Some New Aspects in the Chemistry of 4-Alkylidene-Δ^2-thiazolin-5-ones

By **M. D. Bachi**, Department of Chemistry, The Weizmann Institute of Science, Rehovot, Israel

2-Phenyl-Δ^2-thiazolin-5-one (6) was condensed with various ketones to give 4-alkylidene-2-phenyl-Δ^2-thiazolin-5-one (2). Treatment of these compounds with acylating agents afforded 5-acyloxy-4-alkenyl-2-phenylthiazoles (8) and (9). Sodium borohydride and sodium borodeuteriide reduced the 4-alkylidenethiazolones at the exocyclic double bond to give the respective 4-alkyl-2-phenyl-Δ^2-thiazolin-5-ones (10) and (11).

In the course of our work on β-lactams related to penicillin and cephalosporin, attempts have been made to prepare anhydropenicillin derivatives.[1] It was thought that the anhydropenicillanic acid [1] derivatives (1) might be obtained by reactions of the corresponding 4-alkylidene-Δ^2-thiazolin-5-ones (2) with diphenylketen, by analogy with the reaction of diphenylketen with Δ^2-thiazolines.[2,3] Since this reaction took a different pathway, the chemistry of these thiazolinones has now been investigated. The present paper describes their properties and their reactions with acylating agents and with sodium borohydride.

In principle, reactions of 4-alkylidene-Δ^2-thiazolin-5-ones of type (3) can involve initial attack of various reagents on the C=O, C=C, or C=N double bond. With the exception of the 2-mercapto-derivatives (3; R^1 = SH),[4,5] which, owing to their tautomerism with the 2-thioxo-form, constitute an independent group, little is known about the chemistry of 4-alkylidene-Δ^2-thiazolin-5-ones. The related 4-arylmethylenethiazolinones (3; R^2 = aryl, R^3 = H) undergo ring opening on attack of basic reagents at the 5-position: *e.g.* 4-benzylidene-2-phenyl-Δ^2-thiazolin-5-one (3; $R^1 = R^2$ = Ph, R^3 = H) is hydrolysed by aqueous sodium hydroxide to α-(thio-

[1] The term ' anhydropenicillins ' to designate a group of compounds obtained on a certain rearrangement of penicillins was introduced by S. Wolfe, J. C. Godfrey, C. T. Holdrege, and Y. G. Perron, *J. Amer. Chem. Soc.*, 1963, **85**, 643.

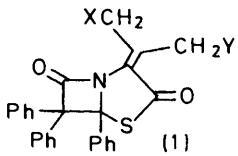
[2] H. T. Clarke, J. R. Johnson, and R. Robinson, eds., ' The Chemistry of Penicillin,' Princeton Univ. Press, Princeton, 1949, p. 973.

[3] R. Pfleger and A. Jäeger, *Chem. Ber.*, 1957, **90**, 2460.

[4] A. H. Cook and J. R. A. Pollock, *J. Chem. Soc.*, 1950, 1898 and previous papers in the same series.

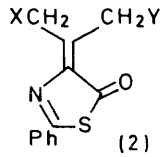
[5] F. P. Doyle, D. O. Holland, W. Marflitt, J. H. C. Nayler, and C. M. O'Connor, *J. Chem. Soc.*, 1955, 1719; F. P. Doyle, D. O. Holland, and J. H. C. Nayler, *ibid.*, p. 2265; F. P. Doyle, D. O. Holland, P. Mamalis, and A. Norman, *ibid.*, 1958, 4605.

benzoylamino)cinnamic acid (4; Z = OH), and aminolysed with piperidine to the piperidino-compound (4; Z = N·[CH_2]$_4$·CH_2).[6] The same thiazolinone is attacked at its exocyclic double bond by benzene in the presence



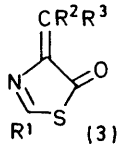
(1)

c: X = Y = H
b: X = Y = OAc

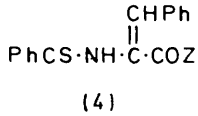


(2)

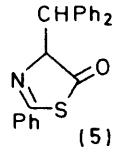
c: X = OAc, Y = H
d: X = H, Y = OAc



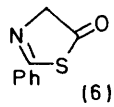
(3)



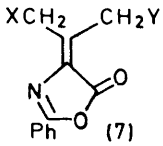
(4)



(5)



(6)



(7)

a: X = Y = H
b: X = Y = OAc
c: X = OAc, Y = H
d: X = H, Y = OAc

or anhydrous aluminum chloride, and by phenylmagnesium bromide, to give, in both cases 4-diphenylmethyl-2-phenyl-Δ^2-thiazolin-5-one (5).[7] A Michael condensation takes place[8] with the potassium salt of dimethyl 3-oxoglutarate. Several reactions involving attack at the C=N double bond of 4-alkylidene- and 4-arylmethylene-Δ^2-oxazolin-5-ones have been reported;[9] for example, it was recently[10] proved by the use of $H_2{}^{18}O$ that the hydrolysis of these oxazolinones by acid involves the addition of the elements of water to the C=N double bond. No parallel work on analogous thiazolinones has been reported.

The 4-alkylidenethiazolinones (2a—d) were prepared by condensation of 2-phenyl-Δ^2-thiazolin-5-one (6)[8,11] with the appropriate ketones in the presence of a basic catalyst. Thus, condensation with acetone in ethanol or propan-2-ol in the presence of benzylamine gave 4-isopropylidene-2-phenyl-Δ^2-thiazolin-5-one (2a); reaction with 1,3-diacetoxypropan-2-one in tetrahydrofuran in the presence of lead(II) acetate gave the diacetoxy-thiazolinone (2b), and condensation with 1-acetoxypropan-2-one gave a mixture of the two isomeric thiazolinones (2c) and (2d). Benzylamine was a poor catalyst for the last two condensations. The thiazolinone (2a) was also prepared by direct condensation of thiobenzoylglycine with acetone in the presence of acetic anhydride under the conditions described for the preparation of 4-isopropylidene-2-phenyl-Δ^2-oxazolin-5-one,[12] but it was accompanied by a large amount of 5-acetoxy-2-phenylthiazole,[11] formed by the competitive *O*-acylation of the intermediate thiazolinone (6). The thiazolinone (2c) was separated from its isomer (2d) by repeated recrystallisations from di-isopropyl ether. When pure (2c) was heated under reflux for a few h in propan-2-ol or treated for a few min with pyridine at room temperature, equilibrium was established and a 1 : 1 mixture of (2c) and (2d) was obtained.

The absolute configurations of the two isomers (2c) and (2d) were deduced from their n.m.r. spectra. Structure (2c) was assigned to the isomer bearing a deshielded methyl group. The deshielding of protons of a β-group *cis* to a carbonyl group in αβ-unsaturated systems is well documented.[13,14] The chemical shifts observed for the β-methyl and β-methylene groups of the thiazolinones (2), along with those reported for the analogous oxazolinones (7),[13] are given in Table 1. The

TABLE 1

N.m.r. data [a] for the thiazolinones (2) and the oxazolinones (7) [b] (δ values in p.p.m.)

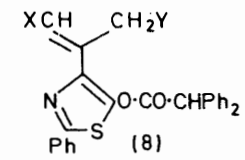
Compound	X	δ(CH_2X)	Y	δ(CH_2Y)
(2a)	H	2·38	H	2·44
(7a)	H	2·33	H	2·39
(2b)	AcO	5·42	AcO	5·42
(7b)	AcO	5·30	AcO	5·40
(2c)	AcO	5·38	H	2·46
(7c)	AcO	5·24	H	2·40
(2d)	H	2·39	AcO	5·38
(7d)	H	2·33	AcO	5·35

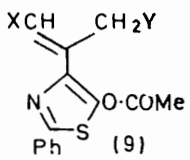
[a] Spectra were recorded with a Varian A60 spectrometer for solutions in deuteriochloroform. [b] Ref. 13.

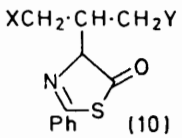
differences in chemical shifts between the methy protons *cis* and *trans* to the carbonyl group either within the same compound (2a) or (7a), or in the *cis–trans* isomers (2c) and (2d) or (7c) and (7d), are of the same magnitude (0·06—0·07 p.p.m.) for the thiazolinones and for the oxazolinones. However, comparison of the chemical shifts of the methylene protons of the β-acetoxymethylene groups indicates that no substantial deshielding effect operates in the thiazolinones while in the oxazolinones the *cis*-methylene protons are deshielded to a larger extent than the respective methyl protons (0·10—0·11 p.p.m.).

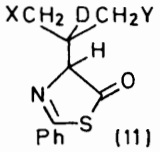
[6] S. I. Lurye and L. G. Gatsenko, *J. Gen. Chem.* (*U.S.S.R.*), 1952, **22**, 321.
[7] R. Filler and Y. S. Rao, *J. Org. Chem.*, 1962, **27**, 3730.
[8] H. Muxfeldt, J. Behling, G. Grethe, and W. Rogalski, *J. Amer. Chem. Soc.*, 1967, **89**, 4991.
[9] W. Steglich, *Fortschr. Chem. Forsch.*, 1969, **12**, 77.
[10] W. Steglich, V. Austel, and A. Prox, *Angew. Chem. Internat. Edn.*, 1968, **7**, 726.
[11] J. B. Jepson, A. Lawson, and V. D. Lawton, *J. Chem. Soc.*, 1955, 1791.
[12] Ref. 2, p. 783.
[13] E. Galantay, A. Szabo, and J. Fried, *J. Org. Chem.*, 1963, **28**, 98.
[14] L. M. Jackman, 'Applications of Nuclear Magnetic Resonance Spectroscopy,' Pergamon, New York, 1959, p. 121; L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 1960, 2881, 2886; K. Brocklehurst, H. S. Price, and K. Williamson, *Chem. Comm.*, 1968, 884.

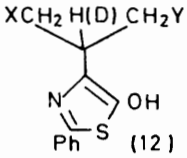
Attempts to prepare the β-lactam (1a) by the reaction of diphenylketen with the thiazolinone (2a) led to a 1 : 1 adduct whose spectral data are in agreement with structure (8a). Similarly the diphenylacetoxythiazole (8b) was obtained when triethylamine was added under high dilution conditions to a boiling solution of (2b) and

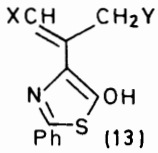

(8)


(9)


(10)


(11)


(12)


(13)

a; X = Y = H c; X = OAc, Y = H
b; X = Y = OAc d; X = H, Y = OAc

diphenylacetyl chloride in dichloromethane. When a solution of the 8 : 1 mixture (see Experimental section) of the two isomeric monoacetoxythiazolinones (2c) and (2d) and diphenylacetyl chloride in dry toluene was treated with triethylamine, the thiazole (8c) was isolated.

O-Acylation of 4-alkylidenethiazolinones (2) involving migration of the exocyclic double bond and concomitant formation of a highly conjugated thiazole system also occurs when other acylating agents are used. These thiazolinones were thus converted into 5-acetoxy-4-alkenylthiazoles (9) by treatment with acetyl chloride and triethylamine or with acetic anhydride and pyridine; (9b) was also obtained upon prolonged heating under reflux of (2b) with acetyl chloride in benzene in the absence of a base. Acetylation of (2c) and (2d) (8 : 1 mixture) with acetyl chloride–triethylamine produced the two isomeric 5-acetoxythiazoles (9c) and (9d) in a 7 : 5 ratio; only (9c) was isolated after treatment with acetic anhydride-pyridine.

The structures of compounds (8) and (9) were substantiated by their n.m.r. spectra (see Table 2). The methyl groups in (8c) and (9c) appear as doublets and the vinyl protons of the enol acetate systems as quartets. Irradiation at the frequencies corresponding to the methyl groups caused the collapse of the quartets to singlets, and irradiation at those of the vinyl protons converted the doublets into singlets. The signals corresponding to the vinyl and phenyl protons in spectra of solutions in deuteriochloroform overlap partially. The use of deuteriobenzene or deuteriobenzene–deuteriochloroform induces a pronounced down-field shift of the signals for the vinyl protons, thus clearly separating them from those for the phenyl protons.

4-Alkylidene-Δ^2-thiazolin-5-ones (2a—d) were reduced by sodium borohydride in tetrahydrofuran or in dimethoxyethane to the respective 4-alkyl-Δ^2-thiazolin-5-ones (10a—d) and with sodium borodeuteriide to the monodeuteriothiazolinones (11a—d). The thiazolinone (2c) or mixtures of (2c) and (2d) gave always, and irrespective of the ratio between the two isomers, the same product, which was shown by its n.m.r. spectrum [15] to consist of a 1 : 1 mixture of two diastereoisomers (11c and d). In a detailed n.m.r. study [15] it was pointed out that in chloroform, benzene, and bromobenzene, the thiazolinones (10) and (11) do exist in their ' oxo ' form

TABLE 2

N.m.r. data for the allylic systems of the 5-acyloxy-4-alkenylthiazoles (8) and (9) (δ values in p.p.m.)

Compound	Solvent	C:CMe	AcO·CH$_2$·C:C	AcO·CH:C	C·C:CH$_2$
(8a)	$CDCl_3$ [a]	2·07 (m)			5·17 (m) 5·58 (m)
(9a)	$CDCl_3$ [a]	2·23 (m)			5·31 (m) 5·80 (m)
(8b)	$CDCl_3$ [a]		5·22 (s)	8·18 (s)	
(9b)	$CDCl_3$ [a]		5·28 (s)	8·25 (s)	
(8c)	$CDCl_3$ [b]	2·00 (d, [d] *J* 1·5 Hz)		7·93 (q, [e] *J* 1·5 Hz)	
	C_6D_6	2·16 (d, *J* 1·5 Hz)		8·33 (q, *J* 1·5 Hz)	
(9c)	$CDCl_3$ [a]	2·17		7·98 (q, *J* 1·5 Hz)	
	C_6D_6 [c]	2·22 (d, [f] *J* 1·5 Hz)		8·23 (q, [g] *J* 1·5 Hz)	
(9d)	$CDCl_3$ [a]		5·13 (m)		5·61 (m) 6·07 (m)
	C_6D_6 [a]		5·21 (m)		5·57 (m) 6·13 (m)

[a] Varian A60. [b] Varian HA 100. [c] Bruker HFX90. [d] Collapses to a singlet on irradiation at δ 7·93 p.p.m. [e] Collapses to a singlet on irradiation at δ 2·00 p.p.m. [f] Collapses to a singlet on irradiation at δ 8·23 p.p.m. [g] Collapses to a singlet on irradiation at δ 2·22 p.p.m.

[15] E. Glotter and M. D. Bachi, *Israel J. Chem.*, 1970, **8**, 633.

while in dimethyl sulphoxide and in pyridine, the enol structure (12) predominates.

The readiness with which the thiazolinones (2) undergo *O*-acylation and the quick equilibration [(2c) ⇌ (2d)] in the presence of pyridine suggest that a ' hydroxy ' form (13) analogous to (12) might exist in equilibrium with the ' oxo ' form (2).

EXPERIMENTAL

M.p.s were determined with a Büchi m.p. apparatus. I.r. spectra were obtained with a Perkin-Elmer Infracord spectrometer. N.m.r. data were usually recorded with a Varian A60 spectrometer, tetramethylsilane being used as internal standard; double-resonance experiments were performed with a Varian HA 100 instrument with the same internal reference, or with a Bruker HFX90 spectrometer with hexamethyldisiloxane as internal standard. Mass spectra were recorded on an Atlas MAT CH4 spectrometer. All reactions were performed under nitrogen in carefully dried solvents. Evaporations were carried out with a rotary evaporator under reduced pressure.

2-Phenyl-Δ²-thiazolin-5-one (6).—Freshly distilled phosphorous tribromide (177 g) was added with stirring during 20 min to a solution of thiobenzoylglycine (68·3 g) in ether (1·5 l). The temperature was kept below the b.p. by occasional immersion in a cooling bath. After being stirred for an additional 20 min at room temperature the mixture was cooled to 0°; the precipitated hydrobromide was then filtered off and washed with ether. It was suspended in ether (1·7 l) and vigorously shaken with aqueous 20% sodium acetate (1·7 l); the ethereal layer was separated, washed with sodium acetate solution, dried, and treated with charcoal. The residue obtained after filtration and evaporation was crystallised from light petroleum to give the thiazolinone (6) (55·5 g, 90%), m.p. 83—84° (lit.,[8] 79—81°; lit.,[11] 84°) (Found: C, 61·3; H, 3·9; N, 7·6; S, 17·85. Calc. for C_9H_7NOS: C, 61·0; H, 4·0; N, 7·9; S, 18·1%), $\nu_{max.}$ ($CHCl_3$), 1730, 1605, and 1580 cm^{-1}, δ ($CDCl_3$) 4·84 (2H, s), 7·4—7·6 (3H, m), and 7·7—7·9 p.p.m. (2H, m). In order to avoid the formation of red by-products, the foregoing work-up should be performed quickly and with the exclusion of air. In contrast to a previous report,[8] pure samples of (6) could be stored for several weeks under nitrogen at 0° without appreciable decomposition.

4-Isopropylidene-2-phenyl-Δ²-thiazolin-5-one (2a).—(*a*) 2-Phenyl-Δ²-thiazolin-5-one (6) (4·0 g) and acetone (2·0 g) in ethanol (35 ml) were warmed to 30° and then treated with benzylamine (0·25 g). The starting material dissolved at once and within a few s the product started to crystallise out. After 3 h the precipitate was filtered off and washed with a small portion of cold ethanol to give the thiazolinone (2a) (3·5 g, 72%), m.p. 99° (lit.,[11] 99°) (Found: C, 66·6; H, 4·95; N, 6·3; S, 15·2. Calc. for $C_{12}H_{11}NOS$: C, 66·35; H, 5·1; N, 6·45; S, 14·8%; *M*, 217), *m/e* 217, $\nu_{max.}$ ($CHCl_3$) 1686, 1616, and 1592 cm^{-1}, δ ($CDCl_3$) 2·38 (3H, s), 2·44 (3H, s), 7·4—7·6 (3H, m), and 7·8—8·0 p.p.m. (2H, m). A similar result (76% yield) was obtained when propan-2-ol was used as solvent.

(*b*) To a suspension of thiobenzoylglycine (29·25 g) and fused sodium acetate (9·15 g) in dry acetone (500 ml) under reflux, acetic anhydride (37·55 g) was added dropwise during 1 h. Heating under reflux was continued for additional 20 h and the mixture was then poured into crushed ice and water (3 l). The voluminous precipitate was collected, washed with water, and dried. The crude product was shown by comparative t.l.c. to consist of a mixture of the thiazolinone (2a) and 5-acetoxy-2-phenylthiazole (an authentic sample was prepared according to ref. 11). Column chromatography over silica gel (700 g) with benzene–light petroleum (b.p. 40—60°) (3 : 7 v/v) as eluant gave the thiazolinone (2a) (16·6 g, 51%), m.p. 98—99° (from ethanol).

4-(2-Acetoxy-1-acetoxymethylethylidene)-2-phenyl-Δ²-thiazolin-5-one (2b).—A solution of the thiazolinone (6) (10·62 g) and 1,3-diacetoxypropan-2-one (41·76 g) in tetrahydrofuran (150 ml) was treated with lead(II) acetate (2·27 g). The mixture was stirred for 3 h at room temperature then diluted with ether, filtered through Celite, and evaporated; the residue was taken up in ether. The solution was washed with aqueous 10% sodium acetate followed by water, dried, and evaporated. The crude product was dissolved in benzene–chloroform (1 : 1 v/v) and filtered through a silica gel column (250 g). The residue (17·3 g) after evaporation was successively recrystallised from ethanol (with charcoal) and methylcyclohexane to give the *thiazolinone* (2b) (12·5 g, 62%), m.p. 113—114° (Found: C, 57·7; H, 4·5; N, 4·5; S, 9·8. $C_{16}H_{15}NO_5S$ requires C, 57·7; H, 4·5; N, 4·2; S, 9·6%), $\nu_{max.}$ ($CHCl_3$) 1736, 1659, and 1616 cm^{-1}, δ ($CDCl_3$) 2·11 (6H, s), 5·42 (4H, s), 7·45—7·65 (3H, m), and 7·85—8·05 p.p.m. (2H, m).

4-(1-Acetoxymethylethylidene)-2-phenyl-Δ²-thiazolin-5-ones (2c) and (2d).—To a solution of 2-phenyl-Δ²-thiazolin-5-one (6) (10·62 g) and 1-acetoxypropan-2-one (27·8 g) in tetrahydrofuran (200 ml) was added lead(II) acetate (2·27 g). After being stirred at room temperature during 3 h the mixture was worked up as described for the preparation of (2b). The crude product (14·7 g) was dissolved in dichloromethane–hexane (1 : 1 v/v) and filtered through a silica gel column. The semisolid residue obtained after evaporation (14·2 g, 86%) was crystallised from propan-2-ol to give a solid (9·5 g), m.p. 51—70°, and an oil (4·7 g). N.m.r. spectra indicated that the crystalline compound consisted of a 5 : 1 mixture of the thiazolinones (2c) and (2d), and the oil was a 1 : 1 mixture of the same two thiazolinones. When the 5 : 1 mixture was recrystallised from propan-2-ol a 3 : 1 [(2c) : (2d)] mixture was obtained, m.p. 60—70° (Found: C, 60·95; H, 4·8; N, 5·2; S, 11·35. Calc. for $C_{14}H_{13}NO_3S$: C, 61·1; H, 4·8; N, 5·1; S, 11·65%), $\nu_{max.}$ (KBr) 1742, 1686, and 1616 cm^{-1}, δ ($CDCl_3$) 2·15 (3H, s), 2·39 (t, *J* 0·8 Hz) and 2·46 (t, *J* 1·1 Hz) (total 3H), 5·38 (2H, m), 7·4—7·6 (3H, m), and 7·8—8·0 p.p.m. (2H, m); recrystallisation from di-isopropyl ether afforded an 8 : 1 [(2c) : (2d)] mixture, which yielded after two more recrystallisations from the same solvent a pure sample of the isomer (2c), m.p. 85—86° (Found: C, 61·2; H, 4·9; N, 5·05; S, 11·4%), $\nu_{max.}$ (KBr) 1742, 1686, and 1616 cm^{-1}, δ ($CDCl_3$) 2·15 (3H, s), 2·46 (3H, t, *J* 1·1 Hz), 5·38 (2H, q, *J* 1·1 Hz), 7·4—7·6 (3H, m), and 7·8—8·0 p.p.m. (2H, m).

Acylation of 4-Isopropylidene-2-phenyl-Δ²-thiazolin-5-one (2a).—(*a*) To a stirred solution of (2a) (1·09 g) in toluene (5 ml) a solution of diphenylketen (0·97 g) in toluene (5 ml) was added during 30 min. After 16 h the solvent was removed and the residue was recrystallised from propan-2-ol and then from methylcyclohexane to give the *diphenylacetoxythiazole* (8a) (1·4 g, 70%), m.p. 111° (Found: C, 75·7; H, 4·9; N, 3·6; S, 8·1. $C_{26}H_{21}NO_2S$ requires C, 75·9; H, 5·1; N, 3·4; S, 7·8%), $\nu_{max.}$ ($CHCl_3$) 1757, 1629, and 1605 cm^{-1}, δ ($CDCl_3$) 2·07 (3H, m), 5·17 (1H, m), 5·30

(1H, s), 5·58 (1H, m), 7·3—7·5 (13H, complex), and 7·8—8·0 p.p.m. (2H, m).

(*b*) To a solution of (2a) (0·34 g) and acetyl chloride (0·62 g) in benzene (20 ml) a solution of triethylamine (0·80 g) in benzene (10 ml) was added during 2 h. After 1 h the mixture was treated with charcoal, filtered through Celite, and evaporated. Recrystallisation of the residue from t-butyl alcohol afforded the *5-acetoxythiazole* (9a) (0·30 g, 58%), m.p. 69° (Found: C, 64·9; H, 5·1; N, 5·6; S, 12·35. $C_{14}H_{13}NO_2S$ requires C, 64·8; H, 5·05; N, 5·4; S, 12·4%), $\nu_{max.}$ (KBr) 1754 and 1618 cm^{-1}, δ ($CDCl_3$) 2·23 (3H, m), 2·30 (3H, s), 5·31 (1H, m), 5·80 (1H, m), 7·3—7·5 (3H, m), and 7·8—8·0 p.p.m. (2H, m).

Acylation of 4-(2-*Acetoxy*-1-*acetoxymethylethylidene*)-2-*phenyl*-Δ^2-*thiazolin*-5-*one* (2b).—(*a*) To a boiling solution of (2b) (1·0 g) and diphenylacetyl chloride (0·76 g), in dichloromethane (60 ml) a solution of triethylamine (0·33 g) in dichloromethane (50 ml) was added during 6 h through a high dilution cycle.[16] After 16 h the solvent was removed, the residue was treated with ether, and the precipitated triethylamine hydrochloride was filtered off. The filtrate was evaporated; recrystallisation of the residue from ethyl acetate–pentane afforded the *diphenylacetoxythiazole* (8b) (0·96 g, 61%), m.p. 131° (Found: C, 68·2; H, 4·5; N, 2·7; S, 5·8. $C_{30}H_{25}NO_6S$ requires C, 68·3; H, 4·8; N, 2·7; S, 6·1%), $\nu_{max.}$ ($CHCl_3$) 1751 and 1718 cm^{-1}, δ ($CDCl_3$) 1·91 (3H, s), 2·24 (3H, s), 5·22 (2H, s), 5·35 (1H, s), 7·3—7·5 (13H, complex), 7·8—8·0 (2H, m), and 8·18 p.p.m. (1H, s).

(*b*) A solution of (2b) (1·0 g) and acetyl chloride (0·6 ml) in benzene (10 ml) was heated under reflux for 40 h. The mixture was evaporated and the residue was dissolved in ether and washed with 5% sodium carbonate and then with water. The ethereal solution was dried, treated with charcoal, and evaporated. Recrystallisation of the residue from ethyl acetate–pentane afforded the *acetoxythiazole* (9b) (0·52 g, 46%), m.p. 96—97°.

(*c*) A solution of (2b) (0·33 g), acetic anhydride (0·31 g), and pyridine (0·4 ml) in benzene (10 ml) was left overnight at room temperature and then worked up as described in (*b*). On recrystallisation from ethyl acetate–pentane the *acetoxythiazole* (9b) was obtained (0·20 g, 54%), m.p. 96—97°.

(*d*) To a solution of (2b) (0·33 g) and acetyl chloride (0·08 g) in benzene (10 ml) a solution of triethylamine (0·10 g) in benzene (5 ml) was added during 20 min with stirring at room temperature. After 1 h the mixture was washed with water, dried, and evaporated. The residue was dissolved in ethyl acetate, treated with charcoal, and recrystallised from ethyl acetate–pentane to give the *acetoxythiazole* (9b) (0·30 g, 79%), m.p. 96—97° (Found: C, 57·7; H, 4·8; N, 3·7; S, 8·7. $C_{18}H_{17}NO_6S$ requires C, 57·6; H, 4·6; N, 3·7; S, 8·5%), $\nu_{max.}$ ($CHCl_3$) 1761 and 1727 cm^{-1}, δ ($CDCl_3$) 2·03 (3H, s), 2·25 (3H, s), 2·36 (3H, s), 5·28 (2H, s), 7·3—7·5 (3H, m), 7·8—8·0 (2H, m), and 8·25 p.p.m. (1H, s).

Acylation of 4-(1-*Acetoxymethylethylidene*)-2-*phenyl*-Δ^2-*thiazolin*-5-*one* (2c and d).—(*a*) To a solution of diphenylacetyl chloride (0·51 g) and an 8 : 1 mixture of the two isomeric thiazolinones (2c) and (2d) (0·55 g) in toluene (20 ml) a solution of triethylamine (0·22 g) in toluene (10 ml) was added dropwise with stirring during 30 min and the mixture was kept overnight. The precipitated triethylamine hydrochloride was filtered off. Evaporation of the filtrate left an oil which crystallised on trituration with propan-2-ol. Recrystallisation from ethyl acetate–hexane gave the *diphenylacetoxythiazole* (8c) (0·49 g, 52%), m.p. 171° (Found: C, 71·6; H, 5·1; N, 3·0; S, 7·05. $C_{28}H_{23}NO_4S$ requires C, 71·6; H, 4·9; N, 3·0; S, 6·8%), $\nu_{max.}$ ($CHCl_3$) 1751 cm^{-1}, δ ($CDCl_3$) (100 MHz) 2·0 (3H, d, *J* 1·5 Hz), 2·17 (3H, s), 5·35 (1H, s), 7·3—7·5 (13H complex), and 7·93 (q, *J* 1·5 Hz) and 7·8—8·0 p.p.m. (m) (total 3H); on irradiation at 200 Hz the quartet at 7·93 collapsed to a singlet; on irradiation at 790 Hz the doublet at 2·0 collapsed to a singlet, δ (C_6D_6–$CDCl_3$, 1 : 1 v/v) 1·81 (3H, s), 2·08 (3H, d, *J* 1·5 Hz), 5·21 (1H, s), 7·0—7·35 (m), 7·7—7·9 (2H, m), and 8·12 (1H, q, *J* 1·5 Hz).

(*b*) A solution of (2c and d) [8 : 1 (2c) : (2d), 0·55 g], acetic anhydride (0·6 ml), and pyridine (0·8 ml) in toluene (10 ml) was left for 48 h at room temperature. The toluene and excess of pyridine were removed and the residue was dissolved in ethyl acetate. The solution was washed with 10% sodium hydrogen carbonate and with brine, dried, treated with charcoal, filtered, and concentrated. Recrystallisation from ethyl acetate–hexane gave the *acetoxythiazole* (9c) (0·40 g, 63%), m.p. 121° (Found: C, 60·7; H, 4·9; N, 4·6; S, 10·2. $C_{16}H_{15}NO_4S$ requires C, 60·6; H, 4·8; N, 4·4; S, 10·1%), $\nu_{max.}$ ($CHCl_3$) 1745 cm^{-1}, δ ($CDCl_3$) 2·17 (d) and 2·22 (s) (total 6H), 2·36 (3H, s), 7·3—7·5 (3H, m), and 7·98 (q, *J* 1·5 Hz), and 7·8—8·0 p.p.m. (m) (total 3H), δ (C_6D_6) (90 MHz) 1·55 (3H, s), 1·58 (3H, s), 2·22 (3H, d, *J* 1·5 Hz), 6·9—7·0 (m), 7·7—7·8 (2H, m), and 8·23 p.p.m. (1H, q, *J* 1·5 Hz); on irradiation at 200 Hz the quartet at 8·23 collapsed to a singlet; on irradiation at 741 Hz the doublet at 2·22 collapsed to a singlet.

(*c*) To a solution of (2c) and (2d) (8 : 1; 0·55 g) and acetyl chloride (0·16 g) in benzene (20 ml) a solution of triethylamine (0·20 g) in benzene (10 ml) was added at room temperature during 30 min. After 1 h the mixture was treated with charcoal, filtered through Celite, and evaporated to give a product (0·40 g, 63%), m.p. 99—105° (from methylcyclohexane). Recrystallisation from ethyl acetate raised the m.p. to 99—107° (Found: C, 60·6; H, 4·8; N, 4·5; S, 10·2%); the n.m.r. spectrum indicated that this product consisted of a mixture of the *acetoxythiazole* (9c) and its *isomeric acetoxythiazole* (9d) in a 7 : 5 ratio. The signals attributed to (9d) are δ ($CDCl_3$) 2·10 (3H, s), 5·13 (2H, m), 5·61 (1H, m), and 6·07 p.p.m. (1H, m); the other signals could not be resolved from the signals of (9c).

Reduction of 4-(2-*Acetoxy*-1-*acetoxymethylethylidene*)-2-*phenyl*-Δ^2-*thiazolin*-5-*one* (2b).—(*a*) To a solution of (2b) (333 mg) in dimethoxyethane (10 ml) at 0°, sodium borohydride (25 mg) was added in portions with stirring during 10 min. After 1 h the solvent was removed and the residue was taken up in ethyl acetate, washed thrice with saturated sodium chloride solution, dried ($CaSO_4$), treated with charcoal, and then filtered through Celite. The filtrate was evaporated and dried (100° at 0·1 mmHg) to give the *thiazolinone* (10b) (323 mg, 96%) as a pure oil (t.l.c.) (Found: C, 57·3; H, 5·2; N, 4·0; S, 9·4. $C_{16}H_{17}NO_5S$ requires C, 57·3; H, 5·1; N, 4·2; S, 9·6%; *M*, 335), *m/e* 335, $\nu_{max.}$ (film) 1739, 1724, 1600, and 1572 cm^{-1}, for n.m.r. data see ref. 15. Thiazolinone (10b) slowly decomposes and cannot be distilled. Deteriorated samples were purified by preparative t.l.c. on silica gel (GF 254, Merck) plates, developed with benzene–ethyl acetate (5 : 1 v/v).

(*b*) Reduction of (2b) with sodium borodeuteriide under the conditions described in (*a*) afforded the *monodeuteriothiazolinone* (11b); for n.m.r. data see ref. 15.

[16] A. C. Cope and E. C. Herrick, *J. Amer. Chem. Soc.*, 1950, **72**, 983.

Reduction of 4-(1-*Acetoxymethylethylidene*)-2-*phenyl*-Δ^2-*thiazolin*-5-*ones* (2c *and* d).—(*a*) The thiazolinone (2c) (412 mg) was reduced with sodium borohydride as described above for the reduction of (2b). The crude compound obtained after the usual work-up (385 mg) was chromatographed on a silica gel (HF, Merck) column. Elution with benzene–ethyl acetate (10 : 1 v/v) under nitrogen pressure gave the thiazolinones (10c and d) (274 mg, 66%) as an oil (Found: C, 60·5; H, 5·2; N, 4·95. Calc. for $C_{14}H_{15}NO_3S$: C, 60·6; H, 5·45; N, 5·05%; *M*, 277), *m/e* 277, $\nu_{max.}$ ($CHCl_3$) 1724, 1603, and 1580 cm^{-1}.

(*b*) Reduction of (2c) or of various mixtures of (2c) and (2d) with sodium borodeuteriide under the conditions described in (*a*) afforded the monodeuteriothiazolinones (11c and d), *m/e* 278. (Calc. for $C_{14}H_{14}{}^2HNO_3S$: *M*, 278), $\nu_{max.}$ ($CHCl_3$) 1724, 1603, and 1580 cm^{-1}, t.l.c. behaviour in various systems identical with (10c and d); for n.m.r. data see ref. 15.

4-*Isopropyl*-2-*phenyl*-Δ^2-*thiazolin*-5-*one* (10a).—(*a*) 4-Isopropylidene-2-phenyl-Δ^2-thiazolin-5-one (2a) was treated with sodium borohydride in tetrahydrofuran as described for the reduction of (2b). The crude product was purified by preparative t.l.c. [benzene–hexane (1 : 1 v/v)] to give (10a) (84%), spectral data identical with those of the thiazolinone obtained from thiobenzoylvaline as described in (*b*).

(*b*) *N*-Thiobenzoylvaline [11] (11·85 g) was treated with phosphorous tribromide as described for the preparation of 2-phenyl-Δ^2-thiazolin-5-one (6) to give the *hydrobromide* of 5-hydroxy-4-isopropyl-2-phenylthiazole [enolic form of (10a)],[15] m.p. 205—206° (from ethanol–ethyl acetate–ether) (Found: C, 48·0; H, 4·5; Br, 26·6; N, 4·7; S, 10·7. $C_{12}H_{14}BrNOS$ requires C, 48·0; H, 4·7; Br, 26·7; N, 4·7; S, 10·7%), $\nu_{max.}$ (KBr) 2850br, 2670br, 1715w, and 1623s cm^{-1}. The free thiazolinone (10a) was obtained from its hydrobromide as described for the preparation of (6). The crude product was distilled (102—104° at 0·1 mmHg) to give an oil (6·48 g, 89%) which did not crystallise (lit.,[11] m.p. 69°) (Found: C, 65·5; H, 5·7; N, 6·5; S, 14·9. Calc. for $C_{12}H_{13}NOS$: C, 65·7; H, 6·0; N, 6·4; S, 14·6%), $\nu_{max.}$ (film) 1724, 1603, and 1575 cm^{-1}; for n.m.r. data see ref. 15.

The author thanks Professor W. Taub for discussions and encouragement and Mr. R. Stuber for technical assistance.

[1/1636 *Received*, 8*th September*, 1971]