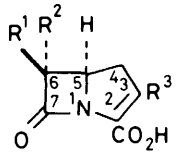
Olivanic Acid Analogues. Part 2.[1] Total Synthesis of Some C(6)-Substituted 7-Oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylates

John H. Bateson, Alison M. Quinn, Terence C. Smale, and Robert Southgate*
Beecham Pharmaceuticals, Research Division, Brockham Park, Betchworth, Surrey RH3 7AJ, U.K.

A number of 6-substituted 7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylates related to the olivanic acids were prepared from the phosphorane (**32**). Generation of the anion α to the azetidin-2-one carbonyl group, followed by reaction with electrophiles and intramolecular cyclisation using the Wittig procedure gave the bicyclic products; in all cases the thermodynamically favoured *trans*-stereochemistry about the azetidinone ring predominated. In contrast, some less readily available *cis*-substituted analogues were obtained from the cyclohexa-1,4-diene derived phosphorane (**61**). The synthetic utility of a masked acetonyl ester group for preparing the free acids of these azabicycloheptene ring systems is described.

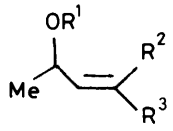
Our preparation of the parent 7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid ring system (**1**), present in olivanic acids[2] such as MM 13902 (**2**), or the related thienamycin[3] (**3**), has already been described.[1] As part of a stepwise approach to the synthesis of analogues of the β-lactam antibiotics, we directed our attention to obtaining some 6-substituted derivatives of (**1**) lacking the C-3 sulphur side-chain of the natural products as found in (**2**) or (**3**). At the outset of this work it was hoped that the cycloaddition reaction of a suitably substituted alkene [MeCH(OR^1)CH=CR^{2}R^3] with chlorosulphonyl isocyanate (CSI) would provide an azetidin-2-one precursor with a substituent at C-3 similar to that of the natural metabolites. The C-4 grouping would ultimately provide the functionality for elaboration to the pyrroline ring.



(**1**) R^1 = R^2 = R^3 = H

(**2**) R^1 = MeCH(*S*), R^2 = H, R^3 = S, NHAc; OSO$_3$H

(**3**) R^1 = H, R^2 = MeCH(*R*), R^3 = S, NH$_2$; OH

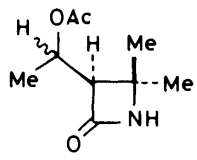


(**4**) R^1 = Ac, R^2 = R^3 = Me

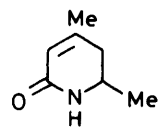
(**5**) R^1 = CH_2Ph, R^2 = R^3 = Me

(**6**) R^1 = Ac, R^2 = H, R^3 = Me

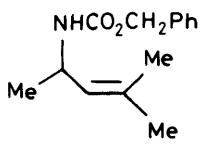
(**7**) R^1 = Ac, R^2 = Ph, R^3 = H



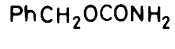
(**8**)



(**9**)



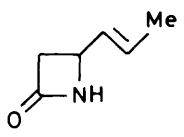
(**10**)



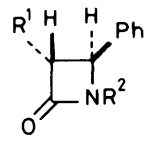
(**11**)

The initial experiments it was decided to use alkenes of type (**4**)—(**7**) carrying phenyl or methyl substituents. In similar cases where the alkene lacks the substituted ethyl group reaction occurs readily to provide the appropriate azetidin-2-ones.[4] Reaction of 4-methylpent-3-en-2-yl acetate (**4**) with CSI, followed by reductive work up,[5] gave only a 4% yield of the two diastereoisomers of the azetidin-2-one (**8**).† The major product was the unexpected dihydropyridone (**9**). The benzyl ether (**5**) underwent a different type of reaction with insertion of the reagent into the carbon–oxygen bond resulting in formation of the urethane (**10**). A small yield of the known benzyl carbamate (**11**) was also obtained. With pent-3-en-2-yl acetate (**6**), reaction with CSI was much slower. The only product identified was the 4-propenylazetidin-2-one (**12**), again in low yield (8%). The *cis*-substituted styrene (**7**) gave a trace amount of one diastereoisomer of the *trans*-product (**13**). It was concluded therefore that the preparation of protected 3-(1-hydroxyethyl)azetidin-2-ones directly by the CSI method was unlikely to be of any synthetic utility.

The generation of a carbanion α to the β-lactam carbonyl



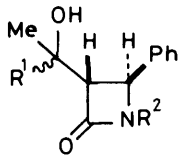
(**12**)



(**13**) R^1 = MeCH(OAc), R^2 = H

(**14**) R^1 = H, R^2 = Me

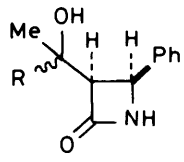
(**15**) R^1 = R^2 = H



(**16**) R^1 = H, R^2 = Me

(**17**) R^1 = R^2 = H

(**18**) R^1 = Me, R^2 = H



(**19**) R = H

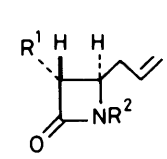
(**20**) R = Me

† All synthetic compounds are racemic; only one enantiomer is depicted.

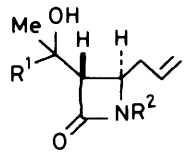
group in simple azetidin-2-ones has been studied by Durst.[6,7] Reaction with a variety of electrophilic reagents gave 3-substituted azetidin-2-ones. We thus turned our attention to this approach. Initially, reaction conditions were established using the readily available 4-phenyl substituted azetidin-2-ones (**14**) and (**15**). Low temperature reaction of the *N*-methylated derivative (**14**) with lithium cyclohexylisopropylamide, followed by acetaldehyde, gave a high yield of the two diastereoisomers of the *trans*-substituted azetidin-2-one (**16**). These could be separated and characterised further as their *O*-acetyl esters. Using (**15**), generation of a dianion is required. This necessitated the use of two equivalents of butyl-lithium at room temperature. Reaction with acetaldehyde under kinetic conditions produced a 50% yield of all four possible diastereoisomers of 3-(1-hydroxyethyl)-4-phenylazetidin-2-one. The ratio of *trans*-products (**17**) to *cis*-products (**19**) was approximately 3:2; one *trans*-isomer of (**17**) and one *cis*-isomer of (**19**) could be isolated in pure form. Reaction of the dianion of (**15**) with acetone gave the *trans*-isomer (**18**) and *cis*-isomer (**20**) in a similar ratio. Durst[7] reported a *trans*:*cis* ratio of 5:1 without separation of the isomers using (**15**) and acetone. The stereochemical assignment of configuration of the β-lactam protons follows from the coupling constants observed between the C-3 and C-4 protons, being 2 Hz for the *trans*-configuration and 6 Hz for the *cis*-configuration.[8]

A similar sequence of reactions was then carried out on the 4-allylazetidin-2-one (**21**), since elaboration of the allyl grouping to provide the bicyclic system (**1**) had previously been demonstrated.[1] Using acetone, a low yield of *trans*-product (**26**) (11%), together with the *cis*-product (**28**) (8%), was obtained. Introduction of the 3-substituent was then tried on the *N*-silylated 4-allylazetidinone (**22**). In most cases characterisation of the products was best achieved after subsequent removal of the silyl group. With acetone, the *trans*-isomer (**26**) was the sole product in high yield. A similar result was obtained using the diphenyl-t-butylsilyl derivative (**23**). With alkyl halides (methyl or ethyl iodide) the *trans*-compounds (**24**) and (**25**) were obtained after desilylation. In the case of methyl iodide a small amount of the *cis*-product (10:1 *trans*:*cis*) was observed. Only in the case of acetaldehyde was any noticeable amount of the *cis*-product obtained. Thus (**22**) gave a mixture of the two diastereoisomers of the *trans*-product (**27**), and the two diastereoisomers of the *cis*-product (**29**); again the *trans*-stereochemistry predominated (5:1 *trans*-*cis*). A pure sample of *trans*-isomer (**30**), having the thienamycin stereochemistry[3,9] at the three contiguous chiral centres, could be separated, but only with some difficulty. A more stereoselective route to (**30**) was achieved by acylation of (**21**) to the thermodynamically favoured (**31**). Reduction of (**31**) with K-Selectride gave predominantly (**30**) (9:1 ratio of *R*:*S* isomers) in the same manner as that reported for other precursors of thienamycin.[9] The ready availability[1] of the phosphorane derivative (**32**) prompted us to perform a similar series of reactions using this azetidin-2-one. In this case the phosphorane grouping provides a means of elaboration to a bicyclic structure by the established Wittig procedure.[1]

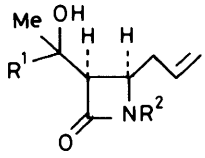
Treatment of (**32**) with lithium cyclohexylisopropylamide followed by acetone gave a 3:1 mixture (71%) of the *trans*- and *cis*-isomers of (**34**). It was found necessary to use two equivalents of the base to generate the C-3 anion efficiently, since with 1 equivalent only unchanged (**32**) was recovered. We attribute this to some initial complexation of the base with the phosphorane grouping. Careful chromatography of the mixture gave the individual isomers, which could be cyclised by our procedure (TFA, −70 °C; O_3; Ph_3P; $NaHCO_3$) described previously for the unsubstituted ring system.[1] Whereas cyclisation leading to the *trans*-isomer (**41**) was rapid (30 min), a much longer period (24 h) was required for total conversion into the *cis*-compound (**48**). It would seem likely therefore, that



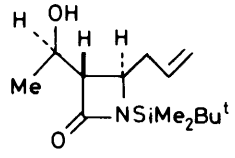
(**21**) $R^1 = R^2 = H$
(**22**) $R^1 = H$, $R^2 = SiMe_2Bu^t$
(**23**) $R^1 = H$, $R^2 = SiPh_2Bu^t$
(**24**) $R^1 = Me$, $R^2 = H$
(**25**) $R^1 = Et$, $R^2 = H$



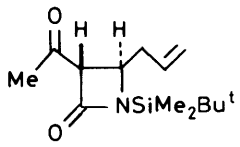
(**26**) $R^1 = Me$, $R^2 = H$
(**27**) $R^1 = H$, $R^2 = SiMe_2Bu^t$



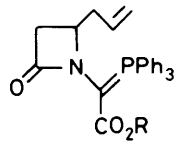
(**28**) $R^1 = Me$, $R^2 = H$
(**29**) $R^1 = H$, $R^2 = SiMe_2Bu^t$

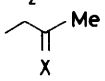


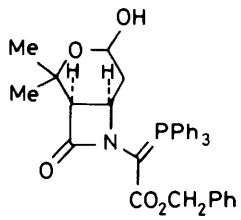
(**30**)



(**31**)



(**32**) R = CH_2Ph
(**33**) R = 



(**53**)

there is some equilibrium between the free aldehyde form and the cyclic hemiacetal (**53**).

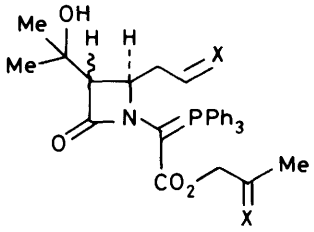
With acetaldehyde a mixture of hydroxyethyl substituted phosphoranes (**35**) was obtained and cyclised similarly. Only two of the four possible diastereoisomers were obtained, suggesting some degree of steric control in the interaction of the enolate. The products were identified as the *trans*-isomer (**42**) and *cis*-isomer (**49**). Subsequently a number of other electrophiles have been used to introduce 3-substituents into the phosphorane (**32**). The final products after cyclisation are listed in Table 1. In many cases it was found more convenient to cyclise the mixture of isomeric phosphoranes and separate the rather less polar bicyclic products.

Only in the case of the 6-hydroxyethyl derivatives (**42**) and (**49**) has the stereochemistry of the side-chain been unequivocally determined. *X*-Ray crystallographic analysis[10] on the *cis*-isomer (**49**) showed the relative stereochemistry to be (5*RS*, 6*RS*, 8*RS*) as in Figure 1. Fractional atomic co-ordinates (Table 2) and selected bond angles and bond lengths (Figure 2) are given in the Experimental section. This stereochemical

arrangement has not yet been found among the 1-azabicycloheptene natural products, although it is reported that a naturally occurring saturated analogue does have the (5*R*, 6*R*, 8*R*) configuration.[11] Although the *trans*-isomer (**42**) was not crystalline, a derivative resulting from addition of thiophenol to the [2,3] double bond was suitable for *X*-ray analysis, and shown to have the (5*RS*, 6*SR*, 8*SR*) stereochemistry.[12] This corresponds to the relative stereochemistry of the *trans*-olivanic acid derivatives and (**42**) has been used to prepare[13] the racemic form of the benzyl ester of the olivanic acid MM 22381.

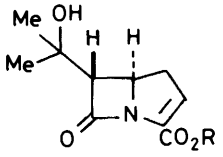
In our experience, the benzyl protecting group in C-3 unsubstituted derivatives is unsuitable for preparing the free acids, since hydrogenolysis leads to reduction of the double bond.[1] Hydrolytic cleavage of the acetonyl ester has been successfully accomplished to prepare (**1**) and the corresponding penem.[1,14] We therefore attempted to introduce substituents at the 3-position of the phosphorane[1] (**33**; X = O). No discrete products could be isolated. Presumably proton abstraction from the activated methylene group of the ester also occurs leading to a more complex reaction mixture; we have observed a similar effect when using the *p*-nitrobenzyl ester. An approach based on using a masked acetonyl ester was therefore tried. The procedure can be illustrated by the preparation of the carpetimycin[15]-type analogues (**57**) and (**59**).

The methylallyl ester phosphorane (**33**; X = CH_2) was prepared from 4-allylazetidin-2-one by standard procedures. Reaction with base and acetone gave a smooth conversion into the *trans*- and *cis*-isomers of (**54**). These were separated and ozonolysed in the usual way thereby effecting cleavage of both double bonds, to give the intermediate aldehyde, now as the acetonyl ester (**55**). Cyclisation then produced the bicyclic esters (**56**) and (**58**), which were efficiently deprotected with 0.1M-aqueous sodium hydroxide to the corresponding salts (**57**) and (**59**). Only the *cis*-isomer (**59**) showed any biological activity.



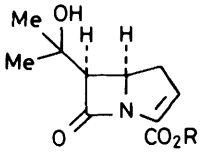
(**54**) X = CH_2

(**55**) X = O



(**56**) R = CH_2Ac

(**57**) R = Na



(**58**) R = CH_2Ac

(**59**) R = Na

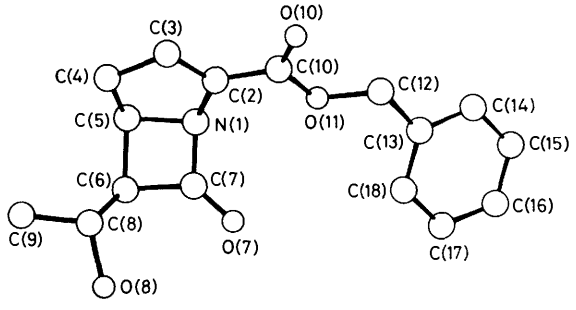
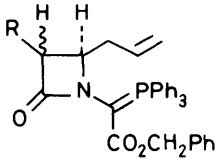
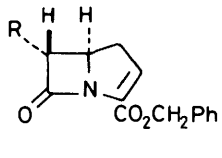
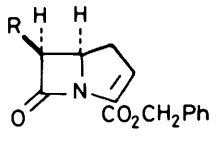
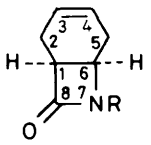


Figure 1. *X*-Ray structure of benzyl 6-(1-hydroxyethyl)-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (**49**)

In another approach to 6-substituted analogues, we have made use of the cyclohexa-1,4-diene-derived azetidin-2-one[16] (**60**), in order to obtain a number of the thermodynamically less favoured *cis*-substituted β-lactam products. Preparation of the phosphorane (**61**; R^1 = CH_2Ph) was by the familiar procedure[1] of condensation with benzyl glyoxylate followed by conversion into the α-chloro ester. Subsequent reaction with triphenylphosphine and 2,6-dimethylpyridine afforded (**61**; R^1 = CH_2Ph). Oxidative cleavage of the double bond of (**61**) as in the 4-allyl series resulted in cyclisation to the 6-oxoethyl substituted azabicycloheptene (**62**). Although isolable, the rather sensitive aldehyde function was best trapped using standard Wittig reagents to provide stable olefinic derivatives such as the ester (**63**), the nitrile (**64**), and the ketone (**65**). A number of esters of the bicyclic system were prepared by this route. These include the pivaloyloxymethyl ester (**66**), the *p*-bromophenacyl ester (**67**), the *p*-nitrobenzyl ester (**68**) and the acetonyl ester (**69**). Only in the case of the acetonyl ester (**69**) could efficient deprotection be achieved to give the sodium salt (**70**). Surprisingly, in spite of the rather different nature of this side-chain compared to the natural products, an unexpected degree of broad-spectrum antibacterial activity was apparent.

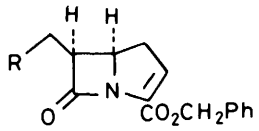
Table 1. Esters of 6-substituted 7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylates

R						
$Me_2C(OH)$	(34)	71%	(41)	25%	(48)	11%
MeCH(OH)	(35)	65%	(42)	17%	(49)	7%
	(36)	64%	(43)	43%	(50)	10%
PhCH(OH)	(37)	63%	(44)	27%	(51)	27%
EtCH(OH)	(38)	72%	(45)	7%	(52)	4%
Me	(39)	19%	(46)	55%	—	—
$PhCH_2$	(40)	32%	(47)	42%	—	—



(60) R = H

(61) R = C(PPh$_3$)CO$_2$R^1

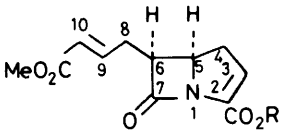


(62) R = CHO

(63) R = MeO$_2$C

(64) R = NC

(65) R = Ac



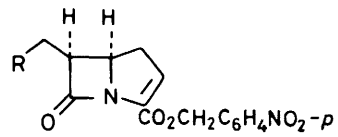
(66) R = CH$_2$OCOBu^t

(67) R = CH$_2$COC$_6$H$_4$Br-*p*

(68) R = CH$_2$C$_6$H$_4$NO$_2$-*p*

(69) R = CH$_2$Ac

(70) R = Na

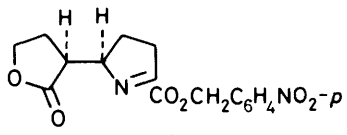


(71) R = CHO

(72) R = HOCH$_2$

(73) R = MeCO$_2$CH$_2$

(74) R = PhNHCO$_2$CH$_2$



(75)

In the case of the *p*-nitrobenzyl ester (**68**) the intermediate aldehyde (**71**) could be isolated as a stable crystalline solid. Careful reduction using 1 equivalent of sodium borohydride led to the formation of the unstable alcohol (**72**), which on attempted purification (silica gel) rearranged. Even at 400 MHz the proton n.m.r. spectrum of this product was of little diagnostic utility. However, the off resonance decoupled ^{13}C n.m.r. spectrum allowed the structural assignment as the 3,4-dihydro-2*H*-pyrrole (**75**). This rearrangement reaction bears a formal resemblance to the acid-catalysed penicillin type rearrangement. It was possible to acetylate the crude alcohol (**72**) to give the more stable ester (**73**), while on reaction with phenylisocyanate the urethane (**74**) was obtained. Details of the biological activity of many of these compounds will be reported elsewhere.

Experimental

U.v. spectra were recorded using Perkin-Elmer 554 and Pye-Unicam SP 8000 and SP7-500 spectrophotometers. Unless stated otherwise, i.r. spectra were recorded for solutions in chloroform, using Perkin-Elmer 197, 457, or 983 machines. ^{1}H N.m.r. spectra were recorded at 60 MHz on a Perkin-Elmer R12 instrument, at 80 MHz on a Varian CFT 20, at 90 MHz on a Perkin-Elmer R32, at 250 MHz on a Bruker WM 250, and at 400 MHz on a Bruker WM 400 instrument, for solutions in $CDCl_3$ with tetramethylsilane as an internal standard (unless otherwise stated). ^{13}C N.m.r. spectra were recorded at 62.89 MHz on a Bruker WM 250 instrument, for $CDCl_3$ solutions, using tetramethylsilane as an internal standard. Mass spectra were determined using an A.E.I. MS9, a VG 7070, or a VG ZAB instrument. The purity of all compounds was tested by t.l.c. analysis using Merck precoated silica gel 60 F_{254} plates (0.2 mm thickness). Preparative chromatography was carried out on columns of Merck silica gel 60 (finer than 230 mesh ASTM, Art. 7729, or 230—400 mesh ASTM, Art. 9385), or mixtures thereof, using the slightly increased pressure provided by a Medcalf Hyflo pump. Solutions were dried internally with magnesium sulphate or with sodium sulphate, and solvents were evaporated under reduced pressure using a rotary evaporator. Dimethylformamide was dried over calcined 4A molecular sieves. Tetrahydrofuran and methylene chloride were dried by distillation from sodium hydride, and from BDH phosphorus pentaoxide drying agent, respectively. Light petroleum refers to the fraction b.p. 60—80 °C. M.p.s were determined with a Kofler hot-stage apparatus and are uncorrected. All compounds prepared are racemic; n.m.r. stereochemical assignments refer to that enantiomer which is depicted.

4-*Methylpent*-3-*en*-2-*yl Acetate* (**4**).—4-Methylpent-3-en-2-ol[17] (2.00 g) in methylene chloride (20 ml) at 0 °C was treated successively with pyridine (1.77 ml) and acetyl chloride (1.57 ml) and was then stirred at room temperature for 2 h. The solution was washed twice with water, then with brine, and finally dried and evaporated. The residue was distilled (water pump) to give the acetate as a colourless liquid (1.8 g, 67%), b.p. 50—52 °C/17 mmHg; $\nu_{max.}$(film) 1 735 and 1 670 cm^{-1}; δ (90 MHz) 1.21 [3 H, d, *J* 6 Hz, *Me*CH(OAc)], 1.67 [6 H, s, CH=C(*Me*)$_2$], 1.94 (3 H, s, MeCO), 5.10 (1 H, br d, *J* 8 Hz, with further fine coupling, =CH–), and 5.58 [1 H, dq, *J* 8 and 6 Hz, MeC*H*(OAc)].

3-(1-*Acetoxyethyl*)-4,4-*dimethylazetidin*-2-*one* (**8**).—4-Methylpent-3-en-2-yl acetate (**4**) (0.90 g) in methylene chloride (10 ml) was cooled to 0 °C and treated with chlorosulphonyl isocyanate (CSI) (0.56 ml). The solution was allowed to warm to room temperature; inspection of the i.r. spectrum indicated that all the CSI had reacted. The reaction mixture was added dropwise to a stirred mixture of sodium sulphite (1.1 g), water (5 ml), and methylene chloride (5 ml). The pH was maintained at 7—8 by simultaneous addition of 10% aqueous potassium hydroxide (*ca.* 10 ml). The mixture was diluted with ethyl acetate (30 ml) and the organic phase was separated, washed with brine, dried and evaporated. The residue (0.48 g) crystallised from ethyl acetate–light petroleum to give 5,6-*dihydro*-4,6-*dimethyl*-2(1H)*pyridone* (**9**) (0.22 g, 28%), m.p. 107—108 °C (Found: M^+, 125.0840. $C_7H_{11}NO$ requires *M*, 125.0841); $\nu_{max.}$ 3 360, 3 180, 1 695, and 1 655 cm^{-1}; δ (90 MHz) 1.24 (3 H, d, *J* 6 Hz, 6-Me), 1.70 (3 H, s, 4-Me), 2.73 (2 H, d, *J* 4 Hz, 5-H$_2$), 4.04 (1 H, complex m, 6-H), 5.32 (1 H, br s, with further fine coupling, 3-H), and 7.45 (1 H, br s, D_2O exch., NH); irradiation at the frequency of the 6-H signal caused the doublets δ 2.73 and 1.24 to collapse to singlets. Chromatography of the mother liquors on silica gel 60 (Art. 7729) gave, successively, the diastereoisomers of the title *azetidinone* (**8**) R_F 0.67 and 0.62, respectively [elution with ethyl acetate–light petroleum (1:1)].

Isomer A (less polar) crystallised from ethyl acetate–light petroleum (0.029 g, 2.5%), m.p. 93—95 °C (Found: M^+, 186.1132. $C_9H_{16}NO_3$ requires *M*, 186.1130); $\nu_{max.}$ 3 380, 1 745, and 1 240 cm^{-1}; δ (90 MHz) 1.30 (3 H, s, 4-Me), 1.37 [3 H, d, *J* 6 Hz, *Me*CH(OAc)], 1.40 (3 H, s, 4-Me), 1.98 (3 H, s, MeCO), 2.92 (1 H, d, *J* 11 Hz, 3-H), 5.19 [1 H, dq, *J* 11 and 6 Hz, C*H*(OAc)], and 6.48 (1 H, br s, NH).

Isomer B (more polar) was isolated as a liquid (0.019 g, 1.6%) (Found: M^+, 186.1130. $C_9H_{16}NO_3$ requires *M*, 186.1130); $\nu_{max.}$(film) 3 370, 1 745, and 1 250 cm^{-1}; δ (90 MHz) 1.42 [3 H, d, *J* 6 Hz, *Me*CH(OAc)], 1.62 (6 H, s, 2 × 4-Me), 2.00 (3 H, s, MeCO), 3.15 (1 H, d, *J* 2 Hz, 3-H), 3.70 [1 H, qd, *J* 6 and 2 Hz, C*H*(OAc)], and 6.29 (1 H, br s, NH).

4-*Benzyloxy*-2-*methylpent*-2-*ene* (**5**).—To 4-methylpent-3-en-2-ol (4.00 g) in dimethylformamide (40 ml) in an atmosphere of

nitrogen was added sodium hydride (80% dispersion in mineral oil; 1.20 g) in portions. The brown solution was stirred at room temperature for 30 min and then cooled to 0 °C. Benzyl bromide (6.84 g, 4.80 ml) was added, and the mixture stirred at room temperature for 3 h. The solvent was evaporated under reduced pressure, and the residue partitioned between ethyl acetate and water. The organic phase was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel 60 (Art. 7729), eluting with ethyl acetate–light petroleum (1:4), to give the benzyl ether (**5**) as a liquid (6.53 g, 86%), $\nu_{max.}$(film) 1 670 cm^{-1}; δ (60 MHz) 1.19 (3 H, d, *J* 6 Hz, 5-H_3), 1.57 and 1.70 (each 3 H, s, $=CMe_2$), 4.05 (1 H, dq, *J* 8 and 6 Hz, C*H*O–CH_2Ph), 4.10 and 4.40 (each 1 H, ABq, *J* 18 Hz, CH_2Ph), 5.05 (1 H, d, *J* 8 Hz, with fine coupling, =CH–), and 7.28 (5 H, s, Ph).

Benzyl 4-*Methylpent*-3-*en*-2-*ylcarbamate* (**10**).—4-Benzyloxy-2-methylpent-2-ene (**5**) (2.00 g) in methylene chloride (10 ml) was cooled to 0 °C and treated with chlorosulphonyl isocyanate (1.49 g) with stirring for 2 h (i.r. monitoring). The solution was added slowly to a mixture of sodium sulphite (3.0 g), water (15 ml) and methylene chloride (10 ml). The pH was maintained at 7—8 by the addition of 10% aqueous potassium hydroxide. Ethyl acetate was added and the organic layer was separated, washed with brine, dried and evaporated. Chromatography of the residue on silica gel 60 (Art. 7729), eluting with ethyl acetate–light petroleum (9:1) gave the title *carbamate* (**10**) as an oil (0.550 g, 22%) (Found: M^+, 233.1416. $C_{14}H_{19}NO_2$ requires *M*, 233.1416); $\nu_{max.}$(film) 3 300, 1 700, and 1 520 cm^{-1}; δ (60 MHz) 1.11 (3 H, d, *J* 6 Hz, 1-H_3), 1.60 (6 H, s, $=CMe_2$), 4.0—4.6 (1 H, m, 4-H), *ca.* 4.5 (1 H, br s, NH), 4.81 (1 H, br d, *J* 7 Hz, =CH–), 4.91 (2 H, s, CH_2Ph), and 7.29 (5 H, s, Ph).

Elution of the column with ethyl acetate–light petroleum (1:1) afforded benzyl carbamate (**11**) (110 mg, 7%), which was recrystallised from ethyl acetate–light petroleum, m.p. 87—89 °C, $\nu_{max.}$ 3 500, 3 400, 1 720, and 1 580 cm^{-1}; δ (60 MHz) 4.92 (2 H, s, CH_2Ph), 5.10 (2 H, br s, NH_2), and 7.30 (5 H, s, Ph).

Pent-3-*en*-2-*yl Acetate* (**6**).—Pent-3-en-2-ol (4.0 g) in methylene chloride (40 ml) was cooled to 0 °C. Pyridine (4.1 ml) and acetyl chloride (3.6 ml) were added and stirring continued at room temperature for 2 h. Water (20 ml) was added, and the methylene chloride layer separated. This was washed with water and brine, then dried and evaporated. The residue was distilled (water pump) to give the acetate (**6**) as a colourless liquid (4.7 g, 79%), b.p. 53 °C/30 mmHg; $\nu_{max.}$(film) 1 735 cm^{-1}; δ (90 MHz) 1.22 (3 H, d, *J* 6 Hz, 1-Me), 1.62 (3 H, d, *J* 5 Hz, 5-Me), 1.96 (3 H, s, MeCO), and 5.0—6.0 (3 H, m, C*H*=C*H*C*H*OAc).

4-(*Prop*-1-*enyl*)*azetidin*-2-*one* (**12**).—To the acetate (**6**) (2.00 g) in methylene chloride (20 ml) was added chlorosulphonyl isocyanate (1.4 ml). The mixture was stirred at room temperature for 8 h (optimum appearance of the i.r. band $\nu_{max.}$ 1 820 cm^{-1}, with concomitant disappearance of that at 2 250 cm^{-1}). Longer reaction times caused complete degradation. The crude *N*-chlorosulphonylazetidinone solution was reduced by dropwise addition, with stirring, to a cooled mixture of sodium sulphite (3.0 g) in water (10 ml) and methylene chloride (10 ml). The aqueous solution was maintained at pH 7—8 by the addition of 10% aqueous potassium hydroxide (*ca.* 25 ml). The mixture was diluted with ethyl acetate (30 ml) and the organic phase was separated, washed with brine, dried and evaporated. The residue was chromatographed on silica gel 60 (Art. 7729), employing gradient elution with ethyl acetate–light petroleum (1:4—1:1), to give *inter alia* the liquid azetidinone[18] (**12**) as the most polar component (0.13 g, 8%) (Found: M^+, 111.0683. C_6H_9NO requires *M*, 111.0684), also *m*/*z* 96 (*M* − Me), 83 (*M* − CO), and 68 (*M* − O=C=NH); $\nu_{max.}$ 3 460, 1 760, and 1 675 cm^{-1}; δ (90 MHz) 1.64 (3 H, d, *J* 5 Hz, =CH*Me*), 2.58 (1 H, dd, *J* 14 and 2 Hz, 3β-H), 3.09 (1 H, ddd, *J* 14, 5, and 2 Hz, 3α-H), 3.97 (1 H, ddd, *J* 6, 5, and 2 Hz, 4α-H), 5.2—6.1 (2 H, m, CH=CH), and 6.88 (1 H, br s, NH).

(*Z*)-4-*Phenylbut*-3-*en*-2-*yl Acetate* (**7**).—(*Z*)-4-Phenylbut-3-en-2-ol[19] (2.0 g) in methylene chloride (20 ml) at 0 °C was treated successively with pyridine (1.3 ml) and acetyl chloride (1.15 ml) and stirred at room temperature for 6 h. Water was added, the organic phase was separated, washed with brine, dried, and evaporated. Chromatography of the residue on silica gel 60 (Art. 9385), eluting with ethyl acetate–light petroleum (1:9), gave the acetate (**7**) as a colourless liquid (2.42 g, 94%), $\nu_{max.}$(film) 1 740, 1 600, and 1 500 cm^{-1}; δ (for alkene) 1.34 (3 H, d, *J* 5.5 Hz, 1-H_3), 1.94 (3 H, s, MeCO), 5.40—6.05 [2 H, m, =C*H*CH(OAc)], 6.52 (1 H, d, *J* 10 Hz, PhC*H*=), and 7.00—7.40 (5 H, m, Ph). The n.m.r. spectrum showed the product to contain *ca.* 25% of the corresponding saturated compound, 4-phenylbutan-2-yl acetate.

(3RS,4RS)-3-(1-*Acetoxyethyl*)-4-*phenylazetidin*-2-*one* (**13**).—(*Z*)-4-Phenylbut-3-enyl acetate (**7**) (2.00 g, 75% pure) in methylene chloride (20 ml) at 0 °C was treated with chlorosulphonyl isocyanate (0.70 ml), and the solution was stirred at room temperature for 24 h. The resulting brown solution was added dropwise to a stirred mixture of sodium sulphite (1.5 g), water (5 ml), and methylene chloride (5 ml), whilst maintaining the pH at 7—8 by addition of 10% aqueous potassium hydroxide. The organic phase was separated, washed with brine, dried, and evaporated. The resulting syrup was chromatographed on silica gel 60 (Art. 7729). Elution with ethyl acetate–light petroleum (gradient elution 1:4—1:1) gave *inter alia* one diastereoisomer of the title azetidinone (**13**) as a gum (0.012 g, 0.8%), $\nu_{max.}$ 3 380, 1 765, 1 740sh, and 1 495 cm^{-1}; δ (90 MHz) 1.37 [3 H, d, *J* 6 Hz, *Me*CH(OAc)], 2.04 (3 H, s, MeCO), 3.13 (1 H, dd, *J* 8 and 2 Hz, 3-H), 4.63 (1 H, d, *J* 2 Hz, 4-H), 5.31 [1 H, dq, *J* 8 and 6 Hz, MeC*H*(OAc)], 6.16 (1 H, br s, NH), and 7.0—7.4 (5 H, m, Ph).

(3RS, 4RS)-3-(1-*Hydroxyethyl*)-1-*methyl*-4-*phenylazetidin*-2-*one* (**16**).—Lithium cyclohexylisopropylamide was prepared from cyclohexylisopropylamine (0.48 g) in tetrahydrofuran (5 ml) in an atmosphere of nitrogen by addition of n-butyl-lithium (1.42 ml of a 2.4M solution in hexane) at −70 °C in the usual manner. To this solution was added 1-methyl-4-phenylazetidin-2-one[6] (**14**) (0.5 g), in tetrahydrofuran (3 ml), and stirring was continued at the low temperature for 5 min. An excess of acetaldehyde (0.85 ml) was added, and after 10 min the reaction mixture was neutralised with acetic acid (0.41 g) and was then allowed to warm to room temperature. Evaporation gave a residue which was partitioned between ethyl acetate and water. The ethyl acetate was separated, washed with brine and then dried and evaporated. Chromatography on silica gel 60 (Art. 7729) [gradient elution with ethyl acetate–light petroleum mixtures (1:1—1:0)] afforded the title compound as a mixture of *trans*-substituted diastereoisomers (**16**) (0.488 g, 80%). Rechromatography (chloroform elution) separated the two components.

Isomer A. The *alcohol* was obtained as a gum (0.285 g, 47%) (Found: M^+, 205.1101. $C_{12}H_{15}NO_2$ requires *M*, 205.1103); $\nu_{max.}$ 3 380 and 1 735 cm^{-1}; δ (90 MHz) 1.34 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 2.72 (3 H, s, 1-Me), 2.82 (1 H, d, *J* 4 Hz, D_2O exch., OH), 3.00 (1 H, br dd, *J* 6 and 2 Hz, 3β-H), 4.12 (1 H, m, br quintet *J* 6 Hz after D_2O exch., CH–O), 4.33 (1 H, d, *J* 2 Hz, 4α-H), and 7.28 (5 H, br s, Ar).

Isomer B. Continued elution afforded the more polar *alcohol* which crystallised from ethyl acetate–light petroleum (0.153 g, 25%), m.p. 76—77 °C (Found: C, 70.4; H, 7.6; N, 6.8.

$C_{12}H_{15}NO_2$ requires C, 70.2; H, 7.4; N, 6.8%); $\nu_{max.}$ 3 370 and 1 735 cm^{-1}; δ (90 MHz) 1.26 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 2.72 (3 H, s, 1-Me), 2.99 (1 H, br dd, *J* 4 and 2 Hz, 3β-H), 3.14 (1 H, d, *J* 4 Hz, D_2O exch., OH), 4.21 (1 H, dq, *J* 4 and 6 Hz after D_2O exch., CH–O), 4.56 (1 H, d, *J* 2 Hz, 4α-H), and 7.28 (5 H, br s, Ar).

(3RS, 4RS)-3-(1-*Acetoxyethyl*)-1-*methyl*-4-*phenylazetidin*-2-*one*.—*Isomer A*. The hydroxyethylazetidinone (**16**) (isomer A) (0.108 g) in methylene chloride (2 ml) was treated with pyridine (0.050 ml) and acetyl chloride (0.045 ml) at 0 °C and stirred at room temperature for 2 h. The mixture was concentrated and partitioned between ethyl acetate and water. The ethyl acetate layer was washed with brine, dried, and evaporated and the residue chromatographed on silica gel 60 (Art. 7729) [elution with ethyl acetate–light petroleum (2:3)]. The corresponding *acetate* was obtained as a gum (0.102 g, 78%) (Found: M^+, 247.1211. $C_{14}H_{17}NO_3$ requires *M*, 247.1208); $\nu_{max.}$ 1 740 and 1 240 cm^{-1}; δ (90 MHz) 1.33 [3 H, d, *J* 6 Hz, *Me*CH(OAc)], 2.00 (3 H, s, OAc), 2.66 (3 H, s, 1-Me), 3.09 (1 H, br m, 3β-H), 4.14 (1 H, d, *J* 2 Hz, 4α-H), 5.28 (1 H, dq, *J* 4.5 and 6 Hz, CH–O), and 7.31 (5 H, s, Ph).

Isomer B. The hydroxyethylazetidinone (**16**) (isomer B) (0.067 g) in methylene chloride (4 ml) was acetylated with pyridine (0.031 ml) and acetyl chloride (0.028 ml) at 0 °C, and then stirred at room temperature for 3 h. Recovery and chromatography as described above for isomer A, gave the corresponding acetate as a gum (0.077 g, 95%), $\nu_{max.}$ 1 745 and 1 240 cm^{-1}; δ (90 MHz) 1.31 [3 H, d, *J* 6 Hz, *Me*CH(OAc)], 1.98 (3 H, s, OAc), 2.68 (3 H, s, 1-Me), 3.00 (1 H, dd, *J* 7 and 2 Hz, 3β-H), 4.31 (1 H, d, *J* 2 Hz, 4α-H), 5.34 (1 H, dq, *J* 7 and 6 Hz, CH–O), and 7.31 (5 H, s, Ph); *m/z* 247 (M^+), 219, 187, and 172.

3-(1-*Hydroxyethyl*)-4-*phenylazetidin*-2-*one*.—To 4-phenylazetidin-2-one (**15**)[5,6] (0.40 g; 2.72 mmol) in tetrahydrofuran (30 ml) in an argon atmosphere at 0 °C, was added butyl-lithium (2.4 ml of a 2.5M solution in hexane; 6.0 mmol). The dark brown solution was stirred for 1 h and then acetaldehyde (0.24 ml) was added, and stirring continued for 10 min. Water (5 ml) was added, and the tetrahydrofuran removed under reduced pressure. Methylene chloride was added, and the organic phase was washed with brine, dried, and evaporated. Chromatography of the residue on silica gel 60 (Art. 7729) [gradient elution with ethyl acetate–light petroleum (3:2)—(1:0)] gave all four racemic diastereoisomers of the title compound (0.260 g, 50%). The least polar fractions from the column contained (n.m.r. spectrum) two *trans*- and one *cis*-substituted azetidinones. Crystallisation (chloroform–light petroleum) afforded a pure *trans*-isomer, (3RS, 4RS)-3-(1-*hydroxyethyl*)-4-*phenylazetidin*-2-*one* (**17**) as needles, m.p. 145—146 °C (Found: C, 68.8; H, 7.0; N, 7.3%; M^+, 191.0946. $C_{11}H_{13}NO_2$ requires C, 69.1; H, 6.9; N, 7.3%; *M*, 191.0946); $\nu_{max.}$ 3 400, 3 250br, and 1 755 cm^{-1}; δ (90 MHz) 1.30 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 2.96 (1 H, dd, *J* 6 and 2 Hz, 3β-H), 4.10 (1 H, br s, OH, D_2O exch.), 4.26 (1 H, m, quintet after D_2O exch., *J* 6 Hz, CH–O), 4.82 (1 H, d, *J* 2 Hz, 4α-H), and 7.40 (6 H, br s, Ar + NH); *m/z* 191, 176, and 148.

The most polar column fractions contained the remaining *cis*-isomer. Crystallisation (chloroform–light petroleum) gave (3RS, 4SR)-3-(1-*hydroxyethyl*)-4-*phenylazetidin*-2-*one* (**19**), m.p. 137—138 °C (Found: C, 69.1; H, 7.1; N, 7.2%; M^+, 191.0945); $\nu_{max.}$ 3 400 and 1 755 cm^{-1}; δ (90 MHz) 0.85 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 2.50 (1 H, br s, OH, D_2O exch.), 3.40 [1 H, dd (after D_2O exch.), *J* 9 and 6 Hz, 3α-H], 3.78 [1 H, dq (after D_2O exch.), *J* 9 and 6 Hz, CH–O], 4.93 (1 H, d, *J* 6 Hz, 4α-H), 6.80 (1 H, br s, NH, D_2O exch.), and 7.40 (5 H, s, Ar); *m/z* 191, 176, and 148.

^1H N.m.r. spectral examination of the crude mixture indicated a *trans*:*cis* product ratio of (3:2) in the four aldol components.

3-(2-*Hydroxypropan*-2-*yl*)-4-*phenylazetidin*-2-*one*.—4-phenylazetidin-2-one (**15**)[6] (0.40 g; 2.72 mmol) in tetrahydrofuran (30 ml) was cooled to 0 °C in an argon atmosphere and treated with butyl-lithium (2.4 ml of a 2.5M solution in hexane; 6 mmol). Stirring was continued for 1 h. An excess of anhydrous acetone (1 ml) was added, and after a further 5 min, the reaction was quenched with water (5 ml). The tetrahydrofuran was evaporated, methylene chloride added, and the organic phase was washed with brine, dried, and evaporated. Chromatography of the residue on silica gel 60 (Art. 7729) [elution with ethyl acetate–light petroleum (7:3)] afforded the (3RS, 4RS)-*isomer* (**18**) of the title compound (240 mg, 43%). Recrystallisation from chloroform–light petroleum gave needles, m.p. 131 °C (Found: M^+, 205.1103. $C_{12}H_{15}NO_2$ requires *M*, 205.1103); $\nu_{max.}$ 3 420, 3 350br, and 1 755 cm^{-1}; δ (90 MHz) 1.33 (3 H, s, Me), 1.44 (3 H, s, Me), 2.31 (1 H, s, OH), 3.05 (1 H, d, *J* 2 Hz, 3β-H), 4.74 (1 H, d, *J* 2 Hz, 4α-H), 6.56 (1 H, br s, NH), and 7.39 (5 H, s, Ph); *m/z* 190, 162, 147, and 106.

Elution of the column with ethyl acetate gave a gum (0.184 g, 33%), shown (n.m.r. spectrum) to be a mixture of the *trans*- and *cis*-substituted β-lactams (**18**) and (**20**) (3:2 ratio). Crystallisation from chloroform–light petroleum gave the (3RS, 4SR)-*isomer* (**20**), m.p. 164 °C (Found: M^+, 205.1101. $C_{12}H_{15}NO_2$ requires *M*, 205.1103); $\nu_{max.}$ 3 420, 3 300br, and 1 755 cm^{-1}; δ (90 MHz) 0.99 (3 H, s, Me), 1.19 (3 H, s, Me), 1.78 (1 H, s, OH), 3.66 (1 H, dd, *J* 6 and 1.5 Hz, 3α-H), 5.05 (1 H, d, *J* 6 Hz, 4α-H), 6.66 (1 H, br s, NH), and 7.45 (5 H, s, Ph); *m/z* 190, 147, and 106.

4-*Allyl*-3-(2-*hydroxypropan*-2-*yl*)*azetidin*-2-*one*.—To 4-allylazetidin-2-one[1] (**21**) (0.250 g, 2.25 mmol) in tetrahydrofuran (25 ml) at −5 °C in an argon atmosphere, was added butyl-lithium (3.0 ml of a 2.5M solution in hexane; 7.5 mmol). After 1 h, anhydrous acetone (1.0 ml) was added, and stirring continued for 10 min. The mixture was quenched with water (5 ml), the tetrahydrofuran evaporated, and the residue diluted with methylene chloride (20 ml). The organic phase was separated, washed with brine, dried, and evaporated. The residue was chromatographed on silica gel 60 (Art. 7729) [gradient elution with ethyl acetate–light petroleum mixtures; (1:1—1:0)] giving recovered allylazetidinone (0.094 g, 38%). Continued elution furnished successively the *cis*- and *trans*-substituted isomers of the title compound. The (3RS, 4RS)-*azetidinone* (**28**) crystallised from ethyl acetate–light petroleum (0.029 g, 8%), m.p. 144 °C (Found: C, 64.2; H, 9.0; N, 8.2. $C_9H_{15}NO_2$ requires C, 63.9; H, 8.9; N, 8.3%); $\nu_{max.}$ 3 400, 1 745, and 1 640 cm^{-1}; δ (90 MHz) 1.35 (3 H, s, Me), 1.51 (3 H, s, Me), 2.18 (1 H, br s, OH), 2.5—2.9 (2 H, m, CH_2), 3.28 (1 H, d, *J* 5 Hz, 3α-H), 3.85 (1 H, td, *J* 9 and 5 Hz, 4α-H), 4.9—6.1 (3 H, m, $CH{=}CH_2$), and 7.20 (1 H, br s, NH).

The (3*RS*, 4*SR*)-azetidinone (**26**) remained a gum (0.042 g, 11%), $\nu_{max.}$ 3 400, 1 750, and 1 640 cm^{-1}; δ (90 MHz) 1.29 (3 H, s, Me), 1.39 (3 H, s, Me), 2.41 (3 H, br t, *J* 6 Hz, CH_2 and OH), 2.88 (1 H, d, *J* 2 Hz, 3β-H), 3.69 (1 H, td, *J* 6 and 2 Hz, 4α-H), 4.9—5.4 (2 H, m, $=CH_2$), 5.89 (1 H, ddt, *J* 18, 9, and 6 Hz, =CH), and 6.50 (1 H, br s, NH).

4-*Allyl*-1-*dimethyl*-*t*-*butylsilylazetidin*-2-*one* (**22**).—The allyl azetidinone (**21**) (15.0 g) and dimethyl-t-butylsilyl chloride (22.5 g) in dimethylformamide (100 ml) were cooled to 0 °C. Triethylamine (15.0 g, 20.7 ml) in dimethylformamide (30 ml) was added, with stirring (20 min), and the mixture was allowed to warm to room temperature over 20 min. The solvent was removed under reduced pressure (oil pump), and the concentrate was partitioned between ethyl acetate and water. The

organic layer was washed with dilute aqueous hydrochloric acid and brine, and dried. The solution was evaporated and the residue chromatographed on a column of silica gel 60 (Art. 7729), eluting with ethyl acetate–light petroleum (2:3). The product was obtained as an oil (23.7 g, 78%), $\nu_{max.}$ 2 960, 2 940, 2 860, 1 730, 1 645, and 840 cm^{-1}; δ (90 MHz) 0.28 (6 H, s, 2 × MeSi), 1.01 (9 H, s, Bu^t), 1.95—2.62 (2 H, m, $CH_2CH{=}CH_2$), 2.65 (1 H, dd, *J* 15.5 and 3 Hz, 3β-H), 3.17 (1 H, dd, *J* 15.5 and 6 Hz, 3α-H), 3.67 (1 H, m, 4α-H), 5.00—5.40 (2 H, m, $=CH_2$), and 5.82 (1 H, m, $CH{=}CH_2$); g.l.c.–m.s. analysis showed the product to be >85% pure; *m/z* (e.i.) 168 (M^+ − Bu^t).

(3RS, 4SR)-4-*Allyl*-3-(2-*hydroxypropan*-2-*yl*)-1-*dimethyl*-t-*butylsilylazetidin*-2-*one*.—A solution of lithium cyclohexylisopropylamide (50 mmol) was prepared as follows. To cyclohexylisopropylamine (6.9 g, 50 mmol) in tetrahydrofuran (250 ml) was added butyl-lithium (25 ml of a 2M solution in hexane; 50 mmol) in an argon atmosphere at −70 °C. The solution was stirred for 10 min. 4-Allyl-1-dimethyl-t-butylsilylazetidin-2-one (**22**) was added and stirring continued for 30 min. Dry acetone (5 ml) was added and after 30 min, the mixture was allowed to warm to room temperature over a period of 1 h. The reaction was quenched with acetic acid (3 ml), the solvents evaporated, and the residue was partitioned between ethyl acetate and brine. The organic phase was dried, evaporated, and chromatographed on silica gel 60 (Art. 7729). Elution with ethyl acetate–hexane (2:3) gave the crude *N*-silylated derivative of (**26**) as an oil (6.25 g, 99%), $\nu_{max.}$ 3 450br, 2 940, 2 860, 1 725, 1 640, and 840 cm^{-1}; δ (90 MHz) 0.22 (3 H, s, MeSi), 0.26 (3 H, s, MeSi), 0.98 (9 H, s, Bu^{t}Si), 1.24 and 1.32 [each 3 H, s, $Me_2C(OH)$], 2.0 (1 H, s, D_2O exch., OH), 2.26 and 2.62 (both 1 H, m, $CH_2CH{=}CH_2$), 2.88 (1 H, d, *J* 3 Hz, 3β-H), 3.53 (1 H, dt, *J* 9 and 3 Hz, 4α-H), 5.00—5.25 (2 H, m, $=CH_2$), and 5.77 (1 H, complex m, $CH{=}CH_2$).

4-*Allyl*-1-*diphenyl*-t-*butylsilylazetidin*-2-*one* (**23**).—To the allylazetidinone (**21**) (1.03 g) and diphenyl-t-butylsilyl chloride (3.18 g) in dimethylformamide (30 ml) at 0 °C, was added triethylamine (1.12 g) in dimethylformamide (5 ml) over 20 min. After a further 40 min, the solvent was evaporated (oil pump) and the residue was partitioned between ethyl acetate and water. The organic layer was washed with dilute aqueous hydrochloric acid and brine, and was then dried and evaporated. The crude product was chromatographed on silica gel 60 (Art. 9385), eluting with ethyl acetate–light petroleum mixtures (0:1—3:7) to give the N-*silylazetidinone* (**23**) as an oil. With time, the product was obtained as needles (2.25 g, 60%), which were washed with cold hexane, and dried *in vacuo*, m.p. 89—90 °C (Found: C, 75.5; H, 7.8; N, 3.9. $C_{22}H_{27}NOSi$ requires C, 75.6; H, 7.8; N, 4.0); $\nu_{max.}$ 2 930, 2 850, 1 725, 1 640, and 1 590 cm^{-1}; δ (250 MHz), 1.22 (9 H, s), 1.73 (2 H, m, $CH_2CH{=}CH_2$), 2.71 (1 H, dd, *J* 15.75, 2 Hz, 3β-H), 3.18 (1 H, dd, *J* 15.75, 5.5 Hz, 3α-H), 3.42 (1 H, m, 4α-H), 4.75 (1 H, dm, *J* 17 Hz) and 4.89 (1 H, dm, *J* 10.5 Hz) ($CH{=}CH_2$), 5.42 (1 H, ddt, *J* 17, 10, and 7 Hz, $CH{=}CH_2$), 7.40—7.66 (10 H, m).

(3RS, 4SR)-4-*Allyl*-3-(2-*hydroxypropan*-2-*yl*)-1-*diphenyl*-t-*butylsilylazetidin*-2-*one*.—A solution of lithium cyclohexylisopropylamide (7 mmol) was prepared from cyclohexylisopropylamine (0.987 g) and butyl-lithium (4.5 ml of a 1.55M solution in hexane) in tetrahydrofuran (40 ml) as described above. To this solution at −70 °C, was added the *N*-diphenyl-t-butylsilylazetidinone (**23**) (1.19 g, 3.4 mmol) in tetrahydrofuran (15 ml) and the solution was stirred for 30 min. Anhydrous acetone (4 ml) was added and stirring was maintained at −70 °C for 30 min, and then at room temperature for 30 min. Acetic acid (0.45 ml) was then added, and the solution was evaporated. The residue was partitioned between ethyl acetate and brine, and the organic phase was dried and evaporated. Chromatography on silica gel 60 [elution with chloroform–ethanol (19:1)], gave the title *azetidinone* as prisms (1.07 g, 92%), m.p. 147 °C (Found: C, 73.6; H, 8.55; N, 3.5. $C_{25}H_{33}NO_2Si$ requires C, 73.7; H, 8.2; N, 3.4%); $\nu_{max.}$ 3 590, 2 970, 2 840, 1 725, 1 640, and 1 590 cm^{-1}; δ (250 MHz) 1.16 (9 H, s, Bu^{t}Si), 1.38 (3 H, s), 1.27 (3 H, s), 1.74 (2 H, m, $CH_2CH{=}CH_2$), 2.93 (1 H, d, *J* 2.5 Hz, 3β-H), 3.36 (1 H, ddd, *J* 7.5, 5.0, and 2.5 Hz, 4α-H), 4.85 (1 H, dd, *J* 16.5 and 2 Hz) and 4.90 (1 H, dd, *J* 10.5 and 2 Hz) ($CH{=}CH_2$), 5.40 (1 H, ddt, *J* 16.5, 10.5, and 7 Hz, $CH{=}CH_2$). ^{1}H N.m.r. analysis of the crude mixture showed the absence of the corresponding *cis*-substituted, (3*RS*, 4*RS*)-isomer.

(3RS, 4SR)-4-*Allyl*-3-(2-*hydroxypropan*-2-*yl*)*azetidin*-2-*one* (**26**).—(i) Via *the* N-*dimethyl*-t-*butylsilyl derivative*. To the crude *N*-dimethyl-t-butylsilyl derivative of (**26**) (5.39 g, 19 mmol) in methanol (50 ml) was added an excess of anhydrous potassium fluoride (1.83 g, 31 mmol) and stirring was continued at room temperature for 30 min. Evaporation of the methanol gave a residue which was partitioned between ethyl acetate and water. The organic phase was separated, washed with brine, dried, and evaporated. The residue was chromatographed on silica gel 60 (Art. 7729) eluting with ethyl acetate–light petroleum (9:1) affording the title azetidinone as an oil (2.01 g, 61%), $\nu_{max.}$ 3 500br, 3 430 (NH), 1 760, and 1 640 cm^{-1}; δ (250 MHz) 1.27 (3 H, s) and 1.39 [3 H, s, $Me_2C(OH)$], 1.66 (1 H, br s, OH, D_2O exch.), 2.40 (2 H, m, $CH_2CH{=}CH_2$), 2.86 (1 H, dd, *J* 3, 1.5 Hz, 3β-H), 3.66 (1 H, ddd, *J* 7.5, 5.5, and 3 Hz, 4α-H), 5.1—5.2 (2 H, m, $CH{=}CH_2$), and 5.74 (1 H, complex m, $CH{=}CH_2$); *m/z* (NH_3; c.i.) 187 (100%; MNH_4^+), 170 (88; MH^+).

(ii) Via *the* N-*diphenyl*-t-*butylsilyl derivative*. The *N*-diphenyl-t-butylsilyl derivative of (**26**), *vide infra* (0.25 g) in methanol (10 ml) was stirred with an excess of anhydrous potassium fluoride (0.10 g) at room temperature for 1.5 h. Recovery and chromatography as in (i) gave the azetidinone (**26**) (0.082 g, 79%), identical (t.l.c. analysis, i.r., n.m.r. spectra) with the sample described above.

4-*Allyl*-1-*dimethyl*-t-*butylsilyl*-3-*methylazetidin*-2-*one*.—[We thank Mr. R. Hickling for the preparation of azetidinones (**24**) and (**25**)]. To cyclohexylisopropylamine (12.4 g, 88 mmol) in tetrahydrofuran (300 ml) was added butyl-lithium (44 ml of a 2M solution in hexane; 88 mmol) in an argon atmosphere at −70 °C. After 5 min, 4-allyl-1-dimethyl-t-butylsilylazetidin-2-one (**22**) (9.0 g, 40 mmol) in tetrahydrofuran (100 ml) was added and stirring continued for 30 min. Methyl iodide (70 ml, 1.1 mol) was added, and stirring maintained at −70 °C for 30 min, and at room temperature for 1 h. Acetic acid (5.0 ml, 88 mmol) was added, and the mixture was evaporated. The residue, in ethyl acetate, was washed with brine, and dried. Evaporation afforded the crude product, which was chromatographed on silica gel 60 (Art. 9385). Elution with ethyl acetate–hexane (1:1) gave the (3*RS*,4*RS*)-*N*-dimethyl-t-butylsilyl derivative of (**24**) as a gum (8.68 g, 91%), $\nu_{max.}$ 2 940, 2 860, 1 725, and 1 640 cm^{-1}; δ (90 MHz) 0.16 (3 H, s, MeSi), 0.20 (3 H, s, MeSi), 0.91 (9 H, s, Bu^{t}Si), 1.21 (3 H, d, *J* 8 Hz, *Me*CH), 1.9—2.6 (2 H, m, $CH_2CH{=}CH_2$), 2.77 (1 H, qd, *J* 8 and 3 Hz, 3β-H), 3.15 (1 H, ddd, *J* 9, 4, and 3 Hz, 4α-H), 4.94—5.21 (2 H, m, $CH{=}CH_2$), and 5.74 (1 H, m, $CH{=}CH_2$). The n.m.r. spectrum indicated the presence (*ca.* 10%) of the corresponding (3*RS*, 4*SR*)-isomer; δ 1.17 (d, *J* 8 Hz).

(3RS, 4RS)-4-*Allyl*-3-*methylazetidin*-2-*one* (**24**).—To the *N*-silylated derivative of (**24**), prepared above (8.60 g, 36 mmol), in tetrahydrofuran (250 ml) was added anhydrous potassium fluoride (3.60 g, 72 mmol) and 18-crown-6 ether (1.0 g, 4 mmol). The mixture was stirred vigorously at room temperature for 5

min. The tetrahydrofuran was evaporated and the residue was partitioned between ethyl acetate and brine. The ethyl acetate layer was separated, dried, evaporated, and the residue was then chromatographed on silica gel 60 (Art. 9385). Elution with ethyl acetate–hexane (3:2) gave the *trans*-substituted isomer (**24**) as a gum (3.80 g, 85%), $\nu_{max.}$ 3 420, 1 755, and 1 640 cm^{-1}; δ (80 MHz) 1.30 (3 H, d, *J* 7 Hz, *Me*CH), 2.36 (2 H, td, *J* 6 and 1 Hz $CH_2CH{=}CH_2$), 2.80 (1 H, qd, *J* 7 and 2 Hz, 3β-H), 3.30 (1 H, td, *J* 6 and 2 Hz, 4α-H), 4.95—5.1 and 5.15—5.25 (2 H, m, $CH{=}CH_2$), 5.8 (1 H, m, $CH{=}CH_2$), and 6.5 (1 H, br s, NH).

Later fractions from the column furnished the corresponding *cis*-substituted (3*RS*, 4*SR*)-isomer of the title compound as a gum (0.39 g, 8%), $\nu_{max.}$ 3 420, 1 755, and 1 640 cm^{-1}; δ (80 MHz) 1.25 (3 H, d, *J* 8 Hz, *Me*CH), 2.2—2.6 (2 H, m, $CH_2CH{=}CH_2$), 3.35 (1 H, qd, *J* 8 and 6 Hz, 3α-H), 3.76 (1 H, dt, *J* 9 and 6 Hz, 4α-H), 5.0—5.15 and 5.15—5.3 (2 H, m, $CH{=}CH_2$), and 5.5—6.1 (2 H, m, $CH{=}CH_2$ and NH).

(3RS, 4RS)-4-*Allyl*-1-*dimethyl*-t-*butylsilyl*-3-*ethylazetidin*-2-*one*.—Lithium cyclohexylisopropylamide (44 mmol) in tetrahydrofuran (150 ml) was prepared at −70 °C in an atmosphere of argon from cyclohexylisopropylamine (6.2 g) and butyllithium (22 ml of a 2M solution in hexane) as previously described. 4-Allyl-1-dimethyl-t-butylsilylazetidin-2-one (**22**) (4.5 g, 20 mmol) in tetrahydrofuran (50 ml) was added and the mixture stirred for 30 min. An excess of iodoethane (93.6 g, 48 ml) was added, and stirring was continued at −70 °C for 30 min and at room temperature for 1 h. Acetic acid (2.5 ml, 44 mmol) was added, the solvents evaporated, and the residue, in ethyl acetate, was washed with brine, dried, and evaporated. Chromatography on silica gel 60 (Art. 7729), eluting with ethyl acetate–hexane (1:3) gave the *N*-dimethyl-t-butylsilyl derivative of (**25**) as an oil (4.03 g, 79%), $\nu_{max.}$ 2 950, 2 870, 1 720, 1 645, and 815 cm^{-1}; δ (60 MHz) 0.12 and 0.16 (each 3 H, s, 2 × MeSi), 0.85 (12 H, m, Bu^{t}Si and CH_2Me), 1.30—2.85 (5 H, m, 3-CH_2, 4-CH_2, and 3β-H), 3.22 (1 H, dt, *J* 9 and 3 Hz, 4α-H), 4.80—5.05 and 5.05—5.25 (2 H, m, $CH{=}CH_2$), and 5.25—6.15 (1 H, m, $CH{=}CH_2$); *m/z* (NH_3; c.i.) 254, (MH^+).

(3RS, 4RS)-4-*Allyl*-3-*ethylazetidin*-2-*one* (**25**).—The silyl derivative of (**25**) (3.95 g) in tetrahydrofuran (100 ml) was deprotected with anhydrous potassium fluoride (1.70 g) in the presence of 18-crown-6 (0.45 g) as described for (**24**). Chromatography afforded the 3-*ethylazetidinone* (**25**) as a gum (1.71 g, 79%) (Found: e.i., $M^+ - CH_2CH{=}CH_2$ 307.0908. $C_{14}H_{15}N_2O_6$ requires 307.0928); $\nu_{max.}$ 3 420, 1 755, and 1 640 cm^{-1}; δ (90 MHz) 1.00 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.78 (2 H, quintet, *J* 7 Hz, MeCH_2), 2.45 (2 H, t, *J* 7 Hz, $CH_2CH{=}CH_2$), 2.79 (1 H, br td, *J* 7 and 2 Hz, 3β-H), 3.45 (1 H, td, *J* 7 and 2 Hz, 4α-H), 5.00—5.18 and 5.22—5.40 (2 H, 2 m, $CH{=}CH_2$), 5.45—6.26 (1 H, m, $CH{=}CH_2$), and 6.85 (1 H, br s, NH); *m/z* (NH_3; c.i. gas) 366 (MNH_4^+), 349 (MH^+).

4-*Allyl*-3-(1-*hydroxyethyl*)-1-*diphenyl*-t-*butylsilylazetidin*-2-*ones* (**27**) *and* (**29**).—(i) Via *direct aldol reaction of azetidinone* (**22**). Lithium cyclohexylisopropylamide in tetrahydrofuran (40 ml) was prepared at −70 °C from cyclohexylisopropylamine (2.76 g) and butyl-lithium (2.6 ml of a 1.55M solution in hexane). To this solution was added the allyl azetidinone (**22**) (2.00 g) in tetrahydrofuran (6 ml). The dark brown solution was stirred at −70 °C for 10 min. An excess of acetaldehyde (1.0 ml) was added and the mixture was allowed to warm to 0 °C. It was then neutralized with acetic acid (2.34 g) and concentrated. The solution in ethyl acetate was washed well with brine, dried, and evaporated. The residue was chromatographed on silica gel 60 (Art. 7729) employing gradient elution with ethyl acetate–light petroleum mixtures (1:9—3:7), to give a mixture of isomers of the title compounds (1.405 g, 59%). The least polar component from the column was a *cis*-substituted (3RS, 4RS)-*hydroxyethylazetidinone* (**29**), obtained as a gum (0.270 g, 11%) [Found: (e.i.) MH^+, 270.1866. $C_{14}H_{28}NO_2Si$ requires 270.1887]; $\nu_{max.}$ 3 470, 2 950, 2 850, 1 720, 1 640, and 840 cm^{-1}; δ (250 MHz) 0.25 (6 H, s, 2 × MeSi), 0.98 (9 H, s, Bu^{t}Si), 1.35 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 2.20 (1 H, br d, *J* 6 Hz, OH, D_2O exch.), 2.51 (1 H, dddt, *J* 16, 6, 4, and 2 Hz) and 2.79 (1 H, dddt, *J* 16, 10, 7 and 2 Hz) ($CH_2CH{=}CH_2$), 3.28 (1 H, dd, *J* 6 and 5 Hz, 3α-H), 3.77 (1 H, ddd, *J* 10, 6, and 4 Hz, 4α-H), 4.19 [1 H, qd, *J* 5 and 6 Hz after D_2O exch., MeC*H*(OH)], 5.12 (1 H, dq, *J* 11 and 2 Hz) and 5.15 (1 H, dq, *J* 18 and 2 Hz) ($CH{=}CH_2$), and 5.81 (1 H, dddd, *J* 18, 11, 7, and 6 Hz, $CH{=}CH_2$); *m/z* 212 (M^+ − Bu^t).

Continued elution of the column afforded a mixture of the *trans*-substituted azetidinones (**27**) (1.135 g, 48%) (*ca.* 1:1 ratio, n.m.r. spectrum). Rechromatography afforded the pure components; the (1′*RS*, 3*RS*, 4*SR*)-isomer remained a gum, $\nu_{max.}$ 3 450, 2 960, 2 860, 1 720, 1 640, and 840 cm^{-1}; δ (250 MHz) 0.23 (3 H, s, MeSi), 0.28 (3 H, s, MeSi), 0.98 (9 H, s, Bu^{t}Si), 1.27 [3 H, d, *J* 7 Hz, *Me*CH(OH)], 2.15—2.28 (1 H, m) and 2.54—2.66 (1 H, m) ($CH_2CH{=}CH_2$), 2.36 (1 H, br s, OH, D_2O exch.), 2.85 (1 H, dd, *J* 7 and 3 Hz, 3β-H), 3.42 (1 H, ddd, *J* 10, 4, and 3 Hz, 4α-H), 3.99 [1 H, br quintet, *J* 7 Hz, MeC*H*(OH)], 5.15 (1 H, br d, *J* 10 Hz) and 5.17 (1 H, br d, *J* 18 Hz) ($CH{=}CH_2$), and 5.74 (1 H, ddt, *J* 18, 10, and 6 Hz, $CH{=}CH_2$); *m/z* (NH_3; c.i.) MH^+, 270. {The n.m.r. spectrum of the trailing fractions indicated the presence of a trace amount of the remaining *cis*-substituted isomer, δ 1.41 [d, *J* 7 Hz, *Me*CH(OH)], 3.32 (dd, *J* 10 and 6 Hz, 3α-H), and 3.84 (ddd, *J* 10, 6, and 4 Hz, 4α-H)}.

The most polar component was the (1′RS, 3SR, 4RS)-*hydroxyethylazetidinone* isomer (**30**), which crystallised from warm hexane, m.p. 79—81 °C (Found: C, 62.6; H, 9.8; N, 5.2. $C_{14}H_{27}NO_2Si$ requires C, 62.4; H, 10.1; N, 5.2%); $\nu_{max.}$ 3 430, 2 930, 2 860, 1 720, 1 640, and 840 cm^{-1}; δ (250 MHz) 0.23 (6 H, s, 2 × MeSi), 0.97 (9 H, s, Bu^{t}Si), 1.23 [3 H, d, *J* 7 Hz, *Me*CH(OH)], 1.97 (1 H, br s, OH, D_2O exch.), 2.2—2.8 (2 H, m, $CH_2CH{=}CH_2$), 2.86 (1 H, dd, *J* 5 and 3 Hz, 3β-H), 3.60 (1 H, dt, *J* 9 and 3 Hz, 4α-H), 3.9—4.3 [1 H, m, MeC*H*(OH)], 5.0—5.3 (2 H, m, $CH{=}CH_2$), and 5.78 (1 H, ddt, *J* 16, 10, and 7 Hz, $CH{=}CH_2$).

(ii) Via *stereoselective reduction of ketone* (**31**). 3-Acetyl-4-allyl-1-dimethyl-t-butylsilylazetidin-2-one (**31**) (*vide infra*) (0.534 g, 2 mmol) in tetrahydrofuran (15 ml) was cooled to 0 °C and potassium tri-s-butylborohydride (K-Selectride) (4.2 ml of a 0.5M solution in tetrahydrofuran; 2.1 mmol) was added. The mixture was stirred at 0—5 °C for 2 h. Saturated aqueous ammonium chloride was added, the mixture was diluted with ethyl acetate, and the organic layer was separated, washed with further portions of ammonium chloride solution, dried, and evaporated. The residue, in toluene (3 ml), was chromatographed on silica gel 60 (1:1 ratio of Art. 9385 and 7729 grades, 13 × 3 cm) eluting with ethyl acetate–light petroleum mixtures (1:3—1:1). The product, obtained as a gum (0.502 g, 91%), was shown (n.m.r. spectrum) to be a 9:1 mixture of the *trans*-substituted isomers of the title hydroxyethylazetidinone (**27**). Crystallisation afforded the major (1′*RS*, 3*SR*, 4*RS*)-isomer (**30**) (0.42 g) m.p. (hexane) 78—80 °C, identical (i.r., n.m.r. spectra) with the sample prepared in (i).

(iii) Via *sodium borohydride reduction of ketone* (**31**). Sodium borohydride (0.01 g) in water (0.5 ml) was added dropwise to the ketone (**31**) (0.055 g) in tetrahydrofuran (1.5 ml) at 0 °C. The reaction mixture was stirred at 5 °C for 1 h and at room temperature for 2 h. Addition of saturated aqueous ammonium chloride and recovery in ethyl acetate was effected as in (ii). Chromatography gave a mixture of the *trans*-substituted isomers (**27**) as a gum (0.041 g, 74%) with a 4:3 ratio of (1′*RS*, 3*SR*, 4*RS*) and (1′*RS*, 3*RS*, 4*SR*) isomers (n.m.r. spectrum).

(3RS, 4SR)-3-*Acetyl*-4-*allyl*-1-*dimethyl*-*t*-*butylsilylazetidin*-2-*one* (**31**).—To cyclohexylisopropylamine (1.252 g, 8.88 mmol) in tetrahydrofuran (30 ml) in an atmosphere of argon at −70 °C, was added butyl-lithium (5.75 ml of a 1.55M solution in hexane). The silylated allylazetidinone (**22**) (1.00 g, 4.44 mmol) in tetrahydrofuran (10 ml) was added, and the mixture stirred for 15 min. *N*-Acetylimidazole (0.980 g, 8.9 mmol) in the minimum amount of dimethylformamide (5 ml) was diluted with tetrahydrofuran. This solution was added dropwise to the cold lithium cyclohexylisopropylamide solution, and stirring was continued at −70 °C for a further 10 min. Saturated aqueous ammonium chloride (20 ml) was added, and the reaction mixture was allowed to warm to room temperature, and diluted with ethyl acetate. The organic layer was washed with brine, dried, and evaporated. The residue was chromatographed on Kieselgel 60 (1:1 ratio Art. 7729 and 9385 grades; 12 × 4 cm), eluting with ethyl acetate–light petroleum (1:3). Early fractions contained a dimeric species, obtained as an oil (104 mg), $\nu_{max.}$ 3 550, 2 940, 2 860, 1 725, 1 640, and 840 cm^{-1}; *m/z* (NH_3; c.i.) 493, (MH^+). [This corresponded to the MH^+ ion arising from the product of aldol reaction of the anion of (**22**) with the ketone (**31**)]. $C_{26}H_{48}N_2O_3Si_2$ requires *M*, 492. Further elution of the column gave the required *ketone* (**31**) as an oil (0.772 g, 65%), $\nu_{max.}$ 2 930, 2 860, 1 735, 1 710, 1 640, and 840 cm^{-1}; δ (250 MHz) 0.23 (3 H, s, MeSi), 0.28 (3 H, s, MeSi), 0.96 (9 H, s, Bu^{t}Si), 2.20 (1 H, m) and 2.60 (1 H, m) ($CH_2CH{=}CH_2$), 2.29 (3 H, s, Ac), 3.89 (1 H, d, *J* 3 Hz, 3β-H), 4.06 (1 H, ddd, *J* 9.5, 4, and 3 Hz, 4α-H), 5.11 (1 H, br d, *J* 11 Hz) and 5.12 (1 H, d, *J* 17 Hz) ($CH{=}CH_2$), and 5.72 (1 H, m, $CH{=}CH_2$), *m/z* (NH_3; c.i.) 285 (MNH_4^+), 268 (MH^+).

Benzyl 4-*Allyl*-3-(2-*hydroxypropan*-2-*yl*)-2-*oxoazetidin*-1-*yl*(*triphenylphosphoranylidene*)*acetates* (**34**).—Lithium cyclohexylisopropylamide was prepared by the addition of butyl-lithium (1.70 ml of a 2.5M solution in hexane) to cyclohexylisopropylamine (0.60 g) in tetrahydrofuran (10 ml) in an atmosphere of argon at −70 °C. The solution was stirred for 10 min, and then benzyl 4-allyl-2-oxoazetidin-1-yl triphenylphosphoranylideneacetate [1] (**32**) (1.00 g) in tetrahydrofuran (10 ml) was added. After 5 min, dry acetone (0.71 ml) was added to the red-brown solution, the cooling bath removed, and the mixture was allowed to warm to 0 °C (10 min). Acetic acid (0.56 g) was added, the solvents were evaporated under reduced pressure, and the residue was chromatographed on silica gel 60 (Art. 7729). Gradient elution with ethyl acetate–light petroleum mixtures (1:1—7:3) gave a mixture of *cis*-(3*RS*, 4*RS*) and *trans*-(3*RS*, 4*SR*) isomers of the title phosphorane (**34**) (0.76 g, 71%), $\nu_{max.}$ 3 000br, 1 735, and 1 620 cm^{-1}.

Careful rechromatography afforded a substantial separation of the *cis*- and *trans*-isomers. These were characterised by subsequent transformation to the respective bicyclic β-lactams (*vide infra*).

Benzyl (5RS, 6RS)-6-(2-*Hydroxypropan*-2-*yl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**48**).—To the *cis*-isomer of the phosphorane (**34**) (0.188 g), in ethyl acetate (14 ml) was added an excess of trifluoroacetic acid (0. 5 ml), and the solution was stirred at room temperature for 30 min; it was then cooled to −70 °C. Ozone was passed into the reaction mixture until it became pale blue. Argon was then bubbled through the cold solution until all the excess of ozone had been purged. Triphenylphosphine (0.085 g) in ethyl acetate (2 ml) was added and the solution maintained at −70 °C for a further 10 min. The reaction flask was transferred to an ice-bath, and saturated aqueous sodium hydrogen carbonate (20 ml) was added, and the mixture was stirred vigorously for 30 min. The ethyl acetate layer was separated, washed with brine, dried, and left at room temperature for 36 h. During this time, the cyclisation reaction was monitored by t.l.c. It was apparent that a polar component, presumed to be the intermediate cyclic hemi acetal (**53**), gradually diminished. This was accompanied by an increase in intensity of a less-polar component, which corresponded to the required *cis*-product. The ethyl acetate was evaporated to give a residue, which was purified by chromatography on silica gel 60 (Art. 9385), eluting with ethyl acetate–light petroleum (1:1). The *bicyclic* β-*lactam* (**48**) crystallised from ethyl acetate–light petroleum (0.048 g, 49%), m.p. 122—124 °C (Found: C, 67.7; H, 6.5; N, 4.5%; M^+, 301.1315. $C_{17}H_{19}NO_4$ requires C, 67.8; H, 6.4; N, 4.7%; *M*, 301.1314); $\lambda_{max.}$(EtOH) 273 nm (ε 4 800 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 2 950br, 1 770, and 1 720 cm^{-1}; δ (90 MHz), 1.30 (3 H, s), 1.54 (3 H, s), 1.74 (1 H, br s, OH), 2.68 (1 H, ddd, *J* 18, 9, and 2.5 Hz, 4-H), 3.59 (1 H, d, *J* 6.5 Hz, 6α-H), 3.83 (1 H, ddd, *J* 18, 9, and 2.5 Hz, 4-H), 4.35 (1 H, dt, *J* 6.5 and 9 Hz, 5α-H), 5.21 and 5.37 (each 1 H, *J* 13 Hz, ABq, CH_2Ph), 6.59 (1 H, t, *J* 2.5 Hz, 3-H), and 7.36 (5 H, br s, Ph).

Benzyl (5RS, 6SR)-6-(2-*Hydroxypropan*-2-*yl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**41**).—The *trans*-isomer of the phosphorane (**34**) (0.365 g) was subjected to an ozonolysis–cyclisation reaction sequence as described in the previous experiment. In this case, however, the formation of the bicyclic β-lactam system was complete after stirring the neutralized ozonolysis reaction mixture at room temperature for only 30 min (t.l.c. analysis). After rapid chromatography, the required *trans*-substituted *bicyclic* β-*lactam* (**41**) was obtained as a gum (0.048 g, 25%) (Found: M^+, 301.1303. $C_{17}H_{19}NO_4$ requires *M*, 301.1314); $\lambda_{max.}$(EtOH) 278 nm; $\nu_{max.}$ 2 950br, 1 780, and 1 720 cm^{-1}; δ (90 MHz) 1.30 (3 H, s), 1.37 (3 H, s), 1.78 (1 H, br s, OH), 2.65 and 2.95 (each 2 H, ddd, *J* 18, 8, and 2 Hz, 4-H_2), 3.16 (1 H, d, *J* 3 Hz, 6β-H), 4.20 (1 H, dt, *J* 3 and 8 Hz, 5α-H), 5.20 (2 H, s, CH_2Ph), 6.36 (1 H, t, *J* 2 Hz, 3-H), and 7.28 (5 H, br s, Ph).

The ozonolysis–cyclisation procedure was also carried out on the unseparated mixture of *cis*- and *trans*-substituted phosphoranes (**34**) (0.76 g). After work-up and chromatographic separation of the resulting bicyclic β-lactams, pure *cis*- (**48**) (0.045 g, 11%) and *trans*- (**41**) (0.100 g, 25%) isomers were obtained.

Benzyl [4-*Allyl*-3-(1-*hydroxyethyl*)-2-*oxoazetidin*-1-*yl*](*triphenylphosphoranylidene*)*acetates* (**35**).—To cyclohexylisopropylamine (0.60 g) in tetrahydrofuran (10 ml) at −70 °C in an argon atmosphere was added butyl-lithium (1.70 ml of a 2.5M solution in hexane), with stirring. After 10 min, the phosphorane (**32**) (1.00 g) in tetrahydrofuran (10 ml) was added and stirring was maintained for 5 min. Acetaldehyde (0.54 ml) was then added, followed, after a further 10 min, by acetic acid (0.56 g). The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel 60 (Art. 7729). Gradient elution with ethyl acetate–light petroleum (1:1—1:0) gave a mixture of the *cis*-(5*RS*, 6*RS*) and *trans*-(5*RS*, 6*SR*) substituted isomers of the title phosphorane (**35**) as a foam (0.71 g, 65%); $\nu_{max.}$ 3 000br, 1 735, and 1 620 cm^{-1}.

Benzyl 6-(1-*Hydroxylethyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylates* (**49**), (**42**).—The mixture of the *cis*- and *trans*-isomers of the phosphorane (**35**) (0.79 g) obtained above, in ethyl acetate (70 ml), was stirred in the presence of trifluoroacetic acid (1.60 g) at room temperature for 30 min. The mixture was cooled to −70 °C, and ozone was passed into the solution until a faint blue colour persisted. Argon was then bubbled through the ozonide solution to remove the excess of ozone. Triphenylphosphine (0.37 g) in ethyl acetate was added, and after 10 min, the reaction flask was transferred to an ice-bath, and saturated aqueous sodium hydrogen carbonate (104

ml) was added to generate the corresponding phosphorane aldehydes. The mixture was stirred vigorously at room temperature for 30 min, and the ethyl acetate layer was then separated and dried. The solution was left at room temperature for 3 days to allow the cyclisation reactions to proceed to completion (t.l.c. analysis). The solvent was then evaporated, and the residual oil was chromatographed rapidly on silica gel 60 (Art. 9385) (80 g) eluting with ethyl acetate–light petroleum mixtures (3:7)—(7:3). Only two of the four possible racemic diastereoisomers of the title compound could be isolated from the reaction mixture, possessing, respectively, *cis*- and *trans*-substitution of the azetidinone ring. The *cis*-(5RS, 6RS, 8RS)-*isomer* (**49**) (0.030 g, 7%) crystallised from ethyl acetate–light petroleum, m.p. 94—99 °C (Found: M^+, 287.1150. $C_{16}H_{17}NO_4$ requires M, 287.1157); $\lambda_{max.}$(EtOH) 270sh nm; $\nu_{max.}$ 3 000br, 1 775, 1 725, and 1 615 cm^{-1}; δ (90 MHz, [$^2H_6$]acetone) 1.25 [3 H, d, *J* 6 Hz, *Me*C(OH)], 2.63 (1 H, ddd, *J* 18, 10, and 2.5 Hz, 4-H), 3.25 (1 H, ddd, *J* 18, 8, and 2.5 Hz, 4-H), 3.51 (1 H, dd, *J* 6 and *ca.* 6 Hz, 6α-H), 4.25 (1 H, ddd, *J* 10, 8, and 6 Hz, 5α-H), overlapping 3.94—4.23 [1 H, m, MeC*H*(OH)], 5.17 (2 H, s, CH_2Ph), 6.46 (1 H, t, *J* 2.5 Hz, 3-H), and 7.22—7.40 (5 H, m, Ph).

Continued elution of the column gave the *trans*-(5RS, 6SR, 8SR)-*isomer* (**42**) as a gum (0.070 g, 17%) (Found: M^+, 287.1156. $C_{16}H_{17}NO_4$ requires M, 287.1157); $\lambda_{max.}$(EtOH) 275 nm; $\nu_{max.}$ 3 000, 1 780, 1 725, and 1 610 cm^{-1}; δ (90 MHz, [$^2H_6$]acetone) 1.25 [3 H, d, *J* 6 Hz, *Me*CH(OH)], 2.77 (2 H, dd, *J* 9 and 2.5 Hz, 4-H_2), 2.96 (1 H, s, OH), 3.31 (1 H, dd, *J* 3.5 and 3 Hz, 6β-H), 4.20 (1 H, td, *J* 9 and 3 Hz, 5α-H) overlapping with 3.94—4.23 [1 H, m, MeC*H*(OH)], 5.17 (2 H, s, CH_2Ph), 6.36 (1 H, t, *J* 2.5 Hz, 3-H), and 7.2—7.5 (5 H, m, Ph).

Benzyl [4-*Allyl*-3-(1-*hydroxycyclohexyl*)-2-*oxoazetidin*-1-*yl*]-*triphenylphosphoranylideneacetates* (**36**).—Lithium cyclohexylisopropylamide in tetrahydrofuran (5 ml) was generated from cyclohexylisopropylamine (0.60 g) and butyl-lithium (2.7 ml of a 1.6M solution in hexane), in the manner described above. The phosphorane (**32**) (1.00 g) in tetrahydrofuran (15 ml) was added, and the resulting red-brown solution was stirred at −70 °C for a further 10 min, and then treated with cyclohexanone (0.40 ml). The mixture was allowed to warm to 0 °C. Neutralisation with acetic acid (0.56 g) and evaporation gave a residue which was partitioned between ethyl acetate and brine. The organic layer was separated, dried, and concentrated. Chromatography on silica gel 60 (Art. 7729), eluting with ethyl acetate–light petroleum mixtures (1:1)—(7:3) gave a mixture of *cis*- and *trans*-substituted isomers of the title phosphorane (**36**) (0.76 g, 64%), $\nu_{max.}$ 3 400, 1 735, and 1 615 cm^{-1}.

Benzyl 6-(1-*Hydroxycyclohexyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]-*hept*-2-*ene*-2-*carboxylates* (**43**) *and* (**50**).—The mixed isomers of the phosphorane (**36**) (0.75 g) in ethyl acetate (50 ml) were stirred at room temperature with trifluoroacetic acid (2.0 ml). Ozonolysis at −70 °C, purging with argon, and addition of triphenylphosphine (0.32 g) in ethyl acetate (5 ml) were conducted as previously described. The mixture was neutralised with saturated aqueous sodium hydrogen carbonate (60 ml), the ethyl acetate layer was separated, washed with brine, dried, and set aside overnight. The solution was concentrated and chromatographed rapidly as before, to give, successively, a *cis*- and a *trans*-substituted isomer of the title compound. The least polar, (5RS, 6RS)-*azabicycloheptene* (**50**) crystallised from ethyl acetate–light petroleum (0.040 g, 10%), m.p. 125—126 °C (Found: C, 70.4; H, 6.8; N, 4.1. $C_{20}H_{23}NO_4$ requires C, 70.4; H, 6.8; N, 4.1%); $\lambda_{max.}$(EtOH), 275 nm (ε 4 240 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 3 600, 1 770, 1 720, and 1 615 cm^{-1}; δ (90 MHz) 1.2—1.9 (10 H, m, cyclohexyl), 1.64 (1 H, s, OH), 2.58 (1 H, ddd, *J* 18, 9, and 3 Hz, 4-H), 3.61 (1 H, d, *J* 5.5 Hz, 6α-H), 3.76 (1 H, ddd, *J* 18, 9, and 3 Hz, 4-H), 4.24 (1 H, td, *J* 9 and 5.5 Hz, 5α-H), 5.11 (1 H, d, *J* 12 Hz) and 5.27 (1 H, d, *J* 12 Hz) (ABq, CH_2Ph), 6.50 (1 H, t, *J* 3 Hz, 3-H), and 7.2—7.4 (5 H, m, Ph).

Further elution of the column provided a corresponding (5RS, 6SR)-*isomer* (**43**), which crystallised from ethyl acetate–light petroleum (0.18 g, 43%), m.p. 102—104 °C (Found: C, 70.4; H, 6.7; N, 4.0. $C_{20}H_{23}NO_4$ requires C, 70.4; H, 6.8; N, 4.1%); $\lambda_{max.}$(EtOH) 279 nm (ε 4 530 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 3 550, 1 775, 1 725, and 1 615 cm^{-1}; δ (90 MHz) 1.2—1.9 (10 H, m, cyclohexyl), 1.75 (1 H, s, OH), 2.66 (1 H, ddd, *J* 18, 8, and 2.5 Hz, 4-H), 2.91 (1 H, ddd, *J* 18, 8, and 2.5 Hz, 4-H), 3.22 (1 H, d, *J* 3 Hz, 6β-H), 4.24 (1 H, td, *J* 8 and 3 Hz, 5α-H), 5.13 and 5.29 (each 1 H, *J* 12 Hz, ABq, CH_2Ph), 6.39 (1 H, t, *J* 2.5 Hz, 3-H), and 7.2—7.4 (5 H, m, Ph).

Benzyl [4-*Allyl*-3-(α-*hydroxybenzyl*)-2-*oxoazetidin*-1-*yl*]*triphenylphosphoranylideneacetates* (**37**).—The phosphorane (**32**) (2.00 g) in tetrahydrofuran (40 ml) was added to a solution of lithium cyclohexylisopropylamide in tetrahydrofuran (20 ml) prepared from cyclohexylisopropylamine (1.20 g) and butyl-lithium (5.30 ml of a 1.6M solution in hexane) in the manner previously described. After 5 min, benzaldehyde (1.0 ml) was added, and the solution kept at −70 °C for 10 min. Acetic acid was then added, and the reaction mixture was allowed to warm to room temperature. Evaporation and chromatography on silica gel 60 (Art. 7729) [elution with ethyl acetate–light petroleum (1:1—3:1)] gave a mixture of (3*RS*, 4*RS*) and (3*RS*, 4*SR*)-isomers of the title phosphorane (**37**) (1.52 g, 63%); $\nu_{max.}$ 3 400, 1 725, and 1 615 cm^{-1}.

Benzyl 6-(α-*Hydroxybenzyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylates* (**51**) *and* (**44**).—A mixture of *cis*- and *trans*-substituted isomers of the phosphorane (**37**) (0.80 g), as obtained above, in ethyl acetate–trifluoroacetic acid was treated successively with ozone, triphenylphosphine (0.34 g), and saturated aqueous sodium hydrogen carbonate (20 ml) under the standard ozonolysis–cyclisation procedure. The resulting solution of phosphorane–aldehydes was set aside at room temperature for 3 days. Evaporation and rapid chromatography of the residue on silica gel 60 (Art. 9385) [elution with ethyl acetate–cyclohexane (1:1)] gave one *cis*- and one *trans*-substituted isomer of the four possible racemic diastereoisomers of the title compound. The (5RS, 6RS) *isomer* (**51**) crystallised from ethyl acetate–light petroleum (0.12 g, 27%), m.p. 124 °C (Found: C, 73.0; H, 5.1; N, 3.6. $C_{22}H_{19}NO_4$ requires C, 73.1; H, 5.3; N, 3.9%); $\lambda_{max.}$(EtOH) 277 nm (ε 4 830 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 3 550, 1 775, 1 725, and 1 610 cm^{-1}; δ (90 MHz, C_6D_6) 1.5—1.9 (1 H, m, 4-H), 2.2—2.7 (2 H, m, 4-H and OH), 3.2—3.7 (2 H, m, 5α-H and 6α-H), 4.43 [1 H, dd, *J* 7 and 3 Hz, PhC*H*(OH)], 5.03 and 5.17 (each 1 H, *J* 12 Hz, ABq, CH_2Ph), 6.12 (1 H, t, *J* 3 Hz, 3-H), and 7.0—7.4 (10 H, m, Ph).

Continued elution of the column gave the (5*RS*, 6*SR*)-isomer (**44**) as a gum (0.12 g, 27%); $\nu_{max.}$ 3 600—3 400, 1 775, 1 715, and 1 610 cm^{-1}; δ (90 MHz, C_6D_6) 1.89 (2 H, dd, *J* 9 and 3 Hz, 4-H_2), 2.70 (1 H, br s, OH), 3.15 (1 H, dd, *J* 5 and 3 Hz, 6β-H), 3.69 (1 H, td, *J* 9 and 3 Hz, 5α-H), 4.67 [1 H, d, *J* 5 Hz, PhC*H*(OH)], 4.95 and 5.09 (each 1 H, *J* 12 Hz, ABq, CH_2Ph), 5.90 (1 H, t, *J* 3 Hz, 3-H), and 6.9—7.4 (10 H, m, Ph).

Benzyl [4-*Allyl*-3-(1-*hydroxypropyl*)-2-*oxoazetidin*-1-*yl*]*triphenylphosphoranylideneacetates* (**38**).—The phosphorane (**32**) (1.00 g, 1.9 mmol) in tetrahydrofuran (15 ml) was added to a solution of lithium cyclohexylisopropylamide, prepared as described above, from cyclohexylisopropylamine (0.60 g, 4.2 mmol) and butyl-lithium (2.7 ml of a solution 1.6M in hexane) at −70 °C. After the mixture had been stirred for 5 min, propanal (1.0 ml) was added, and the solution was then allowed to warm to room temperature. After neutralisation with acetic acid, the

solution was concentrated, diluted with ethyl acetate, washed with brine, and dried. Evaporation gave a gum, which in toluene (5 ml) was chromatographed on silica gel 60 (Art. 7729). Gradient elution with ethyl acetate–light petroleum (1:1—1:0) gave the phosphoranes (**38**) as a foam (0.80 g, 72%).

Benzyl 6-(1-*Hydroxypropyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylates* (**52**) *and* (**45**).—The crude phosphoranes (**38**) (0.800 g) were subjected to the ozonolysis–cyclisation procedure as described for previous examples. The products, in toluene, were chromatographed rapidly on silica gel (Art. 9385) eluting with ethyl acetate–light petroleum mixtures (3:2—7:3), to give a mixture of *cis*- and *trans*-isomers (0.125 g, 30%). Rechromatography afforded successively, samples of the pure components. A (5*RS*, 6*RS*)-isomer (**52**) was obtained as a gum (0.015 g, 4%), $\lambda_{max.}$(EtOH) 270 nm; $\nu_{max.}$ 3 400br, 1 775, 1 710, and 1 610 cm^{-1}; δ (80 MHz, [$^2H_6$]acetone) 0.92 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.52 (2 H, quintet, *J ca.* 7 Hz, MeCH_2), 2.25—2.80 and 2.80—3.25 (each 1 H, m, 4-H_2), 3.60 (1 H, t, *J* 5 Hz, 6α-H), 3.75—4.65 [3 H, m, 5α-H and C*H*(O*H*)], 5.23 (2 H, ABq, CH_2Ph), 6.50 (1 H, t, *J* 2.5 Hz, 3-H), and 7.2—7.5 (5 H, m, Ph); *m/z* (e.i.) 301.

A (5RS, 6SR)-*isomer* (**45**) was also a gum (0.030 g, 7%) (Found: M^+ 301.1318. $C_{17}H_{19}NO_4$ requires *M*, 301.1314); $\lambda_{max.}$(EtOH) 276 nm; $\nu_{max.}$ 3 500br, 1 775, 1 720, and 1 610 cm^{-1}; δ (80 MHz, [$^2H_6$]acetone) 0.95 (3 H, t, *J* 7 Hz, *Me*CH_2), 1.63 (2 H, quintet, *J ca.* 7 Hz, *Me*CH_2), 2.84 (2 H, dd, *J* 9 and 2.5 Hz, 4-H_2), 3.37 (1 H, t, *J* 3.5 Hz, 6β-H), 3.63—3.92 [1 H, m, C*H*(OH)], 4.20 (1 H, dt, *J* 9 and 3.5 Hz, 5α-H), 5.18 (2 H, s, CH_2Ph), 6.03 (1 H, d, *J* 6 Hz, OH, D_2O exch.), 6.40 (1 H, t, *J* 2.5 Hz, 3-H), and 7.05—7.65 (5 H, m, Ph).

Benzyl (3RS, 4RS)-(4-*Allyl*-3-*methyl*-2-*oxoazetidin*-1-*yl*)*triphenylphosphoranylideneacetate* (**39**).—The phosphorane (**32**) (0.50 g) in tetrahydrofuran (5 ml) was added to lithium cyclohexylisopropylamide, prepared in tetrahydrofuran (5 ml) from cyclohexylisopropylamine (0.30 g) and butyl-lithium (0.85 ml of a 2.5M solution in hexane) at −70 °C. The mixture was stirred for 5 min and then an excess of methyl iodide (0.12 ml) was added. After a further 10 min, the reaction vessel was transferred to an ice-bath, and the mixture was neutralised with acetic acid (0.16 ml). The product was recovered in ethyl acetate, and chromatographed on silica gel 60 (Art. 7729). Elution with ethyl acetate–hexane mixtures (1:1—7:3) gave the 3-methylphosphorane (**39**) (0.10 g, 19%), $\nu_{max.}$ 1 735 and 1 610 cm^{-1}. Later fractions from the column contained the unchanged phosphorane (**32**) (0.17 g).

Benzyl (5RS, 6RS)-6-*Methyl*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**46**).—The methylphosphorane (**39**) (0.29 g) was subjected to the standard ozonolysis–cyclisation sequence. Rapid chromatography of the crude product on silica gel 60 (Art. 9385), using gradient elution with ethyl acetate–light petroleum (3:7—3:2) furnished the bicylic *azetidinone* (**46**) as a gum (0.080 g, 55%) (Found: M^+, 257.1051. $C_{15}H_{15}NO_3$ requires *M*, 257.1051); $\nu_{max.}$ 1 780, 1 725, and 1 615 cm^{-1}; δ (90 MHz, [$^2H_6$]acetone) 1.34 (3 H, d, *J* 7 Hz, *Me*CH), 2.85 (2 H, dd, *J* 9 and 2 Hz, 4-H_2), 3.24 (1 H, dq, *J* 3 and 7 Hz, 6β-H), 3.91 (1 H, dt, *J* 3 and 9 Hz, 5α-H), 5.20 (2 H, s, CH_2Ph), 6.45 (1 H, t, *J* 2 Hz, 3-H), and 7.2—7.5 (5 H, m, ArH).

Benzyl (3RS, 4RS)-(4-*Allyl*-3-*benzyl*-2-*oxoazetidin*-1-*yl*)*triphenylphosphoranylideneacetate* (**40**).—The phosphorane (**32**) (1.00 g) in tetrahydrofuran (12 ml) was added to lithium cyclohexylisopropylamide, prepared in tetrahydrofuran (5 ml) from cyclohexylisopropylamine (0.60 g) and butyl-lithium (3.0 ml of a 1.6M solution in hexane) at −70 °C. After 10 min, benzyl bromide (0.36 g) was added and the reaction vessel transferred to an ice-bath. The mixture was neutralised with acetic acid (*ca.* 0.5 g), concentrated, and chromatographed on silica gel 60 (Art. 7729). Elution with ethyl acetate–light petroleum mixtures (1:1—7:3) furnished the benzylphosphorane (**40**) as a foam (0.38 g, 32%), $\nu_{max.}$ 1 730 and 1 610 cm^{-1}. Continued elution afforded the unchanged phosphorane (**32**) (0.42 g).

Benzyl (5RS, 6RS)-6-*Benzyl*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**47**).—Ozonolysis–cyclisation of the phosphorane (**40**) (0.38 g), followed by rapid column chromatography on silica gel 60 (Art. 9385) (elution with ethyl acetate–light petroleum, 3:7) gave the *azetidinone* (**47**) as a gum (0.090 g, 42%), $\nu_{max.}$ 1 785, 1 725, and 1 610 cm^{-1}; δ (90 MHz) 2.63 and 2.76 (each 1 H, dd, *J* 8.5 and 3 Hz, 4-H_2), 2.98 (1 H, d, *J* 9 Hz) and 3.15 (1 H, d, *J* 6 Hz) (PhCH_2CH), 3.40 (1 H, ddd, *J* 9, 6, and 3 Hz, 6β-H), 3.98 (1 H, td, *J* 8.5 and 3 Hz, 5α-H), 5.20 (2 H, s, PhCH_2O), 6.34 (1 H, t, *J* 3 Hz, 3-H), and 7.0—7.4 (10 H, m, 2 × Ph); (Found: M^+, 333.1357. $C_{21}H_{19}NO_3$ requires *M*, 333.1367).

2-*Methylallyl* (4-*Allyl*-2-*oxoazetidin*-1-*yl*)*triphenylphosphoranylideneacetate* (**33**; X = CH_2).—The allylazetidinone (**21**) (2.0 g) and glyoxylic acid hydrate (1.66 g) in dimethylformamide (20 ml) were stirred in the presence of 4A molecular sieves (*ca.* 0.5 g) at room temperature for 2 h. Potassium carbonate (2.5 g) was added, and stirring continued for 15 min. Finally, 2-methylallyl bromide[20] (2.5 g) in dimethylformamide (8 ml) was added, and the mixture stirred for a further 2 h. The solvent was removed under reduced pressure, and the residue, in ethyl acetate, was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel 60 (1:1 ratio grades Art. 9385, 7729; 12 × 4 cm) eluting with ethyl acetate–light petroleum (1:1), to give the epimeric 2-methylallyl (4-allyl-2-oxoazetidin-1-yl)-1-hydroxyacetates as a gum (2.63 g, 61%), $\nu_{max.}$ 3 510br, 1 755, 1 740, 1 660, 1 640, and 915 cm^{-1}; δ (250 MHz) *inter alia* 1.80 (3 H, s), 2.2—2.6 (2 H, m, CH_2CH=CH_2), 2.69 and 2.70 (together 1 H, each dd, *J* 16 and 3 Hz, 3β-H), 3.03 and 3.07 (together 1 H, each dd, *J* 16 and 6 Hz, 3α-H), 3.83 and 3.95 (together 1 H, each m, 4α-H), 4.15 (1 H, br s, OH, D_2O exch.), and 5.42 [1 H, br s, sharpening on D_2O exch., C*H*(OH)]; *m/z* (e.i.) 240 (MH^+); (NH_3; c.i.) 257 (MNH_4^+, and 240 (MH^+).

The epimeric α-hydroxy esters (1.95 g) in tetrahydrofuran (30 ml) were stirred in the presence of thionyl chloride (1.28 ml) and 2,6-dimethylpyridine (2.05 ml) at −20 °C to −10 °C in an argon atmosphere for 1 h. The mixture was filtered through Kieselguhr and the 2,6-dimethylpyridinium chloride was washed well with tetrahydrofuran. The combined filtrate and washings were evaporated under reduced pressure (bath temperature ≯20 °C). Trituration with toluene and evaporation (× 2) afforded the crude α-chloro ester (*ca.* 2.0 g), $\nu_{max.}$ 1 775, 1 765sh, and 1 755 cm^{-1}. The product in dioxane (30 ml) was heated in the presence of triphenylphosphine (2.5 g) and 2,6-dimethylpyridine (2.05 ml) at 55 °C for 12 h. The dark reaction mixture was concentrated, diluted with ethyl acetate, washed with brine (× 3), dried, and evaporated. The residue in toluene (5 ml) was chromatographed on Kieselgel 60 (1:1 mixture Art. 9385 and 7729 grades; 15 × 4 cm) employing gradient elution with ethyl acetate–light petroleum mixtures (1:3—3:1). The title *phosphorane* (**33**, X = CH_2) crystallised from chloroform–ether as prisms (2.61 g, 66% overall from the α-hydroxy ester), m.p. 169—170 °C (Found: C, 74.2; H, 6.3; N, 2.8; P, 6.4. $C_{30}H_{30}NO_3P$ requires C, 74.5; H, 6.25; N, 2.9; P, 6.4%); $\nu_{max.}$ 1 730st (β-lactam + ester), 1 630sh, and 1 610br cm^{-1} (phosphorane).

2-*Methylallyl* [4-*Allyl*-3-(2-*hydroxypropan*-2-*yl*)-2-*oxoazetidin*-1-*yl*]*triphenylphosphoranylideneacetates* (**54**).—To cyclo-

hexylisopropylamine (0.128 g) in tetrahydrofuran (2 ml) at −78 °C in an atmosphere of argon, was added butyl-lithium (0.6 ml of a 1.5M solution in hexane). After 10 min, the 2-methylallylester–phosphorane (**33**, X = CH_2) (0.20 g) in tetrahydrofuran (3 ml) was added, and stirring continued for 10 min. Anhydrous acetone (1.5 ml) was then added to the deep red solution, and the mixture was allowed to warm to room temperature and stirred for a further 15 min. The deep yellow solution was neutralised with acetic acid, concentrated, diluted with ethyl acetate, washed with brine, dried, and evaporated. The residue was then chromatographed on silica gel 60 (Art. 9385) using gradient elution with ethyl acetate–hexane mixtures (1:1—1:0). The leading band contained the (3RS, 4SR)-*trans*-substituted isomer of the title *phosphorane* (**54**; X = CH_2) (0.097 g, 44%). Crystallisation from ethyl acetate gave prisms, m.p. 117—118 °C (Found: C, 73.3; H, 6.7; N, 2.5%; M^+, 541.2369. $C_{33}H_{36}NO_4P$ requires C, 73.2; H, 6.7; N, 2.6%; *M*, 541.2382); $\nu_{max.}$ 1 735, 1 640sh, and 1 610br cm^{-1} (phosphorane).

Continued elution of the column furnished the corresponding (3RS, 4RS)-*cis*-substituted *phosphorane* as a gum (0.040 g, 19%) (Found: M^+, 541.2381. $C_{33}H_{36}NO_4P$ requires *M*, 541.2382); $\nu_{max.}$ 1 735, 1 640sh, and 1 610br cm^{-1}.

Acetonyl (5RS, 6SR)-6-(2-*Hydroxypropan*-2-*yl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**56**).—The *trans*-substituted 2-methylallyl ester–phosphorane (**54**) (0.095 g, 0.175 mmol) in ethyl acetate (16 ml) was equilibrated in the presence of trifluoroacetic acid (2 ml) at room temperature for 30 min. The solution was cooled to −70 °C and ozonolysed in the usual way. Triphenylphosphine (0.092 g, 0.35 mmol) was added, and the solution was allowed to warm to 0 °C over 40 min. Saturated aqueous sodium hydrogen carbonate (60 ml) was added, and the mixture was stirred at room temperature for 3 h, to effect cyclisation of the corresponding acetonyl ester–aldehyde (**55**). The organic layer was separated and the aqueous phase was extracted with further portions of ethyl acetate. The combined organic extracts were dried and evaporated. Rapid column chromatography on silica gel 60 (Art. 9385, 13 × 2.5 cm), eluting with ethyl acetate, gave the *acetonyl ester* (**56**), which crystallised from ethyl acetate–light petroleum (0.0255 g, 54%), m.p. 95—96 °C (Found: C, 58.7; H, 6.3; N, 5.0%; M^+, 267.1108. $C_{13}H_{17}NO_5$ requires C, 58.4; H, 6.4; N, 5.2%; *M*, 267.1106); $\lambda_{max.}$(EtOH) 267 nm (ε 4 460 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 3 600br, 1 775 (β-lactam), 1 730 (acetonyl ester), and 1 610 cm^{-1}; δ (250 MHz) 1.36 and 1.44 [each 3 H, s, Me_2C(OH)], 1.70 (1 H, br s, OH), 2.23 (3 H, s, MeCO), 2.82 (1 H, ddd, *J* 19, 8, and 2.5 Hz, 4-H), 3.01 (1 H, ddd, *J* 19, 10, and 3 Hz, 4-H), 3.27 (1 H, d, *J* 3 Hz, 6β-H), 4.30 (1 H, ddd, *J* 10, 8, and 3 Hz, 5α-H), 4.71 and 4.84 (each 1 H, d, *J* 17 Hz, ABq, CH_2COMe), and 6.60 (1 H, t, *J* 3 Hz, 3-H).

In subsequent experiments reduction of the bis-ozonide using dimethyl sulphide was found to be advantageous.

Acetonyl (5RS, 6RS)-6-(2-*Hydroxypropan*-2-*yl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**58**).—The corresponding *cis*-substituted 2-methylallyl ester–phosphorane (**54**) (0.038 g, 0.07 mmol) was ozonolysed in the established manner. The bis-ozonide was reduced with triphenylphosphine (0.039 g, 0.15 mmol), and the reaction mixture was neutralised with saturated aqueous sodium hydrogen carbonate (30 ml). Cyclisation of the intermediate *cis*-substituted acetonyl ester–aldehyde (**55**) in ethyl acetate was effected by warming to 30 °C for 2 h (t.l.c. analysis). Chromatography as before yielded the *acetonyl ester* (**58**) as a white solid (0.009 g, 48%) (Found: M^+, 267.1090. $C_{13}H_{17}NO_5$ requires *M*, 267.1106); $\lambda_{max.}$ 273 nm (ε 4 220 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 3 580br, 1 775, 1 730, and 1 620 cm^{-1}; δ (250 MHz) 1.28 and 1.51 [each 3 H, s, Me_2C(OH)], 1.63 (1 H, s, OH), 2.23 (3 H, s, MeCO), 2.73 (1 H, ddd, *J* 19, 10, and 3 Hz, 4-H), 3.62 (1 H, d, *J* 6 Hz, 6α-H), 3.85 (1 H, ddd, *J* 19, 9, and 2.5 Hz, 4-H), 4.37 (1 H, ddd, *J* 10, 9, and 6 Hz, 5α-H), 4.71 and 4.84 (each 1 H, d, *J* 17 Hz, ABq, CH_2COMe), and 6.70 (1 H, t, *J* 2.5 Hz, 3-H).

Sodium (5RS, 6SR)-6-(2-*Hydroxypropan*-2-*yl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**57**).—The *trans*-substituted acetonyl ester (**56**) (1.07 g) in tetrahydrofuran (100 ml) and water (30 ml) was cooled to 0 °C. Aqueous sodium hydroxide (0.1M; 40 ml) was added dropwise, and the mixture stirred at 0 °C for 10 min. The tetrahydrofuran was evaporated under reduced pressure and the aqueous concentrate was diluted with water (20 ml), and washed with methylene chloride (×3). The aqueous solution was concentrated and lyophilised to yield the title sodium salt as a solid (0.723 g, 77%), $\lambda_{max.}$(H_2O) 264 nm; δ (250 MHz; D_2O) 1.30 and 1.49 [each 3 H, s, Me_2CH(OH)], 2.75—2.99 (2 H, m, 4-H_2), 3.44 (1 H, d, *J* 3.3 Hz, 6β-H), 4.24 (1 H, td, *J* 10 and 3.3 Hz, 5α-H), and 6.26 (1 H, t, *J ca.* 3 Hz, 3-H).

Further characterisation was achieved by conversion into the corresponding *p*-nitrobenzyl ester. The sodium salt (**57**) (0.720 g) in dimethylformamide was re-esterified with an excess of *p*-nitrobenzyl bromide. Evaporation and chromatography of the residue on silica gel 60 (Art. 9385), eluting with ethyl acetate–hexane (3:1), gave the p-*nitrobenzyl ester* (**57**; R = $CH_2C_6H_4NO_2$-*p*) (0.50 g, 47%), m.p. (EtOAc) 136—144 °C (Found: C, 59.0; H, 5.3; N, 8.1%; M^+, 346.1163. $C_{17}H_{18}N_2O_6$ requires C, 59.0; H, 5.2; N, 8.1%; *M*, 346.1164); $\nu_{max.}$ 1 780, 1 730, 1 610, 1 525, and 1 355 cm^{-1}; δ (250 MHz) 1.38 and 1.47 [each 3 H, s, Me_2C(OH)], 1.71 (1 H, s, OH), 2.81 (1 H, ddd, *J* 19, 8, and 2.75 Hz) and 3.01 (1 H, ddd, *J* 19, 10, and 3 Hz) (4-H_2), 3.29 (1 H, d, *J* 3 Hz, 6β-H), 4.31 (1 H, ddd, *J* 10, 8, and 3 Hz, 5α-H), 5.39 (2 H, ABq, *J* 12 Hz, CH_2Ar), 6.58 (1 H, t, *J ca.* 3 Hz, 3-H), 7.62 and 8.23 (each 2 H, d, *J* 9 Hz, AA′BB′).

Sodium (5RS, 6RS)-6-(2-*Hydroxypropan*-2-*yl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**59**).—The *cis*-substituted acetonyl ester (**58**) (0.564 g) was deprotected with an equimolar amount of 0.1M-aqueous sodium hydroxide as described above. Lyophilisation afforded the sodium salt (**59**) as a solid (0.369 g, 75%), $\lambda_{max.}$(H_2O) 264 nm; δ (250 MHz) (D_2O) 1.30 (3 H, s) and 1.42 [each 3 H, s, Me_2C(OH)], 2.73 (1 H, ddd, *J* 18, 10, and 3 Hz, 4-H), 3.48 (1 H, ddd, *J* 18, 8.5, and 2.5 Hz, 4-H), 3.70 (1 H, d, *J* 6 Hz, 6α-H), 4.34 (1 H, ddd, *J* 10, 8.5, and 6 Hz, 5α-H), and 6.29 (1 H, br t, *J ca.* 3 Hz, 3-H).

Similarly, reaction of the salt (**59**) (0.0315 g) in dimethylformamide (5 ml) with *p*-nitrobenzyl bromide (0.033 g) at room temperature for 2 h, gave, after chromatography, the corresponding p-*nitrobenzyl ester* (**59**; R = $CH_2C_6H_4NO_2$-*p*) (0.0215 g, 61%). Crystallisation from ethyl acetate gave prisms, m.p. 139—144 °C (Found: C, 58.7; H, 5.3; N, 7.9. $C_{17}H_{18}N_2O_6$ requires C, 59.0; H, 5.2; N, 8.1%); $\lambda_{max.}$(EtOH) 269 nm; $\nu_{max.}$ 1 770, 1 730, 1 610, 1 525, and 1 350 cm^{-1}; δ (250 MHz) 1.30 and 1.54 [each 3 H, s, Me_2C(OH)], 2.73 (1 H, ddd, *J* 19, 10, and 3 Hz, 4-H), 3.62 (1 H, d, *J* 6 Hz, 6α-H), 3.85 (1 H, ddd, *J* 19, 9, and 2.5 Hz, 4-H), 4.38 (1 H, ddd, *J* 10, 9, and 6 Hz, 5α-H), 5.38 (2 H, ABq, *J* 12 Hz, CH_2Ar), 6.69 (1 H, t, *J ca.* 3 Hz, 3-H), 7.62 and 8.23 (each 2 H, d, *J* 9 Hz, AA′BB′).

Benzyl (8-*Oxo*-7-*azabicyclo*[4.2.0]*oct*-3-*en*-7-*yl*)-1-*hydroxyacetates*.—Benzyl glyoxylate (2.73 g) was heated in benzene (25 ml) in a Dean-Stark apparatus under reflux for 45 min. 8-Oxo-7-azabicyclo[4.2.0]oct-3-ene[16] (**60**) (1.23 g) was added, and the solution was maintained at reflux for 3 h. Removal of the solvent under reduced pressure, followed by chromatography on silica gel 60 (Art. 7729) eluting with ethyl acetate, gave the two separate epimers of the title *alcohol* (5.75 g, 90%).

Isomer A. M.p. 92—93 °C (Found: C, 66.8; H, 5.9; N, 4.9. $C_{16}H_{17}NO_4$ requires C, 66.9; H, 6.0; N, 4.9%); $\nu_{max.}$ 3 450 and

1 750br cm^{-1}; δ (90 MHz) 1.76—2.73 (4 H, m, 2-H_2 and 5-H_2), 3.12—3.33 (1 H, m) and 3.76—3.93 (1 H, m, 1-H and 6-H), 4.40 (1 H, d, *J* 6 Hz, OH, D_2O exch.), 5.16 (2 H, s, CH_2Ph), 5.47 [1 H, d, *J* 6 Hz, collapsing to s on D_2O exch., C*H*(OH)], 5.67—5.83 (2 H, m, CH=CH), and 7.34 (5 H, m, ArH); *m/z* 287.

Isomer B. M.p. 100—101 °C (Found: C, 67.2; H, 6.0; N, 4.8. $C_{16}H_{17}NO_4$ requires C, 66.9; H, 6.0; N, 4.9%); $\nu_{max.}$ 3 450 and 1 750br cm^{-1}; δ (90 MHz) 1.80—2.63 (4 H, m, 2-H_2 and 5-H_2), 3.13—3.36 (1 H, m) and 3.93—4.13 (1 H, m, 1-H and 6-H), 4.20 (1 H, br s, OH, D_2O exch.), 5.16 (2 H, s, CH_2Ph), 5.50 [1 H, br sharpening to s on D_2O exch., C*H*(OH)], 5.50—6.00 (2 H, m, CH=CH), and 7.34 (5 H, m, Ph); *m/z* M^+, 287.

Benzyl 8-*Oxo*-7-*azabicyclo*[4.2.0]*oct*-3-*en*-7-*yl*(*triphenylphosphoranylidene*)*acetate* (**61**; R^1 = CH_2Ph).—The alcohol, prepared above, as a mixture of epimers (2.2 g) in tetrahydrofuran (50 ml) was cooled to −20 °C. 2,6-Dimethylpyridine (1.5 g) was added, followed by thionyl chloride (1.0 ml). The mixture was stirred at −20 to −10 °C, and the solution was filtered through Kieselguhr and evaporated. The crude α-chloroesters in anhydrous dioxane (20 ml) were stirred with triphenylphosphine (4.02 g) and 2,6-dimethylpyridine (1.64 g) at room temperature overnight. The 2,6-dimethylpyridinium hydrochloride was separated by filtration; the filtrate and washings were evaporated to dryness and chromatographed to give the title phosphorane (**61**; R^1 = CH_2Ph) as an amorphous solid (1.5 g, 37%), $\nu_{max.}$ 1 730 and 1 620 cm^{-1}.

The p-*nitrobenzyl ester–phosphorane* (**61**; R^1 = $CH_2C_6H_4$-NO_2-*p*). This compound was prepared similarly using *p*-nitrobenzyl glyoxylate hydrate, as an amorphous solid (83% from the α-hydroxy ester), $\nu_{max.}$ 1 738, 1 620sh (phosphorane), 1 605, 1 520, and 1 350 cm^{-1}.

The acetonyl ester–phosphorane (**61**; R^1 = CH_2COMe). This compound was obtained *via* acetonyl glyoxylate hydrate. It was obtained as a foam (53% from the α-hydroxy ester), $\nu_{max.}$ 1 740, 1 720sh, and 1 620 cm^{-1} (phosphorane).

The p-*bromophenacyl ester–phosphorane* (**61**; R^1 = CH_2-COC_6H_4Br-*p*). This compound was best prepared employing a stepwise procedure for glyoxylate addition. The azetidinone (**60**) (0.4 g) in dimethylformamide (2 ml) was stirred with glyoxylic acid hydrate (0.32 g) in the presence of hexamethylphosphoric triamide (0.1 ml) and 3A molecular sieves (4 pieces) for 5 h. Potassium carbonate (0.226 g) was added, and the mixture was stirred until effervescence had ceased (5 min). *p*-Bromophenacyl bromide (1.00 g) was added, and the solution stirred at room temperature overnight. The solution was diluted with ethyl acetate, washed with brine (×3), dried, and evaporated to give a gum (1.9 g) which was chromatographed on silica gel 60 (Art. 7729). Elution of the column with ethyl acetate–light petroleum (1:1) gave the *glyoxylate ester* as the separate epimers.

Isomer A. This was a foam, which slowly crystallised from ethyl acetate–light petroleum as needles (0.60 g, 47%), m.p. 135—136 °C (Found: C, 51.9; H, 4.2; Br, 20.0; N, 3.6. $C_{17}H_{16}BrNO_5$ requires C, 51.8; H, 4.1; Br, 20.3; N, 3.6%); $\nu_{max.}$ 3 550br, 1 760sh, 1 750, 1 710, 1 590, and 970 cm^{-1}; δ (90 MHz; [$^2H_6$]DMSO) 1.9—2.8 (4 H, m), 3.35 (1 H, m), 4.17 (1 H, m), 5.55 (2 H, s, CH_2COAr), 5.51 [1 H, d, *J* 6.5 Hz, C*H*(OH); sharpens to s on D_2O exch.], 5.72 (2 H, br s), 6.81 (1 H, d, *J* 6.5 Hz, OH, D_2O exch.), 7.75 and 7.90 (each 2 H, d, *J* 9 Hz, AA′BB′).

Isomer B. This crystallised from ethyl acetate–light petroleum as platelets (0.55 g, 43%), m.p. 144—146 °C (Found: C, 51.7; H, 4.3; Br, 20.6; N, 3.3%); $\nu_{max.}$ 3 200br, 1 760sh, 1 750, 1 710, 1 590, and 965 cm^{-1}; δ (90 MHz, [$^2H_6$]DMSO) 1.9—2.8 (4 H, m), 3.33 (1 H, m), 4.15 (1 H, m), 5.47 [1 H, d, *J* 7 Hz, C*H*(OH); sharpens to s on D_2O exch.], 5.51 (2 H, s, CH_2COAr), 5.71 (2 H, br s), 6.90 (1 H, d, *J* 7 Hz, OH, D_2O exch.), 7.73 and 7.91 (each 2 H, d, *J* 9 Hz, AA′BB′).

The mixture of α-hydroxy-*p*-bromophenacyl ester epimers (0.383 g; 1:1 epimer ratio) in tetrahydrofuran (8 ml), was stirred in the presence of 2,6-dimethylpyridine (0.230 ml) and thionyl chloride (0.139 ml) at −20° to −10 °C for 3.5 h. The mixture was filtered rapidly through Celite, washed well with ethyl acetate, and the filtrate and washings evaporated. The residue in anhydrous dioxane (4 ml) was treated with triphenylphosphine (0.51 g) and 2,6-dimethylpyridine (0.230 ml) at room temperature overnight. Evaporation and chromatography on silica gel 60 (Art. 7729) [elution with ethyl acetate–light petroleum (7:3) gave the p-*bromophenacyl ester—phosphorane* (**61**, R^1 = $CH_2COC_6H_4$Br-*p*) which crystallised from ethyl acetate–ether as rods (0.499 g, 80%), m.p. 200—202 °C (Found: C, 65.7; H, 4.7; Br, 12.1; N, 2.0. $C_{35}H_{29}BrNO_4P$ requires C, 65.8; H, 4.6; Br, 12.5; N, 2.2%); $\nu_{max.}$ 1 740s, 1 710, 1 620, 1 590, and 1 480 cm^{-1}.

The pivaloyloxymethyl ester–phosphorane (**61**; R^1 = CH_2O-COBu^t). This was also prepared by the above method, involving stepwise addition of glyoxylic acid and reaction with pivaloyloxymethyl bromide, prior to phosphorane formation. After chromatography, the phosphorane (**61**; R^1 = CH_2OCOBu^t) was obtained as a foam (0.291 g), $\nu_{max.}$ 1 740 and 1 630 cm^{-1}.

Acetonyl (5RS, 6SR)-6-(2-*Oxoethyl*)-7-*oxo*-1-*azabicyclo*-[3.2.0]*hept*-2-*ene*-2-*carboxylate*.—The phosphorane (**61**; R^1 = CH_2COMe) (0.25 g, 0.50 mmol) in ethyl acetate (50 ml) was stirred with an excess of trifluoroacetic acid (4 ml) for 30 min after which the mixture was cooled to −70 °C. Ozone was passed through the solution until it became pale blue; then the excess of ozone was removed by purging with argon. Triphenylphosphine (0.132 g, 0.50 mmol) was added to the solution and the mixture allowed to warm to room temperature. The solution was neutralised by addition of saturated aqueous sodium hydrogen carbonate (100 ml). The organic phase was separated, washed with brine, and dried. Cyclisation was completed by stirring the ethyl acetate solution for 1 h. Rapid chromatography afforded the unstable title aldehyde (0.044 g, 34%); $\lambda_{max.}$(EtOH) 274 nm; $\nu_{max.}$ 1 775, 1 730, and 1 605 cm^{-1}; δ [250 MHz; $(CD_3)_2CO$] 2.18 (3 H, s), 2.78 (2 H, dd, *J* 9 and 2.5 Hz, 4-H_2), 3.00 (2 H, d, *J* 8 Hz, 8-H_2), 4.08 (1 H, td, *J* 8 and 6 Hz, 6α-H), 4.49 (1 H, td, *J* 9 and 6 Hz, 5α-H), 4.85 (2 H, s), 6.64 (1 H, t, *J* 2.5 Hz, 3-H), and 9.79 (1 H, s, CHO).

Acetonyl (5RS, 6SR)-6-[(E)-3-*Methoxycarbonylallyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**69**).—The crude aldehyde, prepared as described in the previous experiment, in ethyl acetate was stirred with methyl triphenylphosphoranylideneacetate (0.167 g, 0.5 mmol) for 2 h. Concentration of the solution and rapid chromatography on silica gel 60 (Art. 9385), eluting with ethyl acetate–hexane (3:1), yielded the *acetonyl ester* (**69**) [0.027 g, 17% overall from the phosphorane (**61**)], m.p. 110—111 °C (Found: C, 58.65; H, 5.4; N, 4.4%; M^+, 307.1063. $C_{15}H_{17}NO_6$ requires C, 58.6; H, 5.5; N, 4.6%; *M*, 307.1055); $\lambda_{max.}$(EtOH) 271 nm (ε 4 430 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 1 790sh, 1 785, 1 730, 1 660, and 1 620 cm^{-1}; δ (250 MHz) 2.23 (3 H, s, MeCO), 2.53 (1 H, dddd, *J* 16, 10, 7, and 1.5 Hz, 8-H), 2.71—2.82 (3 H, m, 8-H and 4-H_2), 3.77 (3 H, s), 3.79 (1 H, ddd, *J* 10, 6, and 6 Hz, 6α-H), 4.46 (1 H, td, *J* 9 and 6 Hz, 5α-H), 4.73 and 4.82 (each 1 H, *J* 17 Hz, ABq, CH_2COMe), 5.89 (1 H, dt, *J* 15 and 1.5 Hz, 10-H), 6.65 (1 H, t, *J* 2.5 Hz, 3-H), 6.92 (1 H, ddd, *J* 15, 7, 6 Hz, 9-H).

Sodium (5RS, 6SR)-6-[(E)-3-*Methoxycarbonylallyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**70**).—The acetonyl ester (**69**) (0.007 g, 0.02 mmol) in tetrahydrofuran (3 ml) and water (1 ml) was cooled in an ice-bath. Aqueous sodium

hydroxide (0.1M; 0.2 ml, 0.02 mmol) was added dropwise over 1 min. After a further 10 min in the cold, the solution was diluted with water (3 ml) and washed with methylene dichloride (2 × 15 ml). The aqueous solution was lyophilised to yield the title sodium salt (**70**) (5.5 mg), $\lambda_{max.}$(H_2O) 261 nm; δ (250 MHz) (D_2O) 2.69 (4 H, m, 4-H_2 and 8-H_2), 3.75 (3 H, s), 3.88 (1 H, dt, *J* 8 and 5.5 Hz, 6α-H), 4.42 (1 H, td, *J* 9 and 5.5 Hz, 5α-H), 5.98 (1 H, dt, *J* 15 and 1.5 Hz, 10-H), 6.29 (1 H, t, *J* 3 Hz, 3-H), 7.00 (1 H, dt, *J* 15 and 6 Hz, 9-H).

Benzyl (5RS, 6SR)-6-(2-*Oxoethyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]-*hept*-2-*ene*-2-*carboxylate* (**62**).—The phosphorane (**61**; R^1 = CH_2Ph) (0.20 g) was ozonolysed and cyclised using the procedure described above. Rapid chromatography afforded the aldehyde (**62**) as a gum (0.042 g, 39%), $\nu_{max.}$ 1 780, 1 725, and 1 610 cm^{-1}; δ (90 MHz) 2.5—3.00 (4 H, m, 4-H_2 and 8-H_2), 3.87—4.11 (1 H, m, 6α-H), 4.46 (1 H, td, *J* 9 and 6 Hz, 5α-H), 5.21 (2 H, s, CH_2Ph), 6.45 (1 H, t, *J* 2 Hz, 3-H), 7.30 (5 H, s, Ph), and 9.70 (1 H, s, CHO) [irradiation at the frequency of the signals centred δ 2.60 collapsed the 5α-H signal to a doublet (*J* 6 Hz)]; *m*/*z* (e.i.) 285 (M^+).

Benzyl (5RS, 6SR)-6-[(E)-3-*Methoxycarbonylallyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**63**).—The phosphorane (**61**; R^1 = CH_2Ph) (0.20 g) was ozonolysed and cyclised as in the previous experiment. The resulting crude aldehyde (**62**) in chloroform (5 ml) was treated with methyl triphenylphosphoranylideneacetate (0.124 g) and was left at room temperature for 1 h. The solution was evaporated and chromatographed rapidly on silica gel 60 (Art. 9385) to give the *acrylate* (**63**) which crystallised from ether (0.045 g, 35%), m.p. 81—82 °C (Found: M^+, 341.1270. $C_{19}H_{19}NO_5$ requires *M*, 341.1263); $\nu_{max.}$ 1 780, 1 720, 1 650, and 1 610 cm^{-1}; δ (90 MHz) 2.68 (2 H, dd, *J* 9 and 3 Hz, 4-H_2), 2.40—2.90 (2 H, m, 8-H_2), 3.67 (3 H, s, OMe), 3.67—3.74 (1 H, m, 6α-H), 4.35 (1 H, dt, *J* 6 and 9 Hz, 5α-H), 5.20 (2 H, s, CH_2Ph), 5.80 (1 H, br d, *J* 15 Hz, 10-H), 6.45 (1 H, t, *J* 3 Hz, 3-H), 6.84 (1 H, dt, *J* 15 and 6 Hz, 9-H), and 7.32 (5 H, s, Ph). [On irradiation at the frequency of the 4-H_2 signals centred δ 2.6, the 5α-H multiplet simplified to a doublet (*J* 6 Hz), and the 3-H triplet collapsed to a singlet].

Benzyl (5RS, 6SR)-6-[(E)-3-*Cyanoallyl*]-7-*oxo*-1-*azabicyclo*-[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**64**).—The phosphorane (**61**; R^1 = CH_2Ph) was transformed to the crude aldehyde (**62**) as described above. To aldehyde (**62**) in ethyl acetate was added triphenylphosphoranylideneacetonitrile (0.55 g) and the mixture stirred at room temperature for 40 min. The solution was concentrated and chromatographed on silica gel 60 (Art. 9385). Rapid elution with ethyl acetate–light petroleum (3:7) gave the *nitrile* (**64**) which solidified on trituration with ether (0.0237 g, 41%) (Found: M^+, 308.1120. $C_{18}H_{16}N_2O_3$ requires *M*, 308.1161); $\nu_{max.}$ 2 250, 1 785, 1 730, 1 640, and 1 620 cm^{-1}; δ (90 MHz) 2.45—2.90 (2 H, m, 8-H_2), 2.73 (2 H, dd, *J* 9 and 3 Hz, 4-H_2), 3.60—3.90 (1 H, m, 6α-H), 4.40 (1 H, td, *J* 9 and 6 Hz, 5α-H), 5.25 (2 H, s, CH_2Ph), 5.40 (1 H, dd, *J* 16 and 1 Hz, 10-H), 6.53 (1 H, t, *J* 3 Hz, 3-H), 6.60 (1 H, dt, *J* 16 and 7 Hz, 9-H), and 7.30 (5 H, s, Ph).

Benzyl (5RS, 6SR)-6-[(E)-4-*Oxopent*-2-*enyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**65**).—The crude aldehyde (**62**), in ethyl acetate, was prepared from the phosphorane (**61**; R^1 = CH_2Ph) as described in previous experiments. To this solution was added 1-triphenylphosphoranylidenepropan-2-one and the mixture was stirred overnight. Recovery and chromatography as before gave the title *enone* (**65**) as a gum (Found: M^+, 325.1345. $C_{19}H_{19}NO_4$ requires *M*, 325.1376); $\nu_{max.}$ 1 785, 1 730, 1 680 (enone), 1 630, and 1 620 cm^{-1}; δ (90 MHz), 2.25 (3 H, s, COMe), 2.50—3.00 (4 H, m, 8-H_2 and 4-H_2), 3.55—4.95 (1 H, m, 6α-H), 4.40 (1 H, td, *J* 9 and 6 Hz, 5α-H), 5.25 (2 H, s, CH_2Ph), 6.15 (1 H, br d, *J* 16 Hz, 10-H), 6.50 (1 H, t, *J* 3 Hz, 3-H), 6.75 (1 H, dt, *J* 16 and 7 Hz, 9-H), and 7.30 (5 H, s, Ph).

Pivaloyloxymethyl (5RS, 6SR)-6-[(E)-3-*Methoxycarbonylallyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**66**).—The phosphorane (**61**; R^1 = CH_2OCOBu^t) (0.10 g) was processed *via* our standard ozonolysis–cyclisation procedure. Reaction of the intermediate aldehyde with methyl triphenylphosphoranylideneacetate (0.075 g) as before, followed by crystallisation from ether, gave the *pivaloyloxymethyl ester* (**66**) (0.025 g, 38%), m.p. 110—112 °C (Found: C, 59.2; H, 6.4; N, 3.8%; M^+, 365.1498. $C_{18}H_{23}NO_7$ requires C, 59.2; H, 6.3; N, 3.8%; *M*, 365.1475); $\lambda_{max.}$(EtOH) 275 nm (ε 4 060 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 1 785, 1 750, 1 725, 1 660, and 1 610 cm^{-1}; δ (90 MHz) 1.22 (9 H, s, Bu^t), 2.40—2.90 (2 H, m, 8-H_2), 2.75 (2 H, dd, *J* 9 and 3 Hz, 4-H_2), 3.70 (3 H, s, OMe), 3.65—3.90 (1 H, m, 6α-H), 4.40 (1 H, td, *J* 9 and 6 Hz, 5α-H), 5.81 (1 H, dd, *J* 15 and 1 Hz, 10-H), 5.81 and 5.84 (2 H, ABq, CO_2CH_2O), 6.54 (1 H, t, *J* 3 Hz, 3-H), and 6.86 (1 H, dt, *J* 15 and 6 Hz, 9-H).

p-*Bromophenacyl* (5RS, 6SR)-6-[(E)-3-*Methoxycarbonylallyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**67**).—The phosphorane (**61**; R^1 = $CH_2COC_6H_4Br$-*p*) (0.104 g) was converted into the p-*bromophenacyl ester* (**67**) (0.035 g, 43%) by the methods described in the previous examples. The product crystallised from ethyl acetate–light petroleum, m.p. 134—136 °C (Found: C, 53.4; H, 4.1; Br, 17.9; N, 3.2. $C_{20}H_{18}BrNO_6$ requires C, 53.6; H, 4.0; Br, 17.8; N, 3.1%); $\lambda_{max.}$(EtOH) 275infl, 258 (ε 21 990 dm^3 mol^{-1} cm^{-1}), and 210 nm (26 000); $\nu_{max.}$ 1 785, 1 725sh, 1 715, 1 700, 1 660, 1 610, and 1 590 cm^{-1}; δ (90 MHz) 2.45—2.9 (2 H, m, 8-H_2), 2.74 (2 H, dd, *J* 9 and 3 Hz, 4-H_2), 3.68 (3 H, s, OMe), 3.6—3.9 (1 H, m, 6α-H), 4.40 (1 H, td, *J* 9 and 6 Hz, 5α-H), 5.36 (2 H, s, CO_2CH_2CO), 5.80 (1 H, dt, *J* 15 and 1 Hz, 10-H), 6.60 (1 H, t, *J* 3 Hz, 3-H), 6.86 (1 H, dt, *J* 15 and 6 Hz, 9-H), and 7.55 and 7.74 (each 2 H, d, *J* 9 Hz, AA′BB′).

p-*Nitrobenzyl* (5RS, 6SR)-6-(2-*Oxoethyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**71**).—The phosphorane (**61**; R^1 = $CH_2C_6H_4NO_2$-*p*) (5.0 g) was ozonolysed and cyclised in the established manner. Rapid column chromatography of the crude product, in toluene (5 ml), on silica gel 60 (Art. 9385) (15 × 5 cm) [eluting with ethyl acetate–light petroleum (1:1—7:3)] followed by crystallisation from ethyl acetate–ether afforded the stable *aldehyde* (**71**) as off-white prisms (1.32 g, 44%), m.p. 130—132 °C (Found: C, 58.0; H, 4.5; N, 8.4. $C_{16}H_{14}N_2O_6$ requires C, 58.2; H, 4.3; N, 8.5%); $\lambda_{max.}$(EtOH) 263 nm; $\nu_{max.}$ 1 780, 1 730, 1 610, 1 525, and 1 350 cm^{-1}; δ (90 MHz) 2.5—3.2 (4 H, m, 8-H_2 and 4-H_2), 4.05 (1 H, dt, *J* 11 and 6 Hz, 6α-H), 4.53 (1 H, td, *J* 10 and 6 Hz, 5α-H), 5.24 and 5.45 (each 1 H, d, *J* 14 Hz, ABq, CH_2Ar), 6.57 (1 H, t, *J* 3 Hz, 3-H), 7.58 and 8.28 (each 2 H, d, *J* 8 Hz, AA′BB′), and 9.79 (1 H, s, CHO).

p-*Nitrobenzyl* (5RS, 6SR)-6-(3-*Methoxycarbonylallyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylates*.—The phosphorane (**61**; R^1 = $CH_2C_6H_4NO_2$-*p*) (0.40 g) was ozonolysed and cyclised as in the previous experiment, to furnish a solution of the aldehyde (**71**) in ethyl acetate (15 ml). Methyl triphenylphosphoranylideneacetate (0.26 g) was added and the solution was stirred at room temperature for 30 min; it was then evaporated. Rapid chromatography of the residue on silica gel 60 (Art. 9385), eluting with ethyl acetate–light petroleum (7:3) gave the E-*isomer* (**68**) of the title compound as the first band. This crystallised from ethyl acetate–light petroleum as needles [0.132 g, 49% from phosphorane (**61**)], m.p. 156—159 °C

(Found: C, 58.9; H, 4.7; N, 7.1. $C_{19}H_{18}N_2O_7$ requires C, 59.1; H, 4.7; N, 7.25%); $\lambda_{max.}$(EtOH) 269 nm (ε 14 300 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 1 782, 1 722, 1 655, 1 605, 1 525, and 1 350 cm^{-1}; δ (90 MHz) 2.73 (2 H, dd, *J* 9.5 and 3 Hz, 4-H_2), 2.25—2.90 (2 H, m, 8-H_2), 3.69 (3 H, s, OMe), 3.74 (1 H, td, *J* 9.5 and 6 Hz, 6α-H), 4.39 (1 H, td, *J* 9.5 and 6 Hz, 5α-H), 5.20 and 5.42 (each 1 H, *J* 14 Hz, ABq, CH_2Ar), 5.80 (1 H, br d, *J* 16 Hz, 10-H), 6.53 (1 H, t, *J* 3 Hz, 3-H), 6.85 (1 H, dt, *J* 16 and 6 Hz, 9-H), and 7.52 and 8.14 (each 2 H, d, *J* 8 Hz, AA′BB′).

Further elution of the column gave a small amount of the corresponding *Z*-isomer of the product, which crystallised from ether (0.004 g, 2%), m.p. 109—111 °C; $\lambda_{max.}$(EtOH) 269 nm (ε 13 950 dm^3 mol^{-1} cm^{-1}); $\nu_{max.}$ 1 778, 1 720, 1 650, 1 520, and 1 350 cm^{-1}; δ (90 MHz) 2.40—3.50 (4 H, m, 8-H_2 and 4-H_2), 3.66 (3 H, s, OMe), 3.73 (1 H, td, *J* 8 and 6 Hz, 6α-H), 4.35 (1 H, td, *J* 9.5 and 6 Hz, 5α-H), 5.19 and 5.40 (each 1 H, *J* 14 Hz, ABq, CH_2Ar), 5.84 (1 H, d, *J* 11 Hz, 10-H), 6.22 (1 H, ddd, *J* 11, 8, and 6 Hz, 9-H), 6.55 (1 H, t, *J* 3 Hz, 3-H), and 7.52 and 8.14 (2 H, d, *J* 8 Hz, AA′BB′).

p-*Nitrobenzyl* (5RS, 6SR)-6-(2-*Hydroxyethyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**72**).—A suspension of the aldehyde (**71**) (0.050 g; 0.15 mmol) in tetrahydrofuran (2 ml) was cooled to 0 °C. Sodium borohydride (1.437 mg; 0.15 mmol) in water (1 ml) was added dropwise over 2 min. After a further 5 min, pH 7 sodium phosphate buffer (0.05M; 2 ml) was added, and the mixture was diluted with ethyl acetate (10 ml). The organic phase was extracted with brine (3 × 2 ml). The combined aqueous extracts were back-extracted with ethyl acetate. The combined organic extracts were dried and evaporated (without chromatography) to give the unstable alcohol (**72**) (0.047 g, 94%); $\nu_{max.}$ 3 500br, 1 775, 1 730, 1 620sh, 1 610, 1 525, and 1 350 cm^{-1}; δ (80 MHz) 1.8—2.2 (2 H, m, 8-H_2), 2.65 (1 H, br s, D_2O exch., OH), 2.7—2.95 (2 H, m, 4-H_2), 3.80 (2 H, t, *J* 6 Hz, 9-H_2), 4.2—4.6 (2 H, m, 5α-H and 6α-H), 5.26 and 5.97 (each 1 H, *J* 14 Hz, ABq), 6.63 (1 H, t, *J* 3 Hz, 3-H), 7.59 and 8.22 (each 2 H, *J* 9 Hz, AA′BB′). This compound was characterised by conversion into the acetate (**73**) and into the urethane (**74**) (*vide infra*). Work-up without phosphate buffer favoured the formation of large amounts of the isomeric lactone–pyrroline (**75**).

p-*Nitrobenzyl* 2-(2-*Oxotetrahydrofuran*-3-*yl*)-3,4-*dihydro*-2H-*pyrrole*-2-*carboxylate* (**75**).—The alcohol (**72**) (0.040 g) in ethyl acetate (2 ml) was stirred in the presence of silica gel 60 (Art. 9365) (5 mg) at room temperature for 20 h. T.l.c. analysis indicated the complete formation of a less-polar material (R_F 0.37, 0.43 respectively, elution EtOAc). The mixture was passed rapidly through a small column of silica gel 60 (3 × 1 cm). Elution with ethyl acetate gave the isomeric title compound as a gum (0.038 g, 95%) which crystallised (ethyl acetate–ether–light petroleum) as microcrystals (0.035 g), m.p. 117—120 °C (Found: C, 57.9; H, 4.5; N, 8.1. $C_{16}H_{16}N_2O_6$ requires C, 57.8; H, 4.85; N, 8.4%); $\nu_{max.}$ 1 775 (butyrolactone), 1 730 (PNB ester), 1 610, 1 525, and 1 350 cm^{-1}; δ_H (400 MHz) 1.83 (1 H, m), 2.40 (2 H, m), 2.82 (2 H, m), 2.99 (1 H, m), 4.24 (1 H, m), 4.38 (1 H, m), 4.52 (1 H, m), and 7.57 and 8.24 (each 2 H, *J* 9 Hz, AA′BB′), no D_2O exchangeable proton; δ_C (62.89 MHz; $CDCl_3$; Off-resonance decoupled multiplicity, in parentheses), 25.80* (t, C-4′), 26.97* (t, C-4), 36.29 (t, C-3), 44.01 (d, C-3′), 65.88† (t, ArCH_2), 66.72† (t, C-5′), 74.00 (d, C-5), 123.89 (d, Ar C-3, C-5), 128.78 (d, Ar C-2, C-6), 142.34 (s, Ar C-1), 148.1 (s, Ar C-4), 162.17 (s, C-2), 168.75 (s, CO_2R), and 177.06 (s, C-2′ lactone CO) (Found: MH^+, 333.1101. $C_{16}H_{16}N_2O_6$ requires *M*H, 333.1116); *m/z* (e.i.), 275 ($MH^+ - C_2H_2O_2$; 16%), and 248 ($MH^+ - C_4H_5O_2$).

Alternatively, slow chromatography of alcohol (**72**) (0.048 g) on silica gel 60 (Art. 7729) (5 × 2 cm), eluting with ethyl acetate, gave the lactone–pyrroline (**75**) (0.033 g) identical in all respects with the previous sample. T.l.c. analysis indicated that the rearrangement occurred slowly for samples of the alcohol (**72**) stored at −10 °C. In contrast, treatment of the alcohol (**72**) (0.050 g) in dimethylformamide (1 ml) with finely ground potassium carbonate (0.015 g) at room temperature for 2 h did not cause rearrangement. (Signal assignments * and † are interchangeable.)

p-*Nitrobenzyl* (5RS, 6SR)-6-(2-*Acetoxyethyl*)-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**73**).—The aldehyde (**71**) (0.050 g) was converted into the alcohol (**72**) (*ca.* 0.050 g) with sodium borohydride as described above. The material was a foam, and contained no lactone–pyrroline (**75**) (t.l.c. analysis). The alcohol, in pyridine (0.2 ml) was cooled to 0 °C and an excess of acetic anhydride (*ca.* 0.1 ml) was added. The solution was stirred at 0 °C for 1 h. Brine (2 ml) was added, and the mixture was diluted with ethyl acetate (20 ml). The organic layer was washed with further portions of brine (2 × 3 ml), dried, and evaporated. The residue, in toluene (1 ml) was chromatographed on silica gel 60 (Art. 9385) (3.5 × 1.5 cm). Elution with ethyl acetate–light petroleum gave the *acetate* (**73**) [0.037 g, 65% overall from aldehyde (**71**)], which crystallised from chloroform–ether–light petroleum as prisms (0.028 g), m.p. 100—101 °C, (Found: C, 57.7; H, 5.0; N, 7.2. $C_{18}H_{18}N_2O_7$ requires C, 57.8; H, 4.8; N, 7.5%); $\nu_{max.}$ 1 780 (β-lactam), 1 735st (PNB ester + acetate), 1 615, 1 610, 1 525, 1 350, and 1 245 cm^{-1}; δ ([$^2H_6$]acetone; 90 MHz) 1.9—2.15 (2 H, m, 8-H_2), 1.99 (3 H, s, OAc), 2.75—2.95 (2 H, m, 4-H_2), 3.78 (1 H, dt, *J ca.* 6 and 9 Hz, 6α-H), 4.14 (2 H, t, *J* 6 Hz, 9-H_2), 4.43 (1 H, td, *J* 10 and 6 Hz, 5α-H), 5.30 and 5.48 (each 1 H, *J* 14 Hz, ABq), 6.67 (1 H, t, *J* 3 Hz, 3-H), and 7.75 and 8.24 (each 2 H, *J* 9 Hz, AA′BB′); irradiation at the frequency of the 4-H_2 signal simplified the 5-proton resonance to a doublet, *J* 6 Hz, and collapsed the 3-proton resonance to a singlet. Similarly, irradiation at the frequency of the 8-H_2 signal simplified the 6-H resonance to a doublet, *J ca.* 6 Hz and the 9-H_2 signal to a singlet.

Elution of the column with ethyl acetate afforded the lactone–pyrroline (**75**) (0.009 g) (t.l.c. analysis, i.r. spectrum).

p-*Nitrobenzyl* (5RS, 6SR)-6-[2-(*Phenylcarbamoyloxy*)*ethyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* (**74**).—The aldehyde (**71**) (0.050 g) was converted into the alcohol (**72**) (0.048 g) as previously described. This material foamed under reduced pressure and contained no lactone–pyrroline (**75**) (t.l.c. analysis). The alcohol in pyridine (0.2 ml) was stirred with an excess of phenyl isocyanate at 0 °C. The reaction was allowed to warm to room temperature (1.5 h) after which it was diluted with ethyl acetate and washed with brine (2 × 3 ml). The organic layer was dried and evaporated, and the residue, in toluene (1 ml), was chromatographed on silica gel 60 (1:1 mixture, Art. 7729 and 9385 grades; 4 × 1 cm). Elution with ethyl acetate–light petroleum (1:1) afforded diphenylurea, followed by the *urethane* (**74**), which crystallised from chloroform–ethyl acetate as fine needles [0.037 g, 54% overall from (**71**)], m.p. 165—166 °C (Found: C, 61.0; H, 4.6; N, 9.3. $C_{23}H_{21}N_3O_7$ requires C, 61.2; H, 4.7; N, 9.3%); $\nu_{max.}$ 3 445, 1 785 (β-lactam), 1 735st (PNB ester + urethane), 1 610, 1 605, 1 525, 1 445, and 1 350 cm^{-1}; δ ([$^2H_6$]acetone; 80 MHz), 2.12 (2 H, m, 8-H_2), 2.8—3.0 (2 H, m, 4-H_2), 3.81 (1 H, dt, *J* 8 and 7 Hz, 6α-H), 4.23 (2 H, t, *J* 6 Hz, 9-H_2), 4.42 (1 H, td, *J* 10 and 6 Hz, 5α-H), 5.27 and 5.48 (each 1 H, *J* 16 Hz, ABq), 6.66 (1 H, t, *J* 3 Hz, 3-H), 6.97—7.57 (5 H, m, ArH), and 7.72 and 8.23 (each 2 H, *J* 9 Hz, AA′BB′).

Further elution of the column with ethyl acetate afforded the lactone–pyrroline (**75**) (0.014 g; 27%) (t.l.c. analysis, i.r. spectrum).

Table 2. Fractional atomic co-ordinates with standard deviation in parentheses for ester (**49**)

Atom	*x/a*	*y/b*	*z/c*
N(1)	0.8673(3)	0.0025(1)	0.7763(3)
C(2)	0.8152(3)	0.0454(2)	0.6221(3)
C(3)	0.7294(4)	−0.0273(2)	0.4745(3)
C(4)	0.7037(4)	−0.1321(2)	0.5146(4)
C(5)	0.8199(4)	−0.1102(2)	0.7103(4)
C(6)	0.7292(3)	−0.1293(2)	0.8866(3)
C(7)	0.7669(3)	−0.0151(2)	0.9232(3)
O(7)	0.7240(3)	0.0431(1)	1.0277(2)
C(8)	0.5219(4)	−0.1949(2)	0.8649(3)
O(8)	0.4637(3)	−0.1846(1)	1.0422(3)
C(9)	0.4896(4)	−0.3061(2)	0.7964(5)
C(10)	0.8541(4)	0.1549(2)	0.6335(4)
O(10)	0.8011(4)	0.1910(2)	0.5085(3)
O(11)	0.9547(3)	0.2109(1)	0.7955(2)
C(12)	0.9831(7)	0.3182(3)	0.8165(5)
C(13)	1.0805(4)	0.3722(2)	1.0075(4)
C(14)	1.0212(4)	0.3328(2)	1.1575(4)
C(15)	1.1013(7)	0.3867(3)	1.3309(5)
C(16)	1.2414(8)	0.4794(4)	1.3585(7)
C(17)	1.3047(6)	0.5196(3)	1.2127(8)
C(18)	1.2241(5)	0.4656(2)	1.0349(6)

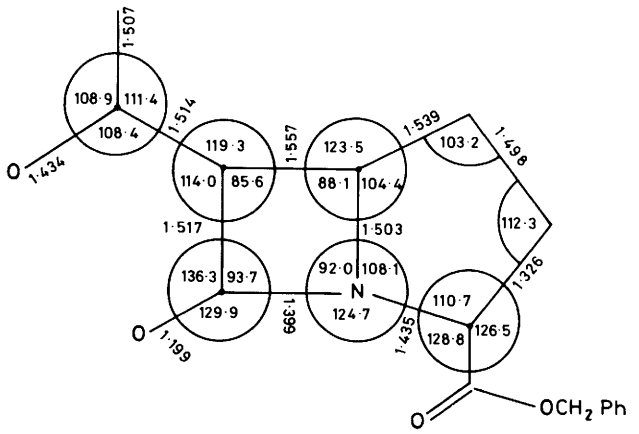


Figure 2. Bond lengths (Å) (standard deviations 0.003—0.006 Å) and bond angles (°) (standard deviations 0.18—0.38°) of ester (**49**)

Crystal Structure Determination of Ester (**49**).—*Crystal data.* $C_{16}H_{17}NO_4$, M = 287.1, Triclinic, space group $P\bar{1}$, a = 7.581(2), b = 14.083(3), c = 7.389(2) Å, α = 97.8(1), β = 96.6(1), γ = 109.3(1)°, Mo-K_α, λ = 0.710 69 Å.

Data Collection.—Reflections were counted for $\theta \leqslant 25°$ (Hilger-Watt Y290 diffractometer, graphite monochromated radiation, λ = 0.710 69 Å). Of a total of 2 556 reflections scanned, 1 862 had $I \geqslant 3\sigma I$ 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 from a difference map and included in the calculations but not refined. The final R-value with all non-hydrogen atoms treated anisotropically was R = 0.051. The standard variations for bond lengths and angles were in the ranges 0.003—0.006 Å and 0.18—0.38°. Tabulations of the bond lengths and bond angles have been treated as a suplementary publication [SUP. No. 56330 (5 pp.)].* The structure factors are available from the Editorial office on request.

* For details of the Supplementary Publications Scheme see Instructions for Authors (1985), *J. Chem. Soc., Perkin Trans. 1*, 1985, Issue 1.

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References

1 Part 1, J. H. Bateson, A. J. G. Baxter, P. M. Roberts, T. C. Smale, and R. Southgate, *J. Chem. Soc., Perkin Trans. 1*, 1981, 3242.
2 A. G. Brown, D. F. Corbett, A. J. Eglington, and T. T. Howarth, *J. Chem. Soc., Chem. Commun.*, 1977, 523.
3 G. Albers-Schönberg, B. H. Arison, O. D. Hensens, J. Hirshfield, K. Hoogsteen, E. A. Kaczka, R. E. Rhodes, J. S. Kahan, F. M. Kahan, R. W. Ratcliffe, E. Walton, L. J. Rushwinkle, R. B. Morin, and B. G. Christensen, *J. Am. Chem. Soc.*, 1978, **100**, 6491.
4 R. Graf, *Justus Liebigs Ann. Chem.*, 1963, **661**, 111.
5 T. Durst and M. J. O'Sullivan, *J. Org. Chem.*, 1970, **35**, 2043.
6 T. Durst and M. J. Lebelle, *Can J. Chem.*, 1972, **50**, 3196.
7 T. Durst, R. Van Den Elzen, and R. Legault, *Can. J. Chem.*, 1974, **52**, 3206.
8 K. D. Barrow and T. M. Spotswood, *Tetrahedron Lett.*, 1965, 3325.
9 F. A. Bouffard and B. G. Christensen, *J. Org. Chem.*, 1981, **46**, 2208.
10 Full atomic co-ordinates, tables of bond angles and bond lengths are available from the Cambridge Crystallographic Data Base.
11 T. Haneishi, M. Nakajima, N. Serizawa, M. Inukai, Y. Takiguchi, M. Arai, S. Satoh, H. Kuwano, and C. Tamura, *J. Antibiot.*, 1983, **36**, 1581.
12 J. H. Bateson, P. M. Roberts, T. C. Smale, and R. Southgate, *J. Chem. Soc., Chem. Commun.*, 1980, 185; a full description will be included in our full paper on thiol addition reactions of C(3)-unsubstituted derivatives.
13 J. H. Bateson, A. J. G. Baxter, K. H. Dickinson, R. I. Hickling, R. J. Ponsford, P. M. Roberts, T. C. Smale, and R. Southgate, 'Recent Advances in the Chemistry of β-Lactam Antibiotics,' ed. G. I. Gregory, Special Publication No. 38, Chemical Society, London, 1981, pp. 291—313.
14 H. R. Pfaendler, J. Gosteli, R. B. Woodward, and G. Rihs, *J. Am. Chem. Soc.*, 1981, **103**, 4526.
15 M. Nakayama, A. Iwasaki, S. Kimura, S. Tanabe, A. Murakami, I. Watanabe, M. Okuchi, H. Itoh, Y. Saino, F. Kobayashi, and T. Mori, *J. Antibiot.*, 1980, **33**, 1388.
16 L. A. Paquette and T. Kakihana, *J. Am. Chem. Soc.*, 1968, **90**, 3897.
17 M. E. Cain, *J. Chem. Soc.*, 1964, 3532.
18 E. J. Moriconi and W. C. Meyer, *J. Org. Chem.*, 1971, **36**, 2841.
19 M. Gaudemar, *Bull. Soc. Chim. Fr.*, 1958, 539.
20 W. J. Jones, W. C. Davies, S. T. Bowden, C. Edwards, V. E. Davis, and L. H. Thomas, *J. Chem. Soc.*, 1947, 1446.

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