Use of Chloroalkenylamines for the Synthesis of 1-Azabicyclo[3.3.0]octane and 1-Azabicyclo[4.3.0]nonane Derivatives

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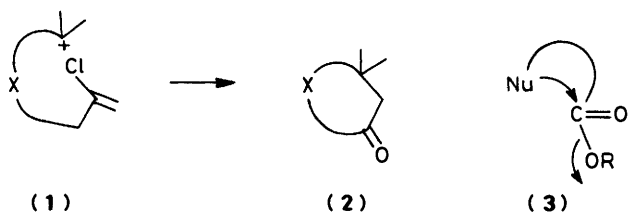
Various *N*-(chloroprop-2-enyl)-, *N*-(3-chlorobut-2-enyl)-, and *N*-(4-chloropent-3- and -4-enyl)-proline derivatives, -succinimides, and -phthalimides have been synthesised and subjected to Lewis acid treatment. The following gave fruitful results: *N*-(4-chloropent-3-enyl)-5-hydroxy-2-pyrrolidone (**25**) gave 1-acetyl-1,2,3,6,7,7a-hexahydropyrrolizin-5-one (**28**); *N*-(4-chloropent-3-enyl)-3-hydroxy-2,3-dihydro-1*H*-isoindol-1-one (**30**) gave 1-*endo*-acetyl-1,2,3,9b-tetrahydropyrrolo[2,1-*a*]isoindol-5-one (**31**) which was isomerised to the *exo*-isomer; *N*-(4-chloropent-3-enyl)-3-methylene-2,3-dihydro-1*H*-isoindol-1-one (**34**) and *N*-(4-chloropent-3-enyl)-3-hydroxy-3-methyl-2,3-dihydro-1*H*-isoindol-1-one (**33**) gave 1-*endo*-acetyl-9b-methyl-1,2,3,9b-tetrahydropyrrolo[2,1-*a*]isoindol-5-one (**35**); *N*-[-2-(3,4-dimethoxyphenyl)ethyl]proline (**42**) gave 8,9-dimethoxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (**43**), *N*-(2-chloroprop-2-enyl)-2-(2-hydroxy-2-propyl)pyrrolidine (**44**) gave 6-chloro-8,8-dimethyl-1,2,3,5,8,8a-hexahydroindolizine (**47**) and 8,8-dimethyl-1,2,3,7,8,8a-hexahydroindolizin-6(5*H*)-one (**48**) which were reduced to the corresponding alcohols; *N*-(4-chloropent-4-enyl)-3-hydroxy-2,3-dihydro-1*H*-isoindol-1-one (**50**) gave 7,8,11,11a-hexahydro-5*H*-azepino[2,1-*a*]isoindole-5,10(9*H*)-dione (**51**).

It is known that carbonium ions react with chloroalkenes to yield carbocyclic and, less frequently, heterocyclic products[1-3] (**1**)→(**2**). It was our objective to extend the usefulness of this



(**1**) (**2**) (**3**)

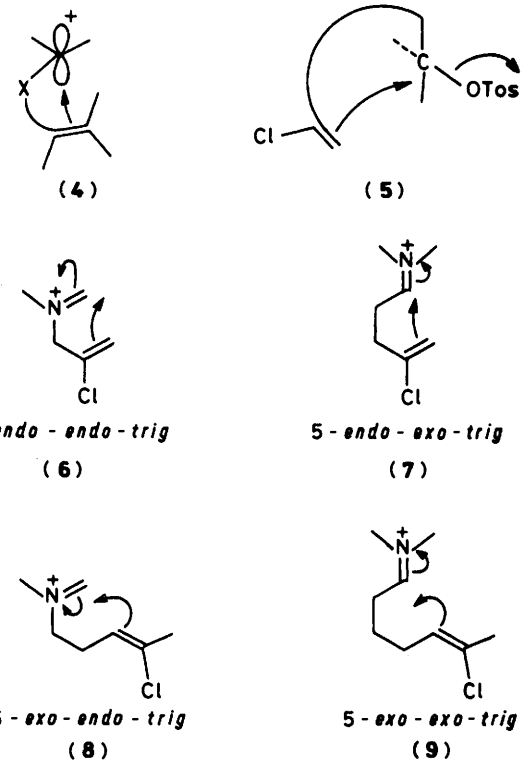
concept by studying the cyclising propensity of various chloroalkenylamines with electrophiles, particularly those that might yield 5,5 or 5,6 ring-fused heterocycles. This paper describes our conclusions based on about two dozen examples.

Results and Discussion

Much of our work was concerned with the attempted syntheses of pyrrolizidine[4] and other 5,5 ring-fused compounds, and Baldwin's rules[5] which concern mainly cyclisation by electron donation into antibonding (LUMO) orbitals [*e.g.* (**3**)] are especially relevant. Although our electrophilic cyclising interactions [*e.g.* (**4**) and (**5**)] require an approximately orthogonal line of approach by the participating centres, models show that Baldwin's rules do provide a good guide to the viability of the proposed reactions, as long as the suggestions of Ben-Ishai[6] are followed; that is that the stereochemistry (*endo* or *exo*) at both termini should be specified.

In our examples, the electrophilic centres are carbonium ions (**4**), potential carbonium ions (**5**) (S_N2), or iminium ions (**6**)—(**9**). These last-named compounds illustrate well the pertinence of Baldwin's rules: there are four modes, (**6**)—(**9**), for electrophilic cyclisation to five-membered rings, arranged here in order of increasing ease of attaining the required bonding.

The first of these, (**6**), is disfavoured and we have found none that is successful. The third, (**8**), and fourth, (**9**), are favoured and we have indeed found that some, though not all, are



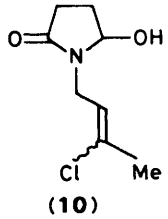
productive. The second type, (**7**), is a borderline case (models), but we had no success in the several examples tried. Models suggest that a 5-*endo*-*exo*-*tet* cyclisation [*cf.* (**5**)] might be more favourable (see below).

We present our results in tabular form, starting with the least favoured. Structural variations include (*a*) changes in stability of the carbonium ions, (*b*) changes in geometry of the chloroalkene, (*c*) use of both stabilised[7] and unstabilised[8] iminium ions, (*d*) comparison of the chloroalkenes with the hopefully more nucleophilic benzene rings, and (*e*) variations in

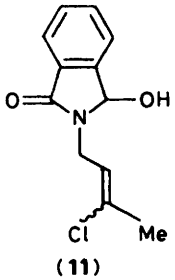
Table.

Entry	Cyclisation mode expected	Starting material	Reagent(s)	Product(s) (yield/%)
1	4-*exo-endo-trig*	(**10**)	HCO_2H	SM[a] (NA[b])
			PPA	Many (Low)
			H_2SO_4	Many (Low)
2	4-*exo-endo-trig*	(**11**)	H_2SO_4	(**12**) (41)→(**13**) (65)
3	5-*endo-endo-trig*	(**14**)	$POCl_3$–HCl	?Dimer + polymers (Low)
4	5-*endo-endo-trig*	(**15**)	$POCl_3$–HCl	Polymer
5	5-*endo-endo-trig*	(**16**)	$POCl_3$–HCl	Polymer
6	5-*endo-endo-trig*	(**17**)	H_2SO_4	Decomp.
7	5-*endo-endo-trig*	(**18**)	H_2SO_4	SM (35) + (**19**) (28)
8	5-*endo-endo-trig*	(**20**)	HCO_2H	Mixture (Low)
			HCl	
			PPA	
9	5-*endo-exo-trig*	(**21**; R = H)	(a) DiBAL; (b) acid	Mixtures (Low)
10	5-*endo-exo-tet?*	(**22**)	BF_3–$CHCl_3$	(**23**) (40)
11	5-*endo-exo-tet*	(**24**)	H_2SO_4 (0 °C)	Mixture
12	5-*exo-endo-trig*	(**25**)	PPA (20 °C)	[(**26**) + (**27**)] (35)→(**28**) (60)
			HCO_2H (100 °C)	SM
13	5-*exo-endo-trig*	(**29**)	$POCl_3$–HCl	Polymer?
14	5-*exo-endo-trig*	(**30**)	H_2SO_4 (0 °C)	(**31**)→(**32**) (64)
15	5-*exo-endo-trig*	(**33**) + (**34**)	H_2SO_4 (0 °C)	(**35**) (67)
16	5-*exo-exo-tet*	(**36**)	H_2SO_4	Isomers (**37**) (78)
17	5-*exo-exo-tet*	(**38**)	H_2SO_4 (0 °C)	Unstable (Low)
18	5-*exo-exo-tet*	(**39**)	H_2SO_4–PPA	Several (Low)
19	5-*exo-exo-tet*	(**40**)	H_2SO_4	Several (Low)
20	5-*exo-exo-tet*	(**41**)	H_2SO_4	Mixture (Low)
21	6-*endo-endo-trig*	(**42**)	$POCl_3$–HCl	(**43**) (62)
22	6-*endo-exo-trig*	(**44**)	H_2SO_4 (0 °C)	[(**47**) + (**48**)] (88)→(**49**) (51)
23	6-*endo-exo-tet*	(**45**)	HCO_2H	Mixture including (**4b**)? (Low)
24	7-*endo-endo-trig*	(**50**)	H_2SO_4 (0 °C)	(**51**) (80)

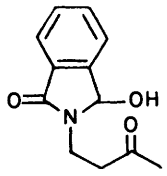
[a]SM = Starting material. [b]NA = not applicable.



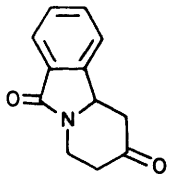
(**10**)



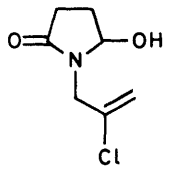
(**11**)



(**12**)



(**13**)



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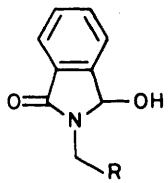
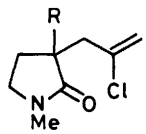
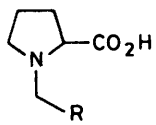


(**18**) R = C(Cl)=CH$_2$
(**19**) R = Ac
(**20**) R = C_6H_4OMe-3



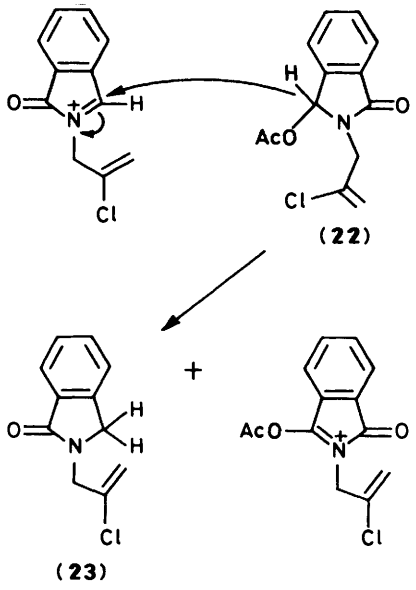
(**21**)



(**14**) R = C(Cl)=CH$_2$
(**15**) R = Ph
(**16**) R = C_6H_4OMe-3

Lewis acids (not all unsuccessful attempts are recorded here). It will be seen that the successful cyclisations are found further down the Table, although we did have unexplained failures amongst the 5-*exo-exo-tet* cases (entries 19, 20).

The following comments are noteworthy. It is assumed that decarbonylation of the proline derivatives (entries 3—5, 13, 21) proceeds *via* the corresponding iminium ions, as demonstrated elegantly by Rapoport and his co-workers:[8] we did not isolate salts of iminium ions. The pioneering and extensive work of Speckamp[9] and his group using hydroxylactams generally assumes the prior formation of an acyliminium ion (*e.g.* $R^1CON^+R^2{=}CHR^3$) which causes rather severe geometrical



Scheme.

restrictions on subsequent five-membered ring forming reactions in several cases (entries 1, 6—8 of Table). We felt that a concerted reaction [*e.g.* (**5**)] would be more favoured (entries 10, 11); thus the choice of cyclising reagent might be crucial in diverting the reaction pathway from '5-*endo*-*endo*-*trig*' to '5-*endo*-*exo*-*tet*'. In the event, the *O*-acetate (**22**) (entry 10) did not cyclise; treatment with boron trifluoride–ether in chloroform gave an unexpected, uncyclised material (**23**) as the only isolable product. We can only postulate that the corresponding iminium ion did form and then possibly abstracted a hydride ion from the starting material as shown (Scheme). Treatment of compound (**18**) with $(CF_3CO)_2O$ or with toluene-*p*-sulphonyl chloride in pyridine had no effect and accordingly we failed to find a successful 5-*endo*-*exo*-*tet* cyclisation.

To summarise, although only a few examples of 5,5 ring-fused compounds were uncovered in this work (entries 12, 14—16), they complement those substitution patterns reported in the literature for pyrrolizidine compounds, which have been fashionable synthetic targets recently, using a variety of approaches.[10–20] The facile synthesis of azepinone derivatives (entry 24) is a significant discovery and should be applicable to other imides. Our results as a whole are useful in making predictions about proposed applications of electrophile + chloroalkene cyclisations.

In some cases (entries 12, 14—22) mixtures of products were obtained and their structures were elucidated by spectroscopic means. This is worthy of some comment.

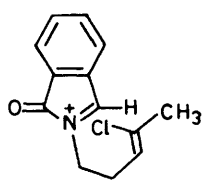
Entry 12. Treatment of the hydroxylactam (**25**) with polyphosphoric acid (PPA) at room temperature gave a new unstable product in low yield. Mass spectral analysis revealed a molecular ion (M^+ 185.0600) which corresponded to $C_9H_{12}ClNO$. Gas liquid chromatography indicated two compounds (50:50) and the i.r. spectrum suggested that a lactam carbonyl and a terminal alkene were present. The n.m.r. spectrum of the compound was complex, but confirmed that the alkenyl proton in the starting material had disappeared. The spectrum showed a new singlet (δ 2.2) which suggested that a vinyl methyl group was present. The analytical data described above are compatible with a mixture of compounds having structures (**26**) and (**27**). Thus, while ring closure has apparently taken place, this has been followed by deprotonation to regenerate the chloroalkenes (**26**) and (**27**) (but see Experimental section). There was no indication of the presence of the hydrolysed compound (**28**) in the mass spectrum. However, treatment of the chloroalkene mixture with concentrated sulphuric acid gave a new compound, the analytical data (mass spectrum, i.r. spectrum, n.m.r. spectrum) of which are consistent with the expected acetylpyrrolizidine (**28**). Gas liquid chromatography indicated that only one compound was present.

Entry 14. Treatment of the hydroxylactam (**30**) with concentrated sulphuric acid at 0 °C gave the acetylpyrroloisoindole derivative (**31**) in moderate yield. Only the thermodynamically less stable *endo*-acetyl epimer (**31**) was isolated. The structure was ascertained by epimerisation and on the basis of the high field n.m.r. spectrum (250 MHz). Treatment of the *endo*-acetyl isomer (**31**) with anhydrous potassium carbonate in dimethyl-

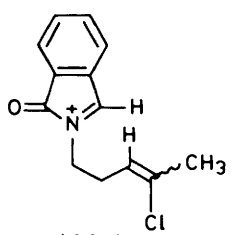
formamide effected complete conversion into the thermodynamically more stable *exo*-acetyl isomer (**32**). Analysis of the crude reaction revealed the presence of the isomer (**32**) as an impurity (10—15%). This impurity was, however, lost on purification. The conversion of the hydroxylactam (**30**) into compounds (**31**) and (**32**) is therefore stereoselective. The high field n.m.r. spectra (250 MHz) of isomers (**31**) and (**32**) are particularly interesting. The actyl methyl group for the *endo*-isomer (**31**) (δ 1.80) is magnetically shielded with respect to the *exo*-isomer (**32**) (δ 2.28). The latter compound exhibits a normal chemical shift for an acetyl methyl group. The origin of this shielding [in (**31**)] is believed to be the aromatic system. The acetyl methyl group in the isomer (**31**) may adopt a conformation in which the relevant protons lie in the shielding zone of the aromatic ring. The corresponding protons in the *exo*-isomer cannot adopt this conformation. For isomer (**31**) the 3-H protons are not equivalent (δ 3.99, 3.48). The downfield proton (3-Hd) appears as a doublet of triplets (^2J = 11.1, ^3J = 8.6 Hz) suggesting a symmetrical disposition of the adjacent 2-H protons. The upfield signal (3-Hu) is obscured by the coincident signal for 1-H_α. From the parameters obtained from the spectrum it is not possible to assign protons 3-Hd and 3-Hu (to 3-H_α and 3-H_β), although Chamberlin and Chung[14] have equated 3-Hd with 3-H_β and 3-Hu with 3-H_α in closely related systems.

The resonance for proton 9b-H [in (**31**)] appears as a doublet (δ 5.00, ^3J 6.8 Hz). For the *exo*-acetyl isomer (**32**) the 3-H protons again are non-equivalent (δ 3.85, 3.55). The downfield signal (3-Hd) is a doublet of triplets (^2J 11.7, ^3J 8.8 Hz). The upfield signal (3-Hu) is a double double doublet (^2J 11.7, ^3J 2.6, 9.3 Hz). The resonance for 1-H_β is a complex multiplet (δ 2.70—2.81) and resonates upfield from the corresponding 1-H_α in the *exo*-isomer (**31**) by *ca.* 0.73 p.p.m. The bridgehead proton (9b-H) for the *exo*-isomer (**32**) appears as a doublet (δ 5.00, ^3J 9.1 Hz). Homonuclear decoupling experiments confirm the assignments made for the spectra of isomers (**31**) and (**32**).

The *endo* selectivity in the cyclisation of the hydroxylactam (**30**) to compound (**31**) can be rationalised by a consideration of the favoured approach of the alkene to the electrophilic centre. The reaction is assumed to take place *via* the acyliminium ion (**31a**) and therefore *via* the favoured '5-*exo*-*endo*-*trig*' mode. The electrophile may, however, add to either side of alkene and the preferred addition governs the stereochemical outcome of the reaction. An examination of molecular models shows that the favoured mode of approach (in terms of the overlap of the π-bond of the alkene with the empty p-orbital in the electrophile) is by structure (**31a**) which would lead to the *endo*-isomer (**31**). A less favoured route is addition of the electrophile to the opposite side of the alkene *via* (**32a**); this would lead to the *exo*-isomer

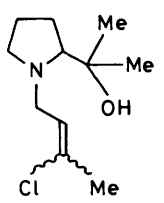


(**31a**)

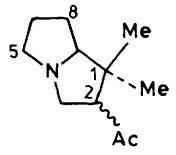


(**32a**)

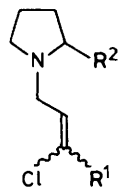
(**32**). Clearly from (**31a**) the alkenyl proton of the starting material eventually becomes the 1-H_α proton in the product (**31**) and from (**32a**) the alkenyl proton becomes the 1-H_β proton of the *exo*-isomer (**32**). It is possible that the addition is stereospecific and that acid-catalysed epimerisation may occur to give the *exo*-isomer (**32**) as an impurity.



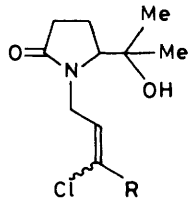
(**36**)



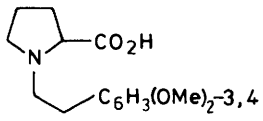
(**37**)



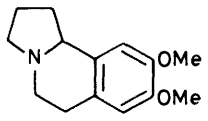
(**38**) R^1 = H, R^2 = C(OH)Me_2
(**39**) R^1 = Me, R^2 = CH_2OH



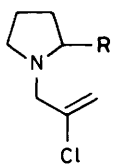
(**40**) R = Me
(**41**) R = H



(**42**)



(**43**)

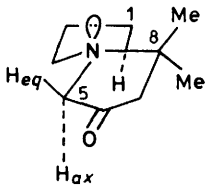


(**44**) R = C(OH)Me_2
(**45**) R = CH_2OH
(**46**) R = CH_2OCHO

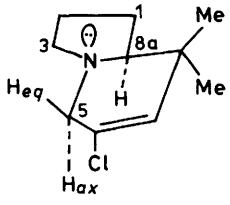
Entry 15. On reaction of *N*-(4-chloropent-3-enyl)phthalimide with methylmagnesium iodide, an inseparable unstable mixture of the hydroxylactam (**33**) and the enamide (**34**) was obtained, and this was stirred with sulphuric acid at 0 °C, affording the *endo*-acetyl compound (**35**) exclusively. As with the analogue (**31**) the acetyl methyl group protons are shielded by the aromatic system (δ 1.75) in compound (**35**). The axial methyl group on C-9b resonates at δ 1.64. The 3-H protons are non-equivalent (δ 4.08, 3.44) and the downfield resonance 3-Hd appears as a doublet of triplets (^2J 11.7, ^3J 8.4 Hz). The upfield resonance 3-Hu is a double double doublet (^2J 11.7, ^3J 4.9, 7.6 Hz). A double doublet (δ 3.26, ^3J 2.7, 5.8 Hz) is assigned to 1-H_α. The close similarity between the n.m.r. spectra of compounds (**31**) and (**35**) confirm the structure of the latter and the stereochemistry at C-1.

Entry 22. The ketone (**48**) and the chloroalkene (**47**) were obtained (70:30 ratio by g.l.c.) in good yield and separated by chromatography with considerable loss due to decomposition. The mass spectrum confirmed the existence of molecular ions for each structure (**48**) and (**47**). The i.r. spectrum for ketone (**48**) indicates a strong ketonic carbonyl absorption (1 720 cm^{-1}) and showed two distinct peaks at 2 775 and 2 720 cm^{-1}. The latter feature, termed 'Bohlmann bands' or '*trans* bands' is characteristic of a *trans*-fused structure in bridgehead nitrogen bicyclic compounds,[21,22] and therefore confirms a *trans*-fused structure for ketone (**48**). These abnormally low frequency C–H stretching absorptions were first observed in quinolizidines and have been shown to be present in *trans*-fused

indolizidines[23] and some rigid piperidines;[24] they occur provided the molecule has hydrogen atoms (on the carbons α to the nitrogen atom) which are antiperiplanar with the lone pair of electrons on the nitrogen atom. The effect has been rationalised by Hamlow, Okuda, and Nakagawa[25] who suggested that a greater p character in the α-C to H_{ax} bond than the α-C to H_{eq} bond would lower the force constant of the former bond with respect to the latter and would therefore lower the stretching frequency of the former relative to the latter. The authors also believed that this phenomenon was the origin of a special shielding effect on the α-axial hydrogens in the ^{1}H n.m.r. spectrum of quinolizidine (H_{eq} δ 2.75, H_{ax} δ 1.82). The high field ^{1}H n.m.r. spectrum (250 MHz) shows this effect with the C-5 hydrogens. A double doublet at δ 3.46 is tentatively assigned as the equatorial hydrogen (5-H_{eq}). The coupling constants can be measured and show a large geminal coupling (14.0 Hz) and an unassigned long-range coupling (1.7 Hz). A doublet at δ 2.70 (^2J 14.0 Hz) is assigned to the axial hydrogen (5-H_{ax}). The bridgehead proton (8a-H, δ 3.05—3.26) is a complex multiplet. The geminal dimethyl resonances (δ 0.92, 0.98) are non-equivalent owing to anisotropic shielding and deshielding. The remaining protons are unresolved and can only be provisionally assigned. The i.r. spectrum for the chloroalkene (**48**) shows a weak internal alkene absorption (1 645 cm^{-1}). As with the ketone (**47**) the presence of 'Bohlmann bands' (2 730, 2 775 cm^{-1}) indicates a *trans*-fused structure.



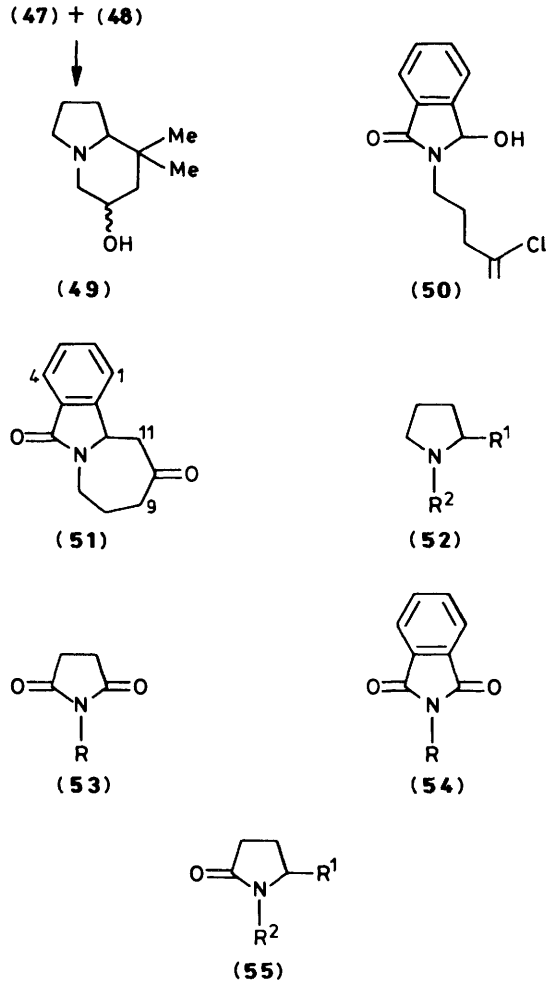
(47)



(48)

The high field ^{1}H n.m.r. spectrum (250 MHz) shows the characteristic non-equivalence for the C-5 hydrogens. A double doublet at δ 3.50 is assigned to the equatorial hydrogen (5-H_{eq}). The coupling constants show a large geminal coupling (15.6 Hz) and an unassigned long-range coupling (0.8 Hz). A double doublet at δ 2.87 is assigned to the axial hydrogen (5-H_{ax}) with some certainty. The geminal (15.6 Hz), and allylic [2.3 Hz, $H(5)_{ax}$–H(7)] coupling constants are confirmed by decoupling experiments. Clearly only 5-H_{ax} can couple allylically to the alkenyl proton (7-H), since the magnitude of an allylic coupling constant depends on the dihedral angle about the carbon-carbon single bond. This is maximum when the allylic C–H bond is perpendicular to the alkene plane [$H(5)_{ax}$–H(7)] and approximately zero when all the nuclei involved are coplanar[26,27] [$H(5)_{eq}$–H(7)]. The alkenyl proton (7-H) at δ 5.60 gives a double doublet with an allylic coupling constant (2.3 Hz) and an unassigned long-range coupling (1.2 Hz). The 5-H proton assignments, proved in this case, confirm the assignments of the corresponding protons in the ketone (**47**) above. The bridgehead proton (8a-H) is a complex multiplet (δ3.15—3.22) in the chloroalkene (**48**). The geminal dimethyl resonances (δ 0.96, 0.98) are non-equivalent, but the separation is less than in the ketone (**47**) suggesting a greater deviation from a chair structure in the six-membered ring in the chloroalkene structure; this is imposed by the two sp^2 hybridised carbon atoms. The remaining protons are unresolved and can only be provisionally assigned.

Owing to the instability of the ketone (**47**), the elemental analysis was unreliable. The ketone was therefore reduced with sodium borohydride to the alcohols (**49**) which gave satisfactory elemental analyses.



Entry 24. The azepinone (**51**) was obtained along with compound (**31**) by cyclisation of a mixture of the phthalimides (**30**) and (**50**). These arose originally because treatment of 5-chloropentan-2-one with PCl_5 gave an inseparable mixture of 2,5-dichloropent-2-ene and 2,5-dichloropent-1-ene. It was convenient to use this mixture for alkylation of phthalimide to give precursors for compounds (**30**) and (**50**) in good yield. Compound (**30**) was also synthesised separately using a pure sample of 2,5-dichloropent-2-ene made from cyclopropyl methyl ketone.[28] Compounds (**51**) and (**31**) were easily separated by chromatography.

Experimental

Several compounds in this work were unstable and repeatedly gave carbon analyses that were 0.5—0.8% in error; in every case, however, t.l.c. and/or g.l.c. analyses indicated that they were single substances.

Compounds referred to as *E* and *Z* were unmeasured mixtures of *E*- and *Z*-chloroalkenyl compounds containing a 3-chloroprop-2-enyl, 3-chlorobut-2-enyl, or 4-chloropent-3-enyl moiety. 2,3-Dichloropropene and 1,3-dichlorobut-2-ene are commercially available.

(E)- *and* (Z)-*Dichloropent-2-ene and* 2,5-*Dichloropent-1-ene.*—5-Chloropentan-2-one (12.06 g, 0.10 mol) in dry dichloro-

methane (50 ml) was added to phosphorus pentachloride (22.9 g, 0.11 mol) in dry dichloromethane (100 ml) and the mixture refluxed for 41 h. The solution was added to ice–water and extracted with dichloromethane. The extract was washed with dilute sodium carbonate solution and water and evaporated to give a crude mixture of products (12.5 g). Distillation (45—60 °C, 30 mmHg) afforded a colourless liquid (7.9 g, 57%) (Found: C, 43.15; H, 5.8. Calc. for $C_5H_8Cl_2$: C, 43.2; H, 5.8%). $\nu_{max.}$ 1 665 (internal alkene), 1 635 cm^{-1} (terminal alkene); δ [(*E*)- and (*Z*)-2,5-dichloropent-2-ene][28] 5.53 (1 H, dt, vinyl), 3.4—3.7 (2 H, dt, CH_2Cl), 2.35—2.8 (2 H, m, CH_2) and 2.1 (3 H, s, CH_3). δ [2,5-dichloropent-1-ene] 5.2 (2 H, s, vinyl), 3.4—3.7 (2 H, t, CH_2), and 1.9—2.2 (2 H, m, CH_2-vinyl) (g.l.c. and ^1H n.m.r. integration suggests an approximately 50:50 ratio of structural isomers).

(E)- *and* (Z)-5-*Bromo*-2-*chloropent*-2-*ene*.—To 2-chloropent-2-en-5-ol[29] (10 g, 0.083 mol) at −10 °C (ice–salt) was added phosphorus tribromide (8.5 g, 0.031 mol) during 30 min. The mixture was left to stand overnight at room temperature, added to water and extracted with dichloromethane. The extract was washed with dilute sodium hydrogen carbonate solution and water and evaporated to give the crude *product* (12 g). Distillation (20 °C, 0.1 mmHg) gave a colourless liquid (8.3 g, 54%) (Found: C. 32.25; H, 4.25. C_5H_8BrCl requires C, 32.75; H, 4.4%); $\nu_{max.}$ 1 660 cm^{-1} (C=C), δ 5.52 (1 H, dt, vinyl), 3.4 (2 H, t, CH_2Br), 2.5—2.9 (2 H, m, CH_2), and 2.1 (3 H, s, CH_3).

Potassium N-(2-*Chloroprop*-2-*enyl*)*prolinate* (**52**; $R^1 = CO_2K$, $R^2 = CH_2CCl{=}CH_2$).—L-Proline (11.5 g, 0.1 mol), 2,3-dichloropropene (12.0 g, 0.109 mol), anhydrous potassium carbonate (20 g), and ethanol (250 ml) were stirred and refluxed for 40 h. The hot mixture was filtered and the solvent was removed under reduced pressure to give a fawn solid. Recrystallisation from ethanol gave the *product* (15.9 g) as the impure potassium salt, $\nu_{max.}$ 3 300—3 500 (OH), 1 550—1 700 cm^{-1} (C=O); δ (D_2O) 5.45 (1 H, s, vinyl), 5.38 (1 H, s, vinyl), 3.55 (1 H, d, CH_2N, ^2J 14.5 Hz), 3.21 (1 H, d, CH_2N, ^2J 14.5 Hz), 2.8—3.2 (2 H, m, CH_2), and 1.5—2.6 (5 H, m, CH_2CH_2, CH).

Ethyl N-(2-*Chloroprop*-2-*enyl*)*prolinate* (**52**; $R^1 = CO_2Et$, $R^2 = CH_2CCl{=}CH_2$).—Crude potassium *N*-(2-chloroprop-2-enyl)prolinate (10 g) and ethanol (400 ml) were heated to reflux. Thionyl chloride (10 ml) was added dropwise and the mixture refluxed for 5 h. The solvent was removed under reduced pressure and to the residue was added dilute potassium carbonate solution and water. Extraction with dichloromethane gave a brown liquid (9.68 g). Kugelrohr distillation (60 °C, 0.25 mmHg) gave a colourless liquid (8.20 g, 60% from proline) (Found: 54.35; H, 7.35; Cl, 16.3; N, 6.5. $C_{10}H_{16}ClNO_2$ requires C, 55.15; H, 7.4; Cl, 16.3; N, 6.45%); $\nu_{max.}$ 1 730 (ester), 1 635 cm^{-1} (C=C); δ 5.47 (1 H, s, vinyl), 5.28 (1 H, s, vinyl), 4.15 (2 H, q, CH_2), 3.0—3.5 (4 H, ms, CH_2), 2.5—2.7 (1 H, m, CH), 1.7—2.2 (4 H, m, CH_2CH_2), and 1.25 (3 H, t, CH_3).

Methyl N-(2-*Chloroprop*-2-*enyl*)*prolinate* (**52**; $R^1 = CO_2Me$, $R^2 = CH_2CCl{=}CH_2$).—Crude potassium *N*-(2-chloroprop-2-enyl)prolinate (1.0 g) and methanol (40 ml) were heated to reflux. Thionyl chloride (0.8 ml) was added dropwise and the mixture refluxed for 5 h. The solvent was removed under reduced pressure and to the residue was added potassium carbonate solution and water. Extraction with dichloromethane gave a brown liquid (0.75 g). Kugelrohr distillation afforded a colourless liquid (0.45 g, 35% from proline) (Found: C, 53.6; H, 7.1; N, 6.55%; M^+, 203.0700. $C_9H_{14}ClNO_2$ requires C, 53.1; H, 7.2; N, 6.9%; *M*, 203.0713); $\nu_{max.}$ 1 740 (ester), 1 635 cm^{-1} (C=C); δ 5.37 (1 H, s, vinyl), 5.26 (1 H, s, vinyl), 3.69 (3 H, s, CH_3), 3.3—3.5 (2 H, m, CH_2), 3.0—3.25 (2 H, m, CH_2), 2.5—2.8 (1 H, m, CH), and 1.7—2.2 (4 H, m, CH_2).

N-(2-*Chloroprop*-2-*enyl*)*proline* (**52**; $R^1 = CO_2H$, $R^2 = CH_2CCl_2{=}CH_2$).—Ethyl *N*-(2-chloroprop-2-enyl)prolinate (2.0 g, 9.2 mmol), sodium hydroxide solution (10.0 ml, 0.02 mol; 2.00M) and ethanol (3 ml) were stirred at room temperature for 21 h. Hydrochloric acid (8.35 ml, 0.02 mol; 2.395M) was added and the solvent was removed under reduced pressure affording a gum. The organic material was dissolved in acetone, the solution was filtered and the solvent removed under reduced pressure to give the *product* (1.59 g, 91%) which slowly solidified (Found: C, 50.15; H, 6.35; Cl, 18.45; N, 7.25. $C_8H_{12}ClNO_2$ requires C, 50.65; H, 6.4; Cl, 18.7; N, 7.4%); $\nu_{max.}$ 3 400 (OH), 1 550—1 675 cm^{-1} (C=O); δ (D_2O) 5.82 (1 H, s, vinyl), 5.72 (1 H, dist. s, vinyl), 4.1 (2 H, s, CH_2N), 3.6—4.1 (2 H, m, CH_2), 3.05—3.45 (1 H, m, CH), and 1.9—2.65 (4 H, ms, CH_2CH_2).

Ethyl Prolinate (**52**; $R^1 = CO_2Et$, $R^2 = H$).—L-Proline (23 g, 0.2 mol) and ethanol (500 ml) were heated to reflux. Thionyl chloride (30 ml) was added dropwise and the mixture refluxed for 5 h. The solvent was removed under reduced pressure and to the residue was added dilute potassium carbonate solution and water. Extraction with dichloromethane gave a brown liquid. Kugelrohr distillation (65 °C, 0.1 mmHg) afforded a colourless liquid (20.4 g, 71%). The ester rapidly dimerised and was redistilled before use. $\nu_{max.}$ 3 340 (NH), 1 725 cm^{-1} (ester); δ 4.16 (2 H, q, CH_2), 3.7 (1 H, m, CH), 2.7—3.2 (2 H, m, CH_2), 2.43 (1 H, s, NH, exch.), 1.6—2.2 (4 H, m, CH_2), and 1.26 (3 H, t, CH_3).

(E)- *and* (Z)-*Ethyl* N-(4-*Chloropent*-3-*enyl*)*prolinate* [*Ethyl Ester of* (**29**)].—Ethyl prolinate (2.73 g, 0.019 mol), 5-bromo-2-chloropent-2-ene (3.87 g, 0.021 mol), anhydrous sodium hydrogen carbonate (1.80 g, 0.021 mol), and dry toluene (25 ml) were stirred at reflux for 12 h. The mixture was added to water and extracted with chloroform to give the crude *product* (4.9 g). Kugelrohr distillation (110 °C, 0.4 mmHg) gave a colourless liquid (3.31 g, 71%) (Found: C, 58.45; H, 8.25; Cl, 14.5; N, 5.7. $C_{12}H_{20}ClNO_2$ requires C, 58.65; H, 8.2; Cl, 14.45; N, 5.7%); $\nu_{max.}$ 1 730 (ester), 1 660 cm^{-1} (C=C); δ 5.5 (1 H, t, vinyl), 4.19 (2 H, q, CH_2), 3.0—3.3 (2 H, m, CH_2), 1.6—2.85 (9 H, ms, remaining protons) 2.1 (3 H, s, CH_3), and 1.28 (3 H, t, CH_3).

(E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)*proline* (**29**).—Ethyl *N*-(4-chloropent-3-enyl)prolinate (0.50 g, 2 mmol), sodium hydroxide (0.20 g, 5 mmol), methanol (3 ml), and water (15 ml) were stirred at room temperature for 16 h. The solution was acidified to pH 6.5 with dilute hydrochloric acid and the water was removed under reduced pressure. Hot acetone was added to the residual solid and the resulting solution was filtered to remove the inorganic material. The acetone solution was concentrated, and the *product* (0.31 g, 70%) separated as white crystals on cooling, m.p. 118—120 °C (from acetone) (Found: C, 55.7; H, 7.5; Cl, 16.65; N, 6.6. $C_{10}H_{16}ClNO_2$ requires C, 55.15; H, 7.4; Cl, 16.3; N, 6.45; $\nu_{max.}$ 3 400 (OH), 1 665 (C=C), and 1 615 cm^{-1} (C=O); δ (D_2O) 5.57 (1 H, dt, vinyl), 3.6—4.1 (2 H, m, CH_2), 3.1—3.45 (2 H, m, CH_2), 2.4—2.75 (3 H, m, CH_2, CH), and 1.6—2.3 (7 H, ms CH_2CH_2, CH_3).

3-(2-*Chloroprop*-2-*enyl*)-N-*methyl*-2-*oxopyrrolidine*-3-*carboxylic Acid* (**21**; R = CO_2H).—Ethyl 3-(2-chloroprop-2-enyl)-*N*-methyl-2-oxopyrrolidine-3-carboxylate (**21**; R = CO_2Et)[30] (2.0 g, 8.7 mmol) in methanol (10 ml) was added to sodium hydroxide (0.73 g, 0.18 mol) in water (20 ml). After being stirred at room temperature for 1 h, the solution was diluted with water (25 ml) and washed with dichloromethane. The liquor was acidified and extracted with dichloromethane to give a solid

product (1.53 g). Recrystallisation from ether afforded a white solid (1.10 g, 58%), m.p. 115—117 °C (decomp.) (Found: C, 49.6; H, 5.4; Cl, 16.2; N, 6.35. $C_9H_{12}ClNO_3$ requires C, 49.65; H, 5.55; Cl, 16.3; N, 6.45%); $\nu_{max.}$ 1 745, 1 725 (CO_2H), and 1 630—1 600 cm^{-1} (lactam, C=C); δ 10.9 (1 H, s, CO_2H, exch.), 5.32 (2 H, s, vinyl), 3.15—3.6 (2 H, m, CH_2N), 3.08 (1 H, d, CH_2-vinyl, *J* 14 Hz) 2.9 (1 H, d, CH_2-vinyl, *J* 14 Hz), 2.9 (3 H, s, CH_3), and 2.1—2.75 (2 H, m, CH_2).

3-(2-*Chloroprop*-2-*enyl*)-N-*methyl*-2-*pyrrolidone* (**21**; R=H).—*N*-Methyl-3-(2-chloroprop-2-enyl)-2-oxopyrrolidine-3-carboxylic acid (1.22 g, 5.6 mmol) was heated at 130 °C under nitrogen until carbon dioxide evolution ceased (20 min). Kugelrohr distillation (85 °C, 0.07 mmHg) gave the *product* as a colourless liquid (0.91 g, 93%) (Found: C, 55.0; H, 7.05; Cl, 20.65; N, 8.0. $C_8H_{12}ClNO$ requires C, 55.35; H, 6.95; Cl, 20.4; N, 8.05%); $\nu_{max.}$ 1 685 (lactam), 1 630 cm^{-1} (C=C); δ 5.22 (2 H, s, vinyl), 3.25—3.45 (2 H, m, CH_2), 2.85 (3 H, s, CH_3), and 1.6—3.1 (5 H, ms, remaining protons).

8,9-*Dimethoxy*-1,2,3,5,6,10b-*hexahydropyrrolo*[2,1-a]*isoquinoline*[31] (**43**).—Phosphorus oxychloride (2.3 ml, 0.025 mol) was added to *N*-[2-(3,4-dimethoxyphenyl)ethyl]proline[32] (**42**) (0.645 g, 2.3 mmol) under nitrogen. The mixture was heated to 100 °C and stirred vigorously for 2.5 min, then cooled (ice–water). Concentrated hydrochloric acid (23 ml) was added and the mixture heated at 50 °C for 20 h. The contents of the flask were basified with sodium carbonate solution and extracted with chloroform to give a fawn solid (0.367 g). Recrystallisation from light petroleum (b.p. 60—80 °C) gave a white crystalline solid (0.330 g, 62%); m.p. 87—88 °C (lit.,[31] m.p. 88—89 °C) (Found: C, 71.6; H, 8.5; N, 5.75. Calc. for $C_{14}H_{19}NO_2$: C, 72.05; H, 8.2; N, 6.0%); $\nu_{max.}$ 1 600 cm^{-1} (aryl); δ 6.56 (1 H, s, aryl), 6.52 (1 H, s, aryl), 3.83 (6 H, s, CH_3O), and 1.5—3.6 (11 H, ms, remaining protons).

N-*Benzylproline*[33] (**52**; $R^1 = CO_2H$, $R^2 = PhCH_2$).—L-Proline (575 g, 0.05 mol), benzyl chloride (7 g, 0.055 mol), anhydrous sodium carbonate (5.3 g) and ethanol (125 ml) were stirred and refluxed for 3 h. The solvent was removed under reduced pressure and the residue was dissolved in water (50 ml). The pH of the solution was adjusted to 6.5 with dilute hydrochloric acid and the solvent was removed under reduced pressure. Recrystallisation of the residue from acetone gave the product as white plates (2.8 g, 27%), m.p. 177—179 °C (lit.,[33] m.p. 176—178 °C) (Found: C, 69.85; H, 7.35; N, 7.15. Calc. for $C_{12}H_{15}NO_2$: C, 70.2; H, 7.35; N, 6.8%); $\nu_{max.}$ 3 400 (OH), 1 640 cm^{-1} (CO_2); δ (D_2O) 7.5 (5 H, s, aryl), 4.38 (2 H, s, CH_2), and 1.9—4.1 (7 H, ms, remaining protons).

N-(m-*Methoxybenzyl*)*proline* (**52**; $R^1 = CO_2H$, $R^2 = CH_2$-C_6H_4OMe-3).—L-Proline (5.75 g, 0.05 mol), *m*-methoxybenzyl chloride (7.83 g, 0.05 mol), anhydrous sodium carbonate (5.3 g), and ethanol (125 ml) were stirred and refluxed for 3 h, and the solvent was removed under reduced pressure. Recrystallisation of the residue from acetone gave the *product* as white crystals (8.3 g, 71%), m.p. 116—119 °C. (Found: C, 66.25; H, 7.5; N, 5.95. $C_{13}H_{17}NO_3$ requires C, 66.4; H, 7.25; N, 5.95%), $\nu_{max.}$ 3 380 (OH), 1 625 (CO_2H), and 1 600 cm^{-1} (aryl); δ (D_2O) 7.40—7.6 (4 H, ms, aryl), 4.37 (2 H, s, CH_2), 3.87 (3 H, s, CH_3O), and 1.6—4.2 (7 H, ms, remaining protons).

2-(2-*Chloroprop*-2-*enyl*)*cyclopentanone*.—*N*-(Cyclopent-1-enyl)morpholine[34] (25 g, 0.163 mol), 2,3-dichloropropene (21.9 g, 0.197 mol), and acetonitrile (200 ml) were refluxed for 21 h. The solvent was removed under reduced pressure and the residue was heated with dilute hydrochloric acid. Extraction with ether afforded the crude *product* (10.1 g). Distillation gave cyclopentanone (2.2 g) and the product (4.89 g) and redistillation of the latter (55 °C, 0.25 mmHg) gave a colourless liquid (3.26 g, 12.5%) (Found: C, 60.4; H, 7.0; Cl, 21.95. $C_8H_{11}ClO$ requires C, 60.55; H, 7.0; Cl, 22.35%); $\nu_{max.}$ 1 740 (C=O), 1 635 cm^{-1} (C=C); δ 5.15 (2 H, s, vinyl), 1.1—3.15 (9 H, ms, remaining protons).

2-(2-*Chloroprop*-2-*enyl*)-1-*methylcyclopentanol* (**24**).—2-(2-Chloroprop-2-enyl)cyclopentanone (1.5 g, 9.5 mmol) was added during 45 min to methylmagnesium iodide (0.0285 mol) prepared from magnesium (0.75 g, 0.0314 mol) and methyl iodide (4.05 g, 0.0285 mol) in ether (75 ml). After 17 h at room temperature, dilute ammonium chloride solution was added. Extraction with dichloromethane afforded the crude *product* (1.59 g). Kugelrohr distillation (82 °C, 0.1 mmHg) gave a colourless liquid (1.4 g, 84%) (Found: C, 62.3; H, 8.7; Cl, 19.8. $C_9H_{15}ClO$ requires C, 61.9; H, 8.65; Cl, 20.3%); $\nu_{max.}$ 3 490 (OH), 1 630 cm^{-1} (C=C); δ 5.15 (2 H, s, vinyl), 1.45—2.8 (10 H, ms, remaining protons), 1.3 (1.5 H, s, *trans*-CH_3), and 1.2 (1.5 H, s, *cis*-CH_3).

N-(2-*Chloroprop*-2-*enyl*)-2-(2-*hydroxy*-2-*propyl*)*pyrrolidine* (**44**).—Methylmagnesium iodide (0.033 mol) was prepared by the addition of methyl iodide (4.68 g, 0.033 mol) to magnesium turnings (0.84 g, 0.035 mol) and dry ether (75 ml) under nitrogen. Ethyl *N*-(2-chloroprop-2-enyl)prolinate (**52**; $R^1 = CO_2Et$, $R^2 = CH_2CCl{=}CH_2$) (2.7 g, 0.010 mol) in dry ether (20 ml) was added dropwise during 15 min, and the mixture was stirred for 15 h, added to water, and acidified with dilute hydrochloric acid. Basification with sodium carbonate solution followed by extraction with chloroform afforded a yellow liquid (1.93 g). Kugelrohr distillation (70 °C, 0.05 mmHg) gave a colourless liquid (1.55 g, 76%) (Found: C, 58.35; H, 8.9; Cl, 17.15; N, 6.75. $C_{10}H_{18}ClNO$ requires C, 58.95; H, 8.9; Cl, 17.4; N, 6.9%); $\nu_{max.}$ 3 450 (OH), 1 640 cm^{-1} (C=C); δ 5.41 (1 H, s, vinyl), 5.27 (1 H, s, vinyl), 3.6 (1 H, d, CH_2N, *J* 15 Hz), 3.3 (1 H, d, CH_2N, *J* 15 Hz), 2.9—3.15 (1 H, m, CH), 2.3—2.8 (2 H, m, CH_2), 2.5 (1 H, s, OH, exch.), 1.5—2.0 (4 H, m, CH_2CH_2), 1.2 (3 H, s, CH_3), and 1.15 (3 H, s, CH_3).

8,8-*Dimethyl*-1,2,3,7,8,8a-*hexahydroindolizin*-6(5H)-*one* (**47**) *and* 6-*Chloro*-8,8-*dimethyl*-1,2,3,5,8,8a-*hexahydroindolizine* (**48**).—Sulphuric acid (60 ml, 96%) was stirred under nitrogen for 15 min; *N*-(2-chloroprop-2-enyl)-2-(2-hydroxy-2-propyl)pyrrolidine (**44**) (1.0 g, 4.9 mmol) was added and stirring continued for 10 min at room temperature. The mixture was added to ice–water, basified with sodium carbonate and extracted with chloroform to give a yellow liquid (0.744 g). Kugelrohr distillation (80 °C, 0.1 mmHg) afforded a colourless liquid (0.65 g, 88% based on ^1H n.m.r.) comprising the ketone (**47**) and the chloroalkene (**48**) in the ratio of 70:30, confirmed by g.l.c. Mass spectral analysis of the mixture indicated the presence of two species: (**47**) (Found: M^+, 167.1319. $C_{10}H_{17}NO$ requires *M*, 167.1310) and (**48**) (Found: M^+ 185.0978. $C_{10}H_{16}ClN$ requires M, 185.0971). Chromatography (15% ether–light petroleum, b.p. 60—80 °C) with 0.44 of material gave the unstable ketone (**47**) (0.185 g) and chloroalkene (**48**) (0.149 g). Kugelrohr distillation of the ketone (**47**) (80 °C, 0.3 mmHg) gave a colourless liquid (0.099 g). Kugelrohr distillation of the chloroalkene (**48**) (60 °C, 0.3 mmHg) gave a colourless liquid (0.096 g): 8,8-*Dimethyl*-1,2,3,7,8,8a-*hexahydroindolizin*-6(5H)-*one* (**47**), $\nu_{max.}$ 2 775, 2 720 (axial; 5-H, 8a-H), 1 720 cm^{-1} (C=O); δ (250 MHz) 3.46 (1 H, dd, ^2J 14.0 Hz, *J* 1.7 Hz, 5-H_{eq}), 3.05—3.13 (1 H, m, 8a-H), 2.70 (1 H, d, ^2J 14.0 Hz, 5-H_{ax}), 2.08—2.26 (4 H, ms, 2 CH_2), 1.71—1.89 (3 H, m, CH_2, CH-*H*), 1.49—1.66 (1 H, m, CH-*H*), 0.98 (3 H, s, CH_3), and 0.92 (3 H, s, CH_3).

6-*Chloro*-8,8-*dimethyl*-1,2,3,5,8,8a-*hexahydroindolizine* (**48**).—(Owing to technical difficulties, an elemental analysis

was not obtained for this compound.) $\nu_{max.}$ 2 775, 2 730 (5-H_{ax}, 8a-H) 1 645 cm^{-1} (C=C); δ (250 MHz) 5.60 (1 H, dd, *J* 2.3, 1.2 Hz), 3.50 (1 H, dd, ^2J 15.6, 0.8 Hz, 5-H_{eq}), 3.15—3.22 (1 H, m, 8a-H), 2.87 (1 H, dd, ^2J 15.6, 2.3 Hz, 5-H_{ax}), 2.02—2.22 (2 H, ms, CH_2, 7-H), 1.50—1.84 (4 H, ms, CH_2, CH_2), 0.98 (3 H, s, CH_3), and 0.96 (3 H, s, CH_3).

8,8-*Dimethyl*-1,2,3,5,6,7,8,8a-*octahydroindolizin*-6-*ol* (**49**).—8,8-Dimethyl-1,2,3,7,8,8a-hexahydroindolizin-6(5*H*)-one (**47**) (0.60 g, 3.6 mmol), sodium borohydride (0.20 g, 5.3 mmol), and ethanol (30 ml) were stirred at room temperature for 16 h. The mixture was added to water and extracted with chloroform to give an oil (0.50 g). Chromatography (acetone) afforded the *product* (0.304 g, 51%), m.p. 55—57 °C, plus a complex mixture of less polar materials (0.150 g) which was not further investigated (Found: C, 71.0; H, 11.3; N, 8.1. $C_{10}H_{19}NO$ requires C, 70.95; H, 11.3; N, 8.3%); $\nu_{max.}$ 3 400 cm^{-1} (OH); δ 3.8—4.0 (1 H, m, CHOH), 2.9—3.2 (2 H, m, CH_2N) 2.4 (1 H, s, OH, exch.), 1.9—2.25 (2 H, m, CH_2N), 1.45—1.9 (5 H, m, 2 CH_2, CH), 1.0—1.35 (2 H, m, CH_2), 1.1 (3 H, s, CH_3), and 0.85 (3 H, s, CH_3).

(E)- *and* (Z)-*Sodium* N-(3-*Chlorobut*-2-*enyl*)*prolinate* [**52**; R^1 = CO_2Na, R^2 = $CH_2CH{=}C(Cl)CH_3$].—L-Proline (11.5 g, 0.10 mol), 1,3-dichlorobut-2-ene (13.6 g, 0.11 mol), anhydrous sodium carbonate (15 g), and ethanol (250 ml) were stirred and refluxed for 21 h. The hot mixture was filtered and the solvent removed under reduced pressure to give the *product* (13.9 g) as the impure sodium salt; $\nu_{max.}$ 3 400 (OH), 1 550—1 770 cm^{-1} (C=O); δ (D_2O) 5.70 (1 H, dt, vinyl), 2.8—3.6 (4 H, ms, 2 CH_2), 2.05—2.55 (1 H, m, CH), 2.13 (3 H, s, CH_3), and 1.6—2.0 (4 H, m, CH_2CH_2).

(E)- *and* (Z)-*Sodium* N-(3-*Chloroprop*-2-*enyl*)*prolinate* (**52**; R^1 = CO_2Na, R^2 = $CH_2CH{=}CHCl$).—L-Proline (11.5 g, 0.10 mol), 1,3-dichloropropene (15.0 g, 0.11 mol), anhydrous sodium carbonate (15 g), and ethanol (250 ml) were stirred and refluxed for 24 h. The hot mixture was filtered and the solvent removed under reduced pressure to give a fawn solid which was washed with ether to give the *product* (16.7 g) as the impure sodium salt; $\nu_{max.}$ 3 400 (OH), 1 500—1 700 cm^{-1} (C=O); δ (D_2O) 5.8—6.4 (2 H, ms, vinyl), 2.8—3.5 (4 H, ms, CH_2CH_2), and 1.5—2.55 (5 H, ms, CH, CH_2CH_2).

(E)- *and* (Z)-*Ethyl* N-(3-*Chlorobut*-2-*enyl*)*prolinate* [**52**; R^1 = CO_2Et, R^2 = $CH_2CH{=}C(Cl)CH_3$].—Crude sodium *N*-(3-chlorobut-2-enyl)prolinate (5.0 g, 0.025 mol) and ethanol (200 ml) were heated to reflux. Thionyl chloride (3.9 ml, 0.043 mol) was added dropwise and the mixture refluxed for 5 h. The solvent was removed under reduced pressure, and to the residue was added dilute sodium carbonate solution and water. Extraction with dichloromethane afforded a brown liquid (4.73 g). Kugelrohr distillation (120 °C, 0.15 mmHg) gave a colourless liquid (4.4 g, 50% from proline) (Found: C, 57.05; H, 7.9; Cl, 15.0; N, 6.06. $C_{11}H_{18}ClNO_2$ requires C, 57.0; H, 7.85; Cl, 15.3; N, 6.05); $\nu_{max.}$ 1 740 (ester), 1 665 cm^{-1} (C=C); δ 5.65 (1 H, dt, vinyl), 4.2 (2 H, q, CH_2), 3.0—3.5 (4 H, ms, 2 CH_2), 2.25—2.6 (1 H, m, CH), 2.13 (3 H, s, CH_3), 1.7—2.2 (4 H, m, CH_2CH_2), and 1.3 (3 H, t, CH_3).

(E)- *and* (Z)-*Ethyl* N-(3-*Chloroprop*-2-*enyl*)*prolinate* (**52**; R^1 = CO_2Et, R^2 = $CH_2CH{=}CHCl$).—Crude sodium *N*-(3-chloroprop-2-enyl)prolinate (10.8 g, 0.057 mol) and ethanol (250 ml) were heated to reflux. Thionyl chloride (10.8 ml, 0.118 mol) was added dropwise and the mixture refluxed for 5 h. The solvent was removed under reduced pressure and to the residue was added water and dilute sodium carbonate solution. Extraction with distillation (100 °C, 0.05 mmHg) gave a colourless liquid (8.8 g, 63% from proline) (Found: C, 55.25; H, 7.45; Cl, 15.9; N, 6.45. $C_{10}H_{16}ClNO_2$ requires C, 55.2; H, 7.4; Cl, 16.3; N, 6.45%); $\nu_{max.}$ 1 730 (ester), 1 630 cm^{-1} (C=C); δ 5.8—6.3 (2 H, m, vinyl), 4.2 (2 H, q, CH_2), 3.0—3.55 (4 H, m, 2 CH_2), 2.25—2.6 (1 H, m, CH), 1.7—2.2 (4 H, m, CH_2), and 1.3 (3 H, t, CH_3).

(E)- *and* (Z)-N-(3-*Chlorobut*-2-*enyl*)-2-(2-*hydroxy*-2-*propyl*)*pyrrolidine* (**36**).—Methylmagnesium iodide (0.033 mol) was prepared by addition of methyl iodide (4.68 g, 0.033 mol) to magnesium turnings (0.84 g, 0.035 mol) and dry ether (75 ml) under nitrogen. Ethyl *N*-(3-chlorobut-2-enyl)prolinate (2.3 g, 0.010 mol) in dry ether (20 ml) was added dropwise to this during 15 min, then dry ether (100 ml) was added and the reaction mixture stirred for 15 h, added to water, acidified with dilute hydrochloric acid, rebasified with sodium carbonate solution, and extracted with chloroform to give a yellow liquid (2.4 g). Kugelrohr distillation (120 °C, 0.2 mmHg) afforded a colourless liquid (1.9 g, 88%) (Found: C, 60.05; H, 9.5; Cl, 16.55; N, 6.4. $C_{11}H_{20}ClNO$ requires C, 60.7; H, 9.25; Cl, 16.3; N, 6.45%); $\nu_{max.}$ 3 430 (OH), 1 665 cm^{-1} (C=C); δ 5.65 (1 H, dt, vinyl), 3.3—3.55 (2 H, m, CH_2), 2.8—3.15 (1 H, m, CH), 2.4—2.7 (3 H, m, CH_2, OH, exch.), 2.1 (3 H, s, CH_3), 1.55—1.85 (4 H, m, CH_2CH_2), 1.21 (3 H, s, CH_3), and 1.13 (3 H, s, CH_3).

2-*Acetyl*-1,1-*dimethyl*-2,3,5,6,7,7a-*hexahydro*-1H-*pyrrolizine* (-1H-*Pyrrolo*[1,2-a]*pyrrole*) (**37**).—Concentrated sulphuric acid (120 ml, 96%) was stirred under nitrogen for 15 min; *N*-(3-chlorobut-2-enyl)-2-(2-hydroxy-2-propyl)pyrrolidine (**36**) (2.09 g, 9.6 mmol) was added and stirring continued for 10 min at room temperature. The mixture was added to ice–water, basified with sodium carbonate, and extracted with chloroform to give a yellow liquid (1.49 g). Kugelrohr distillation (115 °C, 0.1 mmHg) afforded a colourless liquid (1.35 g, 78%) (Found: M^+, 181.1476. $C_{12}H_{19}NO$ requires *M*, 181.1467); $\nu_{max.}$ 1 700 cm^{-1} (C=O); δ 2.40—3.65 (6 H, ms, CH_2CH_2, 2 CH), 2.18 (3 H, s, CH_3CO), 1.50—2.05 (4 H, m, CH_2), 1.25 (2 H, s), 1.2 (1 H, s), 1.05 (1 H, s), and 0.80 (2 H, s).

The hydrochloride was prepared by passing dry hydrogen chloride gas through a solution of the *product* (0.90 g, 5 mmol) in acetone and concentration of the solution under reduced pressure. This afforded the hydrochloride as an oily gum which was recrystallised from acetone to give a fawn crystalline solid (0.466 g, 43%), m.p. 171—173 °C (Found: C, 60.3; H, 9.1; Cl, 16.3; N, 6.1. $C_{11}H_{10}ClNO$ requires C, 60.7; H, 9.25; Cl, 16.2; N, 6.45%); $\nu_{max.}$ 2 900, 2 450 (br N-H^+), 1 690 cm^{-1} (C=O); δ (D_2O) 2.5—4.2 (6 H, m), 2.3 (3 H, s, CH_3CO), 1.7—2.2 (4 H, m, CH_2CH_2), 1.35 (3 H, s, CH_3), and 1.0 (3 H, s, CH_3).

(E)- *and* (Z)-N-(3-*Chloroprop*-2-*enyl*)-2-(2-*hydroxy*-2-*propyl*)*pyrrolidine* (**38**).—Methylmagnesium iodide (0.124 mol) was prepared by addition of methyl iodide (17.6 g, 0.124 mol) to magnesium turnings (3.2 g, 0.132 mol) and dry ether (200 ml) under nitrogen. Ethyl *N*-(3-chloroprop-2-enyl)prolinate (8.2 g, 0.038 mol) in dry ether (50 ml) was added dropwise to this during 15 min. Dry ether (100 ml) was added and the mixture was stirred for 15 h, then added to water, acidified with dilute hydrochloric acid, rebasified with sodium carbonate solution, and extracted with chloroform to give a yellow liquid (5.4 g). Kugelrohr distillation (90 °C, 0.05 mmHg) afforded a colourless liquid (5.0 g, 65%) (Found: C, 58.8; H, 8.85; N, 7.3; M^+, 203.1068. $C_{10}H_{18}ClNO$ requires C, 59.0; H, 8.9; N, 6.9%; *M*, 203.1077); $\nu_{max.}$ 3 420 (OH), 1 620 cm^{-1} (C=C); δ 5.8—6.25 (2 H, ms, vinyl), 2.8—3.6 (3 H, ms, CH_2,CH) 2.3—2.75 (3 H, m, CH_2, OH, exch.), 1.55—1.90 (4 H, m, CH_2), 1.18 (3 H, d, CH_3, and 1.12 (3 H, s, CH_3).

N-(2-*Chloroprop*-2-*enyl*)*prolinol* (**45**).—To lithium aluminium hydride (0.456 g, 0.012 mol) in dry ether (50 ml) under

nitrogen was added ethyl *N*-(2-chloroprop-2-enyl)prolinate [**52**; $R^1 = CO_2Et$, $R^2 = CH_2C(Cl)=CH_2$] (2.62 g, 0.012 mol). The mixture was stirred for 3 h and ethyl acetate (25 ml) was added, followed after 30 min by dilute hydrochloric acid. The ethyl acetate–ether layer was discarded and the liquor basified with sodium carbonate solution and extracted with ether to give a colourless liquid (1.6 g). Kugelrohr distillation (150 °C, 0.1 mmHg) gave the *product* (1.096 g, 52%) (Found: C, 54.1; H, 7.8; N, 8.45. $C_8H_{14}ClNO$ requires C, 54.7; H, 8.05; N, 7.95%); $\nu_{max.}$ 3 400 (OH), 1 635 cm^{-1} (C=C), δ 5.38 (1 H, s, vinyl), 5.28 (1 H, s, vinyl), 3.0—3.7 (6 H, ms, CH_2N, CH_2OH), 2.6—2.9 (1 H, m, CH), 2.8 (1 H, s, OH, exch.), and 1.6—2.0 (4 H, m, CH_2).

(E)- *and* (Z)-N-(3-*Chlorobut*-2-*enyl*)*prolinol* (**39**).—To lithium aluminium hydride (0.44 g, 0.0115 mol) in dry ether (100 ml) under nitrogen was added ethyl *N*-(2-chlorobut-2-enyl)prolinate [**52**; $R^1 = CO_2Et$, $R^2 = CH_2CH=C(Cl)CH_3$] (2.65 g, 0.0115 mol), and the mixture was stirred for 3 h. Ethyl acetate (25 ml) was added, followed after 15 min, by dilute hydrochloric acid, then the ethyl acetate–ether layer was discarded and the aqueous layer basified with sodium carbonate solution and extracted with chloroform to give a colourless liquid (1.7 g). Kugelrohr distillation (90 °C, 0.02 mmHg) gave the *product* (1.39 g, 73%) (Found: C, 56.85; H, 8.85; Cl, 18.45; N, 7.1. $C_9H_{16}ClNO$ requires C, 57.0; H, 8.5; Cl, 18.8; N, 7.4%); $\nu_{max.}$ 3 400 (OH), 1 665 cm^{-1} (C=C); δ 5.6 (1 H, dt, vinyl), 2.90—3.75 (5 H, m, 2 CH_2, CH), 3.03 (1 H, s, OH, exch.), 2.2—2.8 (2 H, m, CH_2), 2.1 (3 H, s, CH_3), and 1.55—2.00 (4 H, m, CH_2).

(E)- *and* (Z)-*Methyl* N-(3-*Chloroprop*-2-*enyl*)-5-*oxoprolinate* [**55**; $R^1 = CO_2Me$, $R^2 = CH_2CH=CHCl$].—To a suspension of sodium hydride (0.34 g, 7.0 mmol, 50%) in dimethylformamide (25 ml) was added methyl pyroglutamate[35] (1.0 g, 7.0 mmol) in dimethylformamide (10 ml) under nitrogen. The mixture was stirred for 1.5 h and 1,3-dichloropropene (0.77 g, 7.0 mmol) in dimethylformamide (10 ml) was added. The mixture was heated at 90 °C for 20 h. A further portion (0.77 g) of 1,3-dichloropropene was added and stirring continued for 5 h. The liquor was added to water and extracted with chloroform to give a crude product (1.75 g). Chromatography (5% acetone–chloroform) afforded an oil (0.9 g). Kugelrohr distillation (140 °C, 0.1 mmHg) gave the *product* (0.71 g, 47%) (Found: C, 50.3; H, 5.5; Cl, 16.5; N, 6.2. $C_9H_{12}ClNO_3$ requires C, 49.65; H, 5.55; Cl, 16.3; N, 6.45%); $\nu_{max.}$ 1 735 (ester), 1 690 (lactam), 1 630 cm^{-1} (C=C); δ 5.65—6.35 (2 H, ms, vinyl), 3.5—4.55 (3 H, ms, CH_2,CH), 3.78 (3 H, s, CH_3), and 1.95—2.7 (4 H, m, CH_2CH_2).

(E)-*and*(Z)-N-(3-*Chloroprop*-2-*enyl*)-2-(2-*hydroxy*-2-*propyl*)-5-*pyrrolidone* (**41**).—To methylmagnesium iodide (0.012 mol), prepared by addition of methyl iodide (1.63 g, 0.012 mol) to cleaned magnesium turnings (0.31 g, 0.013 mol) in dry ether (100 mol), under nitrogen, was added methyl *N*-(3-chloroprop-2-enyl)-5-oxoprolinate (0.50 g, 2.3 mmol) in dry ether (50 ml) during 5 min, and the mixture was stirred at room temperature for 17 h. Ammonium chloride solution was added and the resulting liquor was extracted with chloroform to give the crude product (0.55 g). Chromatography (15% acetone–chloroform) afforded the *product* (0.29 g, 54%) as a colourless gum (Found: C, 55.25; H, 7.75; Cl, 15.9; N, 6.25. $C_{10}H_{16}ClNO_2$ requires C, 55.15; H, 7.4; Cl, 16.3; N, 6.45%); $\nu_{max.}$ 3 390 (OH), 1 660 cm^{-1} (lactam); δ 5.7—6.3 (2 H, ms, vinyl), 3.8—4.5 (2 H, ms, CH_2), 3.45—3.75 (1 H, m, CH), 2.0—2.55 (5 H, ms, CH_2CH_2; OH exch.), 1.27 (3 H, s, CH_3), 1.2 (2 H, s, CH_3), and 1.17 (1 H, s, CH_3).

(E)- *and* (Z)-*Ethyl* (3-*Chlorobut*-2-*enyl*)-5-*oxoprolinate* [**55**; $R^1 = CO_2Et$, $R^2 = CH_2CH=C(Cl)CH_3$].—To a suspension of sodium hydride (1.22 g, 0.0026 mol, 50%) in dimethylformamide (100 ml) was added ethyl pyroglutamate[35] (4.0 g, 0.026 mol) in dimethylformamide (20 ml) under nitrogen. The mixture was stirred for 30 min and 1,3-dichlorobut-2-ene (3.19 g, 0.026 mol) in dimethylformamide (20 ml) was added. The mixture was heated at 90 °C for 20 h. The cooled solution was added to water and extracted with chloroform to give a crude *product* (3.0 g). Kugelrohr distillation (180 °C, 0.1 mmHg) afforded a colourless liquid (2.51 g, 38%) (Found: C, 53.45; H, 6.6; Cl, 15.55; N, 6.0. $C_{11}H_{16}ClNO_3$ requires C, 53.77; H, 6.55; Cl, 14.45; N, 5.7%); $\nu_{max.}$ 1 735 (ester), 1 695 cm^{-1} (lactam); δ 5.48 (1 H, dt, vinyl), 3.7—4.5 (3 H, ms, CH_2, CH), 4.22 (2 H, q, CH_2), 1.95—2.6 (4 H, m, CH_2CH_2), 2.1 (3 H, s, CH_3), and 1.3 (3 H, t, CH_3).

(E)- *and* (Z)-N-(3-*Chlorobut*-2-*enyl*)-2-(2-*hydroxy*-2-*propyl*)-5-*pyrrolidone* (**40**).—To methylmagnesium iodide (0.020 mol) prepared by the addition of methyl iodide (2.90 g, 0.020 mol) to cleaned magnesium turnings (0.54 g, 0.022 mol) in dry ether (175 ml), under nitrogen, was added ethyl *N*-(3-chlorobut-2-enyl)-5-oxoprolinate (1.0 g, 4.1 mmol) in dry ether (50 ml). The mixture was stirred at room temperature for 18 h, ammonium chloride solution was added, and the resulting liquor was extracted with dichloromethane to give a crude product (0.91 g). Chromatography (15% acetone–chloroform) afforded the *product* (0.67 g, 71%) as a colourless oil (Found: C, 57.2; H, 7.9; Cl, 14.6; N, 5.85. $C_{11}H_{18}ClNO_2$ requires C, 57.0; H, 7.85; Cl, 15.3; N, 6.05%); $\nu_{max.}$ 3 380 (OH), 1 660 cm^{-1} (lactam); δ 5.55 (1 H, dt, vinyl), 4.0—4.6 (2 H, m, CH_2N), 3.45—3.65 (1 H, m, CH), 1.5—2.5 (5 H, ms, CH_2CH_2; OH, exch.), 2.1 (3 H, s, CH_3), 1.26 (3 H, s, CH_3), and 1.19 (3 H, s, CH_3).

N-(2-*Chloroprop*-2-*enyl*)*succinimide* (**53**; $R = CH_2CCl=CH_2$).—Succinimide (9.9 g, 0.1 mol), 2,3-dichloropropene (11.67 g, 0.106 mol), anhydrous sodium carbonate (13 g), and ethanol (250 ml) were stirred and heated at reflux for 5 days, a further portion of 2,3-dichloropropene (11.67 g) being added on the third day. The solvent was removed under reduced pressure and dilute hydrochloric acid was added. Extraction with chloroform gave a brown oil (9.8 g). Kugelrohr distillation (120 °C, 0.02 mmHg) gave the *product* (9.1 g, 52%) as a colourless oil (Found: C, 48.45; H, 4.8; Cl, 20.3; N, 7.7; M^+ 173.0242. $C_7H_8ClNO_2$ requires C, 48.45; H, 4.65; Cl, 20.4; N, 8.05%; *M*, 173.0244); $\nu_{max.}$ 1 775, 1 705 (imide), and 1 640 cm^{-1} (C=C); δ 5.4 (2 H, s, vinyl), 4.3 (2 H, s, CH_2), and 2.8 (4 H, s, CH_2); δ_C 177.2 (2 C, s), 135.4 (s), 115.2 (t), 44.0 (t), and 28.3 p.p.m. (2 C, t).

(E)- *and* (Z)-N-(3-*Chlorobut*-2-*enyl*)*succinimide* [**53**; $R = CH_2CH=C(Cl)CH_3$].—Succinimide (9.9 g, 0.1 mol), 1,3-dichlorobut-2-ene (12.5 g, 0.1 mol), anhydrous sodium carbonate (13 g), and ethanol (250 ml) were stirred and heated under reflux for 5 days, a further portion of 1,3-dichlorobut-2-ene (12.3 g) being added on the second day. The hot mixture was filtered and the solvent removed under reduced pressure to give a brown oil (17.2 g). Kugelrohr distillation (150 °C, 0.2 mmHg) gave the *product* (15.0 g), shown by ^1H n.m.r. to be contaminated with 3-oxobutylsuccinimide (10%). An analytical sample was obtained by chromatography (chloroform) (Found: C, 50.75; H, 5.35; Cl, 19.2; N, 7.3; M^+ 187.0400. $C_8H_{10}ClNO_2$ requires C, 51.2; H, 5.35; Cl, 18.9; N, 7.45%; *M*, 187.0400); $\nu_{max.}$ 1 775, 1 700 cm^{-1} (imide); δ 5.5 (1 H, ts, vinyl), 4.25 (2 H, d, CH_2), 2.63 (4 H, m, CH_2), and 2.1 (3 H, s, CH_3).

N-(3-*Oxobutyl*)*succinimide* (**53**; $R = CH_2CH_2COCH_3$).—Impure *N*-(3-chlorobut-2-enyl)succinimide (2.0 g, 0.01 mol) and concentrated sulphuric acid (50 ml) were stirred at room temperature for 2 min and added to ice–water. Extraction with dichloromethane gave a gum (1.3 g). Kugelrohr distillation (140 °C, 0.005 mmHg) gave a colourless liquid (1.02 g, 56%)

which solidified (Found: C, 57.2; H, 6.55; N, 8.5. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%); $\nu_{max.}$ 1 600—1 800 cm^{-1} (imide and ketone); δ 3.75 (2 H, t, CH_2), 2.75 (2 H, t, CH_2CO), 2.7 (4 H, s, CH_2CH_2), and 2.18 (3 H, s, CH_3).

(E)- *and* (Z)-4-*Hydroxy*-N-(3-*chlorobut*-2-*enyl*)*butanamide*.—To *N*-(3-chlorobut-2-enyl)succinimide (3.0 g, 0.016 mol) in aqueous ethanol (200 ml, 90%) at 0 °C was added sodium borohydride (4.1 g, 0.108 mol) and the solution was stirred at 0—5 °C for 1 h. The pH of the solution was maintained at 9—10. A further portion of sodium borohydride (4.1 g) was added and the temperature allowed to rise to 25 °C. The solution was concentrated under reduced pressure at low temperature, water was added to the residue, and the resulting solution was extracted with chloroform to give the *product* (3.00 g, 99%) (Found: C, 49.5; H, 7.6; N, 7.1; M^+, 191.0720. $C_8H_{14}ClNO_2$ requires C, 50.1; H, 7.35; N, 7.3%; *M*, 191.0713); $\nu_{max.}$ 3 280, 3 080 (OH, NH), 1 640 cm^{-1} (amide); δ 6.85 (1 H, s, NHCO, exch.), 5.55 (1 H, dt, vinyl), 4.1 (1 H, s, OH, exch.), 3.8—4.05 (2 H, m, CH_2), 3.63 (2 H, t, CH_2OH, 2.35 (2 H, t, CH_2CO), 2.10 (3 H, s, CH_3), and 1.70—2.00 (2 H, m, CH_2).

(E)- *and* (Z)-4-*Formyloxy*-N-(3-*chlorobut*-2-*enyl*)*butanamide*.—4-Hydroxy-*N*-(3-chlorobut-2-enyl)butanamide (0.50 g, 2.6 mmol) and formic acid (15 ml; 98—100%) were stirred at room temperature for 18 h. The mixture was added to sodium hydrogen carbonate solution and extracted with chloroform to give an oil (0.39 g). Kugelrohr distillation (150 °C, 0.01 mmHg) afforded a colourless oil (0.25 g, 44%) (Found: C, 49.2; H, 6.7; Cl, 15.8; N, 6.3. $C_9H_{14}ClNO_3$ requires C, 49.2; H, 6.45; Cl, 16.15; N, 6.4); $\nu_{max.}$ 3 280 (NH), 1 760 (ester), and 1 645 cm^{-1} (amide); δ 8.05 (1 H, s, OCHO), 6.40 (1 H, s, NHCO, exch.), 5.58 (1 H, dt, vinyl), 4.2 (2 H, t, CH_2), 3.8—4.05 (2 H, m, CH_2), 1.9—2.5 (4 H, m, CH_2CH_2), and 2.1 (3 H, s, CH_3).

(E)- *and* (Z)-N-(3-*Chlorobut*-2-*enyl*)-5-*hydroxy*-2-*pyrrolidone* (**10**).—To *N*-(3-chlorobut-2-enyl)succinimide [**53**; R = CH_2-$CH{=}C(Cl)CH_3$] (2.0 g, 0.011 mol) in aqueous ethanol (85 ml, 90%) at 0 °C was added sodium borohydride (2.73 g, 0.072 mol) and the solution stirred at 0—5 °C for 1 h. The pH of the solution was maintained at 8—9 by frequent addition of hydrochloric acid (6M). A further portion (2.73 g) of sodium borohydride was added and the temperature allowed to rise to 25 °C. The mixture was added to water and extracted with chloroform to give an oil (1.80 g). Chromatography (25% acetone–chloroform) gave the *product* (1.70 g, 84%) (Found: C, 50.5; H, 6.45; Cl, 18.15; N, 7.3. M^+ 189.0552. $C_8H_{12}ClNO_2$ requires C, 50.65; H, 6.4; Cl, 18.7; N, 7.4%; *M*, 189.0557); $\nu_{max.}$ 3 320 (OH), 1 670 cm^{-1} (lactam); δ 5.53 (1 H, dt, vinyl), 5.2 (1 H, m, C*H*OH), 4.83, (1 H, s, OH, exch.), 3.95—4.2 (2 H, m, CH_2), 1.8—2.5 (4H, m, CH_2), and 2.13 (3 H, s, CH_3).

N-(2-*Chloroprop*-2-*enyl*)-5-*hydroxy*-2-*pyrrolidone* (**17**).—To *N*-(2-chloroprop-2-enyl)succinimide (**53**; R = $CH_2CCl{=}CH_2$) (0.50 g, 2.9 mmol) in aqueous ethanol (25 ml), 90%) at 0 °C was added sodium borohydride (0.74 g, 0.019 mol) and the solution stirred at 0—5 °C for 1 h. The pH of the solution was maintained at 8—9 by frequent addition of hydrochloric acid (6M). A further portion (0.74 g) of sodium borohydride was added to water and extracted with chloroform to give an oil (0.125 g). Chromatography (25% acetone–chloroform) afforded the *product* (0.095 g, 19%) (Found: C, 47.35; H, 5.8; Cl, 19.9; N, 7.75. $C_7H_{10}ClNO_2$ requires C, 47.9; H, 5.75; Cl, 20.2; N, 8.0%); $\nu_{max.}$ 3 200 (OH), 1 660 cm^{-1} (lactam); δ 5.37 (2 H, s, vinyl), 5.15—5.35 (1 H, m, C*H*OH) 4.6 (1 H, d, OH, exch.), 4.36 (1 H, d, CH_2N, *J* 16 Hz), 3.87 (1 H, d, CH_2N, *J* 16.Hz), and 1.8—2.8 (4 H, ms, CH_2CH_2).

(E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)*succinimide* [**53**; R = $CH_2CH_2CH{=}C(Cl)CH_3$].—(*a*) Succinimide (2.5 g, 0.025 mol), 2-chloro-5-bromopent-2-ene (5.0 g, 0.027 mol), potassium carbonate (5 g), and ethanol (70 ml) were stirred at reflux for 20 h. The solvent was removed under reduced pressure and the residue was dissolved in dilute hydrochloric acid and extracted with chloroform to give the *product* (3.4 g). Kugelrohr distillation (1.50 °C, 0.1 mmHg) gave a colourless oil which solidified (3.0 g 60%) (Found: C, 53.4; H, 6.1; Cl, 17.1; N, 7.2. $C_9H_{12}ClNO_2$ requires C, 53.6; H, 6.0; Cl, 17.6; N, 6.95%); $\nu_{max.}$ 1 770, 1 700 cm^{-1} (imide); δ 5.45 (1 H, dt, vinyl), 3.6 (2 H, t, CH_2N), 2.7 (4 H, s, CH_2CH_2), 2.25—2.65 (2 H, m, CH_2), and 2.1 (3 H, s, CH_3).

(*b*) To a dispersion of sodium hydride (0.72 g, 0.015 mol, 50%) in dimethylformamide (20 ml) under nitrogen, was added succinimide (1.49 g, 0.015 mol) and the mixture stirred for 30 min at room temperature. 2,5-Dichloropent-2-ene[28] (2.0 g, 0.015 mol) was then added and the mixture heated at 110 °C for 2.5 h. The cooled solution was added to water and extracted with chloroform to give the *product* (1.48 g). The material was washed with light petroleum (b.p. 60—80 °C) and distilled as above to give an oil which solidified (1.33 g, 44%). The material had identical i.r. and n.m.r. spectra with the material obtained in the preceding experiment.

(E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)-5-*hydroxy*-2-*pyrrolidone* (**25**).—To *N*-(4-chloropent-3-enyl)succinimide (0.50 g, 2.5 mmol) in aqueous ethanol (25 ml, 90%) at 0 °C was added sodium borohydride (0.64 g, 0.017 mol) and the solution stirred at 0—5 °C for 1 h with the pH maintained at 8—9 by frequent addition of hydrochloric acid (6M). A further portion (0.64 g) of sodium borohydride was added and the temperature allowed to rise to 25 °C. The mixture was added to water and extracted with chloroform to give an oil (0.47 g). Chromatography (25% acetone–chloroform) afforded the *product* (0.41 g, 80%) (Found: C, 52.9; H, 7.1 Cl, 17.1; N, 6.7. $C_9H_{14}ClNO_2$ requires C, 53.1; H, 6.95; Cl, 17.4; N, 6.9%); $\nu_{max.}$ 3 320 (OH), 1 670 cm^{-1} (lactam); δ 5.45 (1 H, dt, vinyl), 5.25 (1 H, br s, C*H*OH), 5.1—5.3 (1 H, br s, OH, exch.), 3.0—3.6 (2 H, m, CH_2), 2.1 (3 H, s, CH_3), and 1.8—2.6 (6 H, m, CH_2).

Treatment of (E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)-5-*hydroxy*-2-*pyrrolidone* (**25**) *with Polyphosphoric Acid*.—The hydroxylactam (2.0 g, 9.8 mmol) and polyphosphoric acid (80 g) were stirred at room temperature for 50 min, then added to water and extracted with chloroform to give a gum (1.6 g). Chromatography (10% acetone–chloroform) gave a crude product (0.85 g) as an oil. Kugelrohr distillation (140 °C, 0.1 mmHg) gave the *product* (0.70 g) as a colourless oil which darkened rapidly. G.l.c. indicated the presence of two compounds in the ratio *ca.* 1:1 (see Discussion) (Found: M^+, 185.0600. $C_9H_{12}ClNO$ requires *M*, 185.0607); $\nu_{max.}$ 1 680 (lactam), 1 625 cm^{-1} (terminal alkene); δ 5.28 (1 H, s, ?), 5.25 (1 H, dd, ?), and 1.5—4.3 (10 H, ms). It is possible that the 1,2-ene isomer was present.

Treatment of the Chloroalkenyl-lactams (**26**) *and* (**27**) *with Sulphuric Acid*.—The foregoing chloroalkenyl-lactams (0.25 g; 1:1 ratio) and sulphuric acid (15 ml, 96%) were stirred at 0 °C for 30 min. Hydrogen chloride gas was evolved. The mixture was added to ice–water and extracted with chloroform to give the crude product (0.18 g). Kugelrohr distillation (180 °C, 0.4 mmHg) gave a colourless liquid (0.15 g). G.l.c. indicated that only one compound, 1-acetyl-1,2,3,6,7,7a-hexahydropyrrolizin-5-one (**28**), was present (see Discussion) (Found: M^+ 167.0930. $C_9H_{13}NO_2$ requires M, 167.0946); $\nu_{max.}$ 1 700 (ketone), 1 680 cm^{-1} lactam; δ 1.6—4.3 (*ca.* 10 H, ms), and 2.2 (3 H, s, CH_3CO).

N-(2-*Chloroprop*-2-*enyl*)*phthalimide* (**54**; R = $CH_2CCl{=}CH_2$).—Potassium phthalimide (10.0 g, 0.054 mol), 2,3-dichloropropene (5.94 g, 0.054 mol), and dimethylformamide (40 ml) were heated at 100 °C for 2.75 h. The cooled mixture was added to water and extracted with chloroform to give the crude product (9.9 g). Recrystallisation from methanol gave off-white crystals (8.56 g, 72%), m.p. 105—109 °C (Found: C, 59.6; H, 4.0; Cl, 16.4; N, 6.5. $C_{11}H_8ClNO_2$ requires C, 59.6; H, 3.65; Cl, 16.0; N, 6.3%); $\nu_{max.}$ 1 770, 1 700 (imide), 1 635 (C=C), and 1 600 cm^{-1} (aryl); δ 7.65—8.0 (4 H, m, aryl), 5.4 (2 H, s, vinyl), and 4.48 (2 H, s, CH_2).

(E)- *and* (Z)-N-(-3-*Chlorobut*-2-*enyl*)*phthalimide* [**54**; R = $CH_2CH{=}C(Cl)CH_3$].—Potassium phthalimide (10.0 g, 0.054 mol), 1,3-dichlorobut-2-ene (6.70 g, 0.054 mol), and dimethylformamide (40 ml) were heated at 100 °C for 2.5 h. The cooled solution was added to water and extracted with chloroform to give the crude *product* (12.1 g). Recrystallisation from methanol gave white crystals (9.3 g, 78%), m.p. 77—80 °C (Found: C, 61.05; H, 4.2; Cl, 15.35; N, 6.1. $C_{12}H_{10}ClNO_2$ requires C, 61.15; H, 4.3; Cl, 15.35; N, 5.95%); $\nu_{max.}$ 1 770, 1 700 (imide), and 1 600 cm^{-1} (aryl); δ 7.6—8.0 (4 H, m, aryl), 5.62 (1 H, dt, vinyl), 4.44 (2 H, d, CH_2), and 2.12 (3 H, s, CH_3).

(E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)*phthalimide* [**54**; R = $CH_2CH_2CH{=}C(Cl)CH_3$]. Potassium phthalimide (5.4 g, 0.029 mol), 2,5-dichloropent-2-ene (4.0 g, 0.029 mol) and dimethylformamide (20 ml) were heated at 160 °C for 3.25 h. The cooled solution was added to water and extracted with chloroform to give the crude product (6.4 g). Kugelrohr distillation (170 °C, 0.05 mmHg) followed by recrystallisation from methanol gave white crystals (3.6 g, 49%), m.p. 46—49 °C (Found: C, 62.35; H, 5.05; Cl, 14.4; N, 5.45%); $C_{13}H_{12}ClNO_2$ requires C, 62.55; H, 4.85; Cl, 14.2; N, 5.6%); $\nu_{max.}$ 1765, 1640—1745 (imide), and 1610 cm^{-1} (aryl); δ 7.6—8.95 (4 H, m, aryl), 5.48 (1 H, dt, vinyl), 3.6—3.9 (2 H, d, CH_2), 2.25—2.75 (2 H, m, CH_2), and 2.05 (3 H, s, CH_3).

N-(2-*Chloroprop*-2-*enyl*)-3-*hydroxy*-2,3-*dihydro*-1H-*isoindol*-1-*one* (**18**).—To *N*-(2-chloroprop-2-enyl)phthalimide (1.0 g, 4.5 mmol) in aqueous tetrahydrofuran (32 ml, 95%) at 0 °C was added sodium borohydride (0.54 g, 0.014 mol) and the solution stirred at 0—5 °C for 2 h. The pH of the solution was maintained at 8—9 by frequent addition of hydrochloric acid (6M). The mixture was added to water and extracted with chloroform to give the crude product (1.0 g). Chromatography (5% acetone–chloroform) gave a white solid (0.94 g, 93%), m.p. 80—81 °C (Found: C, 59.15; H, 4.5; Cl, 15.9; N, 6.15. $C_{11}H_{10}ClNO_2$ requires C, 59.05; H, 4.5; Cl, 15.85; N, 6.25%); $\nu_{max.}$ 3 310 (OH), 1 675 (lactam), 1 635 (C=C), and 1 600 cm^{-1} (aryl); δ 7.3—7.8 (4 H, m, aryl), 5.79 (1 H, d, C*H*OH), 5.33 (2 H, s, vinyl), 4.62 (1 H, d, OH, exch.), 4.27 (1 H, d, CH_2N, *J* 16 Hz), and 3.93 (1 H, d, CH_2N, *J* 16 Hz).

The O-*acetate* (**22**), obtained by refluxing (**18**) with acetic anhydride, had b.p. 150 °C/0.02 mmHg (Found: C, 59.0; H, 4.65; N, 5.2. $C_{13}H_{12}ClNO_3$ requires C, 58.9; H, 4.55; N, 5.3%); δ 2.15 (3 H, s, CH_3CO), 4.12 (1 H, d, CH_2N, *J* 16 Hz), 4.58 (1 H, d, CH_2N, *J* 16 Hz), 5.38 (2 H, s, vinyl), 7.04 (1 H, s, CHOAc), and 7.5—7.9 (4 H, m, aryl).

N-(2-*Chloroprop*-2-*enyl*)-2,3-*dihydro*-1H-*isoindol*-1-*one* (**23**).—The previous acetate (1.2 g), boron trifluoride–ether (1 cm^3), and chloroform (75 cm^3) were refluxed for 12 h. After washing with aqueous sodium hydrogen carbonate, drying and evaporation, a gum (1.1 g) remained. Flash chromatography yielded the product (400 mg), b.p. 140 °C/0.05 mmHg (Found: C, 63.15; H, 5.1; N, 6.05%; M^+, 209.0404, 207.0439. $C_{11}H_{10}ClNO$ requires C, 63.6; H, 4.85; N, 6.75%; *M*, 209.0421, 207.0451); δ 7.8—7.95 (1 H, m, aryl), 7.3—7.65 (3 H, m, aryl), 5.4 (2 H, s, vinyl), and 4.42 (4 H, 2 s, methylene H); δ_C 48.665 (t), 49.738 (t), 114.678 (t), 122.838 (d), 124.087 (d), 128.175 (d), 131.703 (d), 132.144 (s), 137.378 (s), 141.201 (s), and 168.547 p.p.m. (s).

(E)- *and* (Z)-N-(3-*Chlorobut*-2-*enyl*)-3-*hydroxy*-2,3-*dihydro*-1H-*isoindol*-1-*one* (**11**).—To *N*-(3-chlorobut-2-enyl)phthalimide (1.5 g, 6.4 mmol) in aqueous tetrahydrofuran (48 ml, 95%) at 0 °C was added sodium borohydride (0.77 g, 0.02 mol) and the solution stirred at 0—5 °C for 2 h. The pH of the solution was maintained at 8—9 by frequent addition of hydrochloric acid (6M). The mixture was added to water and extracted with chloroform to give the *product* (1.24 g, 82%) which crystallised on standing, m.p. 102—105 °C (Found: C, 60.65; H, 5.1; Cl, 15.25; N, 5.9. $C_{12}H_{12}ClNO_2$ requires C, 60.65; H, 5.1; Cl, 14.9; N, 5.9%); $\nu_{max.}$ 3 300 (OH), 1 670 (lactam), and 1 615 cm^{-1} (aryl); δ 7.3—7.7 (4 H, m, aryl), 5.7 (1 H, d, CHOH), 5.51 (1 H, dt, vinyl), 4.55 (1 H, d, OH, exch.), 4.05 (2 H, d, CH_2), and 2.1 (3 H, s, CH_3).

(E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)-3-*hydroxy*-2,3-*dihydro*-1H-*isoindol*-1-*one* (**30**).—To *N*-(4-chloropent-3-enyl)phthalimide (0.50 g, 2.0 mmol) in aqueous tetrahydrofuran (21 ml, 95%) at 0 °C was added sodium borohydride (0.24 g, 6.3 mmol) and the solution stirred at 0—5 °C for 1.25 h. The pH of the solution was maintained at 8—9 by frequent addition of hydrochloric acid (6M). The mixture was added to water and extracted with chloroform to give the crude product (0.51 g). Chromatography (5% acetone–chloroform) afforded a colourless gum which crystallised (0.45 g, 89%), m.p. 62—63 °C (Found: C, 61.6; H, 5.5; Cl, 14.45; N, 5.5. $C_{13}H_{14}ClNO_2$ requires C, 62.05; H, 5.6; Cl, 14.1; N, 5.55%); $\nu_{max.}$ 3 260 (OH), 1 670 cm^{-1} (lactam); δ 7.25—7.7 (4 H, m, aryl), 5.6—5.9 (1 H, d, CHOH) 5.4 (1 H, dt, vinyl), 4.45 (1 H, d, OH, exch.), 3.15—3.5 (2 H, m, CH_2), 2.2—2.5 (2H, m, CH_2), and 2.03 (3H, s, CH_3).

1-endo-*Acetyl*-1,2,3,9b-*tetrahydropyrrolo*[2,1-a]*isoindol*-5-*one* (**31**).—To sulphuric acid (30 ml, 96%) at 0 °C was added *N*-(4-chloropent-3-enyl)-3-hydroxy-2,3-dihydro-1*H*-isoindol-1-one (**31**) (0.400 g, 1.59 mmol) and the mixture stirred at 0 °C for 50 min. The mixture was added to water and extracted with chloroform to give the *product* (0.362 g) as a crude oil. Chromatography (10% acetone–chloroform) afforded a white solid (0.219 g, 64%), m.p. 104—107 °C (Found: C, 72.15; H, 6.0; N, 6.2. $C_{13}H_{13}NO_2$ requires C, 72.55; H, 6.1; N, 6.5%); $\nu_{max.}$ 1 700 (C=O), 1 685 cm^{-1} (lactam); δ (250 MHz) 7.77—7.81 (1 H, m, aryl, 6-H), 7.43—7.57 (3 H, m, aryl), 5.00 (1 H, d, ^3J 8.6 Hz, 3-H), 3.41—3.55 (2 H, ms, 1-, 3-H), 2.36—2.60 (2 H, m, 2-H), and 1.80 (3 H, s, CH_3CO).

1-exo-*Acetyl*-1,2,3,9b-*tetrahydropyrrolo*[2,1-a]*isoindol*-5-*one* (**32**).—1-*endo*-Acetyl-1,2,3,9b-tetrahydropyrrolo[2,1-*a*]isoindol-5-one (**31**) (0.185 g, 0.86 mmol), freshly roasted anhydrous potassium carbonate (1.85 g) and dimethylformamide (40 ml) were stirred at room temperature for 6 days. The solvent was removed under reduced pressure and to the residue was added water. Extraction with chloroform gave the *product* (0.185 g) as as a gum. Chromatography (10% acetone–chloroform) afforded a white solid (0.125 g, 68%), m.p. 63—64 °C (Found: C, 72.95; H, 6.1; N, 6.45. $C_{13}H_{13}NO_2$ requires C, 72.55; H, 6.1; N, 6.5%); $\nu_{max.}$ 1 700 (C=O), 1 685 cm^{-1} (lactam); δ (250 MHz) 7.76—7.81 (1 H, m, 6-H), 7.43—7.57 (3 H, m, aryl), 5.00 (1 H, d, ^3J 9.1 Hz, 9b-H), 3.85 (1 H, dt, ^2J 11.7, ^3J 8.8 Hz, 3-H), 3.50—3.59 (1 H, ddd, ^2J 11.7, ^3J 2.6, 9.3 Hz, 3-H), 2.70—2.81 (1 H, m, 1β-H), 2.45—2.64 (2 H, m, 2-H), and 2.28 (3 H, s, CH_3).

(E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)-3-*methylene*-2,3-*dihydro*-1H-*isoindol*-1-*one* (**34**) *and* (E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)-3-*hydroxy*-3-*methyl*-2,3-*dihydro*-1H-*isoindol*-1-*one*

(**33**).—To methylmagnesium iodide (5 mmol), prepared by the addition of methyl iodide (0.72 g, 5 mmol) to cleaned magnesium turnings (0.132 g, 5.5 mmol), in dry ether (50 ml) under nitrogen, was added *N*-(4-chloropent-3-enyl)phthalimide [**54**; R = $CH_2CH_2CH{=}C(Cl)CH_3$] (1.0 g, 4 mmol) and the mixture stirred at room temperature for 12 h. Ammonium chloride solution was added and the resulting solution extracted with chloroform affording a crude gum (1.1 g). Chromatography (10% acetone–chloroform) gave the products as a colourless unstable gum (0.82 g). ^{1}H N.m.r. integration suggested that the product was a mixture of the enamide (**34**) and the hydroxylactam (**33**) (65 and 35% respectively). The unstable mixture was inseparable and was used directly in the next step; $\nu_{max.}$ 3 250 (OH), 1 670 (lactam), 1 625 (C=C); δ [for (*E*)-and (*Z*)-(**33**)] 7.2—7.9 (4 H, m, aryl), 5.4—5.7 (1 H, dt, vinyl), 5.22 (1 H, d, vinyl), 4.95 (0.65 H, d, vinyl), 4.84 (0.35 H, d, vinyl), 3.6—3.9 (2 H, t, CH_2), 2.2—2.8 (2 H, m, CH_2), and 2.1 (3 H, s, CH_3); δ [for (*E*)- and (*Z*)-(**34**)] 7.2—7.9 (4 H, m, aryl), 5.4—5.7 (1 H, dt, vinyl), 4.15 (1 H, br s, OH, exch.), 3.6—3.9 (2 H, t, CH_2), 2.2—2.8 (2 H, m, CH_2), 2.1 (3 H, s, CH_3), 1.72 (2 H, s, CH_3), and 1.70 (1 H, s, CH_3).

1-endo-*Acetyl*-9b-*methyl*-1,2,3,9b-*tetrahydropyrrolo*[2,1-a]-*isoindol*-5-*one* (**35**).—To sulphuric acid (30 ml, 96%) at 0 °C was added the foregoing mixture of the enamide (**34**) and the hydroxylactam (**33**) (0.40 g, 1.6 mmol; 65 and 35% respectively) and the mixture stirred at 0—2 °C for 70 min. The solution was added to water and extracted with chloroform to give crude material (0.35 g). Chromatography (10% acetone–chloroform) gave the *product* [0.30 g, 67%, based on *N*-(4-chloropent-3-enyl)phthalimide], m.p. 114—115 °C (Found: C, 73.35; H, 6.75; N, 6.15. $C_{14}H_{15}NO_2$ requires C, 73.35; H, 6.6; N, 6.1%); $\nu_{max.}$ 1 700 (C=O), 1 685 cm^{-1} (lactam); δ (250 MHz) 7.73—7.76 (1 H, m, 6-H), 7.41—7.57 (3 H, m, 7-, 8-, 9-H), 4.08 (1 H, dt, ^2J 11.7, ^3J 8.4 Hz, 3-H), 3.44 (1 H, ddd, ^2J 11.7, ^3J 4.9, 7.6 Hz, 3-H), 3.26 (1 H, dd, ^3J 2.7, 5.8 Hz, 1α-H), 2.46—2.56 (2 H, m, 2-H), 1.75 (3 H, s, CH_3CO), and 1.64 (3 H, s, CH_3).

(E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)*phthalimide* [**54**; R = $CH_2CH_2CH{=}C(Cl)CH_3$] *and* N-(4-*Chloropent*-2-*enyl*)-*phthalimide* (**54**; R = $CH_2CH_2CH_2CCl{=}CH_2$).—Potassium phthalimide (2.69 g, 0.0145 mol), 2,5-dichloropent-2-ene and 2,5-dichloropent-1-ene (2.0 g, 0.0145 mol; 1:1 ratio), and dimethylformamide (20 ml) were heated at 160 °C for 2 h. The cooled solution was added to water and extracted with chloroform to give the crude *product* (2.64 g). Chromatography (chloroform) gave a colourless gum (2.20 g, 61%) (Found: C, 62.8; H, 5.3; Cl, 14.65; N, 5.8. $C_{13}H_{12}ClNO_2$ requires C, 62.55; H, 4.85; Cl, 14.2; N, 5.6%); $\nu_{max.}$ 1 765, 1 650—1 735 (imide), 1 630 (terminal alkene), and 1 610 cm^{-1}; δ {(*E*)-and (*Z*)-[**54**; R = $CH_2CH_2CH{=}C(Cl)CH_3$]} 7.6—8.95 (4 H, m, aryl), 5.48 (1 H, dt, vinyl), 3.6—3.9 (2 H, d, CH_2), 2.25—2.75 (2 H, m, CH_2), and 2.05 (3 H, s, CH_3). δ [(**54**; R = $CH_2CH_2CH_2CCl{=}CH_2$)] 7.6—8.95 (4 H, m, aryl), 5.15 (2 H, dist. s, vinyl), 3.55—3.85 (2 H, m, CH_2), 2.25—2.75 (2 H, m, CH_2), and 1.75—2.2 (2 H, m, CH_2). (^{1}H N.m.r. integration suggests a *ca.* 1:1 ratio of these structural isomers.)

(E)- *and* (Z)-N-(4-*Chloropent*-3-*enyl*)-3-*hydroxy*-2,3-*dihydro*-1H-*isoindol*-1-*one* (**30**) *and* N-(4-*Chloropent*-4-*enyl*)-3-*hydroxy*-2,3-*dihydro*-1H-*isoindol*-1-*one* (**50**).—To *N*-(4-chloropent-3-enyl)phthalimide [**54**; R = $CH_2CH_2CH{=}C(Cl)CH_3$] and *N*-(4-chloropent-4-enyl)phthalimide (**54**; R = $CH_2CH_2CH_2CCl{=}CH_2$) (1.50 g, 60 mmol; 1:1 ratio) in aqueous tetrahydrofuran (48 ml, 95%) at 0 °C, was added sodium borohydride (0.72 g, 0.019 mol) and the solution stirred at 0—5 °C for 1.25 h. The pH of the solution was maintained at 8—9 by frequent addition of hydrochloric acid (6M). The mixture was added to water and extracted with chloroform to give the crude product (1.69 g). Chromatography (5% acetone–chloroform) afforded a colourless gum (1.44 g, 95%) (Found: C, 61.2; H, 5.8; Cl, 14.7; N, 5.85. $C_{13}H_{14}ClNO_2$ requires C, 62.05; H, 5.6; Cl, 14.1; N, 5.55%); $\nu_{max.}$ 3 300 (OH), 1 670 cm^{-1} (lactam); δ [compound (**30**)] 7.25—7.7 (4 H, m, aryl), 5.6—5.9 (1 H, d, C*H*OH), 5.4 (1 H, dt, vinyl), 4.64 (1 H, d, OH, exch.), 3.15—3.55 (2 H, m, CH_2), 2.2—2.5 (2 H, m, CH_2), and 2.03 (3 H, s, CH_3). δ [compound (**50**)] 7.25—7.7 (4 H, m, aryl), 5.5—5.9 (1 H, d, C*H*OH), 5.15 (2 H, s, vinyl), 4.64 (1 H, d, OH, exch.), 3.15—3.55 (2 H, m, CH_2), 2.2—2.5 (2 H, m, CH_2), 1.6—2.2 (2 H, m, CH_2). (^{1}H N.m.r. integration suggests a *ca.* 1:1 ratio of these structural isomers.)

7,8,11,11a-*Tetrahydro*-5H-*azepino*[2,1-a]*isoindole*-5,10-(9H)-*dione* (**51**) *and* 1-endo-*Acetyl*-1,2,3,9b-*tetrahydro*-5H-*pyrrolo*[2,1-a]*isoindol*-5-*one* (**31**).—To sulphuric acid (60 ml, 96%) at 0 °C was added *N*-(4-chloropent-3-enyl)-3-hydroxy-2,3-dihydro-1*H*-isoindol-1-one and *N*-(4-chloropent-4-enyl)-3-hydroxy-2,3-dihydro-1*H*-isoindol-1-one (1.00 g. 4.00 mmol, 1:1 ratio) and the mixture stirred at 0 °C for 1 h. The mixture was added to water and extracted with chloroform to give the *products* (0.834 g) as an oil. T.l.c. indicated the presence of two compounds. Chromatography (10% acetone–chloroform) gave the *product* (**51**) (0.408 g), m.p. 158—161 °C and compound (**31**) (0.375 g), m.p. 104—107 °C (combined yield, 0.783 g, 91%). 7,8,11,11a-*Tetrahydro*-5H-*azepino*[2,1-a]*isoindole*-5,10(9H)-*dione* (**51**) (*cf.* ref. 36) (Found: C, 72.55; H, 6.55; N, 6.65; M^+, 215.0923. $C_{13}H_{13}NO_2$ requires C, 72.55; H, 6.1; N, 6.5%; *M*, 215.0946); $\nu_{max.}$ 1 700 (ketone), 1 680 (lactam), and 1 615 cm^{-1} (aryl); δ (250 MHz) 7.84—7.87 (1 H, m, 4-H), 7.40—7.62 (3 H, m, 1-, 2-, 3-H), 4.68—4.77 (1 H, m, 7-H), 4.64 (1 H, dd, ^3J 2.4, 11.1 Hz, 11a-H), 3.05—3.16 (2 H, dist. ddt, ^2J 14.3 Hz, 9-H), 2.77 (1 H, dd, ^2J 14.4, ^3J 2.4 Hz, 11-H_{eq}), 2.76—2.87 (1 H, m, 7-H), 1.91—2.21 (2 H, ms, 8-H), and 2.69 (1 H, dd, ^2J 14.4, ^3J 11.1 Hz, 11-H_{ax}). Compound (**31**) had identical i.r. and n.m.r. spectra with the material obtained separately above.

N-(3-*Oxobutyl*)-3-*hydroxy*-2,3-*dihydro*-1H-*isoindol*-1-*one* (**12**).—To sulphuric acid (30 ml, 96%) at 0 °C was added *N*-(3-chlorobut-2-enyl)-3-hydroxy-2,3-dihydro-1*H*-isoindol-1-one (**11**) (0.50 g, 2.1 mmol) and the mixture stirred at room temperature for 1.25 h. The solution was added to ice–water and extracted with chloroform to give the crude product (40.4 g). Chromatography (20% acetone–chloroform) afforded the *product* (0.190 g, 41%) as a white solid, m.p. 107—108 °C (Found: C, 65.5; H, 6.0; N, 6.4. $C_{12}H_{13}NO_3$ requires C, 65.75; H, 6.0; N, 6.4%); $\nu_{max.}$ 3 290 (OH), 1 700 (ketone), 1 685, and 1 670 (lactam) cm^{-1}; δ 7.3—7.75(4 H, m, aryl), 5.8 (1 H, d, C*H*OH), 4.73 (1 H, d, OH, exch.), 3.71 (2 H, t, CH_2N), 2.87 (2 H, t, CH_2CO), and 2.15 (3 H, s, CH_3).

1,3,4,10b-*Tetrahydropyrido*[2,1-a]*isoindole*-2,6-*dione* (**13**).—*N*-(3-Oxobutyl)-3-hydroxy-2,3-dihydro-1*H*-isoindol-1-one (**12**) (0.10 g, 0.46 mmol), ethanol (12 ml), and hydrochloric acid (3.0 ml, 36.5%) were refluxed for 39 h. The solution was added to water and extracted with chloroform to give the *product* (0.097 g) as a yellow gum. Chromatography (15% acetone–chloroform) gave a pure sample (0.060 g, 65%), m.p. 103—107 °C (Found: C, 71.1; H, 5.65; N, 6.65. $C_{12}H_{11}NO_2$ requires C, 71.65; H, 5.50; N, 6.95%); $\nu_{max.}$ 1 700 (ketone), 1 675 cm^{-1} (lactam); δ (250 MHz) 7.88—7.92 (1 H, m, 7-H), 7.40—7.63 (3 H, m, 8-, 9-, 10-H), 4.78 (1 H, m, 4-H_{eq}), 4.71 (1 H, dd, ^3J 12.1, 4.2 Hz, 10b-H), 3.40 (1 H, m, 4-H_{ax}), 3.02 (1 H, dd, ^2J 14.1, ^3J 4.2 Hz, 1-H_{eq}), 2.57 (2 H, m, 3-H), and 2.25 (1 H, dd, ^2J 14.1, ^3J 12.1 Hz, 1-H_{ax}).

N-(2-*Oxopropyl*)-3-*hydroxy*-2,3-*dihydro*-1H-*isoindol*-1-*one* (**19**).—To sulphuric acid (50 ml, 96%) at room temperature was

added *N*-(2-chloroprop-2-enyl)-3-hydroxy-2,3-dihydro-1*H*-isoindol-1-one (**18**) (1.0 g, 4.5 mmol) and the mixture stirred for 90 min at room temperature, then added to ice–water and extracted with chloroform to give a crude gum (0.87 g). Chromatography (15% acetone–chloroform) gave starting material (**18**) (0.33 g) and the *product* (**19**) (0.26 g, 28%), m.p. 115—119 °C (Found: C, 64.2; H, 5.4; N, 6.55. $C_{11}H_{11}NO_3$ requires C, 64.4; H, 5.4; N, 6.8%); $\nu_{max.}$ 3 330 (OH), 1 720 (ketone), and 1 680 cm^{-1} (lactam); δ 7.3—7.8 (4 H, m, aryl), 5.8 (1 H, d, C*H*OH), 4.3 (1 H, d, OH, exch.), 4.25 (2 H, s, CH_2), and 2.17 (3 H, s, CH_3).

N-(2-*Oxopropyl*)*succinimide* (**53**; R = CH_2Ac).—*N*-(2-Chloroprop-2-enyl)succinimide (**53**; R = $CH_2CCl{=}CH_2$) (1.0 g, 5.8 mmol) and polyphosphoric acid (50 g) were stirred and heated at 80—100 °C for 1 h, added to water, and extracted with chloroform to give a fawn solid (0.80 g) (Found: C, 54.0; H, 5.8; N, 8.95. $C_7H_9NO_3$ requires C, 54.2; H, 5.85; N, 9.05%); $\nu_{max.}$ 1 600—1 800 cm^{-1} (imide and ketone CO), δ 4.33 (2 H, s, CH_2N), 2.80 (4 H, s, CH_2), and 2.23 (3 H, s, CH_3).

N-(m-*Methoxybenzyl*)*phthalimide* (**54**; R = $CH_2C_6H_4$-OMe-3).—Potassium phthalimide (1.85 g, 0.01 mol), *m*-methoxybenzyl bromide[37] (2.01 g, 0.01 mol) and dimethylformamide (30 ml) were heated at 90 °C for 1.75 h. The cooled solution was added to water and extracted with chloroform to give the crude *product* (2.2 g). Recrystallisation from methanol gave white needles (1.62 g, 61%), m.p. 125—126 °C (Found: C, 71.3; H, 5.0; N, 5.5. $C_{16}H_{13}NO_3$ requires C, 71.9; H, 4.9; N, 5.25%); $\nu_{max.}$ 1 770, 1 700 (imide), and 1 600 cm^{-1} (aryl); δ 7.5—7.95 (4 H, m, aryl), 6.65—7.35 (4 H, m, aryl) 4.78 (2 H, s, CH_2), and 3.75 (3 H, s, CH_3O).

3-*Hydroxy*-N-(m-*methoxybenzyl*)-2,3-*dihydro*-1H-*isoindol*-1-*one* (**20**).—To *N*-(*m*-methoxybenzyl)phthalimide (0.75 g, 2.8 mmol) in aqueous tetrahydrofuran (27 ml, 95%) at 0 °C was added sodium borohydride (0.33 g, 8.8 mmol) and the solution stirred at 0—5 °C for 1.5 h. The pH of the solution was maintained at 8—9 by frequent addition of hydrochloric acid (6M). The mixture was added to water and extracted with chloroform to give the crude product (0.77 g) as a gum. Trituration with ether afforded the crystalline *product* (0.65 g, 86%), m.p. 109—110 °C (Found: C, 71.35; H, 5.5; N, 5.15. $C_{16}H_{15}NO_3$ requires C, 71.35; H, 5.6; N, 5.2%); $\nu_{max.}$ 3 250 (OH), 1 670 cm^{-1} (lactam); δ 6.6—7.7 (8 H, m, aryl), 5.6 (1 H, d, ^3J 12 Hz, C*H*OH) 4.78 (1 H, d, ^2J 15 Hz, CH_2-aryl), 4.18 (1 H, d, ^2J 15 Hz, CH_2-aryl), 4.08 (1 H, d, ^3J 12 Hz, OH exch.), and 3.63 (3 H, s, CH_3O).

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