Synthesis of Cyclopropa[*d*]thiazolines by a Novel and Efficient Photochemical Rearrangement of 1,3-Thiazines[1]

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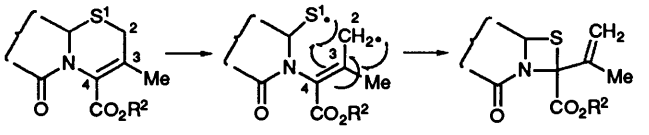
A novel and high yielding photochemical rearrangement has been used to convert the 1,3-thiazines **7** and **11** into the cyclopropa[*d*]thiazolines **10** and **12**, respectively. Use of the substituted thiazine **13** in this reaction gave a high yield of the diastereoisomeric products **14** and **15**.

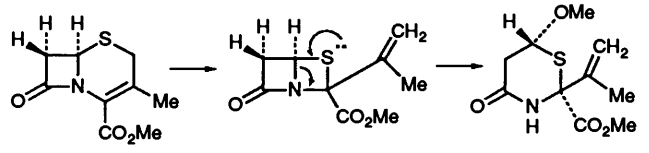
Our discovery[2,3] that *N*-acyl-1,3-thiazines of general structure **1** underwent a novel and high yielding photochemical reaction to afford 1,3-thiazetidines **3** (Scheme 1) not only gave easy access



1 **2** **3**

Scheme 1

to this rare heterocyclic system, but also suggested the intriguing possibility that the β-lactam analogue **5** might be prepared from a cephalosporin **4** using this relatively mild method. The bicyclo[2.2.0] system **5** might be regarded, with penicillins and cephalosporins as part of a homologous series of β-lactams fused to four-, five- and six-membered rings, respectively. It would be the most strained member of the series and, in view of the antibacterial properties of the five- and six-membered analogues, it would be of some considerable interest. In the event, photolysis of the cephalosporin derivative **4** in methanol gave rise to the 1,3-thiazine **6** (Scheme 2), possibly

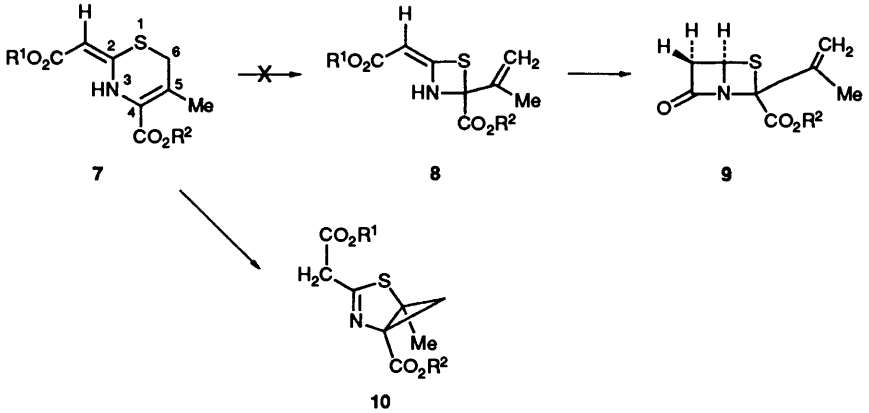


4 **5** **6**

Scheme 2

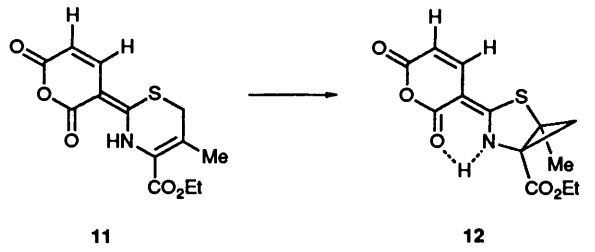
via the intermediate **5**.[4,5] Photolysis in other solvents failed to yield the desired β-lactam **5**. An alternative synthetic route to the β-lactam thiazetidine **5** would be to prepare the thiazetidine **8**, which might be reduced and cyclised to yield the desired β-lactam **9** as in Scheme 3. We therefore irradiated a dilute solution of the thiazine **7** ($R^1 = R^2 = Et$)[6] in either toluene or methanol until the absorption at λ_{max}/nm 336 in the UV spectrum was no longer present. A liquid product, $C_{12}H_{17}NO_4S$, was obtained in 80% yield, which was evidently not the expected thiazetidine **8**. The ^1H NMR spectrum suggested that the product was the cyclopropa[*d*]thiazoline **10**, since the CH_2S singlet present in the ^1H NMR spectrum of the starting material had been replaced by a typically cyclopropyl AB system, J_{AB} 6 Hz, at δ 0.79 and 2.14. The vinylic methyl group at δ 2.30 in the starting thiazine had moved to higher field at δ 1.69 and the olefinic singlet had been replaced by a two proton singlet at δ 3.60. This latter absorption disappeared on shaking with ^2H_2O, indicating the presence of a labile methylene group between imine and ester functionalities. The presence of the imine tautomer **10**, rather than the alternative exocyclic enamine, is not surprising in this compound, in view of the work on similar systems by Toldy *et al.*[7] and it is tempting to imply added stabilisation due to the possibility of the cyclopropa[*d*]thiazoline **10** being regarded as a 'homothiazole'.

When the thiazine anhydride **11**[6] was irradiated in toluene, a solid photoproduct, $C_{13}H_{13}NO_5S$, was obtained in 84% yield (Scheme 4). The absorption at λ_{max}/nm 390 in the UV spectrum of the starting material had shifted to λ_{max}/nm 359 in the UV spectrum of the product and a cyclopropyl AB system was evident in the ^1H NMR spectrum at δ 1.42 and 2.18. The chromophore and the presence of an exchangeable, hydrogen bonded NH proton at δ 10.9 in the ^1H NMR spectrum suggested that, whereas the photoproduct **10** existed as the imine tautomer, the photoproduct **12** existed as the enamine tautomer. The structure **12** was confirmed by X-ray structure



7 **8** **9** **10**

Scheme 3



Scheme 4

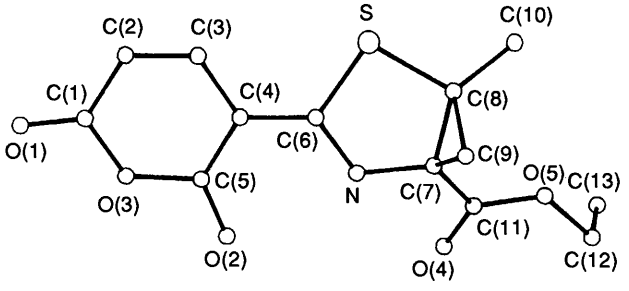


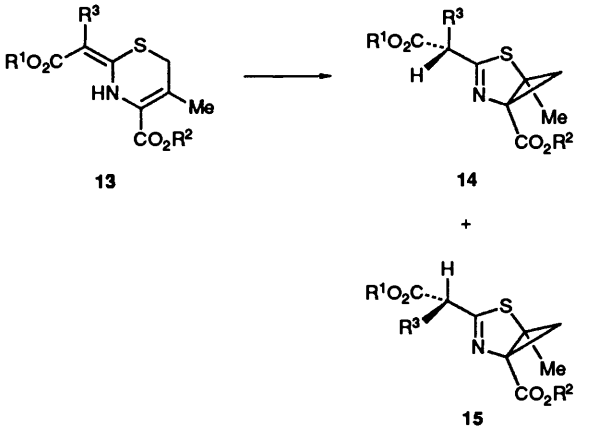
Fig. 1 Molecular structure of the photoproduct **12**

analysis, which gave the molecular conformation shown in Fig. 1. The distinction between the oxygen and nitrogen atoms and the location of the double bonds was effected during the structure refinement by consideration of the atomic temperature factors, bond lengths and hydrogen atom positions.

The six- and five-membered rings together formed an essentially planar entity, the maximum deviation being the sulfur atom, which was 0.08 Å out of the plane on the opposite side from the cyclopropyl ring. The hydrogen atom H(3) bonded to nitrogen was also only 0.06 Å out of this plane, indicating trigonal planar sp^2 hybridisation at nitrogen, due to π-interaction with the C(4)–C(6) double bond. This interaction was reflected in the relatively short N–C(6) bond length of 1.337(8) Å and relatively long C(4)–C(6) double bond length of 1.396(9) Å. The planar configuration at nitrogen also allowed an intramolecular hydrogen bond to be formed between the N–H and the C(5) carbonyl group. The relative distances were N–H(3) 1.05 Å and O(2)···H(3) 1.87 Å. The two non-equivalent S–C bond lengths reflected the difference in hybridisation between the two carbon atoms, with the shorter bond being to the sp^2 hybridised C(6).

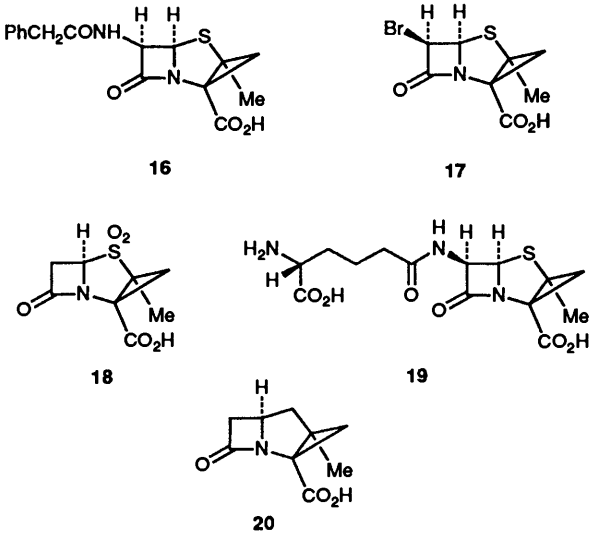
Having discovered a novel and high yielding photochemical reaction, we were curious to examine the photolysis of an alkylated thiazine **13** which, if it resulted in the imine tautomer of the cyclopropa[*d*]thiazoline, then the possibility would arise of the product being one or both of the diastereoisomers **14** or **15**. We were able to prepare the alkylated thiazines **13** (R^1 = R^3 = Me, R^2 = Et), **13** (R^1 = Et, R^2 = R^3 = Me) and **13** (R^1 = R^2 = R^3 = Et) by reaction of the appropriate thioamide with ethyl or methyl 2-oxo-3-methylbut-3-enoate. Alternatively, **13** (R^1 = R^2 = Et, R^3 = Me) was prepared by alkylation of the thiazine **7** (R^1 = R^2 = Et) using methyl iodide and sodium hydride. When the thiazine **13** (R^1 = R^2 = R^3 = Et) was irradiated in toluene, a mixture of approximately equal amounts of the diastereoisomeric cyclopropa[*d*]thiazolines **14** (R^1 = R^2 = R^3 = Et) and **15** (R^1 = R^2 = R^3 = Et) was obtained in 92% yield (Scheme 5). It was found that the hydrogen alpha to both the imine and ester groups was exchangeable with ^2H_2O in the ^1H NMR spectrum as had been the case with the photoproduct **10** (R^1 = R^2 = Et). It appeared, however, that exchange was more rapid in one diastereoisomer than in the other.

We have evidently discovered a novel and high yielding photochemical synthesis of compounds of the general structural



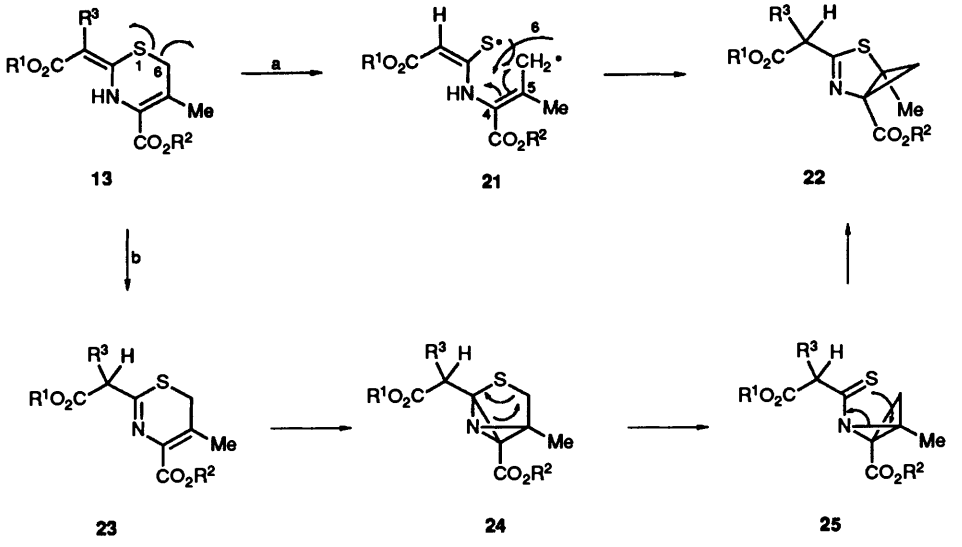
Scheme 5

type shown in **10**, **12**, **14** and **15**. In view of the fact that the β-lactam **16** has been found to be a substrate for bacterial β-lactamases,[8–10] **17** and **18** are β-lactamase inhibitors [10] and **19** is an inhibitor of deacetoxycephalosporin C synthase activity,[11] our reaction may be regarded as producing precursors for the total synthesis of such compounds, which until now have been accessed by partial synthesis from natural products. An olivanic acid analogue **20** of this type has also been synthesised.[12]



The entirely different course of events resultant on photolysis of *N*-acylated thiazines **1** and their unacylated counterparts **13** deserves some comment. The former reaction can be rationalised as in Scheme 1 by photolytic cleavage of the sulfur to allylic carbon bond, S–C-2, in **1** giving the diradical **2**. The sulfur radical may then attack one end of the allylic radical made up of C-2, C-3 and C-4 to yield the product **3**. If the sulfur to allylic carbon, S–C-6, cleavage is also the first step in the photochemical transformation of unacylated thiazines **13** outlined in Scheme 6(a), then the allylic radical system C-6, C-5, C-4 will be conjugated with the lone pair on nitrogen. This may encourage attack of sulfur at C-5 in the middle of the allylic system, rather than at C-4 as was the case with the acylated compound **1**. The sequence of events shown in **21** would then lead to the product **22**.

An alternative and, to us, more convincing explanation of the results is that tautomerism to the heterodiene **23** is possible in the unacylated compound **13**, but not in the acylated



Scheme 6

compound **1**. The diene **23** might then undergo bicyclobutane formation[13] to yield **24**, which could rearrange, *via* the thioamide **25**, to the product **22** as shown in Scheme 6(b).

Experimental

M.p.s were determined on a Kofler hot stage apparatus. IR spectra were recorded on Perkin-Elmer 257 and 477 spectrometers and UV spectra in methanol on a Pye-Unicam SP800 spectrophotometer. ^{1}H NMR spectra were obtained using Varian EM360 (60 MHz), Perkin-Elmer R32 (90 MHz), JEOL FX-90 (90 MHz) and Bruker WH360 (360 MHz) instruments and ^{13}C NMR spectra using JEOL EC-100 (25.1 MHz) and Bruker WH360 (90.5 MHz) instruments; *J* values are given in Hz. Mass spectra were obtained by Mr A. Greenway on AEI-MS30, and Kratos MS25 and MS80 instruments using electron impact (EI) ionisation and combustion analyses were recorded by Mrs G. Olney and Miss. K. Plowman, University of Sussex, and by the microanalytical laboratory, ICI Pharmaceuticals. Thin layer chromatography was carried out using Kieselgel Merck GF_{254} of thickness 0.25 mm for analytical work and of thickness 0.75 mm for preparative work. Flash chromatography was conducted using PF_{254} silica gel.

Ethyl (5-Ethoxycarbonyl-1-methyl-2-thia-4-azabicyclo-[3.1.0]*-hex-3-en-3-yl)acetate* **10** ($R^1 = R^2 =$ Et).—A solution of ethyl 2,3-dihydro-2-ethoxycarbonylmethylene-5-methyl-6*H*-1,3-thiazine-4-carboxylate **7** ($R^1 = R^2 =$ Et)[6] (200 mg, 0.738 mmol) in dry de-gassed toluene (*ca.* 200 cm^3) and acetone (*ca.* 10–20 cm^3) was irradiated in an atmosphere of nitrogen, using a Hanovia immersion medium pressure 125 W lamp with a Pyrex filter. The reaction was monitored by loss of the λ_{max}/nm 336 absorption of the dihydrothiazine in the UV spectrum. After the reaction was complete (2–3 h), the solvent was removed under reduced pressure to give a dark oil. Preparative TLC (silica, Et_2O) gave the pure liquid photoproduct, **10** ($R^1 = R^2 =$ Et) (122 mg, 61%); b.p. *ca.* 160 °C at 0.5 mmHg (Found: C, 53.2; H, 6.4; N, 4.9. $C_{12}H_{17}NO_4S$ requires: C, 53.1; H, 6.3; N, 5.2%); *m/z* 271 (M^+); λ_{max}/nm 262 and 292 (log ε 3.42 and 3.40); ν_{max}(film)/cm^{-1} 1770–1640br; δ_H(C^2HCl_3; 60 MHz) 0.79 and 2.14 (2 × 1 H, 2 × d, 2 × J_{AB} 6, cyclopropyl CH_2), 1.25 (3 H, t, *J* 7.5, *Me*CH_2O), 1.31 (3 H, t, *J* 7.5, *Me*CH_2O), 1.69 (3 H, s, *Me*-C), 3.60 (2 H, s, N=CCH_2CO_2Et—exchangeable with ^2H_2O), 4.18 (2 H, q, *J* 7.5, CH_2O) and 4.31 (2 H, q, *J* 7.5, CH_2O).

5-(5-*Ethoxycarbonyl*-1-*methyl*-2-*thia*-4-*azabicyclo*[3.1.0]*hex*-3-*ylidene*)*glutaconic Anhydride* **12**.—A suspension of 5-(2,3-dihydro-4-ethoxycarbonyl-5-methyl-6*H*-1,3-thiazin-2-ylidene)-glutaconic anhydride **11**[6] (50 mg, 0.17 mmol) in dry distilled de-gassed toluene (*ca.* 200 cm^3) was irradiated using a Hanovia photochemical reactor fitted with a 125 W medium pressure lamp and equipped with a water-cooled Pyrex jacket as a filter under nitrogen for *ca.* 6 h, when the absorption at λ_{max}/nm 390 in the UV spectrum was replaced by a band at λ_{max}/nm 359. Further irradiation had little effect on this absorption. The solvent was removed under reduced pressure and the yellow crystalline product was purified by preparative TLC (silica gel; Et_2O + *ca.* 1% acetic acid). The resultant off-white crystalline product (42 mg, 84%) was found to be pure, but was recrystallised from dichloromethane and diethyl ether or light petroleum (40–60 °C) for analysis. When photolysis was carried out in toluene and acetone, the reaction was completed in *ca.* 1 h. The product appeared as white needles, m.p. 147–149 °C (Found: C, 52.8; H, 4.45; N, 4.7. $C_{13}H_{13}NO_5S$ requires: C, 52.9; H, 4.4; N, 4.7%); λ_{max}/nm 286 and 359 (log ε 3.62 and 4.43); ν_{max}(Nujol)/cm^{-1} 3250 and 1526 (NH), 1740 (CO_2Et), 1725sh and 1587 [anhydride C=O (2)] and 1546 (exocyclic C=C); δ_H(C^2HCl_3; 90 MHz) 1.37 (3 H, t, *J* 7, CH_3CH_2O), 1.42 and 2.18 (2 × 1 H, 2 × d, 2 × *J* 6.1, cyclopropyl CH_2), 1.80 (3 H, s, CH_3–C), 4.38 (2 H, q, *J* 7, MeCH_2O), 5.67 and 7.08 (2 × 1 H, d × d, 2 × *J* 9.3, HC=) and 10.90 (1 H, s, NH—exchanges with ^2H_2O); δ_C(C^2HCl_3; 25.1 MHz), 14.24 (q, CH_3CH_2O), 17.42 (q, CH_3-cyclopropyl), 27.48 (cyclopropyl CH_2), 40.81 (s, S–C), 54.65 (s, NCCO_2), 63.23 (t, OCH_2Me), 103.61 and 143.41 (2 × d, *C*=) and 165.95 and 170.83 (2 × s, 2 × C=O). Other resonances were indistinguishable.

Ethyl 2,3-*Dihydro*-2-(1-*methoxycarbonylethylidene*)-5-*methyl*-6H-1,3-*thiazine*-4-*carboxylate* **13** ($R^1 = R^3 =$ Me, $R^2 =$ Et).—2-Methoxycarbonylthiopropionamide* (1 g, 6.8 mmol) and freshly prepared, distilled ethyl 3-methyl-2-oxobut-3-enoate[14] (1.2 g, 8.45 mmol) were dissolved in dry dioxane (25 cm^3) and the solution was saturated with anhydrous hydrogen chloride at 0 °C and left sealed for 15 h in the dark at room temp. The solvent was removed under reduced pressure at *ca.* 20 °C to give a yellow crystalline mass. Recrystallisation from ethanol gave pale yellow crystals of the thiazine (1.06 g, 58%).

* Obtained as a gift from ICI Pharmaceuticals.

Table 1 Final atomic coordinates ($\times 10^4$) with estimated standard deviations in parentheses

	x	*y*	*z*
S	3030	2606(2)	−1470
N	5144(6)	4354(5)	−9(8)
O(1)	321(8)	8809(6)	−3935(8)
O(2)	4702(6)	7064(5)	−471(8)
O(3)	2455(6)	7868(5)	−2146(7)
O(4)	7474(6)	4229(5)	3294(6)
O(5)	7783(6)	1969(5)	2943(6)
C(1)	972(9)	7760(8)	−3368(11)
C(2)	365(9)	6382(8)	−3825(11)
C(3)	1236(8)	5314(7)	−3063(10)
C(4)	2782(7)	5421(6)	−1877(9)
C(5)	3410(9)	6773(6)	−1396(11)
C(6)	3692(8)	4289(7)	−1111(9)
C(7)	5928(7)	3091(6)	580(9)
C(8)	4858(8)	1883(6)	−187(9)
C(9)	6111(8)	2164(7)	−919(9)
C(10)	4773(9)	592(7)	838(11)
C(11)	7115(8)	3172(6)	2435(9)
C(12)	9074(9)	1909(8)	4689(10)
C(13)	8604(11)	1845(11)	6318(12)

Table 2 Intramolecular distances and angles with estimated standard deviations in parentheses

(a) Bond lengths (Å)

S–C(6)	1.742(7)	C(1)–C(2)	1.454(11)
S–C(8)	1.804(6)	C(2)–C(3)	1.329(10)
N–C(6)	1.337(8)	C(3)–C(4)	1.429(9)
N–C(7)	1.426(8)	C(4)–C(5)	1.439(9)
O(1)–C(1)	1.194(9)	C(4)–C(6)	1.396(9)
O(2)–C(5)	1.211(9)	C(7)–C(8)	1.529(9)
O(3)–C(1)	1.391(9)	C(7)–C(9)	1.528(10)
O(3)–C(5)	1.385(8)	C(7)–C(11)	1.483(8)
O(4)–C(11)	1.209(8)	C(8)–C(9)	1.502(11)
O(5)–C(11)	1.325(8)	C(8)–C(10)	1.504(10)
O(5)–C(12)	1.471(8)	C(12)–C(13)	1.477(14)

(b) Bond angles (°)

C(8)–S–C(6)	93.5(3)	C(8)–C(7)–N	110.1(5)
C(7)–N–C(6)	117.6(5)	C(9)–C(7)–N	116.8(6)
C(5)–O(3)–C(1)	125.2(5)	C(9)–C(7)–C(8)	58.9(5)
C(12)–O(5)–C(11)	117.6(5)	C(11)–C(7)–N	113.3(5)
O(3)–C(1)–O(1)	116.7(7)	C(11)–C(7)–C(8)	126.1(6)
C(2)–C(1)–O(1)	126.4(7)	C(11)–C(7)–C(9)	121.4(6)
C(2)–C(1)–C(3)	116.9(6)	C(7)–C(8)–S	106.6(4)
C(3)–C(2)–C(1)	119.1(6)	C(9)–C(8)–S	116.4(4)
C(4)–C(3)–C(2)	124.1(6)	C(9)–C(8)–C(7)	60.5(5)
C(5)–C(4)–C(3)	117.9(6)	C(10)–C(8)–S	113.7(5)
C(6)–C(4)–C(3)	123.5(6)	C(10)–C(8)–C(7)	126.0(5)
C(6)–C(4)–C(5)	118.6(6)	C(10)–C(8)–C(9)	123.0(6)
O(3)–C(5)–O(2)	116.0(6)	C(8)–C(9)–C(7)	60.6(5)
C(4)–C(5)–O(2)	127.2(6)	O(5)–C(11)–O(4)	125.4(6)
C(4)–C(5)–O(3)	116.7(6)	C(7)–C(11)–O(4)	123.4(6)
N–C(6)–S	112.0(5)	C(7)–C(11)–O(5)	111.1(5)
C(4)–C(6)–S	123.0(5)	C(13)–C(12)–O(5)	112.9(7)
C(4)–C(6)–N	125.0(6)		

The product rapidly decomposed at room temperature in air but could be stored under nitrogen at *ca.* −30 °C; m.p. 59–61 °C (Found: C, 53.1; H, 6.4; N, 5.1. $C_{12}H_{17}NO_4S$ requires: C, 53.1; H, 6.3; N, 5.2%); *m/z* 271 (M^+); $\nu_{max}(CCl_4)/cm^{-1}$ 1730 (unsaturated ester) and 1660 (C=C); λ_{max}/nm 226, 292 and 347; $\delta_H(C^2HCl_3$; 60 MHz) 1.38 (3 H, t, *J* 7, CH_3CH_2O), 1.90 (3 H, s, CH_3C=), 2.29 (3 H, s, CH_3C=), 3.29 (2 H, s, CH_2S), 3.74 (3 H, s, CH_3O) and 4.34 (3 H, q, *J* 7, CH_2O).

Ethyl 2,3-*Dihydro*-2-(1-*ethoxycarbonylethylidene*)-5-*methyl*-6H-1,3-*thiazine*-4-*carboxylate* **13** ($R^1 = R^2 = Et$, $R^3 = Me$).*—A solution of the thiazine **7** ($R^1 = R^2 = Et$)[6] (200 mg, 0.74 mmol) in dry THF (10 cm^3) was added to a solution of benzene-washed sodium hydride (20 mg, 0.83 mmol) in dry THF (10 cm^3) at 0 °C. The solution was stirred at 0 °C for 1 h and methyl iodide (105 mg, 0.74 mmol) was added. The solution was allowed to warm to room temp. over a further 2 h and partitioned between water and chloroform. The organic layer was dried (Na_2SO_4) and the solvent was removed under reduced pressure to yield a red oil, which was chromatographed (silica gel, ether–light petroleum, 1:1) to yield the thiazine as a yellow solid, which was recrystallised from ethanol (80 mg, 38%), m.p. 71–73 °C; *m/z* 285 (M^+); λ_{max}/nm 226, 291 and 348 (log ε 3.97, 3.72 and 4.15); $\nu_{max}(KBr)/cm^{-1}$ 1694 and 1653 (ester C=O); $\delta_H(C^2HCl_3$; 360 MHz) 1.25 (3 H, t, *J* 7.2, OCH_2CH_3), 1.33 (3 H, t, *J* 7.2, OCH_2CH_3), 1.85 (3 H, s, CH_3C=), 2.23 (3 H, s, CH_3C=), 3.24 (2 H, s, CH_2S), 4.16 (2 H, q, *J* 7.2, $CO_2CH_2CH_3$), 4.29 (2 H, q, *J* 7.2, $CO_2CH_2CH_3$) and 8.79 (1 H, br, NH); $\delta_C(C^2HCl_3$; 90.55 MHz) 14.11 (OCH_2CH_3), 14.24 (OCH_2CH_3), 14.48 (CH_3C=), 19.49 (CH_3C=), 31.37 (CH_2S), 59.46 ($CO_2CH_2CH_3$), 61.41 ($CO_2CH_2CH_3$), 91.91 and 120.11 (2 × C=), 126.66 ($NCCO_2CH_2CH_3$), 152.72 (NCS), 163.04 and 168.71 (2 × C=O).

Methyl 2,3-*Dihydro*-2-(*ethoxycarbonylethylidene*)-5-*methyl*-6H-1,3-*thiazine*-4-*carboxylate* **13** ($R^1 = Et$, $R^2 = R^3 = Me$).*—Freshly prepared methyl 2-oxo-3-methylbut-3-enoate[6] (2.8 g, 21.9 mmol) and 2-ethoxycarbonyl-2-thiopropionamide† (3.53 g, 21.9 mmol) were dissolved in dry dioxane (40 cm^3) and the solution was saturated with hydrogen chloride gas at 0 °C. This was left to stand overnight at room temp., and the solvent was removed under reduced pressure to give an orange oil which crystallised on standing and was recrystallised from ethanol to give the thiazine as yellow needles (3.97 g, 67%), m.p. 74–76 °C (Found: C, 52.8; H, 6.4; N, 5.2. $C_{12}H_{17}NO_4S$ requires: C, 53.1; H, 6.3; N, 5.2%); *m/z* 271 (M^+); λ_{max}/nm 226, 291 and 348 (log ε 4.24, 4.00 and 4.43); $\nu_{max}(KBr)/cm^{-1}$ 1694 and 1652 (α,β-unsaturated esters); $\delta_H(C^2HCl_3$; 360 MHz) 1.21 (3 H, t, *J* 7, OCH_2CH_3), 1.80 (3 H, s, CH_3C=), 2.19 (3 H, s, CH_3C=), 3.25 (2 H, s, CH_2S), 3.79 (3 H, s, OCH_3) and 4.11 (2 H, q, *J* 7, OCH_2CH_3); $\delta_C(C^2HCl_3$; 90.55 MHz) 14.12 (OCH_2CH_3), 14.32 (CH_3C=), 19.44 (CH_2S), 31.08 (CH_3C=), 52.04 (OCH_2CH_3), 59.44 (OCH_3), 120.81 (NC=C), 126.42 ($NCCO_2CH_3$) and 163.33 and 168.72 (2 × C=O).

Ethyl 2,3-*Dihydro*-2-(1-*ethoxycarbonylpropylidene*)-5-*ethyl*-6H-1,3-*thiazine*-4-*carboxylate* **13** ($R^1 = R^2 = R^3 = Et$).—A solution of freshly prepared distilled ethyl 3-methyl-2-oxobut-3-enoate[14] (0.9 g, 6.34 mmol) and 2-ethoxycarbonylthiobutyramide* (1 g, 5.71 mmol) in dry dioxane (15 cm^3) was saturated with anhydrous hydrogen chloride at 0 °C. The solution was kept sealed in the dark for 18 h at room temp. and the solvent was removed under reduced pressure at *ca.* 20 °C. The product was recrystallised from ethanol to give white crystals of the fairly air-stable product (1.5 g, 88%), m.p. 58–61 °C (Found: C, 56.1; H, 7.1; N, 4.7. $C_{14}H_{21}NO_4S$ requires: C, 56.2; H, 7.0; N, 4.7%); *m/z* 299 (M^+); ν_{max}(Nujol)/cm^{-1} 1735, 1720, 1690, 1660 and 1570; λ_{max}/nm 223, 291 and 347 (log ε 4.01, 3.76 and 4.20); $\delta_H(C^2HCl_3$; 60 MHz) 1.00 (3 H, t, *J* 8, CH_3CH_2), 1.30 (3 H, t, *J* 7.5, CH_3CH_2O), 1.38 (3 H, t, *J* 7.5, CH_3CH_2O), 2.30 (3 H, s, CH_3C=), 3.30 (2 H, s, CH_2S), 4.23 (2 H, q, *J* 7.5, CH_2O) and 4.34 (2 H, q, *J* 7.5, CH_2O); $\delta_C(C^2HCl_3$; 25.1 MHz) 14.20, 14.56 and 14.74 (3 × q, 3 × CH_3), 19.72 (q, CH_3C=), 22.81 (t, CH_2C=), 31.19 (t, CH_2S), 59.46 and 61.52 (2 × t, 2 × CH_2O), *ca.* 98 (br s, CH_2CCO_2), 120.98 (s, C=), 126.62 (s, $NCCO_2$), 153.32 (s, NCS) and 163.15 and 168.67 (2 × s, 2 × CO_2).

* This experiment was completed by Dr D. Loakes.

Ethyl 2-(5-Ethoxycarbonyl-1-methyl-2-thia-4-azabicyclo-[3.1.0]hex-3-en-3-yl)butanoate **14** + **15** ($R^1 = R^2 = R^3 = Et$).—A solution of ethyl 2-3-dihydro-2-(1-ethoxycarbonylpropylidene)-5-methyl-6*H*-1,3-thiazine-4-carboxylate **13** ($R^1 = R^2 = R^3 = Et$) (50 mg, 0.167 mmol) in toluene (*ca.* 200 cm^3) and acetone (*ca.* 10 cm^3) was de-gassed and irradiated under nitrogen with a Hanovia immersion medium pressure 125 W mercury-arc lamp using a Pyrex filter. The reaction was seen to be complete within *ca.* 40 min by loss of the λ_{max}/nm 347 band in the UV spectrum. The solvent was removed under reduced pressure to give the diastereoisomeric products **14** and **15** as a dark oil, which could be further purified by preparative TLC (silica gel, Et_2O), (46 mg, 92%); *m/z* 299.1189 ($C_{14}H_{21}NO_4S$ requires 299.1191); λ_{max}/nm 225sh, 259 and 297; ν_{max}(film)/cm^{-1} 1770–1650; $\delta_H(C^2HCl_3$; 90 MHz) 0.66 and 0.74 (1 H, 2 × d, *J* 6, diastereoisomeric cyclopropyl CH), 0.91 and 0.99 (3 H, 2 × overlapping t, 2 × *J* 7.5, diastereoisomeric *Me*-CH_2C), 1.25–1.40 (6 H, m, 2 × *Me*CH_2O), 1.66 (3 H, s, *Me*C=), 1.7–2.2 (2 H, m, diastereoisomeric MeCH_2C=), 2.11 (1 H, d, *J* 6, cyclopropyl CH), 3.55 and 3.58 (1 H, 2 × t, 2 × *J* 7.2, diastereoisomeric Et*CH*CO_2Et), 4.20 and 4.28 (2 × 1 H, 2 × q, *J* ca. 7, diastereoisomeric CH_2O) and 4.28 (2 H, q, *J ca.* 7, CH_2O). The δ 3.55 triplet exchanged with ^2H_2O in *ca.* 20 min whilst the δ 3.58 triplet required > 1 h.

X-Ray Structure Determination of the Photoproduct **12**.—*Crystal data.* $C_{13}H_{13}NO_5S$, M = 295.3, monoclinic, a = 9.417(7), b = 9.748(6), c = 7.745(6) Å, β = 110.42(4)°, U = 666.3 Å^3, Z = 2, D_c = 1.47 g cm^{-3}, $F(000)$ = 308. Mo-Kα radiation, λ = 0.710 69 Å, μ = 2.6 cm^{-1}. Space group *Pc*, from systematic absences of *h0l* for *l* odd and successful structure refinement.

A clear needle-shaped crystal *ca.* 0.3 × 0.1 × 0.05 mm was used for data collection on a Hilger and Watts Y290 four circle diffractometer. Accurate cell parameters were derived from the setting angles for 12 reflections. Intensities for $hk \pm l$ reflections with $2 < \theta < 25°$ were measured by a $\omega/2\theta$ step scan using monochromated Mo-Kα radiation. The intensities of three standard reflections monitored every 100 reflections showed no significant variation. After correction for Lorentz and polarisation effects but not for absorption, 1197 non-zero reflections were used in the structure analysis.

The systematic absences in the data indicate either space group *P2/c* or *Pc*. The latter was presumed and was confirmed by the successful structure analysis. The positions of the non-hydrogen atoms were derived by routine heavy atom methods and refined anisotropically by full matrix least squares to a residual R = 0.076. The positions of the hydrogen atoms were then taken from an angle-weighted difference map and held fixed with a common U_{iso} of 0.08 Å^2. Further least squares refinement converged at R = 0.0603, R' = 0.0689 with a maximum shift to error ratio of 0.01 and a final difference map was everywhere <0.3 eÅ^{-3}. A comparable refinement as the opposite enantiometer converged at R = 0.0604, R' = 0.0690. The final atom coordinates and bond lengths and angles are listed (Tables 1 and 2, respectively) for the former refinement.

The structure solution and refinement were done with the SHELX program system of G. M. Sheldrick and atomic scattering factors and dispersion corrections were taken from ref. 15. Lists of hydrogen atom coordinates and temperature factors have been deposited at the Cambridge Crystallographic Data Centre.* Tables of structure factors are available from one of the authors (P. B. H.).

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* For details of the CCDC deposition scheme see, 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1992, Issue 1.

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