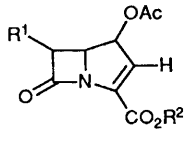
Olivanic Acid Analogues. Part 9.[1] Allylic Oxidative Functionalisation of Substituted Azetidinones: Synthesis of Some 4-Acyloxy-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylates

John H. Bateson,* Alison M. Robins and Robert Southgate
SmithKline Beecham Pharmaceuticals, Research Division, Brockham Park, Betchworth, Surrey RH3 7AJ, UK

Sharpless oxidation (Bu^tO_2H, SeO_2) of the protected allyl azetidinone **7** gave the allylic alcohol **8** which was transformed to the 5,6-*trans*-4α-acetoxyolivanic acid derivative **16**. Kharasch–Sosnovsky benzoyloxylation ($PhCO_3Bu^t$, CuCl, PhH, heat) of the silylated 7-azabicyclo[4.2.0]oct-3-enes **17b,c** provided *inter alia* allylic benzoates **18b,c** and **21b,c**. These were synthetic precursors of the 5,6-*cis*-olivanic acid analogues **23** and **26**, which contain 8- and 4α-benzoyloxy groups, respectively.

In parallel with the discovery[2] of '1β-methylcarbapenems', synthetic carbapenem antibiotics which are insensitive to renal dehydropeptidases, other reports have drawn attention to comparable derivatives containing oxygen substituents at the allylic position. These include the simple acetoxy derivative **1** (R^1 = H) prepared from 4-vinylazetidinone,[3] together with 4-hydroxy,[4] and 4-methoxy[4,5] variants of **1**. The 4-acyloxy-olivanic acids **1** [R^1 = $MeCH(OH)^-$], together with corresponding derivatives in the 1-carbadethiacephem series,[6] may be envisaged as activated '*endo*-substituted' analogues of the naturally occurring 3-acetoxymethylcephems **2**.



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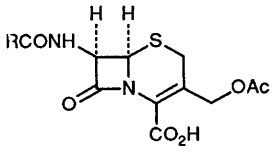

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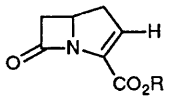
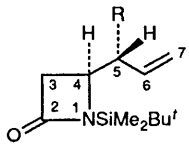


3; R = PNB ($CH_2C_6H_4NO_2$-*p*)
4; R = Na

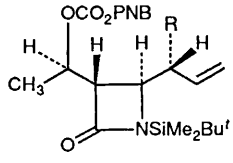
Results and Discussion

We now describe in full[7] our synthesis of type **1** olivanic acid derivatives, employing two distinct strategies involving allylic oxidation reactions of olefinic precursors. As a result of the labile nature of the parent ester **3** and its sodium salt **4**,[8] we were unable to achieve functionalisation at C-4 of the bicyclic species† using allylic oxidation (*vide infra*) or bromination conditions. Also, to our surprise, 4-allyl-1-dimethyl-*tert*-butylsilylazetidinones were resistant to radical bromination (NBS, AIBN, PhH, heat).

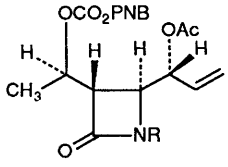
In contrast, *N*-silylated azetidinones **5** and **7**[9] were oxidised allylically under Sharpless' conditions (Bu^tO_2H, SeO_2, MDC, 50 °C)[10,11] to provide alcohols **6** and **8**, respectively (yields *ca.* 35% after recycling of recovered starting material). Whereas product **6** was a single component, **8** was a mixture (8:1) of alcohol epimers. For the major component, double resonance experiments obtained a value $^3J_{4,5}$ of 1–2 Hz, although this does not permit conclusive assignment of stereochemistry. Acetylation of alcohol **8** provided acetate **9** (86%) and this material gave access to 4-acetoxyolivanic acid derivatives with the *trans*-configuration of C-5 and C-6 protons. Desilylation to **10** with potassium fluoride in methanol and conversion into phosphorane **12** *via* glyoxylate **11** followed our established procedures.[8,9] Ozonolysis of the double bond, with oxidative work-up of the ozonide with *m*-chloroperbenzoic acid, gave carboxylic acid **13** (86%), m.p. 251–253 °C. Activation as the mixed diethylphosphonic anhydride, followed by displacement with lithium pyrimidine-2-thiolate afforded the pyrimidinyl thioester **14**. Wittig cyclisation in refluxing toluene (2.5 h) then gave the bicyclic azetidinone **15** (68%) [ν_{max} 1795 cm^{-1}; δ_H 4.17 (1 H, dd, *J* 6 and 4 Hz, 5-H) and 6.64 (1 H, d, *J* 6 Hz, 4-H)]. The geminal coupling constant $^3J_{4,5}$ 6 Hz) correlates with that found by Reuschling for a 6-unsubstituted analogue **1** (R^1 = H, R^2 = PNB),[3] and by Rosati for a 4-hydroxy derivative[4b] related to our own compound **15**. Recent results of Coulton



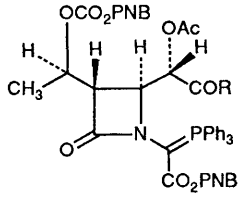
5; R = H
6; R = OH



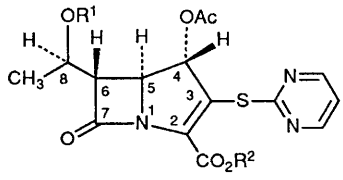
7; R = H
8; R = OH
9; R = OAc



10; R = H
11; R = CH(OH)CO_2PNB
12; R = C(PPh_3)CO_2PNB



13; R = OH
14; R = S-(pyrimidin-2-yl)

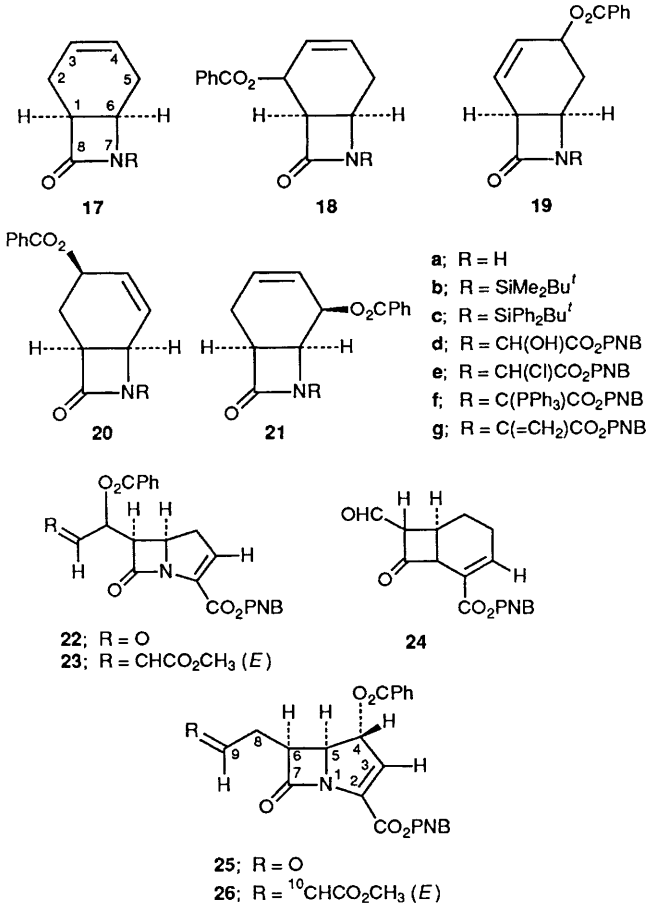


15; R^1 = PNBOCO, R^2 = PNB
16; R^1 = H, R^2 = Na

† This paper employs systematic numbering based on the azabicyclo-[3.2.0]hept-2-ene system throughout. Trivial numbering in respect of the term 'carbapenem' does not apply.

et al. from these laboratories have demonstrated[12] an α-face stereochemistry for the acetoxy group present in the γ-lactam analogue of **1**. These observations prompt us provisionally also to assign the thermodynamically favoured 4α-stereochemistry to acetate **15**. This represents the (4*RS*,5*RS*,6*RS*,8*SR*) relative stereochemistry and implies that precursor allylic alcohol **8** possesses (3*RS*,4*RS*,6*SR*) stereochemistry as depicted. Hydrogenolysis of ester **15** gave the sodium salt **16** in good yield (*ca.* 75%). However, it did not possess the level of broad-spectrum antibacterial activity exhibited by its 4-unsubstituted counterpart, prepared previously in these laboratories.[13] UV spectroscopic evidence did, however, indicate that the compound was unstable in aqueous solution. This may be rationalised in terms of nucleofugal activation by the acetoxy group during hydrolysis of the β-lactam.

The second approach comprises a development of our previously described[8] strategy for the synthesis of *cis*-carbapenems from the β-lactam **17a**, derived from cyclohexa-1,4-diene. *N*-Silylation of this compound (Me_2Bu^tSiCl, imidazole, DMF) gave **17b**. Unsurprisingly, this was not oxidised allylically under Sharpless' conditions, since this is a general property of endocyclic olefins.[10]



In contrast, compound **17b** proved to be a substrate for the Kharasch–Sosnovsky allylic benzoyloxylation reaction (PhCO_3Bu^t, CuCl, PhH, heat, 24 h),[14,15] which has been employed successfully to functionalise at the C-2 position of a cephem system.[16] We obtained all four possible allylic monobenzoate regioisomers **18b** (25%), **19b** (17%), **20b** (18%) and **21b** (20%). Each was a single stereoisomer. A similar reaction of the *N*-diphenyl-*tert*-butylsilylazetidinone **17c** directed the oxidation to favour **18c** (35%) at the expense of the 5-benzoyloxy isomer **21c** (6%). Desilylation (KF, MeOH) gave the unprotected

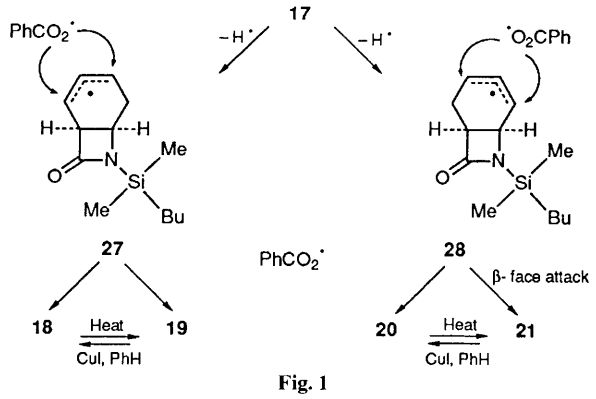


Fig. 1

isomers **18a**–**21a**. More conveniently, the crude oxidation products were desilylated *in situ* prior to separation. In this way, **17c** provided **18a** (26%), **19a** (18%), **20a** (8%) and **21a** (6%) in the designated overall yields. In each case the regiochemistry of substitution was proven rigorously by ^1H NMR double-resonance experiments; initial irradiation at the frequency of the NH proton signal permitted assignment of the proton topology. [Interestingly, for all isomers $^4J_{1,NH}$ *ca.* 1 Hz and $^3J_{6,NH}$ 0. This was confirmed conclusively for isomer **20a** by a SIMPLE[17] experiment. Partial deuteriation of the NH proton produced isotope shifts in the ^{13}C resonances δ_C 46.6 and 43.7 ppm of −20 and −128 ppb, respectively. These magnitudes indicate carbons sited 3 and 2 bonds from the deuterium and thereby locate C-1 and C-6. Individual proton decoupled ^{13}C spectra then identified the corresponding one-bond proton partners as the β-lactam protons, δ_H 3.66 (C-1) and δ_H 4.11 (C-6) ppm.]. Stereochemical assignments for the benzoyloxy groups are less certain owing to the possibility of two distinct conformations for the cyclohexenyl ring of each isomer. However, for the isomer pair **20a** and **21a**, evidence thus far accumulated corroborates the β-face stereochemistry. For compound **20a** the ^1H NMR spectrum shows $^3J_{1,2}$ 7 and $^3J_{2,3}$ 10.5 Hz. Examination of molecular models shows that only for the 3β-benzoyloxy stereochemistry, in the conformation permitting its favoured pseudoequatorial configuration, will the two couplings both be predicted to be of this magnitude. For the case of compound **21a**, its allylic counterpart, a 5β-configuration correlates stereochemically with the only configuration that is possible for its azabicycloheptene derivative **25** (*vide infra*). These conclusions suggest that the *N*-silyl substituent may direct the approach of benzoyloxy radicals to the more hindered β-face of the allylic radical intermediate **28** (Fig. 1), perhaps as a consequence of the silicon–oxygen interaction.

In the case of the *N*-diphenyl-*tert*-butyl series, the product yields indicate a preference for benzoates **18c** and **19c** and therefore also for the formation of radical **27**.

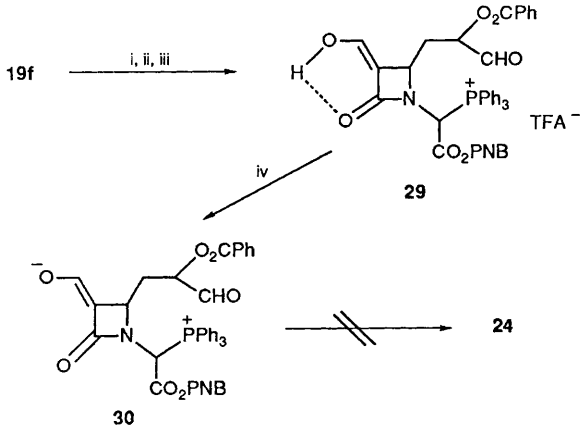
In order to determine the extent of allylic rearrangement of reaction products during the course of the benzoyloxylation, TBDMS compounds **19b** and **21b** were each heated in refluxing benzene in the presence of copper(I) chloride overnight. Desylation of the crude products provided respectively **18a** and **19a** (1:9) and **20a** and **21a** (1:5) (^1H NMR), indicating that equilibration of the allylic benzoate pairs is established under the reaction conditions (Fig. 1). These are much milder than those normally required by the uncatalysed reaction.[18,19] Thus, during the allylic functionalisation reaction it is likely that the yield of benzoates **18** and **20** is enhanced at the expense of isomers **19** and **21**. A (3,3)-sigmatropic shift interconversion mechanism would require the same substituent configuration for the isomers comprising each allylic pair.

Each isomer **18a**–**21a**, in turn, was converted *via* glyoxylates

18d–21d and α-chloro esters **18e–21e** into the corresponding phosphoranes **18f–21f** using our established methods.[8,9] Further characterisation of the latter was achieved by conversion into the crystalline, substituted acrylate derivatives **19g–21g** with aqueous formaldehyde.[1] An ozonolysis–cyclisation sequence[8] with phosphorane **18f** gave α-benzoyloxy aldehyde **22** (65%), which was characterised further by reaction with methoxycarbonylmethylenetriphenylphosphorane to afford the (*E*)-enoate **23**.

Ozonolysis–cyclisation of phosphorane **21f** similarly provided the bicyclic formyl benzoate **25** (29%) $^3J_{4,5}$ 7.5 Hz. This was also characterised by reaction with the stabilised phosphorane to give the *E*-enoate **26** (66%). A better yield overall (63%) of **26** could be obtained by trapping of **25** *in situ* prior to chromatography. Examination of molecular models indicates conclusively that in the *cis*-β-lactam series, it is impossible to accommodate a β-acyloxy substituent at C-4 without incurring severe non-bonded interactions with the C-6 substituent. Under these circumstances, it is unlikely that the intramolecular Wittig cyclisation would occur. Accordingly, we are confident in assigning (4*RS*,5*SR*,6*SR*) (4α-benzoyloxy group) relative stereochemistry to aldehyde **25** and its derivatives. Retention of stereochemistry during the cyclisation correlates with 5β-benzoyloxy stereochemistry in azabicyclooctanes **21**.

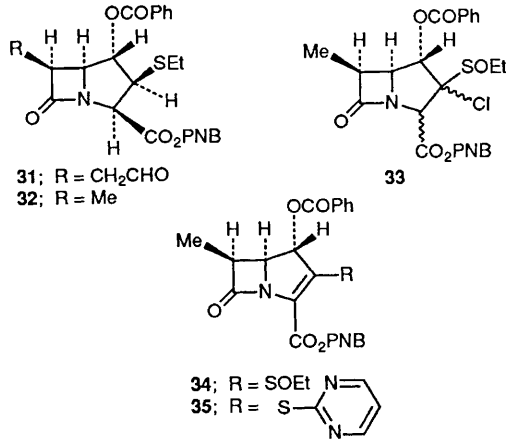
Ozonolysis–cyclisation failed to produce any bicyclic β-lactam products from phosphorane isomers **19f** and **20f**. This may be understood in the latter instance owing to the reluctance for formation of a 1-azabicyclo[2.2.0]hex-2-ene. For **19f**, which should function as the precursor of a 1-azabicyclo[4.2.0]oct-2-ene ('1-dethia-1-carbacephem') **24**, other factors must come into play. We postulate (Scheme 1) that hydroxymethylene intermediate **29** is deprotonated by the sodium hydrogencarbonate to generate an unreactive betaine **30** in preference to an ylide. Accordingly, cyclisation cannot occur. A similar situation was encountered by Woodward in his initial studies on penem synthesis.[20]



Scheme 1 *Reagents:* i, EtOAc–TFA, RT; ii, O_3, −70 °C; iii, Ph_3P (1 mol equiv.), −70–0 °C; iv, $NaHCO_3$, H_2O, 0 °C–RT

We have also investigated some additional reactions of the formyl benzoate **25**. Addition of ethanethiol to the Δ^2-double bond gave a single adduct.[21,22]

This is assigned as the 2β-carboxy,3β-sulphide isomer **31** (66%) on steric grounds, a product of *trans*-addition. Decarbonylation of aldehyde **31** using Wilkinson's catalyst gave[22] the 6β-methyl derivative **32** as an oil (82%). An α-chloro sulphoxidation reaction sequence (i, iodobenzene dichloride, pyridine, MDC, H_2O; ii, DBU, EtOAc)[21] provided the Δ^2-3-ethylsulphinyl compound **34** *via* α-chloro sulphoxide **33**. We were unable to achieve a sulphoxide-displacement reaction[23] with this substrate using sodium pyrimidine-2-thiolate, and thus could not obtain an analogue **35** of acetate **15**. We attribute this



to steric hindrance by the 4α-benzoyloxy group. The 2β-carboxy group configuration is favoured in **31**[21] and retained in **32**,[22] since epimerisation would give rise to an unfavourable 1,3-*syn* interaction with the 4α-benzoyloxy group.

Experimental

The experimental techniques, materials, solvents and spectroscopic instrumentation employed in this work were as described in Parts 2[9] and 4[24] of the series. IR spectra were recorded for chloroform solutions and NMR spectra were obtained in $CDCl_3$. Coupling constants are in Hz.

All compounds prepared are racemic; NMR stereochemical assignments refer to that enantiomer which is depicted.

Organic solutions were dried internally using anhydrous sodium sulphate. Merck silica gel 60 Art. 7729 is finer than 230 mesh ASTM; Art. 9385 is 230–400 mesh ASTM.

4α-*Acetoxy Series*

(4*RS*)-1-*Dimethyl*-tert-*butylsilyl*-4-[(1*SR*)-1-*hydroxyprop*-2-*enyl*]*azetidin*-2-*one* **6**.—To a solution of 4-allyl 1-dimethyl-*tert*-butylsilylazetidin-2-one **5**[9] (10.0 g) in dichloroethane (60 ml) was added selenium dioxide (2.47 g, 0.5 mol equiv.), followed by *tert*-butyl hydroperoxide (TBHP) (3.5 mol equiv.) [prepared by extraction of 70% aqueous TBHP (25 ml) with dichloroethane (40 ml) and adding the organic phase].[11] The solution was stirred at 50 °C for 5 days. The reaction mixture was cooled and shaken with saturated aqueous sodium sulphite. The organic layer was washed with brine, dried and concentrated under reduced pressure. The residue was chromatographed on silica gel (Art. 7729), eluting with ethyl acetate–hexane (3:7) to give recovered azetidinone **5** (6.2 g, 62%). Later fractions contained alcohol **6** (2.35 g, 22%), which was an oil, ν_{max}/cm^{-1} 3450br, 3000–2860, 1735, 1645 and 1610; δ_H(90 MHz) 0.26 (3 H, s), 0.29 (3 H, s), 0.98 (9 H, s), 1.98 (1 H, br s, OH, D_2O exch.), 2.94 (2 H, m, 3-H_2), 3.66 (1 H, m, 4-H), 4.39 (1 H, dm, *J* 5, C*H*OH), [5.25 (1 H, ddd, *J* 10, 2 and 1.5) and 5.38 (1 H, ddd, *J* 16, 2 and 1.5) (=CH_2)] and 5.79 (1 H, ddd, *J* 16, 10 and 5, C*H*=CH_2); *m*/*z* CI (NH_3) 242 (MH^+). Recycling of the recovered **5** provided a further amount of alcohol (1.2 g), raising the yield to *ca.* 33%.

A similar experiment employing salicylic acid (0.1 mol equiv.) as additive[11] gave alcohol **6** (21%), but with poorer recovery of the starting material (32%).

(3RS,4RS)-1-*Dimethyl*-tert-*butylsilyl*-4-[(1SR)-1-*hydroxyprop*-2-*enyl*]-3-[(1SR)-1-p-*nitrobenzyloxycarbonyloxyethyl*]-*azetidin*-2-*one* **8**.—To a solution of (3*RS*,4*SR*)-4-allyl-1-dimethyl-*tert*-butylsilyl-3-[(1*SR*)-1-*p*-nitrobenzyloxycarbonyloxyethyl]azetidin-2-one **7**[9] (6.83 g) in dichloroethane (20 ml) was added selenium dioxide (1.69 g, 1 mol equiv.) followed by

TBHP (8 ml of the solution in dichloroethane,[11] *ca.* 4 mol equiv.), and the mixture was stirred at 45–50 °C for 24 h. Work-up and chromatography as for alcohol **6** gave recovered **7** (2.65 g, 39%) and then alcohol **8** as an oil (8:1 ratio of isomers) (1.77 g, 25%), ν_{max}/cm^{-1} 3450br, 2960–2860, 1745, 1610, 1525 and 1350; δ_H(250 MHz) (major component) 0.24 (3 H, s), 0.32 (3 H, s), 1.00 (9 H, s), 1.36 [3 H, d, *J* 7, C*H*$_3$CH(OR)], 2.61 (1 H, br s, OH, D$_2$O exch.), 3.39 (1 H, dd, *J* 6 and 3, 3-H), 3.69 (1 H, t, *J ca.* 2.5, 4-H), 4.41 [1 H, br d, *J* 6, C*H*(OH)], 5.13 [1 H, quin., *J ca.* 6, CH$_3$C*H*(OR)], 5.24 (2 H, s, C*H*$_2$Ar), [5.21 (1 H, br d, *J* 11) and 5.39 (1 H, dd, *J* 17 and *ca.* 2) (=CH$_2$)], 5.79 (1 H, ddd, *J* 17, 11 and 6, C*H*=CH$_2$) and 7.54 (2 H, *J* 9) and 8.24 (2 H, *J* 9) (AA′BB′).

Recycling of the recovered **7** gave a further quantity of alcohol **8** (0.628 g), raising the yield to 35%.

(3RS,4RS)-4-[(1SR)-1-*Hydroxyprop*-2-*enyl*]-3-[(1SR)-1-p-*nitrobenzyloxycarbonyloxyethyl*]*azetidin*-2-*one*.—A solution of alcohol **8** (0.20 g) in methanol (5 ml) was stirred with potassium fluoride (0.028 g) at room temperature for 15 min. The methanol was evaporated and the residue partitioned between ethyl acetate and brine. The organic layer was dried and chromatographed on silica gel. Elution with ethyl acetate gave the title azetidinone (0.087 g, 55%), ν_{max}/cm^{-1} 3500–3200, 3390, 1755, 1740, 1610, 1525 and 1350; δ_H(90 MHz) 1.40 [3 H, d, *J* 6, C*H*$_3$CH(OR)], 2.82 (1 H, br s, OH), 3.24 (1 H, dd, *J* 6 and 2, 3-H), 3.47 (1 H, dd, *J* 4 and 2, 3-H), 4.21 [1 H, br m, C*H*(OH)], 5.22 (2 H, s, CH$_2$Ar), 5.0–5.5 [3 H, m, CH$_3$C*H*(OR) and =CH$_2$], 5.71 (1 H, ddd, *J* 16, 10 and 6, C*H*=CH$_2$), 6.32 (1 H, br s, NH) and [7.50 (2 H, *J* 9) and 8.23 (2 H, *J* 9) (AA′BB′)]; *m*/*z* CI (NH$_3$) 351 (MH$^+$); EI Found: 293.0773. $C_{13}H_{13}N_2O_6$ requires *M* − CH$_2$=CH–CH(OH), 293.0774.

(3RS,4RS)-4-[(1SR)-1-*Acetoxyprop*-2-*enyl*]-1-*dimethyl*-tert-*butylsilyl*-3-[(1SR)-1-p-*nitrobenzyloxycarbonyloxyethyl*]-*azetidin*-2-*one* **9**.—A solution of alcohol **8** (1.77 g) in methylene dichloride (50 ml) at 0 °C was treated successively with triethylamine (1.07 ml, 2 mol equiv.), acetic anhydride (0.73 ml, 2 mol equiv.) and dimethylaminopyridine (DMAP) (0.05 g, 0.1 mol equiv.). The solution was stirred at room temperature for 1.5 h, and then evaporated. The residue, in ethyl acetate, was washed with brine (×2), dried and concentrated. Chromatography on silica gel (Art. 7729), eluting with ethyl acetate–hexane (1:2) gave acetate **9** as a gum (1.67 g, 86%), ν_{max}/cm^{-1} 2950–2860, 1755, 1740, 1610, 1525 and 1350; δ_H(250 MHz) 0.21 (3 H, s), 0.29 (3 H, s), 0.96 (9 H, s), 1.39 [3 H, d, *J* 6, CH$_3$CH(OR)], 2.11 (3 H, s, OAc), 3.37 (1 H, dd, *J* 6 and 3, 3-H), 3.75 (1 H, dd, *J* 3 and 2, 4-H), 5.13 [1 H, quin, *J* 6, CH$_3$C*H*(OR)], 5.23 (2 H, s, C*H*$_2$Ar), 5.28 (1 H, br d, *J* 10) and 5.35 (1 H, br d, *J* 16) (=CH$_2$), 5.51 [1 H, br dd, *J* 6 and 2 CH(OAc)], 5.72 (1 H, ddd, *J* 16, 10 and 6, C*H*=CH$_2$) and 7.52 (2 H, *J* 9) and 8.24 (2 H, *J* 9) (AA′BB′); *m*/*z* (EI) Found: 449.1377. $C_{20}H_{25}N_2O_8Si$ requires M^+ − Bu^t, 449.1380.

(3RS,4RS)-4-[(1SR)-1-*Acetoxyprop*-2-*enyl*]-3-[(1SR)-1-p-*nitrobenzyloxycarbonyloxyethyl*]*azetidin*-2-*one* **10**.—A solution of acetate **9** (0.50 g) in methanol (15 ml) was stirred with potassium fluoride (0.57 g, 2 mol equiv.) at room temperature for 10 min. Recovery in ethyl acetate (*vide supra*) and chromatography on silica gel (Art. 7729) eluting with ethyl acetate–hexane (1:1) provided β-lactam **10** (0.273 g, 71%), ν_{max}/cm^{-1} 3420, 1775sh, 1765, 1745, 1610, 1525 and 1350; δ_H(250 MHz) 1.42 [3 H, d, *J* 6, C*H*$_3$CH(OR)], 2.10 (3 H, s, OAc), 3.27 (1 H, dd, *J* 6.5 and 2, 3-H), 3.80 (1 H, dd, *J* 4 and 2, 4-H), 5.14 [1 H, quin, *J* 6, CH$_3$C*H*(OR)], 5.25 (2 H, s, C*H*$_2$Ar), 5.32 (1 H, br d, *J* 10) and 5.41 (1 H, br d, *J* 17) (=CH$_2$), 5.44 [1 H, *J* 6 and 4, CH(OAc)], 5.78 (1 H, ddd, *J* 17, 10 and 6, C*H*=CH$_2$), 5.80 (1 H, br s, NH) and 7.54 (2 H, *J* 9) and 8.25 (2 H, *J* 9) (AA′BB′); *m*/*z* CI (NH$_3$) 393 (MH$^+$) and 410 (MNH$_4^+$); EI Found: 293.0771. $C_{13}H_{13}N_2O_6$ requires [M^+ − CH$_2$=CH(OAc)], 293.0774.

p-*Nitrobenzyl* {(3RS,4RS)-4-[(1SR)-1-*Acetoxyprop*-2-*enyl*]-3-[(1SR)-1-p-*nitrobenzyloxycarbonyloxyethyl*]-2-*oxoazetidin*-1-*yl*}(*triphenylphosphoranylidene*)*acetate* **12**.—The azetidinone **9** (0.630 g) was heated in benzene (25 ml) with *p*-nitrobenzyl glyoxylate (0.548 g) in a Dean-Stark apparatus for 36 h. Water (2 ml) was added to the cooled solution, which was stirred overnight. The rehydrated excess of reagent separated from solution and was removed by filtration. The filtrate was concentrated and chromatographed on silica gel (Art. 9385). Elution with ethyl acetate–hexane (1:1) gave glyoxylate ester **11** (0.598 g, 62%), ν_{max}/cm^{-1} 3500, 1775, 1740, 1610, 1525 and 1350. This was converted into the title phosphorane **12** by use of our established methods.[8,9] It was obtained as a pale yellow foam (0.716 g, 85%), ν_{max}/cm^{-1} 1755, 1745, 1620br, 1610, 1525 and 1350; *m*/*z* (EI) 845 (M^+).

p-*Nitrobenzyl* {(3RS,4RS)-4-[(1RS)-*Acetoxy*(*carboxy*)-*methyl*]-3-[(1SR)-1-p-*nitrobenzyloxycarbonyloxyethyl*]-2-*oxoazetedin*-1-*yl*}(*triphenylphosphoranylidene*)*acetate* **13**.—Phosphorane **12** (0.177 g) in methylene dichloride–ethyl acetate (6:1, 35 ml) was stirred with trifluoroacetic acid (TFA) (2 ml) for 30 min. The solution was cooled to −65 °C and ozonolysed. After purging of the excess of ozone with argon gas, *m*-chloroperbenzoic acid (0.041 g, 1.1 mol equiv.) was added, the solution warmed to room temperature and the mixture was stirred overnight. The solution was evaporated and the residue, in toluene, chromatographed on silica gel (Art. 9385). Elution with ethanol–ethyl acetate (1:9) gave the *carboxy phosphorane* **13** (0.145 g, 86%) as a white solid, m.p. 251–253 °C (Found: C, 59.9; H, 4.15; N, 4.7. $C_{44}H_{38}N_3O_{14}P$ requires C, 61.2; H, 4.4; N, 4.9%); ν_{max}(KBr)/cm^{-1} 3500–3400, 1740, 1680, 1630–1600, 1525 and 1350.

p-*Nitrobenzyl* {3RS,4RS)-4-{(1RS)-(*Acetoxy*)[*pyrimidin*-2-*ylthio*)*carbonyl*]*methyl*}-3-[(1SR)-1-p-*nitrobenzyloxycarbonyl-oxyethyl*]-2-*oxoazetidin*-1-*yl*}(*triphenylphosphoranylidene*)-*acetate* **14**.—The carboxy phosphorane **13** (0.129 g) in dry THF in an argon atmosphere was treated with triethylamine (0.024 ml, 1.2 mol equiv.), followed by diethyl chlorophosphate (0.031 g, 1.2 mol equiv.) and the mixture was stirred at room temperature for 1.5 h. Lithium pyrimidine-2-thiolate[1] (0.021 g, 1.2 mol equiv.) was added, and the suspension stirred for 6 h. The mixture was evaporated, and the residue in ethyl acetate was washed with brine, dried, evaporated and chromatographed on silica gel (Art. 9385). Elution with ethyl acetate–hexane (1:1) gave the title compound **14** as a gum (0.053 g, 29%); ν_{max}/cm^{-1} 1755, 1630–1620, 1610, 1555, 1525, 1385 and 1350.

p-*Nitrobenzyl* (4RS,5RS,6RS)-4-*Acetoxy*-6-[(1SR)-1-p-*nitro-benzyloxycarbonyloxyethyl*]-7-*oxo*-3-(*pyrimidin*-2-*ylthio*)-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* **15**.—A solution of the *S*-ester phosphorane **14** (0.035 g) in anhydrous toluene (35 ml; degassed in a stream of argon gas) was heated at reflux in an argon atmosphere for 2.5 h. The mixture was filtered and evaporated, and the residue chromatographed rapidly on silica gel (Art. 9385) to give the *bicyclic azetidinone* **15** as a gum (0.017 g, 68%) (Found: M^+, 679.1182. $C_{30}H_{25}N_5O_{12}S$ requires *M*, 679.1220); λ_{max}(EtOH) 328 and 362 nm; ν_{max}/cm^{-1} 1795, 1745, 1610, 1560, 1525, 1385 and 1350; δ_H(250 MHz) 1.50 [3 H, d, *J* 6.5, C*H*$_3$CH(OR)], 1.89 (3 H, s), 3.81 (1 H, dd, *J* 6 and 4, 6-H), 4.17 (1 H, dd, *J* 6 and 5-H), 5.23 (2 H, s, ArC*H*$_2$OCO$_2$), *ca.* 5.28 [1 H, m, CH(OR)], 5.33 (*J* 14) and 5.48 (*J* 14) (2 H, ABq, ArCH$_2$OCO), 6.64 (1 H, d, *J* 6, 4-H), 7.09 (1 H, t, *J* 5,

pyrimidine 4-H), 7.56, 7.62, 8.20 and 8.23 (each 2 H, *J* 9) (2 × AA′BB′) and 8.54 (2 H, d, *J* 5, 2 × pyrimidinyl 3-H).

Sodium (4RS,5RS,6RS)-4-*Acetoxy*-6-[(1SR)-1-*hydroxyethyl*]-7-*oxo*-3-(*pyrimidin*-2-*ylthio*)-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* **16**.—A solution of *p*-nitrobenzyl ester **15** (0.017 g) in dioxane (6 ml) was added to a 'prehydrogenated' suspension of 10% Pd–C catalyst in dioxane–water (3:2; 10 ml). The ester was shaken in an atmosphere of hydrogen gas for 2 h. Sodium hydrogen carbonate (0.002 g, *ca.* 1 mol equiv.) in water (1 ml) was added, and the mixture filtered through Celite. The filtrate was evaporated, and the aqueous residue was extracted with diethyl ether. The aqueous solution, $\lambda_{max}(H_2O)$ 278 and 243 nm, was estimated to contain *ca.* 75% yield of sodium salt **16**.

Benzyloxy Series

(1RS,6SR)-7-*Dimethyl*-tert-*butylsilyl*-7-*azabicyclo*[4.2.0]*oct*-3-*en*-8-*one* **17b**.—β-Lactam **17a** (0.40 g) and dimethyl-*tert*-butylsilyl chloride (0.49 g) in dry DMF were stirred in the presence of triethylamine (0.25 ml) for 0.5 h. The mixture was diluted with ethyl acetate, washed with brine and the organic layer dried and evaporated. The residue was chromatographed on silica gel (Art. 9385). Elution with ethyl acetate–hexane (1:1) gave the *title silane* **17b** as an oil (0.77 g, 99%) (Found: MH^+, 238.1628. $C_{13}H_{24}NOSi$ requires *M* + 1, 238.1627; $M - CH_3^+$, 222.1306. $C_{12}H_{20}NOSi$ requires *M* − 15, 222.1298; $M - Bu^t$, 180.0863. $C_9H_{14}NOSi$ requires *M* − 57, 180.0845); ν_{max}/cm^{-1} 3000–2860, 1730, 1255 (SiMe) and 840; δ_H(90 MHz) 1.1 (3 H, s) and 1.22 (3 H, s) (2 × SiMe), 1.95 (9 H, s), 1.8–2.6 (4 H, m, 2-H_2 and 5-H_2), 3.38 (1 H, dt, *J* 6.5 and 2, 1-H), 3.90 (1 H, m, $W_{\frac{1}{2}}$ 7, 6-H) and 5.81 (2 H, m, $W_{\frac{1}{2}}$ 18, 3-H and 4-H).

(1RS,6SR)-7-*Diphenyl*-tert-*butylsilyl*-7-*azabicyclo*[4.2.0]*oct*-3-*en*-8-*one* **17c**.—This compound was prepared similarly from β-lactam **17a** (0.50 g) and diphenyl-*tert*-butylsilyl chloride (1.12 g) in DMF (5 ml) in the presence of imidazole (0.553 g) for 3 days. The *title silane* crystallised as prisms ($CHCl_3$–hexane) (1.233 g, 72%), m.p. 119–120 °C (Found: C, 76.4; H, 7.6; N, 3.9. $C_{23}H_{27}NOSi$ requires C, 76.4; H, 7.5; N, 3.9%), ν_{max}/cm^{-1} 3080–2870, 1735 and 1590; δ_H(90 MHz) 1.17 (9 H, s), 1.61 (2 H, m, 5-H_2), [2.00 (1 H, dm, *J* 18) and 2.5 (1 H, ddd, *J* 18, 7 and 2) (5-H_2)], 3.41 (1 H, td, *J* 6.5 and 2, 1-H), 3.69 (1 H, m, $W_{\frac{1}{2}}$ 8, 6-H), 5.50 (1 H, m, $W_{\frac{1}{2}}$ 10, 4-H) and 5.89 (1 H, m, $W_{\frac{1}{2}}$ 10, 3-H).

Benzoyloxylation of N-*Silylated* 7-*Azabicyclo*[4.2.0]*oct*-3-*en*-8-*ones*.—*Method* (*i*). Dimethyl-*tert*-butylsilane **17b** (5.0 g) in benzene (50 ml) containing copper(I) chloride (0.02 g) was heated under reflux in an argon atmosphere. *tert*-Butyl perbenzoate (4.2 ml) in benzene (20 ml) was added dropwise over 45 min, and the mixture was heated under reflux for a further 16 h. The pale green solution was evaporated, and the residue chromatographed on silica gel (Art. 7385). Elution with ethyl acetate–hexane (1:9–1:4) afforded the silylated allylic benzoates in order: **18b** (1.87 g, 25%), **19b** (1.27 g, 17%), **20b** (1.35 g, 18%) and **21b** (1.49 g, 20%).

A similar experiment with diphenyl-*tert*-butylsilane **17c** (2.0 g) as substrate provided **18c** (0.91 g, 35%), **19c** (0.57 g, 22%), **20c** (0.24 g, 9%) and **21c** (0.15 g, 6%).

Each silane, in turn was deprotected using potassium fluoride in methanol to give azetidinones **18a–21a** (*vide infra*) (63–72%).

Method (*ii*). More conveniently, benzoyloxylation was followed by desilylation prior to separation, *e.g.*: silane **17c** (15.0 g) in benzene (400 ml) containing copper(I) chloride (0.040 g) was heated under reflux in an argon atmosphere. *tert*-Butyl perbenzoate (8.5 ml) in benzene (100 ml) was added (1.5 h) and the mixture heated under reflux for 16 h. The mixture was cooled and evaporated to give a residue, which was taken up in methanol (150 ml). Potassium fluoride (2.65 g, 1.1 mol equiv.) was added and the suspension was stirred at room temperature for 10 min. The methanol was evaporated and the residue partitioned between ethyl acetate and brine. Evaporation of the organic layer gave an oil which was chromatographed on silica gel (Art. 9385) (20 × 6 cm), eluting with ethyl acetate–hexane (1:1). The four azetidinones **18a–21a** were obtained in the order below.

(1RS,5SR,6RS)-8-*Oxo*-7-*azabicyclo*[4.2.0]*oct*-3-*en*-5-*yl benzoate* **21a**. This compound crystallised from ethyl acetate–hexane as off-white needles (0.595 g, 6%), m.p. 156–158 °C (Found: C, 68.8; H, 5.4; N, 6.0. $C_{14}H_{13}NO_3$ requires C, 69.1; H, 5.4; N, 5.8%), ν_{max}/cm^{-1} 3410, 1760, 1715 and 1600; δ_H 2.50 (2 H, t, *J ca.* 4, 2-H_2), 3.54 (1 H, dq, *J* 5 and 1, 1-H), 4.01 (1 H, dd, *J* 5 and 2, 6-H), 5.49 (1 H, br dd, *J* 4 and 2, 5-H), 5.96–6.30 (2 H, m, 3-H and 4-H), 6.54 (1 H, br s, N-H), 7.26–7.67 (3 H, m) and 8.00 (2 H, dd, *J* 8 and 2, (Ph); double-resonance experiments indicated $^4J_{1,NH}$ 1, $^3J_{6,NH}$ 0 and $^3J_{5,6}$ 2.

(1RS,2SR,6RS)-8-*Oxo*-7-*azabicyclo*[4.2.0]*oct*-3-*en*-2-*yl benzoate* **18a**. Crystallisation of this compound from ethyl acetate–hexane gave prisms (2.63 g, 26%), m.p. 168 °C (Found: C, 69.0; H, 5.4; N, 5.7%), ν_{max}/cm^{-1} 3420, 1760, 1715 and 1600; δ_H 2.50 (2 H, m, $W_{\frac{1}{2}}$ 6, 5-H_2), 3.71 (1 H, br dd, *J* 5 and 2, 1-H), 4.13 (1 H, m, $W_{\frac{1}{2}}$ 7, 6-H), 5.66 (1 H, dd, *J* 6 and 2, 2-H), 5.9–6.3 (2 H, m, 3-H and 4-H), 6.33 (1 H, br s, N-H), 7.25–7.63 (3 H, m) and 7.97 (2 H, dd, *J* 8 and 2, (Ph); double-resonance experiments showed $^3J_{1,2}$ 2.

(1RS,4RS,6SR)-8-*Oxo*-7-*azabicyclo*[4.2.0]*oct*-2-*en*-4-*yl benzoate* **19a**. This compound crystallised from ethyl acetate–hexane as matted needles (1.79 g, 18%), m.p. 115 °C (Found: C, 68.9; H, 5.4; N, 6.0%) ν_{max}/cm^{-1} 3410, 1760, 1715, 1600 and 1580; δ_H 1.57 (1 H, 7 lines, *J* 14, 10.5 and 4, 5-H), 2.60 (1 H, ddd, *J* 14, 5 and 1, 5-H), 3.77 (1 H, m, 1-H), 4.10 (1 H, m, 6-H), 5.60 (1 H, br ddd, *J* 10.5, 5 and 2, 4-H), 5.86–6.25 (2 H, m, 2-H and 3-H), 6.36 (1 H, br, N–H), 7.28–7.7 (3 H, m) and 8.03 (2 H, dd, *J* 8 and 2) (Ph); double-resonance experiments showed $^3J_{4,5}$ 10.5 and 5, and $^3J_{3,4}$ 2.

(1RS,3SR,6RS)-8-*Oxo*-7-*azabicyclo*[4.2.0]*oct*-4-*en*-3-*yl benzoate* **20a**. This compound crystallised from ethyl acetate as rosettes of needles (0.828 g, 8%), m.p. 158–160 °C (Found: C, 68.8; H, 5.45; N, 5.9%), ν_{max}/cm^{-1} 3400, 1750, 1715, 1600 and 1580; δ_H 1.87 (1 H, ddd, *J* 13.5, 10.5 and 7, 2-H), 2.58 (1 H, ddd, *J* 13.5, 6 and 3, 2-H), 3.66 (1 H, br 7 lines, *J* 7, 6 and 3, 1-H), 4.11 (1 H, dd, *J* 6 and 5, 6-H), 5.59 (1 H, br dd, *J* 10.5 and 6, 3-H), 5.98–6.27 (2 H, m, 4-H and 5-H), 6.45 (1 H, br s, N–H), [7.27–7.65 (3 H, m) and 8.04 (2 H, dd, *J* 8 and 2) (Ph)]; double-resonance experiments confirm $^3J_{2,3}$ 10.5 and 6, and $^3J_{3,4} < 1$.

Isomerisation of Benzoates **19b** *and* **21b**.—Benzoate isomers **19b** and **21b** (0.025 g) in benzene (*ca.* 1 ml) containing copper(I) chloride (0.001 g) were each heated in turn in an argon atmosphere overnight. The solvent was evaporated and each residue, in methanol, was desilylated by stirring it with potassium fluoride (0.005 g) for 10 min. Recovery [method (ii)] gave mixtures of the crude benzoates (0.014 g), (**18a**:**19a** 1:9) and (**20a**:**21a** 1:5), respectively (^{1}H NMR).

Phosphorane Formation and Characterisation.—Each allylic benzoate **18a–21a**, in turn, was converted (i, glyoxylic acid hydrate, DMF, 4A molecular sieves; ii, *p*-nitrobenzyl bromide, potassium carbonate) into the glyoxylate esters **18d–21d**, and thence to the phosphoranes **18f–21f** *via* α-chloro esters **18e–21e**, using methods which we have previously described in detail;[8,9,24] *e.g.* phosphorane **18f** was obtained from **18a** in 60% overall yield as a crisp foam: ν_{max}/cm^{-1} 1740, 1710, 1615br, 1605, 1320 and 1345.

Each phosphorane was characterised by conversion of an aliquot into the corresponding acrylate ester **18g**–**21g** with aqueous formaldehyde.[1]

p-*Nitrobenzyl* (1RS,2SR,6RS)-2-(2-*Benzoyloxy*-8-*oxo*-7-*aza*-*bicyclo*[4.2.0]-*oct*-3-*en*-7-*yl*)*acrylate* **18g**.—Phosphorane **18a** (0.040 g) in benzene (3 ml) was heated in the presence of an excess of 40% aqueous formaldehyde (0.2 ml) in an argon atmosphere at reflux for 10 min. The mixture was diluted with ethyl acetate, washed with brine and the organic layer was dried and evaporated. The residue was chromatographed on silica gel (Art. 9385). Elution with ethyl acetate–hexane (1:1) gave a gum which crystallised (ethyl acetate–hexane) as needles (0.022 g, 84%), m.p. 110–111 °C (Found: C, 64.0; H, 4.5; N, 6.1%; M^+, 448.1277. $C_{24}H_{20}N_2O_7$ requires C, 64.3, H, 4.5; N, 6.25; *M*, 448.1267), ν_{max}/cm^{-1} 1750, 1725, 1715sh, 1605, 1520 and 1350; δ_H(250 MHz) 2.4–2.61 (2 H, m, 5-H_2), 3.87 (1 H, dd, *J* 5 and 2, 1-H), 4.84 (1 H, m, 6-H), 5.31 (1 H, *J* 14) and 5.37 (1 H, *J* 14) (ABq), 5.71 (1 H, dd, *J* 6 and 2, 2-H), 6.00 (1 H, m) and 6.28 (1 H, m) (3-H and 4-H), 6.08 (1 H, s) and 6.22 (1 H, s) (=CH_2), 7.44 (3 H, m) and 7.99 (2 H, dd, *J* 8 and 2 Hz) (Ph), and 7.47 (2 H, *J* 9) and 8.27 (2 H, *J* 9) (AA′BB′). Compounds **19**–**21** were prepared similarly.

p-*Nitrobenzyl* (1RS,4RS,6SR)-2-(4-*benzoyloxy*-8-*oxo*-7-*aza*-*bicyclo*[4.2.0]*oct*-2-*en*-7-*yl*)*acrylate* **19g**. From phosphorane **19f**, as a gum (73%) (Found: M^+, 448.1284), ν_{max}/cm^{-1} 1750, 1725, 1720sh, 1610, 1525 and 1350; δ_H (250 MHz) *inter alia* 5.49 (1 H, m, $W_{\frac{1}{2}}$ 11, 4-H), 6.11 (1 H, s) and 6.16 (1 H, s) (=CH_2).

p-*Nitrobenzyl* (1RS,3RS,6RS)-2-(3-*benzoyloxy*-8-*oxo*-7-*aza*-*bicyclo*[4.2.0]*oct*-4-*en*-7-*yl*)*acrylate* **20g**. From phosphorane **20f**, as prisms (ethyl acetate–hexane) (90%), m.p. 113 °C (Found: C, 64.1; H, 4.4; N, 6.25%; M^+, 448.1281), ν_{max}/cm^{-1} 1750, 1730, 1725sh, 1610, 1525 and 1350; δ_H(250 MHz) *inter alia* 5.55 (1 H, br dd, *J* 10 and 6, 3-H), and 5.98 (1 H, s) and 5.28 (1 H, s) (=CH_2).

p-*Nitrobenzyl* (1RS,5SR,6RS)-2-(5-*benzoyloxy*-8-*oxo*-7-*aza*-*bicyclo*[4.2.0]*oct*-3-*en*-7-*yl*)*acrylate* **21g**. From phosphorane **21f** as fine prisms (ethyl acetate–diethyl ether–hexane) (91%), m.p. 115–116 °C (Found: C, 64.3; H, 4.55; N, 6.2%; M^+, 448.1239), ν_{max}/cm^{-1} 1750sh, 1720, 1605, 1525 and 1350; δ_H(250 MHz) *inter alia* 5.54 (1 H, dd, *J* 6 and 2, 5-H), 6.07 (1 H, s) and 6.19 (1 H, s) (=CH_2).

Ozonolysis–Cyclisation of Phosphoranes **18f**–**21f**[8,9]

p-*Nitrobenzyl* (5RS,6RS)-6-[1-*Benzoyloxy*-2-*oxoethyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* **22**.—Phosphorane **18f** (1.20 g) was subjected to the ozonolysis–cyclisation sequence which we have previously described in detail. Rapid chromatography on silica gel (Art. 9385), eluting with ethyl acetate–hexane (4:1) gave the labile *benzoyloxy aldehyde* **22** as a gum (0.504 g, 65%) (Found: M^+, 450.1075. $C_{23}H_{18}N_2O_8$ requires *M*, 450.1063), ν_{max}/cm^{-1} 1785, 1735sh, 1725st, 1610, 1520 and 1350; δ_H(250 MHz) 2.86 (1 H, ddd, *J* 20, 10.5 and 3) and 2.97 (1 H, ddd, *J* 20, 8.5, and 3) (4-H_2), 3.99 (1 H, t, *J* 6, 6-H), 4.58 (1 H, ddd, *J* 10.5, 8.5 and 6, 5-H), 5.33 (1 H, *J* 15) and 5.47 (1 H, *J* 15) (ABq, ArCH_2), 5.58 (1 H, dd, *J* 6 and 1, 1′-H), 6.57 (1 H, t, *J* 3, 3-H), 7.4–7.7 (5 H, m, PhH_3 + PNB AA′), 8.05 (2 H, m, PhH_2), 8.24 (2 H, d, *J* 9, PNB BB′) and 9.67 (1 H, d, *J* 1, 2′-H).

p-*Nitrobenzyl* (5RS,6RS)-6-[(*E*)-1-*Benzoyloxy*-3-*methoxy*-*carbonylallyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxyl*-*ate* **23**.—Benzoyloxy aldehyde **22** (0.061 g) in ethyl acetate (2 ml) was stirred with methoxycarbonylmethylenetriphenyl-phosphorane (0.053 g) at room temperature for 1.5 h. The mixture was evaporated and the residue chromatographed on silica gel (Art. 9385), eluting with ethyl acetate–hexane (2:3). The major component, the (*E*)-*enoate* **23** crystallised from ethyl acetate–hexane as needles (0.034 g, 50%), m.p. 130 °C (Found: C, 61.8; H, 4.45; N, 5.4%; M^+, 506.1277. $C_{26}H_{22}N_2O_9$ requires C, 61.7; H, 4.4; N, 5.5%; *M*, 506.1325), ν_{max}/cm^{-1} 1785, 1725st, 1720sh, 1660, 1650, 1610, 1520 and 1345; δ_H 2.85 (2 H, dm, *J* 9, 4-H_2), 3.71 (3 H, s), 4.13 (1 H, t, *J* 6, 6-H), 4.49 (1 H, ddd, *J* 9.5, 8 and 6, 5-H), 5.26 (1 H, *J* 14) and 5.46 (1 H, *J* 14) (ABq, ArCH_2), 6.00 (1 H, t, *J ca.* 6, 1′-H), 6.12 (1 H, d, *J* 16, 3′-H), 6.46 (1 H, t, *J* 3, 3-H), 6.98 (1 H, dd, *J* 16 and 6, 2′-H), 7.2–7.6 (3 H, m, PhH_3), 7.59 (2 H, d, *J* 9, PNB AA′), 7.99 (2 H, m, PhH_2) and 8.22 (2 H, dd, *J* 9, PNB BB′). Earlier fractions contained the *Z*-isomer as a less pure gum (0.11 g); ν_{max}/cm^{-1} (*inter alia*) 1785 and 1725; δ_H (*inter alia*) 5.98 (1 H, d, *J* 11, 3′-H).

p-*Nitrobenzyl* (4RS,5SR,6SR)-4-*Benzoyloxy*-7-*oxo*-6-(2-*oxo*-*ethyl*)-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* **25**.—Phosphorane **21f** (0.42 g) was subjected to ozonolysis–cyclisation as for isomer **18f**. Work-up with triphenylphosphine (0.168 g) and recovery in ethyl acetate was followed by evaporation and rapid chromatography of the residue on silica gel (Art. 9385). Elution with ethyl acetate–hexane (3:4) gave *aldehyde* **25** as a gum (0.080 g, 29%) (Found: M^+, 450.1068. $C_{23}H_{18}N_2O_8$ requires *M*, 450.1063); ν_{max}/cm^{-1} 2725, 1790, 1735sh, 1730, 1610, 1525 and 1350; δ_H(250 MHz) 2.98 (1 H, dd, *J* 19 and 7) and 3.23 (1 H, dd, *J* 19 and 9.5) (8-H_2), 4.22 (1 H, dt, *J* 9.5 and 7, 6-H), 4.63 (1 H, dd, *J* 7.5 and 7, 5-H), 5.35 (1 H, *J* 14) and 5.49 (1 H, *J* 14) (ABq, ArCH_2), 6.24 (1 H, dd, *J* 7.5 and 2.5, 4-H), 6.62 (1 H, d, *J* 2.5, 3-H), 7.49 (2 H, m, PhH_2), 7.64 (3 H, m, PhH + PNB AA′), 7.95 (2 H, m, PhH_2), 8.26 (2 H, d, *J* 9, PNB BB′) and 9.50 (1 H, s, 9-H).

p-*Nitrobenzyl* (4RS,5SR,6SR)-4-*Benzoyloxy*-6-[(*E*)-3-*meth*-*oxycarbonylallyl*]-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carb*-*oxylate* **26**.—Reaction of aldehyde **25** (0.020 g) in ethyl acetate (2 ml) with methoxycarbonylmethylenetriphenylphosphorane (0.014 g) for 2 h gave, after chromatography (*cf.* **25**) the *enoate* **26** as a gum (0.017 g, 76%). Alternatively, phosphorane **21f** (0.250 g) was ozonolysed and cyclised (*vide supra*). The solution of crude aldehyde **25** was then treated with the stabilised phosphorane (0.133 g, 1.1 mol equiv.). Chromatography afforded *enoate* **26** (0.116 g, 63%) (Found: M^+, 506.1285. $C_{26}H_{22}N_2O_9$ requires *M*, 506.1325), λ_{max}(EtOH) 270 and 233 nm; ν_{max}/cm^{-1} 1790, 1725st, 1660, 1605, 1525 and 1360; δ_H(250 MHz) 2.76 (2 H, 7 lines, *J* 8, 6.5 and 8-H_2), 3.68 (3 H, s), 3.91 (1 H, q, *J ca.* 7, 6-H), 4.53 (1 H, dd, *J* 8 and 7, 5-H), 5.34 (1 H, *J* 13) and 5.48 (1 H, *J* 13) (ABq, ArCH_2), 5.72 (1 H, dt, *J* 16 and 1.5, 10-H), 6.29 (1 H, dd, *J* 8 and 3, 4-H), 6.63 (1 H, d, *J* 3, 3-H), 6.79 (1 H, dt, *J* 16 and 6.5, 9-H), 7.46 (2 H, m, PhH_2), 7.64 (3 H, m, PhH + PNB AA′), 7.95 (2 H, br d, *J ca.* 8, PhH_2) and 8.25 (2 H, d, *J* 9, PNB BB′); decoupling experiments confirmed $^3J_{3,4}$ 3 and $^3J_{4,5}$ 8).

Phosphoranes **19f** and **20f** gave no bicyclic β-lactam products on subjection to ozonolysis–cyclisation.

Reactions of Aldehyde **25**

p-*Nitrobenzyl* (2RS,3SR,4SR,5SR,6SR)-4-*Benzoyloxy*-3-*ethylthio*-7-*oxo*-6-(2-*oxoethyl*)-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate* **31**.—Aldehyde **25** (0.040 g) in DMF (1 ml) was stirred with ethanethiol (0.006 g) in the presence of potassium carbonate (0.001 g) for 5 min.[21] The mixture was diluted with ethyl acetate (10 ml), washed well with brine (×3), dried and evaporated. The residue was chromatographed on silica gel, eluting with ethyl acetate–hexane (1:1) to give the *adduct* **31**, a single isomer, as a gum (0.030 g, 66%) (Found: M^+, 512.1235. $C_{25}H_{24}N_2O_8S$ requires *M*, 512.1253), ν_{max}/cm^{-1} 2730, 1770, 1725, 1610, 1520 and 1350; δ_H(250 MHz) 1.31 (3 H, t, *J* 6.5, CH_3CH_2), 2.72 (2 H, q, *J* 6.5, CH_2CH_2), 3.01 (1 H, d, *J* 8, 8-H_2),

3.86 (1 H, dd, *J* 7 and 2, 3-H), 4.08 (1 H, dt, *J* 8 and 6, 6-H), 4.64 (1 H, dd, *J* 6 and 3, 5-H), 4.82 (1 H, d, *J* 7, 2-H), 5.29 (2 H, s, $ArCH_2$), 4.59 (1 H, br dd, *J* 3 and 2, 4-H), 7.43–7.68 (5 H, m, PhH_3 + PNB AA′), 7.92 (2 H, m, PhH_2), 8.23 (2 H, d, *J* 9, PNB BB′) and 9.61 (1 H, s, 9-H); decoupling experiments confirmed $^3J_{3,4}$ 2 and $^3J_{4,5}$ 3.

p-*Nitrobenzyl* (2RS,3SR,4SR,5SR,6SR)-4-*Benzoyloxy*-3-*ethylthio*-6-*methyl*-7-*oxo*-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate* **32**.—Aldehyde (0.045 g) was heated in methylene dichloride (5 ml) with tris(triphenylphosphine)rhodium(I) chloride (0.081 g) in an argon atmosphere at reflux for 16 h.[22] The mixture was cooled and evaporated, and the residue, in toluene, was chromatographed on silica gel (Art. 7729). Elution with ethyl acetate–hexane (1:4) gave the 6β-*methyl derivative* **32** as an oil (0.035 g, 82%) (Found: M^+, 484.1271. $C_{24}H_{24}N_2O_7S$ requires *M*, 484.1304), ν_{max}/cm^{-1} 1770, 1750sh, 1720, 1605, 1520 and 1350; δ_H(250 MHz) 1.28 (3 H, d, *J* 8, 8-H_3), 1.30 (3 H, t, *J* 7, CH_3CH_2), 2.71 (2 H, q, *J* 7, CH_3CH_2), 3.76 (1 H, dq, *J* 7 8 and 6, 6-H), 3.82 (1 H, dd, *J* 7 and 3, 3-H), 4.43 (1 H, dd, *J* 6 and 4, 5-H), 4.84 (1 H, d, *J* 7, 2-H), 5.30 (2 H, s, $ArCH_2$), 5.67 (1 H, dd, *J* 4 and 3, 4-H), 7.4–7.65 (5 H, m, PhH_3 + PNB AA′), 7.98 (2 H, br d, *J ca.* 8, PhH_2) and 8.24 (2 H, d, *J* 9, PNB BB′); decoupling experiments confirmed that $^3J_{3,4}$ 3 and $^3J_{4,5}$ 4.

p-*Nitrobenzyl* (4RS,5RS,6RS)-4-*Benzoyloxy*-3-*chloro*-3-*ethylsulphinyl*-6-*methyl*-7-*oxo*-1-*azabicyclo*[3.2.0]*heptane*-2-*carboxylate* **33**.—6-Methyl compound **32** (0.035 g) in methylene dichloride (3 ml) containing pyridine (0.020 g, 3 mol equiv.) and water (*ca.* 0.0015 g, 1 mol equiv.) was stirred with iodobenzene dichloride (0.045 g, 2 mol equiv.) at 0 °C for 30 min.[21] Evaporation gave a residue which was chromatographed rapidly on silica gel (Art. 9385). Elution with ethyl acetate–hexane (1:1) provided the α-chloro sulphoxide **33** as a gum (0.025 g, 65%), ν_{max}/cm^{-1} 1780, 1750sh, 1730, 1605, 1525 and 1345; δ_H(250 MHz) 1.38 (3 H, d, *J* 7, 8-H_3), 1.41 (3 H, t, *J* 7, CH_3CH_2), 3.07 (1 H, m) and 3.30 (1 H, m) (CH_3CH_2), 3.87 (1 H, dq, *J* 7 and 6, 6-H), 4.63 (1 H, dd, *J ca.* 8 and 6, 5-H), 5.12 (1 H, s, 2-H), 5.30 (2 H, s, $ArCH_2$), 6.28 (1 H, d, *J* 8, 4-H), 7.50 (2 H, m, PhH_2), 7.63 (3 H, m, PhH + PNB AA′), 8.05 (2 H, m, PhH_2) and 8.27 (2 H, PNB BB′); *m*/*z* 527 and 534 (wk) (M^+).

p-*Nitrobenzyl* (4RS,5RS,6RS)-4-*Benzoyloxy*-3-*ethylsulphinyl*-6-*methyl*-7-*oxo*-1-*azabicyclo*[3.2.0]*hept*-2-*ene*-2-*carboxylate* **34**.—α-Chloro sulphoxide **33** in ethyl acetate (3 ml) was stirred with DBU (0.007 g, 1 mol equiv.) in an argon atmosphere for 2 h. The solution was diluted with ethyl acetate, washed with brine (× 3), dried and evaporated.[21] The resulting crude Δ²-ethylsulphinyl compound **34** was obtained as a gum (0.020 g, 85%), λ_{max}(EtOH) 270 nm; ν_{max}/cm^{-1} 1795, 1720st, 1640, 1605, 1520 and 1345.

Attempted Ethylsulphinyl Displacement of **34**.—Δ²-Sulphoxide **34** in dry DMF (8 ml) containing sodium pyrimidine-2-thiolate (0.004 g) was stirred at −35 °C for 1.5 h.[23] The solution was diluted with ethyl acetate and washed well with water and brine. TLC analysis (ethyl acetate–hexane 3:1) showed only one mobile compound **34**. The IR spectrum of an aliquot showed that the latter was present only in low quantity, and that much decomposition had occurred.

DBU Stability of Esters **15** *and* **26**.—An aliquot of each ester (0.005 g) in ethyl acetate (5 ml) was stirred at room temperature in the presence of DBU (*ca.* 0.001 g) for 3 h. The solution was washed with brine, and the ester recovered by evaporation of the dried organic phase. Both remained unchanged (TLC, NMR).

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