideration of the structure-activity relationships, nineteen 2- or 4-thiazolylmethyl cyclopropanecarboxylates, including three benzyl-thiazolylmethyl chrysanthemates (IVf, Xb and Xc), were prepared from thioamides and α -haloketones or α -haloaldehydes and examined for insecticidal activity against houseflies. All those with benzyl substitutions on the thiazole ring were ineffective, as were the other substituents. Only 4,5,6,7-tetrahydrobenzothiazolylmethyl chrysanthemate and 2,2,3,3-tetramethylcyclopropanecarboxylate (Xf and XI_f) possessed about the same order of activity as allethrin, and their activities were 0.61 and 1.56 $\mu\text{g}/\text{fly}$ respectively.

Resmethrin (I), 5-benzyl-3-furylmethyl *dl*-*cis*, *trans*-chrysanthemate, was one of the most potent pyrethroids synthesized by Elliott *et al.*, and was found to be comparable to the organophosphorous insecticides in potency.¹⁾

From a consideration of the structure-activity relationships, Elliott *et al.* proposed the term "planar activating nucleus" and considered that the furan ring in I, the benzene ring in the benzyl esters, or cyclopentenolone in the natural pyrethrins and allethrin correspond to the nucleus, and constitute an important factor in the activity of the pyrethroid molecule.²⁾

It was of interest to determine if the insecticidal activity of I was maintained after replacement of the furan ring with other heterocyclic rings containing two hetero atoms. To that end, nineteen new cyclopropanecarboxylic esters, including three benzyl-thiazolylmethyl chrysanthemates (IVf, Xb and Xc), were]

synthesized and examined for insecticidal activity.

Thiazolylmethyl derivatives, the alcoholic components of these esters, were prepared by either procedure A or B, shown in Charts 1 and 2. The thioamides (IIa—f), which were prepared from the corresponding nitriles according to the method outlined by Bernthsen,³⁾ were condensed with sym-dichloroacetone in refluxing benzene to give the substituted chloromethylthiazoles (IIIa—f). Esterification of

I

[†] New Insecticidal Cyclopropanecarboxylic Esters, Part II.

^{††} Part I; K. Sota, T. Amano, M. Aida, K. Noda, A. Hayashi and I. Tanaka, *Agr. Biol. Chem.*, **35**, 968 (1971).

CHART 1

	a	b	c	d	e	f	g
R ₂ ;	CH ₃	C ₆ H ₅ CH ₂	H	CH ₃	CH ₃		
R ₃ ;	H	H	C ₆ H ₅ CH ₂	CH ₃	CH ₂ CH=CH ₂		

X ; Cl or Br

R, R'; same as in Chart 1

CHART 2

these chloromethyl compounds with potassium chrysanthemate or 2,2,3,3-tetramethylcyclopropanecarboxylate in refluxing isopropyl alcohol gave the corresponding esters (IVa~f).

On the other hand, seven 2-thiazolylmethyl alcohols and eleven esters were synthesized by procedure B. Benzoyl thioglycolamide (VI), obtained by a slight modification of the method of Olin,⁴⁾ using triethylamine instead of triethanolamine, was allowed to react with the appropriate α -haloketone or α -haloaldehyde in benzene to give the thiazolylmethyl compounds (VIIIa~f). The benzyloxy-methyl thiazoles (VIIIa~f) were hydrolysed and then esterified using the appropriate cyclopropanecarbonyl chloride to give the desired thiazolylmethyl esters (Xa~g and XIId~f).

Among these cyclization compounds, the 2-methyl (IIIa),⁵⁾ 2-phenyl (IIIe),⁶⁾ 4-methyl (VIIIa),⁷⁾ and 4,5-dimethyl (VIIIId)⁸⁾ thiazolyl compounds have been previously synthesized by direct heating of the two reaction materials. However, presuming a lack of stability of the chloromethyl compounds, we attempted to use a solvent such as benzene, and obtained the thiazoles in moderate yield.

In the IR spectra, all of these thiazoles showed thiazole band II⁹⁾ at 1520~1555 cm⁻¹

and a characteristic band¹⁰⁾ in the 1460~1500 cm⁻¹ region, and a weak thiazole band I⁹⁾ was observed only in some thiazoles in the 1585~1685 cm⁻¹ region. In the NMR spectra, all the thiazolylmethyl esters showed proton signals due to the chrysanthemoyl moiety, δ 1.70 (6H, s, (CH₃)₂C=C), 1.12 and 1.24 (3H each, s each, gem-diCH₃), 4.71~4.99 (1H, m, Me₂C=CH), or 2,2,3,3-tetramethylcyclopropanecarbonyl, δ 1.23 (12H, d, $J=4.2$ cps, 2 $\times$ gem-diCH₃), and signals due to thiazolylmethyl, as shown in Table IV.

Physical constants and analytical data for these esters are summarized in Tables I, II, and III.

Insecticidal data for these esters by the topical application method and the spray chamber method¹¹⁾ against houseflies are summarized in Tables V, VI, and VII respectively, and a comparison of the activity of benzo-thiazolylmethyl and 4,5,6,7-tetrahydrobenzo-thiazolylmethyl esters (Xg, XIg, Xf and XIIf) is shown in Table VIII.

As shown in Table V, the majority of 4-thiazolylmethyl esters were ineffective, though the 2-isopropyl-substituted ester (IVd) was about 1/4 as toxic as allethrin. The data in Table VI indicated that the mono-substituted 2-thiazolylmethyl esters were also inactive. As

TABLE I. 2-SUBST-4-THIAZOLYLMETHYL CHRYSANTHEMATES

No.	R ₁	bp °C (mmHg)	n_D^{20}	Formula	Anal. (%)					
					C	Calcd. H	N	C	Found H	N
IVa	CH ₃	115~6 (0.12)	1.5199	C ₁₅ H ₂₁ NO ₂ S	64.48	7.58	5.01	64.76	7.55	5.02
IVb	C ₂ H ₅	125~6 (0.03)	1.5164	C ₁₆ H ₂₃ NO ₂ S	65.49	7.90	4.77	65.86	8.00	4.61
IVc	C ₃ H ₇ (<i>n</i>)	145~6 (0.18)	1.5145	C ₁₇ H ₂₅ NO ₂ S	66.41	8.20	4.56	66.69	8.25	4.44
IVd	C ₃ H ₇ (<i>i</i>)	131 (0.10)	1.5138	C ₁₇ H ₂₅ NO ₂ S	66.41	8.20	4.56	66.49	8.25	4.35
IVe	C ₆ H ₅	180~1 (0.20)	1.5760	C ₂₀ H ₂₃ NO ₂ S	70.36	66.79	4.10	70.32	6.08	4.04
IVf	C ₆ H ₅ CH ₂	176~7 (0.02)	1.5538	C ₂₁ H ₂₅ NO ₂ S	70.95	7.09	3.94	71.27	7.00	3.86

TABLE II. 4-(AND/OR)-5-SUBST.-2-THIAZOLYMETHYL CHRYSANTHEMATES

No.	R ₂	R ₃	bp °C (mmHg)	n _D ²⁰	Formula	Anal. (%)					
						C	Calcd. H	N	C	Found H	N
Xa	CH ₃	H	118~9 (0.08)	1.5177	C ₁₅ H ₂₁ NO ₂ S	64.48	7.58	5.01	64.96	7.61	5.03
Xb	C ₆ H ₅ CH ₂	H	175~8 (0.03)	1.5530	C ₂₁ H ₂₅ NO ₂ S	70.95	7.09	3.94	71.27	7.02	3.86
Xc	H	C ₆ H ₅ CH ₂	181~4 (0.04)	1.5526	C ₂₁ H ₂₅ NO ₂ S	70.95	7.09	3.94	71.38	7.08	3.87
Xd	CH ₃	CH ₃	131 (0.05)	1.5171	C ₁₆ H ₂₃ NO ₂ S	65.49	7.90	4.77	65.90	7.99	4.36
Xe	CH ₃	CH ₂ =CHCH ₂	146~7 (0.10)	1.5186	C ₁₈ H ₂₅ NO ₂ S	67.69	7.89	4.39	68.20	8.08	3.90
Xf			150~2 (0.06)	1.5322	C ₁₈ H ₂₅ NO ₂ S	67.69	7.89	4.39	67.85	8.04	4.66
Xg			167~9 (0.10)	1.5612	C ₁₈ H ₂₁ NO ₂ S	68.55	6.71	4.44	68.72	6.84	4.13

TABLE III. SUBSTITUTED THIAZOLYMETHYL 2,2,3,3-TETRAMETHYLCYCLOPROPANECARBOXYLATES

No.	R	mp °C bp °C (mmHg)	n _D ²⁰	Formula	C	Calcd. H	Anal. (%)			
							N	C	Found H	N
4-Thiazolymethyl esters										
Vb	2-C ₂ H ₅	108 (0.02)	1.5107	C ₁₄ H ₂₁ NO ₂ S	62.89	7.92	5.24	62.99	7.96	5.38
Vf	2-C ₆ H ₅ CH ₂	84~5	—	C ₁₉ H ₂₃ NO ₂ S	69.27	7.04	4.25	69.23	7.03	4.08
2-Thiazolymethyl esters										
XId	4,5-diCH ₃	145~7 (0.90)	1.5046	C ₁₄ H ₂₁ NO ₂ S	62.89	7.92	5.24	62.96	8.12	5.09
XIe	4-CH ₃ , 5-CH ₂ CH=CH ₂	135~6 (0.10)	1.5131	C ₁₆ H ₂₃ NO ₂ S	65.49	7.90	4.77	65.72	7.96	4.48
XIf	4,5-	143~6 (0.14)	1.5274	C ₁₆ H ₂₃ NO ₂ S	65.49	7.90	4.77	65.76	7.92	4.38
XIg	4,5-	80.5~81.0	—	C ₁₆ H ₁₉ NO ₂ S	66.41	6.62	4.84	66.45	6.76	4.67

represented by resmethrin (I), benzyl substituents on furan, thiophene, and benzene rings make the esters effective with regard to insecticidal activity. However, in the case of the thiazole series, all the benzyl compounds were ineffective, as well as the other substituents. On the other hand, it has been observed that di-substitutions on the thiazole ring in 2-thiazolymethyl esters show a tendency to

increase the potency, and in particular 4,5,6,7-tetrahydrobenzothiazolymethyl chrysanthemate (Xf) was the most potent of these esters, with an activity about 1.5 times as that of allethrin.

This compound possesses a structure in which two adjacent substituents are fused to each other, and the molecule closely resembles phthalthrin (XII). In fact, regarding the

TABLE IV. SPECTRAL DATA FOR ESTERS IV, V, X, AND XI

No.	C=O	IR (cm ⁻¹) thiazole band		CH=CH ₂	CH ₂ O	thiazole proton	NMR (δ ppm) others
IVa	1725	1530	1495		* 5.06 s	6.97 s	2.63 (s, 2-CH ₃)
IVb	1725	1530	1485		* 5.06 s	7.04 s	2.94 (q, $J=7.8$ cps, 2-CH ₂ Me)
IVc	1730	1530	1485		5.19 s	7.15 s	2.98 (t, $J=7.2$ cps, 2-CH ₂ Et)
IVd	1730	1530	1480		5.18 s	7.11 s	2.95~3.57 (se, $J=7.2$ cps, 2-CH(Me) ₂) 1.38 (d, $J=7.2$ cps, 2-C(CH ₃) ₂)
IVe	1725	1525	1505		* 5.21 s	7.18 s	7.26~7.50, 7.74~8.16 (each m, Ph)
IVf	1725	1530	1495		5.14 s	7.12 s	7.31 (s, Ph), 4.24 (s, CH ₂ Ph)
Xa	1730	1530	1485		* 5.24 s	6.78 s	2.39 (s, 4-CH ₃)
Xb	1730	1520	1500		* 5.27 s	6.61 s	3.99 (s, CH ₂ Ph), 7.13 (s, Ph)
Xc	1730	1530	1495		* 5.18 s	7.29 s	4.04 (s, CH ₂ Ph), 7.14 (s, Ph)
Xd	1730	1555	1485		* 5.19 s		2.28 (s, 5-CH ₃), 2.34 (s, 4-CH ₃)
Xe	1725	1545	1480	1630 985 910	5.25 s		5.57~6.21 (m, CH ₂ CH=CH ₂), 3.44 (d, $J=6$ cps, CH ₂ CH=CH ₂), 2.31 (s, 4-CH ₃)
Xf	1725	1550	1485		5.27 s		2.59~2.96 (m, 4,7-CH ₂ ×2), 1.83~2.04 (m, 5,6-CH ₂ ×2)
Xg	1725	1520	1460		5.50 s		7.79~8.16, 7.19~7.57 (m, Ph)
Vb	1730	1535	1480		* 5.00 s	7.02 s	2.92 (q, $J=7.8$ cps, 2-CH ₂ Me)
Vf	1715	1535	1495		* 5.04 s	7.03 s	4.17 (s, CH ₂ Ph), 7.26 (s, Ph)
XId	1720	1550	1480		5.21 s		2.32 (s, 4,5-diCH ₃)
XIe	1730	1550	1480	1645 990 910	5.21 s		5.57~6.25 (m, CH ₂ CH=CH ₂), 3.44 (d, $J=6$ cps, CH ₂ CH=CH ₂), 2.31 (s, 4-CH ₃)
XIf	1725	1550	1480		5.24 s		2.59~2.97 (m, 4,7-CH ₂ ×2), 1.72~2.07 (m, 5,6-CH ₂ ×2)
XIg	1735	1525	1480		5.38 s		7.62~8.04, 7.19~7.53 (m, Ph)

* determined in CCl₄ solution

TABLE V. INSECTICIDAL ACTIVITY OF 2-SUBST.-4-THIAZOLYLMETHYL CHRYSANTHEMATES

No.	R ₁	Topical application LD ₅₀ (μ g/fly)	Spray method	
			KT ₅₀	Mortality (%)
IVa	CH ₃	>5	4'11''	63.1
IVb	C ₂ H ₅	>5	3'13''	74.4
IVc	C ₃ H ₇ (<i>n</i>)	>5	3'52''	64.0
IVd	C ₃ H ₇ (<i>i</i>)	3.56	3'02''	83.3
IVe	C ₆ H ₅	>5	3'44''	64.0
IVf	C ₆ H ₅ CH ₂	>5	3'57''	66.6
	allethrin*	1.03		

* *dl-cis*, *trans*-chrysanthemate

TABLE VI. INSECTICIDAL ACTIVITY OF 4-AND/OR 5-SUBST.-2-THIAZOLYLMETHYL CHRYSANTHEMATES

No.	R ₂	R ₃	Topical application LD ₅₀ (μg/fly)	KT ₅₀	Spray method Mortality (%)
Xa	CH ₃	H	> 5	> 30'	11.1
Xb	C ₆ H ₅ CH ₂	H	> 5	9'23''	21.4
Xc	H	C ₆ H ₅ CH ₂	> 5	8'58''	60.4
Xd	CH ₃	CH ₃	> 5	7'38''	37.7
Xe	CH ₃	CH ₂ CH=CH ₂	4.34	8'21''	32.0
Xf			0.61	3'31''	91.8
Xg			> 5	14'31''	77.4
	allethrin*		1.03		

* *dl-cis, trans*-chrysanthemate.

TABLE VII. INSECTICIDAL ACTIVITY OF SOME 2- OR 4-THIAZOLYLMETHYL 2,2,3,3-TETRAMETHYLCYCLOPROPANE CARBOXYLATES

No.	R	Topical application LD ₅₀ (μg/fly)	KT ₅₀	Spray method Mortality (%)
4-thiazolylmethyl esters				
Vb	2-C ₂ H ₅	> 5	3'11''	62.5
Vf	2-C ₆ H ₅ CH ₂	> 5	2'58''	78.1
2-thiazolylmethyl esters				
XId	4,5-diCH ₃	> 5	17'52''	23.9
XIe	4-CH ₃ , 5-CH ₂ CH=CH ₂	> 5	13'52''	36.9
XIf	4,5-	1.56	6'22''	70.7
XIg	4,5-	> 5	23'29''	21.0
	allethrin*	1.03		

* *dl-cis, trans*-chrysanthemate.

activity of esters of the maleimide series, constituting the planar activating nucleus in XII, Kato *et al.* have reported¹²⁾ that mono-substitution in maleimidomethyl chrysanthemates was ineffective, and phthalimidomethyl

chrysanthemate was less active than the tetrahydro-type ester (XII). As shown in Table VIII, it was found that the benzothiazolylmethyl esters (Xg and XIg) were about 1/40 as active as the corresponding tetrahydro-type

TABLE VIII. COMPARISON OF THE ACTIVITY OF BENZOTHAZOLYLMETHYL ESTERS AND THEIR 4,5,6,7-TETRAHYDRO COMPOUNDS

No.	LD ₅₀ (μ g/fly)	Relative potency
Xf	0.61	165
Xg	25.3	4
XIf	1.56	64
XIg	> 40	< 2.5
allethrin*	1.03	100

* *dl-cis,trans*-chrysanthemate.

esters (Xf and XIf).

These structure-activity relationships of the maleimidomethyl ester series coincided fairly exactly with those of the thiazolylmethyl ester series in our present study, and with respect to rapid paralytic effect, these two series are also similar to each other. These facts suggest that the thiazole ring may be similar to maleimide rather than furan, thiophene, and benzene as a planar activating nucleus. Considering its potent paralytic effect, Xf would not be characterized as a resmethrin type, but as a pathaltrin type of pyrethroid.

Recently, to correlate biological activity with chemical structure, regression analysis using the effect of substituents has been carried out by Hanch-Fujita *et al.*¹³⁻¹⁶⁾ However, it was difficult to account for the structure-activity relationships of this series by applying the method of Hansch-Fujita to our specific data, since high activity was observed only in tetrahydro-type esters (Xf and XIf) and not in the other esters.

Some pyrethroids containing the tetramethylene substituent on the alcoholic side, phthalthrin (XII), benzyl¹⁷⁾ and thenyl¹⁸⁾ series esters, had already been prepared and were found to be active. These tetrahydro-type esters are effective, even though not so powerful as resmethrin, in a wide range of types of planar activating nucleus, whereas the benzyl substituent was not always effective as a substituent of the planar activating nucleus for insect toxicity, as seen in our present study.

It may be inferred that a simple steric structure common to these tetrahydro-type esters is a primary factor for insect toxicity of pyrethroids. If we consider the receptor theory that drugs exert their effects by interacting with certain receptors in the tissues, the postulated receptor for pyrethroids will have a shape complementary to that of these tetrahydro-type esters (XII and Xf).

On the other hand, all the 2,2,3,3-tetramethylcyclopropanecarboxylates shown in Table VII were less active than the corresponding chrysanthemates, as observed in allethrolone.¹⁹⁾

EXPERIMENTAL

Synthesis. All mp's and bp's are uncorrected. IR spectra refer to films for liquids and nujol mulls for solid samples. NMR spectra were recorded at 60 MHz in CDCl₃ with TMS as an internal standard unless otherwise stated.

Thioamides (II). These thioamides, synthesized from the corresponding nitriles, were identified by the disappearance of the C $\equiv$ N band (2250 cm⁻¹) and the appearance of a C=S band (1630 cm⁻¹) in the IR spectra.

1) **Thioisobutyramide (II_d).** To a solution of 75 g of isobutyronitrile in 250 g of 10% NH₃-EtOH, H₂S gas was introduced with stirring at room temperature. The gas flow was maintained sometimes over 3 days to keep the solution under saturation. The resultant reaction mixture was concentrated to give a residue which was chromatographed on silica gel (Wako gel C-200). Elution with benzene afforded 11.8 g (10.5%) of the thioisobutyramide (II_d), mp 45.5~46.0°C (from benzene-hexane) (lit.²⁰⁾ mp 41°C). *Anal.* Found: C, 46.29; H, 8.74; N, 12.91. *Calcd.* for C₄H₉NS: C, 46.56; H, 8.79; N, 13.57%.

Thiobutyramide (II_c). Bp 96°C/0.55 mmHg (lit.²⁰⁾ bp 88.5°C/0.11 mmHg), thiopropionamide (II_b), mp 41~3°C (lit.²⁰⁾ mp 40°C), and phenylthioacetamide (II_f), mp 96~8°C (lit.³¹⁾ mp 97.5~8°C) were similarly prepared. Thioacetamide (II_a) and thiobenzamide (II_e) were commercial reagents.

2) **Benzoyl thioglycolamide (VI).** To a solution of 27.8 g of (Et)₃N and 32 g of benzoyl glycolonitrile²¹⁾

in 310 ml of EtOH, H₂S gas was introduced with stirring at room temperature, and by working up as described for IIId, 22.2 g (57%) of white needle-like crystals were obtained, mp 104~5°C (from benzene-hexane) (lit.⁴¹ mp 103°C).

α-Haloketones and α-haloaldehydes (VII). 1-Chloro-3-phenyl-2-propanone (VIIb); bp 100°C/1.2 mmHg (lit.²²¹ bp 96~8°C/1 mmHg), 2-chloro-3-phenylpropionaldehyde (VIIc); bp 105°C/17 mmHg (lit.²³¹ bp 104~6°C/12 mmHg), 4-acetyl-4-chloro-1-butene (VIIe); bp 56~62°C/18 mmHg (lit.²⁴¹ bp 44~45.5°C/11 mmHg), and 2-bromocyclohexanone (VIIf); bp 100~2°C/16 mmHg (lit.²⁵¹ bp 112~3°C/20 mmHg) were synthesized according to the above references, respectively. Monochloroacetone (VIIa) and 3-chloro-2-butanone (VIId) were obtained from a commercial source.

Cyclization of thioamides to thiazolymethyl compounds 4-Chloromethylthiazoles (III). Procedure A

One example of this step is shown.

2-Isopropyl-4-chloromethylthiazole (IIId). To a solution of 11.0 g of thioisobutyramide, was added dropwise with stirring a solution of 13.6 g of (ClCH₂)₂CO in 30 ml of benzene, while maintaining the reaction temperature between 70~75°C, and the mixture was stirred for another 3 hr at that temperature. To the resultant mixture was added a small portion of ice-water and 30 ml of 25% NaOH solution. The benzene layer was separated and the aqueous layer was extracted with benzene. The benzene solution was dried and evaporated *in vacuo*. The residual oil was distilled *in vacuo* to give 7.3 g (39%) of IIId, bp 54~7°C/0.07 mmHg. IR (cm⁻¹): 1520 (band II), 1485, 720 (CCl). NMR δ: 1.39 (6H, d, *J*=6.8 cps, C(CH₃)₂), 3.24 (1H, se, *J*=6.8 cps, CH(Me)₂), 4.68 (2H, s, CH₂Cl), 7.30 (1H, s, ring H). *Anal.* Found: C, 47.78; H, 5.76; N, 7.44. Calcd. for C₇H₁₀CINS: C, 47.86; H, 5.74; N, 7.97%.

2-n-Propyl-4-chloromethylthiazole (IIIf). Bp 65~6°C/0.03 mmHg. NMR δ: 0.98 (3H, t, *J*=6.5 cps, CH₃), 1.78 (2H, se, *J*=6.5 cps, CH₂Me), 2.95 (2H, t, *J*=6.5 cps, CH₂Et), 4.64 (2H, s, CH₂Cl), 7.14 (1H, s, ring H). IR (cm⁻¹): 1520, 1485 (band II), 720 (CCl). *Anal.* Found: C, 48.24; H, 5.78; N, 8.08. Calcd. for C₇H₁₀CINS: C, 47.86; H, 5.74; N, 7.97%.

2-Benzyl-4-chloromethylthiazole (IIIf). Bp 152~4°C/17 mmHg. IR (cm⁻¹): 1686 (band I), 1600 (Ph), 1495, 720 (CCl). NMR δ: 4.20 (2H, s, CH₂Ph),

4.54 (2H, s, CH₂Cl), 7.07 (1H, s, ring H), 7.29 (5H, s, Ph-H).

2-Ethyl-4-chloromethylthiazole (IIIf). Bp 63~5°C/0.05 mmHg. IR (cm⁻¹): 1520 (band II), 1485, 720 (CCl).

2-Methyl-4-chloromethylthiazole (IIIf). Bp 60~3°C/2 mmHg (lit.⁵¹ bp 84°C/10 mmHg).

2-Phenyl-4-chloromethylthiazole (IIIf). Bp 121~3°C/0.55 mmHg (lit.²⁶¹ mp 50~1°C).

2-Hydroxymethylthiazoles IX. Procedure B

5-Allyl-4-methyl-2-hydroxymethylthiazole (IXe). To a solution of 6.0 g of benzoyl thioglycolamide (VI), was added dropwise, with stirring, a solution of 4.1 g of 4-acetyl-4-chloro-1-butene (VIIe) in 30 ml of benzene, while maintaining the reaction temperature between 70~5°C. The mixture was then refluxed for another 3 hr at that temperature, and by working up as above for IIId, 5.3 g (60%) of 2-benzoyloxymethyl-4-methyl-5-allylthiazole (VIIIe) was obtained, bp 152~5°C/0.09 mmHg. IR (cm⁻¹): 1725 (C=O), 1600 (Ph), 1545 (band II), 1490, 990, 920 (—CH=CH₂). NMR δ: 2.33 (3H, s, CH₃), 3.43 (2H, d, *J*=5.9 cps, CH₂CH=CH₂), 4.84~5.24 (2H, m, CH=CH₂), 5.49 (2H, s, OCH₂), 5.65~6.24 (1H, m, CH=CH₂), 7.19~7.62 (3H, m, Ph-H_{3,4,5}), 7.85~8.20 (2H, m, Ph-H_{2,6}). *Anal.* Found: C, 65.62; H, 5.66; N, 4.79. Calcd. for C₁₅H₁₅NO₂S: C, 65.92; H, 5.53, N, 5.13%. To a solution of 80 ml of 5% KOH-EtOH solution, 5.3 g of VIIIe was added and the mixture was left to stand overnight. After filtration of the precipitated crystals and evaporation of the solvent, the residue was extracted with ether and dried. After evaporation of the ether, the residual oil was distilled *in vacuo* to give 2.8 g (85%) of IXe, bp 103~4°C/0.1 mmHg. IR (cm⁻¹): 3205 (OH), 1550 (band II), 1475, 1635, 985, 915 (CH=CH₂).

2-Benzoyloxymethyl-4,5,6,7-tetrahydrobenzothiazole (VIIIIf). Bp 173~6°C/0.11 mmHg. IR (cm⁻¹): 1720 (C=O), 1600 (Ph), 1550 (band II), 1490. NMR δ: 1.71~2.00 (4H, m, 5,6-CH₂CH₂), 2.61~3.01 (4H, m, 4,7-CH₂CH₂), 5.58 (2H, s, OCH₂), 7.25~7.75 (3H, m, Ph-H_{3,4,5}), 8.01~8.28 (2H, m, Ph-H_{2,6}). *Anal.* Found: C, 65.80; H, 5.65; N, 4.59. Calcd. for C₁₆H₁₅NO₂S: C, 65.91; H, 5.53; N, 5.12%.

2-Hydroxymethyl-4,5,6,7-tetrahydrobenzothiazole (IXf). Bp 130~3°C/1 mmHg. IR (cm⁻¹): 3205 (OH), 1670 (band I), 1550 (band II), 1485.

2-Hydroxymethyl-4-benzylthiazole (IXb). Bp 145°C/

0.2 mmHg. IR (cm^{-1}): 3200 (OH), 1600 (Ph), 1525 (band II), 1495. Anal. Found: C, 64.46; H, 5.47; N, 6.62. Calcd. for $\text{C}_{11}\text{H}_{11}\text{NOS}$: C, 64.36; H, 5.40; N, 6.82%.

2-Benzoyloxymethyl-5-benzylthiazole (XIIIc). Bp $200\sim 2^\circ\text{C}/0.2\text{ mmHg}$. IR (cm^{-1}): 1725 (C=O), 1600 (Ph), 1525 (band II), 1495. NMR δ : 4.04 (2H, s, CH_2Ph), 5.47 (2H, s, OCH_2), 7.17 (5H, s, $\text{C}_6\text{H}_5\text{CH}_2$), 7.29 (1H, s, ring H), 7.30~7.50 (3H, m, $\text{PhCO}_2(3,4,5)$), 7.89~8.40 (2H, m, $\text{PhCO}_2(2,6)$).

2-Hydroxymethyl-5-benzylthiazole (IXc). Crude oil was obtained and was employed for the next step without further purification.

2-Benzoyloxymethyl-4,5-dimethylthiazole (VIIIId). Crude oil IR (cm^{-1}): 1725 (C=O), 1600 (Ph), 1520 (band II), 1480.

2-Hydroxymethyl-4,5-dimethylthiazole (IXd). Bp $106\sim 7^\circ\text{C}/0.8\text{ mmHg}$ (lit.⁸⁾ bp $144\sim 6^\circ\text{C}/17\text{ mmHg}$. IR (cm^{-1}): 3205 (OH), 1555 (band II), 1475.

2-Benzoyloxymethyl-4-methylthiazole (VIIIa). Bp $121\sim 2^\circ\text{C}/0.15\text{ mmHg}$ (lit.⁷⁾ bp $125\sim 7^\circ\text{C}/0.1\text{ mmHg}$. IR (cm^{-1}): 1725 (C=O), 1600 (Ph), 1585 (band I), 1530 (band II), 1490.

2-Hydroxymethyl-4-methylthiazole (IXa). Crude oil (lit.⁷) bp $86^\circ\text{C}/0.1\text{ mmHg}$ was employed for the next step without further purification.

2-Hydroxymethylbenzothiazole (IXg). Mp $91\sim 92.5^\circ\text{C}$ (lit.²⁷) mp $93\sim 4^\circ\text{C}$. IR (cm^{-1}): 3145 (OH), 1595 (Ph), 1520 (band II), 1460.

Esters of chrysanthemic or 2,2,3,3-tetramethylcyclopropanecarboxylic acid

Esters from 4-chloromethylthiazoles (IV and V). The following two typical reactions are given here, and the other esters were similarly prepared (Tables I and III).

2-Benzyl-4-thiazolylmethyl chrysanthemate (IVf). To a solution of K *dl-cis,trans*-chrysanthemic acid in 15 ml of isoPrOH, 2.3 g of IIIf was added and heated under reflux for 12 hr. The reaction mixture was evaporated and extracted with ether. The organic layer was washed with aq Na_2CO_3 solution and dried over anhydrous MgSO_4 . After evaporation of the solvent, the residual oil was distilled *in vacuo* to give 2.4 g (67%) of IVf.

2-Ethyl-4-thiazolylmethyl 2,2,3,3-tetramethylcyclopropanecarboxylate (Vb). To a solution of K 2,2,3,3-tetramethylcyclopropanecarboxylate (from 1.4 g of KOH and 2.8 g of 2,2,3,3-tetramethylcyclopropanecarboxylic acid) in 25 ml of isoPrOH, 3.2 g of IIIb was added and heated under reflux for 12 hr. The reaction mixture was concentrated and extracted with ether. The extract was washed with aq Na_2CO_3 solution and dried (MgSO_4). After evaporation of the solvent, the residual oil was distilled *in vacuo* to give 3.5 g (66%) of Vb.

Esters from 2-hydroxymethylthiazoles (X and XI). The following typical reactions are given, and the other esters were similarly prepared (Tables II and III).

4-Methyl-2-thiazolylmethyl chrysanthemate (Xa). 4.1 g of *dl-cis,trans*-chrysanthemoyl chloride in 35 ml of benzene was added to a solution of 3.2 g of IXa and 5 ml of $(\text{Et})_3\text{N}$ in 35 ml of benzene at $0\sim 5^\circ\text{C}$ with stirring, then allowed to stand overnight at room temperature. The mixture was shaken with water, 10% HCl, 5% Na_2CO_3 , and water and dried (MgSO_4). After evaporation of the solvent, distillation *in vacuo* gave 4.4 g (72%) of the ester (Xa).

4-Methyl-5-allyl-2-thiazolylmethyl 2,2,3,3-tetramethylcyclopropanecarboxylate (XIe). 2.0 g of 2,2,3,3-tetramethylcyclopropanecarbonyl chloride in 20 ml of benzene was added to a solution of 2.4 g of IXe and 3.0 ml of $(\text{Et})_3\text{N}$ in 30 ml of benzene at $0\sim 5^\circ\text{C}$ with stirring, then allowed to stand overnight at room temperature. The mixture was shaken with water, 10% HCl, 5% Na_2CO_3 , and water and dried (MgSO_4). After evaporation of the solvent, distillation *in vacuo* afforded 2.7 g (73%) of the ester (XIe).

Evaluation of insecticidal activities

Topical application method. Susceptible houseflies ("Takatsuki"), *Musca domestica vicina* Macq., were treated on the dorsum of the thorax with 0.5 μl of an acetone solution of the test compound by means of a micrometer syringe, and kept at $24\sim 27^\circ\text{C}$. Mortality accounts were made after twenty-four hours.

Spray chamber method. The knockdown test was carried out according to the method of Nagasawa¹¹⁾ against houseflies by spraying 0.5 ml of 1% Deo-base solution of the test compound, and KT_{50} and Mortality (%) after twenty-four hours were assessed.

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