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Efficient Synthesis of 3-Mono and Disubstituted Lactams using Meerwein Eschenmoser [3,3] Sigmatropic Rearrangements.

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Abstract: 3-Allyl substituted five six and seven membered ring lactams, are readily available in good yields and reasonable selectivity by a formal Meerwein Eschenmoser [3,3] rearrangement, using readily available methoxymethyleniminium salts and lithium alkoxides derived from allyl alcohols.

The stereoselective formation of new carbon carbon bonds β to a nitrogen atom is a process that is fundamental in alkaloid synthesis. To date Diels Alder reactions of acrylamides[1], alkylation of enamines[2] and anions derived from amides, thioamides[3] and imides[4] have been the most popular methods for achieving this transformation. In acyclic systems the Meerwein Eschenmoser variation of the Claisen rearrangement (**1**⟶**2**) has also been used to a limited extent, but has the disadvantage that the starting ketene-N,O-allyl acetals are difficult to obtain in all but the simplest of cases[5]. Sigmatropic rearrangement with ring expansion of exocyclic ketene-N,O acetals have been successfully employed in the synthesis of seven membered ring lactams[6]. In this work multistep procedures were required to generate the required ketene-N,O acetals. Welsh first reported that formal Meerwein Eschenmoser Claisen rearrangements could be effected in acyclic systems, simply by treating methoxymethyleniminium salts with allyl lithium alkoxides[7]. Recently we reported in preliminary form[8] **Scheme1**, that this chemistry could be extended to lactams and now report in detail the findings of that study. The results of this study are summarised in **Table 1.**

(1) **(2)**

A number of methods were employed for the synthesis of the methoxymethyleniminium salts (**3**). The most convenient method consisted of treating the corresponding tertiary lactam with methyl triflate in methylene chloride as solvent[7]. This reaction was complete in one hour at room temperature. Alternatively dimethyl sulphate could be used as the methylating agent, but because of its lower reactivity it was necessary to heat the reagents at 50°C in the absence of solvent for three hours to effect quantitative salt formation[9]. Alternatively the methoxymethyleniminium triflate and methyl sulphate salts could be obtained by treating the corresponding iminoethers with methyl triflate or dimethyl sulphate respectively. Imino methylethers (which are readily available from corresponding secondary lactams[10]) were more reactive towards the methylating agents than the

tertiary amides. All four methods were used for preparing the salts in essentially quantitative yield. In the case of the N-methyl-3-allyl substituted lactams (**Table 1** enteries **c** and **k**), the corresponding salts could only be made by treating the tertiary amide with methyl triflate. Due to the unstable and hygroscopic nature of the methoxymethyleniminium salts no attempts were made at purification and characterisation. Instead the salts were used immediately in their crude form for the rearrangement.

Table 1

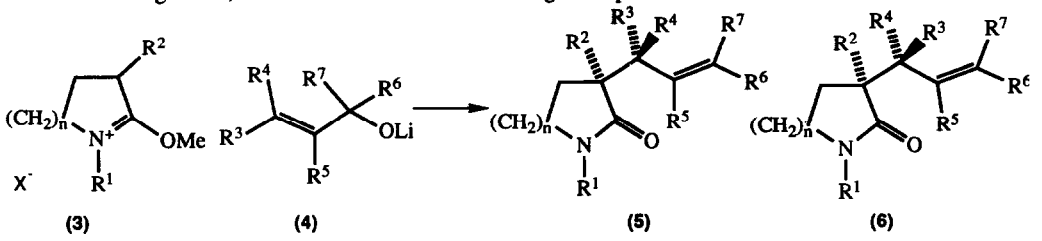
5, 6	n	R^1	R^2	R^3	R^4	R^5	R^6	R^7	Ratio **(5):(6)**	Time(hr)	Yield (%)
a	1	Me	H	H	H	H	H	H	-	12	64
b	1	Me	H	Me	H	H	H	H	5.5:1	12	64
c	1	Me	Allyl	Me	H	H	H	H	6.5:1	12	85
d	1	Me	H	H	H	H	Me	Me	-	12	68
e	1	Me	H	H	Et	H	H	H	1:5	12	31*
f	1	Me	H	Me	H	H	Me	H	9:1	12	67
g	1	Me	H	H	H	Me	Bu^n	H	-	24	53, 39*
h	1	Bn	H	Me	H	H	H	H	11:1	24	92
i	2	Me	H	H	H	H	H	H	-	12	85
j	2	Me	H	Me	H	H	H	H	1.5:1	12	72
k	2	Me	Allyl	Me	H	H	H	H	5:1	24	73
l	3	Me	H	H	H	H	H	H	-	12	68

*Only one mol of alcohol used.

The lithium alkoxide was conveniently prepared by adding n-butyllithium in hexane (1.6M), to the allyl alcohol in THF as the solvent. The freshly prepared crude methoxymethyleniminium salt was suspended in dry THF, this was added to the lithium alkoxide in THF and the resulting mixture was boiled under reflux for the time given in **Table 1**. In order to obtain acceptable yields of the 3-substituted lactams, it was necessary to use a two fold access of lithium alkoxide w.r.t. the salt. Yields of 3-mono and 3-disubstituted lactams obtained, are calculated on the amount of methoxymethyleniminium salt used and as can be seen from **Table 1** range from good to excellent. In all cases studied varying amounts (5-20%) of the the N-methyl unsubstituted lactam was produced as a by-product, which could be readily removed by flash chromatography. The reaction works well for primary secondary and even tertiary lithium allyl alkoxides (**Table 1** enteries **a**, **f** and **d**) and for lactam ring sizes ranging from five to seven. When a substituent was already present on the 3-position of the lactam (**Table 1** enteries **c** and **k**), then a quaternary chiral centre was formed in good yield and with reasonable stereoselectivity.

In the case of salt (**3, n=1**) reacting with crotyl alkoxide (**Table 1** entry **b**), two diastereoisomers were produced on rearrangement, with reasonable selectivity. The isomer ratios could be readily determined by proton nmr spectroscopy. In all cases were crotyl alcohol was used as a substrate (**Table 1** enteries **b**, **c**, **f**, **h**, **j**, and **k**), the methyl group attached to the allylic carbon atom on the side chain had a lower chemical shift value for the major isomer and these signals was used for the quantification of the diastereoisomers. In the case of the six membered ring salt (**3, n=2**) reacting with crotyl alkoxide (**Table 1** entry **j**), the stereoselectivity of the

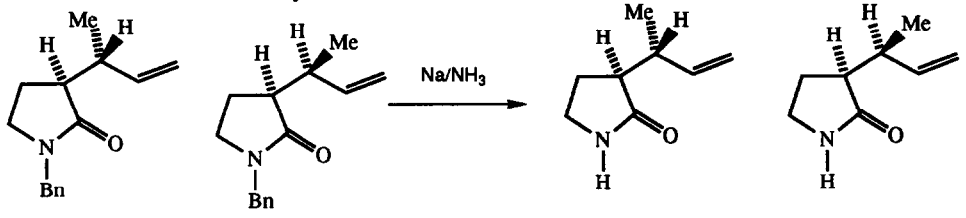
rearrangement appears to be poor. Stopping the reaction after 10% consumption of starting salt showed an isomer ratio of (**5j:6j** 10:1), which progressively got worse as the reaction proceeded. In the case of (**5k**) when a quatenary chiral centre was produced the stereoselectivity was good. These two observations suggest the the piperidinone (**5j**) is epimerising under the basic reaction conditions. The reason why this should happen in the six membered ring series, but not in the five membered rings is at present unclear to us.



(3) (4) (5) (6)

Scheme1

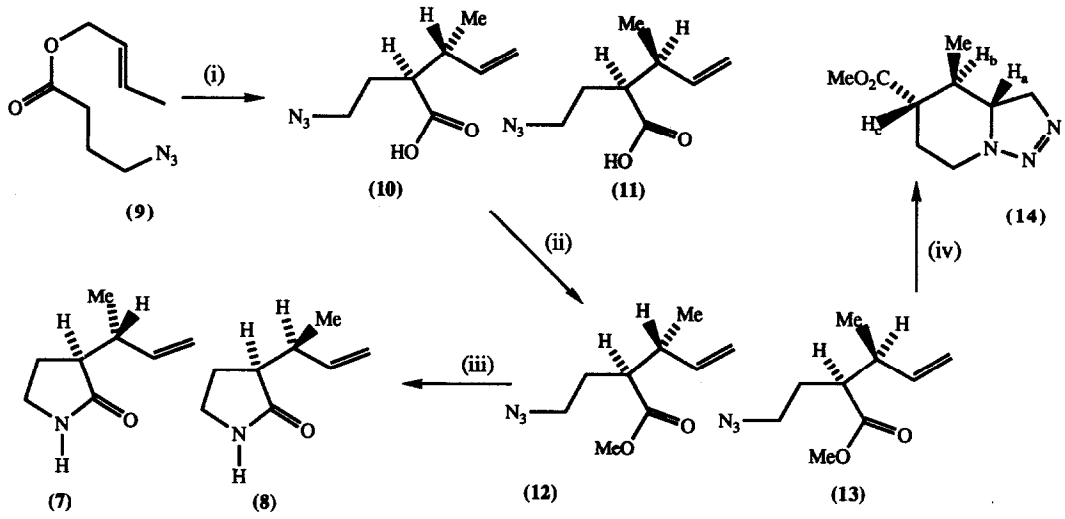
One example of an N-benzylmethoxymethyleniminium salt (**Table 1** entry **h**) was studied. The diastereoselectivity on rearrangement with crotyl alcohol was substantially higher 10:1 than in the N-methyl case 5.5:1 and the chemical yield was also higher. The benzyl group group on the amide was readily removed with sodium in liquid ammonia to give the secondary lactams (**7**) and (**8**), (85%) without any epimerisation at the chiral centre next to the amide carbonyl group. Therefore this methodology can be successfully applied to the synthesis of 3-substituted secondary lactams.



(5h) (6h) (7) (8)

In the cases were diastereoisomers were produced, which contained a hydrogen at each of the new chiral centres (**Table 1** enteries **b** and **j**), the proton coupling constants between these hydrogens was measured in an attempt to assign the relative stereochemistry of (**5**) and (**6**) respectively. In each case this coupling constant for the minor isomer was greater than that for the major. Because the difference in coupling constants between the diastereoisomers was very small, (1 Hz and 1.4Hz for **b** and **j** respectively) no information on the relative stereochemistry of the diastereoisomers could be obtained.

In order to solve this stereochemical problem authentic samples of diastereoisomers (**7**) and (**8**) were synthesised, **Scheme 2**. Hence Ireland Claisen rearrangement of crotyl ester (**9**) (under conditions that are presumed to give the E-trimethylsilylenol ether) give a 1:3 mixture of diastereoisomers (**10**) and (**11**)[11]. This rearrangement itself is worthy of comment. It is well known that ester enolates react with azides to give triazolinones[12]. However the desired Ireland Claisen reaction proceeded cleanly without any triazolinone side products. This appears to be the first report of an Ireland Claisen rearrangement in a substance containing azide functionality. Esterification of the acids using Shaw's procedure[13] give the methyl esters (**12**) and (**13**) ratio 1:3. Reduction of the azide functionality with triphenyl phosphine and water[14] give an intermediate amino ester (not isolated), which readily cyclised in boiling THF to give the lactams (**8**) and (**7**) ratio 3:1.

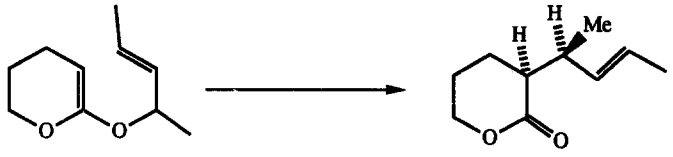


Reagents: (i) LDA followed by Me_3SiCl, (ii) Sodium hydroxide, methyl iodide, (iii) Triphenyl phosphine, water. (iv) 2 years neat, room temperature.

Scheme 2

On sitting at room temperature for two years, substrates (**12**) and (**13**) underwent intramolecular 1,3-dipolar cycloaddition to give a 70:5:15:10 mixture of four stereoisomeric cycloadducts (**14**). Closely related intramolecular cycloadditions of this type have previously been reported by Logothetis[15], with reaction times of several months. Clearly the major cycloadduct must be derived from the major diastereoisomer of the Ireland Claisen rearrangement (**13**). On examination of the proton nmr spectrum of the major isomer (**14**), it was found that J_{HaHb} = 11.0Hz and J_{HbHc} = 11.5Hz. This confirmed that H_a, H_b and H_c were all axial and that H_b was *trans* to both H_a and H_c. This fortutitous cycloaddition therefore gives a derivative in which the relative stereochemistry of (**13**) is unambiguously assigned.

The major lactam diastereoisomer derived from the unambiguous synthesis and that derived from the Meerwein Eschenmoser rearrangement product (**5h** and **6h**), followed by N-debenzylation were different. The predominant transition state for the Meerwein Eschenmoser rearrangement must therefore be chair like to give (**5h**) as the major diastereoisomer. Lythgoe has previously reported[16] that the ketene allyl acetal (**15**) rearranges predominantly via a boat transition state to give (**16**) as the major diastereoisomer. It appears in our case, that simply replacing a oxygen atom in the ring for an alkylated nitrogen atom is enough to reverse the diastereoselectivity of this reaction.



(15) (16)

The relative stereochemistry of diastereoisomers (**5** and **6b, c, e, f, j, k**), was then assigned by assuming that these also were the products of chair transition states and by comparing their proton nmr spectra to that of (**5h**) and (**6h**). In particular the methyl doublet resonances of the major diastereoisomer for lactams produced from E-crotyl alcohol (**5**), consistently had a lower chemical shift value than that of the minor

diastereoisomer (**6**) and the chemical shift for the proton on the chiral centre on the ring, consistently had a higher value for (**5**) than that for (**6**).

When (+)-R- 2-methylhept-2-en-3-ol was used as substrate (**Table 1** entry **g**) then the S-lactam (**5g**) was produced as as essentially one enantiomer (as determined using the chiral shift reagent Eu(hfc)$_3$) Due to the broading of the signals exact quantification was difficult but it was estimated that the ee was greater that 95%. This result is strange in that asymmetric induction at this centre would only of been predicted to be as good as the diastereoselectivity, (note the previous highest recorded de was 84% (**Table 1** entry **h**)). The latent diastereoselctivity for this alcohol must therefore be very high.

Experimental

General remarks.

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Microanalyses were obtained using a Perkin Elmer 2400 CHN elemental analyser. Infra red spectra were recorded on a Perkin Elmer 983G infra red spectrometer as potassium bromide (KBr) discs (solids), or liquid films (liquids). Mass spectra were recorded using an updated MS902 and accurate molecular masses were determined by the peak matching method using perfluorokerosene as standard reference. Nuclear magnetic resonance (nmr) were recorded at 300MHz using a General Electric QE nmr spectrometer and at 500MHz using a General Electric OMEGA nmr spectrometer. Chemical shifts are given in parts per million (δ) downfield from tetramethylsilane as an internal standard and coupling constants are given in hertz. Unless otherwise stated, deuterochloroform was used as solvent. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad. Flash chromatography was performed using air pressure to maintain a flow rate at 5ml/min and silica refers to Silica Gel 60 (Merck 9385). Analytical thin layer chromatography (t.l.c.) was carried out on Merck Kieselgel 60F_{254} plates and were visualised using a Hanovia Chromatolite ultraviolet lamp, or iodine. All solvents were purified and dried according to standard procedures. The term petroleum ether refers to that fraction of petroleum with a boiling point between 40^{0}C and 60^{0}C. Ether refers to diethyl ether.

General Procedure for the Preparation of Methoxymethyleniminium Triflate Salts.

The tertiary amide or the imino ether was dissolved in dry methylene chloride (2ml per mmol) and stirred at room temperature. One mol equivalent of methyltrifluoromethane sulphonate (methyl triflate) was added to this solution dropwise. This mixture was stirred at room temperature for 1 hour. The methylene chloride was removed under high vacuum to give the salt in quantitative yield. The salt was then suspended in THF (7ml per mmol) and this solution was used directly for the next stage.

General Procedures for the Preparation of Methoxymethyleniminium Methyl Sulphate Salts.

A ; From Imino ethers.

The imino ether was stirred in methylene chloride (1ml per mmol) at 0^{0}C and dimethyl sulphate (1molar equivalent) was added dropwise to this over a half hour. Upon completion of this addition the reaction mixture was stirred at room temperature for a further 10 hours. The methylene chloride was removed under high vacuum to give the salt in quantitative yield. The salt was then suspended in THF (7ml per mmol) and this solution was used directly for the next stage.

B ; From N-Substituted Lactams.

A mixture of the required N-substituted lactam and dimethyl sulphate (1 molar equivalent) were heated, with stirring, to between 50°C and 60°C for 3 hours. The heavy oil was allowed to cool to room temperature, then suspended in THF (7ml per mmol). This solution was used directly for the next stage.

The salts were made as they were required and no attempt was made at purification.

General Procedure for the [3, 3] Sigmatropic Rearrangements.

To a stirred solution of the allylic alcohol (2 mols) in dry THF (3ml per mmol) under an atmosphere of nitrogen, was added 1.6M *n*-butyllithium solution in hexane (2 mols) dropwise over 15 minutes. This mixture was allowed to stir for a further 15 minutes after which the desired methoxymethylene iminium salt (1 mol) in dry THF (7ml per mmol) was added all at once and the resulting reaction mixture was heated on an oil bath at a temperature of 70°C for time stated in **Table 1**. The THF was removed under reduced pressure and the residue was dissolved in methylene chloride (30ml) and this was washed with saturated $NaHCO_3$ (aq) (2 x 20ml) and brine (1 x 20ml). The organic layer was then dried ($MgSO_4$) and then concentrated *in vacuo*. The crude product was purified by flash chromatography, followed by short path reduced pressure distillation. Yields given refer to homogeneous compounds obtained after flash chromatography and the solvent quoted for the R_f value was the solvent used for the chromatography. When nmr data is given for minor isomers in diastereoisomer mixtures, only the distinct peaks that are not overlapping with the major isomer are given.

1-Methyl-3-(prop-2'-en-1'-yl)pyrrolidin-2-one (5a).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=1, 8g, 36mmol) with allyl alcohol (4.2g, 72mmol) and 45ml of 1.6M n-butyllithium solution to yield (**5a**, 3.22g, 64%; b.p. 54°C at 0.5mmHg) as a clear oil (ether, R_f = 0.82). $C_8H_{13}NO$ requires C 69.03, H 9.41, N 10.06%. Found C 68.89, H 9.32, N 10.32%. m/e (%) 139(M^+, 100), 124(9.41), 98(36.14). ν_{max} (cm^{-1}) 3531, 3071, 2969, 2927, 1682, 1497, 1468. δ 1.74 (1H, dq, *J* = 12.8, 8.1, NCH2C$\underline{H}_A$H$_B$), 2.12(2 x H, m, NCH2CH$_A$$\underline{H}_B$ and -C$\underline{H}_A$H$_B$CH=C), 2.50(1H, m, CH$_A$$\underline{H}_B$CH=C), 2.56(1H, m, NCOC$\underline{H}$), 2.85(3H, s, N-C$\underline{H}_3$), 3.29(2H, m, NC$\underline{H}_A\underline{H}_BCH_2$), 5.03(1H, d, *J* = 11.2, CH$_2$CH=C$\underline{H}_A$H$_B$), 5.11(1H, d, *J* = 16.1, CH$_2$CH=CH$_A$$\underline{H}_B$) 5.80(1H, m, -CH$_2C\underline{H}$=CH$_2$). ^{13}C δ 22.9, 34.5, 40.2, 42.7, 46.6, 115.7, 134.6, 171.2.

3-(But-3'-en-2'-yl)-1-methylpyrrolidin-2-ones (5b) and (6b).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=1, 3.0g, 13mmol) with crotyl alcohol (1.87g, 26mmol) and 16.2ml of 1.6M n-butyllithium solution to yield (**5b,6b**, 1.3g, 64%; b.p. 68-69°C at 0.5mmHg) as a clear oil (ether, R_f = 0.48). Flash chromatography failed to separate the diastereoisomers. $C_9H_{15}NO$ Requires C 70.55, H 9.87, N 9.14%. Found C 70.39, H 9.59, N 8.93%. m/e (%) 153(52.78), 138(14.21), 98(57.31). ν_{max} (cm^{-1}) 3475, 3074, 2927, 2872, 1679, 1635, 1498, 1430, 1398. Nmr analysis indicated a 5.5:1 mixture of diastereoisomers. δ (major isomer) 0.98(3H, d, *J* = 7.0, -CHC$\underline{H}_3$), 1.81(1H, dq, *J* = 15.7, 6.6, N-CH$_2$C$\underline{H}_A$H$_B$), 2.05(1H, m, N-CH$_2$CH$_A$$\underline{H}_B$), 2.55(1H, td, *J* = 8.3, 3.6, NCOC$\underline{H}$), 2.79(1H, m, -C$\underline{H}$CH$_3$), 2.85(3H, s, N-C$\underline{H}_3$), 3.29(2H, m, NCC$\underline{H}_A\underline{H}_B$), 5.05(1H, d, *J* = 10.3, CH=C$\underline{H}_A$H$_B$), 5.06(1H, d, *J* = 17.1, CH=CH$_A$$\underline{H}_B$), 5.80(1H, m, -CH$\underline{C}$H=CH$_2$). δ (minor isomer) 1.10(3H, d, *J* = 7.0, C$\underline{H}_3$CH), 2.47(1H, td, *J* = 8.5, 4.6, NCOC$\underline{H}$), 5.72(1H, m, C$\underline{H}$=CH$_2$).

3-(But-3'-en-2'-yl)-1-methyl-3-(prop-2'-en-1'-yl)pyrrolidin-2-one (5c) and (6c).

Obtained on reaction of methoxymethyleniminium triflate salt (**3c**, n=1, 3.5g, 11.7mmol) with crotyl alcohol (1.58g, 22mmol) and 13.7ml of 1.6M n-butyllithium solution to yield (**5c,6c** 1.9g, 85%; b.p. 77°C at 0.05 mmHg) as a clear oil (ether, R_f = 0.29). Flash chromatography failed to separate the diastereoisomers.

$C_{12}H_{19}NO$ Requires C 74.57, H 9.91, N 7.25%. Found C 73.99, H 9.74, N 7.15%. H.R.M.S. $C_{12}H_{19}NO$ Requires 193.1466. Found 193.1465. m/e (%) 193(73.12), 178(34.19), 152(37.85), 138(91.18), 137(100), 97(12.9), 82(14.62). ν_{max} (cm^{-1}) 3460, 3071, 2969, 2914, 1685, 1635, 1500, 1460, 1399, 1268. Nmr analysis indicated a 5.5:1 ratio of diastereoisomers. δ (major isomer) 0.94(3H, d, J = 6.8, -CHC$\underline{H}_3$), 1.78 (1H, dt, J = 14.1, 7.1, $NCH_2CH_A\underline{H}_B$), 2.02(1H, dt, J = 14.2, 6.5, $NCH_2CH_A\underline{H}_B$), 2.16(1H, dd, J = 8.6, 13.4, -$CH_A\underline{H}_BCH$=), 2.36 (1H, dd, J = 6.2, 13.4, -$CH_A\underline{H}_BCH$=C), 2.52 (1H, dq, J = 7.0, 8.0, -C$\underline{H}CH_3CH$), 2.84(3H, s, N-C$\underline{H}_3$), 3.19(2H, m, $NCH_A\underline{H}_BCH_2$), 5.05(4H, m, CH_2CH=C$\underline{H}_2$ and -$CH(CH_3)CH$=C$\underline{H}_2$), 5.66(2H, m, -$CH_2C\underline{H}$=CH_2 and -$CH(CH_3)C\underline{H}$=CH_2). δ (minor isomer) 1.01(3H, d, J = 6.7, C$\underline{H}_3CH$), 1.95(1H, m, $NCH2CH_A\underline{H}_B$), 5.81(1H, m, C$\underline{H}$=CH_2).

3-(But-2'-en-1-yl)-1,3'-dimethylpyrrolidin-2-one (5d).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=1, 3.0g, 13mmol) with 2-methyl-3-buten-2-ol (2.24g, 26mmol) and 16.2ml of 1.6M n-butyllithium solution to yield (**5d**, 1.5g, 68%; b.p. 89-91°C at 0.6mmHg) as a clear oil (ether, R_f = 0.17). $C_{10}H_{17}NO$ Requires C 71.81, H 10.25, N 8.38%. Found C 71.62, H 10.11, N 8.30%. m/e (%) 167(35.94), 152(4.60), 98(44.80). ν_{max} (cm^{-1}) 3448, 2962, 2919, 1684, 1497, 1262. δ 1.63 and 1.70(2 x 3H, 2s, CH=C(C$\underline{H}_3$)$_2$), 1.70(1H, m, $NCH_2CH_A\underline{H}_B$), 2.00(1H, m, $NCH_2CH_A\underline{H}_B$), 2.14 and 2.39(2x1H, 2xm, -$CH_A\underline{H}_BCH$=C), 2.42(1H, m, NCOC$\underline{H}$), 2.84(3H, s, N-C$\underline{H}_3$), 3.28(2H, m, $NCH_A\underline{H}_BCH_2$), 5.09(1H, t, J = 6.1, -$CH_2C\underline{H}$=$C(CH_3)_2$). ^{13}C δ 16.8, 23.0, 24.8, 28.4, 28.6, 40.9, 46.6, 120.1, 132.6, 175.4.

1-Methyl-3-(pent-2'-en-3'-yl)pyrrolidin-2-one (5e) and (6e).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=1, 5.7g, 25mmol) with *cis* -2-penten-1-ol (2.3g, 28mmol) and 15.6ml of 1.6M n-butyllithium solution to yield (**6e**, 1.1g, 26%; and **5e**, 0.21g, 5%; b.p. 60°C at 0.2mmHg) as clear oils. In this case the two diastereoisomers separated by flash chromatography (ether, major isomer (**6e**) R_f = 0.13, minor isomer (**5e**) R_f = 0.16). Nmr analysis of the crude reaction mixture indicated a 4.5:1 ratio of diastereoisomers. $C_{10}H_{17}NO$ Requires C 71.81, H 10.25, N 8.38%. Found C 71.77, H 10.13, N 8.30%. m/e (%) 167(8.56), 152(2.51), 138(8.21), 98(39.69), 83(0.41). ν_{max} (cm^{-1}) 3471, 3072, 2956, 2929, 2782, 1684, 1635, 1429, 1397, 1304. Major isomer (**6e**) δ 0.91(3H, t, J = 7.2, -$CH_2C\underline{H}_3$), 1.48(2H, dq, J = 7.2, 7.6, $CHC\underline{H}_2CH_3$), 1.88(1H, m, $NCH_2CH_A\underline{H}_BCH$), 2.03(1H, m, $NCH_2CH_A\underline{H}_BCH$), 2.54(2H, m, NCOC$\underline{H}$), and -C$\underline{H}(C_2H_5)CH$=$CH_2$), 2.82(3H, s, NC$\underline{H}_3$), 3.32(2H, m, $NCH_A\underline{H}_BCH_2$), 5.09(1H, d, J = 11.2, CH=C$\underline{H}_A\underline{H}_B$), 5.10(1H, d, J = 16.3, CH=C$\underline{H}_A\underline{H}_B$), 5.58(1H, m, C$\underline{H}$=$CH_2$). Minor Isomer (**5e**). H.R.M.S $C_{10}H_{17}NO$ Requires 167.1310. Found 167.1309. δ 0.87(3H, t, J = 7.5, -$CH_2C\underline{H}_3$), 1.44(2H, m, -$C\underline{H}_2CH_3$), 1.88 and 2.05(2 x H, m, $NCH_2C\underline{H}_A\underline{H}_BCH$), 2.34(1H, m, NCOC$\underline{H}$), 2.55(1H, m, C$\underline{H}CH$=$CH_2$), 2.83(3H, s, N-C$\underline{H}_3$), 3.26(2H, m, NC$\underline{H}_A\underline{H}_B$), 5.07(2H, m, -$CH(C_2H_5)CH$=C$\underline{H}_A\underline{H}_B$), 5.64(1H, m, C$\underline{H}$=$CH_2$).

1-Methyl-3-(pent-3'-en-2'-yl)pyrrolidin-2-one (5f) and (6f).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=1, 3.0g, 13mmol) with *trans* -3-penten-2-ol (2.2g, 26mmol) and 16.2ml of 1.6M n-butyllithium solution to yield (**5f**, **6f**, 1.5g, 67%; b.p. 64-65°C at 0.1mmHg) as a clear oil (ether, R_f = 0.18). Flash chromatography failed to separate the diastereoisomers. $C_{10}H_{17}NO$ Requires C 71.81, H 10.25, N 8.38%. Found C 71.43, H 10.01, N 8.19%. H.R.M.S. $C_{10}H_{17}NO$ Requires 167.1310. Found 167.1309. m/e (%) 167(M^+, 62.08), 152(32.50), 98(53.35), 83 (0.83). ν_{max} (cm^{-1}) 3436, 3023, 2955, 2920, 1679, 1497, 1452, 1399, 1254. Nmr analysis

indicated a 9:1 mixture of diastereoisomers. δ (major isomer) 0.94(3H, d, J = 6.9, -CHC$\underline{H}_3$), 1.65(3H, d, J = 5.2, CH=CHC$\underline{H}_3$), 1.81 and 2.05(2 x m, 2 x 1H, NCH$_2$C$\underline{H}_A\underline{H}_B$), 2.55(1H, m, NCOC$\underline{H}$), 2.71(1H, m, -C$\underline{H}CH_3$), 2.84(3H, s, N-C$\underline{H}_3$), 3.29(2H, m, NC$\underline{H}_A\underline{H}_B$), 5.44(2H, m, J = 16.2, from decoupling methyl group at 0.94, -C$\underline{H}$=C$\underline{H}$). ^{13}C δ (major isomer) 13.7, 16.7, 18.4, 28.3, 35.4, 45.1, 46.7, 123.1, 133.0, 174.4. δ(minor isomer) 1.07(3H, d, J = 7.9, -CHC$\underline{H}_3$).

1,2'-Dimethyl-3-(hept-2'-en-1'-yl)pyrrolidin-2-one (5g).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=1, 4.3g, 19mmol) with 2-methyl-1-hepten-3-ol (4.9g, 38mmol) and 23.7ml of 1.6M n-butyllithium solution to yield (**5g**, 2.1g, 53%; b.p. 96-97°C at 0.1mmHg) as a clear oil (ether, R_f = 0.26). $C_{13}H_{23}NO$ Requires C 74.59, H 11.08, N 6.69%. Found C 74.23, H 10.92, N 6.41%. m/z (%) 209(M^+, 15.06), 110(0.75), 95(1.12). ν_{max} (cm^{-1}) 3469, 2950, 2923, 2853, 1688, 1496, 1430, 1398. δ 0.89(3H, t, J = 7.2, CH$_2$C$\underline{H}_3$), 1.30(4H, m, -CH$_2$(C$\underline{H}_2$)$_2$CH$_3$), 1.60(3H, s, $\underline{H}_3$CC=CH-), 1.66(1H, dq, J = 15.2, 4.8, NCH$_2$C$\underline{H}_A$H$_B$CH), 1.83(1H, m, NCH$_2$CH$_A\underline{H}_B$CH) 1.90(2H, m, -C$\underline{H}_A\underline{H}_B$(CH$_2$)$_2CH_3$), 2.04(1H, m, C$\underline{H}_AH_BCH_3$C=CH-), 2.57(1H, m, NCOC$\underline{H}$), 2.67(1H, d, J = 17.1, CH$_A\underline{H}_B$C(CH$_3$)=C), 2.85(3H, s, N-C$\underline{H}_3$), 3.28(2H, m, N$\underline{C}$H$_A\underline{H}_B$CH$_2$), 5.16(1H, t, J = 7.3, C=C$\underline{H}$CH$_2$). ^{13}C δ 12.9, 14.6, 21.3, 23.0, 26.6, 28.7, 30.2, 39.1, 40.4, 46.5, 125.9, 131.3, 171.8.

(R)-2-Methyl-1-hepten-3-ol[17] was used as substrate on one tenth of the above scale and using one mol of alcohol per mol of salt give S (+)-(**5g**, 39%) $[\alpha]_D$ = + 47°, (c = 1.36, $CHCl_3$). In the presence of Eu(hfc)$_3$ the methyl group (δ = 1.60) in the racemic sample split into two signals. In the lactam derived from (R)-2-methyl-1-hepten-3-ol only one signal could be seen at the same concentration. Broading of signals makes exact quantification difficult, but the ee is certainly greater than 95%. Absolute stereochemistry was assigned by assuming a chair transition state.

1-Benzyl-3-(but-3'-en-2'-yl)pyrrolidin-2-one (5h) and (6h).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=1 R^1=Bn, 3.0g, 10mmol) with crotyl alcohol (1.44g, 20mmol) and 12.5ml of 1.6M n-butyllithium solution to yield (**5h**,**6h** 2.1g, 92%; b.p. 122 -124°C at 0.3mmHg) as a clear oil (ether, R_f = 0.49). Flash chromatography did not separate the diastereoisomers. $C_{15}H_{19}NO$ Requires C 78.56, H 8.35, N 6.11%. Found C 78.27, H 8.29, N 6.05%. m/z (%) 229(M^+ 49.51), 174(62.78). ν_{max} (cm^{-1}) 3446, 3025, 2960, 2869, 1683, 1491, 1450, 1259. Nmr analysis indicated an 11:1 ratio of diastereoisomers. δ(major isomer) 1.0(3H, d, J = 5.9, -CHC$\underline{H}_3$), 1.81 and 1.97(2 x 1H, 2xm, NCH$_2$C$\underline{H}_A\underline{H}_B$), 2.74(1H, td, J = 8.8, 3.8, NCOC$\underline{H}$), 2.85(1H, m, -C$\underline{H}$CH$_3$), 3.16 (2H, m, NC$\underline{H}_A\underline{H}_B$), 4.38 and 4.54(2x1H, 2xd, J = 14.6, N-C$\underline{H}_A\underline{H}_B$-Ph), 5.01(1H, d, J = 11.4, CH=C$\underline{H}_A$H$_B$), 5.03(1H, d, J = 16.4, CH=CH$_A\underline{H}_B$), 5.83 (1H, m, -CHC$\underline{H}$=CH$_2$), 7.33 (5H, Ar-$\underline{H}$). ^{13}C δ (major isomer) 13.2, 18.6, 36.4, 44.0, 45.1, 45.7, 112.9, 118.3, 126.5, 127.1, 127.6, 140.6, 174.3. δ (minor isomer) 1.12(3H, d, J = 6.8, C$\underline{H}_3$CH), 2.51(1H, td, J = 8.4, 5.6, NCOC$\underline{H}$), 5.73(1H, m, C$\underline{H}$=CH$_2$).

1-Methyl-3-(prop-2'-en-1'-yl)piperidin-2-one (5i).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=2, 6.4g, 26.8mmol) with allyl alcohol (3.4g, 59mmol) and 33.7ml of 1.6M n-butyllithium solution to yield (**5i**, 3.4g, 85%; b.p. 68-69°C at 0.5 mmHg) as a clear oil (ether, R_f = 0.27) . $C_9H_{15}NO$ Requires C 70.55, H 9.87, N 9.14%. Found C 70.16, H 9.63, N 8.98%. H.R.M.S. $C_9H_{15}NO$ Requires 153.1154. Found 153.1152. m/e (%) 153 (M^+, 100), 138 (14.81), 112 (24.07). ν_{max} (cm^{-1}) 3461, 3070, 2934, 2861, 1639, 1497, 1243. δ 1.52(1H, *ddt*, J = 12.8, 9.0, 1.2, C$\underline{H}_A$H$_B$CHCO), 1.75(1H, m, CH$_A\underline{H}_B$CHCO) 1.80 and 1.94(2 x 1H, 2xm, NCH$_2$C$\underline{H}_{AB}$),

2.25(1H, dt, J = 13.8, 7.9, -C$\underline{H_A}H_B$CH=C), 2.34 (1H, m, NCO$\underline{H}$), 2.72(1H, m, CH$_A\underline{H_B}$CH=C), 2.93(3H, s, N-C$\underline{H_3}$), 3.27(2H, m, NC$\underline{H_A}\underline{H_B}CH_2$), 5.02(1H, d, J = 12.1, CH=C$\underline{H_A}$H$_B$), 5.04(1H, d, J = 16.9, CH=CH$_A\underline{H_B}$), 5.75(m, 1H, CH$_2$C$\underline{H}$=CH$_2$). ^{13}C δ 20.4, 25.0, 30.8, 35.2, 40.0, 49.1, 115.5, 135.5, 170.9.

3-(But-3'-en-2'-yl)-1-methylpiperidin-2-one (5j) and (6j).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=2, 3.0g, 12.5mmol) with crotyl alcohol (1.8g, 25mmol) and 15.6ml of 1.6M n-butyllithium solution to yield (**5j, 6j**, 1.5g, 72%; b.p. 88°C at 0.6 mmHg) as a clear oil (ether, R$_f$ = 0.41). Flash chromatography failed to separate the diastereoisomers. $C_{10}H_{17}NO$ Requires C 71.81, H 10.25, N 8.38%. Found C 71.74, H 10.06, N 8.29%. m/z (%) 167 (M$^+$, 14.93), 152 (72.97), 112(82.43), 97(6.08). ν_{max} (cm^{-1}) 3450, 3074, 2935, 2865, 1634, 1495, 1345. Nmr analysis indicated a 1.5:1 mixture of diastereoisomers. δ (major isomer) 0.93(3H, d, J = 6.8, -CHC$\underline{H_3}$), 1.55 and 1.80(2 x 1H, 2 x m, NCH$_2$CH$_2$C$\underline{H_A}\underline{H_B}$), 1.72 and 1.91(2 x 1H, 2 x m, NCH$_2$C$\underline{H_A}\underline{H_B}CH_2$), 2.34(1H, ddd, J = 3.1, 5.4, 9.8, NCOC$\underline{H}$), 2.95(3H, s, N-C$\underline{H_3}$), 3.15(1H, m, C$\underline{H}$CH$_3$) 3.21 (2H, m, NC$\underline{H_2}$CH$_2$), 5.05 (2H, m, CH=C$\underline{H_2}$), 5.83(1H, m, -CHC$\underline{H}$=CH$_2$) ^{13}C δ(major isomer) 12.9, 20.6, 21.4, 33.9, 36.2, 45.1, 49.1, 112.7, 135.9, 171.5. δ(minor isomer) 1.06(3H, d, J = 7.1, C$\underline{H_3}$CH), 2.10(1H, ddd, J = 4.5, 6.2, 10.2, NCOC$\underline{H}$), 5.75(1H, m, C$\underline{H}$=CH$_2$).

3-(But-3'-en-2'-yl)-1-methyl-3-(prop-2'-en-1'-yl)piperidin-2-one (5k) and (6k).

Obtained on reaction of methoxymethyleniminium triflate salt (**3**, n=2, R^2=allyl, 3.5g, 11.0mmol) with crotyl alcohol (1.6g, 22mmol) and 13.7ml of 1.6M n-butyllithium solution to yield (**5k,6k** 1.9g, 84%; b.p. 64°C at 0.05mmHg) as a clear oil (ether, R$_f$ = 0.29). Flash chromatography failed to separate the diastereoisomers. $C_{13}H_{21}NO$ Requires C 75.31, H 10.21, N 6.76%. Found C 75.27, H 10.13, N 6.66%. m/e (%) 207 (M$^+$, 93.99), 102(41.52), 116(68.35), 152(100), 151(70.17), 137(6.97). ν_{max} (cm^{-1}) 3430, 3069, 2933, 2867, 1631, 1493, 1205. Nmr analysis indicated a 5.5:1 ratio of diastereoisomers. δ (major isomer) 0.95(3H, d, J = 6.9, -CHC$\underline{H_3}$), 1.55 and 1.73(2 x 1H, 2 x m, C$\underline{H_A}\underline{H_B}$CCO), 1.73 and 1.83(2 x 1H, 2 x m, NCH$_2$C$\underline{H_A}\underline{H_B}$), 2.14(1H, dd, J = 8.5, 13.4, -C$\underline{H_A}$H$_B$CH=CH$_2$), 2.52(1H, dd, J = 13.5, 6.0, -CH$_A\underline{H_B}$CH=CH$_2$), 2.73(m, 1H, -C$\underline{H}$CH$_3$), 2.96(3H, N-C$\underline{H_3}$), 3.24(2H, m, NC$\underline{H_A}\underline{H_B}$), 5.04(4H, m, -CH$_2$CH=C$\underline{H_2}$ and CH(CH$_3$)CH=C$\underline{H_2}$), 5.70(1H, ddd, J = 17.0, 10.2, 8.8, CH(CH$_3$)C$\underline{H}$=CH$_2$), 5.75(1H, m, CH$_2$C$\underline{H}$=CH$_2$). ^{13}C δ (major isomer) 15.2, 20.0, 22.2, 26.2, 34.4, 43.8, 44.7, 49.1, 115.2, 116.0, 134.5, 138.4, 170.4. δ (minor isomer) 0.98(3H, d, J = 6.8, C$\underline{H_3}$CH).

1-Methyl-3-(prop-2'-en-1'-yl)-hexahydroazepin-2-one (5l).

Obtained on reaction of methoxymethyleniminium methyl sulphate salt (**3**, n=3, 2.2g, 7.6mmol) with allyl alcohol (0.97g, 15.2mmol) and 10.9ml of 1.6M n-butyllithium solution to yield (**5l**, 0.99g, 71%; b.p. 97-98°C at 6mmHg) as a colourless oil (ether, R$_f$ = 0.54). $C_{10}H_{17}NO$ Requires C 71.81, H 10.25, N 8.38%. Found C 71.69, H 10.13, N 8.33%. m/z (%) 167 (100), 152(17.63), 126(18.56), 111(4.06). υ_{max} (cm^{-1}) 3479, 3069, 2923, 2852, 1638, 1484, 1452, 1427. δ 1.31, 1.48 and 1.72(4H, 3xm, N-CH$_2$(C$\underline{H_2}$)$_2$-), 1.72 and 1.92(2 x 1H, NCOCHC$\underline{H_A}\underline{H_B}$-), 2.07(1H, m, NCOC$\underline{H}$), 2.62(2H, m, -C$\underline{H_A}\underline{H_B}$CH=CH$_2$), 2.99(3H, s, N-C$\underline{H_3}$), 3.14 (1H, dd, N-C$\underline{H_A}H_B$(CH$_2$)$_2$- and 3.54(1H, dd, N-CH$_A\underline{H_B}$) 5.05(2H, m, CH=C$\underline{H_2}$), 5.84(1H, m, -CH$_2C\underline{H}$=CH$_2$). ^{13}C δ 25.5, 27.8, 27.9, 34.2, 35.3, 41.7, 48.9, 114.6, 135.9, 175.1.

3-(But-3'-en-2'-yl)pyrrolidin-2-ones (7) and (8).

Liquid ammonia (50ml) was added to a solution of (**5h,6h**, 1.0g, 4.4mmol) in ethanol (1ml). Small pieces of sodium (420mg, 18.3mmol) were slowly added to this solution. The blue colour of the solvated electrons initially was immediately discharged but as time proceeded (10min) the blue colour persisted. After 3hr

all the ammonia had evaporated. Ethanol 10ml was cautiously added (to destroy any residual sodium). The ethanol was removed under reduced pressure and water (10ml) was added and and this was extracted with methylene chloride (3x20ml). The combined extracts were dried over magnesium sulphate and concentrated. Short path distillation gave (**7,8**, 0.52g, 85%; b.p. 84°C at 0.1mmHg) as a clear oil. Nmr analysis showed it to be an 11:1 mixture of diastereoisomers (**7:8**). $C_8H_{13}NO$ Requires C 69.03, H 9.41, N 10.06%. Found C 68.77, H 9.31, N 10.41%. m/z (%) 139(M^+, 40.89), 84(49.41), 83(7.81). υ_{max} (cm^{-1}) 3223, 3077, 2959, 2874, 1688, 1635, 1455, 1274. δ(major) 1.03(3H, d, *J* = 6.5, $C\underline{H}_3CH$) 1.80 and 2.10(2x1H, 2xm, $NCH_2C\underline{H}_A\underline{H}_B$), 2.52(1H, td, *J* = 9.1, 5.3Hz, $COC\underline{H}$), 5.06(2H, m, $CH=C\underline{H}_2$), 5.82(1H, m, $C\underline{H}=CH_2$), 6.21(1H, s, N-H). δ(minor) 1.12(3H, d, *J* = 6.9, $C\underline{H}_3CH$) 1.80 and 2.10(2x1H, 2xm, $NCH_2C\underline{H}_A\underline{H}_B$), 2.43(1H, td, *J* = 10.2, 7.9, $COC\underline{H}$), 5.06(2H, m, $CH=C\underline{H}_2$), 5.79(1H, m, $-CHC\underline{H}=CH_2$), 6.21(1H, s, N-H).

2-Butenyl-4-chlorobutanoate.

4-Chlorobutyrl chloride (10g, 71mmol) was dissolved in dry ether (50ml) and this was stirred at 0°C. Crotyl alcohol (5.6g, 77.7mmol) in dry ether (10ml) was then added dropwise over 30 minutes and the resulting solution was allowed to warm to room temperature, whereupon it was stirred for a further 3 hours. A saturated solution of $NaHCO_3$(aq) (20ml) was cautiously added to the reaction mixture and this was stirred for a further 30 minutes. The ethereal layer was then separated, dried ($MgSO_4$) and the solvent removed *in vacuo*. Distillation gave 2-butenyl-4-chlorobutanoate (10.3g, 82%; b.p. 64°C at 0.05mmHg) as a colourless oil (ether, R_f = 0.79). $C_8H_{13}ClO_2$ Requires C 54.40, H 7.42%. Found C 54.29, H 7.37%. m/e (%) 176(M^+, 4.4), 105(100). ν_{max} (cm^{-1}) 3016, 2958, 1730, 1443. δ 1.72(3H, d, *J* = 6.4, $CH=CH-C\underline{H}_3$), 2.01(2H, m, $ClCH_2\,C\underline{H}_2CH_2$-), 2.51(2H, t, *J* = 7.2, $C\underline{H}_2$-CO), 3.60(2H, t, *J* = 6.4, $Cl\underline{CH}_2$), 4.53(2H, d, *J* = 6.6, $-C\underline{H}_2CH=C$), 5.56(1H, m, $CH=C\underline{H}CH_3$), 5.80(1H, m, $-CH_2C\underline{H}=C$). ^{13}C δ 16.7, 26.6, 30.2, 43.1, 64.3, 123.9, 130.6, 171.4.

2-Butenyl-4-azidobutanoate (9)

Sodium azide (2.8g, 43mmol) was added to a stirred solution of 2-butenyl-4-chlorobutanoate (5.0g 28.3mmol) in dimethylsulphoxide (50ml) and the resulting suspension was heated at 45-50°C for 24hr. The reaction mixture was cooled to room temperature, water (30ml) was added and this was extracted with ether (3x30ml). The combined ethereal extracts were washed with brine 3x(20ml), dried ($MgSO_4$) and the solvent removed *in vacuo*, without heating to yield the product as a brown oil. Flash chromatography gave 2-butenyl-4-azidobutanoate (**9**, 4.2g, 82%) as a clear oil (ether, R_f = 0.77). Due to the potential explosion hazard none of the azides were distilled. $C_8H_{13}N_3O_2$ Requires C 52.44, H 7.15, N 22.94%. Found C 52.13, H 6.94, N 22.66%. m/z (%) 141(M^+-N_3, 0.29), 112(24.2), 70(5.08), 42(63.69). ν_{max} (cm^{-1}) 3441, 3018, 2939, 2871, 2095, 1729, 1417, 1257. δ 1.72(d, 3H, *J* = 6.3, $CH=CHC\underline{H}_3$), 1.92(2H, m, $N_3CH_2\,C\underline{H}_2CH_2$-), 2.39(2H, t, *J* = 6.9, $C\underline{H}_2$-CO), 3.35(2H, t, *J* = 7.1 $N_3C\underline{H}_2$), 4.51(2H, d, *J* = 6.1, $-C\underline{H}_2CH=C$), 5.58(m, 1H, $CH=C\underline{H}CH_3$), 5.79(m, 1H, $-CH_2C\underline{H}=CH$). ^{13}C δ 16.7, 23.2, 30.1, 49.6, 64.3, 123.9, 130.6, 171.4.

2-(2'-Azidoethyl)-3-methyl-4-pentenoic acids (10) and (11).

n-Butyllithium (10.6ml, 1.6M) was added dropwise over five minutes a solution of diisopropyl amine (1.82g, 18.0mmol) in dry THF (50ml) at -78°C. The cooling bath was then removed and the solution allowed to warm to -30°C after which it was recooled to -78°C. 2-Butenyl-4-azidobutanoate (3g, 16.4mmol) was then added dropwise at a rate so as to maintain the temperature at -78°C. After 5 minutes trimethylsilylchloride (1.95g, 18.1mmol) was added and the cooling bath removed to allow the reaction mixture to return to room

temperature, after which it was heated to 60°C for 30 minutes. After cooling to room temperature dry methanol (5.8g, 180mmol) was added and the reaction mixture was stirred for 10 minutes longer. Aqueous sodium hydrogen carbonate solution (20ml, 5%) was then added to the reaction mixture and this was extracted with ether (2 x 20ml). The aqueous layer was then acidified to pH 1 with concentrated hydrochloric acid and this was extracted with methylene chloride (3 x 30ml). The combined organic extracts were then dried ($MgSO_4$) and the solvent removed *in vacuo*. Flash chromatography gave 2-(2'-azidoethyl)-3-methyl-4-pentenoic acids (**10,11**, ratio 1:3, 2.2g, 73%) as a clear oil (ether, R_f = 0.21). No separation of the diastereoisomers was effected by the chromatography. $C_8H_{13}N_3O_2$ Requires C 52.44, H 7.15, N 22.94%. Found C 52.24, H 6.96, N 22.89%. m/e (%) 141(1.31), 140(14.57), 138(0.29) 128(3.0), 96(4.27). ν_{max} (cm^{-1}) 3077, 2930, 2879, 2103, 1706, 1637, 1456, 1291. δ (major) 1.09(3H, d, *J* = 6.6, -CHC<u>H</u>$_3$), 1.83(2H, m, $N_3CH_2C\underline{H}_2CH$), 2.38(1H, m, -C<u>H</u>CH$_3$), 3.28 and 3.44(2 x 1H, 2xm, $N_3C\underline{H}_2CH_2C$), 5.09(2H, m, CH=C<u>H</u>$_2$), 5.61(1H, m, -CHC<u>H</u>=CH$_2$), 9.62(1H, s, -COO<u>H</u>). ^{13}C δ 17.4, 28.0, 39.4, 47.3, 48.6, 114.4, 139.3, 179.6. δ(minor) 1.07(3H, d, *J* = 6.8, -CHC<u>H</u>$_3$), 1.78(1H, m, $N_3CH_2CH\underline{H}_A$), 5.8(1H, m, C<u>H</u>=CH$_2$).

Methyl-2-(2'-azidoethyl)-3-methyl-4-pentenoates (12) and (13).

2-(2'-Azidoethyl)-3-methyl-4-pentenoic acids (**10, 11,** 1.7g, 9.3mmol) were dissolved in 2M potassium hydroxide solution (10ml). Methyl iodide (3.9g, 27.9mmol) dissolved in dimethyl sulphoxide (20ml) was added all at once to the hydroxide solution. The resulting red homogeneous solution was stirred at room temperature for 2 hours after which it was poured into water (30 ml) and extracted with methylene chloride (3x30ml). The combined extracts were washed with water (3x10ml), dried ($MgSO_4$) and the solvent removed *in vacuo*. Flash chromatography gave methyl-2-(2'-azidoethyl)-3-methyl-4-pentenoates (**12,13**, 1.5g, 82%) as a clear oil (ether R_f = 0.77). $C_9H_{15}N_3O_2$ Requires C 54.80, H 7.67, N 21.31%. Found C 53.54, H 7.51, N 21.09%. m/z (%) 155(M^+ -N_3, 5.88), 154(4.58), 140(4.21), 138(6.21), 96(15.61). ν_{max} (cm^{-1}) 3326, 3075, 2949, 2873, 2107, 1733, 1433, 1348, 1264. Nmr analysis indicated a 1:3 ratio of diasteroisomers. δ (major isomer) 1.01(d, 3H, *J* = 6.4, -CHC<u>H</u>$_3$), 1.80(2H, m, $N_3CH_2C\underline{H}_2$), 2.4(1H, m, $N_3CH_2CH_2C\underline{H}$), 2.48(1H, m, -C<u>H</u>CH$_3$), 3.18 and 3.34(2 x 1H, 2 x m, $N_3C\underline{H}_A\underline{H}_B$), 3.71(3H, s, OC<u>H</u>$_3$), 5.04(2H, m, CH=C<u>H</u>$_2$), 5.61(1H, m, -CHC<u>H</u>=CH$_2$) ^{13}C δ (major isomer) 17.4, 27.1, 39.8, 47.4, 48.8, 50.6, 114.6, 139.7, 174.0.

3-(But-3'-en-2'-yl)pyrrolidin-2-ones (7) and (8).

To a solution of methyl-2-(2'-azidoethyl)-3-methyl-4-pentenoates (**12,13**, 3.3g, 16.7mmol) in THF (50ml) was added triphenylphosphine (4.3g, 16.7mmol) and water (0.37g, 21mmol). This mixture was stirred at room temperature for 4 hours, after which ^{31}P nmr analysis showed quantitative formation of triphenylphosphine oxide. The reaction mixture was then heated under reflux for 24 hours, cooled and the solvent removed *in vacuo*. The residue was then dissolved in a 1:1 mixture of ether/petroleum ether and the precipitated triphenylphosphine oxide was removed by filtration and washed thoroughly with cold ether. Once more the solvent was removed *in vacuo* and the crude brown oil was purified by flash chromatography (silica, ether/methanol, 95/5 R_f = 0.41) and reduced pressure distillation to give (**7, 8**, 1.1g, 47%; b.p. 84°C at 0.1mmHg) as a colourless oil. $C_8H_{13}NO$ Requires C, 69.03, H, 9.41, N, 10.06%. Found C 68.92, H 9.32, N 10.08%. m/z (%) 139(M^+, 40.89), 84(49.81) 83(7.81). ν_{max} (cm^{-1}) 3223, 3077, 2959, 2874, 1688, 1635, 1455, 1274. Nmr analysis indicated a 3:1 ratio of isomers. δ (major isomer) 1.12(3H, d, *J* = 7.0, -CHC<u>H</u>$_3$), 1.80 and 2.10(2 x 1H, 2xm, $NCH_2C\underline{H}_A\underline{H}_B$), 2.43(1H, dt, NCOC<u>H</u>), 2.79(1H, m, -C<u>H</u>), 3.28(2H, m, $NC\underline{H}_A\underline{H}_BCH_2$), 5.06(2H, m, CH=C<u>H</u>$_2$), 5.79(1H, m, -CHC<u>H</u>=CH$_2$), 6.21(1H, s, N-<u>H</u>). δ(minor isomer)

1.03(3H, d, J = 6.5, CH_3CH) 1.80 and 2.10(2x1H, 2xm, $NCH_2CH_AH_B$), 2.52(1H, td, J = 9, 5, COCH), 5.06(2H, m, $CH=CH_2$), 5.82(1H, m, $-CHCH=CH_2$), 6.21(1H, s, N-H).

Triazoline (14).

A neat sample of pure methyl-2-(2'-azidoethyl)-3-methyl-4-pentenoates (**12,13**) was left in a sealed sample tube at room temperature for approximately two years. Nmr indicated no alkene present and a 70:5:15:10 mixture of stereoisomeric products. $C_9H_{15}N_3O_2$ Requires C 54.80, H 7.67, N 21.31%. Found C 53.66, H 7.49, N 21.01%. m/z (%) 198(M^++1, 3.2) 169(1.5), 154(14.3), 69(100). δ(major) 0.79(3H, d, J = 6.6, CH_3CH), 1.42(1H, qdd, J = 6.6, 11.0, 11.3, CH_3CH), 1.64(1H, ddd, J = 4.7, 12.8, 17.9, $CH_{ax}CH_2N$), 1.82(1H, m, $CH_{eq}HCH_2N$), 2.17(1H, dt, J = 3.0, 11.0, $CHCO_2Me$), 3.02(1H, dt, J = 3.0, 11.0, N-CH-CHMe), 3.39(1H, ddd, J = 3.3, 13.2, 14.3, CH_{ax}-N), 3.66(3H, s, OCH_3), 3.96(1H, dd, J = 9.8, 15.4Hz, N=N-CH_{ax}), 4.17(1H, dd, J = 5.0, 15.2, N=N-CH_{eq}H), 4.47(1H, ddd, J = 0.7, 5.7, 13.5, CH_{eq}H-N).

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