Use of π-Allyltricarbonyliron Lactam Complexes in the Preparation of Nocardicin Derivatives: Synthesis of (−)-3-Oxo-1-[(p-benzyloxyphenyl)-benzyloxycarbonylmethyl]azetidin-2-one
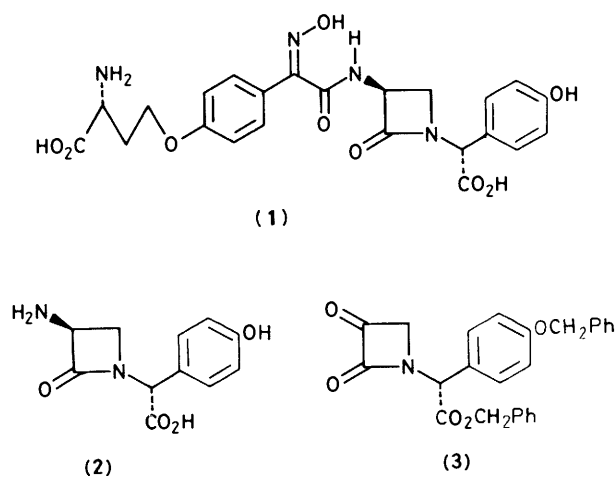
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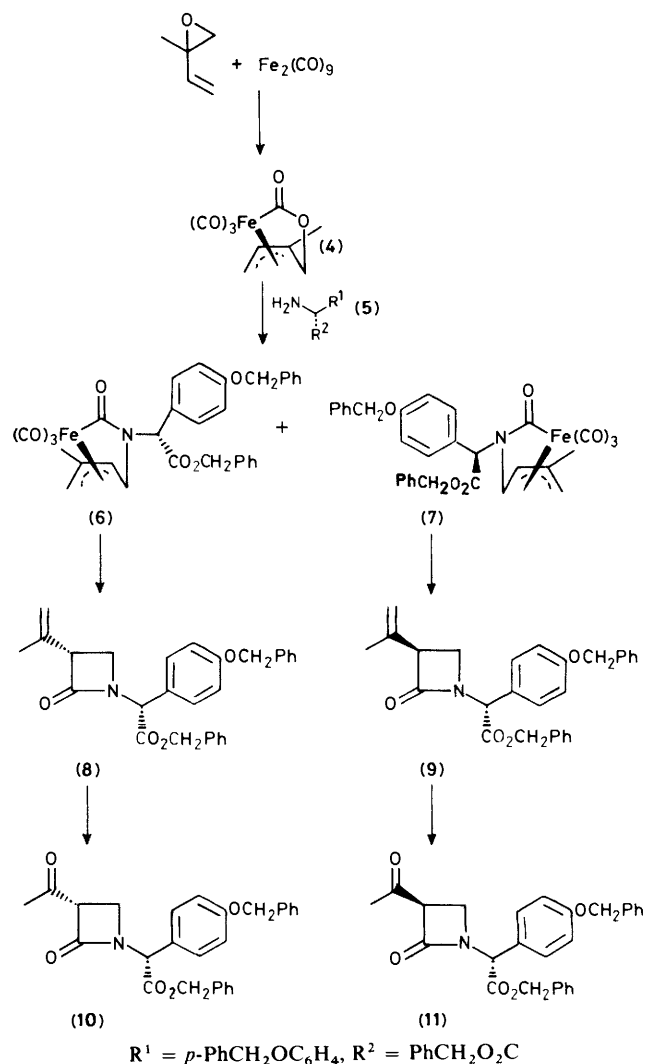*Department of Chemistry, Imperial College of Science and Technology, London SW7 2AY, England*

A short five-step synthesis, in 79% overall yield, of (−)-3-oxo-1-[(p-benzyloxyphenyl)benzyloxy-carbonylmethyl]azetidin-2-one (3), a precursor for nocardicin synthesis has been developed from isoprene monoepoxide. The key steps of the procedure rely on the efficient transformation of 2–4-η³-(1-formyloxy-2-methylbut-3-en-2-ylato)tricarbonyliron into the corresponding diastereoisomeric lactam complexes (6) and (7) using D-(−)-benzyl-(p-benzyloxyphenyl)glycinate (5) and ZnCl₂·TMEDA (TMEDA = tetramethylethylenediamine), and their oxidation with ceric ammonium nitrate to 3-isopropenylazetidinone derivatives.

The nocardicin antibiotics, typified by nocardicin A (1) were first isolated from *Nocardia* species in 1976.[1] Interest in the synthesis of these novel monocyclic β-lactams has been prompted by the wide spectrum of activity they have exhibited against Gram-negative bacteria. Examination of the various published syntheses[2-7] showed that a general precursor for the nocardicins was 3-aminonocardicinic acid (2). This had been prepared previously by Ban[5] in racemic form using a reductive amination sequence from the azetidine-2,3-dione (3).

Here we describe a novel route using iron carbonyl complexes for the preparation of compound (3) in its optically pure form. The chemistry is based upon earlier observations, where it was shown that π-allyltricarbonyliron lactone complexes could be converted into the corresponding lactam derivatives which upon oxidation with ceric ammonium nitrate, afford azetidin-ones.[8-10] The tricarbonyliron lactone complex precursor (4) was prepared from the quantitative reaction of isoprene monoepoxide with nonacarbonyldi-iron in tetrahydrofuran (THF) at room temperature according to our previously published procedure.[11] The requisite, suitably protected N-substituent could then be introduced in its entirety by reaction of the lactone complex (4) with the dibenzylated derivative of

D-(−)-p-hydroxyphenylglycine (5) in the presence of ZnCl₂·TMEDA without epimerisation at the chiral centre. The diastereoisomeric lactam complexes (6) and (7) obtained in 94.5% combined yield, could be readily separated by silica
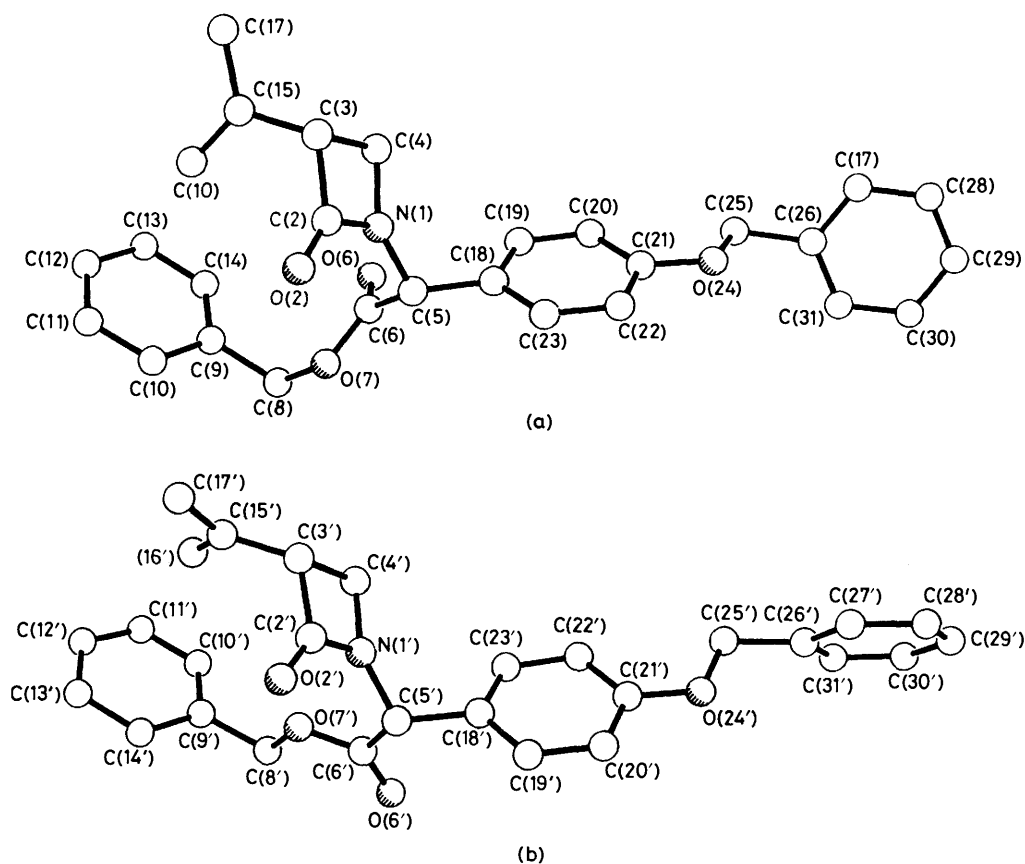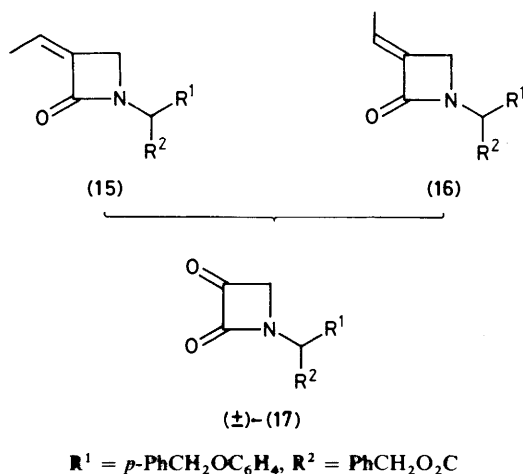

R¹ = p-PhCH₂OC₆H₄, R² = PhCH₂O₂C

(a)

(b)

Figure. The molecular structure of 1-(3R)-[(1'R)-(p-benzyloxyphenyl)benzyloxycarbonylmethyl]-3-isopropenylazetidin-2-one (8) showing (a) and (b) the two conformations of the molecule in the crystal and giving the crystallographic numbering scheme.

gel chromatography. The structural assignment for these two diastereoisomers follows from highfield ^{1}H n.m.r. studies and from an X-ray crystallographic structure determination of a subsequent derivative. Oxidation of the lactam complex (6) with cerium(IV) at −30 °C afforded the azetidinone (8) in an excellent 99% yield. The relative stereochemistry of the appending isopropenyl substituent at C-3 in this compound follows from comparison with similar molecules and was confirmed by X-ray crystallographic analysis (see Figure). This determination also provides evidence for the structure assigned to the original complex (6). Similar oxidation of the diastereoisomer (7) gave the azetidinone (9) in 87% yield. Efforts were then made to convert the isopropenyl substituted azetidinones (8) and (9) into nocardicin precursors. Low temperature (−78 °C) ozonolysis of (8) gave the 3α-acetyl-β-lactam (10) while similar treatment of (9) afforded (11). Although each acetyl derivative was characterised spectroscopically using freshly prepared materials, as a result of the acidity of the 3-H proton, rapid epimerisation occurred upon storage at 0 °C over 16 h to give a 1:1 mixture. Reduction of the freshly prepared 3-α-acetyl derivative (10) with K-Selectride at −78 °C furnished a 3:1 mixture of the diastereoisomeric alcohols (12) and (13) in 64% yield, which were inseparable by chromatography. Treatment of the 3β-acetyl derivative (11) with the weakly basic zinc borohydride reagent gave a 1.2:1 ratio of separable diastereoisomeric alcohols in 80% yield which we believe to be (13) and (14) formed by non-selective reduction of the carbonyl function. This lack of selectivity is in contrast to other reports on 3-acetyl-azetidinones.[12] The major isomer in this last reaction was found to have an ^{1}H n.m.r. spectrum identical with the minor isomer

(10) ⟶

(12)   3 : 1   (13)

(11) ⟶

(14)   1 : 1·2   (13)

$R^1 = p\text{-PhCH}_2OC_6H_4, \quad R^2 = PhCH_2O_2C$
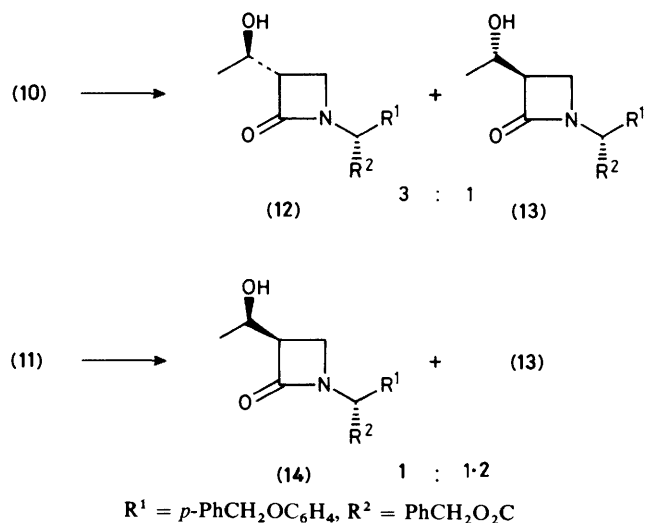
obtained from the K-Selectride reaction of (10). From these and later results, it appears that the Selectride reagent is sufficiently basic to cause some epimerisation prior to reduction, but that reduction of the carbonyl group is selective. Indeed, separate treatment of a 1:1 mixture of (10) and (11) with K-Selectride gave the same alcohols, albeit in a different ratio. Evidence to support the stereochemical assignment for the alcohols (12), (13), and (14) is provided by their subsequent elimination products. Treatment of the diastereoisomeric mixture (13) and

(15)

(16)

(±)-(17)

$R^1 = p\text{-PhCH}_2\text{OC}_6\text{H}_4$, $R^2 = \text{PhCH}_2\text{O}_2\text{C}$

chiral centre adjacent to the lactam nitrogen would not be lost and hence permit preparation of the 3-oxoazetidinone (3) in its optically pure form. To this end we found that treatment of a 1:1 mixture of the 3-acetyl derivatives (10) and (11) obtained by quantitative ozonolysis of a crude mixture of (8) and (9), with dimethyl-t-butylsilyl triflate at 0 °C in the presence of triethylamine gave the enol ether (19) also in essentially

(10) + (11) ⟶

(19)

(−)-(3)

$R^1 = p\text{-PhCH}_2\text{OC}_6\text{H}_4$, $R^2 = \text{PhCH}_2\text{O}_2\text{C}$

(14) with methanesulphonyl chloride gave the corresponding mesylates. Regiospecific elimination with diazabicycloundecene (DBU), proceeded slowly to give an isomeric mixture of the olefins (15) and (16) which are chromatographically separable. Similar exposure of the mesylates derived from (12) and (13) with DBU gave predominantly the E-ene lactam (16). The stereochemical assignments of (15) and (16) are made on the basis of the known anisotropy effects due to the carbonyl group,[13] which profoundly influences the chemical shifts of the methyl and vinyl protons, e.g. δ 2.02 and 5.62 for the methyl and vinyl protons respectively in compound (15) and 1.68 and 6.17 for similar protons in (16). In view of the predominant anti-elimination of alcohol mesylates,[12b] the Z,E-mixture of ene lactams must have arisen from a threo-, erythro-mixture of alcohols as in (13) and (14). Conversely, the E-ene lactam (16) could only have been derived from an erythro-mixture in accord with the assigned structures for (12) and (13).

Although the elimination sequence appeared to be successful, a polarimetry measurement of the isomeric mixture of ene lactams showed that racemisation had apparently occurred at the chiral centre. The base lability at this activated benzylic position has been commented on previously.[3,4,14] Alternative conditions for effecting elimination of the mesylates without epimerisation at the activated centre were investigated but without success. Ozonolysis of the ene lactams (15) and (16) at −25 °C gave the racemic 3-oxoazetidinone (17) in 84% yield, characterised by its high carbonyl stretching frequency of $v_{max.}$ 1 855 cm^{-1}.
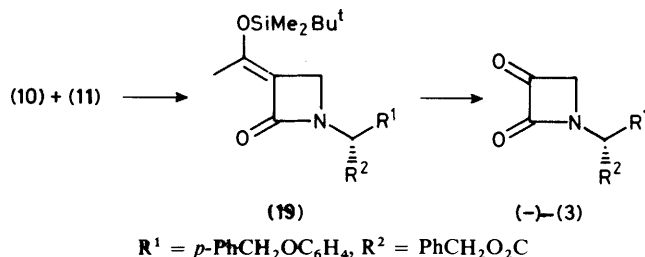
In an effort to prepare potentially interesting pharmaceutical compounds related to the nocardicins in which the C-3 position contained a hydroxyethyl substituent, a group common to many β-lactam antibiotics,[15] the 3-acetylazetidinones (10) and (11) were reduced with K-Selectride to give a diastereoisomeric mixture of alcohols [mainly (12) and (13)] in 64% yield. These were deprotected using Pd—C in a hydrogen atmosphere to afford the free carboxylic acid (18) (82%). However, on

(18)

biological evaluation, this mixture of compounds (18) only showed very low levels of antibiotic activity.

Owing to the epimerisation problem noted earlier, an alternative route was sought whereby the configuration at the

quantitative yield. Isolation of this compound was unnecessary since ozonolysis of the crude reaction mixture, followed by reductive work-up, gave optically pure (−)-3-oxoazetidinone (3) in 84% yield. The whole sequence described above leading to (3) in five steps from isoprene epoxide proceeds in a remarkably high 79% overall yield.

Since 3-oxoazetidinone (17) has been converted into 3-aminonocardicinic acid[5] (2) and hence the nocardicins, this new route should be considered as a potential enantioselective synthesis of these systems. All attempts to use the existing chirality of the 3β-acetylazetidinone (11) in a direct synthesis of (−)-3-aminonocardicinic acid by way of a Beckmann-type reaction were unsuccessful. This was attributed to the reluctance of the β-lactam nucleus to stabilise a partial positive charge at C-3 in the transition state for migration.

Experimental

Preparation of 2—4-η³-(1-{[(1'R)-(p-Benzyloxyphenyl)-(benzyloxycarbonyl)methyl]formylamino}-3-methylbut-3-en-2-ylato)tricarbonyliron (6) and (7).—To a stirred solution of the lactone complex (4) (838 mg, 2.9 mmol) and ZnCl$_2$·TMEDA (1.46 g, 5.8 mmol) in ether–THF (1:1; 30 ml), D-(−)-benzyl-(p-benzyloxyphenyl)glycinate (5) (4.03 g, 11.6 mmol) (prepared from its hydrochloride salt by shaking an ethereal suspension with anhydrous NaHCO$_3$) in ether–THF (1:1; 7 ml) was added under argon. After 5 h, a further quantity of the lactone complex (4) (227 mg, 0.8 mmol) was added to the reaction mixture. After a further 3.5 h, the reaction mixture was diluted with ether (120 ml) and washed with 6% aqueous HCl (2 × 30 ml). The aqueous layers were re-extracted with ether (60 ml) and the combined organic extracts washed with water and then brine and, finally, dried. Removal of solvent gave a foam which was carefully

chromatographed using a solvent gradient (25—45% ether–petroleum) to give the complex (6) (1.276 g, 60.5%) as a form, $\nu_{max.}$ 3 050, 2 980, 2 930, 2 070, 2 010, 1 995, 1 735, 1 610, 1 580, 1 505, 1 395, 1 380, 1 280, 1 250, 1 160, and 1 005 cm^{-1}; δ (250 MHz) 1.97 (3 H, s, 3-Me), 2.85 (1 H, dd, J 12 and 7 Hz, 1-H), 3.07 (1 H, d, J 1.5 Hz, 4′-H), 3.33 (1 H, br d, J 12 Hz, 1′-H), 3.59 (1 H, dd, J 1.5 and 1.5 Hz, 4-H), 4.15 (1 H, br d, J 7 Hz, 2-H), 5.02 (2 H, s, PhCH$_2$), 5.07 (1 H, d, J_{AB} 16 Hz, PhCH$_2$), 5.19 (1 H, d, J_{AB} 16 Hz, PhCH$_2$), 6.00 (1 H, s, NCH), 6.87 (2 H, d, J_{AB} 8 Hz, Ar), 6.97 (2 H, d, J_{AB} 8 Hz, Ar), and 7.22—7.46 (10 H, m, Ph); m/z 441 [M^+ − Fe(CO)$_3$ < 1%], 375, and 242 [Found: C, 63.35; H, 4.6; N, 2.3%; M^+ − Fe(CO)$_3$, 441.1935. C$_{30}$H$_{27}$NFeO$_7$ requires C, 63.28; H, 4.78; N, 2.40%; M^+ − Fe(CO)$_3$, 441.1940] and the complex (7) (0.708 g, 34%) as a foam, $\nu_{max.}$ 3 040, 2 950, 2 920, 2 870, 2 070, 2 010, 1 995, 1 735, 1 605, 1 585, 1 450, 1 400, 1 375, 1 260, 1 160, and 1 000 cm^{-1}; δ (250 MHz) 1.92 (3 H, s, 3-Me), 2.64 (1 H, d, J 1.5 Hz, 4-H), 2.82 (1 H, br d, J 12 Hz, 1′-H), 3.50 (1 H, dd, J 1.5 and 1.5 Hz, 4′-H), 3.66 (1 H, dd, J 12 and 7 Hz, 1-H), 4.22 (1 H, br d, J 7 Hz, 2-H), 5.02 (2 H, s, PhCH$_2$), 5.18 (2 H, s, PhCH$_2$), 5.72 (1 H, s, NCH), 6.87 (2 H, d, J_{AB} 8 Hz, Ar), 6.97 (2 H, d, J_{AB} 8 Hz, Ar), and 7.20—7.46 (10 H, m, Ph) [Found: C, 63.5; H, 4.55; N, 2.35%; M^+ − Fe(CO)$_3$, 441.1937. C$_{30}$H$_{27}$-FeNO$_7$ requires C, 63.28; H, 4.78; N, 2.40%; M^+ − Fe(CO)$_3$, 441.1940].

Preparation of (3R)-1-[(1R′)-(p-*Benzyloxyphenyl*)benzyloxy-carbonylmethyl]-3-isopropenylazetidin-2-one (8).—A solution of the lactam (6) (1.126 g, 1.98 mmol) in ethanol (70 ml) was cooled to −30 °C and a solution of ceric ammonium nitrate (5.42 g, 9.9 mmol) in ethanol (70 ml) was added with stirring over a period of 10 min. The reaction was allowed to warm to room temperature over 2 h, whereupon the solvent was removed and the residue partitioned between water (60 ml) and CH$_2$Cl$_2$ (220 ml). The organic layer was further washed with water (60 ml) and brine (60 ml) to give, after drying and chromatography (45% ether–petroleum), the *azetidinone* (8) (0.865 g, 99%) as an oil which slowly crystallised as white rosettes, m.p. 68 °C; $[\alpha]_D^{22}$ −52.1° (c, 2.0 in CHCl$_3$); δ (250 MHz) 1.79 (3 H, s, Me), 3.18 (1 H, dd, J 5.5 and 5.5 Hz, cis-4-H), 3.51 (1 H, dd, J 5.5 and 3.0 Hz, trans-4-H), 3.70 (1 H, dd, J 5.5 and 3.0 Hz, 3-H), 4.92 (2 H, m, CH$_2$), 5.06 (2 H, s, PhCH$_2$), 5.19 (2 H, s, PhCH$_2$), 5.62 (1 H, s, NCH), 6.94 (2 H, d, J_{AB} 8.5 Hz, Ar), 7.16 (2 H, d, J_{AB} 8.5 Hz, Ar), and 7.21—7.46 (10 H, m, Ph); $\nu_{max.}$ 3 080, 3 060, 3 020, 2 980, 1 750, 1 735, 1 645, 1 610, 1 585, 1 500, 1 455, 1 380, 1 260, 1 225, 1 165, 1 010, and 910 cm^{-1}; m/z 441 (M^+, 1%), 373, 306, 238, and 91 (100) (Found: C, 76.4; H, 6.2, N, 3.15%; M^+, 441.1944. C$_{28}$H$_{27}$NO$_4$ requires C, 76.17; H, 6.16; N, 3.17%; M^+, 441.1940).

Preparation of (3S)-1-[(1′R)-(p-*Benzyloxyphenyl*)benzyloxy-carbonylmethyl]-3-isopropenylazetidin-2-one (9).—Ceric ammonium nitrate (2.75 g, 5.0 mmol) in ethanol (40 ml) was added dropwise to a cooled (−30 °C) solution of the lactam complex (7) (558 mg, 0.98 mmol) in ethanol (25 ml) with stirring. The reaction mixture was allowed to warm to room temperature over 2 h, when solvent was removed and the gummy residue partitioned between CH$_2$Cl$_2$ (180 ml) and 3% aqueous NaHCO$_3$. The organic phase was washed sequentially with water and brine, and evaporated and the residue chromatographed (45% ether–petroleum) to give the azetidinone (9) (378 mg, 87%) as a colourless oil, $[\alpha]_D^{22}$ −140.0° (c, 1.5 in CHCl$_3$); $\nu_{max.}$ 3 070, 3 040, 2 980, 1 750, 1 735, 1 645, and 1 260 cm^{-1}; δ (250 MHz) 1.65 (3 H, s, Me), 2.96 (1 H, dd, J 5.0 and 2.1 Hz, trans-4-H), 3.75 (1 H, dd, J 5.3 and 5.0 Hz, cis-4-H), 3.83 (1 H, m, 3-H), 4.86 (2 H, m, =CH$_2$), 5.06 (2 H, s, PhCH$_2$), 5.20 (2 H, s, PhCH$_2$), 5.64 (1 H, s, NCH), 6.94 (2 H, d, J_{AB} 8.9 Hz, Ar), 7.17 (2 H, d, J_{AB} 8.9 Hz, Ar), and 7.20—7.46 (10 H, m, Ph); m/z 441

(M^+, 1%), 373, 306, 238, and 91 (100) (Found: C, 76.25; H, 6.3; N, 3.10%; M^+, 441.1931. C$_{28}$H$_{27}$NO$_4$ requires C, 76.17; H, 6.16; N, 3.17%; M^+ 441.1940).

Preparation of (3R)-3-*Acetyl*-1-[(1′R)-(p-*benzyloxyphenyl*)-benzyloxycarbonylmethyl]azetidin-2-one (10).—A solution of the isopropenylazetidinone (8) (120 mg, 0.27 mmol) in CH$_2$Cl$_2$ (10 ml) was treated with ozone at −78 °C until no starting material was present by t.l.c. (60% ether–petroleum). Dimethyl sulphide was added and the reaction warmed to room temperature and stirred for 1 h. Removal of solvent gave a single diastereoisomeric ketone (10) (120 mg, 100%) as a syrup, $\nu_{max.}$ (film) 3 080, 3 060, 3 030, 1 750, 1 740, 1 722, 1 610, 1 510, and 1 240 cm^{-1}; δ (250 MHz) 2.30 (3 H, s, COCH$_3$), 3.09 (1 H, dd, J 5.4 and 5.4 Hz, cis-4-H), 3.94 (1 H, dd, J 5.4 and 2.9 Hz, trans-4-H), 4.01 (1 H, dd, J 5.4 and 2.9 Hz, 3-H), 5.06 (2 H, s, PhCH$_2$), 5.19 (2 H, s, PhCH$_2$), 5.56 (1 H, s, NCH), 6.96 (2 H, d, J_{AB} 8.8 Hz, Ar), 7.10 (2 H, d, J_{AB} 8.8 Hz, Ar), and 7.21—7.45 (10 H, m, Ph); m/z 443 (M^+, <1%), 353, 308 (100), 212, and 91 (Found: M^+, 443.1722. C$_{27}$H$_{25}$NO$_5$ requires M, 443.1733).

Preparation of (3S)-3-*Acetyl*-1-[(1′R)-(p-*benzyloxyphenyl*)-benzyloxycarbonylmethyl]azetidin-2-one (11).—A solution of the alkenylazetidinone (9) (164 mg, 0.37 mmol) in CH$_2$Cl$_2$ (10 ml) was treated with ozone at −78 °C, until t.l.c. (60% ether–petroleum) indicated the disappearance of all starting material. The mixture was then stirred with dimethyl sulphide for 1 h at room temperature after which the solvent was removed to afford a single diastereoisomeric ketone (11) (164 mg, 100%) which showed an i.r. spectrum similar to that of (10) above, δ (250 MHz) 2.26 (3 H, s, COCH$_3$), 3.47 (1 H, dd, J 5.4 and 2.9 Hz, trans-4-H), 3.56 (1 H, dd, J 5.4 and 5.4 Hz, cis-4-H), 4.20 (1 H, dd, J 5.4 and 2.9 Hz, 3-H), 5.04 (2 H, s, PhCH$_2$), 5.18 (2 H, s, PhCH$_2$), 5.55 (1 H, s, NCH), 6.96 (2 H, d, J_{AB} 8.5 Hz, Ar), 7.10 (2 H, d, J_{AB} 8.5 Hz, Ar), and 7.21—7.45 (10 H, m, Ph).

Reduction of (3R)-3-*Acetyl*-1-[(1′R)-(p-*benzyloxyphenyl*)-benzyloxycarbonylmethyl]azetidin-2-one (10).—To a cooled (0 °C) solution of the freshly prepared crude ketone (10) in THF (2 ml), K-Selectride (0.5M-solution in THF; 1.1 ml) was added and the reaction stirred for a further 0.25 h. The mixture was quenched with water, warmed to room temperature, and extracted with ethyl acetate to give the hydroxyethyl-azetidinones (12) and (13) (77 mg, 64%) in a 3:1 ratio as a syrup, $[\alpha]_D^{22}$ −30.3° (c, 0.65 in CH$_2$Cl$_2$); $\nu_{max.}$(film) 3 400, 3 080, 3 060, 3 030, 2 920, 1 740, 1 610, 1 570, 1 510, and 1 240 cm^{-1}; (13) δ (250 MHz) 1.18 (3 H, d, J 6 Hz, Me), 2.91 (1 H, dd, J 5.5 and 2.5 Hz, trans-4-H), 3.21 (1 H, ddd, J 6.5, 5.5, and 2.5 Hz, 3-H), 3.48 (1 H, dd, J 5.5 and 5.5 Hz, cis-4-H), 3.91 (1 H, dq, J 6.5 and 6 Hz CHOH), 5.02 (2 H, s, PhCH$_2$), 5.17 (2 H, s, PhCH$_2$), 5.60 (1 H, s, NCH), 6.92 (2 H, d, J_{AB} 8.5 Hz, Ar), 7.16 (2 H, d, J 8.5 Hz, Ar), and 7.22—7.44 (10 H, m, Ph); (12) δ (250 MHz), 1.25 (3 H, d, J 6 Hz, Me), 3.10 (1 H, m, 3-H), 3.40 (1 H, dd, J 6 and 5.5 Hz, cis-4-H), 4.08 (1 H, dq, J 6 and 5.5 Hz, CHOH), 5.04 (2 H, s, PhCH$_2$), 5.17 (2 H, s, PhCH$_2$), 5.57 (1 H, s, NCH), 6.92 (2 H, d, J_{AB} 8.5 Hz, Ar), 7.15 (2 H, d, J_{AB} 8.5 Hz, Ar), and 7.22—7.44 (10 H, m, Ph); m/z 445 (M^+, <1%), 310 (100), 266, and 91 (Found: M^+, 445.1890. C$_{27}$H$_{27}$NO$_5$ requires M, 445.1889).

Reduction of (3S)-3-*Acetyl*-1-[(1′R)-(p-*benzyloxyphenyl*)-benzyloxycarbonylmethyl]azetidin-2-one (11) *with Zinc Boro-hydride.*—The freshly prepared 3-acetylazetidinone (11) was stirred in ether (8 ml) at 0 °C and Zn(BH$_4$)$_2$ (0.13M solution in ether; 1.0 ml) was added. After 0.5 h, the reaction was quenched with water at 0 °C and the mixture extracted with ethyl acetate. Chromatography (ether) provided a 1:1.2 diastereoisomeric mixture of the hydroxyethylazetidinones (14) and (13) (132 mg, 80%); $[\alpha]_D^{22}$ −139.3° (c, 0.9 in CHCl$_3$); $\nu_{max.}$ 3 400, 3 080, 3 060, 3 030, 1 920, 1 740, 1 610, 1 570, 1 510, and 1 240 cm^{-1}; (14) δ

(250 MHz) 1.21 (3 H, d, *J* 7.5 Hz, Me), 3.08 (1 H, dd, *J* 5.5 and 2.5 Hz, *trans*-4-H), 3.22 (1 H, m, 3-H), 3.58 (1 H, dd, *J* 5.5 and 5.5 Hz, *cis*-4-H), 4.02 (1 H, dq, *J* 7.5 and 5.5 Hz, C*H*OH), 5.01 (2 H, s, PhC*H*₂), 5.17 (2 H, s, PhC*H*₂), 6.00 (1 H, s, NCH), 6.91 (2 H, *J*$_{AB}$ 8.5 Hz, Ar), 7.16 (2 H, d, *J*$_{AB}$ 8.5 Hz, Ar), and 7.22—7.44 (10 H, m, Ph).

Preparation of (Z)- and (E)-3-Ethylidene-1-[(p-benzyloxyphenyl)benzyloxycarbonylmethyl]azetidin-2-ones **(15)** *and* **(16).**—The diastereoisomeric mixture of β-lactams **(13)** and **(14)** (108 mg, 0.24 mmol) in CH₂Cl₂ (3 ml) was stirred with triethylamine (67 μl, 0.48 mmol) and methanesulphonyl chloride (27 μl, 0.35 mmol) at 0 °C, for 0.5 h. The reaction mixture was diluted with CH₂Cl₂ (25 ml) and washed with 0.1M-HCl (3 ml), water (2 × 3 ml), and brine (5 ml), and then dried and evaporated to provide the corresponding mesylates, as a syrup, $\nu_{max.}$ 3 030, 2 920, 1 755, 1 740, 1 610, 1 350, 1 240, 1 175, and 910 cm⁻¹; *m/z* 522 (*M*⁺, <1%), 418, 387, 290, and 91 (100). To a stirred solution of the crude mesylates in CH₂Cl₂ (0.75 ml) at 0 °C, DBU (40 μl, 0.26 mmol) was added and the reaction followed by t.l.c. (ether). After 5 h, the reaction mixture was diluted with CH₂Cl₂ (20 ml) and washed with 10% aqueous citric acid, water, and brine. Removal of the solvent furnished an isomeric mixture of enelactams (85 mg, 67%) which were chromatographically separated (50% ether–petroleum) to give the (Z)-*azetidin-2-one* **(15)**, $\nu_{max.}$ 3 040, 2 890, 1 740, 1 610, 1 510, 1 380, 1 250, and 1 195 cm⁻¹; δ (90 MHz) 2.02 (3 H, d, *J* 7.0 Hz, Me), 3.46 (1 H, d, *J*$_{AB}$ 7.0 Hz, 4-H), 3.98 (1 H, d, *J*$_{AB}$ 7.0 Hz, 4-H), 5.04 (2 H, s, PhC*H*₂), 5.18 (2 H, s, PhC*H*₂), 5.62 (1 H, q, *J* 7.0 Hz, vinyl H), 5.68 (1 H, s, NCH), 6.91 (2 H, d, *J*$_{AB}$ 8.9 Hz, Ar), 7.13 (2 H, d, *J*$_{AB}$ 8.9 Hz, Ar), and 7.15—7.44 (10 H, m, Ph) and the (E)-*azetidin-2-one* **(16)**, $\nu_{max.}$ 2 960, 2 870, 1 735, 1 610, 1 305, and 1 180 cm⁻¹; δ (90 MHz) 1.68 (3 H, d, *J* 7.0 Hz, Me), 3.54 (1 H, d, *J*$_{AB}$ 7.1 Hz, 4-H), 4.07 (1 H, d, *J*$_{AB}$ 7.1 Hz, 4-H), 5.05 (2 H, s, PhC*H*₂), 5.19 (2 H, s, PhC*H*₂), 5.68 (1 H, s, NCH), 6.17 (1 H, q, *J* 7.0 Hz, vinyl H), 6.92 (2 H, d, *J*$_{AB}$ 8.8 Hz, Ar), 7.17 (2 H, d, *J*$_{AB}$ 8.8 Hz, Ar), and 7.18—7.46 (10 H, m, Ph); *m/z* 427 (*M*⁺, <1%), 292, and 91 (100) (Found: C, 75.65; H, 6.0; N, 3.15%. C₂₇H₂₅NO₄ requires C, 75.85; H, 5.89; N, 3.28%).

Preparation of (E)-3-Ethylidene-1-[(p-benzyloxyphenyl)-benzyloxycarbonylmethyl]azetidin-2-one **(16).**—A solution of methanesulphonyl chloride (23 mg, 0.20 mmol) in CH₂Cl₂ (0.5 ml) was added to a solution of the hydroxyethylazetidinones **(12)** and **(13)** (58 mg, 0.13 mmol) and triethylamine (36 μl, 0.26 mmol) in CH₂Cl₂ (3.5 ml) at 0 °C. After 1 h, the reaction was diluted with CH₂Cl₂ (10 ml), washed with 0.1M-aqueous HCl (2 ml), water, 5% aqueous NaHCO₃, and brine, dried, and evaporated to furnish the crude mesylates which were dissolved in CH₂Cl₂ (300 μl) and treated with DBU (22 mg, 0.22 mmol) at 0 °C. The reaction mixture was stirred for 3.5 h and then diluted with CH₂Cl₂ (10 ml) and washed with 10% aqueous citric acid, water, and brine. It was then dried (MgSO₄) and evaporated to give the *E*-enelactam **(16)** (54 mg, 97%), identical with previously prepared material above.

Preparation of 1-[(p-Benzyloxyphenyl)benzyloxycarbonylmethyl]azetidine-2,3-dione **(17).**—The enelactams **(15)** and **(16)** (60 mg, 0.14 mmol) in CH₂Cl₂ (8 ml) were treated with ozone at −25 °C until no starting material remained (by t.l.c.). Dimethyl sulphide was added, and the reaction stirred for 2 h. Solvent was removed and the residue chromatographed (80% ether–petroleum) to give the keto-lactam **(17)** (47 mg, 84%) as a syrup, $\nu_{max.}$ 2 920, 1 855, 1 780, 1 740, 1 610, 1 510, and 1 195 cm⁻¹; δ (250 MHz) 3.68 (1 H, d, *J* 10.2 Hz, 4-H), 4.31 (1 H, d, *J* 10.2 Hz, 4-H), 5.08 (2 H, s, PhC*H*₂), 5.22 (2 H, d, *J* 2.5 Hz, PhC*H*₂), 5.94 (1 H, s, NCH), 6.96 (2 H, dd, *J* 7.1 and 2.3 Hz, Ar), 7.16 (2 H, dd, *J* 7.1 and 2.3 Hz, Ar), and 7.21—7.48 (10 H, m, Ph).

Preparation of 3-(1'-Hydroxyethyl)-1-[(1'R)-(p-hydroxyphenyl)carboxymethyl]azetidin-2-ones **(18)** *and* **(19).**—A mixture of azetidin-2-ones **(10)** and **(11)** (70 mg, 0.16 mmol) in

Table 1. Atomic co-ordinates (× 10⁴) and temperature factors (Å² × 10³)

Atom	x	y	z
N(1)	2 438(5)	7 361(5)	8 803(1)
C(2)	1 605(6)	6 114(6)	8 948(1)
O(2)	−303(5)	5 603(4)	8 965(1)
C(3)	3 898(7)	5 737(5)	9 077(1)
C(4)	4 751(7)	7 158(7)	8 903(1)
C(5)	1 311(7)	8 575(5)	8 632(1)
C(6)	1 003(6)	10 155(6)	8 790(1)
O(6)	2 484(5)	11 142(5)	8 845(1)
O(7)	−1 091(4)	10 272(4)	8 872(1)
C(8)	−1 646(8)	11 663(6)	9 048(1)
C(9)	−1 093(7)	12 240(6)	9 330(1)
C(10)	−2 604(8)	10 337(8)	9 474(1)
C(11)	−2 130(11)	9 949(9)	9 736(1)
C(12)	−171(12)	10 472(10)	9 852(1)
C(13)	1 343(10)	11 400(9)	9 711(1)
C(14)	834(8)	11 779(8)	9 451(1)
C(15)	4 052(7)	6 015(6)	9 370(1)
C(16)	2 544(9)	6 977(9)	9 495(1)
C(17)	5 950(9)	5 229(9)	9 502(1)
C(18)	2 494(6)	8 806(5)	8 372(1)
C(19)	4 429(7)	9 687(6)	8 342(1)
C(20)	5 478(7)	9 824(6)	8 102(1)
C(21)	4 514(7)	9 037(6)	7 884(1)
C(22)	2 590(7)	8 109(6)	7 909(1)
C(23)	1 572(7)	8 001(6)	8 152(1)
C(24)	5 384(5)	9 069(4)	7 635(1)
C(25)	7 170(8)	10 165(7)	7 585(1)
C(26)	7 592(7)	10 171(7)	7 293(1)
C(27)	9 456(8)	9 442(7)	7 197(1)
C(28)	9 887(9)	9 459(8)	6 928(1)
C(29)	8 429(10)	10 227(9)	6 760(1)
C(30)	6 543(10)	10 959(9)	6 854(1)
C(31)	6 112(8)	10 942(8)	7 121(1)
N(1')	4 825(6)	4 080(6)	6 285(1)
C(2')	6 606(8)	3 514(10)	6 166(1)
O(2')	8 415(6)	4 166(9)	6 125(1)
C(3')	5 495(9)	1 903(7)	6 085(1)
C(4')	3 414(9)	2 647(8)	6 217(1)
C(5')	4 378(8)	5 703(8)	6 401(1)
C(6')	2 896(13)	6 770(9)	6 227(1)
O(6')	1 863(11)	7 963(8)	6 302(1)
O(7')	2 831(6)	6 299(5)	5 979(1)
C(8')	1 342(12)	7 224(11)	5 801(1)
C(9')	1 391(11)	6 394(10)	5 537(1)
C(10')	−302(12)	5 443(13)	5 457(1)
C(11')	−353(15)	4 661(15)	5 225(1)
C(12')	1 340(16)	4 772(17)	5 065(2)
C(13')	3 160(16)	5 738(18)	5 130(1)
C(14')	3 180(13)	6 607(12)	5 376(1)
C(15')	5 431(11)	1 462(9)	5 803(1)
C(16')	3 993(15)	2 080(13)	5 631(1)
C(17')	7 206(16)	473(18)	5 723(1)
C(18')	3 524(7)	5 566(7)	6 680(1)
C(19')	4 768(7)	6 223(7)	6 890(1)
C(20')	4 010(7)	6 057(7)	7 146(1)
C(21')	2 052(7)	5 233(7)	7 193(1)
C(22')	753(7)	4 561(8)	6 986(1)
C(23')	1 549(7)	4 780(8)	6 730(1)
O(24')	1 447(5)	5 125(4)	7 453(1)
C(25')	−484(8)	4 188(8)	7 510(1)
C(26')	−848(7)	4 174(6)	7 804(1)
C(27')	718(8)	3 468(7)	7 974(1)
C(28')	313(8)	3 422(7)	8 243(1)
C(29')	−1 647(8)	4 080(8)	8 338(1)
C(30')	−3 189(8)	4 760(7)	8 169(1)
C(31')	−2 780(7)	4 818(7)	7 903(1)

Table 2. Bond lengths (Å)

N(1)–C(2)	1.341(5)	N(1)–C(4)	1.460(5)
N(1)–C(5)	1.453(5)	C(2)–O(2)	1.207(5)
C(2)–C(3)	1.525(6)	C(3)–C(4)	1.533(6)
C(3)–C(15)	1.503(6)	C(5)–C(6)	1.510(6)
C(5)–C(18)	1.516(5)	C(6)–O(6)	1.207(5)
C(6)–O(7)	1.321(5)	O(7)–C(8)	1.468(6)
C(8)–C(9)	1.497(6)	C(9)–C(10)	1.374(7)
C(9)–C(14)	1.357(6)	C(10)–C(11)	1.385(7)
C(11)–C(12)	1.356(9)	C(12)–C(13)	1.376(10)
C(13)–C(14)	1.377(7)	C(15)–C(16)	1.347(7)
C(15)–C(17)	1.440(7)	C(18)–C(19)	1.358(6)
C(18)–C(23)	1.388(5)	C(19)–C(20)	1.385(5)
C(20)–C(21)	1.382(6)	C(21)–C(22)	1.369(6)
C(21)–O(24)	1.374(5)	C(22)–C(23)	1.389(6)
O(24)–C(25)	1.401(6)	C(25)–C(26)	1.506(6)
C(26)–C(27)	1.352(5)	C(26)–C(31)	1.370(7)
C(27)–C(28)	1.393(6)	C(28)–C(29)	1.346(8)
C(29)–C(30)	1.359(9)	C(30)–C(31)	1.384(7)
N(1')–C(2')	1.309(7)	N(1')–C(4')	1.454(7)
N(1')–C(5')	1.450(7)	C(2')–O(2')	1.214(7)
C(2')–C(3')	1.499(9)	C(3')–C(4')	1.538(8)
C(3')–C(15')	1.470(8)	C(5')–C(6')	1.494(8)
C(5')–C(18')	1.522(6)	C(6')–O(6')	1.199(9)
C(6')–O(7')	1.314(6)	O(7')–C(8')	1.450(8)
C(8')–C(9')	1.496(8)	C(9')–C(10')	1.316(11)
C(9')–C(14')	1.363(9)	C(10')–C(11')	1.332(11)
C(11')–C(12')	1.308(12)	C(12')–C(13')	1.361(15)
C(13')–C(14')	1.428(12)	C(15')–C(16')	1.303(10)
C(15')–C(17')	1.384(13)	C(18')–C(19')	1.382(6)
C(18')–C(23')	1.357(7)	C(19')–C(20')	1.392(6)
C(20')–C(21')	1.361(6)	C(21')–C(22')	1.397(6)
C(21')–O(24')	1.376(5)	C(22')–C(23')	1.401(6)
O(24')–C(25')	1.404(6)	C(25')–C(26')	1.511(6)
C(26')–C(27')	1.374(6)	C(26')–C(31')	1.362(6)
C(27')–C(28')	1.392(7)	C(28')–C(29')	1.371(7)
C(29')–C(30')	1.352(7)	C(30')–C(31')	1.376(6)

Table 3. Bond angles (°)

C(2)–N(1)–C(4)	94.6(3)	C(2)–N(1)–C(5)	130.9(3)
C(4)–N(1)–C(5)	134.1(4)	N(1)–C(2)–O(2)	130.2(4)
N(1)–C(2)–C(3)	92.7(3)	O(2)–C(2)–C(3)	137.0(4)
C(2)–C(3)–C(4)	84.7(3)	C(2)–C(3)–C(15)	115.4(3)
C(4)–C(3)–C(15)	116.7(4)	N(1)–C(4)–C(3)	87.9(3)
N(1)–C(5)–C(6)	107.4(3)	N(1)–C(5)–C(18)	112.5(3)
C(6)–C(5)–C(18)	115.2(3)	C(5)–C(6)–O(6)	124.8(4)
C(5)–C(6)–O(7)	110.6(3)	O(6)–C(6)–O(7)	124.5(4)
C(6)–O(7)–C(8)	117.9(3)	O(7)–C(8)–C(9)	111.3(4)
C(8)–C(9)–C(10)	119.7(4)	C(8)–C(9)–C(14)	121.7(4)
C(10)–C(9)–C(14)	118.5(4)	C(9)–C(10)–C(11)	120.5(5)
C(10)–C(11)–C(12)	120.0(6)	C(11)–C(12)–C(13)	120.2(5)
C(12)–C(13)–C(14)	118.9(5)	C(9)–C(14)–C(13)	121.9(5)
C(3)–C(15)–C(16)	121.4(4)	C(3)–C(15)–C(17)	115.1(4)
C(16)–C(15)–C(17)	123.4(4)	C(5)–C(18)–C(19)	124.8(3)
C(5)–C(18)–C(23)	117.3(3)	C(19)–C(18)–C(23)	117.8(3)
C(18)–C(19)–C(20)	122.5(4)	C(19)–C(20)–C(21)	118.8(4)
C(20)–C(21)–C(22)	120.2(4)	C(20)–C(21)–O(24)	124.6(4)
C(22)–C(21)–O(24)	115.2(4)	C(21)–C(22)–C(23)	119.7(4)
C(18)–C(23)–C(22)	120.9(4)	C(21)–O(24)–C(25)	118.6(3)
O(24)–C(25)–C(26)	108.9(4)	C(25)–C(26)–C(27)	120.8(4)
C(25)–C(26)–C(31)	120.6(4)	C(27)–C(26)–C(31)	118.6(4)
C(26)–C(27)–C(28)	121.5(4)	C(27)–C(28)–C(29)	119.5(5)
C(28)–C(29)–C(30)	119.7(5)	C(29)–C(30)–C(31)	120.8(5)
C(26)–C(31)–C(30)	119.9(5)	C(2')–N(1')–C(4')	94.9(5)
C(2')–N(1')–C(5')	130.7(5)	C(4')–N(1')–C(5')	133.6(4)
N(1')–C(2')–O(2')	131.0(7)	N(1')–C(2')–C(3')	94.0(4)
O(2')–C(2')–C(3')	134.9(6)	C(2')–C(3')–C(4')	84.3(4)
C(2')–C(3')–C(15')	118.3(5)	C(4')–C(3')–C(15')	120.9(5)
N(1')–C(4')–C(3')	86.8(4)	N(1')–C(5')–C(6')	112.5(4)
N(1')–C(5')–C(18')	112.4(4)	C(6')–C(5')–C(18')	112.7(4)
C(5')–C(6')–O(6')	124.5(4)	C(5')–C(6')–O(7')	113.9(6)
O(6')–C(6')–O(7')	121.7(6)	C(6')–O(7')–C(8')	117.0(5)
O(7')–C(8')–C(9')	107.9(6)	C(8')–C(9')–C(10')	120.2(6)
C(8')–C(9')–C(14')	120.8(6)	C(10')–C(9')–C(14')	119.0(6)
C(9')–C(10')–C(11')	123.1(7)	C(10')–C(11')–C(12')	120.9(9)
C(11')–C(12')–C(13')	120.2(9)	C(12')–C(13')–C(14')	118.6(8)
C(9')–C(14')–C(13')	118.1(8)	C(3')–C(15')–C(16')	124.1(6)
C(3')–C(15')–C(17')	114.8(6)	C(16')–C(15')–C(17')	120.7(7)
C(5')–C(18')–C(19')	120.4(4)	C(5')–C(18')–C(23')	120.9(4)
C(19')–C(18')–C(23')	118.7(4)	C(18')–C(19')–C(20')	120.2(4)
C(19')–C(20')–C(21')	120.4(4)	C(20')–C(21')–C(22')	120.8(4)
C(20')–C(21')–O(24')	116.2(4)	C(22')–C(21')–O(24')	123.1(4)
C(21')–C(22')–C(23')	117.2(4)	C(18')–C(23')–C(22')	122.7(4)
C(21')–O(24')–C(25')	117.6(3)	O(24')–C(25')–C(26')	110.0(4)
C(25')–C(26')–C(27')	120.9(4)	C(25')–C(26')–C(31')	120.1(4)
C(27')–C(26')–C(31')	119.0(4)	C(26')–C(27')–C(28')	119.8(4)
C(27')–C(28')–C(29')	119.9(5)	C(28')–C(29')–C(30')	120.0(4)
C(29')–C(30')–C(21')	120.1(5)	C(26')–C(31')–C(30')	121.1(4)

ethanol (10 ml) with 10% palladium on charcoal (10 mg) was stirred in a pressure bottle under 2 atm of hydrogen for 2 h. The suspension was filtered through a pad of Celite and the filtrate concentrated to give the debenzylated azetidin-2-ones (18) (35 mg, 82%), $\nu_{max.}$ 3 400, 3 050, 2 960, 2 930, 2 900, 2 600, 1 740, 1 610, 1 510, 1 380, 1 240, and 1 015 cm^{-1}; δ (250 MHz; D$_2$O) 1.03 (3 H, d, J 7.0 Hz, Me), 2.85 (1 H, m, *trans*-4-H), 3.15 (1 H, m, 3-H), 3.42 (1 H, m, *cis*-4-H), 3.90 (1 H, m, CH$_3$C*H*OH), 5.30 (1 H, s, NCH), 6.79 (4 H, d, J 8.3 Hz, Ar); (19) δ (250 MHz, D$_2$O), 1.13 (3 H, d, J 7.0 Hz, CH$_3$), 3.08, 3.15, and 3.28 (3 H, m, 3-H, *trans*-4-H and *cis*-4-H), 4.02 (1 H, m, CH$_3$C*H*OH), 5.26 (1 H, s, NC*H*Ar), and 6.79 and 7.12 (3 H, d, J 8.3 Hz, Ar).

Preparation of (−)-1-[(p-Benzyloxyphenyl)benzyloxycarbonylmethyl]azetidine-2,3-dione (3).—Dimethyl t-butylsilyltrifluoromethane sulphonate (34 μl, 0.15 mmol) was added dropwise to a stirred solution of the diastereoisomeric mixture of acetylazetidinones (10) and (11) (63 mg, 0.14 mmol) and triethylamine (26 μl, 0.19 mmol) in 1,2-dichloroethane (1 ml) under argon at 0 °C. After 10 min the reaction mixture was diluted with CH$_2$Cl$_2$ (80 ml) and methanol (8 ml) and treated with ozone at −78 °C until no starting material was present by t.l.c. (60% ether–petroleum). Powdered zinc (373 mg, 5.7 mmol) and glacial acetic acid (1 ml) were then added and the solution warmed to room temperature. It was then passed through a pad of Celite and the solvent removed to leave a residue which was partitioned between water (5 ml) and diethyl ether (10 ml). The organic phase was then washed with water (5 ml) and dried. Solvent was removed and the residue chromatographed [80% ether–petroleum (b.p. 40—60 °C)] to give the azetidine-2, 3-di-

one (3) as a syrup (49 mg, 84%) the spectral data for which were identical with those of compound (17); $[\alpha]_D^{29}$ −33.2° (*c*, 0.46 in CHCl$_3$).

Crystallographic Analyses of (3R)-1-[(1'R)-(p-Benzyloxyphenyl)benzyloxycarbonylmethyl]-3-isopropenylazetidin-2-one (8).—C$_{28}$H$_{27}$O$_4$N, M = 441.5, monoclinic, a = 5.929(1) b = 7.985(1), c = 50.712(13) Å, β = 91.31(2)°, U = 2 400 Å^3, space group $P2_1$, Z = 4 (two crystallographically independent molecules in the asymmetric unit), D_c = 1.23 g cm^{-3}. Refined unit-cell parameters were obtained by centring 25 reflections on a Nicolet R3m diffractometer. 3 534 Independent reflections were measured (θ ⩽ 58°) with Cu-K_α radiation (graphite monochromator) and using ω scans. 2 797 Had $|F_o| > 3\sigma(|F_o|)$ and were considered to be observed. The data were corrected for Lorentz and polarisation factors; no absorption correction was applied.

Despite the presence of 66 non-hydrogen atoms in the asymmetric unit, the structure was solved straightforwardly by

direct methods and ΔE-map recycling. The non-hydrogen atoms were refined anisotropically. The positions of the β-lactam (C-3 and C-3′) hydrogen atoms, also those of the methyl groups were found in a ΔF-map. The former were refined isotropically and the methyl groups were refined as rigid bodies. All the other hydrogen atom positions were idealised (C–H = 0.96 Å), assigned isotropic thermal parameters, $U(H) = 1.2$ U_{eq} (C) and allowed to ride on their parent carbons. Refinement was by block-cascade full-matrix least-squares to $R = 0.051$, $R_w = 0.052$, $[w^{-1} = \sigma^2(F) + 0.000\,55F^2]$. Computations were carried out on an Eclipse S140 Computer using the SHELXTL program system.[16] The fractional atomic co-ordinates are given in Table 1. Tables 2 and 3 give the bond lengths and valence angles. The fractional co-ordinates of the hydrogen atoms and their isotropic thermal parameters and the thermal parameters of the non-hydrogen atoms, have been deposited as Supplementary Data, Sup. No. 56307 (6 pp.).* The observed and calculated structure factors are available on request from the Editorial office.

The two crystallographically independent molecules have markedly different conformations [Figures 1 (a), (b)]; whereas in both molecules the lactam and phenyl rings are similarly orientated with respect to each other, notably both the propenyl group and the benzyl ester carbonyl adapt very different orientations to the lactam ring in the two molecules. The N(1),C(5),C(6),O(6) torsion angle is 76° cf. 161° for N(1′),C(5′),C(6′),O(6′) and the C(4),C(3),C15),C(16) torsion angle is 78° cf. 21° for C(4′),C(3′),C(15′),C(16′). The terminal benzyl ring [C(26)—C(31)] is also differently orientated.

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

References
1 H. Aoki, H. Sakai, M. Kohsaka, T. Konomi, J. Hosada, Y. Kubochi, E. Iguchi, and H. Imanaka, J. Antibiot., 1976, 29, 492; M. Hashimoto, T. Komori, and T. Kamiya, J. Am. Chem. Soc., 1976, 98, 3023; J. Antibiot., 1976, 29, 890.
2 T. Kamiya, M. Hashimoto, O. Nakaguchi, and T. Oku, Tetrahedron, 1979, 35, 323.
3 G. A. Koppel, L. McShane, F. Jose, and R. D. G. Cooper, J. Am. Chem. Soc., 1978, 100, 3933.
4 H. H. Wasserman and D. L. Hlasta, J. Am. Chem. Soc., 1978, 100, 6780.
5 K. Chiba, M. Mori, and Y. Ban, J. Chem. Soc., Chem. Commun., 1980, 770.
6 P. G. Mattingly and M. J. Miller, J. Org. Chem., 1981, 46, 1557.
7 M. Hatanaka, N. Noguchi, and T. Ishimaru, Bull. Chem. Soc. Jpn., 1982, 55, 1234.
8 G. D. Annis, E. M. Hebblethwaite, and S. V. Ley, J. Chem. Soc. Chem. Commun., 1980, 297.
9 G. D. Annis, E. M. Hebblethwaite, S. T. Hodgson, D. M. Hollinshead, and S. V. Ley, J. Chem. Soc., Perkin Trans. 1, 1983, 2851.
10 S. T. Hodgson, D. M. Hollinshead and S. V. Ley, J. Chem. Soc., Chem. Commun., 1984, 494.
11 A. M. Horton, D. M. Hollinshead and S. V. Ley, Tetrahedron, 1984, 40, 1737.
12 (a) F. A. Bouffard and B. G. Christensen, J. Org. Chem., 1981, 46, 2208; (b) F. Pacquet and J. d'Angelo, Tetrahedron Lett., 1982, 23, 2777; (c) T. Kametani, T. Nagahara, and M. Ihara, Heterocycles, 1981, 16, 539.
13 E.g. L. M. Jackman and S. Sternhell, 'Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry' 2nd edn., Pergamon Press, Oxford, 1978.
14 C. A. Townsend and L. T. Nguyen, Tetrahedron Lett., 1982, 23, 4859.
15 E.g. R. W. Ratcliffe and G. Albers-Schönberg, in 'Chemistry and Biology of β-Lactam Antibiotics', Ed. R. B. Morin and M. Gorman, Acad. Press, N.Y. 1982, vol. 2, 227.
16 G. M. Sheldrick, SHEXTL An Integrated System for Solving, Refining, and Displaying Crystal Structures from Diffraction Data, University of Gottingen, Federal Republic of Germany, Revision 4.0, 1983.