Olivanic Acid Analogues. Part 5.[1] Synthesis of 3-Alkylthio and 3-Alkylsulphinyl Analogues *via* Michael Addition of Thiols to 3-Unsubstituted 1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylates. X-Ray Molecular Structure of (2*RS*,3*RS*,5*SR*)-Benzyl 3-Ethylthio-7-oxo-1-azabicyclo[3.2.0]heptane-2-carboxylate and (2*RS*,3*SR*,5*SR*,6*RS*,1'*RS*)- and (2*RS*,3*SR*,5*RS*,6*SR*,1'*SR*)-Benzyl 3-Chloro-6-(1-hydroxyethyl)-7-oxo-3-[(*SR*)-phenylsulphinyl]-1-azabicyclo[3.2.0]heptane-2-carboxylate

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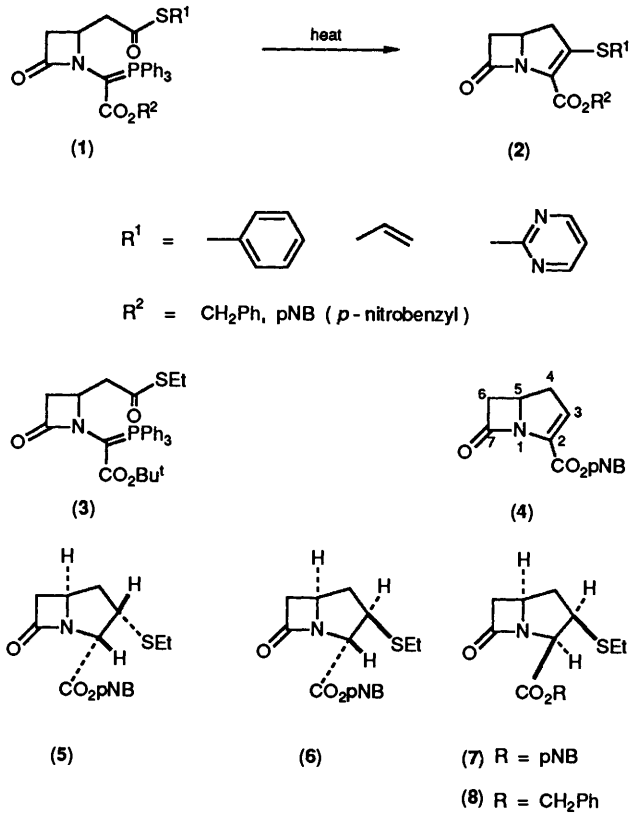
Reaction of thiols with 1-azabicyclo[3.2.0]hept-2-ene-2-carboxylates results in Michael addition to the double bond, producing in high yield 2-thio-substituted 1-azabicyclo[3.2.0]heptane-2-carboxylates; the major products such as the ethylthio adducts (**5**) and (**7**) are those of *trans*-addition to the double bond. Oxidation of these major adducts with iodobenzene dichloride in the presence of aqueous pyridine results in highly regio- and stereo-specific oxidation to α-chlorosulphoxides as in compounds (**27**) and (**28**); base-catalysed elimination produces the Δ^2-unsaturated α- and β-sulphoxides (**31**) and (**32**). Oxidation of the thiol addition products with iodobenzene dichloride–pyridine under anhydrous conditions gives the Δ^3-unsaturated isomers such as (**35**) and (**36**) rather than the α-chloro sulphide products; equilibration with base results in a mixture of the Δ^3- and Δ^2-isomers which can be separated. Deprotection gives the bioactive Δ^2-sodium salts [*e.g.*, (**40**)], while the corresponding Δ^3-salts (**38**) and (**39**) show no antibacterial properties.

We have previously demonstrated the utility of the intramolecular thiol ester–phosphorane cyclisation to synthesise olivanic acid (1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate; 1-carbapenem) analogues bearing a 3-sulphur substituent,[2] *e.g.* (**1**) ⟶ (**2**). However, in the case of the ethylthiol ester (**3**) we were unable to isolate or detect any of the desired bicyclic product (**2**; R^1 = Et, R^2 = Bu^t). This failure to effect cyclisation prompted us to seek an alternative method for introducing alkylthio substituents. This has been achieved using readily available 3-unsubstituted compounds such as (**4**).[3,4,†]

Michael reaction with thiols in the presence of base provided in high yield the products resulting from addition to the double bond. These saturated sulphides have been used to obtain unsaturated Δ^2- and Δ^3-analogues either at the sulphoxide or at the sulphide oxidation level. Thus, reaction of compound (**4**) in dimethylformamide (DMF) in the presence of potassium carbonate and ethanethiol gave a separable mixture of the isomeric products (**5**) (49%), (**6**) (6%), and (**7**) (26%).‡ The major products (**5**) and (**7**) were those resulting from *trans*-addition of thiol to the double bond. Isomer (**7**) was converted into isomer (**6**) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), suggesting that the presence of compound (**6**) in the reaction mixture is the consequence of a base-catalysed epimerisation of product (**7**). This observation, together with the characteristic lower field ^{1}H NMR shift of the 2-proton in compounds (**5**) and (**6**) having the 'natural' stereochemistry (as designated in penicillins) compared with compound (**7**) with the 'unnatural' configuration, allowed the assignments of stereochemistry to be made as shown.[5] An X-ray analysis of the analogous benzyl ester (**8**) confirmed these assignments and



† Numbering based on the 1-azabicyclo[3.2.0]heptane ring system.
‡ All compounds are racemic; only one enantiomer is depicted for convenience.

showed clearly the sulphur and carboxy substitutents to have a *cis*-relationship (Figure 1). Fractional atomic co-ordinates (Table 1) and selected bond angles and bond lengths (Figure 4) are given in the Experimental section.

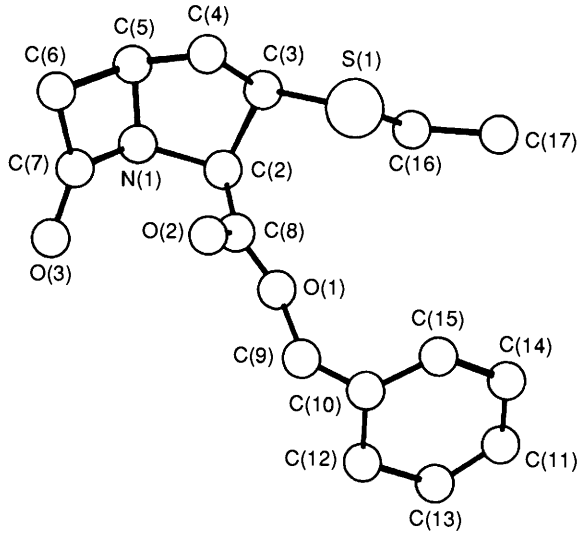


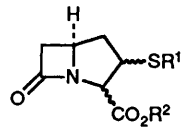
Figure 1. X-Ray structure of benzyl 3-ethylthio-7-oxo-1-azabicyclo-[3.2.0]heptane-2-carboxylate (**8**).

Other examples derived from compound (**4**) or the corresponding benzyl ester are shown in structures (**9**)–(**12**). These cover aliphatic, aromatic, and heterocyclic thiols and include the acetamidoethylthio substituent found in many carbapenem natural products.[2] In most cases the isomers could be separated by chromatographic procedures, the stability of the products being much greater than that of the corresponding unsaturated compounds. The thiol addition reaction appears to be general, although variations in isomer ratio have been observed depending on the nature of the thiol, the reaction time, and whether performed on isolated or crude bicyclic material.

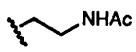
A *trans* 6-(1-hydroxyethyl) side-chain did not interfere with the reaction so that substrate (**13**)[6] on reaction with thiophenol produced a 3:1 mixture (49%) of products (**14**) and (**15**), together with *cis*-isomer (**16**) (13%). Addition of acetamidoethanethiol to compound (**13**) resulted in a separable mixture of all three isomers (**17**) (16%), (**18**) (36%), and (**19**) (14%). In another series the *p*-bromophenacyl ester of the *cis*-subsituted bicyclic β-lactam, compound (**20**),[6] gave adducts (**21**), (**22**), and (**23**) in an overall yield of 56%. Little indication of addition to the C-6 side-chain double bond was apparent. These products could readily be deprotected to provide the corresponding sodium salts (**24**), (**25**), and (**26**). Whereas the salt of compound (**20**) exhibited some antibacterial activity,[6] the saturated adducts (**24**)–(**26**) were inactive. It should be noted that the latter are considerably more stable than those with the Δ^2-double bond present.

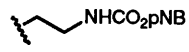
Attention was next turned to the synthesis of the unsaturated ring system found in the natural products. This was achieved initially in two stages, providing esters of Δ^2-unsaturated sulphoxide isomers. Oxidation of either of the two major adducts with two mol equiv. of iodobenzene dichloride (IBD)[7,*] in wet chloroform in the presence of pyridine was found to be highly stereo- and regio-specific, giving a single α-chloro sulphoxide isomer in each case. Under these conditions ethylthiol adducts (**5**) and (**7**) gave chloro sulphoxides (**27**) and (**28**) respectively. In each case spectroscopic evidence suggested

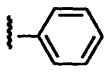
* (Dichloroiodo)benzene.

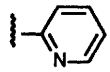


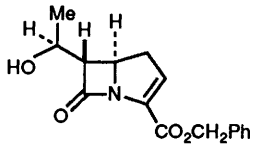
R^2 = CH_2Ph or pNB

(**9**) R^1 = 

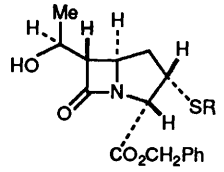
(**11**) R^1 = 

(**10**) R^1 = 

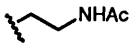
(**12**) R^1 = 

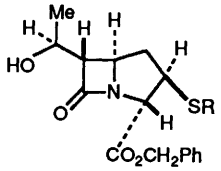


(**13**)

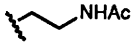


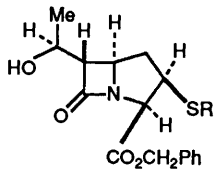
(**14**) R = Ph

(**17**) R = 

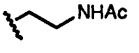


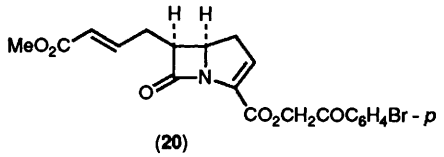
(**15**) R = Ph

(**18**) R = 



(**16**) R = Ph

(**19**) R = 



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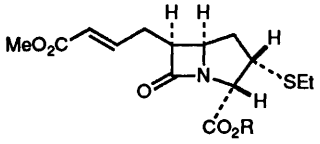
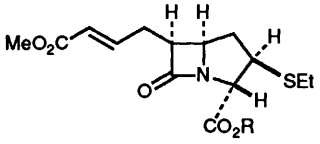


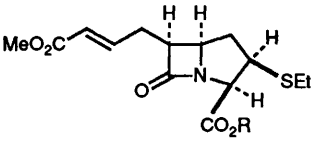
(**21**) R = $CH_2COC_6H_4Br$-*p*

(**24**) R = Na



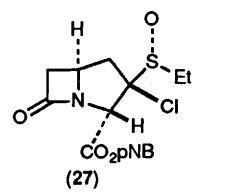
(**22**) R = $CH_2COC_6H_4Br$-*p*

(**25**) R = Na



(**23**) R = $CH_2COC_6H_4Br$-*p*

(**26**) R = Na



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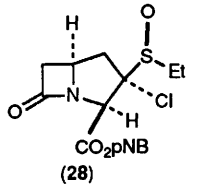

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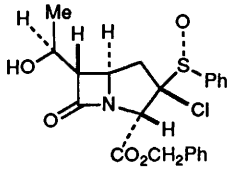

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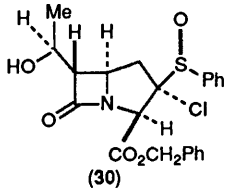

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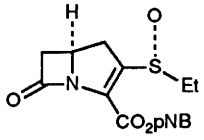

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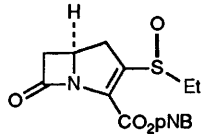

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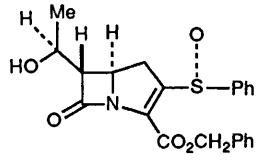

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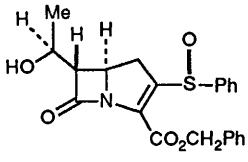


(34)

chlorination had occurred with retention of stereochemistry at C-3 as shown. For isomer (**6**) oxidation was not selective and a mixture of diastereoisomers was obtained. Confirmation of the stereochemical assignments for the major products was confirmed unambiguously in the case of benzene thiol adducts (**14**) and (**15**) by X-ray crystallography. Oxidation of compound (**14**) [as a 3:1 mixture with isomer (**15**)] gave, as the major product, compound (**29**) (Figure 2); isomer (**16**) produced chloro sulphoxide (**30**) (Figure 3). Fractional atomic co-ordinates (Tables 2 and 3) and bond angles and bond lengths (Figures 5 and 6) are again given for both isomers in the Experimental section.

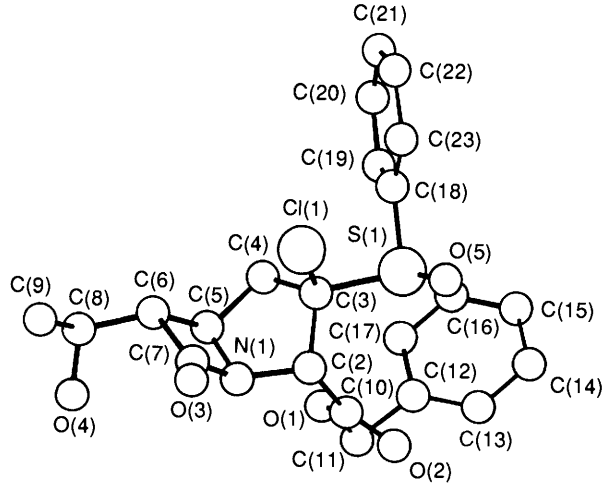


Figure 2. X-Ray structure of chloro sulphoxide (**29**).

Treatment of chloro sulphoxides (**27**) and (**28**) in ethyl acetate with DBU gave a rapid conversion into the α- or β-sulphoxide of the Δ^2-unsaturated esters (**31**) and (**32**), respectively. The

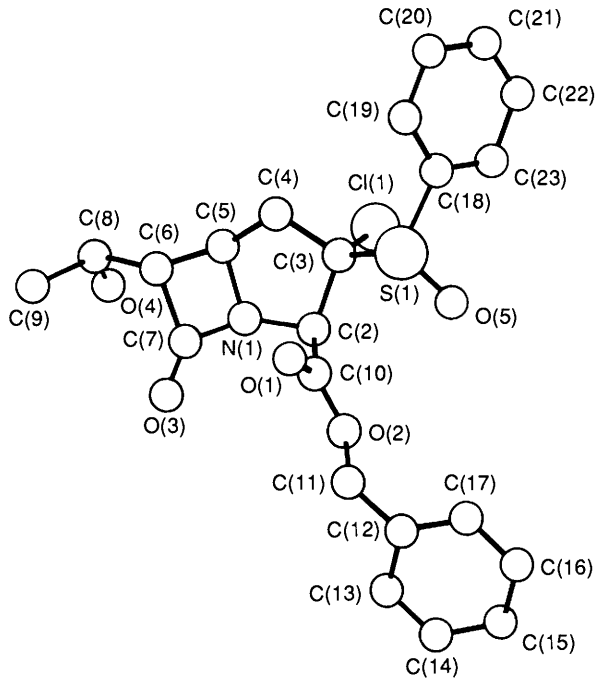
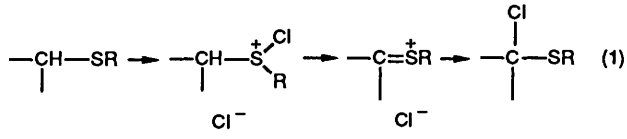


Figure 3. X-Ray structure of chloro sulphoxide (**30**).

oxidation product of minor isomer (**6**) produced a mixture of sulphoxides. Similarly, in the 6-(1-hydroxyethyl) series elimination readily occurred to give sulphoxides (**33**) and (**34**). After work-up, many of the products were of high purity and often crystalline. In the latter form these sulphoxides were stable, but non-crystalline products were best kept in solution. Attempts to purify the sulphoxides further by chromatography resulted in extensive degradation. Similarly, hydrogenolysis to remove the acid protecting group (benzyl or *p*-nitrobenzyl) again resulted in decomposition, indicating an extremely labile family of compounds. Attempted reduction of sulphoxide to sulphide was also unsuccessful.

Our approach was then directed to carrying out a similar sequence of reactions, but at the sulphide oxidation level, by way of an α-chloro sulphide derivative. We anticipated that the oxidation with IBD in the absence of water would produce a sulphonium intermediate capable of rearranging in a Pummerer-like manner, to form an α-chloro sulphide[8,9] [equation (1)].

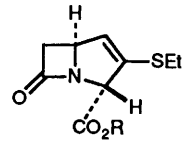


(1)

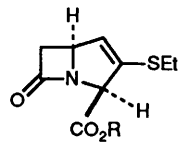
Subsequent elimination would produce the required unsaturated analogue at desired oxidation level. A somewhat unexpected result was obtained.

When isomers (**5**), (**6**), and (**7**) were oxidised with IBD in dry benzene containing pyridine, we could isolate in each case some 50% of the corresponding Δ^3-isomer. Thus compounds (**5**) and (**6**) both gave Δ^3-compound (**35**), while isomer (**7**) formed the C-2 epimeric product (**36**). With base the latter was immediately converted into compound (**35**). Thus all three isomers could be channelled into the Δ^3-product (**35**). Equilibration of compound (**35**) with a catalytic amount of DBU gave some 30% of the desired Δ^2-sulphide (**37**) and 50% of recovered compound (**35**) after chromatographic separation. Characteristically, the Δ^2- and Δ^3-isomers exhibited a vinyl sulphide absorption in the IR spectrum at 1 560–1 575 cm^{-1} for compound (**35**) and 1 540–

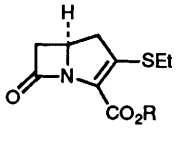
1 550 cm^{-1} for isomer (**37**). Further, in Δ^3-isomers (**35**) and (**36**) the ^1H NMR spectrum clearly revealed an allylic coupling between 4-H and 2-H of 1.5 Hz, as well as long-range couplings between 2-H and 5-H for isomer (**35**) ($^4J_{2\beta,5\alpha}$ 3.5 Hz) and 2-H and 6-H for isomer (**36**) ($^5J_{2\alpha,6\alpha}$ 1.5 Hz).



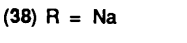
(**35**) R = pNB



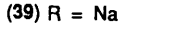
(**36**) R = pNB



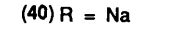
(**37**) R = pNB



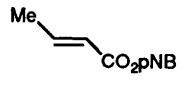
(**38**) R = Na



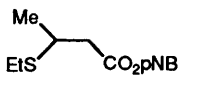
(**39**) R = Na



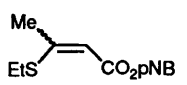
(**40**) R = Na



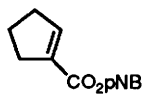
(**41**)



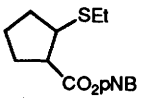
(**42**)



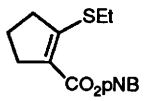
(**43**)



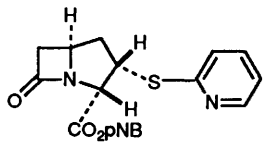
(**44**)



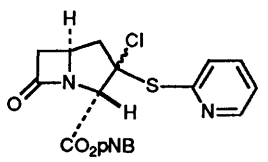
(**45**)



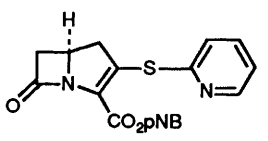
(**46**)



(**47**)



(**48**)



(**49**)

No α-chloro sulphide was isolated with the ethylthio series or any other alkyl-substituted compound. On occasions minor amounts of the Δ^2-isomer could be detected in the reaction mixture. Although less convenient, other halogen sources such as *N*-chlorosuccinimide (NCS)[10] or chlorine[11] itself worked equally successfully. Hydrogenolysis of the esters (**35**)–(**37**) readily gave the sodium salts. The Δ^3-compounds (**38**) and (**39**) were very stable but inactive; Δ^2-salt (**40**) was more labile and showed an appreciable level of antibacterial activity. The integrity of these preparations was confirmed by conversion into their biologically labile phthalidyl esters (see Experimental section), of which the Δ^2-isomer demonstrated *in vivo* activity. Application of this procedure to C-6 substituted analogues, particularly the synthesis of natural products such as the olivanic acids MM 22381[2] and PS-5,[12] will form the subject of a further full paper in the series.

The outcome of the IBD oxidation led us to examine the sequence with some model series. Use of thiol adduct (**42**), derived from the crotonate ester (**41**), gave only the expected mixture of (*E*)- and (*Z*)- double-bond isomers (**43**) with no evidence for any β,γ-product. Similarly the cyclopentene ester (**44**) produced adduct (**45**) and subsequently product (**46**). One must conclude that in our bicyclic system the strained steric environment of the intermediate in the oxidation sequence is such that there is a marked preference for elimination to the observed deconjugated product rather than that seen with a simple linear or cyclic case.

Only on one occasion have we isolated a 2-chloro sulphide, hitherto the putative intermediate in these reactions. This was with the major isomer (**47**) resulting from addition of pyridine-2-thiol. Here reaction with IBD provided a new product with spectroscopic evidence incompatible with the Δ^3-isomer, but consistent with α-chloro sulphide (**48**). Further evidence for structure (**48**) was obtained on treatment with DBU, when a rapid conversion into Δ^2-compound (**49**) occurred. This product was identical with an authentic sample of compound (**49**) synthesised by an alternative procedure.[13]

Experimental

The experimental techniques, materials, solvents, and spectroscopic instrumentation employed in this work were as described in Parts 2[6] and 4[1] of the series. Unless stated otherwise, IR spectra were recorded for chloroform solutions, and NMR spectra were obtained in $CDCl_3$. IBD was prepared[14] from chlorine gas and iodobenzene in chloroform. It was crystallised from chloroform–hexane, air dried, and stored in sealed vessels at 0 °C. Solvents for the anhydrous IBD oxidations were obtained as follows. Benzene was dried over sodium wire and distilled; dichloromethane was passed through basic alumina, refluxed over BDH phosphorus pentaoxide–silica gel drying agent (Trockenmittel®), and distilled therefrom; pyridine was dried over potassium hydroxide and distilled. Biogel® P2 refers to 200–400 mesh grade. All compounds prepared are racemic; NMR stereochemical assignments refer to that enantiomer which is depicted.

p-*Nitrobenzyl* 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate*.—*Method A*. To a stirred suspension of *p*-nitrobenzyl 7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate[3] (**4**) (1.15 g, 4 mmol) in dry DMF (10 ml) at ambient temperature was added ethanethiol (0.25 g, 0.3 ml, 4 mmol), followed by potassium carbonate (0.055 g, 0.4 mmol). The orange mixture was stirred for 30 min. After dilution with ethyl acetate (100 ml), the solution was washed successively with water and brine and then dried. Evaporation gave the crude adducts, which were chromatographed on silica gel (Art. 7729). Gradient elution with ethyl acetate–light petroleum mixtures gave the following three isomers of the *title carboxylate*, in order of elution.

(i) (2RS,3RS,5RS)-*Isomer* (**5**) obtained as white crystals (from EtOAc–light petroleum) (0.681 g, 49%), m.p. 79–80.5 °C (Found: C, 55.0; H, 5.3; N, 7.8. $C_{16}H_{18}N_2O_5S$ requires C, 54.9; H, 5.1; N, 8.0%); ν_{max} 1 765, 1 755sh, 1 522, and 1 350 cm^{-1}; δ_H(90 MHz) 1.23 (3 H, t, *J* 7 Hz), 2.20 (2 H, dd, *J* 8 and 6.5 Hz, 4-H_2), 2.56 (2 H, q, *J* 7 Hz), 2.75 (1 H, dd, *J* 16 and 2 Hz, 6-H^β), 3.38 (1 H, dd, *J* 16 and 5 Hz, 6-H^α), 3.62 (1 H, td, *J* 8 and 6.5 Hz, 3-H^β), 3.96–4.25 (1 H, m, 5-H), 4.78 (1 H, d, *J* 6.5 Hz, 2-H^β), 5.25 (2 H, s, CH_2Ar), and 7.51 (2 H, *J* 7.5 Hz) and 8.17 (2 H, *J* 7.5 Hz) (AA′BB′).

(ii) (2RS,3SR,5RS)-*Isomer* (**6**) was obtained as a gum (0.078 g, 6%) (Found: M^+, 350.0952. $C_{16}H_{18}N_2O_5S$ requires *M*, 350.0936); ν_{max} 1 760, 1 750, 1 520, and 1 325 cm^{-1}; δ_H(90 MHz) 1.21 (3 H, t, *J* 7 Hz), 1.63 (1 H, ddd, *J* 13, 9, and 8 Hz, 4-H), 2.35–2.90 [4 H, including 2.56 (2 H, q, *J* 7 Hz, CH_2Me), 2.77 (1 H, dd, *J* 16 and 2 Hz, 6-H^β), and 1 H, 4-H], 3.29 (1 H, dd, *J* 16 and 4.5 Hz, 6-H^α), 3.55–3.97 (2 H, m, 3-H^α and 5-H), 4.33 (1 H, d, *J* 6 Hz, 2-H^β), 5.24 (2 H, s, CH_2Ar), and 7.47 (2 H, *J* 8 Hz) and 8.15 (2 H, *J* 8 Hz) (AA′BB′).

(iii) (2RS,3RS,5SR)-*Isomer* (**7**) was crystallised from ethyl acetate–light petroleum as plates (0.362 g, 26%), m.p. 97–98 °C (Found: C, 54.85; H, 5.3; N, 7.8%); ν_{max} 1 765, 1 745, 1 520, and

1 345 cm^{-1}; δ_H(90 MHz) 1.21 (3 H, t, *J* 7 Hz), 1.91 (1 H, ddd, *J* 12, 12, and 10 Hz, 4-H), 2.30 (1 H, ddd, *J* 12, 6, and 6 Hz, 4-H), 2.55 (2 H, q, *J* 7 Hz), 2.79 (1 H, dd, *J* 16 and 2 Hz, 6-H$^{\beta}$), 3.11 (1 H, dd, *J* 16 and 4 Hz, 6-H$^{\alpha}$), 3.50–3.85 (2 H, m, 3-H$^{\alpha}$ and 5-H), 4.14 (1 H, d, *J* 7 Hz, 2-H$^{\alpha}$), 5.26 (2 H, s, CH_2Ar), and 7.52 (2 H, *J* 8 Hz) and 8.14 (2 H, *J* 8 Hz) (AA'BB').

Method B [No isolation of intermediate ester (**4**)]. A stirred suspension of *p*-nitrobenzyl (4-allyl-2-oxoazetidin-1-yl)triphenylphosphoranylideneacetate[3] (1.066 g) in ethyl acetate (100 ml) at ambient temperature under argon was treated with trifluoroacetic acid (TFA) (3.08 ml) for 15 min. The clear solution obtained was cooled (−70 °C) and the product was cyclised by treatment with ozonised oxygen in the manner which we have previously described.[3] The crude product, shown (TLC) to contain mainly the bicyclic ester (**4**) together with triphenylphosphine, was evaporated to dryness (room temperature) and the residue was immediately redissolved in dry DMF. To the solution was added ethanethiol (0.15 ml) followed by potassium carbonate (0.027 g) and the mixture was stirred at room temperature for 1.5 h. The red reaction mixture was diluted with ethyl acetate, washed, and dried, and the crude products were chromatographed as described in Method A. The three isomers of the title ester were obtained in the following yields overall from the phosphorane: (**5**) (0.167 g, 25%), (**6**) (0.095 g, 14%), and (**7**) (0.090, 14%).

The following compounds were prepared similarly, using Method A.

Benzyl 3-ethylthio-7-oxo-1-azabicyclo[3.2.0]*heptane-2-carboxylate*. From benzyl 7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate[3] (0.060 g) and ethanethiol (0.10 ml). The (2*RS*,3*RS*,5*RS*)-isomer and (2*RS*,3*SR*,5*RS*)-isomer were obtained as an inseparable, gummy mixture (0.038 g, 56%) (4:1 ratio) (Found: M^+, 305.1057. Calc. for $C_{16}H_{19}NO_3S$: *M*, 305.1085); ν_{max} 1 770 and 1 750 cm^{-1}; δ_H(major isomer) 1.17 (3 H, t, *J* 7 Hz, SCH_2Me), 2.16 (2 H, dd, *J* 9 and 6 Hz, 4-H_2), 2.54 (2 H, q, *J* 7 Hz), 2.70 (1 H, dd, *J* 16 and 2.5 Hz, 6-H$^{\beta}$), 3.33 (1 H, dd, *J* 16 and 5 Hz, 6-H$^{\alpha}$), 3.55 (1 H, td, *J* 9 and 7 Hz, 3-H$^{\beta}$), 4.06 (1 H, tdd, *J* 6.5 and 2.5 Hz, 5-H), 4.72 (1 H, d, *J* 7 Hz, 2-H$^{\beta}$), 5.12 (2 H, s, CH_2Ph), and 7.29 (5 H, s, CH_2Ph). The presence of the minor component was evident from the signal at δ_H 4.35 (d, *J* 5 Hz, 2-H$^{\beta}$).

(2RS,3RS,5SR)-*Isomer* (**8**) was obtained as needles (from EtOAc–light petroleum) (0.017 g, 22%), m.p. 62–64 °C (Found: C, 62.8; H, 6.2; N, 4.3. $C_{16}H_{19}NO_3S$ requires C, 62.9; H, 6.3; N, 4.6%); ν_{max} 1 770 and 1 740 cm^{-1}; δ 1.17 (3 H, t, *J* 7 Hz, SCH_2Me), 1.93 (1 H, td, *J* 12 and 10 Hz, 4-H), 2.25 (1 H, dt, *J* 12 and 6 Hz, 4-H), 2.54 (2 H, q, *J* 7 Hz), 2.79 (1 H, dd, *J* 16 and 2.5 Hz, 6-H$^{\beta}$), 3.08 (1 H, dd, *J* 16 and 4 Hz, 6-H$^{\alpha}$), 3.5–3.8 (2 H, m, 3-H$^{\alpha}$ and 5-H), 4.10 (1 H, d, *J* 7 Hz, 2-H$^{\alpha}$), 5.17 (2 H, s, CH_2Ph), and 7.30 (5 H, s, CH_2Ph).

Benzyl 3-(2-acetamidoethylthio)-7-oxo-1-azabicyclo[3.2.0]*heptane-2-carboxylate* (**9**; R^2 = CH_2Ph). From benzyl (5*RS*)-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate[3] (0.56 g) and 2-acetamidoethanethiol[15] (0.302 g). The isomers were eluted in the following order.

(2RS,3SR,5RS)-*Isomer* (2α,3β). A gum (0.361 g, 43%) (Found: M^+, 362.1294. $C_{18}H_{22}N_2O_4S$ requires *M*, 362.1300); ν_{max} 3 480, 1 765, 1 745sh, 1 670, and 1 520 cm^{-1}; δ_H 1.59 (1 H, dt, *J* 13 and 7 Hz, 4-H), 1.90 (3 H, s), 2.4–2.9 (5 H, m, 3-H$^{\alpha}$, 4- and 6-H, and CH_2S), 3.1–3.4 (3 H, m, 6-H and CH_2N), 3.6–4.0 (1 H, m, 5-H), 4.34 (1 H, d, *J* 5 Hz, 2-H$^{\beta}$), 5.13 (2 H, s, CH_2Ph), 6.22 (1 H, br s, NH), and 7.29 (5 H, s, Ph).

The (2RS,3RS,5RS)-*isomer* (2α,3α) was also a gum (0.192 g, 22%) (Found: M^+, 362.1315); ν_{max} 3 460, 1 765, 1 745sh, 1 665, and 1 515 cm^{-1}; δ_H 1.90 (3 H, s), 2.16 (2 H, dd, *J* 8 and 5 Hz, 4-H_2), 2.5–2.9 (3 H, m, 6-H and CH_2S), 3.2–3.5 (3 H, m, 6-H and CH_2N), 3.57 (1 H, br q, *J* 8 Hz, 3-H$^{\beta}$), 4.03 (1 H, qd, *J* 5 and 2.5 Hz, 5-H), 4.70 (1 H, d, *J* 7 Hz, 2-H$^{\beta}$), 5.14 (2 H, s, CH_2Ph), 6.20 (1 H, br s, NH), and 7.29 (5 H, s, Ph).

The (2RS,3RS,5SR)-*isomer* (2β,3β) (0.145 g, 17%) had m.p. 117–118 °C (from $CHCl_3$–light petroleum) (Found: C, 59.6; H, 6.1; N, 7.7. $C_{18}H_{22}N_2O_4S$ requires C, 59.7; H, 6.1; N, 7.7%); ν_{max} 1 765, 1 740, 1 665, and 1 510 cm^{-1}; δ_H 1.92 (3 H, s), 1.9–2.5 (2 H, m, 4-H_2), 2.5–2.8 (2 H, m, CH_2S), 2.77 (1 H, dd, *J* 16 and 3 Hz, 6-H$^{\beta}$), 3.11 (1 H, dd, *J* 16 and 4 Hz, 6-H$^{\alpha}$), 3.2–3.5 (2 H, m, CH_2N), 3.5–3.9 (2 H, m, 3-H$^{\alpha}$ and 5-H), 4.11 (1 H, d, *J* 7 Hz, 2-H$^{\alpha}$), 5.20 (2 H, s, CH_2Ph), 6.00 (1 H, br s, NH), and 7.37 (5 H, br s, Ph); *m/z* (EI) M^+, 362.

p-*Nitrobenzyl 3-(2-acetamidoethylthio)-7-oxo-1-azabicyclo*[3.2.0]*heptane-2-carboxylate* (**9**; R^2 = *pNB*). From *p*-nitrobenzyl ester (**4**) (0.284 g) and 2-acetamidoethanethiol[15] (0.131 g). Silica gel chromatography with ethyl acetate as eluant, gave a gum (0.183 g, 46%) shown (NMR) to be a mixture of the 2α,3α- and 2α,3β-isomer of the title ester (1:2 ratio). These compounds were separated by rechromatography with chloroform–ethanol eluant mixtures.

The (2*RS*,3*SR*,5*RS*)-isomer (2α,3β; major component) was a gum, ν_{max} 3 460, 1 768, 1 755sh, 1 675, 1 522, and 1 345 cm^{-1}; δ_H 1.65 (1 H, ddd, *J* 13, 8.5, and 7.5 Hz, 4-H), 1.96 (3 H, s), 2.50–3.10 [4 H, including 4-H, 2.69 (t, *J* 6 Hz) and 2.75 (t, *J* 6 Hz) (CH_2S), and 2.81 (1 H, dd, *J* 16 and 2 Hz, 6-H$^{\beta}$)], 3.28–3.52 (3 H, m, CH_2N and 6-H$^{\alpha}$), 3.70–4.01 (2 H, 3-H$^{\alpha}$ and 5-H), 4.39 (1 H, d, *J* 6 Hz, 2-H$^{\beta}$), 5.29 (2 H, s, CH_2Ar), 6.12 (1 H, br s, NH), and 7.53 (2 H, *J* 8.5 Hz) and 8.21 (2 H, *J* 8.5 Hz) (AA'BB').

The (2*RS*,3*RS*,5*RS*)-isomer (2α,3α; minor component) was also obtained as a gum; ν_{max} 3 480, 1 775, 1 758sh, 1 678, 1 522, and 1 350 cm^{-1}; δ_H 1.95 (3 H, s), 2.20 (2 H, dd, *J* 8.5 and 6.5 Hz, 4-H_2), 2.69 and 2.76 (each 1 H, t, *J* 6 Hz) (CH_2S), 2.76 (1 H, dd, *J* 16 and 2.5 Hz, 6-H$^{\beta}$), 3.2–3.8 [4 H, comprising 3.33 (2 H, t, *J* 6 Hz, CH_2N), 3.65 (1 H, td, *J* 8.5 and 6.5 Hz, 3-H$^{\beta}$) and 6-H$^{\alpha}$], 3.93–4.20 (1 H, m, 5-H), 4.78 (1 H, d, *J* 6.5 Hz, 2-H$^{\beta}$), 5.27 (2 H, s, CH_2Ar), 6.03 (1 H, br s, NH), and 7.54 (2 H, *J* 8.5 Hz) and 8.21 (2 H, *J* 8.5 Hz) (AA'BB').

Continued elution of the first column with ethanol–ethyl acetate (1:9) provided the (2*RS*,3*RS*,5*SR*)-isomer (2β,3β) as a gum (0.071 g, 21%); ν_{max} 3 460, 1 770, 1 745, 1 675, 1 522, and 1 350 cm^{-1}; δ_H 1.89 (1 H, ddd, *J* 12, 12, and 6 Hz, 4-H), 1.96 (3 H, s), 2.34 (1 H, ddd, *J* 12, 12, and 10 Hz, 4-H), 2.69 (2 H, td, *J* 6 and 3 Hz, CH_2S), 2.77 (1 H, dd, *J* 16 and 3 Hz, 6-H$^{\beta}$), 3.13 (1 H, dd, *J* 16 and 4.5 Hz, 6-H$^{\alpha}$), 3.33 (2 H, t, *J* 6 Hz, CH_2N), 3.60–3.89 (2 H, m, 3-H$^{\alpha}$ and 5-H), 4.16 (1 H, d, *J* 7 Hz, 2-H$^{\alpha}$), 5.29 (2 H, s), 6.07 (1 H, br s, NH), and 7.57 (2 H, *J* 8.5 Hz) and 8.20 (2 H, *J* 8.5 Hz) (AA'BB').

Benzyl 7-oxo-3-phenylthio-1-azabicyclo[3.2.0]*heptane-2-carboxylate* (**10**; R^2 = CH_2Ph). From benzyl (5*RS*)-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate[3] and thiophenol. The (2*RS*,3*RS*,5*RS*)- (major) and (2*RS*,3*SR*,5*RS*)-isomer were inseparable and were isolated as a gum [(4:1) ratio, 27%] [Found: (for mixture) M^+, 353.1102. Calc. for $C_{20}H_{19}NO_3S$: *M*, 353.1085]; ν_{max} 1 760 and 1 740sh cm^{-1}; δ_H(2α,3α-major isomer) 2.23 (1 H, dd, *J* 9 and 4 Hz, 4-H), 2.27 (1 H, dd, *J* 9 and 4 Hz, 4-H), 2.68 (1 H, dd, *J* 16 and 2.5 Hz, 6-H$^{\beta}$), 3.31 (1 H, dd, *J* 16 and 5 Hz, 6-H$^{\alpha}$), 3.90 (1 H, td, *J* 9 and 7 Hz, 3-H$^{\beta}$), 4.10 (1 H, br m, 5-H$^{\alpha}$), 4.74 (1 H, d, *J* 7 Hz, 2-H$^{\beta}$), 5.12 (2 H, s), and 7.1–7.4 (10 H, m, 2 × Ph). The minor isomer (2α,3β) had δ_H 4.38 (d, *J* 5 Hz, 2-H$^{\beta}$).

The (2RS,3RS,5SR)-*isomer* was crystallised from ether (19%), m.p. 84–85 °C (Found: C, 68.1; H, 5.6; N, 3.9. $C_{20}H_{19}NO_3S$ requires C, 68.0; H, 5.4; N, 4.0%); ν_{max} 1 765 and 1 740 cm^{-1}; δ_H 2.05 (1 H, td, *J* 12 and 10 Hz, 4-H), 2.56 (1 H, dt, *J* 12 and 5 Hz, 4-H), 2.81 (1 H, dd, *J* 16 and 2.5 Hz, 6-H$^{\beta}$), 3.10 (1 H, dd, *J* 16 and 4 Hz, 6-H$^{\alpha}$), 3.5–3.8 (1 H, m, 5-H$^{\alpha}$), 3.96 (1 H, ddd, *J* 12, 7, and 5 Hz, 3-H$^{\alpha}$), 4.16 (1 H, d, *J* 7 Hz, 2-H$^{\alpha}$), 5.19 (2 H, s), and 7.1–7.4 (10 H, m, 2 × Ph).

p-*Nitrobenzyl 3-[2-(p-Nitrobenzyloxycarbonylamino)ethylthio]-7-oxo-1-azabicyclo*[3.2.0]*heptane-2-carboxylate* (**11**; R^2 = *pNB*). This was prepared from *p*-nitrobenzyl ester (**4**)

(0.576 g) and *p*-nitrobenzyloxycarbonylaminoethanethiol[16] (0.512 g).

The (2*RS*,3*RS*,5*RS*)- and (2*RS*,3*SR*,5*RS*)-isomer (2α,3α) and (2α,3β) were obtained as an inseparable mixture (0.765 g, 70%); (5:7 ratio), ν_{max} 3 460, 1 770, 1 730, 1 520, and 1 350 cm^{-1}; δ_H 1.47–2.91 (4-H_2, 5-H, CH_2S, and 6-H), 2.19–4.21 (5 H, 3-, 5-, and 6-H and CH_2N), 4.39 [7/12 H, d, *J* 6 Hz, 2-H$^{\beta}$ (2α, 3β)], 4.79 [5/12 H, d, *J* 7 Hz, 2-H$^{\beta}$ (2α, 3α)], 5.18 (s) and 5.27 (s) (together 4 H, CH_2Ph), ~5.2 (1 H, br s, NH), and 7.40–7.60 (4 H) and 8.15 and 8.18 (together 4 H, each d, *J* 8 Hz) (2 × AA'BB').

The (2*RS*,3*RS*,5*SR*)-isomer (2β,3β) was isolated as a foam (0.18 g, 17%); ν_{max} 3 460, 1 770, 1 740sh, 1 730, 1 520, and 1 350 cm^{-1}; δ_H 1.89 (1 H, ddd, *J* 12, 12, and 9.5 Hz, 4-H), 2.32 (1 H, ddd, *J* 12, 6, and 6 Hz, 4-H), 2.72 (2 H, t, *J* 6 Hz, CH_2S), 2.80 (1 H, dd, *J* 16 and 3 Hz, 6-H$^{\beta}$), 3.13 (1 H, dd, *J* 16 and 4.5 Hz, 6-H$^{\alpha}$), 3.31. (2 H, t, *J* 6 Hz, CH_2N), 3.57–3.87 (2 H, m, 3-H$^{\alpha}$ and 5-H), 4.16 (1 H, d, *J* 7.5 Hz, 2-H$^{\alpha}$), 5.19 and 5.30 (each 2 H, s, CH_2Ar), ~5.2 (1 H, br s, NH), and 7.48, 7.56, 8.17, and 8.18 (each 2 H, *J* 8 Hz) (2 × AA'BB').

p-*Nitrobenzyl* 7-*oxo*-3-(*pyridin*-2-*ylthio*)-1-*azabicyclo*[3.2.0]-*heptane*-2-*carboxylate* (**12**; R^2 = *pNB*). From *p*-nitrobenzyl carboxylate (**4**) (0.26 g) and pyridine-2-thiol (0.22 g, 2 mol equiv.).

(2RS,3RS,5RS)-*Isomer* (2α,3α) (**47**) (0.148 g, 41%) had m.p. 138–139 °C (Found: C, 57.3; H, 4.3; N, 10.4%; M^+, 399.0890. $C_{19}H_{17}N_3O_5S$ requires C, 57.1; H, 4.3; N, 10.5%; *M*, 399.0888); ν_{max} 1 770, 1 750, 1 520, and 1 350 cm^{-1}; δ_H 2.34 (2 H, dd, *J* 8 and 6 Hz, 4-H_2), 2.84 (1 H, dd, *J* 16 and 3 Hz, 6-H$^{\beta}$), 3.43 (1 H, dd, *J* 16 and 6 Hz, 6-H$^{\alpha}$), 4.05–4.30 (1 H, m, 5-H), 4.77 (1 H, td, *J* 8 and 7 Hz, 3-H$^{\beta}$), 5.06 and 5.25 (2 H, ABq, *J* 13 Hz, CH_2Ar), 5.22 (1 H, d, *J* 7 Hz, 2-H$^{\beta}$), 6.92–7.55 (3 H, m, pyridyl-H_3), 7.28 (2 H, *J* 8 Hz) and 8.05 (2 H, *J* 8 Hz) (AA'BB'), and 8.39–8.46 (1 H, m, pyridyl-H).

The remaining isomers (0.094 g, 26%) were difficult to separate; small aliquots were purified for characterisation: (2RS,3SR,5RS)-*isomer* (2α,3β) remained a gum (Found: M^+, 399.0863); ν_{max} 1 765, 1 750sh, 1 520, and 1 350 cm^{-1}; δ_H 1.91 (1 H, ddd, *J* 12, 8, and 2 Hz, 4-H), 2.65–2.95 (1 H, ddd, 4-H), 2.80 (1 H, dd, *J* 15 and 3 Hz, 6-H$^{\beta}$), 3.35 (1 H, dd, *J* 15 and 6 Hz, 6-H$^{\alpha}$), 3.85–4.15 (3 H, m, 2-, 3-, and 5-H), 5.23 (2 H, s, CH_2Ar), 6.90–7.60 (3 H, m, pyridyl-H_3), 7.45 (2 H, *J* 8 Hz) and 8.15 (2 H, *J* 8 Hz) (AA'BB'), and 8.25 (1 H, m, pyridyl-H).

(2RS,3RS,5SR)-*Isomer* (2β,3β) had m.p. 172–174 °C (Found: M^+, 399.0902); ν_{max} 1 765, 1 740, 1 520, and 1 350 cm^{-1}; δ_H 1.86–2.54 (2 H, m, 4-H_2), 2.87 (1 H, dd, *J* 16 and 3 Hz, 6-H$^{\beta}$), 3.20 (1 H, dd, *J* 16 and 6 Hz, 6-H$^{\alpha}$), 3.70–3.95 (1 H, m, 5-H), 4.50 (1 H, d, *J* 7 Hz, 2-H$^{\alpha}$), 4.94 (1 H, ddd, *J* 12, 7, and 6 Hz, 3-H$^{\beta}$), 5.14 and 5.32 (2 H, ABq, *J* 14 Hz, CH_2Ar), 6.90–7.50 (3 H, m, pyridyl-H_3), 7.32 (2 H, *J* 8 Hz) and 8.08 (2 H, *J* 8 Hz) (AA'BB'), and 8.36–8.46 (1 H, m, pyridyl-H).

Benzyl (5RS,6SR,1'SR)-6-(1-*Hydroxyethyl*)-7-*oxo*-3-*phenylthio*-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate*. This was prepared from benzyl (5*RS*,6*SR*,1'*SR*)-6-(1-hydroxyethyl)-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (**13**)[6] (0.300 g) and thiophenol (0.12 ml). Chromatography of the crude products on silica gel, with ethyl acetate–light petroleum (1:1) as eluant, gave an inseparable mixture (0.204 g, 57%) of the (2*RS*,3*RS*,5*SR*,6*RS*,1'*RS*)-isomer (**14**) and (2*RS*,3*SR*,-5*SR*,6*RS*,1'*RS*)-isomer (**15**) (2:1 ratio) of the *title carboxylic ester*. This was a gum (Found: M^+, 397.1364. Calc. for $C_{22}H_{23}NO_4S$: *M*, 397.1346), ν_{max} 3 470, 1 760, 1 740, and 1 585 cm^{-1}; δ_H 1.28 [3 H, d, *J* 7 Hz, *Me*CH(OH)], 1.7–2.6 (3 H, m, 4-H_2 and OH), 3.02 [2/3 H, dd, *J* 6 and 3 Hz, 6-H$^{\beta}$ of isomer (**14**)], 3.21 [1/3 H, dd, *J* 6 and 2.5 Hz, 6-H$^{\beta}$ of isomer (**15**)], 3.7–4.3 [3 H, m, 3- and 5-H, and MeC*H*(OH)], 4.43 [1/3 H, d, *J* 4 Hz, 2-H$^{\beta}$ of isomer (**15**)], 4.76 [2/3 H, d, *J* 7 Hz, 2-H$^{\beta}$ of isomer (**14**)], 5.06 (2/3 H, s) and 5.15 (1/3 H, s) (CH_2Ph), and 7.1–7.5 (10 H, m, 2 × Ph).

Elution with ethyl acetate–light petroleum (7:3) gave the (2RS,3RS,5RS,6SR,1'SR)-*isomer* (**16**) (0.055 g, 15%), m.p. 111–112 °C (from EtOAc–light petroleum) (Found: C, 66.4; H, 6.1; N, 3.4. $C_{22}H_{23}NO_4S$ requires C, 66.5; H, 5.8; N, 3.5%); ν_{max} 3 480, 1 765, 1 740, and 1 585 cm^{-1}; δ_H 1.30 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 2.07 (1 H, td, *J* 12 and 10 Hz, 4-H), 2.14 (1 H, s, OH), 2.38 (1 H, dt, *J* 12 and 5 Hz, 4-H), 3.16 (1 H, dd, *J* 4.5 and 2.5 Hz, 6-H$^{\beta}$), 3.66 (1 H, ddd, *J* 10, 5, and 2.5 Hz, 5-H), 3.8–4.2 [2 H, m, 3-H$^{\alpha}$ and MeC*H*(OH)], 4.18 (1 H, d, *J* 7 Hz, 2-H$^{\alpha}$), 5.20 (2 H, s, CH_2Ph), and 7.1–7.4 (10 H, m, 2 × Ph).

Benzyl 3-(2-*Acetamidoethylthio*)-6-(1-*hydroxyethyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate* (**17**)–(**19**).—To a solution of benzyl (5*RS*,6*SR*,1'*SR*)-6-(1-hydroxyethyl)-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (**13**)[6] (0.440 g) in dry DMF (5 ml) under argon was added 2-acetamidoethanethiol (0.200 g), followed by powdered potassium carbonate (0.106 g). The mixture was stirred at room temperature for 1 h, then concentrated under reduced pressure, and the residue was partitioned between ethyl acetate and brine. The organic phase was dried and evaporated, and the residue was chromatographed on silica gel (Art. 7729) to give a mixture of three isomers of the *title sulphide* (0.517 g, 83%). Rechromatography [elution with ethanol–chloroform (1:9)] permitted partial separation. The three isomers eluted in the following order; pure isolated yields are quoted.

(2RS,3SR,5SR,6RS,1'RS)-*Isomer* (**18**) was obtained as a *chloroform hemisolvate* (0.256 g, 36%), m.p. 94–96 °C (from chloroform–light petroleum) (Found: C, 52.7; H, 5.8; N, 6.0%; M^+, 406.1562. $C_{20}H_{26}N_2O_5S \cdot 0.5CHCl_3$ requires C, 52.8; H, 5.7; N, 6.0%; *M*, 406.1562); ν_{max} 3 460, 3 380, 1 760, 1 665, and 1 515 cm^{-1}; δ_H 1.32 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 1.69 (1 H, dt, *J* 14 and 6 Hz, 4-H), 1.95 (3 H, s), 2.4–3.0 (4 H, m, 4-H, SCH_2, and OH), 3.18 (1 H, dd, *J* 5 and 2 Hz, 6-H$^{\beta}$), 3.2–3.5 (2 H, m, NCH_2), 3.73 (1 H, td, *J* 6 and 4 Hz, 3-H$^{\alpha}$), 3.85 (1 H, td, *J* 6 and 2 Hz, 5-H$^{\alpha}$), 4.0–4.3 [1 H, m, MeC*H*(OH)], 4.42 (1 H, d, *J* 4 Hz, 2-H$^{\beta}$), 5.17 (2 H, s, CH_2Ph), 6.10 (1 H, br s, NH), and 7.34 (5 H, s, Ph).

(2RS,3RS,5SR,6RS,1'RS)-*Isomer* (**17**) was isolated as a gum (0.122 g, 16%) (Found: M^+, 406.1542); ν_{max} 3 470, 2 980, 1 765, 1 670, and 1 515 cm^{-1}; δ_H 1.29 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 1.92 (3 H, s), 2.0–2.3 (2 H, m, 4-H_2), 2.68 (1 H, br s, OH), 2.57 and 2.76 (each 1 H, dt, *J* 12 and 6 Hz) (SCH_2), 3.05 (1 H, dd, *J* 5 and 3 Hz, 6-H$^{\beta}$), 3.32 (2 H, q, *J* 6 Hz, NCH_2), 3.53 (1 H, td, *J* 9 and 7 Hz, 3-H$^{\beta}$), 3.9–4.3 [2 H, m, 5-H$^{\alpha}$ and MeC*H*(OH)], 4.74 (1 H, d, *J* 7 Hz, 2-H$^{\beta}$), 5.17 (2 H, s, CH_2Ph), 6.10 (1 H, br s, NH), and 7.34 (5 H, s, Ph).

(2RS,3RS,5RS,6SR,1'SR)-*Isomer* (**19**) was also a gum (0.107 g, 14%) (Found: M^+, 406.1561); ν_{max} 3 480, 2 980, 1 770, 1 745, 1 675, and 1 515 cm^{-1}; δ_H 1.29 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 1.89 (1 H, td, *J* 12 and 10 Hz, 4-H), 1.90 (3 H, s), 2.27 (1 H, dt, *J* 12 and 6 Hz, 4-H), 2.53 and 2.71 (each 1 H, dt, *J* 12 and 6 Hz, SCH_2), 3.07 (1 H, dd, *J* 5 and 2 Hz, 6-H$^{\beta}$), 3.28 (2 H, q, *J* 6 Hz, NCH_2), 3.6–3.9 (2 H, m, 3-H$^{\alpha}$), 4.0–4.2 [1 H, m, MeC*H*(OH)], 4.11 (1 H, d, *J* 7 Hz, 2-H$^{\alpha}$), 5.19 (2 H, s, CH_2Ph), 6.03 (1 H, br s, NH), and 7.56 (5 H, s, Ph).

Conversion of (2RS,3RS,5SR)-p-*Nitrobenzyl* 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate* (**7**) *to its* (2RS,3SR,5RS)-*Epimer* (**6**).—To a solution of the ester (**7**) (0.048 g) in ethyl acetate (2 ml) was added DBU (0.0048 g). The solution darkened. After remaining at room temperature overnight, the solution was diluted with ethyl acetate, washed successively with water and brine, dried, and evaporated. The residue, now richer in ester isomer (**6**) (TLC) was redissolved in dichloromethane (2 ml), and the process was repeated. Evaporation gave a gum (0.029 g, 60%), identical (TLC, NMR) with the 3-epimer (**6**).

Similarly, the corresponding 2β,3β-benzyl ester (**8**) in

dichloromethane was converted into its 3α-epimer overnight in the presence of a catalytic amount of DBU.

p-Bromophenacyl 3-Ethylthio-6-[(E)-3-methoxycarbonylallyl]-7-oxo-1-azabicyclo[3.2.0]heptane-2-carboxylates.—These were prepared from *p*-bromophenacyl 8-oxo-7-azabicyclo-[4.2.0]oct-3-en-7-yl(triphenylphosphoranylidene)acetate[6] by a cyclisation–thiol addition sequence: a solution of the phosphorane (5.0 g) in ethyl acetate (400 ml) was treated at room temperature with TFA (80 ml) for 30 min. The solution was ozonolysed at −70 °C for 20 min, and triphenylphosphine (2.64 g, 1 mol equiv.) was added. The mixture was warmed to 0 °C, saturated aqueous sodium hydrogen carbonate was added cautiously, and neutralisation was completed by the addition of solid sodium hydrogen carbonate. The solution was washed with saturated aqueous sodium chloride and was then dried (Na_2SO_4). Methoxycarbonylmethylenetriphenylphosphorane (3.0 g, 1.1 mol equiv.) was added, and the solution was stirred at room temperature for 1 h. Evaporation gave *p*-bromophenacyl 6-[(*E*)-3-methoxycarbonylallyl]-7-oxo-1-azabicyclo[3.2.0]-hept-2-ene-2-carboxylate (**20**),[6] containing triphenylphosphine oxide.

To a solution of the crude ester (**20**) in DMF (15 ml) was added ethanethiol (0.485 g, 0.585 ml, 1 mol equiv.), together with finely ground, anhydrous potassium carbonate (1.08 g, 1 mol equiv.), and the suspension was stirred for 30 min. The reaction mixture was diluted with ethyl acetate, washed with brine, dried, and evaporated to give a gum (7.85 g), which was chromatographed on silica gel (Art. 7729) (20 × 4 cm). Elution of the column with ethyl acetate–light petroleum (1:5) gave the double-bond isomer of compound (**21**), *p-bromophenacyl* (2RS,3RS,5SR,6RS)-3-*ethylthio*-6-[(Z)-3-*methoxycarbonylallyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate*, which crystallised from ethyl acetate–light petroleum (1:1) as prisms (0.125 g, 3%), m.p. 92 °C (Found: C, 51.4; H, 4.8; N, 2.8; S, 6.4. $C_{22}H_{24}BrNO_6S$ requires C, 51.8; H, 4.7; N, 2.7; S, 6.3%); ν_{max} 1 765sh, 1 760, 1 720sh, 1 710, 1 650, and 1 590 cm^{-1}; δ_H(90 MHz) 1.25 (3 H, t, *J* 7 Hz), 2.20 (2 H, m, 4-H_2), 2.5–3.2 (2 H, m, 1′-H_2), 2.64 (2 H, q, *J* 7 Hz), 3.3–3.7 (2 H, m, 3-H^{β} and 6-H^{α}), 3.67 (3 H, s), 4.18 (1 H, m, $w_{\frac{1}{2}}$ 14 Hz, 5-H^{α}), 4.79 (1 H, d, *J* 7 Hz, 2-H^{β}), 5.17 (1 H, *J* 16 Hz) and 5.39 (1 H, *J* 16 Hz) (ABq), 5.85 (1 H, br d, *J* 11 Hz, 3′-H), 5.22 (1 H, ddd, *J* 11, 8, and 7 Hz, 2′-H), and 7.55 (2 H, *J* 8 Hz) and 7.74 (2 H, *J* 8 Hz) (AA′BB′). Irradiation at the frequency of the 2$^{\beta}$-proton located the resonance for the 3$^{\beta}$-proton at δ 3.50.

Continued elution [ethyl acetate–light petroleum (1:3)] gave a mixture of isomers (**21**) and (**22**) (1.912 g). Crystallisation (ethyl acetate–light petroleum) afforded the (2RS,3RS,5SR,-6RS)-*isomer* (**21**) of the *title compound* as needles (0.648 g, 16%), m.p. 133–134 °C (Found: C, 51.8; H, 4.5; N, 2.7; S, 6.3%); λ_{max}(EtOH) 218sh and 258 nm (ε 9 200); ν_{max} 1 760, 1 720sh, 1 710, 1 660, and 1 590 cm^{-1}; δ_H 1.24 (3 H, t, *J* 7 Hz), 2.05–2.30 (2 H, m, 4-H_2), 2.4–2.8 (2 H, m, 1′-H_2), 2.64 (2 H, q, *J* 7 Hz), 3.27–3.65 (2 H, m, 3- and 6-H^{β}), 3.69 (3 H, s), 4.05 (1 H, m, $w_{\frac{1}{2}}$ 13 Hz, 5-H^{α}), 4.80 (1 H, d, *J* 7 Hz, 2-H^{β}), 5.20 (1 H, *J* 17 Hz) and 5.41 (1 H, *J* 17 Hz) (ABq), 5.83 (1 H, br d, *J* 15 Hz, 3′-H), 6.87 (1 H, dt, *J* 15 and 6 Hz, 2′-H), and 7.56 (2 H, *J* 8 Hz) and 7.4 (2 H, *J* 8 Hz) (AA′BB′).

Rechromatography of the mother liquors gave mixed fractions (0.185 g), together with the pure (2*RS*,3*SR*,5*SR*,6*RS*)-isomer (**22**) as a foam (0.595 g, 15%), ν_{max} 1 760s, 1 720, 1 710, 1 660, and 1 590 cm^{-1}; δ_H1.28 (3 H, t, *J* 7 Hz), 1.2–2.3 (1 H, m, 4-H), 2.4–2.8 (3 H, m, 4-H and 1′-H_2), 2.72 (2 H, q, *J* 7 Hz), 3.6 (1 H, br m, 6-H^{α}), 3.72 (3 H, s), 4.1 (2 H, br m, 3- and 5-H^{α}), 4.46 (1 H, d, *J* 5 Hz, 2-H^{β}), 5.20 (1 H, *J* 17 Hz) and 5.41 (1 H, *J* 17 Hz) (ABq), 5.83 (1 H, br d, *J* 15 Hz, 3′-H), 6.87 (1 H, dt, *J* 15 and 6 Hz, 2′-H), and 7.58 (2 H, *J* 8 Hz) and 7.72 (2 H, *J* 8 Hz) (AA′BB′).

Finally, elution with ethyl acetate–light petroleum (1:1) provided the (2RS,3RS,5RS,6SR)-*isomer* (**23**) as a gum (0.750 g). Rechromatography, followed by trituration with ether, gave microcrystals (0.685 g, 17%), m.p. 86–88 °C (Found: C, 51.8; H, 4.7; N, 2.7; S, 6.0%); ν_{max} 1 765, 1 750, 1 720sh, 1 710, 1 660, and 1 590 cm^{-1}; δ_H 1.25 (3 H, t, *J* Hz), 2.10 (2 H, t, *J* 9 Hz, 4-H_2), 2.64 (4 H, m), 3.36 (1 H, m, $w_{\frac{1}{2}}$ 13 Hz, 6-H^{α}), 3.5–4.0 (2 H, m, 3- and 5-H^{α}), 3.69 (3 H, s), 4.23 (1 H, d, *J* 8 Hz, 2-H^{α}), 5.25 (1 H, *J* 18 Hz) and 5.45 (1 H, *J* 18 Hz) (ABq), 5.82 (1 H, br d, *J* 15 Hz, 3′-H), 6.87 (1 H, dt, *J* 15 and 6 Hz, 2′-H), and 7.55 (2 H, *J* 8 Hz) and 7.75 (2 H, *J* 8 Hz) (AA′BB′).

Total yield of thiol adducts was 2.238 g (56% overall from phosphorane).

Sodium 3-Ethylthio-6-[(E)-3-methoxycarbonylallyl]-7-oxo-1-azabicyclo[3.2.0]heptane-2-carboxylates.—(a) (2RS,3RS,5SR,6RS)-*Isomer* (**24**). A solution of *p*-bromophenacyl ester (**21**) (0.125 g) in anhydrous DMF (0.25 ml) was stirred with an excess of sodium thiophenoxide (0.020 g, ~1.5 mol equiv.) at 0 °C under argon for 3.5 h. Cold ether (10 ml) was added dropwise, and the solution was stirred at 0 °C for 30 min. The solution was decanted and the residue was washed well with further portions of cold, dry ether to give *sodium salt* (**24**) as the *DMF hemisolvate* (0.074 g, 65%), m.p. 215–218 °C [Found: C, 49.8; H, 5.5; N, 5.3%. $C_{14}H_{18}NNaO_5S \cdot 0.5HCON(CH_3)_2$ requires C, 50.0; H, 5.8; N, 5.7%]; ν_{max} 1 750, 1 720, 1 665 (DMF), 1 655sh, and 1 605 cm^{-1}; δ(D_2O) 1.09 (3 H, t, *J* 8 Hz), 1.98 (2 H, t, *J* 7 Hz, 4-H_2), 2.3–2.6 (2 H, m), 2.53 (2 H, q, *J* 8 Hz), 2.71 (s) and 2.87 (s) (together 3 H, DMF), 3.60 (3 H, s), 3.67 (1 H, q, *J* ~6 Hz, 6-H^{α}), 4.12 (1 H, q, *J* ~6 Hz, 5-H^{α}), 4.32 (2 H, d, *J* 7 Hz, 2-H^{α}), 5.85 (1 H, br d, *J* 16 Hz, 3′-H), 6.89 (1 H, dt, *J* 16 and 6 Hz, 2′-H), and 7.84 (0.5 H, br s, DMF).

Further evidence for the integrity of the sodium salt preparation was obtained by benzylation. A suspension of the salt (**24**) (0.02 g) in DMF (0.2 ml) was stirred with an excess of benzyl bromide (0.05 ml) overnight. Recovery and chromatography on silica gel (Art. 7729) [elution with ethyl acetate–light petroleum (1:4)] afforded the *benzyl ester* of compound (**24**) as a gum (0.019 g) (Found: M^+, 403.1450. $C_{21}H_{25}NO_5S$ requires *M*, 403.1453); ν_{max} 1 760, 1 735, 1 720, and 1 660 cm^{-1}; δ_H 1.18 (3 H, t, *J* 7 Hz), 2.0–2.30 (2 H, m, 4-H_2), 2.3–2.75 (2 H, m, 1′-H_2), 2.56 (2 H, q, *J* 7 Hz), 3.2–3.7 (2 H, m, 3-H^{β} and 6-H^{α}), 3.72 (3 H, s), ~4.1 (1 H, br m, 5-H^{α}), 4.69 (1 H, d, *J* 7 Hz, 2-H^{β}), 5.15 (2 H, s), 5.82 (1 H, br d, *J* 15 Hz, 3′-H), 6.85 (1 H, dt, *J* 15 and 6 Hz), and 7.33 (5 H, s, Ph).

(b) (2RS,3SR,5SR,6RS)-*Isomer* (**25**). This was prepared from *p*-bromophenacyl ester (**22**) (0.085 g) as described above: the sodium salt (**25**), an off-white powder (0.038 g), had ν_{max} 1 755, 1 720, and 1 600 cm^{-1}. The *benzyl ester* was a gum (Found: M^+, 403.1481); ν_{max} 1 765, 1 740, 1 725, and 1 655 cm^{-1}; δ_H 1.17 (3 H, t, *J* 7 Hz), 1.4–2.8 (2 H, m, 4-H_2), 2.4–2.8 (2 H, m, 1′-H_2), 2.55 (2 H, q, *J* 7 Hz), ~3.15 (1 H, m, 3-H^{α}), ~3.55 (1 H, m, 6-H^{α}), 3.68 (3 H, s), 4.96 (1 H, m, 5-H^{α}), 4.27 (1 H, d, *J* 6 Hz, 2-H^{β}), 5.14 (2 H, s), 5.80 (1 H, br d, *J* 15 Hz, 3′-H), 6.84 (1 H, m, 2-H), and 7.25 (5 H, s, Ph).

(c) (2RS,3RS,5RS,6SR)-*Isomer* (**26**). This was prepared from *p*-bromophenacyl ester (23) (0.077 g). The sodium salt was obtained as a gum (0.045 g), ν_{max} 1 750, 1 720, and 1 610 cm^{-1}. The *benzyl ester* crystallised from ethyl acetate–light petroleum as needles, m.p. 117 °C (Found: C, 62.1; H, 6.5; N, 3.4%; M^+, 403.1453. $C_{21}H_{25}NO_5S$ requires C, 62.5; H, 6.2; N, 3.5%; *M*, 403.1453); ν_{max} 1 765, 1 720, and 1 655 cm^{-1}; δ_H 1.17 (3 H, t, *J* 7 Hz), 1.9–2.1 (2 H, m, 4-H_2), 2.3–2.6 (2 H, m, 1′-H_2), 2.54 (2 H, q, *J* 7 Hz), 3.28 (1 H, m, 6-H^{α}), 3.5–3.9 (2 H, m, 3- and 5-H^{α}), 3.67 (3 H, s), 4.09 (1 H, d, *J* 8 Hz, 2-H^{α}), 5.13 (2 H, s), 5.69 (1 H, dt, *J* 15 and 1 Hz, 3′-H), 6.78 (1 H, dt, *J* 15 and 6 Hz, 2′-H), and 7.30 (5 H, s, Ph).

α-Chlorosulphoxidation Reaction.—(2RS,3SR,5RS)-*p-Nitrobenzyl 3-Chloro-3-[(SR)-ethylsulphinyl]-7-oxo-1-azabicyclo-*

[3.2.0]*heptane-2-carboxylate* (**27**).—*p*-Nitrobenzyl ester (**5**) (0.215 g, 0.61 mmol) was dissolved in chloroform (20 ml) and the solution was treated with pyridine (0.164 g, 2.07 mmol, 3.4 mol equiv.) and water (~ 0.110 g). The stirred mixture was cooled to −20 °C and freshly prepared IBD[14] (0.506 g, 1.84 mmol) was added. The mixture was stirred under argon for 45 min, then was concentrated under reduced pressure, and the residue was chromatographed on silica gel 60 (Art. 7729), with rapid elution with ethyl acetate–light petroleum (1:1–3:2). The single *α-chlorosulphoxide isomer* (**27**) was obtained as a white solid (0.147 g, 60%), which crystallised from ethyl acetate–light petroleum as needles, m.p. 104–108 °C (Found: C, 48.2; H, 4.3; N, 7.0. $C_{16}H_{17}ClN_2O_6S$ requires C, 47.95; H, 4.2; N, 7.0%); ν_{max} 1 780, 1 730, 1 522, and 1 350 cm^{-1}; δ_H 1.37 (3 H, t, *J* 7.5 Hz), 2.41 (1 H, dd, *J* 14 and 2 Hz, 4-H), 2.97 (1 H, dd, *J* 14 and 7 Hz, 4-H), 3.10 (2 H, q, *J* 7.5 Hz), 3.23 (1 H, dd, *J* 16 and 3 Hz, 6-H$^{\beta}$), 3.50 (1 H, dd, *J* 16 and 5.5 Hz, 6-H$^{\alpha}$), 4.15–4.40 (1 H, m, 5-H$^{\alpha}$), 5.06 (1 H, s, 2-H$^{\beta}$), 5.20 (2 H, s), and 7.50 (2 H, *J* 8 Hz) and 8.15 (2 H, *J* 8 Hz) (AA′BB′).

The following compounds (**28**)–(**30**) were prepared similarly, using IBD (2.2 mol equiv.), pyridine (3.3 mol equiv.), and water (>1 mol equiv.).

(2RS,3SR,5SR)-p-*Nitrobenzyl* 3-*Chloro*-3-[(SR)-*ethylsulphinyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate* (**28**). This was prepared from 2β-*p*-nitrobenzyl ester (**7**) (0.072 g) (−20 to 0 °C; 30 min; and 0 °C, 1 h). The title α-chloro sulphoxide (**28**) was obtained as a gum (0.060 g, 73%), ν_{max} 1 775, 1 742, 1 522, and 1 345 cm^{-1}; δ_H 1.37 (3 H, t, *J* 7 Hz), 2.31 (1 H, dd, *J* 13 and 5 Hz, 4-H), 2.59 (1 H, dd, *J* 13 and 9 Hz, 4-H), 2.90 (1 H, dd, *J* 16 and 2 Hz, 6-H$^{\beta}$), 3.24 (1 H, dd, *J* 16 and 5 Hz, 6-H$^{\alpha}$), ~3.0 (2 H, m, SC*H*$_2$Me), 4.12–4.38 (1 H, m, 5-H$^{\alpha}$), 4.43 (1 H, s, 2-H$^{\alpha}$), 5.29 (2 H, s), and 7.53 (2 H, *J* 8 Hz) and 8.05 (2 H, *J* 8 Hz) (AA′BB′). Lack of stability necessitated its immediate conversion into dehydro derivative (**32**).

(2RS,3SR,5SR,6RS,1′RS)-*Benzyl* 3-*Chloro*-6-(1-*hydroxyethyl*)-7-*oxo*-3-[(SR)-*phenylsulphinyl*]-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate* (**29**). This was prepared from a (2:1) mixture of 2α,3α-(**14**), and 2α,3β-(**15**) thiophenol adducts (2 h). The *title α-chloro sulphoxide* (**29**) crystallised from chloroform–light petroleum as needles (48%), m.p. 154–159 °C (Found: C, 58.9; H, 4.7; N, 3.2. $C_{22}H_{22}ClNO_5S$ requires C, 59.0; H, 5.0; N, 3.1%); ν_{max} 3 480, 1 780, and 1 745 cm^{-1}; δ_H 1.28 (3 H, d, *J* 6 Hz, Me), 1.77 (1 H, br d, *J* 15 Hz, 4-H), 1.87 (1 H, br s, OH), 2.92 (1 H, dd, *J* 15 and 9 Hz, 4-H), 3.42 (1 H, dd, *J* 5 and 3 Hz, 6-H$^{\beta}$), 3.9–4.3 [2 H, m, 5-H and MeC*H*(OH)], 5.05 (1 H, s, 2-H$^{\beta}$), 5.25 (2 H, s, C*H*$_2$Ph), and 7.1–7.7 (10 H, m, 2 × Ph).

(2RS,3SR,5RS,6SR,1′SR)-*Benzyl* 3-*Chloro*-6-(1-*hydroxyethyl*)-7-*oxo*-3-[(SR)-*phenylsulphinyl*]-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate* (**30**). The preparation from 2β,3β-thiophenol adduct (**16**) required 5 h at room temperature for completion. The *title α-chloro sulphoxide* (**30**) (67%) crystallised from ethyl acetate–light petroleum, m.p. 141–143 °C (Found: C, 58.7; H, 4.8; N, 3.1%); ν_{max} 3 480, 1 780, and 1 740 cm^{-1}; δ_H 1.32 (3 H, d, *J* 16 Hz, Me), 1.70 (1 H, dd, *J* 12.5 and 5 Hz, 4-H), 2.02 (1 H, br s, OH), 2.53 (1 H, dd, *J* 12.5 and 9 Hz, 4-H), 3.25 (1 H, dd, *J* 15 and 2.5 Hz, 6-H$^{\beta}$), 3.9–4.3 [2 H, m, 5-H and MeC*H*(OH)], 4.45 (1 H, s, 2-H$^{\alpha}$), 5.30 (2 H, s, C*H*$_2$Ph), and 7.2–7.8 (10 H, m, 2 × Ph).

Dehydrochlorination Reactions of α-Chloro Sulphoxides.—(5RS)-p-*Nitrobenzyl* 3-[(SR)-*Ethylsulphinyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**31**). A stirred solution of the chloro sulphoxide (**27**) (0.147 g, 0.272 mmol) in ethyl acetate (30 ml) at room temperature was treated with DBU (0.056 g, 0.272 mmol, 1 mol equiv.). After 10 min, the mixture was washed successively with water and brine, dried, and evaporated. The resulting gum was triturated with ether, and the white solid was crystallised from ethyl acetate–light petroleum to give the *title sulphoxide* (**31**) as a single isomer (0.114 g, 100%), m.p. 111–112 °C (decomp.) (Found: C, 52.45; H, 4.6; N, 7.75. $C_{16}H_{16}N_2O_6S$ requires C, 52.75; H, 4.40; N, 7.7%); λ_{max}(EtOH) 268 (ε 12 200) and ~310infl nm (6 500); ν_{max} 1 790s, 1 718w, 1 522, 1 350, and 1 322 cm^{-1}; δ_H 1.36 (3 H, t, *J* 7 Hz), 2.92 (2 H, q, *J* 7.5 Hz), 3.09 (1 H, dd, *J* 16.5 and 2.5 Hz, 6-H$^{\beta}$), 3.21 (2 H, d, *J* 8 Hz, 4-H$_2$), 3.56 (1 H, dd, *J* 16.5 and 5.5 Hz, 6-H$^{\alpha}$), 4.11–4.45 (1 H, m, 5-H$^{\alpha}$), 5.22 (1 H, *J* 14 Hz) and 5.42 (1 H, *J* 14 Hz) (ABq), and 7.57 (2 H, *J* 8 Hz) and 8.16 (2 H, *J* 8 Hz) (AA′BB′).

The following Δ^2-esters (**32**)–(**34**) were prepared similarly. In this series, the final products decomposed when chromatographed on silica gel or 'Florisil'. They were, however, obtained in high purity after an aqeuous 'wash'. Crystalline compounds were stable; non-crystalline products were best stored in ethyl acetate solution at 0 °C.

(5RS)-p-*Nitrobenzyl* 3-[(RS)-*Ethylsulphinyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**32**). This was prepared from chloro sulphoxide (**28**) (0.077 g). Recovery and crystallisation from ethyl acetate–light petroleum gave the *title sulphoxide* (0.049 g, 70%), m.p. 110–113.5 °C (Found: C, 52.5; H, 4.4; N, 7.6%); λ_{max}(EtOH) 269 (ε 11 300) and 310infl nm (6 500); ν_{max} 1 795, 1 720br w, 1 525, 1 350, and 1 320 cm^{-1}; δ_H 1.35 (3 H, t, *J* 7.5 Hz), 2.93 (2 H, q, *J* 7.5 Hz), 3.03 (1 H, dd, *J* 16 and 2.5 Hz, 6-H$^{\beta}$), 3.07 (1 H, dd, *J* 19 and 7.5 Hz, 4-H), 3.57 (1 H, dd, *J* 19 and 9.5 Hz, 4-H), 4.20–4.53 (1 H, m, 5-H$^{\alpha}$), 5.21 (1 H, *J* 14 Hz) and 5.45 (1 H, *J* 14 Hz) (ABq), and 7.55 (2 H, *J* 8 Hz) and 8.17 (2 H, d, *J* 8 Hz) (AA′BB′).

(5RS,6SR,1′SR)-*Benzyl* 6-(1-*Hydroxyethyl*)-7-*oxo*-3-[(RS)-*phenylsulphinyl*]-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**33**). This was prepared from a suspension of α-chloro sulphoxide isomer (**29**) (0.031 g) in ethyl acetate, and DBU (0.011 g). Crystallisation from ethyl acetate–light petroleum gave the *title sulphoxide* (**33**) (0.015 g, 53%) as a *hydrate*, m.p. 104–109 °C (Found: C, 62.0; H, 5.4; N, 3.1. $C_{22}H_{21}NO_5S \cdot H_2O$ requires C, 61.5; H, 5.4; N, 3.25%); λ_{max}(EtOH) 302 nm; ν_{max} 3 420, 1 790, 1 730, 1 625, and 1 590 cm^{-1}; δ_H 1.32 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 1.80 (1 H, br s, OH), 2.73 (1 H, dd, *J* 19 and 11 Hz, 4-H), 3.26 (1 H, dd, *J* 19 and 8 Hz, 4-H), 3.39 (1 H, dd, *J* 4 and 2 Hz, 6-H$^{\beta}$), 3.9–4.3 [2 H, m, 5-H and MeC*H*(OH)], 5.28 (1 H, *J* 12 Hz) and 5.45 (1 H, *J* 12 Hz) (ABq, C*H*$_2$Ph), and 7.2–7.7 (10 H, m, 2 × Ph); *m/z* (EI) 393.1058 $(M - H_2O)^+$. $C_{22}H_{19}NO_4S$ requires *m/z*, 393.1032.

(5RS,6SR,1′SR)-*Benzyl* 6-(1-*Hydroxyethyl*)-7-*oxo*-3-[(SR)-*phenylsulphinyl*]-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**34**). This was obtained as a gum from α-chloro sulphoxide isomer (**30**) in quantitative yield, λ_{max}(EtOH) 298 nm; ν_{max} 3 430, 1 790, and 1 725 cm^{-1}; δ_H 1.29 (3 H, d, *J* 7 Hz), 1.88 (1 H, br s, OH), 2.49 (1 H, dd, *J* 18 and 8 Hz, 4-H), 3.12 (1 H, dd, *J* 5 and 3 Hz, 6-H$^{\beta}$), 3.48 (1 H, dd, *J* 18 and 10.5 Hz, 4-H), 3.9–4.5 [2 H, m, 5-H and MeC*H*(OH)], 5.36 (2 H, s, C*H*$_2$Ph), and 7.2–7.8 (10 H, m, 2 × Ph).

(2RS,5RS)-p-*Nitrobenzyl* 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-3-*ene*-2-*carboxylate* (**35**).—*Method A*. To a solution of ester (**5**) [(2*RS*,3*RS*,5*RS*)-isomer] (0.28 g, 0.80 mmol) in sodium-dried benzene (12 ml) at room temperature was added dry pyridine (0.14 g, 1.77 mmol, 2.2 mol equiv.) under argon. The solution was cooled (+4 °C) close to its freezing point and IBD[14] (0.245 g, 0.88 mmol, 1.1 mol equiv.) was added in one portion. The mixture was stirred rapidly to give a clear solution, which was stored in a refrigerator (+8 °C) for 2.25 h. The reaction mixture was filtered through Kieselguhr and the orange filtrate was reduced in volume (~2 ml). Rapid chromatography on silica gel 60 (Art. 7729) with ethyl acetate–light petroleum (1:1) as eluant gave the *title* Δ^3-*vinyl sulphide* (**35**) (0.159 g), contaminated with a trace of ester (**5**). Addition of diethyl ether afforded pure compound (**35**) as white crystals (0.13 g, 46%), m.p. 82–82.5 °C (Found: C, 55.1; H, 4.8; N, 8.0. $C_{16}H_{16}N_2O_5S$ requires C, 55.14; H, 4.60; N, 8.05%); ν_{max} 1 780,

1 760, 1 575 (vinyl sulphide), 1 530, and 1 355 cm^{-1}; δ_H 1.31 (3 H, t, *J* 7 Hz), 2.83 (2 H, q, *J* 7 Hz), ~2.9 (1 H, m, 6-H$^{\beta}$), 3.42 (1 H, dd, *J* 16 and 5 Hz, 6-H$^{\alpha}$), 4.54–4.70 (1 H, m, 5-H), 5.17 (1 H, dd, *J* 3.5 and 1.5 Hz, 2-H$^{\beta}$), 5.30 (2 H, s, CH_2Ar), 5.80 (1 H, dd, *J* ~1.5 and 1.5 Hz, 4-H), and 7.55 (2 H, *J* 8.5 Hz) and 8.24 (2 H, 8.5 Hz) (AA'BB).

In similar experiments we sometimes isolated small quantities (~5–10%) of the more polar, isomeric Δ^2-vinyl sulphide (**37**) (*vide infra*).

Method B. The procedure was as described in Method A using ester (**5**) (0.070 g, 0.20 mmol), except that NCS (0.030 g, 0.22 mmol, 1.1 mol equiv.) was added in place of IBD. The clear solution was kept in the refrigerator for 24 h, and then at room temperature for 4 h. Work-up and chromatography gave Δ^3-vinyl sulphide (**35**) (0.032 g, 45%), identical with the previous sample in all respects.

Method C. To a solution of *p*-nitrobenzyl ester (**5**) (0.080 g) in anhydrous dichloromethane (6 ml) under argon was added dry pyridine (0.044 g). The stirred solution was cooled to −70 °C and treated with a solution of chlorine (0.018 g) in dry tetrachloromethane (0.25 ml). The reaction vessel was placed in an ice-bath (20 min) and then in a refrigerator (1.5 h). Work-up and chromatography provided the title compound (**35**) (0.042 g).

Reaction with (2RS,3SR,5RS)-*Isomer* (**6**).—A solution of the carboxylic ester (**6**) (0.11 g) in dry benzene (6 ml) was treated with IBD (0.94 g) in the presence of pyridine according to Method A. The title compound (**35**) (0.42 g, 38%) was obtained. A similar experiment with isomer (**6**) (0.220 g), employing chloroform as the solvent, together with an excess of IBD (0.347 g, 2 mol equiv.) in the presence of pyridine (0.15 ml), led to the isolation of (2RS,5RS)-p-*nitrobenzyl* 4-*chloro*-3-*ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-3-*ene*-2-*carboxylate* (0.011 g, 5%), m.p. 114–119 °C (from Et_2O) (Found: M^+, 382.0396. $C_{16}H_{15}ClNO_5S$ requires *M*, 382.0390); ν_{max} 1 785, 1 755, 1 522, and 1 345 cm^{-1}; δ_H 1.20 (3 H, t, *J* 8 Hz), 2.85 (2 H, q, *J* 8 Hz, CH_2Me), 3.00 (1 H, dd, *J* 16.5 and 2.5 Hz, 6-H$^{\beta}$), 3.45 (1 H, dd, *J* 16.5 and 5 Hz, 6-H$^{\alpha}$), 4.25 (1 H, ddd, *J* 2.5 and ~2 Hz, 5-H), 5.15 (1 H, d, *J* 2.5 Hz, 2-H$^{\beta}$), 5.26 (2 H, s, CH_2Ar), and 7.48 (2 H, *J* 8.5 Hz) and 8.25 (2 H, *J* 8.5 Hz) (AA'BB'). We consider this material to arise as a consequence of overchlorination of the double bond present in product (**35**). [The second product obtained was the Δ^3-vinyl sulphide (**35**) (0.034 g).]

(2RS,5SR)-p-*Nitrobenzyl* 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-3-*ene*-2-*carboxylate* (**36**).—A solution of the (2*RS*,3*RS*,5*SR*)-*p*-nitrobenzyl isomer (**7**) (0.07 g) in dry benzene (3 ml) under argon was treated with IBD (0.06 g) in the presence of pyridine (0.035 g) according to Method A. The chromatographed Δ^3-*vinyl sulphide* (**36**) was crystallised from ether to give a microcrystalline solid (0.030 g, 43%), m.p. 106–107 °C (Found: C, 55.0; H, 4.6; N, 7.9. $C_{16}H_{16}N_2O_5S$ requires C, 55.14; H, 4.60; N, 8.05%); ν_{max} 1 778, 1 750, 1 575w (vinyl sulphide), 1 522, and 1 350 cm^{-1}; δ_H 1.30 (3 H, t, *J* 7 Hz), 2.82 (2 H, q, *J* 7 Hz), 2.93 (1 H, dd, *J* 15.5 and 2.5 Hz, 6-H$^{\beta}$), 3.18 (1 H, ddd, *J* 15.5, 4.5, and 1.5 Hz, 6-H$^{\alpha}$), 4.34–4.62 (2 H, 2- and 5-H$^{\alpha}$), 5.19 and 5.38 (2 H, ABq, *J* 15 Hz, CH_2Ar), 5.77 [1 H, dd, *J* ~1.5 and 1.5 Hz (collapsing to s on irradiation at the signal centred δ 4.50), 4-H], and 7.55 (2 H, *J* 8.5 Hz) and 8.50 (2 H, *J* 8.5 Hz) (AA'BB').

Conversion of (2RS,5SR)-p-*Nitrobenzyl* 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-3-*ene*-2-*carboxylate* (**36**) *into its* (2RS,5RS)-*Epimer* (**35**).—To a solution of the 2β-carboxylic ester (**36**) (0.004 g) in dry dichloromethane (0.5 ml) at room temperature was added DBU (~1 mg). After 5 min, TLC indicated that complete conversion into the 2α-epimer (**35**) had occurred. After 4 h, the corresponding Δ^2-isomer (**37**) (*vide infra*; following experiment) was evident. Its presence in the equilibrium mixture was confirmed by the UV spectrum [λ_{max}(EtOH) 320 nm].

(5RS)-p-*Nitrobenzyl* 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**37**).—A solution of the Δ^3-2α-carboxylate (**35**) (0.208 g) in dry dichloromethane at ambient temperature under argon was stirred in the presence of DBU (0.034 g, 0.4 mol equiv.) for 2.5 h. The yellow solution was washed with brine, filtered, and evaporated. Chromatography on 'Florisil' (15 g; 200–300 Mesh) with ethyl acetate–light petroleum (1:1) as eluant gave recovered ester (**35**) (0.10 g, 48% recovery) followed by the *title* Δ^2-*carboxylic ester* (**37**) as yellow plates (0.060 g, 29%), m.p. 134.5–139 °C (from EtOAc–light petroleum) (Found: C, 54.9; H, 4.8; N, 8.0. $C_{16}H_{16}N_2O_5S$ requires C, 55.14; H, 4.60; N, 8.05%); λ_{max}(EtOH) 268 (ε 10 300) and 320 nm (12 200); ν_{max} 1 780, 1 700, 1 550w, 1 520, and 1 345 cm^{-1}; δ_H 1.32 (3 H, t, *J* 7.5 Hz), 2.85 (2 H, q, *J* 7.5 Hz), 2.93 (1 H, dd, *J* 16 and 2.5 Hz, 6-H$^{\beta}$), 2.99 (1 H, dd, *J* 18 and 8.5 Hz, 4-H), 3.28 (1 H, dd, *J* 18 and 8.5 Hz, 4-H), 3.49 (1 H, dd, *J* 16 and 5.5 Hz, 6-H$^{\alpha}$), 4.23 (1 H, tdd, *J* 8.5, 5.5, and 2.5 Hz, 5-H), 5.22 and 5.48 (2 H, ABq, *J* 14 Hz, CH_2Ar), and 7.62 (2 H, d, *J* 8 Hz) and 8.20 (2 H, d, *J* 8 Hz) (AA'BB').

Sodium 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**40**).—A catalyst of 5% palladium on charcoal (0.073 g), suspended in dioxane–water (2:1) (10 ml) was prehydrogenated (H_2, 1 atm) at room temperature for 20 min. A solution of the Δ^2-*p*-nitrobenzyl ester (**37**) (0.060 g) in dioxane (4 ml) was added to the catalyst suspension. After the mixture had been shaken under hydrogen for 3 h, aq. sodium hydrogen carbonate (0.0145 g in 2 ml) was added, and the catalyst was removed by filtration on Kieselguhr. The filtrand was washed well with further portions of water, the combined filtrate and washings were evaporated to remove dioxane and the cloudy aqueous residue was shaken with ethyl acetate (×2). The aqueous phase was concentrated by evaporation at room temperature and the residue was chromatographed on Bio-Gel® P2, and eluted with deionised water containing butan-1-ol (1%). The fractions were monitored by UV spectroscopy. Those containing the title salt (λ_{max} 295 nm) were combined and evaporated. Re-evaporation from ethanol (×3) and then toluene gave the salt (**40**) as a pale yellow, hygroscopic solid (0.020 g, 49%), ν_{max}(KBr) 1 750br and 1 600 cm^{-1}; λ_{max}(EtOH) 295 nm. The salt was characterised by conversion into its phthalidyl ester (*vide infra*).

(2RS,5RS)-*Sodium* 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-3-*ene*-2-*carboxylate* (**38**).—This was prepared from Δ^3-2α-carboxylic ester (**35**) (0.400 g) (30 min), and was obtained as a pale yellow solid (0.243 g, 90%); ν_{max}(KBr) 1 762 and 1 612 cm^{-1}; $\delta_H(D_2O)$ 1.25 (3 H, t, *J* 7.5 Hz), 2.85 (2 H, q, *J* 7.5 Hz), 2.86 (1 H, dd, *J* 17 and 2.5 Hz, 6-H$^{\beta}$), 3.40 (1 H, dd, *J* 17 and 5 Hz, 6-H$^{\alpha}$), 4.80 (1 H, m, 2-H$^{\beta}$), 5.85 (1 H, m, 4-H), and ~4.6 (1 H, m, 5-H).

(2RS,5SR)-*Sodium* 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-3-*ene*-2-*carboxylate* (**39**).—This was prepared from Δ^3-2β-carboxylic ester (**36**) (0.025 g). The title salt was obtained as a pale yellow solid (0.006 g, 36%); ν_{max}(KBr) 1 760–1 750br and 1 620–1 610 cm^{-1}; $\delta_H(D_2O)$ 1.29 (3 H, t, *J* 7.5 Hz), 2.65–3.40 [4 H, including 2.87 (2 H, q, *J* 7.5 Hz), and 6-H_2], 5.88 (1 H, br s, 4-H), and ~4.5 (2 H, m, 2-H$^{\alpha}$ and 5-H).

Phthalidyl 3-*Ethylthio*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate*.—*Method A.* A suspension of the Δ^2-sodium salt (**40**) (0.0056 g) in dry DMF (2 ml) was stirred with bromophthalide (0.005 g) at room temperature for 1.5 h. The mixture was diluted with ethyl acetate, washed successively with water

and brine, and the filtrate was dried and evaporated. Chromatography on 'Florisil' (2 g; 200–400 Mesh) with ethyl acetate–light petroleum (1:1) as eluant gave the epimeric phthalide esters of compound (**40**) as a white solid (2.8 mg) (from Et_2O), identical (TLC, UV, IR) with the mixture of epimers described below.

Method B by isomerisation of the Δ^3*-phthalidyl esters of compound* (**38**). A solution of the esters (*vide infra*) (0.090 g) in dichloromethane (4 ml) was stirred in the presence of DBU (0.017 g) under argon at room temperature for 2.5 h. The yellow solution was washed with brine, and the organic layer was dried and evaporated. Chromatography on silica gel (Art. 9385; 5 g) with ethyl acetate–light petroleum (1:1) as eluant gave recovered Δ^3-esters (0.021 g). Elution with ethyl acetate afforded a gum; trituration with ether gave the Δ^2-phthalidyl ester epimers of compound (**40**) (1:1 ratio) as a white solid (0.0225 g). The ethereal washings on evaporation gave a further amount of starting material (0.007 g).

On other occasions the phthalidyl esters of compound (**40**) were separated by chromatography. The *least polar isomer* was obtained as white crystals, m.p. 175–185 °C (decomp.) (from EtOAc) (Found: C, 59.1; H, 4.4; N, 4.0%; M^+, 345.0665. $C_{17}H_{15}NO_5S$ requires C, 59.1; H, 4.35; N, 4.1%; *M*, 345.0669); λ_{max}(EtOH) 230 (ε 11 800), 274 (2 780), and 329 nm (13 500); ν_{max} 1 790 and 1 720 cm^{-1}; δ_H 1.35 (3 H, t, *J* 7.5 Hz), 2.88 (2 H, q, *J* 7.5 Hz), 2.90 (1 H, dd, *J* 16 and 2.5 Hz, 6-H$^{\beta}$), 2.98 (1 H, dd, *J* 18 and 8 Hz, 4-H), 3.32 (1 H, dd, *J* 18 and 8.5 Hz, 4-H), 3.45 (1 H, dd, *J* 16 and 6 Hz, 6-H$^{\alpha}$), 4.00–4.35 (1 H, m, 5-H), 7.44 (1 H, s, OCHO), and 7.37–7.90 (4 H, ArH).

The *more polar isomer* was obtained as prisms, m.p. 172–175 °C (from EtOAc) (Found: C, 58.8; H, 4.3; N, 4.0%); λ_{max}(EtOH) 230 (ε 10 050), 282 (2 400), and 328 nm (10 470); ν_{max} 1 790 and 1 720 cm^{-1}; δ_H 1.30 (3 H, t, *J* 7.5 Hz), 2.84 (2 H, q, *J* 7.5 Hz), 2.88 (1 H, dd, *J* 16 and 3 Hz, 6-H$^{\beta}$), 2.99 (1 H, dd, *J* 18 and 8.5 Hz, 4-H), 3.28 (1 H, dd, *J* 18 and 8.5 Hz, 4-H), 3.45 (1 H, dd, *J* 16 and 5.5 Hz, 6-H$^{\alpha}$), 4.00–4.35 (1 H, m, 5-H), 7.49 (1 H, s, OCHO), and 7.40–7.97 (4 H, m, ArH).

(2RS,5RS)-*Phthalidyl 3-Ethylthio-7-oxo-1-azabicyclo*[3.2.0]*hept-3-ene-2-carboxylate*.—This was prepared from Δ^3-sodium salt (**38**) (0.114 g) as described in method A. The title ester, a 1:1 mixture of phthalide epimers, remained a gum (0.108 g) (Found: M^+, 345.0667. Calc. for $C_{17}H_{15}NO_5S$: *M*, 345.0669); ν_{max} 1 790 and 1 780 cm^{-1}; δ_H 1.28 and 1.30 (together 3 H, each t, *J* 7.5 Hz), 2.81 and 2.82 (together 2 H, each q, *J* 7.5 Hz), 2.83 (1 H, dd, *J* 16 and 2.5 Hz, 6-H$^{\beta}$), 3.39 (1 H, dd, *J* 16 and 5.5 Hz, 6-H$^{\alpha}$), 4.60 (1 H, m, 5-H), 5.12 (1 H, dd, *J* 3 and 2 Hz, 2-H$^{\beta}$), 5.80 (1 H, dd, *J* 3 and 2 Hz, 4-H), 7.40 (1 H, s, CO_2CH), and 7.40–8.00 (4 H, ArH).

p-*Nitrobenzyl Crotonate* (**41**).—A suspension of crotonic acid (2.0 g) in DMF (20 ml) was cooled to 0 °C. Triethylamine (2.8 g, 3.9 ml) was added, followed by *p*-nitrobenzyl bromide (5.0 g), and the solution was stirred at room temperature for 1.5 h. The mixture was diluted with ethyl acetate, washed successively with water (×2) and brine (×2), and the organic layer was dried ($MgSO_4$). Evaporation gave a solid, which was crystallised from ethyl acetate–light petroleum to give *ester* (**41**) as off-white crystals (4.22 g, 82%), m.p. 84–85 °C (Found: C, 59.6; H, 4.9; N, 6.2. $C_{11}H_{11}NO_4$ requires C, 59.7; H, 5.0; N, 6.3%); λ_{max}(EtOH) 264 nm (ε 10 000); ν_{max} 1 720, 1 660, 1 610, 1 525, and 1 350 cm^{-1}; δ_H(90 MHz) 1.90 (3 H, dd, *J* 7 and 2 Hz), 5.27 (2 H, s), 5.88 (1 H, dq, *J* 16 and 1 Hz, 2-H), 7.07 (1 H, dq, *J* 16 and 7 Hz, 3-H), and 7.52 (2 H, *J* 9 Hz) and 8.20 (2 H, *J* 9 Hz) (AA′BB′).

p-*Nitrobenzyl* 3-(*Ethylthio*)*butanoate* (**42**).—A solution of the crotonate ester (**41**) (1.0 g) in DMF (3 ml) was stirred with ethanethiol (0.280 g, 0.335 ml) in the presence of potassium carbonate (0.063 g, 0.1 mol equiv.) at room temperature for 15 min. The mixture was diluted with ethyl acetate, washed well with water and brine successively, and was dried. Evaporation gave the *ester* (**42**) as an oil (1.250 g, 97%) (Found: M^+, 283.0859. $C_{13}H_{17}NO_4S$ requires *M*, 283.0878); ν_{max} 1 735, 1 610, 1 525, and 1 350 cm^{-1}; δ_H(90 MHz) 1.23 (3 H, t, *J* 7.5 Hz, SCH_2Me), 1.33 (3 H, d, *J* 7 Hz, 4-H_3), 2.49 (1 H, dd, *J* 15 and 7 Hz) and 2.71 (1 H, dd, *J* 15 and 7 Hz) (2-H_2), 2.56 (2 H, q, *J* 7.5 Hz, SCH_2Me) 3.23 (1 H, quin., *J* 7 Hz, 3-H), 5.23 (2 H, s), and 7.52 (2 H, *J* 9 Hz) and 8.21 (2 H, *J* 9 Hz) (AA′BB′).

p-*Nitrobenzyl* 3-(*Ethylthio*)*but-2-enoate* (**43**).—A solution of the 3-(ethylthio)butanoate ester (**42**) (0.20 g) in dry benzene (3 ml) containing pyridine (0.056 g, 2 mol equiv.) was cooled to 5 °C. IBD (0.097 g, 1 mol equiv.) was added, and the mixture was stirred for 2 h. The crude reaction mixture was chromatographed rapidly on silica gel 60 (Art. 7729) (8 × 2 cm) with ethyl acetate–light petroleum (1:19) as eluant to give *inter alia* the *Z-isomer* of the *title ester*. It crystallised (ethyl acetate–light petroleum) as microcrystals (0.065 g, 33%), m.p. 94–96 °C (Found: C, 55.7; H, 5.2; N, 4.9; S, 11.2. $C_{13}H_{15}NO_4S$ requires C, 55.5; H, 5.4; N, 5.0; S, 11.4%); λ_{max}(EtOH) 216infl (ε 7 700) and 278 nm (25 400); ν_{max} 1 710, 1 610sh, 1 595, 1 520, 1 350, and 1 175 cm^{-1}; δ_H(90 MHz) 1.36 (3 H, t, *J* 7.5 Hz, SCH_2Me), 2.39 (3 H, s, 4-H_3), 2.84 (2 H, q, *J* 7.5 Hz, SCH_2Me), 5.24 (2 H, s), 5.58 (1 H, s, 2-H), and 7.51 (2 H, *J* 9 Hz) and 8.20 (2 H, *J* 9 Hz) (AA′BB′).

Later fractions were crystallised from ethyl acetate–light petroleum to give the E-*isomer* of the *title ester* as needles (0.058 g, 29%), m.p. 107–110 °C (Found: C, 55.4; H, 5.4; N, 4.9; S, 10.9%); λ_{max}(EtOH) 216infl (ε 8 300) and 290 nm (18 500); ν_{max} 1 695, 1 610, 1 580, 1 525, 1 350, and 1 175 cm^{-1}; δ_H 1.32 (3 H, s, *J* 7.5 Hz, SCH_2Me), 2.25 (3 H, d, *J* ~1 Hz, 4-H_3), 2.89 (2 H, q, *J* 7.5 Hz, SCH_2Me), 5.24 (2 H, s), 5.85 (1 H, q, *J* <1 Hz, 2-H), and 7.50 (2 H, *J* 9 Hz) and 8.20 (2 H, *J* 9 Hz) (AA′BB′).

p-*Nitrobenzyl Cyclopentene-1-carboxylate* (**44**).—A suspension of cyclopentene-1-carboxylic acid[17] (0.5 g) (Pfalz and Bauer) in DMF (3 ml) was stirred in the presence of triethylamine (1 ml) at room temperature until homogeneous. *p*-Nitrobenzyl bromide (1.08 g) was added, and the mixture was stirred for 2.5 h, then diluted with ethyl acetate, and washed successively with 0.5M-hydrochloric acid, aqueous sodium hydrogen carbonate, and brine, and dried. Evaporation gave ester (**44**) as a brown solid, which was recrystallised from diethyl ether–light petroleum as off-white needles (0.780 g, 71%), m.p. 78 °C (lit.,[18] 74–76 °C) (Found: C, 62.85; H, 5.45; N, 5.6. Calc. for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.3; N, 5.7%); ν_{max} 1 710, 1 630, 1 610, 1 520, and 1 350 cm^{-1}; δ_H(90 MHz) 1.85–2.3 (2 H, m), 2.4–2.9 (4 H, m), 5.36 (2 H, s), 7.00 (1 H, br s, 2-H), and 7.64 (2 H, *J* 9 Hz) and 8.34 (2 H, *J* 9 Hz) (AA′BB).

p-*Nitrobenzyl* 2-*Ethylthiocyclopentanecarboxylate* (**45**).—Ester (**44**) (0.650 g) in DMF (8 ml) was stirred with ethanethiol (0.164 g, 0.195 ml) in the presence of potassium carbonate (0.030 g) at room temperature for 15 min. The mixture was diluted with ethyl acetate, washed with brine, and dried. Evaporation and chromatography of the residue on silica gel 60 [Art. 9385 (15 × 3 cm) and elution with ethyl acetate–light petroleum (1:9)] provided, as the only products, a ~1:1 mixture of the *trans*- and *cis*-adduct of the title ester (**45**) (0.701 g, 86%). Rechromatography of the mixture provided pure samples of the respective components [silica gel 60 Art. 7729; elution with ethyl acetate–light petroleum (1:19)].

(1RS,2SR)-*Isomer* (least polar) was an oil [Found: (EI) M^+, 309.1044. $C_{15}H_{19}NO_4S$ requires *M*, 309.1035]; ν_{max} 1 730, 1 610, 1 520, and 1 350 cm^{-1}; δ_H(90 MHz) 1.21 (3 H, t, *J* 7.5 Hz, SCH_2Me), 1.4–2.3 (6 H, m), 2.54 (2 H, q, *J* 7.5 Hz, SCH_2Me),

2.65–2.9 (1 H, m), 3.37 (1 H, q, *J* 7 Hz), 5.22 (2 H, s), and 7.52 (2 H, *J* 9 Hz) and 8.23 (2 H, *J* 9 Hz) (AA'BB').

(1RS,2RS)-*Isomer* (more polar) was also an oil [Found: (EI) M^+, 309.1027]; ν_{max}($CHCl_3$) 1 730, 1 610, 1 520, and 1 350 cm^{-1}; δ_H(90 MHz) 1.20 (3 H, t, *J* 7.5 Hz, SCH_2Me), 1.6–2.3 (6 H, m), 2.65 (2 H, q, *J* 7.5 Hz, SCH_2Me), 3.04–3.43 (2 H, m), 5.22 (2 H, s), and 7.55 (2 H, *J* 9 Hz) and 8.21 (2 H, *J* 9 Hz) (AA'BB').

Isomerisation with DBU.—A mixture of *trans*- and *cis*-isomer of compound (**45**) [0.38 g, ~2:3 ratio] was dissolved in ethyl acetate (10 ml) and the solution was stirred with DBU (0.03 g) for 7 days. Isomerisation in favour of the *trans*-isomer was evident [^{1}H NMR spectrum: ratio (9:1)].

p-*Nitrobenzyl* 2-*Ethylthiocyclopentene*-1-*carboxylate* (**46**).—(a) Via trans-*Adduct.* (1*RS*,2*SR*)-*p*-Nitrobenzyl-2-ethylthiocyclopentanecarboxylate (**45**) (0.500 g), anhydrous dichloromethane (8 ml), pyridine (0.258 ml, 2 mol equiv.), and IBD (0.445 g, 1 mol equiv.) was left together at −5 °C for 16 h. The mixture was diluted with chloroform and chromatographed on silica gel 60 (Art. 9385). Elution with ethyl acetate–light petroleum (1:9) gave unchanged ester (**45**) (0.036 g recovery), followed by the *vinyl sulphide* (**46**); the latter was crystallised from ethyl acetate–light petroleum as matted needles (0.170 g, 72%), m.p. 120 °C (Found: C, 58.45; H, 5.6; N, 4.4; S, 10.15. $C_{15}H_{17}NO_4S$ requires C, 58.6; H, 5.6; N, 4.6; S, 10.4%); λ_{max}(EtOH) 292 nm (ε 16 770); ν_{max} 1 690, 1 610, 1 565 (vinyl sulphide), 1 525, and 1 350 cm^{-1}; δ_H(90 MHz) 1.65 (3 H, t, *J* 7.5 Hz), 1.6–2.2 (2 H, m, 4-H_2), 2.3–2.9 (4 H, m, 3- and 5-H_2), 2.90 (2 H, q, *J* 7.5 Hz), 5.21 (2 H, s), and 7.58 (2 H, *J* 9 Hz) and 8.25 (2 H, *J* 9 Hz) (AA'BB').

A similar experiment with anhydrous benzene as solvent gave a much slower conversion into vinyl sulphide (**46**) (17% after 16 h).

(b) Via cis-*Adduct.* A solution of (1*RS*,2*RS*)-*p*-nitrobenzyl 2-ethylthiocyclopentanecarboxylate (**45**) (0.265 g) in dry dichloromethane (4 ml) containing pyridine (0.136 ml, 2 mol equiv.) and IBD (0.236 g) was kept at −5 °C for 16 h. Chromatography as described in (a) led to the isolation of unchanged ester (**45**) (0.074 g recovery) together with the vinyl sulphide (**46**) (0.288 g, 65%), identical in all respects with the previous sample.

(c) *From cyclopentene*-1-*carboxylic acid.* Repetition of the sequence starting from cyclopentene-1-carboxylic acid (0.50 g), followed by esterification, thiol addition (without separation of adducts), and IBD oxidation (25 h), gave the crystalline vinyl sulphide (**46**) (1.00 g) in 73% yield overall.

(2RS,5RS)-p-*Nitrobenzyl* 3-*Chloro*-7-*oxo*-3-(*pyridin*-2-*ylthio*)-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate* (**48**).—To a stirred solution of (2*RS*,3*RS*,5*RS*)-ester isomer (**47**) (0.050 g) in anhydrous benzene (2 ml) at 5 °C were added dry pyridine (0.025 g, 2.6 mol equiv.) and IBD (0.041 g, 1.2 mol equiv.). The mixture was stored at 5 °C for 22 h. Further amounts of pyridine (0.010 g) and IBD (0.025 g) were added to complete the reaction (8 h). The mixture was chromatographed rapidly on a short column of silica gel 60 (Art. 9385), with ethyl acetate–hexane (1:1) as eluant, to provide the unstable title chloro sulphide as a gum (0.018 g), which crystallised (0.014 g, 28%) (from ethyl acetate–ether); ν_{max} 1 760 and 1 735 cm^{-1}; δ_H 2.86 (1 H, dd, *J* 16 and 3 Hz, 6-H^β), 2.95 (2 H, d, *J* 7 Hz, 4-H_2), 3.42 (1 H, dd, *J* 16 and 6 Hz, 6-H^α), 4.10–4.40 (1 H, m, 5-H^α), 5.22 (1 H, *J* 14 Hz) and 5.40 (1 H, *J* 14 Hz) (ABq, CH_2Ar), 5.68 (1 H, s, 2-H^β), 7.05–7.44 (3 H, m, pyridyl-H_3), 7.63 (2 H, *J* 9 Hz) and 8.21 (2 H, *J* 9 Hz) (AA'BB'), and 8.40–8.53 (1 H, m, pyridyl-H); double-resonance experiments confirmed the A_2MB_2 system for the 6-H_2/5-H/4-H_2 resonances.

On treatment of an aliquot with DBU, the Δ^2-ester (**49**) was produced. The was identical {TLC [R_f 0.19, elution with ethyl acetate–light petroleum (7:3)]} with the sample prepared below.

Table 1. Fractional atomic co-ordinates for ester (**8**).

Atom	*x*	*y*	*z*
S(1)	0.454(2)	0.900(1)	0.895(3)
O(1)	0.493(4)	0.587(2)	0.846(1)
O(2)	0.139(4)	0.677(2)	0.826(1)
O(3)	0.196(4)	0.669(2)	0.725(1)
N(1)	0.412(4)	0.835(2)	0.764(1)
C(2)	0.515(5)	0.792(3)	0.810(1)
C(3)	0.495(6)	0.931(3)	0.835(1)
C(4)	0.254(6)	0.990(3)	0.816(1)
C(5)	0.310(6)	0.973(3)	0.767(1)
C(6)	0.101(5)	0.923(3)	0.733(1)
C(7)	0.220(5)	0.790(3)	0.736(1)
C(8)	0.378(6)	0.681(3)	0.827(1)
C(9)	0.395(7)	0.471(4)	0.868(1)
C(10)	0.540(7)	0.417(4)	0.898(1)
C(11)	0.598(8)	0.674(4)	0.458(1)
C(12)	0.809(8)	0.706(4)	0.387(1)
C(13)	0.622(8)	0.742(4)	0.419(1)
C(14)	0.700(9)	0.563(4)	0.469(1)
C(15)	0.884(8)	0.522(4)	0.438(1)
C(16)	0.276(6)	0.635(3)	0.091(1)
C(17)	0.307(8)	0.644(4)	0.040(1)

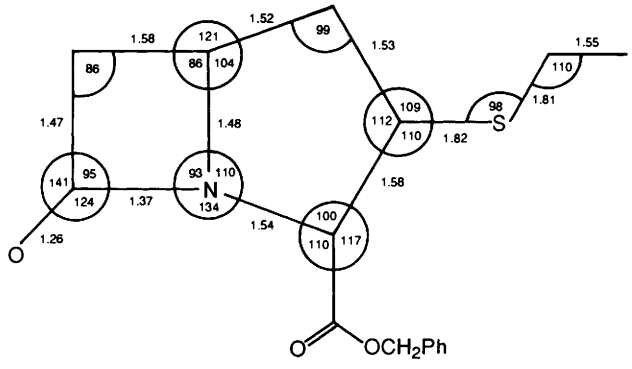


Figure 4. Bond lengths (Å) (standard deviations 0.03–0.04 Å) and bond angles (°) (standard deviations 1–3°) of ester (**8**).

p-*Nitrobenzyl* 7-*Oxo*-3-(*pyridin*-2-*ylthio*)-1-*azabicyclo*[3.2.0]-*hept*-2-*ene*-2-*carboxylate* (**49**).—Ester isomer (**47**) (0.280 g) was oxidised in dry benzene (10 ml) with IBD (0.26 g) in the presence of pyridine (0.14 g) at 5–10 °C as described above. The reaction mixture contained α-chloro sulphide (**48**) {TLC [R_f 0.40, EtOAc–light petroleum (7:3)]}. DBU (0.150 g) was added portionwise at room temperature (20 min) and the mixture was diluted with dichloromethane, washed with brine, dried, and evaporated. The residue was chromatographed rapidly on silica gel 60 (Art. 9385). Gradient elution with ethyl acetate–light petroleum (1:4–1:1) gave recovered ester (**47**) (0.034 g recovery). Elution with ethyl acetate–light petroleum (7:3) gave the title Δ^2-*ester* (**49**), which crystallised from ethyl acetate–diethyl ether (0.070 g, 25%), m.p. 87–89 °C (Found: M^+, 397.0726. $C_{19}H_{15}N_3O_5S$ requires *M*, 397.0732); λ_{max}(EtOH) 263 (ε 11 400) and 319 nm (12 800); ν_{max} 1 785, 1 710, 1 610, 1 580, 1 520, and 1 350 cm^{-1}; δ_H 2.90 (1 H, dd, *J* 16 and 10 Hz) and 3.35 (1 H, dd, *J* 16 and 8 Hz) (4-H_2), 2.90 (1 H, dd, *J* 16 and 3 Hz, 6-H^β), 3.35 (1 H, dd, *J* 16 and 6 Hz, 6-H^α), 4.05–4.25 (1 H, m, 5-H^α), 5.25 (1 H, *J* 14 Hz) and 5.50 (1 H, *J* 14 Hz) (ABq, CH_2Ar), 7.10–7.50 (3 H, m, pyridyl-H_3), 7.63 (2 H, *J* 8 Hz) and 8.20 (2 H, *J* 8 Hz) (AA'BB'), and 8.50–8.60 (1 H, m, pyridyl-H).

Table 2. Fractional atomic co-ordinates for chloro sulphoxide ester (**29**).

Atom	*x*	*y*	*z*
Cl(1)	0.117 5(1)	0.933 2(2)	0.968 6(1)
S(1)	0.290 2(1)	0.921 0(2)	0.999 2(1)
O(1)	0.291 2(3)	0.610 4(4)	1.092 9(4)
O(2)	0.307 7(3)	0.604 2(6)	0.908 4(4)
O(3)	0.013 9(3)	0.641 8(5)	0.953 4(4)
O(4)	−0.013 6(3)	0.496 3(5)	0.760 0(4)
O(5)	0.286 1(3)	0.950 1(5)	0.880 3(4)
N(1)	0.133 0(4)	0.641 0(5)	1.051 7(4)
C(2)	0.192 0(5)	0.703 4(6)	0.982 3(5)
C(3)	0.194 4(4)	0.842 6(6)	1.031 8(5)
C(4)	0.181 2(4)	0.823 3(6)	1.156 3(5)
C(5)	0.131 0(4)	0.700 5(6)	1.164 8(5)
C(6)	0.041 8(4)	0.712 2(6)	1.152 7(5)
C(7)	0.053 2(4)	0.658 1(6)	1.034 9(6)
C(8)	0.011 8(4)	0.365 8(7)	0.770 6(7)
C(9)	0.093 2(5)	0.353 7(9)	0.805 0(9)
C(10)	0.269 7(4)	0.633 9(7)	0.988 2(6)
C(11)	0.369 6(4)	0.558 1(8)	1.113 8(6)
C(12)	0.429 0(4)	0.664 3(7)	1.114 5(6)
C(13)	0.475 3(5)	0.685 7(8)	1.024 2(6)
C(14)	0.527 6(5)	0.787(1)	1.023 2(8)
C(15)	0.532 8(5)	0.870(1)	1.112 1(9)
C(16)	0.486 5(6)	0.848(1)	1.202 9(8)
C(17)	0.434 7(5)	0.747 7(9)	1.205 2(6)
C(18)	0.277 1(4)	1.068 9(7)	1.072 8(5)
C(19)	0.308 8(4)	1.078 1(8)	1.180 1(6)
C(20)	0.300 3(5)	1.193(1)	1.237 2(6)
C(21)	0.262 0(6)	1.294 2(9)	1.192 1(8)
C(22)	0.231 7(6)	1.287 3(8)	1.086 9(8)
C(23)	0.240 3(5)	1.172 6(8)	1.025 0(6)

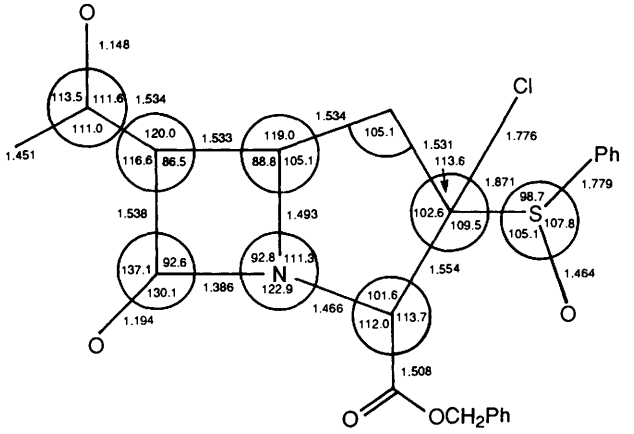


Figure 5. Bond lengths (Å) (standard deviations 0.005–0.012 Å) and bond angles (°) (standard deviations 0.29–0.80°) of chloro sulphoxide (**29**).

The product was identical in all respects with material prepared in these laboratories by intramolecular Wittig cyclisation.[13]

Crystal Structure Determination of Ester (**8**).—*Crystal data.* $C_{16}H_{19}NO_3S$, M = 305.1, orthorhombic, space group $P2_12_12_1$, a = 5.37(1), b = 9.91(1), c = 29.90(2) Å, Mo-K_α, λ = 0.710 69 Å.

Data collection. Reflections were measured to $\theta \leqslant 22°$ (Mo-K_α radiation, graphite monochromator, λ = 0.710 69 Å). Of a total of 1 191 reflections scanned 894 had a net count $\geqslant 2\sigma(I)$ and were used in the refinement. The structure was solved by MULTAN; refinement was confined to a full-matrix least-squares using isotropic temperature factors only. No attempt was made to look for or to include hydrogen atoms. The final R-value was R = 0.17. Atomic co-ordinates are in Table 1 and bond lengths and bond angles in Figure 4.*

Table 3. Fractional atomic co-ordinates for chloro sulphoxide ester (**30**).

Atom	*x*	*y*	*z*
Molecule 1			
Cl(1)	0.826 4(3)	1.073 7(2)	0.701 8(4)
S(1)	0.798 9(3)	0.9627	0.507 0(3)
O(1)	0.575(1)	0.886 7(5)	0.551(1)
O(2)	0.448 5(9)	0.970 9(6)	0.453(1)
O(3)	0.466(1)	0.908 3(6)	0.795(1)
O(4)	0.647(1)	0.984 7(6)	1.108(1)
O(5)	0.719(1)	1.005 0(6)	0.394(1)
N(1)	0.626(1)	0.981 9(5)	0.785(1)
C(2)	0.625(1)	0.995 0(7)	0.645(1)
C(3)	0.772(1)	0.993 9(8)	0.666(1)
C(4)	0.834(1)	0.951 2(6)	0.794(1)
C(5)	0.756(1)	0.967 4(6)	0.890(1)
C(6)	0.699(1)	0.916 8(7)	0.952(1)
C(7)	0.569(1)	0.933 3(6)	0.836(1)
C(8)	0.702(2)	0.925 1(9)	1.104(1)
C(9)	0.632(2)	0.871(1)	1.144(2)
C(10)	0.550(1)	0.942 0(9)	0.543(1)
C(11)	0.361(2)	0.924 9(9)	0.347(2)
C(12)	0.286(2)	0.965 4(8)	0.229(1)
C(13)	0.169(2)	0.989(1)	0.226(2)
C(14)	0.099(2)	1.027(1)	0.117(3)
C(15)	0.144(3)	1.042(1)	0.011(3)
C(16)	0.254(3)	1.014(2)	0.005(2)
C(17)	0.329(2)	0.979(1)	0.119(2)
C(18)	0.960(1)	0.986 9(8)	0.538(1)
C(19)	1.052(1)	0.942 7(7)	0.614(2)
C(20)	1.180(2)	0.960(1)	0.646(2)
C(21)	1.208(2)	1.018(1)	0.598(2)
C(22)	1.117(2)	1.060 5(9)	0.526(2)
C(23)	0.988(2)	1.045 7(7)	0.497(2)
Molecule 2			
Cl(1′)	0.769 9(4)	1.121 6(2)	0.121 9(4)
S(1)	0.800 3(4)	1.231 6(2)	0.321 3(4)
O(1′)	1.027(1)	1.306 0(6)	0.278(1)
O(2′)	1.152 2(9)	1.223 0(5)	0.376(1)
O(3′)	1.127(1)	1.286 8(7)	0.035(1)
O(4′)	0.946(1)	1.212 6(6)	−0.281(1)
O(5′)	0.883(1)	1.190 3(6)	0.432(1)
N(1′)	0.968(1)	1.214 0(6)	0.036(1)
C(2′)	0.974(1)	1.199 8(6)	0.180(1)
C(3′)	0.827(1)	1.202 7(6)	0.162(1)
C(4′)	0.769(1)	1.244 8(8)	0.035(1)
C(5′)	0.837(1)	1.229 7(8)	−0.060(1)
C(6′)	0.898(1)	1.284 0(7)	0.128(2)
C(7′)	1.017(2)	1.267 0(9)	−0.006(2)
C(8′)	0.897(1)	1.273(1)	−0.276(1)
C(9′)	0.969(2)	1.323(1)	−0.320(2)
C(10′)	1.055(1)	1.250 2(7)	0.281(2)
C(11′)	1.235(2)	1.268 5(8)	0.480(2)
C(12′)	1.317(1)	1.227 4(7)	0.593(1)
C(13′)	1.440(2)	1.211(1)	0.593(2)
C(14′)	1.517(2)	1.172(1)	1.698(3)
C(15′)	1.472(3)	1.148(2)	0.799(3)
C(16′)	1.354 1(3)	1.167(1)	0.803(2)
C(17′)	1.276(1)	1.206 3(9)	0.698(2)
C(18′)	0.634(1)	1.205 3(7)	0.282(1)
C(19′)	0.545(2)	1.253 2(9)	0.215(2)
C(20′)	0.416(2)	1.230(1)	0.185(2)
C(21′)	0.390(2)	1.172(1)	0.219(2)
C(23′)	0.485(2)	1.131(1)	0.295(2)
C(22′)	0.611(2)	1.149(1)	0.323(2)

* *Supplementary data* (see section 5.6.3 of Instructions for Authors, in the January issue). H-Atom co-ordinates and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

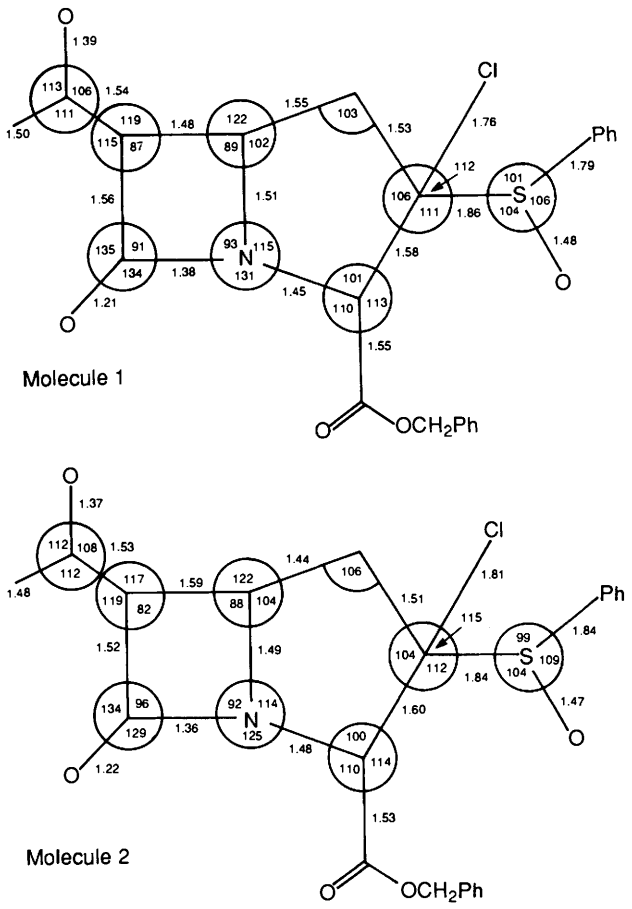


Figure 6. Bond lengths (Å) (standard deviations (0.011–0.03 Å) and bond angles (°) (standard deviations 0.7–2°) of chloro sulphoxide ester (**30**).

Crystal Structure Determination of Chloro Sulphoxide Ester (**29**).—*Crystal data.* $C_{22}H_{22}ClNO_5S$, M = 447.9, monoclinic, space group $P2_1/c$, a = 17.074(5), b = 10.311(4), c = 12.037(4) Å, β = 90.6(1)°, Mo-K_α, λ = 0.71 69 Å.

Data Collection. Reflections were counted for θ ≤ 23°. Of a total of 2 963 reflections 1 714 had a net count ≥3.0 σ(I) and were used in the refinement. The structure was solved by MULTAN and refined by full-matrix least-squares with C, O, N anisotropic. The hydrogen atoms were located on a difference map and included in the calculations but not refined. The final R-value was R = 0.061. Atomic co-ordinates are shown in Table 2 and bond lengths and bond angles in Figure 5.*

Crystal Structure Determination of Chloro Sulphoxide Ester (**30**).—*Crystal data.* $C_{22}H_{22}ClNO_5S$, M = 447.9, monoclinic, space group $P2_1$, a = 1.144(4), b = 20.780(5), c = 10.158(4) Å, β = 109.7(1)°, Mo-K_α, λ = 0.710 69 Å.

Data collection. Reflections were counted for θ ≤ 25°. Of a total of 4 018 reflections 2 143 had a net count ≥3.0 σ(I) and 2 497 had a net count ≥2.0 σ(I). The structure was solved by MULTAN and refined by least-squares as for compound (**29**). The final R-value was 0.086. It should be noted that the unit-cell volume clearly showed two molecules of the β-lactam in the asymmetric unit, the co-ordinates of which correspond to the two enantiomers. Atomic co-ordinates for both molecules are shown in Table 3, and bond lengths and bond angles are shown in Figure 6.*

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