

Studies related to Penicillins. Part 26.¹ Conversion of Potassium Benzylpenicillinate into 1-Substituted Derivatives of 3-Phenylacetamidoazetidine-2,4-dione²

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A new method for the synthesis of azetidine-2,4-diones, involving a Norrish Type II photoreaction of 4-pyruvoylazetidin-2-ones, has been devised. The process features in two strategies in which potassium benzylpenicillinate (**17a**) is converted into 1-substituted 3-phenylacetamidoazetidine-2,4-diones.

In one strategy, (1*R*,5*S*)-3-benzyl-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-7-ones substituted at position 6 by methyl, *p*-nitrobenzyl, and methoxymethyl esters of a 1-carboxy-2-methylprop-1-enyl moiety [*i.e.* compounds (**14a–c**)] were treated with pyruvic acid. A displacement reaction ensued in which the acid cleaved the C-5–O-4 bond of the substrate with an inversion of configuration to give the corresponding 1-substituted (3*R*,4*R*)-3-phenylacetamido-4-pyruvoyloxyazetidin-2-ones (**10a–c**). Under photolytic conditions, compounds (**10a–c**) were converted into the 1-substituted 3-phenylacetamidoazetidine-2,4-diones (**15a,b,e**). The oxadiazabicycloheptenones (**14a–c**) were derived from the corresponding 1-substituted (2*R*,3*S*)-4-oxo-3-phenylacetamidoazetidine-2-sulphinic acids (**19a–c**) by a novel oxidative desulphinylation induced by lead(IV) acetate.

In the second strategy, (1*S*,5*R*)-3-benzyl-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-7-ones substituted at position 6 by 1-methoxycarbonyl-2-methylprop-1-enyl, (1*S*)-1-methoxycarbonyl-2-methyl-2-methylthiopropyl, and (3*R*)-4,4-dimethyl-2-oxothietan-3-yl entities [*i.e.* compounds (**13a**), (**18a**), and (**25**)] were treated with pyruvic acid to give the corresponding (3*S*,4*S*)-3-phenylacetamido-4-pyruvoyloxyazetidin-2-ones (**9a**), (**22**), and (**24**). Whereas the photolyses of compounds (**9a**) and (**24**) proceeded in the expected manner to give the azetidinediones (**15a**) and (**23**), loss of methanethiol accompanied the Norrish Type II reaction of the pyruvate (**22**) to give the azetidinedione (**15a**).

The methoxymethyl ester (**15e**) was transformed into the carboxylic acid (**15c**) by the action of trifluoroacetic acid. Compound (**15c**) lacked antibacterial activity and β -lactamase inhibitory properties.

The notion that appropriate monocyclic β -lactams may be endowed with substantial antibacterial activity was boosted in 1976 with the discovery of the nocardins.³ In particular, nocardicin A (**1**) was found to inhibit the growth of several Gram-negative bacteria. The monobactams—reported in 1981 by workers at Takeda⁴ and Squibb⁵—are currently the most important group of monocyclic β -lactam derivatives. Natural representatives are unsubstituted at position 4, incorporate an acylamino group at position 3, and a sulphy moiety at position 1; additionally, a methoxy function may be present at position 3. Whereas no nocardicin representative is of clinical value, monobactam derivatives, *e.g.* aztreonam (**2**),⁶ are used to treat infections caused by Gram-negative bacteria. Around 1975, we initiated some work aimed at the preparation of novel monocyclic β -lactams which, we hoped, would possess antibacterial activity. At that time, it was known that compounds (**3**)⁷ and (**4**)⁸ were bioinactive. To be effective, monocyclic azetidinediones of type (**5**) should be able to permeate through the bacterial cell walls and bind with the carboxypeptidases/transpeptidases (EnzXH), enzymes which are located in the cell membrane and involved in cell wall biosynthesis; the enzyme–substrate complexes should then react to give species of type (**6**).⁹ The acylating power of a β -lactam derivative is one factor which may influence bioactivity and, accordingly, we decided to prepare compounds which would be more reactive than the azetidinediones (**3**) and (**4**). One series of substances, which was expected to meet this requirement, was azetidinediones of type (**7**). In this paper, we describe our efforts to prepare such compounds.

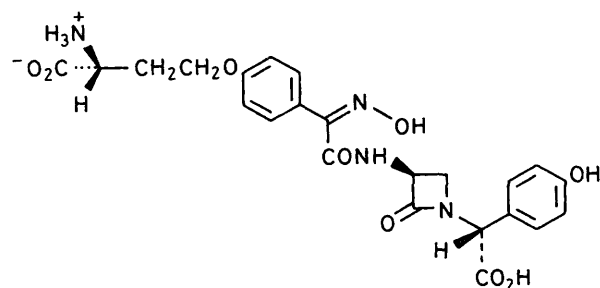
Results and Discussion

At the outset of our studies, four methods had been developed for the synthesis of azetidine-2,4-diones: the cycloaddition of ketenes with isocyanates,^{10,11} the condensation of malonyl chlorides with amino compounds,^{11–13} the cyclodehydration of malonamic acids,¹⁴ and the reaction of phosphacumulene ylides with carbon dioxide.¹⁵ However, none of these procedures appeared to be suitable for the derivation of compounds of type (**7**) and, indeed, no example of an azetidine-2,4-dione incorporating an acylamino group at position 3 had been reported. The nearest relative to such a compound was the spiro derivative (**8**);¹³ not surprisingly, it was devoid of microbial activity.

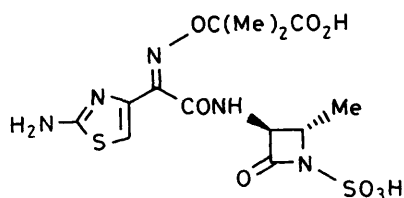
The report by Brandt *et al.*,¹⁶—that 4-thioxoazetidin-2-ones could be prepared from 4-acylmethylthioazetidin-2-ones by a Norrish Type II photoelimination—suggested that azetidine-2,4-diones might be accessible by photolysis of 4-acylmethoxyazetidin-2-ones. However, the finding by Binkley¹⁷—that pyruvoyl esters of secondary alcohols were converted into ketones, acetaldehyde, and carbon monoxide when irradiated in benzene—suggested that azetidinediones of types (**9**) and (**10**) might serve as precursors of the target systems. Based upon earlier experience, in which it was established that the oxadiazabicycloheptenone (**11**) reacted with acetic acid to give the *trans*-acetoxiazetidinone (**12**),¹⁸ we anticipated that pyruvates of types (**9**) and (**10**) would be accessible from the reaction of oxadiazabicycloheptenones of types (**13**) and (**14**) with pyruvic acid. With a view to preparing the azetidinedione (**15a**), compounds (**13a**)^{19,20} and (**14a**) were selected for an initial study.

The oxadiazabicycloheptenone (**13a**) was prepared from the mercury(II) derivative (**16**)¹⁸ [available from the reaction of

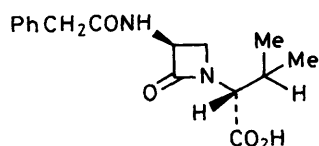
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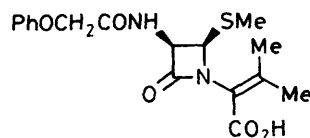
(1)



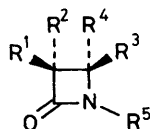
(2)



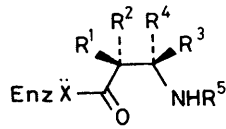
(3)



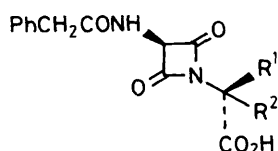
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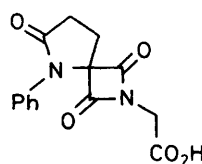
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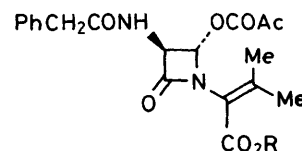
(6)



(7)

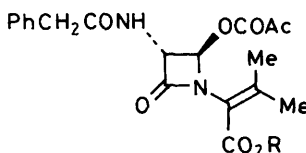


(8)



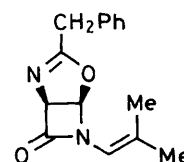
(9)

a; R = Me

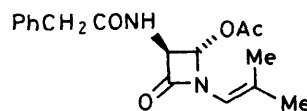


(10)

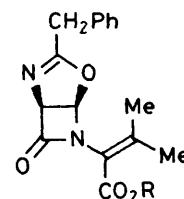
R
a; Me
b; CH₂C₆H₄NO₂-p
c; CH₂OMe



(11)

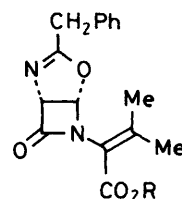


(12)



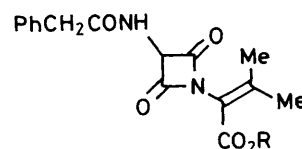
(13)

a; R = Me



(14)

R
a; Me
b; CH₂C₆H₄NO₂-p
c; CH₂OMe



(15)

R
a; Me
b; CH₂C₆H₄NO₂-p
c; H
d; Na
e; CH₂OMe

potassium benzylpenicillinate (17a) with Hg(OAc)₂ in HOAc and treatment of the product with pyridine] by slight modifications of the published procedure.²⁰ Thus the mercury(II) derivative (16) was converted into the methylthiobutanoate (18a) [26% yield after SiO₂ chromatography based on (17a)] by the action of sodium sulphide and iodomethane in *N,N*-dimethylformamide (DMF). Compound (18a) was oxidised, as described earlier,²⁰ to the sulfoxide (18b) which underwent thermolysis in boiling ethyl acetate to give the butenoate (13a) [80% yield after SiO₂ chromatography based on (18a)].

It was envisaged that the oxadiazabicycloheptenone (14a) would be accessible from the *trans*-azetidinesulphinic acid (19a)²¹ [itself prepared from (17b) by the action of 1,5-diazabicyclo[4.3.0]non-5-ene (DBN)]. A brief study of oxidants revealed that lead(IV) acetate was effective in bringing about the (19a)→(14a) transformation. Thus when treated in dichloromethane with the reagent and sodium hydrogen carbonate, the sulphinic acid (19a) was transformed into the crystalline

oxadiazabicycloheptenone (14a), isolated in 60% yield after silica gel fractionation. The properties of compound (14a) matched those of its enantiomer (13a) and its optical rotation {[α]_D -53° (CHCl₃)} was of opposite sign but similar magnitude to that of the enantiomer (13a).

Compounds (13a) and (14a) reacted with pyruvic acid in the prescribed manner to give the *trans*-pyruvoyloxazetidinones (9a) and (10a), respectively. The former product, isolated as a crystalline solid in 72% yield, showed [α]_D -35° (CH₂Cl₂); the latter product, obtained as a crystalline material in 76% yield, showed [α]_D +36° (CH₂Cl₂). Spectroscopically, the two materials were indistinguishable.

Irradiation of 1% solutions of the pyruvates (9a) and (10a) in benzene, followed by silica gel purification, gave the crystalline

azetidinone (15a) in *ca.* 78% yield. The structure of compound (15a) followed from its analytical and spectral properties. In common with other azetidinones,¹¹ the material showed a weak i.r. absorption at 1885 cm⁻¹ and a strong one at 1745 cm⁻¹ for the asymmetric and symmetric carbonyl stretches, respectively. The intensities of these signals were reversed in the Raman spectrum. The ¹H n.m.r. spectrum (CDCl₃) showed all the expected signals and, in particular, the 3-hydrogen atom of the four-membered ring appeared as a doublet at δ 4.75 which was coupled (*J* 7 Hz) to the adjacent amido proton at δ 7.11. Three carbonyl resonances were apparent in the ¹³C n.m.r. spectrum (CDCl₃): one at δ 158.3 attributed to the side-chain amide, one at δ 168.3 ascribed to the ring carbonyl groups,¹⁵ and one at δ 172.8 for the ester carbonyl moiety. As well as featuring weak peaks at *m/z* 330 and 298, attributed to the molecular ion and to the molecular ion minus methanol, the mass spectrum showed strong peaks at *m/z* 175 and 91, ascribed to the species (20) and C₇H₇⁺, respectively.

The azetidinone (15a) failed to inhibit the growth of a range of Gram-positive and -negative bacteria. It also displayed no activity against several β-lactamases. In the hope that it would fare better, the acid (15c) was sought. Since attempts to prepare compound (15c) from the methyl ester (15a) were unsuccessful, the synthesis of compound (15b) was next considered. The *p*-nitrobenzyl ester moiety is known to be an effective precursor of the carboxylic acid group in sensitive β-lactam substrates; moreover, its hydrogenolysis in the presence of sodium hydrogen carbonate can lead directly to the sodium salt.²²

The oxadiazabicycloheptenone (14b) was prepared as a crystalline solid in 65% yield by oxidation of the sulphonic acid (19b)²¹ with lead(IV) acetate in dichloromethane in the presence of sodium hydrogen carbonate. Treatment of compound (14b) with pyruvic acid provided the *trans*-pyruvoyloxyazetidinone (10b) as an almost pure syrup in *ca.* 75% yield. When irradiated in benzene, the pyruvate (10b) was converted into the azetidinone (15b) which, after silica gel purification, was isolated as a syrup in 46% yield.

Disappointingly, when hydrogenolysed over 10% palladium-charcoal [in THF, and in EtOH-H₂O (4:1) containing NaHCO₃ (1 mol equiv.)], the *p*-nitrobenzyl ester (15b) was converted into mixtures of products which showed no evidence for the presence of the hoped for materials (15c,d).

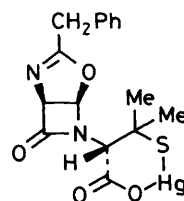
The finding that the azetidinone (15a) was unaffected by neat trifluoroacetic acid over a three-day period suggested that compound (15c) might be accessible from a precursor bearing an acid-labile ester function. Accordingly, the synthesis of the methoxymethyl ester (15e) was undertaken.

When treated in dichloromethane with triethylamine and chloromethyl ether, the acid (17c)²³ was transformed into the crystalline methoxymethyl ester (17d) in 91% yield. Compound (17d) reacted with DBN in dichloromethane to give, after an acidic work-up, the *trans*-azetidinesulphonic acid (19c) as a syrup in 47% yield. Not surprisingly, compound (19c)—incorporating a strong acid moiety and an acid-sensitive ester function—was unstable and had to be processed rapidly. However, when subjected to the action of lead(IV) acetate, it was converted into the required oxadiazabicycloheptenone (14c), albeit in only poor yield (24% after SiO₂ purification). Compound (14c), which was a syrup, reacted with pyruvic acid to give mainly the *trans*-pyruvoyloxyazetidinone (10c) which, without purification, was irradiated in benzene. Following silica gel fractionation of the crude product, the azetidinone (15e) was obtained as a syrup in 26% yield [based upon (14c)].

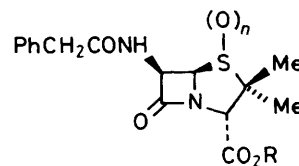
In the presence of trifluoroacetic acid, the methoxymethyl ester (15e) was transformed in 30% yield into the required acid (15c). As well as being analytically and spectroscopically characterised, compound (15c) was treated with diazomethane to give a crystalline product which was identical with the methyl

ester (15a). Disappointingly, the acid (15c) lacked antibacterial activity and β-lactamase-inhibitory properties.

With a view to reducing the electron-withdrawing influence of the ring nitrogen substituent, attention was turned to the synthesis of azetidinones of type (21). The initial target was the butanoate (21a) which, it was envisaged, would be accessible from compound (18a).²⁰

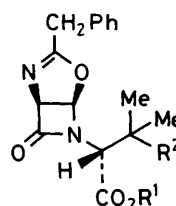


(16)



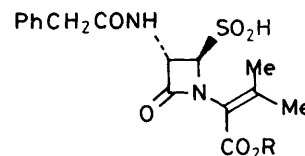
(17)

R	n
a; K	0
b; Me	2
c; H	2
d; CH ₂ OMe	2



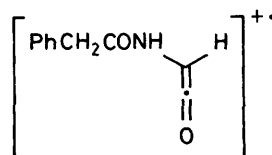
(18)

R ¹	R ²
a; Me	SMe
b; Me	S(-O)Me

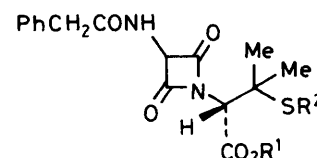


(19)

R
a; Me
b; CH ₂ C ₆ H ₄ NO ₂ - <i>p</i>
c; CH ₂ OMe



(20)



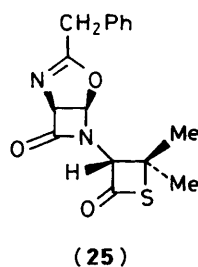
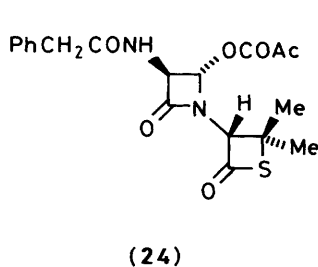
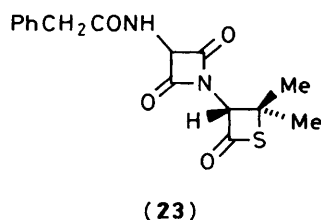
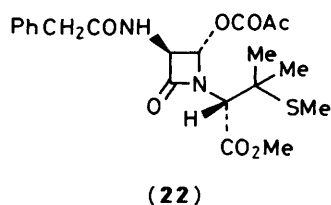
(21)

a; R¹ = R² = Me

Pyruvic acid reacted with the oxadiazabicycloheptene (18a) in the prescribed manner to give the *trans*-pyruvoyloxyazetidinone (22) in 56% yield. However, under photolytic conditions, compound (22) was transformed in 43% yield into the butanoate (15a). Clearly, a β-elimination of methanethiol had accompanied the Norrish Type II process.

The synthesis of the thietanone (23) was next investigated. In this compound and its projected precursor (24), a β-elimination of the aforementioned type is unlikely. Moreover, there is the possibility of transforming the product (23) into a target of type (21).

In the presence of pyruvic acid, the oxadiazabicycloheptenone (25)²⁴ was transformed into the *trans*-pyruvoyloxyazetidinone (24), isolated as an almost pure syrup in *ca.* 88% yield. Under the usual photolytic conditions, compound (24) gave rise to the



required azetidinedione (23) (43% yield after SiO₂ chromatography). Attempts to open the thietanone ring of compound (25) without disrupting the azetidinedione function were unsuccessful.

The present results are of interest in three respects. First, they provide the technology for converting penicillins into 3-acylaminoazetidine-2,4-diones. Secondly, they reveal that the Binkley photoreaction can be employed to generate an oxo moiety adjacent to a β -lactam nitrogen atom. Thirdly, they exemplify a new means of preparing oxadiazabicycloheptenones of type (14). Such compounds have been shown to be valuable intermediates in the synthesis of antibacterially active 1-oxaceph-2-ems.²⁵

During the course of and subsequent to this work, other routes to azetidine-2,4-diones have been published. One procedure, reported by Bachi and his co-workers, involves the oxidation of 4-thioxoazetidin-2-ones with ozone or *m*-chloroperoxybenzoic acid.²⁶ Another process, developed by the groups of Maruyama and Kanoaka, entails the irradiation of succinimides and *N*-formyl α,β -unsaturated carboxamides.²⁷ A third method, described by Aoyama and his co-workers, involves the photolysis of *N*-acyl α -oxoamides.²⁸ Finally, Cainelli *et al.*, have recently shown that the cyclocondensation of malonamic esters can be effected by triethylaluminium.²⁹

Experimental

Dry dichloromethane was prepared by distilling it from calcium chloride flakes. Dry benzene was obtained by leaving the solvent over sodium wire and distilling it prior to use. Ethereal diazomethane was generated by adding a solution of Diazald in diethyl ether to potassium hydroxide in aqueous ethanol.³⁰ Photolyses were conducted at 15 °C in a pyrex vessel using a Hanovia medium-pressure u.v. lamp. The Raman spectrum was measured with a modified Cary Model 81 instrument. A Bruker HX90E spectrometer was used to record the ¹³C n.m.r.

spectrum. For other instrumental details and for chromatographic techniques, see Part 20.³¹

Methyl (2S)-2-[(1S,5R)-3-Benzyl-7-oxo-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-6-yl]-3-methyl-3-methylthiobutanoate (18a).—Potassium benzylpenicillinate (17a) (3.73 g, 10 mmol) was converted into compound (16) (2.56 g, 48%) by the literature procedure.¹⁸ Sodium sulphide nonahydrate (2.30 g, 9.6 mmol) was added to a stirred suspension of compound (16) (2.56 g, 4.8 mmol) in DMF (50 cm³) followed, after 5 min, by iodomethane (2.91 g, 20 mmol). After 15 h, the solvent was evaporated off and ethyl acetate was added. Insoluble material was filtered off and the filtrate was washed ($\times 4$) with brine. Evaporation of the dried organic layer and purification of the resultant syrup by silica gel chromatography (Et₂O as eluant) gave the title compound (18a) [0.88 g, 26% based upon (17a)] as a white solid. After recrystallisation from chloroform–light petroleum, the sample possessed m.p. 97–98 °C (lit.,²⁰ 97–99 °C); [α]_D +14° (CHCl₃) [lit.,²⁰ +8° (CHCl₃)]; δ (60 MHz; CDCl₃) 1.00 and 1.10 (each 3 H, s, together CMe₂), 1.94 (3 H, s, SMe), 3.65 (5 H, s, CO₂Me and PhCH₂), 4.30 (1 H, s, 2-H), 5.05 and 6.03 (each 1 H, d, *J* 3.5 Hz, together 2 \times β -lactam-H), and 7.20 (5 H, s, Ph).

Methyl 2-[(1S,5R)-3-Benzyl-7-oxo-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-6-yl]-3-methylbut-2-enoate (13a).—Using the literature procedure,²⁰ the methylthiobutanoate (18a) (0.362 g, 1.0 mmol) was converted into the sulphoxide (18b), isolated as a ca. 1:1 mixture of diastereoisomers δ (60 MHz; CDCl₃) 0.92, 1.00, and 1.04 (1.5, 3, and 1.5 H, each s, together CMe₂), 2.10 (3 H, s, SMe), 3.43 and 3.53 (3.5 and 1.5 H, each s, together CO₂Me and PhCH₂), 4.18 and 4.27 (each 0.5 H, s, together, 2-H), 4.93, 5.93, and 6.05 (1, 0.5, and 0.5 H, each d, *J* 3.5 Hz, together 2 \times β -lactam-H), and 7.05 (5 H, s, Ph).

A solution of product (18b) in ethyl acetate (50 cm³) was heated under reflux for 0.5 h. Evaporation of the solvent and purification of the product by silica gel chromatography (Et₂O as eluant) gave the title compound (13a) (0.251 g, 80%) as a white solid. After recrystallisation from chloroform–diethyl ether, the sample displayed m.p. 121–122 °C (lit.,¹⁹ 123 °C); [α]_D +56° (1% in CHCl₃) [lit.,¹⁹ +65° (CHCl₃)]; δ (60 MHz; CDCl₃) 1.50 and 2.16 (each 3 H, s, together CMe₂), 3.70 (2 H, s, PhCH₂), 3.73 (3 H, s, CO₂Me), 5.23 and 5.98 (each 3 H, d, *J* 3.5 Hz, together 2 \times β -lactam-H), and 7.34 (5 H, s, Ph).

Methyl 2-[(1R,5S)-3-Benzyl-7-oxo-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-6-yl]-3-methylbut-2-enoate (14a) (With C.M. Pant).—Lead(IV) acetate (0.443 g, 1 mmol) was added to a stirred solution of the sulphonic acid (19a) (0.380 g, 1 mmol) in dry dichloromethane (10 cm³) followed by sodium hydrogen carbonate (0.084 g, 1 mmol). After 4 h, the mixture was filtered and the filtrate diluted with dichloromethane and washed with aqueous sodium hydrogen carbonate. Evaporation of the dried (MgSO₄) organic layer gave a syrup which was fractionated by silica gel chromatography [PhH–Et₂O (9:1) as eluant] to afford the title compound (14a) (0.188 g, 60%). After recrystallisation from chloroform–diethyl ether, the sample possessed m.p. 120–121 °C; [α]_D –53° (1.2% in CHCl₃); ν_{\max} (KBr) *inter alia* 1765 (β -lactam C=O), 1715 (ester C=O), and 1655 cm^{–1} (C=N); λ_{\max} (EtOH) 214 nm (ϵ 10 700); *m/z* (e.i.) *inter alia* 314 (*M*⁺), 160, and 91 (C₇H₇⁺, base peak) (Found: C, 64.9; H, 5.8; N, 8.8. C₁₇H₁₈N₂O₄ requires C, 64.95; H, 5.75; N, 8.90%). The ¹H n.m.r. spectrum of the sample matched that of its enantiomer (13a).

Methyl 3-Methyl-2-[(3S,4S)-2-oxo-3-phenylacetamido-4-pyrrovoxyazetidin-1-yl]but-2-enoate (9a).—The oxadiazabicycloheptenone (13a) (0.235 g, 0.75 mmol) was dissolved in

the minimum volume or redistilled pyruvic acid and the solution left for 16 h. Dichloromethane was then added and the solution washed well with aqueous sodium hydrogen carbonate followed by water. Evaporation of the dried (MgSO_4) organic layer gave the *title compound* (**9a**) (0.217 g, 72%) in an almost pure state. After recrystallisation from chloroform–diethyl ether, the sample (0.142 g, 47%) possessed m.p. 136–137 °C; $[\alpha]_D - 35^\circ$ (CH_2Cl_2); $\nu_{\text{max.}}$ (KBr) *inter alia* 3 300 (NH), 1 785 (β -lactam C=O), 1 740 (ester C=O), 1 725 (unsat. ester C=O), and 1 665 cm^{-1} (amide C=O); $\lambda_{\text{max.}}$ (EtOH) 225sh nm (ϵ 10 000); δ (60 MHz; CDCl_3) 2.02 and 2.23 (each 3 H, s, together CMe_2), 2.46 (3 H, s, COMe), 3.63 (2 H, s, PhCH_2), 3.75 (3 H, s, CO_2Me), 4.90 (1 H, dd, J 7 and 1 Hz, NHCHCH), 6.28 (1 H, d, J 1 Hz, CHCHOCO), 6.68br (1 H, d, J 7 Hz, CONHCH), and 7.30 (5 H, s, Ph) [addition of D_2O caused the signal at δ 6.68 to disappear and that at δ 4.90 to collapse to a d (J 1 Hz)]; m/z *inter alia* 314 ($M^+ - \text{C}_3\text{H}_4\text{O}_3$), 160, and 91 (C_7H_7^+ , base peak) (Found: C, 59.5; H, 5.2; N, 6.9. $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_7$ requires C, 59.70; H, 5.50; N, 6.95%).

Methyl 3-Methyl-2-[(3R,4R)-2-oxo-3-phenylacetamido-4-pyrroloxyazetidin-1-yl]but-2-enoate (10a).—The oxadiazabicycloheptenone (**14a**) (0.314 g, 1.0 mmol) was treated with redistilled pyruvic acid as described for compound (**13a**). Work-up as before gave the *title compound* (**10a**) (0.305 g, 76%) in an almost pure state. After crystallisation from chloroform–light petroleum, the sample (0.210 g, 52%) displayed m.p. 136–138 °C; $[\alpha]_D + 36^\circ$ (0.5% in CH_2Cl_2); $\lambda_{\text{max.}}$ (EtOH) 225sh nm (ϵ 10 500) (Found: C, 59.6; H, 5.2; N, 6.8. $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_7$ requires C, 59.70; H, 5.50; N, 6.95%). The i.r., ^1H n.m.r., and mass spectra of the sample were identical with those of its enantiomer (**9a**).

Photolysis of the Pyruvate (10a).—A solution of the pyruvate (**10a**) (0.286 g, 0.711 mmol) in dry benzene (250 cm^3) was irradiated with u.v. light. The reaction was monitored by ^1H n.m.r. spectroscopy and, after 40 h, when all the reactant had disappeared, the solvent was evaporated off and the residue purified by silica gel chromatography (PhH– Et_2O , gradient elution) to yield *methyl 2-(2,4-dioxo-3-phenylacetamidoazetidin-1-yl)-3-methylbut-2-enoate* (**15a**) (0.193 g, 82%). The sample, after recrystallisation from chloroform–diethyl ether, was obtained as needles, m.p. 130–131 °C; $\nu_{\text{max.}}$ (KBr) *inter alia* 3 300 (NH), 1 885w and 1 745s (azetidinedione C=O), 1 730 (ester C=O), and 1 655 cm^{-1} (amide C=O); $\nu_{\text{max.}}$ (Raman) *inter alia* 1 883s and 1 750w (azetidinedione C=O), 1 730 (ester C=O), and 1 638 cm^{-1} (amide C=O); $\lambda_{\text{max.}}$ (EtOH) 221 (ϵ 8 900) and 288 nm (1 800); δ (60 MHz; CDCl_3) 2.08 and 2.28 (each 3 H, s, together CMe_2), 3.51 (2 H, s, PhCH_2), 3.67 (3 H, s, CO_2Me), 4.75 (1 H, d, J 7 Hz, NHCH), 7.11 (1 H, d, J 7 Hz, CONHCH), and 7.21 (5 H, s, Ph) (addition of D_2O caused the signal at δ 7.11 to disappear and that at δ 4.75 to collapse to a s); δ (22 MHz; CDCl_3 ; ^1H -decoupled spectrum) 22.0 (CMe), 23.4 (CMe), 42.4 (OMe), 52.2 (CH_2Ph), 64.4 (NHCH), 115.9, 127.6, 129.1, 129.4, and 133.8 (ArC and olefinic C), 158.3 (CONH), 168.3 (azetidinedione CO), and 172.8 p.p.m. (CO_2Me); m/z (e.i.) *inter alia* 330 (M^+), 298 ($M^+ - \text{CH}_4\text{O}$), 175 ($\text{C}_{10}\text{H}_9\text{NO}_2^+$), and 91 (C_7H_7^+ , base peak) (Found: C, 61.9; H, 5.5; N, 8.3%. M^+ 330.1249. $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_5$ requires C, 61.80; H, 5.50; N, 8.45%; M , 330.1216).

Photolysis of the Pyruvate (9a).—The pyruvate (**9a**) (0.201 g, 0.5 mmol) was photolysed as described for its enantiomer (**10a**). Work-up and purification of the product as before gave a material (0.124 g, 75%) that was identical with the azetidinedione (**15a**) by ^1H n.m.r. spectroscopy.

p-Nitrobenzyl 2-{(1R,5S)-3-Benzyl-7-oxo-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-6-yl}-3-methylbut-2-enoate (14b) (With C.M. Pant).—Lead(IV) acetate (0.353 g, 0.796 mmol) was added

to a stirred solution of the sulphinic acid (**19b**)²¹ (0.400 g, 0.798 mmol) in dichloromethane (10 cm^3) followed by sodium hydrogen carbonate (0.067 g, 0.798 mmol). After 4 h, the mixture was filtered and the filtrate diluted with dichloromethane and washed with aqueous sodium hydrogen carbonate. Evaporation of the dried (MgSO_4) organic layer and purification of the product by silica gel chromatography [PhH– Et_2O (1:1) as eluant] gave the *title compound* (**14b**) (0.225 g, 65%). After recrystallisation from chloroform–diethyl ether, the sample possessed m.p. 91–93 °C; $[\alpha]_D - 20^\circ$ (0.7% in CHCl_3); $\nu_{\text{max.}}$ (KBr) *inter alia* 1 775 (β -lactam C=O), 1 710 (ester C=O), 1 645 ($\text{C}=\text{N}$), and 1 610 cm^{-1} ($\text{C}=\text{C}$); $\lambda_{\text{max.}}$ (EtOH) 218 (ϵ 18 000) and 262 nm (12 700); δ (60 MHz; CDCl_3) 1.54 and 2.24 (each 3 H, s, together CMe_2), 3.70 (2 H, s, PhCH_2), 5.28 and 6.00 (each 1 H, d, J 3.5 Hz, together $2 \times \beta$ -lactam-H), 5.33 (2 H, s, $\text{CO}_2\text{CH}_2\text{C}_6\text{H}_4$), 7.40 (5 H, s, Ph), and 7.60 and 8.40 (each 2 H, d, separation 8 Hz, together C_6H_4); m/z (e.i.) *inter alia* 435 (M^+), 276, 274, 160, 159 (base peak), 137, 136, and 91 (C_7H_7^+) (Found: C, 63.7; H, 4.8; N, 9.6%. M^+ , 435.1433. $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_6$ requires C, 63.45; H, 4.85; N, 9.65%, M^+ , 435.1430).

p-Nitrobenzyl 3-Methyl-2-[(3R,4R)-2-oxo-3-phenylacetamido-4-pyrroloxyazetidin-1-yl]but-2-enoate (10b).—Compound (**14b**) (0.250 g, 0.574 mmol) was dissolved in the minimum volume of redistilled pyruvic acid and the solution was left for 15 h. Ethyl acetate was then added and the solution was washed with aqueous sodium hydrogen carbonate followed by water. Evaporation of the dried (MgSO_4) organic layer gave the *title compound* (**10b**) (0.226 g, ca. 75%) as a slightly impure yellow syrup, $\nu_{\text{max.}}$ (film) *inter alia* 3 300 (NH), 1 780 (β -lactam C=O), 1 730 (ester and ketone C=O), and 1 680 cm^{-1} (amide C=O); δ (60 MHz; CDCl_3) *inter alia* 2.02, 2.21, and 2.35 (each 3 H, s, together CMe_2 and COMe), 3.53 (2 H, s, PhCH_2), 4.74 (1 H, d, J 7 Hz, NHCHCH), 5.23 (2 H, s, $\text{OCH}_2\text{C}_6\text{H}_4$), 6.35 (1 H, s, CHCHOCO), 6.92 (1 H, d, J 7 Hz, CONHCH), 7.22 (5 H, s, Ph), and 7.44 and 8.08 (each 2 H, d, separation 8 Hz, together C_6H_4) (addition of D_2O caused the signal at δ 6.92 to disappear and that at δ 4.74 to collapse to a s); m/z (e.i.) *inter alia* 435 ($M^+ - \text{C}_3\text{H}_4\text{O}_3$), 299 ($M^+ - \text{C}_{10}\text{H}_{10}\text{NO}_3$), 160, 159, 137, 136, and 91 (C_7H_7^+ , base peak).

Photolysis of the Pyruvate (10b).—A solution of the pyruvate (**10b**) (0.226 g, 0.432 mmol) in dry benzene (45 cm^3) was irradiated with u.v. light. The reaction was monitored by ^1H n.m.r. spectroscopy and, after 30 h, when all the reactant had disappeared, the solvent was evaporated off. Purification of the residue by silica gel chromatography (light petroleum– EtOAc , gradient elution) gave *p-nitrobenzyl 2-(2,4-dioxo-3-phenylacetamidoazetidin-1-yl)-3-methylbut-2-enoate* (**15b**) (0.089 g, 46%) as a chromatographically homogeneous pale yellow syrup, $\nu_{\text{max.}}$ (film) *inter alia* 3 350 (NH), 1 880w and 1 745s (azetidinedione C=O), and 1 670 cm^{-1} (amide C=O); $\lambda_{\text{max.}}$ (EtOH) 208 (ϵ 31 500) and 258 nm (14 000); δ (60 MHz; CDCl_3) 2.16 and 2.33 (each 3 H, s, together CMe_2), 3.63 (2 H, s, PhCH_2), 4.64 (1 H, d, J 7 Hz, NHCH), 5.20 (2 H, s, $\text{OCH}_2\text{C}_6\text{H}_4$), 6.17br (1 H, d, J 7 Hz, CONHCH), 7.28 (5 H, s, Ph), and 7.46 and 8.17 (each 2 H, d, separation 8 Hz, together C_6H_4) (addition of D_2O caused the signal at δ 6.17 to disappear and that at δ 4.64 to collapse to a s); m/z (e.i.) 451 (M^+), 298 ($M^+ - \text{C}_7\text{H}_7\text{NO}_3$), 272, 250, 174, 137, 136, 105, and 91 (C_7H_7^+ , base peak) (Found: M^+ , 451.1374. $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_7$ requires M , 451.1379).

Methoxymethyl Benzylpenicillinate 1,1-Dioxide (17d).—Triethylamine (18.5 cm^3 , 123 mmol) was added to a stirred ice-cooled suspension of the acid (**17c**)²³ (45.0 g, 123 mmol) in dichloromethane (50 cm^3) followed by chloromethyl methyl ether (11.4 cm^3 , 123 mmol) (added in drops over 20 min). After 30 min, the mixture was allowed to warm to room temperature,

diluted with chloroform, and washed with 0.1M hydrochloric acid ($\times 3$). Evaporation of the dried (MgSO_4) organic layer gave the *title compound* (**17d**) (46.0 g, 91%). The sample, after recrystallisation from chloroform-diethyl ether, showed m.p. 167–168 °C; $[\alpha]_D^{25} +96^\circ$ (1% in EtOH); $\nu_{\text{max.}}$ (KBr) *inter alia* 3 280 (NH), 1 805 (β -lactam C=O), 1 765 and 1 745 (ester C=O), and 1 655 cm^{-1} (amide C=O); $\lambda_{\text{max.}}$ (EtOH) 205 (ϵ 13 700) and 258 nm (270); δ (60 MHz; CDCl_3) 1.38 and 1.56 (each 3 H, s, together 2-Me₂), 3.48 (3 H, s, OMe), 3.62 (2 H, s, PhCH_2), 4.44 (1 H, s, 3-H), 4.77 (1 H, d, J 4 Hz, 5-H), 5.34 (2 H, centre of AB q, J 6 Hz, separation of inner lines 6 Hz, OCH_2O), 6.10 (1 H, dd, J 10 and 4 Hz, 6-H), 7.10br (1 H, d, J 10 Hz, CONHCH), and 7.25 (5 H, s Ph) [addition of D_2O caused the signal at δ 7.10 to disappear and that at δ 6.10 to collapse to a d (J 4 Hz)]; m/z (e.i.) *inter alia* 411 (M^+), 346 ($M^+ - \text{O}_2\text{S}$), 256 ($M^+ - \text{C}_3\text{H}_5\text{O}_5\text{S}$), and 91 (C_7H_7^+ , base peak) (Found: C, 52.4; H, 5.5; N, 6.8; S, 7.9. $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}_7\text{S}$ requires C, 52.65; H, 5.40; N, 6.85; S, 7.80%).

(2R,3S)-1-(1-Methoxymethoxycarbonyl-2-methylprop-1-enyl)-4-oxo-3-phenylacetamidoazetidine-2-sulphinic Acid (**19c**).—95% DBN (12.5 cm^3 , 96 mmol) in dichloromethane (50 cm^3) was added to a solution of compound (**17d**) (40.8 g, 99.4 mmol) in dichloromethane (200 cm^3). The reaction was monitored by t.l.c. and, when the starting material had disappeared, the mixture was washed with dilute hydrochloric acid ($\times 3$) followed by water. The organic layer was then extracted with aqueous sodium hydrogen carbonate. After acidification with dilute hydrochloric acid, the aqueous layer was extracted with chloroform. Removal of the solvent from the organic layer gave the *title compound* (**19c**) (19.2 g, 47%) as a pale yellow syrup. $[\alpha]_D^{25} +22^\circ$ (7% in EtOH); $\nu_{\text{max.}}$ (film) *inter alia* 3 300 (NH), 1 775 (β -lactam C=O), 1 720 (ester C=O), and 1 660 cm^{-1} (amide C=O); $\lambda_{\text{max.}}$ (EtOH) 216 nm (ϵ 7 800); δ (60 MHz; CDCl_3) 2.00 and 2.25 (each 3 H, s, together CMe₂), 3.37 (3 H, s, OMe), 3.60 (2 H, s, PhCH_2), 4.70 (1 H, d, J 2 Hz, 2-H), 5.10–5.40 (3 H, m, together 3-H and OCH_2O), 7.21 (5 H, s, Ph), 8.08br (1 H, d, J 5 Hz, CONHCH), and 9.90br (1 H, s, SO_2H); m/z (e.i.) *inter alia* 344 ($M^+ - \text{HO}_2\text{S}$), 300, 286, 282, 274, 148, 118 ($\text{C}_8\text{H}_6\text{O}^+$), and 91 (C_7H_7^+ , base peak) (Found: $M^+ - \text{HO}_2\text{S}$, 344.1388. $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_5$ requires m/z 344.1372).

Methoxymethyl 2-[(1R,5S)-3-Benzyl-7-oxo-4-oxa-2,6-diazabicyclo[3.2.0]hept-2-en-6-yl]-3-methylbut-2-enoate (**14c**).—Sodium hydrogen carbonate (3.13 g, 37.3 mmol) was added to a stirred solution of the sulphinic acid (**19c**) (15.30 g, 37.3 mmol) in dichloromethane (60 cm^3) followed by lead(IV) acetate (16.53 g, 37.3 mmol). After 1 h, the mixture was diluted with chloroform and washed with aqueous sodium hydrogen carbonate followed by water. Evaporation of the dried (MgSO_4) organic layer and purification of the syrup (6.45 g) by silica gel chromatography ($\text{PhH-Et}_2\text{O}$, gradient elution) gave the *title compound* (**14c**) (3.08 g, 24%) as a pale yellow syrup. $[\alpha]_D^{25} -42^\circ$ (4% in EtOH); $\nu_{\text{max.}}$ (film) *inter alia* 1 780 (β -lactam C=O), 1 720 (ester C=O), and 1 650 cm^{-1} (C=N); $\lambda_{\text{max.}}$ (EtOH) 211 (ϵ 10 000) and 282 nm (1 000); δ (60 MHz; CDCl_3) 1.53 and 2.20 (each 3 H, s, together CMe₂), 3.48 (3 H, s, OMe), 3.73 (2 H, s, PhCH_2), 5.26 and 6.07 (each 1 H, d, J 3 Hz, together 2 \times β -lactam-H), 5.33 (2 H, s, OCH_2O), and 7.40 (5 H, s, Ph); m/z (e.i.) *inter alia* 344 (M^+), 299 ($M^+ - \text{C}_2\text{H}_5\text{O}$), and 91 (C_7H_7^+ , base peak) (Found: M^+ , 344.1379. $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_5$ requires M , 344.1372).

Methoxymethyl 2-(2,4-Dioxo-3-phenylacetamidoazetidin-1-yl)-3-methylbut-2-enoate (**15e**).—Compound (**14c**) (0.305 g, 0.887 mol) was dissolved in redistilled pyruvic acid (5 cm^3) and the mixture stirred vigorously for 10 min. Dichloromethane was then added and the solution was washed well with aqueous sodium hydrogen carbonate. Evaporation of the dried (MgSO_4) organic layer gave a yellow syrup (0.272 g) which was mainly

methoxymethyl 3-methyl-2-[(3R,4R)-2-oxo-3-phenylacetamido-4-pyruvoyloxyazetidin-1-yl]but-2-enoate (**10c**); $\nu_{\text{max.}}$ (film) *inter alia* 3 300 (NH), 1 780 (β -lactam C=O), 1 760–1 720 (ester and ketone C=O), and 1 660 cm^{-1} (amide C=O); δ (60 MHz; CDCl_3) *inter alia* 2.03, 2.24, and 2.50 (each 3 H, s, together CMe₂ and COMe), 3.44 (3 H, s, OMe), 3.60 (2 H, s, PhCH_2), 4.88 (1 H, dd, J 7 and 1 Hz, NHCHCH), 5.26 (2 H, s, OCH_2O), 6.30 (1 H, d, J 1 Hz, CHCHOCO), and 7.2br (6 H, s, CONH and Ph).

A solution of the crude pyruvate (**10c**) (0.141 g) in dry benzene (50 cm^3) was irradiated with u.v. light. Evaporation of the solvent after 48 h and purification of the residue by silica gel chromatography ($\text{PhH-Et}_2\text{O}$, gradient elution) gave the *title compound* (**15e**) [0.043 g, 26% based upon (**14c**)] as a colourless syrup. $\nu_{\text{max.}}$ (film) *inter alia* 3 320 (NH), 1 880w and 1 750s (azetidinedione C=O), 1 720sh (ester C=O), and 1 650sh cm^{-1} (amide C=O); δ (60 MHz; CDCl_3) 2.16 and 2.33 (each 3 H, s, together CMe₂), 3.41 (3 H, s, OMe), 3.61 (2 H, s, PhCH_2), 4.73 (1 H, d, J 7 Hz, NHCH), 5.23 (2 H, s, OCH_2O), 6.26br (1 H, d, J 7 Hz, CONHCH), and 7.23 (5 H, s, Ph) (addition of D_2O caused the signal at δ 6.26 to disappear and that at δ 4.73 to collapse to a s); m/z (e.i.) *inter alia* 299 ($M^+ - \text{C}_2\text{H}_5\text{O}_2$), 298 ($M^+ - \text{C}_2\text{H}_6\text{O}_2$), 272 ($M^+ - \text{C}_3\text{H}_4\text{O}_3$), 175 ($\text{C}_{10}\text{H}_9\text{NO}_2^+$), 118, and 91 (C_7H_7^+ , base peak).

2-(2,4-Dioxo-3-phenylacetamidoazetidin-1-yl)-3-methylbut-2-enoic Acid (**15c**).—Trifluoroacetic acid (0.1 cm^3) was added to a solution of the methoxymethyl ester (**15e**) (0.181 g, 0.5 mmol) in deuteriochloroform (1 cm^3). When the reaction was complete by ^1H n.m.r. spectroscopy, the solvent was evaporated off. The resultant solid was treated with ice-cold chloroform and the mixture filtered to give the *title compound* (**15c**) (0.047 g, 30%). After recrystallisation from ethanol, the sample possessed m.p. 168–170 °C; $\nu_{\text{max.}}$ (KBr) *inter alia* 3 420 and 3 240 (OH and NH), 1 880w and 1 745s (azetidinedione C=O), 1 710 (acid C=O), 1 675 and 1 650 (amide C=O), and 1 630 cm^{-1} (C=C); δ [60 MHz; $(\text{CD}_3)_2\text{SO}$] 1.94 and 2.24 (each 3 H, s, together CMe₂), 3.57 (2 H, s, PhCH_2), 5.40 (1 H, d, J 7 Hz, NHCH), 7.27 (5 H, s, Ph), and 9.04 (1 H, d, J 7 Hz, CONHCH) (addition of D_2O caused the signal at δ 9.04 to disappear and that at δ 5.40 to collapse to a s); m/z (e.i.) *inter alia* 298 ($M^+ - \text{H}_2\text{O}$), 272 ($M^+ - \text{CO}_2$), 175 ($\text{C}_{10}\text{H}_9\text{O}_2^+$), 154, 153, 118 ($\text{C}_8\text{H}_6\text{O}^+$), and 91 (C_7H_7^+ , base peak) (Found: C, 60.5; H, 5.0; N, 8.9. $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_5$ requires C, 60.75; H, 5.10; N, 8.85%).

Reaction of the Butenoic Acid (**15c**) with Diazomethane.—The butenoic acid (**15c**) (0.027 g, 0.85 mmol) was treated with an excess of diazomethane in diethyl ether at 0 °C. Evaporation of the solvent, after 15 min, left a white solid (0.025 g, 89%) which was identical (t.l.c. and ^1H n.m.r. spectroscopy) with the methyl ester (**15a**).

Methyl (2S)-3-Methyl-3-methylthio-2-[(3S,4S)-2-oxo-3-phenylacetamido-4-pyruvoyloxyazetidin-1-yl]butanoate (**22**).—Compound (**18a**) (0.181 g, 0.5 mmol) was dissolved in the minimum volume of pyruvic acid and the solution was left for 48 h. Chloroform was then added and the solution was washed well with aqueous sodium hydrogen carbonate followed by water. Evaporation of the dried (MgSO_4) organic layer gave a gum which was dissolved in chloroform. Addition of light petroleum to the solution induced the precipitation of the *title compound* (**22**) (0.126 g, 56%) as an amorphous pale yellow solid, $[\alpha]_D^{25} +12^\circ$ (1.5% in EtOH); $\nu_{\text{max.}}$ (KBr) *inter alia* 3 400 (NH), 1 780 (β -lactam C=O), 1 750br (ester and ketone C=O), and 1 665 cm^{-1} (amide C=O); $\lambda_{\text{max.}}$ (EtOH) 210 (ϵ 9 200), 275 (2 600), and 311 nm (1 700); δ (60 MHz; CDCl_3) 1.50 (6 H, s, CMe₂), 2.03 and 2.48 (each 3 H, s, together SMe and COMe), 3.60 (5 H, s, CO_2Me and CH_2Ph), 4.45 (1 H, d, J 7 Hz, NHCHCH), 4.50 (1

H, s, NCHCO_2Me), 6.18 (1 H, d, J 7 Hz, CONHCH), 6.70 (1 H, s, CHCHOCO), and 7.26 (5 H, s, Ph) (addition of D_2O caused the signal at δ 6.18 to disappear and that at δ 4.45 to collapse to a s); m/z (e.i.) *inter alia* 450 (M^+), 363 ($M^+ - \text{C}_3\text{H}_3\text{O}_3$), 362 ($M^+ - \text{C}_3\text{H}_4\text{O}_3$), 315 ($M^+ - \text{C}_4\text{H}_7\text{O}_3\text{S}$), 274, 91 (C_7H_7^+ , base peak), and 89.

Photolysis of the Pyruvate (22).—A solution of the pyruvate (22) (0.080 g, 0.18 mmol) in dry benzene (30 cm^3) in a pyrex vessel was irradiated with u.v. light. After 30 h, when no starting material remained according to ^1H n.m.r. spectroscopy, the mixture was filtered (to remove a small amount of precipitated material). Removal of the solvent from the filtrate left a residue (0.025 g, 43%) which was identical (t.l.c. and ^1H n.m.r. spectroscopy) with the azetidinone (15a).

(3R)-4,4-Dimethyl-3-[(3S,4S)-2-oxo-3-phenylacetamido-4-pyruvoyloxyazetidin-1-yl]thietan-2-one (24).—Compound (25)²⁴ (0.265 g, 0.84 mmol) was dissolved in the minimum volume of pyruvic acid and the solution was left for 8 h. After dilution with chloroform, the solution was washed well with aqueous sodium hydrogen carbonate followed by water. Evaporation of the dried (MgSO_4) organic layer gave the title compound (24) (0.297 g, ca. 88%) as an almost pure colourless syrup with the following properties: $[\alpha]_D -64^\circ$ (3.4% in CHCl_3); ν_{max} (film) *inter alia* 3360 (NH), 1785 (β -lactam C=O), 1755 (ester C=O), 1740 (thietanone and ketone C=O), and 1655 cm^{-1} (amide C=O); λ_{max} (EtOH) 218 (ϵ 9 000) and 275 nm (800); δ (60 MHz; CDCl_3) 1.76 and 1.90 (each 3 H, s, together 4-Me₂), 2.50 (3 H, s, COMe), 3.57 (2 H, s, PhCH_2), 4.80 (1 H, dd, J 8 and 1 Hz, NHCHCH), 5.13 (1 H, s, 3-H), 6.17 (1 H, d, J 1 Hz, CHCHOCO), 6.70br (1 H, d, J 8 Hz, CONHCH), and 7.20 (5 H, s, Ph) [addition of D_2O caused the signal at δ 6.70 to disappear and that at δ 4.80 to collapse to a d (J 1 Hz)]; m/z (e.i.) 317 ($M^+ - \text{C}_3\text{H}_3\text{O}$), 298, 159 (base peak), and 91 (C_7H_7).

Photolysis of the Pyruvate (24).—A solution of the pyruvate (24) (0.217 g, 0.537 mmol) in dry benzene (55 cm^3) was irradiated with u.v. light. After 36 h, when no starting material remained (^1H n.m.r. spectroscopy), the solvent was removed and the residue purified by silica gel chromatography (PhH-Et₂O, gradient elution) to give (3R)-4,4-dimethyl-3-(2,4-dioxo-3-phenylacetamidoazetidin-1-yl)thietan-2-one (23) (0.077 g, 43%) as a pale yellow syrup, $[\alpha]_D -19^\circ$ (0.5% in CHCl_3); ν_{max} (film) *inter alia* 3300 (NH), 1880w (azetidinone C=O), 1750 (azetidinone and thietanone C=O), and 1660 cm^{-1} (amide C=O); λ_{max} (EtOH) 218 (ϵ 8 000) and 283 nm (1 900); δ (60 MHz; CDCl_3) 1.79 and 1.85 (each 3 H, s, 4-Me₂), 3.53 (2 H, s, PhCH_2), 4.74 (1 H, d, J 7 Hz, NHCH), 5.19 (1 H, s, 3-H), 6.68br (1 H, d, J 7 Hz, CONHCH), and 7.15 (5 H, s, Ph) (addition of D_2O caused the signal at δ 6.68 to disappear and that at δ 4.74 to collapse to a s); m/z (e.i.) 332 (M^+), 298 ($M^+ - \text{H}_2\text{S}$), 202, 175 ($\text{C}_{10}\text{H}_9\text{NO}_2^+$), and 91 (C_7H_7^+ , base peak) (Found: M^+ , 332.0827. $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_4\text{S}$ requires M , 332.0831).

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