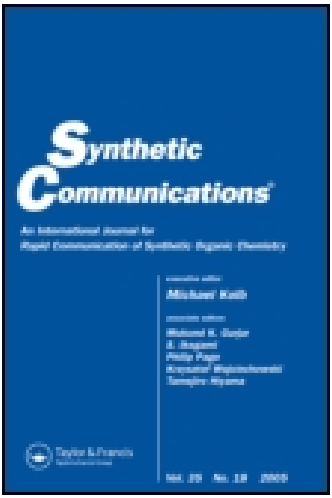

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SYNTHESIS OF EXOCYCLIC ENAMIDES VIA STEREOCONTROLLED ALLYLIC ISOMERIZATION AND 1,3-TRANSPOSITION

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SYNTHESIS OF EXOCYCLIC ENAMIDES VIA STEREOCONTROLLED ALLYLIC ISOMERIZATION AND 1,3-TRANSPOSITION

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ABSTRACT

In the presence of pyridinium *para*-toluenesulfonate (PPTS) an allylic alcohol moiety exocyclic to a lactam ring undergoes allylic isomerisation, or if the solvent is nucleophilic, 1,3-transposition can occur. All the rearrangements occurred with stereocontrol.

Acyclic enamides are valuable precursors for asymmetric reduction to chiral nitrogen compounds,[1] among other uses in synthesis. However, cyclic enamides, in which the double bond is exocyclic, are less common,[2] and perhaps in consequence have been used relatively little in synthesis. Most of those that have been prepared possess an alkoxycarbonyl group attached to

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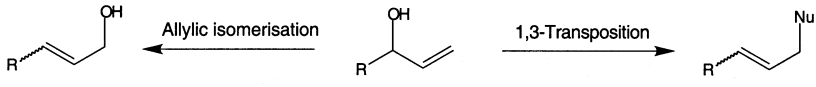
the exocyclic double bond,[3] formed for example at high temperatures by the condensation of stabilised ylides with cyclic imides.[4] We here report mild and stereocontrolled routes to enamides containing an hydroxymethyl, hydroxyalkyl, or bromomethyl group.

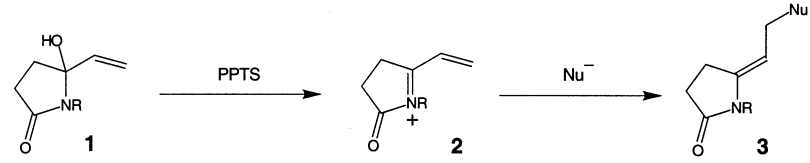
We reasoned that the ability of allylic alcohols to undergo allylic isomerisation or 1,3-transposition reactions[5] (Scheme 1) could be exploited in the context of the lactams **1**. The intramolecular transpositions frequently occur with excellent stereocontrol owing to sigmatropic rearrangements.[6,7] On the other hand, intermolecular 1,3-transpositions can be troublesome; early work showed that mineral acids often gave equilibrium mixtures or were incompatible with other functional groups.[8] Such 1,3-transpositions have been improved by the use of a catalytic combination of tetrabutylammonium perrhenate and *para*-toluenesulfonic acid,[9] but even so tertiary allylic alcohols underwent dehydration rather than isomerisation.



Scheme 1. Modes of reactions of an allylic alchol.

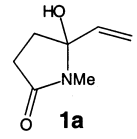
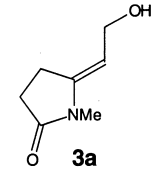
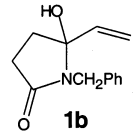
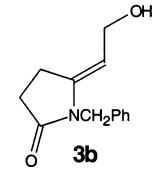
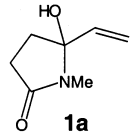
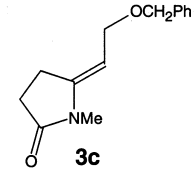
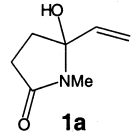
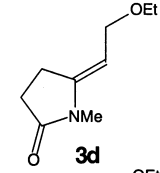
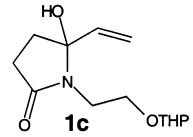
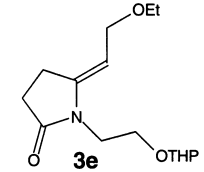
We report here some allylic isomerisations and 1,3-transpositions of tertiary allylic alcohols of type **1** with a catalytic amount of pyridinium para-toluenesulfonate (PPTS)[10] to give primary allylic alcohols and allylic ethers (Table 1). An acyliminium species **2**, an excellent electrophile,[11] is believed to be formed, followed by nucleophilic attack (Scheme 2). By other means, peroxides and allyl bromides can be prepared. For all of the above reactions, NMR data were consistent with the presence of only one alkene isomer, and in one case (bromide **6**, Scheme 4), that was shown by nOe experiments to have the *E*-configuration, as in **3**.

Table 1 shows some allylic isomerisations and 1,3-transpositions of the tertiary allylic alcohols **1**. Non-nucleophilic solvents such as dichloromethane (entry 1) have been used to effect allylic isomerisation.[12]

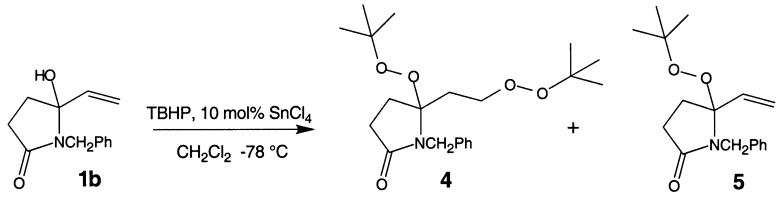


Scheme 2. Stereocontrolled rearrangements of allylic alcohols.

Table 1. Reaction of Allylic Alcohols with PPTS

Entry	Allylic Alcohol	Conditions	Products	Yield (%)
1	 **1a**	CH_2Cl_2 2 h	 **3a**	72
2	 **1b**	CH_2=CHOAc 0.5 h	 **3b**	40
3	 **1a**	$PhCH_2OH$ 2 h	 **3c**	81
4	 **1a**	EtOH 0.5 h	 **3d**	71
5	 **1c**	EtOH 0.5 h	 **3e**	98

It was hoped that the use of vinyl acetate as the solvent would generate the vinyl ether, prior to a [3,3]-sigmatropic rearrangement; however, only allylic isomerisation was observed (entry 2). The use of alcohols as solvents gave allylic ethers in all cases (entries 3–5). Treatment of 5-hydroxy-1-(2-hydroxyethyl)-5-vinyl-2-pyrrolidinone with PPTS in dichloromethane induced decomposition, no intramolecular 1,3-transposition (with or without cycli-



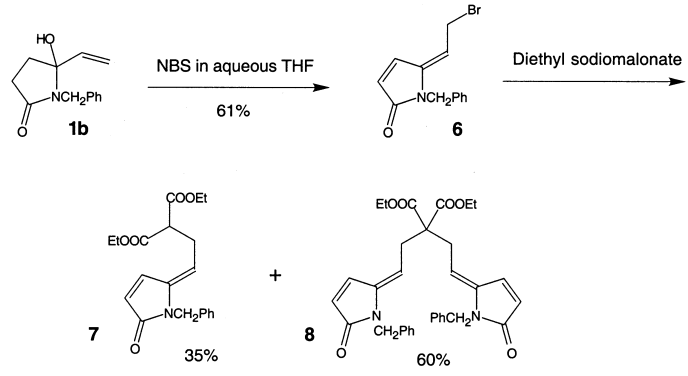
Scheme 3. Diperoxide formation involving a 1,3-transposition.

sation) being observed, so that protection of the hydroxy group as **1c** proved necessary.

Reaction of **1b** with an alkyl peroxide nucleophile was also effective; in tin (IV) chloride (10 mol%) in the presence of *tert*-butyl hydroperoxide (2.3 mol equiv.) gave the α,γ-diperoxide **4** (Scheme 3). Formation of the peroxides **4** and **5** is believed to involve acyliminium cations generated by attack of $SnCl_4$ on the hydroxy group of **1b** and subsequent expulsion of an oxo-tin moiety.

Treatment of allylic alcohol **1b** with *N*-bromosuccinimide in aqueous THF also induced 1,3-transposition, affording the allylic bromide **6** (Scheme 4) as a single diastereoisomer.[9] The bromide **6** underwent displacement with malonate anion to give esters **7** and **8**, showing that the functionalised allylic lactams can be used in C–C bond formation.

In conclusion, allylic isomerisations and transpositions have been shown to occur with PPTS under mild conditions, compatible with sensitive functionality. The formation of free hydroxyl groups is notable, and was not directly achievable *via* rearrangements of unsaturated esters.[7] The stereocontrolled formation of an exocyclic allylic alcohol unit is well-suited to



Scheme 4. Oxidative transposition followed by alkylation of malonate.

further functionalisation, *e.g.* asymmetric epoxidation, and hence may find use in total synthesis. The uses of other nucleophiles such as thiols or amines for these 1,3-transposition reactions are to be investigated.

EXPERIMENTAL

General. All melting points were determined on a microscope hot-stage apparatus. ^{1}H and ^{13}C NMR spectra were run on a Bruker AM-250 instrument at 250 and 68.8 MHz respectively. Combustion analyses were carried out using a Perkin Elmer 2400 CHN elemental analyzer. Mass spectra were obtained on a Kratos MS-50 RF spectrometer. Infrared spectra were recorded on a Perkin Elmer FT-IR 1720 instrument. Thin-layer chromatography was performed on Merck 0.2 mm aluminium-backed silica gel 60 F_{254} plates and visualized using an alkaline $KMnO_4$ spray or by ultraviolet light. Flash column chromatography was performed using Merk 0.040 to 0.063 mm, 230 to 400 mesh silica gel. Petroleum ether (40–60°C fraction) and ethyl acetate were distilled before use; tetrahydrofuran was distilled from sodium and benzophenone; dichloromethane was distilled from calcium hydride. Evaporation refers to the removal of solvent under reduced pressure.

The following compounds were prepared by literature procedures: 5-hydroxy-1-methyl-5-vinyl-2-pyrrolidinone;[13] and 1-(2-hydroxyethyl)-2,5-pyrrolidinedione.[14]

***N*-Methylsuccinimide**. A mixture of succinimide (5.0 g, 50.5 mmol), methyl iodide (7.88 g, 55.5 mmol) and anhydrous potassium cabonate (8.37 g, 60.6 mmol) was heated at reflux in anhydrous acetone (75 ml) for 4 h and give a fine precipitate of potassium bromide. After cooling to 20°C the mixture was filtered and the acetone evaporated to give a solid, to which a small amount of dichloromethane was added. Filtration gave ***N*-Methylsuccinimide** as a white solid (5.59 g, 98%); mp 68–70°C (ethyl acetate/petroleum ether), lit.[15] mp 64°C.

***N*-Benzylsuccinimide**. A mixture of succinimide (2.0 g, 20.2 mmol), benzyl bromide (3.80 g, 22.2 mmol) and anhydrous potassium carbonate (3.35 g, 24.2 mmol) was heated at reflux in anhydrous acetone (30 ml) for 2.5 h, and gave a fine white precipitate of potassium bromide. After cooling to 20°C the mixture was filtered and the acetone evaporated to give a pale orange solid which was recrystallised from ethyl acetate/light petroleum ether to give ***N*-benzylsuccinimide** as white platelets (3.06 g, 94%); mp 103–104°C, lit.[16] mp 100–103°C; ^{1}H NMR ($CDCl_3$) δ 7.45–7.10 (5H, m, Ar), 4.61 (2H, s, CH_2Ph), 2.64 (4H, s, CH_2CO); ^{13}C NMR ($CDCl_3$) δ 176.9 (s), 135.8 (s), 128.9 (d), 128.6 (d), 128.0 (d), 42.4 (t) 28.2 (t).

5-Hydroxy-1-(2-hydroxyethyl)-5-vinylpyrrolidin-2-one. To a stirred solution of 1-(2-hydroxyethyl)pyrrolidine-2,5-dione (2.0 g, 14.0 mmol) in THF (100 ml), cooled to −78°C, was added vinylmagnesium bromide (34.9 ml, 34.9 mmol, 1 M solution in THF) dropwise. The cooling bath was then removed and the mixture stirred at 20°C for 1.5 h. It was then poured onto saturated ammonium chloride (40 ml), the layers separated and the aqueous layer extracted with ether (2 × 20 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to give an orange oil. This was purified by column chromatography (95:5 ethyl acetate: 40–60°C petroleum ether) to give **5-hydroxy-1-(2-hydroxyethyl)-5-vinylpyrrolidin-2-one** as a colourless oil (0.39 g, 16%); IR, ν_{max} (thin film): 3340 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.85 (1H, dd, $J = 15.5$ Hz, $J = 8.0$ Hz, =CH), 5.40 (1H, dd, $J = 15.5$ Hz, $J = 1.3$ Hz, $=CH_2$), 5.33 (1H, dd, $J = 8.0$ Hz, $J = 1.3$ Hz, $=CH_2$), 5.05–3.40 (4H, m), 2.40–2.05 (4H, m); ^{13}C NMR ($CDCl_3$) δ 176.1 (s), 139.2 (d), 117.3 (t), 98.3 (s), 39.4 (t), 65.5 (t), 30.4 (t), 28.3 (t); m/z (EI): 171 (M^+, 37%), 155 (16%), 145 (20%), 115 (39%), 82 (41%), 55 (100%); HRMS, M^+ found 171.0903, $C_8H_{13}NO_3$ requires 171.0895.

1-[2-(Tetrahydropyran-2-yloxy)ethyl]pyrrolidine-2,5-dione. To 1-(2-hydroxyethyl)pyrrolidine-2,5-dione (3.0 g, 21.0 mmol) in dichloromethane (150 ml) was added dihydropyran (2.64 g, 31.4 mmol) then pyridinium *para*-toluenesulfonate (0.53 g, 2.10 mmol) and the mixture heated at reflux for 40 min. It was then cooled, washed with half-saturated brine, dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography (60:40 ethyl acetate: 40–60°C petroleum ether) to give **1-[2-(tetrahydropyran-2-yloxy)ethyl]pyrrolidine-2,5-dione** as a white microprisms (4.42 g, 93%); mp 82–84°C (ethyl acetate/petroleum ether); IR, ν_{max} (nujol mull): 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.80 (1H, m, OC*H*O), 3.90–3.40 (6H, m), 2.71 (4H, s, $COCH_2$), 1.85–1.40 (6H, 3); ^{13}C NMR ($CDCl_3$) δ 177.1 (s), 98.2 (d), 63.0 (t), 62.3 (t), 38.3 (t), 30.4 (t), 28.2 (t), 25.4 (t), 19.3 (t); m/z (EI): 227 (M^+, 100%), 207 (56%), 186 (22%), 155 (32%), 108 (72%); HRMS, M^+ found 227.1146, $C_{11}H_{17}NO_4$ requires 227.1157.

1-Benzyl-5-hydroxy-5-vinylpyrrolidin-2-one (1b). *N*-benzylsuccinimide (2.0 g, 10.6 mmol) in THF (80 ml) was cooled in an ice-salt mixture and treated dropwise with vinylmagnesium bromide (15.9 ml, 15.9 mmol, 1M solution in THF). When the addition was complete the mixture was allowed to stir at 0°C for 1.5 h. It was then poured onto saturated aqueous ammonium chloride (40 ml), the layers separated and the aqueous layer extracted with diethyl ether (3 × 15 ml). The combined organic extracts were dried ($MgSO_4$), evaporated, and the residue purified by column chromatography (55:45 ethyl acetate: 40–60°C petroleum ether) to give **1b** as an oily solid (2.14 g, 93%); IR, ν_{max} (thin film): 3330, 1670, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35–7.10 (5H, m, Ar), 5.66 (1H,

dd, $J = 17.0$ Hz, $J = 11.0$ Hz, $=CH$), 5.42 (1H, dd, $J = 17.0$ Hz, $J = 1.0$ Hz, $=CH_2$), 5.17 (1H, dd, $J = 11.0$ Hz, $J = 1.0$ Hz, $=CH_2$), 4.35 (2H, s, NCH_2), 2.70–1.90 (4H, m); ^{13}C NMR ($CDCl_3$) δ 175.7 (s), 139.2 (d), 138.2 (s), 128.4 (d), 128.3 (d), 127.1 (d), 116.6 (t), 91.3 (s), 43.0 (t), 34.3 (t), 29.1 (t); m/z (EI): 217 (M^+, 22%), 199 (89%), 170 (60%), 146 (11%), 106 (62%), 91 (100%), 84 (42%), 65 (62%); HRMS, M^+ found 217.1102, $C_{13}H_{15}NO_2$ requires 217.1103.

5-Hydroxy-1-[2-(tetrahydropyran-2-yloxy)ethyl]-5-vinylpyrrolidin-2-one (1c). To a solution of 1-[2-(tetrahydropyran-2-yloxy)ethyl]pyrrolidine-2,5-dione (2.0 g, 8.80 mmol) in THF (70 ml), cooled to −78°C, was added vinylmagnesium bromide (13.2 ml, 13.2 mmol, 1M solution in THF) dropwise. When the addition was complete the mixture was stirred at 20°C for 4 h. It was then poured onto saturated ammonium chloride (30 ml), the layers separated and the aqueous layer extracted with diethyl ether (2×20 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to give an orange oil which was purified by column chromatography (70:30 ethyl acetate: 40–60°C petroleum ether) to give **1c** as a colourless oil (1.24 g, 55%), IR, ν_{max} (thin film): 3330, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.82 (1H, m, $=CH$), 5.64–5.50 (1H, m, $=CH_2$), 5.44–5.30 (1H, m, $=CH_2$), 4.64 (1H, m, $OCHO$), 4.00–3.35 (6H, m), 3.20–3.04 (1H, m), 2.80–2.55 (1H, m), 2.45–2.25 (1H, m), 2.20–1.30 (7H, m); ^{13}C NMR ($CDCl_3$) δ 176.7 (s), 176.6 (s), 139.9 (d), 117.5 (t), 117.3 (t), 98.9 (d), 98.8 (d), 90.1 (s), 65.6 (t), 65.2 (t), 62.5 (t), 62.3 (t), 40.1 (t), 39.7 (t), 34.0 (t), 33.8 (t), 30.1 (t), 29.3 (t), 25.2 (t), 25.0 (t), 19.4 (t), 19.2 (t); m/z (FAB): 278 (MNa^+, 32%), 256 (20%), 238 (70%), 172 (32%), 154 (100%), 111 (28%); HRMS, MNa^+ found 278.1380, $C_{13}H_{21}NO_4Na$ requires 278.1368.

5-(2-Hydroxyethylidene)-1-methylpyrrolidin-2-one (3a). To a solution of 5-hydroxy-1-methyl-5-vinylpyrrolidin-2-one[13] (0.20 g, 1.42 mmol) in ethanol free dichloromethane (10 ml) was added pyridinium *para*-toluenesulfonate (36 mg, 0.14 mmol). The mixture was then stirred at 20°C for 2 h, diluted with diethyl ether, washed with half-saturated brine and the organic layer dried ($MgSO_4$) and evaporated to give an oil which was purified by column chromatography (90:10 ethyl acetate: 40–60°C petroleum ether) to give **3a** as a colourless oil (142 mg, 71%); IR, ν_{max} (thin film): 3380, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.84 (1H, tt, $J = 7.5$ Hz, $J = 2.0$ Hz, $=CH_2$) 3.98 (2H, d, $J = 7.5$ Hz, CH_2OH), 2.88 (3H, s, CH_3), 2.70 (2H, m, CH_2CO), 2.45 (2H, m, $=CCH_2$); ^{13}C NMR ($CDCl_3$) δ 175.8 (s), 145.8 (s), 96.4 (d), 65.5 (t), 28.6 (t), 26.6 (q), 21.2 (t); m/z (EI) 141 (M^+, 48%), 124 (100%), 119 (13%), 114 (47%), 98 (42%), 88 (33%), 84 (69%), 68 (59%), 57 (79%); HRMS, M^+ found 141.0783, $C_7H_{11}NO_2$ requires 141.0790.

1-Benzyl-5-(2-hydroxyethylidene)pyrrolidin-2-one (3b). To a solution of **1b** (0.1 g, 0.46 mmol) in vinyl acetate (5 ml) was added pyridinium *para*-toluenesulfonate (13 mg, 0.046 mmol) and the solution stirred at 20°C for 0.5 h. Sodium hydrogen carbonate (0.2 g) was added and the solution filtered and evaporated. The residue was purified by column chromatography (80:20 ethyl acetate: 40–60°C petroleum ether) to give **3b** as a clear oil (40 mg, 40%); IR, ν_{max} (thin film): 3380, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–7.00 (5H, m, Ar), 4.82 (1H, tt, $J = 7.5$ Hz, $J = 2$ Hz, $=CH$), 4.68 (2H, s, CH_2Ph), 8.83 (2H, d, $J = 7.5$ Hz, CH_2OH), 2.70–2.40 (4H, m); ^{13}C NMR ($CDCl_3$) δ 175.9 (s), 144.2 (s), 136.0 (s), 128.7 (d), 127.4 (d), 127.3 (d), 97.7 (d), 65.0 (t), 43.9 (t), 28.6 (t), 21.3 (t); m/z (FAB): 218 (M^+, 72%), 197 (32%), 182 (62%), 160 (100%), 139 (25%); HRMS, MH^+ found 218.1181, $C_{13}H_{16}NO_2$ requires 218.1190.

5-(2-Benzyloxyethylidene)-1-methylpyrrolidin-2-one (3c). A mixture of 5-hydroxy-1-methyl-5-vinylpyrrolidin-2-one[13] (0.20 g, 1.42 mmol) and benzyl alcohol (4.0 g, 37 mmol) in THF (15 ml) was cooled to 0°C and then treated with a catalytic quantity of pyridinium *para*-toluenesulfonate. The mixture was then stirred at 20°C for 2 h, diluted with diethyl ether (20 ml) and washed with half-saturated brine. The organic layer was dried ($MgSO_4$) and evaporated to give an oil which was purified by Kugelrohr distillation (90°C/0.2 mm Hg) followed by column chromatography (30:70 ethyl acetate: 40–60°C petroleum ether) to give **3c** as a light orange oil (0.25 g, 81%); IR, ν_{max} (thin film): 1690, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (5H, m, Ar), 4.90 (1H, tt, $J = 7.5$ Hz, $J = 2.0$ Hz, $=CH$) 4.52 (2H, s, CH_2Ph), 4.05 (2H, d, $J = 7.5$ Hz, CH_2OBn), 2.95 (3H, s, CH_3), 2.80–2.60 (2H, m, CH_2CO), 2.55–2.40 (2H, m, $=CCH_2$); ^{13}C NMR ($CDCl_3$) δ 175.8 (s), 145.9 (s), 138.2 (s), 128.4 (d), 127.9 (d), 127.7 (d), 96.5 (d), 72.2 (t), 65.4 (t), 28.6 (t), 26.6 (q), 21.2 (t); m/z (FAB): 232 (MH^+, 35%), 212 (100%), 98 (42%), 67 (49%); HRMS, MH^+ found 232.1348, $C_{14}H_{18}NO_2$ requires 232.1357.

5-(2-Ethoxyethylidene)-1-methylpyrrolidin-2-one (3d). To a solution of 5-hydroxy-1-methyl-5-vinylpyrrolidin-2-one[13] (0.20 g, 1.42 mmol) in ethanol (15 ml) at 20°C was added a catalytic quantity of pyridinium *para*-toluenesulfonate. The mixture was then stirred for 30 min at 20°C and the ethanol evaporated at 30°C to give an oil which was purified by column chromatography (70:30 ethyl acetate: 40–60°C petroleum ether) to give **3d** as an orange oil (0.17 g, 71%); IR, ν_{max} (thin film) 1690, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.84 (1H, tt, $J = 7.5$ Hz $J = 2.0$ Hz, $=CH$), 3.98 (2H, d, $J = 7.5$ Hz, CH_2OEt), 3.48 (2H, q, $J = 7.5$ Hz), 2.88 (3H, s, CH_3), 2.70 (2H, m, CH_2CO), 2.45 (2H, m, $=CCH_2$), 1.16 (3H, t, $J = 7.5$ Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 175.8 (s), 145.5 (s), 96.7 (d), 65.6 (t), 28.6 (t), 26.5 (q), 21.1 (t), 15.3 (q); m/z (EI): 169 (M^+, 25%), 140 (18%),

124 (100%), 114 (54%), 96 (21%), 68 (20%), 55 (15%); HRMS, M^+ found 169.1093, $C_9H_{15}NO_2$ requires 169.1103.

5-(2-Ethoxyethylidene)-1-[2-(tetrahydropyran-2-yloxy)ethyl]-pyrrolidin-2-one (3e). To solution of 5-hydroxy-1-[2-(tetrahydropyran-2-yloxy)ethyl]-5-vinylpyrrolidin-2-one (0.24 g, 0.94 mmol) in ethanol (8 ml) at 20°C was added pyridinium *para*-toluenesulfonate (24 mg, 0.094 mmol). The mixture was then stirred for 0.5 h and quenched by adding solid sodium hydrogen carbonate. It was then filtered and evaporated at 20°C. The residue was purified by column chromatography (65:35 ethyl acetate: 40–60°C petroleum ether) to give **3e** as a light orange oil (0.26 g, 98%): IR, ν_{max} (thin film): 1690, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.06 (1H, tt, $J = 7.5$ Hz, $J = 2.1$ Hz $=CH$), 4.62 (1H, t, $J = 3.5$ Hz, $OCHO$), 4.02 (2H, d, $J = 7.5$ Hz, $CH_2OCH_2CH_3$), 3.85–3.40 (8H, m), 2.76 (2H, t, $J = 7.5$ Hz, CH_2CO), 2.49 (2H, m, $=CCH_2$), 1.90–1.40 (6H, m), 1.22 (3H, t, $J = 7.5$ Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 175.7 (s), 144.1 (s), 98.4 (d), 97.0 (d), 65.7 (t), 65.3 (t), 63.1 (t), 61.9 (t), 39.6 (t), 30.4 (t), 28.5 (t), 25.4 (t), 21.3 (t), 19.1 (t), 15.2 (q); m/z (FAB): 154 (74%), 136 (100%), 126 (41%); HRMS, M^+ found 283.1776, $C_{15}H_{25}NO_4$ requires 283.1784.

Reaction of 1-Benzyl-5-hydroxy-5-vinylpyrrolidin-2-one (1b) with *tert*-Butyl Hydroperoxide and with tin (IV) Chloride. *Caution: care should be exercised and correct procedures followed*[17] *when handling with tert-butyl hydroperoxide and the alkyl peroxide products*. A solution **1b** (0.3 g, 1.38 mmol) in dichloromethane (20 ml) was cooled to −78°C and treated dropwise with tin (IV) chloride (37 mg, 0.14 mmol, 10 mol %) followed by *tert*-butyl hydroperoxide (**Caution**: 0.52 ml, 3.18 mmol, 6.08 M solution in dichloromethane). The mixture was then stirred at −78°C for 2 h, poured onto ice (15 g) and the layers separated. The aqueous layer was extracted with dichloromethane (3 × 10 ml) and the combined organic extracts dried ($MgSO_4$) and evaporated to give an oil which was purified by column chromatography (14:86 ethyl acetate: 40–60°C petroleum ether) to give the diperoxide **4** as a colourless oil (69 mg, 13%); IR, ν_{max} (thin film): 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35–7.10 (5H, m, Ar), 4.79 (1H, d, $J = 15.5$ Hz, CH_2Ph), 4.12 (1H, d, $J = 15.5$ Hz, CH_2Ph), 3.87 (2H, t, $J = 7.0$ Hz, CH_2OO), 2.70–1.70 (6H, m), 1.20 (9H, s, ^{t}Bu), 1.15 (9H, s, ^{t}Bu); ^{13}C NMR ($CDCl_3$) δ 177.0 (s), 138.6 (s), 128.4 (d), 127.7 (d), 127.0 (d), 98.2 (s), 80.1 (s), 79.9 (s), 69.8 (t), 42.8 (t), 34.7 (t), 30.2 (t), 28.7 (t), 26.5 (q), 26.3 (q); m/z (FAB): 380 (MH^+, 100%), 290 (90%), 234 (14%), 216 (16%), 190 (65%); HRMS, MH^+ found 380.2450, $C_{21}H_{34}NO_5$ requires 380.2437; and the peroxide **5** as a colourless oil (136 mg, 33%); IR, ν_{max} (thin film): 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.20 (5H, m, Ar), 5.62 (1H, d, $J = 17.5$ Hz, $J = 11.0$ Hz, $=$ CH), 5.35 (1H, dd, $J = 17.5$ Hz, $J = 1.5$ Hz $=CH_2$), 5.16 (1H, dd, $J = 11.0$ Hz, $J = 1.5$ Hz, CH_2), 4.63 (1H, d, $J =$

15.5 Hz, CH_2Ph), 4.16 (1H, d, $J = 15.5$ Hz, CH_2Ph), 2.55–2.35 (2H, m, CH_2CO), 2.20–2.00 (2H, m, CH_2) 1.15 (9H, s, ^{t}Bu); ^{13}C NMR ($CDCl_3$) δ 177.0 (s), 138.5 (s), 136.2 (d), 128.6 (d), 127.9 (d), 127.3 (d), 117.7 (d), 97.6 (s), 80.0 (s), 43.4 (t), 32.0 (t), 30.7 (t), 26.6 (q); m/z (FAB): 290 (MH^+, 100%), 234 (18%), 216 (31%), 190 (67%); HRMS, MH^+ found 290.1770, $C_{17}H_{24}NO_3$ requires 290.1756.

1-Benzyl-5-(2-bromoethylidene)-3-pyrrolidin-2-one (6). A solution of **1b** (0.2 g, 0.92 mmol) in THF (5 ml) and water (1 ml) was cooled to 0°C and treated portion-wise with *N*-bromosuccinimide (0.18 g, 1.01 mmol). When the addition was complete the mixture was stirred at 20°C for 20 h. Diethyl ether (5 ml) and water (5 ml) were then added, and the layers separated. The aqueous layer was extracted with diethyl ether (2 × 4 ml), the combined organic extracts washed throughly with saturated aqueous sodium hydrogen carbonate (8 ml) then brine (5 ml), and dried ($MgSO_4$). Evaporation gave a residue which was purified by column chromatography (50:50 ethyl acetate: 40–60°C petroleum ether) to give **6** as a dark red solid (156 mg, 61%), mp 82–84°C (ethyl acetate/petroleum ether); IR, ν_{max} (nujol mull): 1705, 1680, 1645 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.40–7.05 (6H, m), 6.35 (1H, dd, $J = 6.0$ Hz, $J = 2.0$ Hz, =C*H*CO), 5.51 (1H, dt, $J = 9.0$ Hz, $J = 2.0$ Hz, =C*H*CH$_2$Br), 4.82 (2H, s, CH_2Ph), 4.18 (2H, d, $J = 9.0$ Hz, CH_2Br); ^{13}C NMR ($CDCl_3$) δ 169.9 (s), 142.3 (s), 136.6 (s), 132.0 (d), 128.7 (d), 127.5 (d), 126.8 (d), 125.6 (d), 109.2 (d), 42.7 (t), 26.7 (t); m/z (EI): 277 (M^+, ^{79}Br, 13%), 233 (11%), 198 (100%), 91 (78%), 65 (11%); HRMS, M^+ found 277.0105, $C_{13}H_{12}NO^{79}Br$ requires 277.0102

Reaction of 1-Benzyl-5-(2-bromoethylidene)-3-pyrrolin-2-one (6) with Diethyl Sodiomalonate. Sodium hydride (24 mg, 0.79 mmol, 80% dispersion in oil) was washed twice with THF, then THF (10 ml) was added. The mixture was cooled to 0°C and treated dropwise with diethyl malonate (0.13 g, 0.79 mmol) in THF (5 ml). It was then stirred at 0°C for 0.5 h and a solution of **6** (0.20 g, 0.72 mmol) in THF (5 ml) was added dropwise. When the addition was complete the mixture was stirred 20°C for 3 h, poured onto saturated aqueous ammonium chloride (10 ml) and the layers separated. The aqueous layer was exracted with ether (2 × 5 ml) and the combined organic extracts dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography (30:70 then 40:60 ethyl acetate: 40–60°C petroleum ether) to give **7** as a dark red oil (91 mg, 35%); IR, ν_{max} (thin film): 1735, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.40–7.10 (6H, m), 6.27 (1H, dd, $J = 6.0$ Hz, $J = 1.5$ Hz, =C*H*CO), 5.28 (1H, t, $J = 8.5$ Hz, =C*H*CH$_2$), 4.80 (2H, s, CH_2Ph), 4.12 (4H, q, $J = 7.0$ Hz, OCH$_2$), 3.36 (1H, t, $J = 7.5$ Hz, COC*H*CO), 2.84 (2H, dd, $J = 8.5$ Hz, J =7.5 Hz = CHCH_2), 1.21 (6H, t, $J = 7.0$ Hz, CH$_3$); ^{13}C NMR ($CDCl_3$) δ 170.1 (s), 168.3 (s), 141.3 (s), 137.1

(s), 132.9 (d), 128.6 (d), 127.3 (d), 126.9 (d), 124.8 (d), 110.1 (d), 61.7 (t), 52.0 (t), 51.7 (d), 26.9 (t), 14.0 (q); m/z (FAB): 358 (MH^+, 100%), 342 (62%), 305 (31%), 276 (48%), 243 (56%); HRMS, MH^+ found 358.1660, $C_{20}H_{24}NO_5$ requires 358.1654; and **8** as a dark red oil (226 mg, 60%); IR, ν_{max} (thin film): 1735, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.05 (10H, m, Ar), 6.67 (2H, dd, $J = 5.5$ Hz, $J = 2.0$ Hz, $CH{=}CHCO$), 6.12 (2H, dd, $J = 5.5$ Hz, $J = 2.0$ Hz, $=CHCO$), 5.02 (2H, $J = 8.0$ Hz, $=CHCH_2$), 4.76 (4H, s, CH_2Ph), 4.09 (4H, q, $J = 7.0$ Hz, OCH_2CH_3), 2.58 (4H, d, $J = 8.0$ Hz, $=CHCH_2$), 1.17 (6H, t, $J = 7.0$ Hz, $2CH_3$); ^{13}C NMR ($CDCl_3$) δ 170.0 (s), 169.8 (s), 141.5 (s), 137.2 (s), 132.3 (d), 128.7 (d), 127.5 (d), 127.2 (d), 124.8 (d), 107.9 (d), 61.8 (t), 57.6 (s), 42.6 (t), 30.7 (t), 14.0 (q); m/z (FAB): 555 (MH^+, 100%), 464 (21%), 371 (31%), 308 (41%), 296 (34%), 284 (24%), 262 (21%), 218 (45%), 210 (39%); HRMS, MH^+ found 555.2488, $C_{33}H_{35}N_2O_6$ requires 555.2495.

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