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ADDITION REACTIONS OF THIAZOL-5(4H)-ONES—II[1]

CYCLOADDITION AND MICHAEL ADDITION REACTIONS OF 4-SUBSTITUTED 2-PHENYLTHIAZOL-5(4H)-ONES

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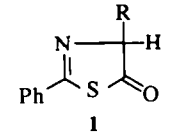
Abstract—The mixture of adducts formed under mild conditions between a 4-substituted 2-phenylthiazol-5(4H)-one and an electron-deficient alkene is shown to include a stable cycloadduct and a Michael adduct formed through the 2- or the 4-position of the thiazolone. The reaction can be diverted towards the Michael adduct entirely, by adding traces of aqueous alkali to the reactants in acetone solution. A novel type of 1:2-adduct is present in the reaction mixture, and is shown to be formed through reaction of the cycloadduct with the alkene. A product formed by extrusion of carbonyl sulphide from the cycloadduct is the same as that obtained from the analogous oxazolone and the alkene, but generally the differences between the propensity of oxazolones and thiazolones to undergo various types of addition reaction with representative dipolarophiles are shown to be substantial.

Addition reactions of different types have been reported for 4-substituted 2-aryloxazol-5(4H)-ones (**1**; O in place of S), including cycloaddition reactions[2] and Michael addition reactions involving either the 2- or the 4-position of the oxazolone ring.[3] We expected that a different pattern of addition reactivity would be shown by 4-substituted 2-phenylthiazol-5(4H)-ones (**1**) since in comparison with corresponding oxazolones these compounds exist in solution to a greater extent in enolic and mesoionic tautomeric forms at the expense of the keto-tautomeric form, indicating a different electron distribution on ring atoms and on the exocyclic O atom in the two series.[4] 2-Phenylthiazol-5(4H)-one (**1**; R = H) differs from its 4-substituted homologues in existing in the keto-tautomeric form, and like the corresponding oxazolone undergoes condensation reactions typical of an active methylene compound,[5] rather than cycloaddition or Michael addition reactions.

Initial studies of the reaction between 4-substituted 2-phenylthiazol-5(4H)-ones (**1**) and electron-deficient alkenes soon confirmed our expectation that there would be substantial differences in the addition behaviour of thiazolones compared with that of oxazolones, and the broad study reported here reveals several examples of concurrent operation of different addition mechanisms involving thiazolones, with novel features in comparison with oxazolone reactions. In particular, thiazolone-alkene cycloadducts (**2**) are generally stable and only reluctantly undergo the extrusion step which is typical of the cycloaddition reactions of oxazol-5(4H)-ones with dipolarophiles.[2]

Reactions of 4-substituted 2-phenylthiazol-5(4H)-ones with alkenes. Alkene adducts (**2–5**) isolated from reactions with thiazolones under mild conditions include two types (**2** and **4**) which have not been obtained previously in corresponding reactions with oxazolones, although a cycloadduct has been assumed to be an intermediate in the well-established 2-pyrroline synthesis using oxazolones and alkenes.[2]

4-Methyl-2-phenylthiazol-5(4H)-one (**1**; R = Me)[6] gave three products (**2–4**) on reaction with maleic anhydride in acetone solution at room temperature during 4–12 hr, two of which were 1:1-adducts, and the third incorporated two molecules of alkene and one of thiazolone. The



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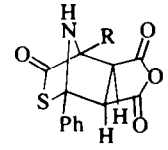
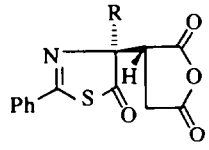


2: R = Me

2a: S in place of NH, NPh in place of –O–, R = Ph



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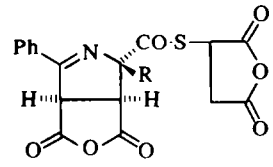

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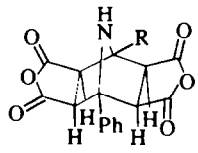

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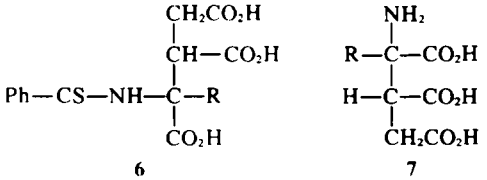
1:1-adducts were respectively the cycloadduct (**2**) and the Michael adduct (**3**; R = Me), structure and stereochemistry being assigned on the basis of spectroscopic data and chemical properties. We have been able to demonstrate that the 1:2-adduct (**4**; R = Me) arises by further reaction of the cycloadduct (**2**) with maleic anhydride, though we have not found conditions for the isomerisation of **2** into (**3**; R = Me), or vice versa, and we conclude that the cycloadduct (**2**) and the Michael adduct (**3**; R = Me) are formed through concurrent addition processes, the cycloadduct from the mesoionic tautomer of (**1**; R = Me), and the Michael adduct from either (**1**; R = Me) or from its enol-tautomer. Further discussion of the course of the reaction leading to the Michael adduct is included later in this paper.

The *exo*-stereochemistry shown in **2** is assigned on the basis of NMR data, the coupling constant for the ring-junction protons (J = 7·0 Hz) being consistent with

their *endo*-orientation by analogy with structure assignments to similar 2,4-diphenyl-1,3-dithiol-5-one–alkene cycloadducts[7] (e.g. J = 9·6 Hz for *endo*-adduct **2a** from N-phenylmaleimide and the dithiolone, and J = 6·8 Hz for the *exo*-isomer), and for corresponding bicyclo[2.2.1]hexanes.[8]

The cycloadduct (**2**) gave an N-acetyl derivative in high yield with acetic anhydride and pyridine, and it was unchanged after 12 hr in refluxing toluene. Its stability was further demonstrated by the presence of a molecular ion in its mass spectrum. In contrast, the putative oxazolone-alkene cycloadduct (**2**; O in place of S) loses CO_2 so readily that it has escaped isolation in all previous studies;[2] however, the analogous loss of carbonyl sulphide from **2** is a prominent fragmentation mode under electron impact, as shown by a peak at (M-60) in its mass spectrum.

The isomeric 1:1-adduct (**3**) obtained from the same reaction mixture showed mass spectrometric fragmentation behaviour consistent with addition of the thiazolone to the alkene through the 4-position of the thiazolone; hydrolysis into a thiobenzamidotricarboxylic acid (**6**; R = Me) with alkali, and into the corresponding aminotricarboxylic acid (**7**; R = Me) with 6N HCl, provides conclusive proof of structure, and the formation of a pyrrolidone (**8**), which give an anhydride (**9**) on treatment with acetic anhydride and pyridine, through acid hydrolysis of the analogous Michael adduct (**3**; R = Ph) from 2,4-diphenylthiazol-5(4H)-one, proves the *erythro*-configuration shown in structures **3**, **6** and **7** for the phenyl compounds, and this is assumed for the methyl compounds too. Alkaline hydrolysis of the 1:2-adduct (**4**;



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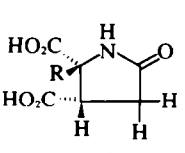

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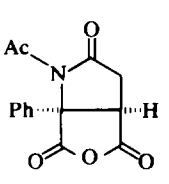

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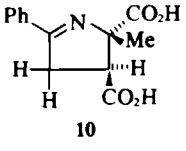

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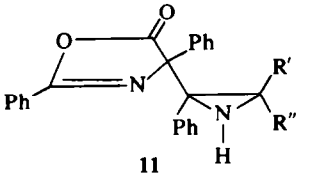
R = Me) gave the 1-pyrroline (**10**); we deduce that decarboxylation of the intermediate tricarboxylic acid involves loss of the C-3 carboxy group since this is part of a β-ketimino-acid system.

Although the formation of **3** is easily rationalised on the basis of a Michael addition reaction sequence, with the cycloadduct (**2**) or the enol-tautomer of the thiazolone (**1**) acting as base, the stereospecificity of the addition might imply that an ene reaction mechanism operates in the formation of **3**. The sole relevant example of an ene reaction arises in the stereospecific addition of 2,4-diphenyloxazol-5(4H)-one to 2-phenyl-3H-azirines, leading to **11**.[9] Analogous adducts are formed between 2-benzyl-4-methyloxazol-5(4H)-one and 4,4-dimethylthiazoline-5-carboxylic acid,[10] and between 4-substituted 2-phenyloxazol-5(4H)-ones and alkenes or alkynes,[3] but the stereochemistry of these adducts has not been investigated.

The yield of (**3**; R = Me) was increased considerably, and the other adducts (**2** and **4**; R = Me) were not formed, when two drops of 2N NaOH were added to an otherwise identical reaction mixture to that leading to all three adducts (**2**, **3** and **4**); this tends to support the assignment of the Michael addition reaction mechanism for the formation of **3**. Furthermore, the opposite stereochemistry would be predicted for **3** on the basis of the optimum encounter mode for the reactants participating in an ene reaction.[cf 9]



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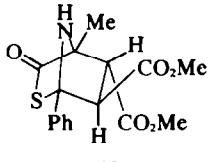
In addition to the Michael adduct (**3**; R = Ph), the cycloadduct-alkene extrusion product (**5**; R = Ph) was also obtained from 2,4-diphenylthiazol-5(4H)-one and maleic anhydride. Neither the cycloadduct (**2**; R = Ph) nor the 1:2-adduct (**4**; R = Ph) was obtained, and although the yield of **5** was reduced to 5% on conducting the reaction under the mildest possible conditions (room temperature in acetone solution during 24 hr) we were still unable to isolate a cycloadduct, but the yield of the Michael adduct (**3**; R = Ph) was increased under these conditions. A similar result was obtained for the two thiazolones (**1**; R = Me, Ph) in reactions with dimethyl fumarate; whereas the 4-methylthiazolone gave a mixture of the cycloadduct (**12**) and the product (**13**) of further reaction with extrusion between **12** and the alkene, no corresponding cycloadduct was obtained in the reaction of the 4-phenyl-thiazolone with dimethyl fumarate, which gave two cycloadduct extrusion products (**13**; R = Ph) and the 1-pyrroline (**14**).



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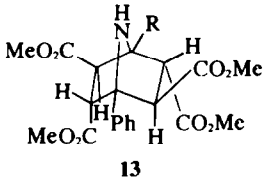

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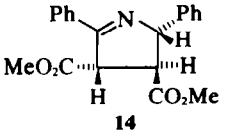

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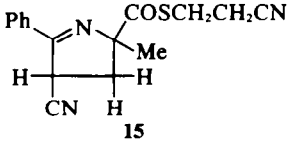

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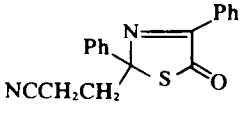

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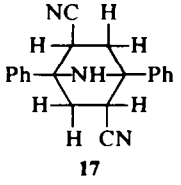

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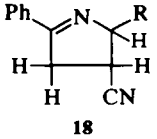

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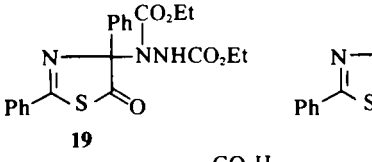
The two thiazolones (1; R = Me, Ph) also differed in their addition reactions with acrylonitrile; no cycloadduct was isolated in either case, but the 4-methylthiazolone gave the 1:2-adduct (**15**) in low yield, while the 4-phenylthiazolone gave as major product a Michael adduct involving reaction through the 2-position of the thiazolone ring (**16**). The 1-pyrroline (**18**; R = Ph) and the cycloadduct-extrusion product (**17**; R = Ph) were also formed from the 4-phenylthiazolone, but in very low yield.

Differences with corresponding oxazolone reactions revealed in this study, viz. the greater tendency to undergo Michael addition reactions shown by the thiazolones, and the greater stability of thiazolone-alkene cycloadducts, are exemplified further for other unsaturated systems later in this paper; generally, the thiazolones show diminished cycloaddition reactivity in comparison with corresponding oxazolones, and the nature of the 4-substituent is important in determining the proportions of the adducts and their extrusion products. The novel type of adduct exemplified by **4** and **15** arises as a result of the reluctance of the cycloadducts to extrude carbonyl sulphide, making feasible the alternative reaction path involving attack at sulphur by the alkene, resulting in ring-opening. The stability of the cycloadducts (**2**) is partly determined, however, by the nature of the ring-junction substituents.

Reactions of 4-substituted 2-phenylthiazol-5(4H)-ones with azo-compounds. Whereas the 4-phenylthiazolone (1; R = Ph) reacted with diethyl azodicarboxylate and with 4-phenyl-1,2,4-triazolin-3,5-dione to give Michael adducts (**19**; R = Ph, and **20**; R = Ph respectively), the 4-methylthiazolone (1; R = Me) failed to react with diethyl azodicarboxylate but gave the corresponding adduct (**20**; R = Me) with the triazolindione. The adducts **20** were characterised by hydrolysis into the N - thiobenzoyl - α - (1 - phenylurazol - 3 - yl) - α - amino - acids (**21**); the hydrazine (**19**) on alkaline hydrolysis, however, gave only N-thiobenzoyl-α-aminophenylacetic acid as a result of hydrolytic ring-opening of the thiazolone accompanied by the presumed reversal of the addition reaction between the thiazolone and the azo-compound.



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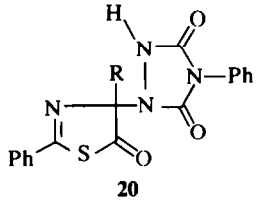

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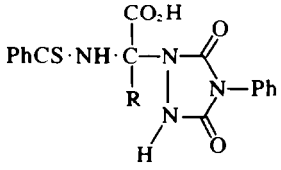

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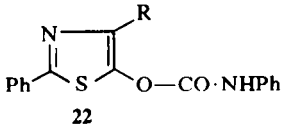
Corresponding reactions reported for mesoionic oxazolones[11] lead to cycloadducts, and the formation of Michael adducts from the thiazolones provides a further indication of the diminished cycloaddition reactivity of the thiazolones, The formation of **19** and **20** can be represented equally satisfactorily by Michael addition or ene addition mechanisms, though the ease with which the triazolindione gives the adduct (**20**; R = $CHMe_2$) by reaction with the thiazolone (1; R = $CHMe_2$) in CH_2Cl_2 (in which the thiazolone is in the keto-tautomeric form[4]) suggests that the Michael addition route is more likely to be the correct interpretation of the course of these reactions, as with those of alkenes.

Reactions of 4-substituted 2-phenylthiazol-5(4H)-ones with N-morpholino-1-cyclohexene. N-Thiobenzoyl-amino-acid morpholides (**23**) were obtained from reactions between the thiazolones and the enamine, apparently through aminolysis of the thiazolone; mesoionic oxazolones give cycloadducts with enamines,[12] together with N-benzoylamino-acid morpholides in some cases.

Reactions of 4-substituted 2-phenylthiazol-5(4H)-ones with heterocumulenes. Although mesoionic oxazolones and thiazolones give cycloadducts with isocyanates,[13] the thiazolones (**1**) react with phenyl isocyanate through an alternative reaction path to give the carbamates (**22**). This behaviour is consistent with the greater nucleophilicity of the exocyclic O atom in these compounds, in comparison with correspondingly-substituted oxazolones, as already revealed in the behaviour of thiazolones and oxazolones towards acetylating agents. While thiazolones yield 5-acetoxythiazoles with acetic anhydride,[14] oxazolones are unchanged by similar treatment; indeed, cyclisation of α-benzamido-acids with acetic anhydride is a standard preparative procedure in the 2-phenyloxazolone series. Acetyl derivatives of oxazolones formed under different conditions have been shown to involve the 4-position of the ring,[15] though recently[16] the intermediacy of N-acetyloxazolonium betaines has been advocated to explain the formation of N-acetyl-2-pyrrolines and 2-diacetylamino-cyclobutanones in oxazolone-alkene-acetic anhydride reaction mixtures.

No adducts were formed between the thiazolones (1; R = Me, Ph) and phenyl isothiocyanate or carbon disulphide, although mesoionic counterparts of **1** have been shown to give the products of cycloaddition-extrusion with these heterocumulenes.[13]

Reactions of 4-substituted 2-phenylthiazol-5(4H)-ones with alkynes. In contrast with results described in preceding paragraphs, the reactions of thiazolones with dimethyl acetylenedicarboxylate to give pyrroles are entirely comparable with those of corresponding oxazolones.[2] Pyrroles (**24**; R = Me, Ph) prepared in this way were identical with those obtained from corresponding oxazolones (1; O in place of S) with dimethyl acetylenedicarboxylate in refluxing xylene during 5 hr. We find, however, that pyrroles are formed under mild conditions (room temperature in acetone solution during 24 hr) when thiazolones are used in this synthesis.



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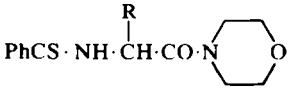

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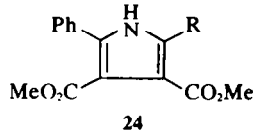

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EXPERIMENTAL

General. Reaction mixtures were shielded from light with aluminium foil. NMR spectra were measured using a Perkin-Elmer R10 spectrometer operating at 60 MHz, with TMS as internal standard. Mass spectra were measured at 70 eV either by Dr. J. R. Chapman (AEI Scientific Apparatus Ltd., Manchester) using an AEI MS30 instrument, or by Dr. B. J. Millard (School of Pharmacy, University of London) using an AEI MS9 instrument. Elemental analyses were performed by Mr. S. Bance and Staff, May & Baker Ltd., Dagenham, Essex.

Reaction of 2,4-diphenylthiazol-5(4H)-one with maleic anhydride

A soln of 2,4-diphenylthiazol-5(4H)-one[6] (7·6 g; 0·03 mol) and maleic anhydride (5·88 g; 0·06 mol) in acetone (250 ml) was set aside at room temp. during 12 hr. The residue obtained on evaporation *in vacuo* was triturated with petrol (b.p. 60–80°), and the resulting yellow solid was triturated with warm methylene chloride; the residue was recrystallised from acetonitrile to give **5** (R = Ph), 0·67 g (5%), m.p. 260° (dec), lit.[2] m.p. 260° (dec); Found: C, 67·3; H, 4·2; N, 3·3; $C_{22}H_{15}O_6N$ requires: C, 67·85; H, 3·9; N, 3·6%.

The methylene chloride soln gave **3** (R = Ph), 3·4 g (28%), as colourless crystals on concentration, m.p. 136–137° after recrystallisation from MeOH. (Found: C, 64·8; H, 3·7; N, 4·13; S, 9·0; $C_{19}H_{13}NO_4S$ requires: C, 64·95; H, 3·75; N, 4·0; S, 9·15%); IR: ν_{max} 1860, 1780 (anhydride), 1710 (thiazolone CO), 1600 cm^{-1} (C = N); UV: λ_{max} (log ϵ) 210 nm (4·17), 245 (4·25), and 270 sh (3·68); NMR ($PhNO_2$): τ 5·35 (1H, –CH–CO–, q, J_{AX} = 9·2 Hz, J_{BX} = 4·5 Hz), 6·55 (1H, –CH–CH_2–, q, J_{AB} = 19 Hz, J_{AX} = 9·2 Hz), 7·28 (1H, –CH–CH_2–, q, J_{AB} = 19 Hz, J_{BX} = 4·5 Hz); MS: *m/e* 105 (50%), 115 (70), 121 (Ph.CS^+: 100), 251 (30), 323 (M-28; 50), 351 (M: 0·04).

(ii) A soln of 2,4-diphenylthiazol-5(4H)one (0·76 g; 3 mmol) and maleic anhydride (0·78 g; 8 mmol) in toluene (10 ml) was maintained at 50° during 1 hr. Evaporation *in vacuo* and recrystallisation of the residue from acetonitrile gave **5** (R = Ph), m.p. 260° (dec), 0·43 g (37%).

Hydrolysis of the Michael adduct (**3**; R = Ph)

(i) *Alkaline hydrolysis.* To the adduct (0·35 g; 1 mmol) in dioxan (1 ml) was added N NaOH (2 ml; 2 equiv). The mixture was acidified after 12 hr at room temp. and extracted with ether; evaporation of the dried ($MgSO_4$) ether extracts gave **6** (R = Ph), m.p. 133° after crystallisation from benzene. (Found: C, 58·8; H, 4·5; N, 3·45; S, 8·3. $C_{19}H_{17}NO_6S$ requires: C, 58·9; H, 4·45; N, 3·6; S, 8·3%); UV ($CHCl_3$): λ_{max} 250 nm (log ϵ 4·04), 285 sh (3·81), 395 (2·30); NMR (acetone-$^2H_6$): τ −0·05 (1H, –NH–, broad s, exchanged with ^2H_2O), 0·40 (3H, –CO_2H, broad s, exchanged with ^2H_2O), 1·90–2·15 (4H, ArH, m), 2·40–2·80 (6H, ArH, m), 5·80 (1H, –CH–CH_2, q, J_{AX} = 10·3, J_{BX} = 3·4 Hz), 7·00 (1H, –CH–CH_2–, q, J_{AB} = 17·1, J_{AX} = 10·3 Hz), 7·55 (1H, –CH–CH_2–, q, J_{AB} = 17·1, J_{BX} = 3·4 Hz).

(ii) *Acid hydrolysis.* The adduct **3** (R = Ph; 1·4 g; 4 mmol) and 6N HCl (10 ml) were heated at 120° in a sealed tube during 12 hr. The cooled mixture was filtered, and the evaporated filtrate was triturated with ether; the residue was crystallised (charcoal) from water, to give **8** (R = Ph), 0·78 g (79%), m.p. 242–244° (dec). (Found: C, 57·5; H, 4·45; N, 5·4; $C_{12}H_{11}NO_5$ requires: C, 57·85; H, 4·45; N, 5·6%); IR (Nujol): ν_{max} 3300 (–NH–), 2600 (H-bonded OH), 1710 (–CO–NH–), 1690, 1620 (–CO_2H and –CO_2^-) cm^{-1}; NMR(dimethylsulphoxide-$^2H_6$): τ −2·2 (2H, CO_2H, broad s, exchanged with ^2H_2O), 1·1(1H, NH, s, exchanged with ^2H_2O), 2·6 (5H, ArH, s), 5·95–6·15 (1H, –CH–CH_2–, m), 7·45–7·65 (2H, –CH–CH_2–, M). Treatment of **8** (R = Ph; 0·25 g; 1 mmol) with Ac_2O (5 ml) containing one drop of pyridine under reflux during 30 min, followed by evaporation and crystallisation from $CHCl_3$ gave 1-acetyl-5-phenyl-2-pyrrolidone-4,5-dicarboxylic acid anhydride (0·17 g; 62%), m.p. 186–188°. (Found: C, 61·5; H, 4·0; N, 5·2; $C_{14}H_{11}NO_5$ requires: C, 61·55; H, 4·05; N, 5·1%); IR (Nujol): ν_{max} 1860, 1780 (anhydride), 1730 (pyrrolidone C=O), 1700 (acetyl C=O); NMR (acetone-$^2H_6$): τ 2·6 (5H, ArH, s), 5·90–6·2 (1H, –CH–CH_2, m), 6·80–7·10 (2H, –CH–CH_2–, m).

Reaction of 4-methyl-2-phenylthiazol-5(4H)-one with maleic anhydride

(i) A soln of the thiazolone[6] (7·0 g, 0·036 mol) and maleic anhydride (3·57 g; 0·036 mol) in acetone (500 ml) was set aside at room temp. during 4 hr, then evaporated *in vacuo*. The resulting yellow oil was triturated with petrol (b.p. 80–100°) and the residual pale yellow solid was extracted with boiling $CHCl_3$; the residue, **4** (R = Me), 1·41 g (10%), had m.p. 178–181° (Found: C, 55·8; H, 3·4: N, 3·8; S, 8·4. $C_{18}H_{13}NO_7S$ requires: C, 55·8; H, 3·4; N, 3·6; S, 8·3%) after crystallisation from MeCN. IR (Nujol): ν_{max} 1860, 1780 (anhydride), 1680 (thiolester), 1620 cm^{-1} (C=N). NMR (C^2H_3CN): τ 1·65–1·85 (2H, ArH, m), 2·2–2·4 (3H, ArH, m), 4·7 (1H, N=C–CH–CH–, d, J = 9·0 Hz), 5·4 (1H, –CH–CH_2–, q, J_{AX} = 10 Hz, J_{BX} = 7 Hz), 5·7 (1 H, N=C–CH–CH–, d, J = 9 Hz), 6·4 (1H, –CH–CH_2, q, J_{AX} = 10 Hz, J_{AB} = 19 Hz), 7·0 (1H, –CH–CH_2–, q, J_{BX} = 7 Hz, J_{AB} = 19 Hz), 8·3 (3H, –CH_3, s). MS: *m/e* 104 (25%), 115 (50), 131 (40), 156 (100), 157 (60), 228 (90), 229 (25), 261 (2), no M^+. Concentration of the $CHCl_3$ extract gave the cycloadduct **2**, 4-methyl-1-phenyl-2-thia-7-azabicyclo[2.2.1]heptan-3-one *exo*-5,6-dicarboxylic anhydride (3·38 g; 32%), m.p. 130–1° (dec). Found: C, 57·9; H, 3·8; N, 4·78; S, 11·1. $C_{14}H_{11}NO_4S$ requires: C, 58·15; H, 3·85; N, 4·85; S, 11·1%; IR: ν_{max} 3350 (NH), 1840, 1780 (anhydride C=O), 1680 cm^{-1} (thiolester C=O). UV (MeOH): λ_{max} 213 (log ϵ 3·98), 248 nm (3·94); NMR ($PhNO_2$): τ 5·25 (1H, –CH–CH–, d, J = 7·0 Hz), 5·82 (1H, –NH–, broad s, exchanged with ^2H_2O), 6·13 (1H, –CH–CH–, d, J = 7·0 Hz), 8·08 (3H, CH_3, s); MS: *m/e* 104 (20%), 115 (45), 131 (14), 156 (100), 157 (65), 228 (77), 229 (44), 261 (12), 289 (M^+, 0·07%). The adduct **3** (R = Me) was also isolated from the $CHCl_3$ extract by fractional crystallisation; 1·58 g (15%) was obtained, m.p. 150–1°. (Found: C, 58·0; H, 3·85; N, 4·8; S, 11·1. $C_{14}H_{11}NO_4S$ requires: C, 58·15; H, 3·85; N, 4·85; S, 11·1%); IR (Nujol): ν_{max} 1860, 1780 (anhydride C=O), 1710 (thiazolone C=O), 1600 (C=N); UV (MeOH): λ_{max} 209 (log ϵ 4·08), 243 (4·17), 270 nm (sh, 3·57). NMR (C^2HCl_3): τ 1·95–2·15 (2H, ArH, m), 2·20–2·50 (3H, ArH, m), 6·35 (1H, –CH–CH_2, q, J_{AX} = 9·0, J_{BX} = 5·0 Hz), 6·95 (1H, –CH–CH_2–, q, J_{AX} = 9·0, J_{AB} = 18·0 Hz), 7·65 (1H, –CH–CH_2–, q, J_{AB} = 18·0, J_{BX} = 5·0 Hz), 8·20 (3H, CH_3, s); MS: *m/e* 103 (23), 104 (69), 105 (95), 121 (100), 189 (55), 261 (90), 289 (M^+, 0·3%).

(ii) Reaction of the thiazolone with 2 equiv maleic anhydride as in (i) above also gave adducts **4**, **2** and **3**; (R = Me), but in yields 40, 5 and 8% respectively.

(iii) Reaction of the thiazolone with maleic anhydride as in (i) but with the addition of 2 drops 2N NaOH gave only **3** (R = Me) in 45% yield.

Reaction of the cycloadduct **2** *with maleic anhydride*

A soln of the cycloadduct (0·289 g) and maleic anhydride (0·098 g) in acetone (10 ml) was heated under reflux during 12 hr, then evaporated and worked up to give the 1:2-adduct (**4**; R = Me), 0·053 g (14%).

Hydrolysis of 2-(4-*methyl*-2-*phenylthiazol*-5-*on*-4-*yl*) *succinic anhydride, the Michael adduct* (**3**; R = Me)

(i) *Alkaline hydrolysis.* To the Michael adduct (0·289 g; 1 mmol) in dioxan (1 ml) was added N NaOH (2 ml, 2 equiv). After 12 hr at room temp. the soln was acidified and extracted with ether. The dried ($MgSO_4$) ether extracts were evaporated and the residue was crystallised from petrol (b.p. 60–80°) to give **6** (R = Me), 0·170 g (53%), m.p. 79–81°. (Found: C, 51·7; H, 4·7; N, 4·3; S, 9·8. $C_{14}H_{15}NO_6S$ requires: C, 51·7; H, 4·65; N, 4·3; S, 9·85%); UV ($CHCl_3$): λ_{max} 248 (log ϵ 4·12), 285 (3·73), 392 nm (2·24). NMR (acetone-$^2H_6$): τ 0·6 (1H, NH, broad s, exchanged with ^2H_2O), 1·0 (3H, CO_2H, broad s, exchanged with ^2H_2O), 2·0–2·3 (2H, ArH, m), 2·4–2·7 (3H, ArH, m), 6·6 (1H, –CH–CH_2–, q, J_{AX} = 8·5, J_{BX} = 5·0 Hz), 7·15 (1H, –CH–CH_2–, q, J_{AX} = 8·5, J_{AB} = 17·0 Hz), 7·45 (1H, –CH–CH_2–, q, J_{AB} = 17·0, J_{BX} = 5·0 Hz), 8·0 (3H, CH_3, s).

(ii) *Acid hydrolysis.* The Michael adduct (1·16 g, 4 mmol) was heated at 120° in 6N HCl during 12 hr. The mixture was filtered after cooling, and the residue obtained on evaporation of the filtrate was purified by chromatography on silica gel, using the

upper phase from an equilibrated *n*-butanol:acetic acid:water mixture (4:1:5) as eluant. 50 Ml fractions were collected, and those shown by TLC to contain a single ninhydrin-positive component (R_F 0·07 in n-butanol:acetic acid:water = 4:1:5) were combined and evaporated. The residue on crystallisation from water gave **7** (R = Me), 0·089 g (11%), as the hydrate, m.p. 151-2°. (Found: C, 37·6; H, 6·2; N, 6·3. $C_7H_{11}NO_6$, H_2O requires: C, 37·65; H, 5·85; N, 6·25%); IR (Nujol): ν_{max} 3100 (NH), 1700 (CO_2H), 1610 cm^{-1} (CO_2^-); MS: *m/e* 70 (43%), 97 (22), 119 (8), 142 (100), 177 (6), 205 (M^+, 0·3).

Hydrolysis of S-(2,5-dioxotetrahydrofuran-3-yl)-5-methyl-2-phenyl-1-pyrroline 3,4-dicarboxylic anhydride 5-thiolcarboxylate (the 1:2-adduct, **4**; R = Me)

The 1:2-adduct (0·774 g, 2 mmol) was dissolved in 1N NaOH (15 ml); after 15 min at room temp., the soln was acidified and extracted with ether, and the colourless oil obtained on evaporation of the dried ($MgSO_4$) ether soln was crystallised from EtOAc, giving **8** (R = Me) (0·060 g; 12%), as the hydrate, m.p. 163–4° (dec.). (Found: C, 61·6; H, 5·35; N, 5·48. $C_{13}H_{13}NO_4$, $\frac{1}{2}H_2O$ requires: C, 61·7; H, 5·45; N, 5·55%); IR (Nujol): ν_{max} 1700 (CO_2H), 1600 cm^{-1} (C=N); UV (MeOH): λ_{max} 210 nm (log ϵ 3·98), 246 (4·09); NMR ($C^2H_3O^2H$): τ 2·0–2·3 (2H, ArH, m), 2·4–2·6 (3H, ArH, m), 5·7–6·6 (3H, –CH–CH_2–, m) 8·5 (3H, CH_3, s); MS: *m/e* 103 (8%), 104 (20), 105 (20), 115 (25), 158 (80), 202 (100), 247 (M^+, 0·5).

Acetylation of the cycloadduct **2**

The cycloadduct **2** (0·289 g, 1 mmol) was dissolved in Ac_2O (10 ml) containing one drop of pyridine. The soln was evaporated after 10 min at room temp., and the residual oil was triturated with ether to give a colourless solid, which give the N-acetyl derivative (0·13 g, 39%), m.p. 137–9° (dec) after recrystallisation from $CHCl_3$. (Found: C, 58·0; H, 4·0; N, 4·25; S, 9·5. $C_{16}H_{13}NO_5S$ requires: C, 58·0; H, 3·95; N, 4·25; S, 9·7%); IR (Nujol); ν_{max} 1850, 1780 (anhydride), 1700 (amide), 1680 (thiolester C=O) cm^{-1}; NMR (dimethyl sulphoxide-$^2H_6$): τ 2·5 (5H, ArH, s), 4·6 (1H, –CH–CH, d, J = 7·0 Hz), 5·6 (1H, –CH–CH–, d, J = 7·0 Hz), 7·5 (3H, CH_3CO, s), 8·45 (3H, CH_3, s).

Reaction of 2,4-diphenylthiazol-5(4H)-one with dimethyl fumarate

(i) A soln of the thiazolone (1·01 g, 4 mmol) and dimethyl fumarate (5·76 g, 40 mmol) in toluene (150 ml) was heated under reflux during 2 hr, then evaporated *in vacuo*. Trituration of the residual oil with MeOH, and recrystallisation of the resulting solid from MeOH, gave **13** (R = Ph), m.p. 197–8° (lit.[2]197–8°), 1·2 g (62%). Found: C, 64·85; H, 5·65; N, 2·9. Calc. for $C_{26}H_{27}NO_8$: C, 64·7; H, 5·75; N, 3·2%.

(ii) A soln of the thiazolone (1·01 g, 4 mmol) and dimethyl fumarate (0·58 g, 4 mmol) in toluene was treated as in (i), and worked up to give **14** (0·80 g; 60%), m.p. 137–8°, lit.[2] m.p. 137–8°. (Found: C, 71·4; H, 5·7; N, 4·0. Calc. for $C_{20}H_{19}NO_4$: C, 71·2; H, 5·7; N, 4·15%). Satisfactory agreement of spectroscopic data with those reported for this compound in Ref.[2] was obtained.

(iii) Reactions of the thiazolone with dimethyl fumarate under mild conditions (as described above for reactions with maleic anhydride) gave back the thiazolone; no Michael adduct could be obtained from these reactants in acetone soln to which two drops N NaOH had been added.

Reaction of 4-methyl-2-phenylthiazol-5(4H)-one with dimethyl fumarate

(i) A soln of the thiazolone (0·955 g, 5 mmol) and dimethyl fumarate (0·76 g, 5·3 mmol) in toluene (10 ml) was heated under reflux during 2 hr, then evaporated almost to dryness; petrol (b.p. 40–60°) was added, and the ppt (0·65 g, 39%), m.p. 110–5°, was crystallised from MeOH to give **13** (R = Me), 0·080 g, (4%), m.p. 181–5° (Found: C, 60·0; H, 6·2; N, 3·2. $C_{21}H_{25}NO_8$ requires: C, 60·15; H, 6·0; N, 3·35%); IR (Nujol): ν_{max} 3350 (NH), 1730 cm^{-1} (ester C=O); NMR (C^2HCl_3): τ 2·4–2·8 (5H, ArH, m), 5·75 (1H, –CH–CH–, d, J = 6·0 Hz), 6·20 (3H, MeO, s), 6·25 (3H, MeO, s), 6·30 (3H, MeO, s), 6·55 (1H, –CH–CH–, d, J = 6·0 Hz), 6·70(3H, MeO, s), 6·70–6·85 (2H, –CH, m), 7·50 (1H, NH, s, exchanged with ^2H_2O), 8·40 (3H, CH_3–C, s); MS: *m/e* 216 (100%), 184 (73), 274 (67), 419 (M^+, 5%). The second crop from the mixture was the cycloadduct (**12**), m.p. 114–5° (0·510 g, 30%), 4-methyl-1-phenyl-2-thia-7-azabicyclo[2.2.1]heptan-3-one *exo*-5-*endo*-6-dicarboxylic acid dimethyl ester. (Found: C, 57·3; H, 5·1; N, 4·1; S, 9·6. $C_{16}H_{17}NO_5S$ requires: C, 57·3; H, 5·1; N, 4·2, S, 9·55%); IR (Nujol): ν_{max} 3350 (NH), 1720 (ester C=O), 1690 cm^{-1} (thiolester C=O); NMR (C^2HCl_3): τ 2·4 (5H, ArH, s), 5·7 (1H, –CH–CH–, d, J = 5·0 Hz), 6·15 (3H, MeO, s), 6·40 (1H, –CH–CH–, d, J = 5·0 Hz), 6·70 (3H, MeO, s), 7·05 (1H, –NH, broad s, exchanged with ^2H_2O), 8·20 (3H, CH_3–C, s); MS: *m/e* 104 (14), 115 (15), 131 (20), 156 (20), 184 (29), 215 (37), 242 (100), 274 (17), 275 (10), 307 (M^+ – CO, 1%).

(ii) Under the conditions described in (i) above, the thiazolone (2·87 g, 15 mmol) and dimethyl fumarate (5·47 g, 38 mmol) gave an increased yield (2·6 g, 42%) of **13** (R = Me), the product of reaction of the cycloadduct with the alkene.

(iii) The thiazolone (0·382 g, 2 mmol) and dimethyl fumarate (0·576 g, 4 mmol) in acetone during 12 hr at room temp. gave **12** (0·42 g, 63%) as sole product. Under identical conditions but with the addition of two drops 2N NaOH, the cycloadduct was formed in similar yield as sole product.

Reaction of 2,4-diphenylthiazol-5(4H)-one with acrylonitrile

(i) A soln of the thiazolone (1·01 g, 4 mmol) in acrylonitrile (5·3 g, 0·1 mol) was heated under reflux during 2 hr, then evaporated to dryness *in vacuo*. These residual oil on trituration with petrol (b.p.60–80°) and MeOH gave **16** m.p. 190–8° (0·61 g, 50%), m. p. 200–1° (dec) after recrystallisation from MeOH (0·23 g, 19%). (Found: C, 70·4; H, 4·6; N, 9·1; S, 10·4. $C_{18}H_{14}N_2OS$ requires: C, 70·55; H, 4·6; N, 9·15; S, 10·45%); IR (Nujol): ν_{max} 1740 (C=O), 1590 cm^{-1} (C=N); UV (MeOH): λ_{max} 208 (log ϵ 4·34), 254 (4·32), 274 nm (4·30); NMR (C^2HCl_3): τ 1·9–2·1 (2H, ArH, m), 2·4–2·7 (8H, ArH, m), 6·1–6·5 (4H, –CH_2–CH_2–, m); MS: *m/e* 103 (25%), 104 (27), 115(95), 121 (8), 160 (25), 175 (27), 193 (17), 203 (50), 219 (100), 246 (9), 278 (4), 306 (M^+, 63). Fractional crystallisation of the petrol extracts gave **17** (R = Ph, or its 2,6-dicyano-isomer) 0·032 g (3%), m.p. 215–7°, and **18** (R = Ph), m.p. 127–8°. Both these products were obtained[2] from corresponding reaction of 2,4-diphenyloxazol-5(4H)-one with acrylonitrile, and m.p. and IR data[2] were identical with those obtained in the present work; similar uncertainty concerning the position of the cyano-groups in **17** has been recorded.[2]

(ii) The thiazolone was recovered from a soln in acetone in the presence of excess acrylonitrile after 24 hr at room temp. However, an equivalent mixture to which two drops 2N NaOH had been added gave the adduct **16** in 20% yield after 24 hr at room temp.

Reaction of 4-methyl-2-phenylthiazol-5(4H)-one with acrylonitrile

(i) A soln of the thiazolone (0·24 g, 1·25 mmol) in acrylonitrile (1·7 g, 32 mmol) was kept at 60° during 45 min, and evaporated to dryness *in vacuo*. The residue on crystallisation from MeOH gave **15** (0·021 g; 6%), m.p. 105–6°. (Found: C, 65·0; H, 5·15; N, 14·2; S, 10·5. $C_{16}H_{15}N_3OS$ requires: C, 64·6; H, 5·1; N, 14·15; S, 10·8%); IR (Nujol): ν_{max} 2250 (C≡N), 1680 (C=O), 1610 cm^{-1} (C=N); NMR (dimethylsulphoxide-$^2H_6$): τ 1·9–2·2 (2H, ArH, m), 2·3–2·6 (3H, ArH, m), 6·2–6·7 (3H, –CH–CN, CH_2–C=N–, m), 6·9–7·2 (4H, –S–CH_2–CH_2–CN, m), 8·45 (3H, CH_3, s). MS: *m/e* 103 (14%), 104 (26), 114(6), 115 (24), 140 (13), 156 (5), 168 (9), 183 (100), 269 (1), 297 (M^+, 1).

(ii) The thiazolone was recovered from a soln in acetone containing excess acrylonitrile, after 48 hr at room temp.; and also from a similar mixture containing two drops 2N NaOH.

Reaction of 4-methyl-2-phenylthiazol-5(4H)-one with phenyl isocyanate

A soln of the thiazolone (0·38 g, 2 mmol) in phenyl isocyanate (5·45 g, 43 mmol) was kept at 50° during 10 min, then evaporated *in vacuo* to give **22** (R = Me), m.p. 110–4°, and m.p. 114–6° (0·495 g, 80%) after recrystallisation from petrol (b.p. 80–100°). (Found: C, 65·7; H, 4·6; N, 9·0; S, 10·4. $C_{17}H_{14}N_2O_2S$ requires: C, 65·8; H, 4·55; N, 9·05; S, 10·35%); IR (Nujol): ν_{max} 3350 (NH), 1730 (C=O), 1600 (C=N), 1550 cm^{-1} (amide II); UV (Et_2O): λ_{max} 232 (log ϵ

2·5–2·8 (8H, ArH, m); MS: *m/e* 103 (53%), 119 (100), 121 (95), 130 (58), 163 (95), 191 (M–PhNCO; 10).

Reaction of 2,4-diphenylthiazol-5(4H)-one with phenyl isocyanate

A soln of the thiazolone (0·25 g, 1 mmol) in phenyl isocyanate (5·54 g) was kept at room temp. during 15 min, during which time **22** (R = Ph) started to crystallise out. Evaporation *in vacuo*, and trituration of the residue with petrol (b.p. 80–100°) gave 0·20 g (54%) of the phenylcarbamoyloxy-thiazole, m.p. 146–7°. (Found: C, 70·8; H, 4·3; N, 7·5; S, 8·7. $C_{22}H_{16}N_2O_2S$ requires: C, 70·95; H, 4·35; N, 7·5; S, 8·6%); IR (Nujol): ν_{max} 3350 (NH), 1720 (C=O), 1600 (C=N), 1530 cm^{-1} (amide II); UV (Et_2O): λ_{max} 230 (log ϵ 4·36), 270 (4·02), 300 (4·00), 320 nm (4·04); NMR (C^2HCl_3): τ 2·0–2·3 (2H, ArH, m), 2·5–2·8 (13H, ArH, m); MS: *m/e* 103 (38%), 119 (100), 121 (95), 148 (10), 165 (22), 193 (95), 225 (98), 253 (M–PhNCO; 20).

Attempted reactions of 2-phenylthiazol-5(4H)-ones with phenyl isothiocyanate

The 4-methyl and 4-phenyl-thiazolones were recovered in nearly quantitative yield from solns in toluene or in acetone which had been heated under reflux during 48 hr; also from solns in phenyl isothiocyanate which were maintained at 100° during 48 hr.

Reaction 2,4-diphenylthiazol-5(4H)-one with 4-phenyl-1,2,4-triazolin-3,5-dione

(i) A soln of the thiazolone (0·25 g, 1 mmol) and the triazolindione[17] (0·175 g, 1 mmol) in acetone (10 ml) changed colour from red to pale yellow during 10 min. Evaporation *in vacuo* and trituration with petrol (b.p. 60–80°) gave **20** (R = Ph), 0·324 g (76%), m.p. 182–4° (dec) after crystallisation from MeOH. (Found: C, 64·8; H, 3·9; N, 12·9; S, 7·5. $C_{23}H_{16}N_4O_3S$ requires: C, 64·45; H, 3·75; N, 13·05; S, 7·5%); IR (Nujol): ν_{max} 3100 (NH), 1760, 1740 (urazole C=O), 1700 (thiazolone C=O), 1590 (C=N) cm^{-1}; NMR (dimethylsulphoxide-$^2H_6$): τ −0·55 (1H, NH, broad s, exchanged with ^2H_2O), 1·8–2·1 (2H, ArH, m), 2·2–2·7 (13H, ArH, m); MS: *m/e* 121 (100), 252 (47), 400 (0·5), 428 (M^+, 0·20).

(ii) The same reactants in refluxing toluene during 1 hr gave **20** (R = Ph) in 52% yield.

Reaction of 4-methyl-2-phenylthiazol-5(4H)-one with 4-phenyl-1,2,4-triazolin-3,5-dione

Reactions conducted as in (i) and (ii) above for the 2,4-diphenylthiazolone gave 4 - phenyl - 1 - (4 - methyl - 2 - phenylthiazol - 5 - on - 4 - yl) urazole (**20**; R = Me), m.p. 106–8° from CCl_4-petrol (b.p. 60–80°), in yields (i) 58% and (ii) 32%, respectively. (Found: C, 58·7; H, 3·8; N, 15·4; S, 8·6. $C_{18}H_{14}N_4O_3S$ requires: C, 59·0; H, 3·85; N, 15·3; S, 8·75%); IR and NMR spectra showed the expected differences from those of the phenyl analogue above.

Reaction of 4-isopropyl-2-phenylthiazol-5(4H)-one[6] *with 4-phenyl-1,2,4-triazolin-3,5-dione*

The reaction conducted as in (i) above gave **20** (R = $CHMe_2$) in 77% yield, m.p. 194–5° from acetone. (Found: C, 61·2; H, 4·55; N, 14·4; S, 8·4. $C_{20}H_{18}N_4O_3S$ requires: C, 60·85; H, 4·6; N, 14·2; S, 8·1%) through the colour change indicating the completion of reaction occurred after 1 hr.

Hydrolysis of Michael adducts (**20**; R = Ph), *and* (**20**; R = Me).

To a soln of the adduct (1 mmol) in dioxan (1 ml) was added N NaOH (1 ml). After 15 min at room temp. the reaction soln was acidified to Congo Red and extracted with ether to give **21** (R = Ph), m.p. 101–3° after crystallisation from benzene-ether (Found: C, 62·1; H, 5·45; N, 10·8; S, 6·05. $C_{23}H_{18}N_4O_4S$, $C_4H_{10}O$ requires: C, 62·3; H, 5·4; N, 10·75; S, 6·15%) from **20** (R = Ph), and the corresponding derivative **21** (R = Me), m.p. 89–92° after crystallisation from CCl_4 (Found: C, 56·5; H, 4·4; N, 14·9; S, 8·1. $C_{18}H_{16}N_4O_4S$ requires: C, 56·25; H, 4·2; N, 14·55; S, 8·35%) from **20** (R = Me), yields 67 and 57%, respectively.

Reaction of 2,4-diphenylthiazol-5(4H)-one with diethyl azodicarboxylate

(i) A soln of the thiazolone (0·25 g, 1 mmol) and diethyl azodicarboxylate (0·52 g, 3 mmol) in acetone (20 ml) was evaporated after 12 hr at room temp. to give an oil which, on trituration with benzene gave **19**, m.p. 135–6° (dec), 0·146 g (34%), after recrystallisation from petrol (b.p. 80–100°). (Found: C, 59·3; H, 5·0; N, 9·8; S, 7·3. $C_{21}H_{21}N_3O_5S$ requires: C, 59·0; H, 4·95; N, 9·85, S, 7·5%); IR (Nujol): ν_{max} 3250 (NH), 1740, 1710 (ester C=O), 1700 (thiazolone C=O), 1590 (C=N), 1560 cm^{-1} (amide II); NMR (C^2HCl_3): τ 1·9–2·1 (2H, ArH, m), 2·1–2·8 (8H, ArH, m), 3·5 (1H, NH, broad s, exchanged with ^2H_2O), 5·9 (4H, CH_3–CH_2, q, J = 7·0 Hz), 8·8 (6H, CH_3–CH_2, t, J = 7·0 Hz); MS: *m/e* 104 (24%), 121 (100), 163 (5), 222 (11), 250 (16), 252 (24), 294 (8), 399 (6), 427 (M^+, 0·02).

(ii) The reactants in refluxing toluene during 2 hr gave the adduct in 45% yield.

Reaction of N,N'-diethoxycarbonyl-N-(2,4-diphenylthiazol-5-on-4-yl)hydrazine **19** *with aqueous alkali*

The adduct **19** (0·427 g, 1 mmol) was dissolved in dioxan (1 ml), and after adding 2N NaOH (2 ml, 2 equiv), the mixture was set aside during 4 hr at room temp. Acidification to Congo Red and extraction with ether gave N-thiobenzoyl-DL-α-aminophenylacetic acid (m.p. and m.m.p. 145°, identical spectra).

Attempted reaction of 4-methyl-2-phenylthiazol-5(4H)-one with diethyl azodicarboxylate

Reactions conducted as for the 2,4-diphenylthiazolone failed to give the corresponding adduct, though loss of the thiazolone was shown through changes in absorption spectra; small yields of diethyl hydrazine-1,2-dicarboxylate, m.p. 134–5° (lit.[18] m.p. 135°) were isolated from every experiment.

Reaction of 4-substituted 2-phenylthiazol-5(4H)-ones with N-morpholino-1-cyclohexene

The 4-phenyl- or the 4-methylthiazolone **1** (1 mmol) was dissolved in toluene (5 ml) containing morpholinocyclohexene (0·35 g, 2 mmol), and heated under reflux during 1 hr. The yellow oil obtained on evaporation in vacuo gave **23** (R = Ph), 65%, m.p. 124–6° (Found: C, 67·2; H, 5·7; N, 8·0; S, 9·3. $C_{19}H_{20}N_2O_2S$ requires: C, 67·0; H, 5·9; N, 8·25; S, 9·4%) or the analogue **23** (R = Me), 90%, m.p. 157–9° (Found: C, 60·4, H, 6·45; N, 10·0; S, 11·7. $C_{14}H_{18}N_2O_2S$ requires: C, 60·5; H, 6·5; N, 10·05; S, 11·5%) respectively, as sole isolated products. Spectroscopic data were consistent with the structures assigned to the products, by analogy with corresponding data for N-thiobenzoyl-amino-acid amides.[6]

Reaction of 2,4-diphenylthiazol-5(4H)-one with dimethyl acetylenedicarboxylate

(i) A soln of the thiazolone (0·253 g, 1 mmol) and dimethyl acetylenedicarboxylate (0·355 g, 2·5 mmol) in toluene (5 ml) was heated under reflux during 4 hr. The pale yellow oil obtained by evaporation of the mixture *in vacuo* gave **24** (R = Ph), 0·30 g (90%), m.p. 149–150° (lit.[2] 149–150°) after trituration with petrol (b.p. 60–80°) and crystallisation from MeOH (Found: C, 72·0; H, 5·3; N, 4·15; Calc. for $C_{20}H_{19}NO_4$: C, 71·6; H, 5·1; N, 4·2%).

(ii) The same quantities of reactants in acetone (10 ml) gave the pyrrole (0·185 g, 52%) after 24 hr at room temp., and working up as in (i) above.

Reaction of 4-methyl-2-phenylthiazol-5(4H)-one with dimethyl acetylenedicarboxylate

(i) A soln of the thiazolone (0·955 g, 5 mmol) and dimethyl acetylenedicarboxylate (1·42 g, 10 mmol) in toluene (10 ml) was heated under reflux during 6 hr, and worked up as described above for corresponding mixtures obtained from the diphenylthiazolone, to give **24** (R = Me), 0·98 g (66%), m.p. 126–8° (lit.[2] 127–8°) after crystallisation from MeOH (Found: C, 65·8; H, 5·5; N, 5·3; calc for $C_{15}H_{15}NO_4$: C, 65·9; H, 5·55; N, 5·1%).

(ii) The same quantities of reactants in acetone (10 ml) gave the pyrrole (0·655 g, 48%) after 24 h at room temp., and working up as in (i) above.

Reaction of 4-carboxymethyl-2-phenylthiazol-5(4H)-one (**1**; R = CH_2CO_2H) *with dimethyl acetylenedicarboxylate*

Reaction of **1** (R = CH_2CO_2H) with excess dimethyl acetylenedicarboxylate in refluxing toluene during 6 hr, and working up as described above for corresponding reaction mixtures gave **24**

(R = CH_2CO_2H), 70%, m.p. 176–7° from benzene (Found: C, 59·9; H, 4·8; N, 4·3; $C_{16}H_{15}NO_6$ requires: C, 60·55; H, 4·75; N, 4·4%); IR (Nujol): ν_{max} 3350 (-NH-), 1725 (CO_2Me C=O), 1695 cm^{-1} (CO_2H C=O).

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