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Rearrangement of ammonium ylides produced by intramolecular reaction of catalytically generated metal carbenoids. Part 1. Synthesis of cyclic amines

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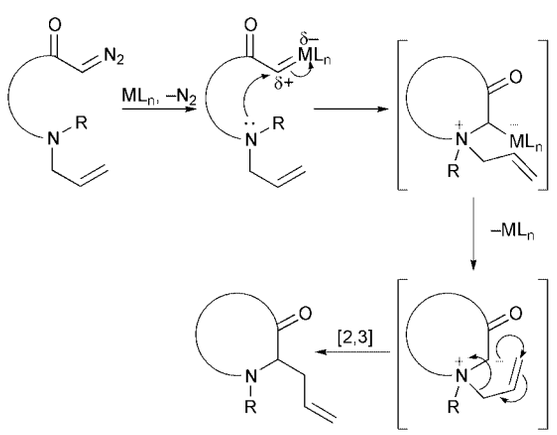
Cyclic amines have been prepared in good yield by [2,3]-rearrangement of ammonium ylides produced by intramolecular reaction of copper carbenoids tethered to allylic amines. Copper(II) acetylacetonate is the optimum catalyst for carbenoid/ylide generation from the diazo ketone precursor, and reactions must be performed at elevated temperatures in order to obtain reasonable reaction rates and high yields. The reaction has been used to prepare five- to eight-membered cyclic amines. In cases where the substrate possesses a substituent on the tether connecting the diazo group to the allylic amine, tandem ylide formation and rearrangement delivers a high yield of the expected 2,5-dialkylpyrrolidinone or 2,6-dialkylpiperidinone, but low levels of diastereocontrol are obtained.

Two new methods have been developed for the synthesis of diazo ketones containing a nucleophilic allylic amine substituent. The first method involves conjugate addition of allylic amines to unsaturated diazo ketones and is high yielding but of limited scope. The alternative general sequence involving nitrogen protection, α-diazo ketone formation, deprotection and allylation can be used to prepare the substrates required for intramolecular tandem ylide formation and rearrangement.

Introduction

The formation of ylides by the reaction of catalytically generated metal carbenoids with amines, ethers and sulfides is a very attractive alternative to traditional methods of ylide generation,[1] which generally involve deprotonation or desilylation of the corresponding onium salts.[2] In general, the generation of ylides from carbenoids involves mild reaction conditions and requires only a small amount of an appropriate copper or rhodium catalyst.[1] In recent years, several groups, including our own, have investigated the synthesis of reduced cyclic amines, ethers and sulfides from metal carbenoids by *intramolecular* generation and subsequent rearrangement of ammonium,[1,3–5] oxonium[1,6–9] and sulfonium ylides.[1,10]

Natural products containing cyclic amine units are ubiquitous, and these alkaloids frequently possess potent biological activity. Consequently, the development of new and more efficient methods for the stereoselective synthesis of cyclic amines continues to be a burgeoning area of research. In principle, the intramolecular generation of cyclic ammonium ylides from metal carbenoids and their subsequent rearrangement could provide a wide range of cyclic amines of the type found in natural products. In recent seminal studies, West has thoroughly investigated the synthesis of pyrrolidines, piperidines and morpholines by [1,2] Stevens rearrangement of catalytically generated cyclic ammonium ylides.[3] In this paper, we disclose the results of a systematic study concerning the [2,3] rearrangement of ammonium ylides generated from copper carbenoids in an *intramolecular* fashion (Scheme 1), and define the scope and limitations of this tandem process for the synthesis of cyclic amines.[4]



Scheme 1

Results and discussion

Initial studies focused on the construction of simple cyclic amines by tandem catalytic ammonium ylide generation and rearrangement (Scheme 1). In order to investigate the reaction in detail, an efficient route was required for the preparation of the α-diazo ketones containing allylic amines required to serve as cyclisation precursors. At the outset, substrate preparation posed a significant problem because nucleophilic amines are generally incompatible with most of the conventional methods employed for α-diazo ketone formation. Consequently, it was necessary either to protect the amino group prior to diazo ketone formation or to introduce the amine functionality after preparation of the diazo ketone.

The α-diazo ketone precursors required for the synthesis of pyrrolidines, were prepared using a route in which the allylic amine group was introduced after preparation of the diazo ketone (Scheme 2). The diazo ketone required for this approach, 4-bromo-1-diazobutan-2-one (**1**),[11] was prepared in 82% yield by treatment of 3-bromopropanoic acid with oxalyl chloride in

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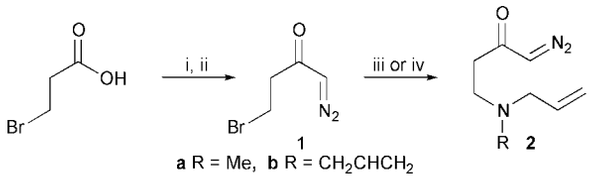


Scheme 2 *Reagents and conditions*: (i), $(COCl)_2$, DMF (cat.), CH_2Cl_2, 0 °C; (ii), CH_2N_2, Et_2O, 0 °C ⟶ rt (82%, 2 steps); (iii), $MeNHCH_2CHCH_2$, Et_3N, EtOAc, 0 °C ⟶ rt (**2a**, 77%); (iv), DBN, hydroquinone, Et_2O, −10 °C then $NH(CH_2CHCH_2)_2$, Et_2O, 0 °C ⟶ rt (**2b**, 73%).

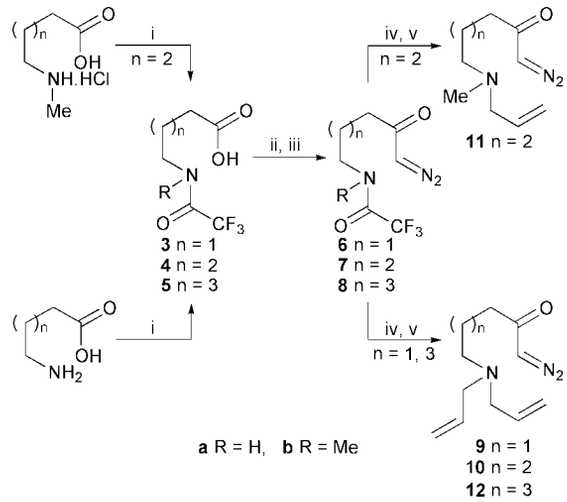
the presence of a sub-stoichiometric amount of *N,N*-dimethylformamide, and reaction of the resulting acid chloride with a large excess of diazomethane. Treatment of the α-diazo ketone **1** with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) at −10 °C resulted in elimination of HBr and produced a solution of α-diazo methyl vinyl ketone.[11] The solution of the α,β-unsaturated diazo ketone was filtered and immediately added to a solution of diallylamine at 0 °C to give the cyclisation precursor **2b** in 73% yield. The cyclisation precursor **2a** was prepared in 77% yield by addition of *N*-methylallylamine to the α-diazo ketone **1** at room temperature.

The conjugate addition approach was only applicable to the synthesis of the precursors required for pyrrolidine synthesis, and so a general method for the preparation of longer-chain cyclisation precursors was still required. The most obvious solution to the problem was to employ a strategy in which the amino functionality of an amino acid was protected during conversion of the carboxylic acid group into the corresponding α-diazo ketone. Subsequent deprotection and allylation at nitrogen would then provide the required cyclisation precursor.

The number of candidate *N*-protecting groups was limited because α-diazo ketones are incompatible with many of the methods commonly used for *N*-deprotection *e.g.* treatment with acid or hydrogenolysis. Of the commonly used protecting groups, the trifluoroacetyl group was deemed to have the appropriate reactivity profile because it is compatible with many of the methods used for diazo ketone synthesis and can be removed under relatively mild alkaline conditions.[12] Another candidate protecting group would have been the Fmoc group, which has been used by Coutts and Saint for *N*-protection during the synthesis of diazo ketones from amino acids.[13]

Protection of 4-aminobutanoic acid using trifluoroacetic anhydride gave low yields of the amide **3a**, and so alternative protection conditions were investigated (Scheme 3). Reaction of the amino acid with ethyl trifluoroacetate in the presence of triethylamine gave the trifluoroacetamide **3a** in 89% yield,[12] and this was then converted into the α-diazo ketone **6a** in 80% yield using standard conditions. Subsequent treatment of the amide **6a** with potassium carbonate in aqueous ethanol resulted in extremely slow deprotection and afforded none of the free amine. In contrast, exposure of the amide **6a** to a saturated aqueous solution of barium hydroxide at room temperature resulted in complete consumption of the starting material in less than 20 minutes.[14] The resulting free amino α-diazo ketone product was not isolated, but was treated with allyl bromide to give the desired cyclisation precursor **9** in 48% yield over two steps.

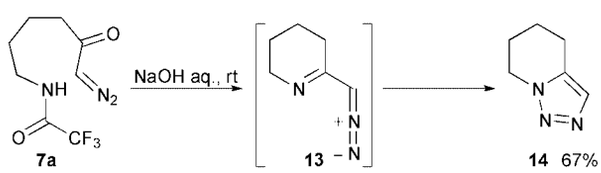
Two longer chain analogues (**11** and **12**) of the precursor **9** were prepared in a similar manner (Scheme 3). The synthesis of the diazo ketone **11** commenced with conversion of the hydrochloride salt of 5-(*N*-methylamino)pentanoic acid into the trifluoroacetamide **4b** by treatment with ethyl trifluoroacetate and excess triethylamine in methanol at room temperature. The starting material was prepared in 47% yield by heating commercially available *N*-methylpiperidin-2-one with concentrated hydrochloric acid in a sealed tube.[15] Conversion of the acid **4b** into the α-diazo ketone **7b** *via* the acid chloride was accomplished in 79% yield using the standard protocol. Removal of



Scheme 3 *Reagents and conditions*: (i), CF_3CO_2Et, Et_3N, MeOH, rt (**3a**, 89%; **4a**, 90%; **4b**, 63%; **5a**, 76%); (ii), $(COCl)_2$, DMF (cat.), CH_2Cl_2, 0 °C; (iii), CH_2N_2, Et_2O, 0 °C ⟶ rt (**6a**, 80%; **7a**, 83%; **7b**, 79%; **8a**, 82%, 2 steps); (iv), $Ba(OH)_2$ aq. or NaOH aq., rt; (v), CH_2CHCH_2Br, K_2CO_3, THF, rt (**9**, 48%; **11**, 37%; **12**, 54%, 2 steps).

the protecting group was effected by treatment of the amide **7b** with aqueous sodium hydroxide at room temperature, and the resulting amine was immediately alkylated to provide the cyclisation precursor **11**. The cyclisation precursor **12** was prepared from 6-aminohexanoic acid by the analogous sequence of trifluoroacetamide protection, diazo ketone formation, *N*-deprotection and dialkylation with allyl bromide.

The attempted synthesis of the cyclisation precursor **10** was unsuccessful. Although the amide **7a** was prepared from 5-aminopentanoic acid in good yield by trifluoroacetylation and subsequent diazo ketone formation using the standard protocol, deprotection under basic aqueous conditions delivered the triazole **14** rather than the required amino-substituted diazo ketone (Scheme 4). The outcome of the reaction was unantici-

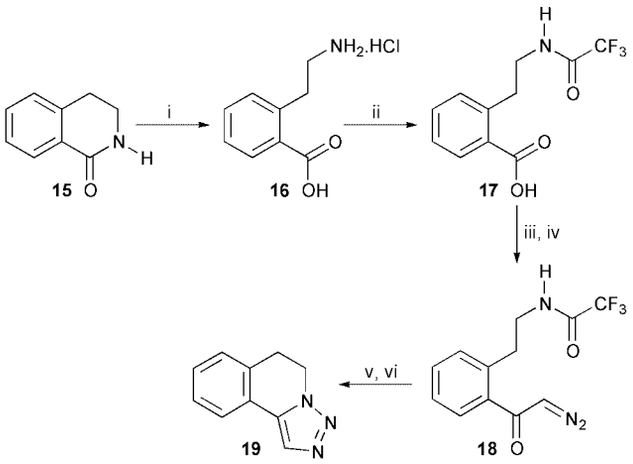


Scheme 4

pated, but it is probable that the triazole **14** was formed by cyclisation of the intermediate diazo imine **13** produced by intramolecular condensation. It is well known that related diazo imines undergo cyclisation to give triazoles.[16] When allylation was performed without purification of the intermediate amine after deprotection, a small amount of the desired product was obtained but the major product was the triazole **14**.

The problem of competitive triazole formation during deprotection was also observed when the trifluoroacetyl group was removed from the α-diazo ketone **18** prepared from the lactam **15** (Scheme 5). Reaction of the lactam **15** with concentrated hydrochloric acid at high temperature in a sealed tube afforded the amino acid hydrochloride salt **16** in 59% yield, and the amino functionality was protected by trifluoroacetylation. The acid **17** was then converted into the α-diazo ketone **18** in 82% yield using the standard protocol, and subsequent hydrolysis of the trifluoroacetyl group with aqueous barium hydroxide delivered a 57% yield of the triazole **19** instead of the required amine.

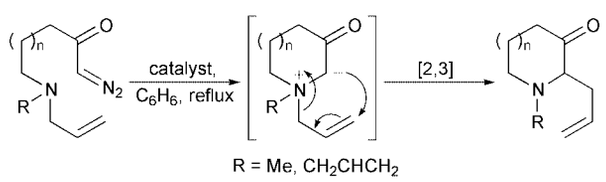
It is significant that competitive triazole formation was only encountered when deprotection of the substrates (**7a** and **18**) afforded a free primary amino group which could condense



Scheme 5 *Reagents and conditions*: (i), HCl conc., 165 °C (59%); (ii), CF_3CO_2Et, Et_3N, MeOH, rt (69%); (iii), $(COCl)_2$, DMF (cat.), CH_2Cl_2, 0 °C; (iv), CH_2N_2, CH_2Cl_2–Et_2O, 0 °C ⟶ rt (82%, 2 steps); (v), $Ba(OH)_2$ aq., rt; (v), CH_2CHCH_2Br, K_2CO_3, THF, rt (57%).

with the ketone carbonyl group to produce a six-membered cyclic imine. Triazole formation was not observed during the deprotection of substrates possessing either a longer or shorter chain between the amide and diazo ketone, or during the deprotection of amides in which an *N*-alkyl substituent prevented imine formation by the resulting secondary amine.

The metal-catalysed tandem ammonium ylide generation and [2,3]-rearrangement reactions of the α-diazo ketone substrates were explored (Scheme 6). Cyclisation reactions were



Substrate	R	n	Catalyst	Product	Yield (%)
2a	CH_3	0	$Cu(acac)_2$	**20**	73
2a	CH_3	0	$Rh_2(OAc)_4$	**20**	58
2b	CH_2CHCH_2	0	$Cu(acac)_2$	**21**	76
2b	CH_2CHCH_2	0	$Rh_2(OAc)_4$	**21**	70
9	CH_2CHCH_2	1	$Cu(acac)_2$	**22**	79
9	CH_2CHCH_2	1	$Rh_2(OAc)_4$	**22**	74
11	CH_3	2	$Cu(acac)_2$	**23**	84
11	CH_3	2	$Rh_2(OAc)_4$	**23**	56
12	CH_2CHCH_2	3	$Cu(acac)_2$	**24**	39
12	CH_2CHCH_2	3	$Rh_2(OAc)_4$	**24**	5

Scheme 6

performed by slow addition of a dilute solution of the α-diazo ketone to a solution of the catalyst (2 mol%) at room temperature or reflux. In preliminary studies, the cyclisation reactions of substrates **2a** and **2b** were performed in a variety of solvents at room temperature or reflux and copper(II) acetylacetonate and rhodium(II) acetate were employed as the catalysts. Copper-catalysed reactions required temperatures of >35 °C to initiate carbenoid generation, and reactions performed at reflux in low boiling solvents (*e.g.* dichloromethane) required extended reaction times and delivered poor yields of the pyrrolidinones. The poor performance of copper catalysts at lower reaction temperatures is attributable to competitive coordination of the amine to the metal centre, which blocks the vacant coordination site(s) required for carbenoid formation. Competitive coordination has been proposed by Doyle *et al.* to explain similar results obtained from *intermolecular* reactions of rhodium carbenoids with amines.[17]

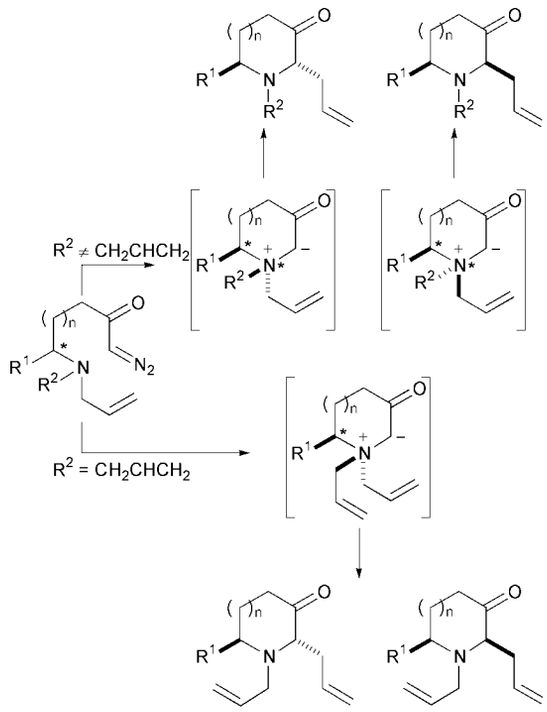
After considerable experimentation, it was found that copper- and rhodium-catalysed reactions proceeded at a satisfactory rate when performed in benzene at reflux. Under these conditions, the copper(II) acetylacetonate catalysed reactions of the precursors **2a** and **2b** proved to be highly effective, and the pyrrolidinones **20** and **21** were obtained in yields of 73% and 76% respectively. Lower yields of the pyrrolidinones were obtained when rhodium(II) acetate was employed as the catalyst under identical conditions (58% and 70% respectively). It is noteworthy that yields of the pyrrolidinone **21** obtained from the reactions of the *diallyl* substrate **2b** were generally higher than the yields of the pyrrolidinone **20** obtained from reactions of the diazo ketone **2a**.

The cyclisation reactions of diazo ketones **9**, **11** and **12** were also performed in benzene at reflux. Cyclisation of the substrate **9** proceeded to give the piperidinone **22** in 79% yield when copper(II) acetylacetonate was used as the catalyst. When copper(II) hexafluoroacetylacetonate and rhodium(II) acetate were employed as the catalysts, yields of 73% and 74% were obtained. Treatment of the α-diazo ketone **11** with copper(II) acetylacetonate in benzene at reflux gave the azepinone **23** in 84% yield. The use of copper(II) hexafluoroacetylacetonate or rhodium(II) acetate as the catalyst gave lower yields (58% and 56%) of the azepinone **23**. Finally, the copper(II) acetylacetonate catalysed reaction of the substrate **12** afforded the azocinone **24** in 39% yield. Copper(II) hexafluoroacetylacetonate was then employed as a catalyst in an attempt to improve the yield of the azocinone **24**. Although this complex is an excellent catalyst for the synthesis of cyclic ethers from diazo ketones and has been used to prepare an 8-membered cyclic ether,[4b] the azocinone **24** was formed in only 13% yield when this complex was used to cyclise substrate **12**. Rhodium(II) acetate also proved to be an inferior catalyst, and the azocinone **24** was obtained in only 5% yield when this complex was used.

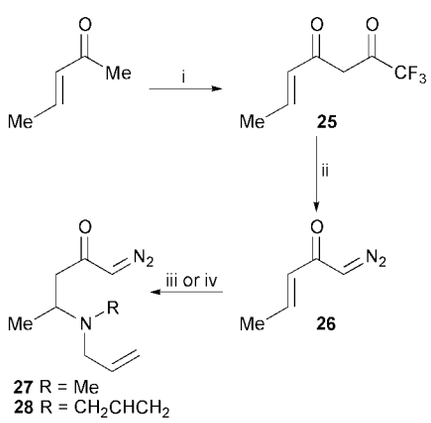
The results described above are consistent with those obtained by West and co-workers during the synthesis of cyclic amines by [1,2]-rearrangement of ammonium ylides generated by copper-catalysed reaction of α-diazo ketones.[3e] They have shown that higher yields of medium-ring cyclic amines are obtained when ammonium ylides are generated from copper carbenoids rather than rhodium carbenoids, and have used the tandem catalytic ylide generation and [1,2]-Stevens rearrangement reaction to synthesise the alkaloid (−)-epilupinine.[3c,3f]

At this stage in our study, the tandem carbenoid insertion and ylide rearrangement reaction had been used to prepare relatively unsubstituted cyclic amines from achiral substrates, and the issue of diastereocontrol had not been investigated. Cyclisation of diazo ketones bearing a substituent on the tether joining the diazo group to the allylic amine would result in two possible diastereoisomeric products, and the origin of the stereocontrol should depend on the nature of the substituents on the nitrogen atom (Scheme 7). In the case where the nitrogen atom possesses two non-equivalent substituents, ammonium ylide formation results in the creation of an additional stereogenic centre (*) at nitrogen. Provided that ylide formation is not reversible, the stereochemical outcome of the reaction is determined at this stage because each diastereoisomeric ylide undergoes stereospecific rearrangement.[18] In contrast, a substrate possessing two identical substituents reacts to give an ammonium ylide without the creation of an additional stereogenic centre (Scheme 7). In this case, a single ammonium ylide is generated and the level of diastereocontrol is dictated by the relative propensity of the diastereotopic allyl groups to undergo subsequent [2,3]-rearrangement.

A series of substituted precursors was prepared in order to explore the stereochemical outcome during the formation of pyrrolidines and piperidines. The α-diazo ketone precursors required for pyrrolidine synthesis were prepared by conjugate addition of either diallylamine or *N*-methylallylamine to an unsaturated diazo ketone (Scheme 8). The unsaturated diazo



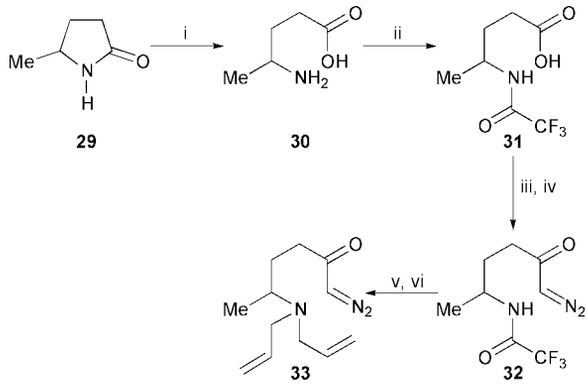
Scheme 7



Scheme 8 *Reagents and conditions*: (i), LiHMDS, −78 °C then $CF_3CO_2CH_2CF_3$, −78 °C; (ii), MsN_3, Et_3N, MeCN, rt (77%, 2 steps); (iii), $MeNHCH_2CHCH_2$, Et_2O, rt (**27**, 85%); (iv), $NH(CH_2CHCH_2)_2$, Et_2O, rt (**28**, 64%).

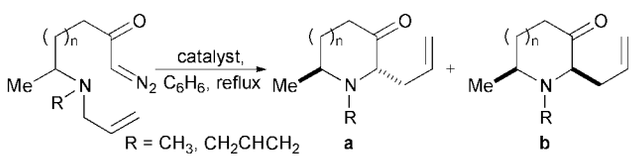
ketone **26** was prepared using Danheiser's two step diazo transfer sequence.[19] Thus, deprotonation of pent-3-en-2-one with lithium hexamethyldisilazane and reaction of the resulting enolate with 2,2,2-trifluoroethyl trifluoroacetate afforded the 1,3-dicarbonyl compound **25**. The β-diketone was immediately treated with methanesulfonyl azide and triethylamine to deliver the α-diazo ketone **26** in 77% yield over two steps.[19] Subsequent conjugate addition with either *N*-methylallylamine or diallylamine at room temperature then afforded the precursors **27** and **28** in yields of 85% and 64% respectively. The conjugate addition reaction of diallylamine proved to be capricious and often failed to proceed to completion, resulting in a difficult separation of the required product **28** from the starting materials.

The final substrate to be investigated, α-diazo ketone **33**, was prepared from the lactam **29** by a route in which nitrogen was protected using the trifluoroacetyl group (Scheme 9). The lactam **29** was first heated at reflux in 6 M HCl to afford the amino acid **30** in 76% yield.[15] *N*-Protection then gave the required trifluoroacetamide **31** in high yield and this was converted into the corresponding α-diazo ketone **32** *via* the acid chloride using the standard method (Scheme 9). Deprotection was accomplished by treatment of the amide **32** with a saturated aqueous solution of barium hydroxide, and immediate alkylation then delivered the desired cyclisation precursor **33** in modest yield over two steps.



Scheme 9 *Reagents and conditions*: (i), 6 M HCl, reflux (76%); (ii), CF_3CO_2Et, Et_3N, MeOH, rt (89%); (iii), $(COCl)_2$, DMF (cat.), CH_2Cl_2, 0 °C; (iv), CH_2N_2, Et_2O, 0 °C ⟶ rt (68%, 2 steps); (v), $Ba(OH)_2$ aq., rt; (vi), CH_2CHCH_2Br, K_2CO_3, THF, rt (31%, 2 steps).

The cyclisation reactions of the α-diazo ketones **27**, **28** and **33**, were then investigated (Scheme 10). Reactions were performed by slow addition of a dilute solution of the α-diazo ketone to a solution of the catalyst (2 mol%) in benzene at reflux. The reaction of diazo ketone **28** proceeded to deliver a mixture of the pyrrolidinones **35a**–**b** in excellent yield but with little diastereocontrol (≤2 : 1), and the choice of catalyst had little influence on either the yield or stereochemical outcome of the reaction. However, purification of the mixture of pyrrolidinones **35a**–**b** on silica gel resulted in epimerisation and led to a dramatic change in the diastereoisomeric ratio. Prolonged exposure of the mixture to silica gel returned an 8 : 1 mixture of isomers, as judged by NMR, but it was not possible to determine the relative configuration of each isomer using NOE difference spectroscopy because there was significant overlap of signals in the ^{1}H NMR spectrum. However, based on our results from related cyclic ethers, the *cis*-isomer **35b** is likely to be the thermodynamically favoured product arising from epimerisation.[4a]



Substrate	R	n	Catalyst	Product (Ratio)	Yield (%)
27	CH_3	0	$Cu(acac)_2$	**34** (1:1)	70
27	CH_3	0	$Rh_2(OAc)_4$	**34** (1:1)	62
28	CH_2CHCH_2	0	$Cu(acac)_2$	**35** (1.7:1)	84
28	CH_2CHCH_2	0	$Rh_2(OAc)_4$	**35** (2:1)	83
33	CH_2CHCH_2	1	$Cu(acac)_2$	**36** (1:1)	72
33	CH_2CHCH_2	1	$Rh_2(OAc)_4$	**36** (1:1)	70

Scheme 10

When one of the allyl groups was replaced by a methyl substituent, there was no diastereocontrol; the copper(II) acetylacetonate mediated cyclisation of the diazo ketone **27** afforded a 1 : 1 mixture of the isomers **34a**–**b** in a combined yield of 70% (Scheme 10). Increasing the size of the alkyl substituent resulted in a diminished yield without a significant improvement in the level of diastereocontrol. When the crude mixture of the isomers **34a**–**b** was purified by column chromatography, epimerisation occurred and a single isomer was isolated. As in the case above, overlapping signals in the ^{1}H NMR spectrum

precluded confirmation of the relative stereochemistry using NOE difference spectroscopy. As a result, the relative stereochemistry of the major isomer isolated after epimerisation was not determined unambiguously, but it is likely that the isomer **34b** was the major product for the reasons outlined above.

The cyclisation of the α-diazo ketone **33** proceeded in good yield but a 1 : 1 mixture of **36a**–**b** was obtained (Scheme 10). Epimerisation was encountered when the mixture was exposed to silica gel, and this resulted in a moderate preference (2 : 1 as judged by NMR) for one of the diastereoisomers. However, it was not possible to separate the diastereoisomers by column chromatography and once again NOE difference spectroscopy could not be used to determine the relative stereochemistry because there was insufficient separation of signals in the ^{1}H NMR spectrum.

The low levels of diastereocontrol obtained upon cyclisation of diazo ketones **27**, **28** and **33** contrast with results obtained from the copper-mediated cyclisation reactions of related oxygen-containing diazo ketones to give five- and six-membered cyclic ethers.[8a,8c] It is surprising that the levels of diastereocontrol are so low irrespective of whether the nitrogen centre possesses one or two allyl groups which can participate in the [2,3]-rearrangement of the putative ammonium ylide intermediate.

In summary, we have developed two new methods for the synthesis of diazo ketone precursors containing a nucleophilic allylic amine substituent. Although the preparation of cyclisation precursors by conjugate addition of allylic amines to unsaturated diazo ketones is of limited scope, the alternative sequence of nitrogen protection, α-diazo ketone formation, deprotection and allylation, is general and can be used to prepare a wide range of cyclisation precursors in reasonable yield. We have also demonstrated that copper(II) acetylacetonate is the best catalyst for carbenoid/ylide generation and that reactions must be performed at elevated temperatures in order to obtain reasonable reaction rates and high yields. The reaction has been used to prepare five- to seven-membered cyclic amines in good yield and eight-membered cyclic amines in modest yield. However, when the tandem intramolecular ammonium ylide formation and rearrangement reaction is used to prepare dialkyl- pyrrolidines or piperidines, it is not possible to achieve high levels of diastereocontrol directly from the cyclisation reaction. In addition, we have found that the propensity of the cyclic amine products to undergo epimerisation upon purification would complicate matters even if high levels of diastereocontrol were achievable during the reaction.

Experimental

General

Air and/or moisture sensitive reactions were performed under an atmosphere of nitrogen in oven or flame dried apparatus. Organic solvents and reagents were dried and distilled using standard methods: tetrahydrofuran (potassium–benzophenone ketyl), diethyl ether (sodium metal–benzophenone ketyl), methanol (magnesium methoxide), ethyl trifluoroacetate (anhydrous calcium chloride), allyl bromide (anhydrous magnesium sulfate), benzene, dichloromethane and triethylamine (calcium hydride). All other solvents and reagents were used as received from commercial suppliers. All reactions were monitored by thin layer chromatography using plastic- or aluminium-backed silica gel 60 F_{254} plates. Thin layer chromatography plates were viewed under UV light or were visualised using either basic potassium permanganate solution or acidic ethanolic anisaldehyde solution. Flash column chromatography was performed using Merck 7734 grade silica gel or Fluka silica gel 60 (220–440 mesh). Melting points were determined using either Büchi 510 or Reichert hot-stage melting point apparatus. IR spectra were recorded as potassium bromide disks, as liquid films on sodium chloride plates, or as solutions in chloroform, using either a Perkin–Elmer 1720X or 1600 series FTIR spectrometer. ^{1}H NMR spectra were recorded using a Bruker DRX500 (500 MHz), AM400 (400 MHz) or WM250 (250 MHz) spectrometer. ^{1}H NMR data are expressed as chemical shifts in ppm from an internal standard of tetramethylsilane followed by the number of protons, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad), coupling constant(s) J (Hz), and assignment. ^{13}C NMR spectra were recorded using a JEOL EX270 (67.5 MHz), Bruker AM400 (100 MHz) or Bruker DRX500 (125 MHz) instrument and multiplicities were obtained using a DEPT sequence. ^{13}C NMR chemical shifts are expressed in parts per million downfield from tetramethylsilane or the sodium salt of 3-(trimethylsilyl)-propanesulfonic acid. High resolution mass spectra (HRMS) were obtained using an AEI MS902 or VG Micromass 70E mass spectrometer, using electron impact (EI), chemical ionisation (CI) or fast-atom bombardment (FAB). Microanalysis was performed by the microanalysis section of the School of Chemistry, University of Nottingham, UK.

General procedure for the preparation of α-diazo ketones

Oxalyl chloride was added dropwise to a solution of the carboxylic acid in dry dichloromethane at room temperature or 0 °C. A small amount of dry dimethylformamide was added, and the resulting mixture was stirred at room temperature or 0 °C for the time indicated. The solvent was removed *in vacuo* and the residue dissolved in dry diethyl ether. The ethereal solution was added slowly to a solution of diazomethane in diethyl ether at 0 °C, and the resulting solution was stirred at 0 °C and then at room temperature. The remaining diazomethane was consumed by dropwise addition of glacial acetic acid and the solution was neutralised with a saturated aqueous solution of sodium bicarbonate. The organic phase was separated, the aqueous phase extracted with diethyl ether and the combined organic extracts were dried before removal of the solvent *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the *α-diazo ketone*.

4-Bromo-1-diazobutan-2-one 1[11]**.** Following the general procedure, the acid chloride was prepared by the reaction of 3-bromopropanoic acid (1.14 g, 7.45 mmol) with oxalyl chloride (3.00 cm^3, 34.4 mmol) and dry dimethylformamide (one drop) in dry dichloromethane (45 cm^3) at room temperature for 2 h. The acid chloride was dissolved in dry diethyl ether (30 cm^3) and added to a solution of diazomethane (~33 mmol) in diethyl ether (120 cm^3) at 0 °C. The mixture was stirred at 0 °C for 30 min and then at room temperature for a further 45 min. The remaining diazomethane was consumed with glacial acetic acid (3.50 cm^3, 61.1 mmol). Purification by flash column chromatography on silica gel (diethyl ether–hexane, 1 : 1) afforded the *α-diazo ketone* **1** (1.08 g, 82%) as a yellow liquid; ν_{max}(film)/cm^{-1} 3096, 2108, 1634; δ_H (250 MHz, $CDCl_3$) 5.31 (1H, br s, CHN_2), 3.62 (2H, t, J 6.7, CH_2Br), 2.90 (2H, t, J 6.7, CH_2CO); δ_C (67.8 MHz, $CDCl_3$) 191.5 (CO), 55.8 (CH), 43.3 ($BrCH_2$), 26.5 (CH_2CO); *m*/*z* (EI) 175.9579 (M^+. $C_4H_5BrN_2O$ requires 175.9585).

4-(*N*-Methyl-*N*-allylamino)-1-diazobutan-2-one 2a. *N*-Methylallylamine (0.50 g, 7.0 mmol) and triethylamine (1.13 cm^3, 8.11 mmol) were dissolved in dry ethyl acetate (15 cm^3). The mixture was cooled to 0 °C and a solution of 4-bromo-1-diazobutan-2-one (**1**) (1.36 g, 7.68 mmol) in dry ethyl acetate (15 cm^3) was added over 30 s. The resulting solution was stirred at 0 °C for 25 min and at room temperature for 15 h. The mixture was then diluted with a saturated aqueous solution of sodium bicarbonate (40 cm^3) and extracted with diethyl ether (3 × 40 cm^3). The combined organic extracts were dried over anhydrous potassium carbonate and the solvent removed

in vacuo. The residue was purified by flash column chromatography on silica gel (1% triethylamine in diethyl ether) to give the *α-diazo ketone* **2a** (0.91 g, 77%) as a green liquid; ν_{max}(film)/cm^{-1} 3080, 2977, 2793, 2104, 1641, 998, 920; δ_H (250 MHz, $CDCl_3$) 5.84 (1H, ddt, *J* 17.1, 10.2 and 6.5, C*H*=CH_2), 5.39 (1H, br s, CHN_2), 5.18 (1H, dtd, *J* 17.1, 1.1, 0.7, *trans* CH=CH_2), 5.15 (1H, dtd, *J* 10.2, 1.1, 0.7, *cis* CH=CH_2), 3.01 (2H, ddd, *J* 6.5, 1.1, 1.1, CH_2CH=CH_2), 2.70 (2H, t, *J* 7.0, NCH_2CH_2), 2.53–2.45 (2H, m, CH_2CO), 2.23 (3H, s, CH_3); δ_C (67.8 MHz, $CDCl_3$) 193.7 (CO), 135.2 (CH), 117.6 (CH_2), 60.6 (CH_2), 54.6 (CH_2), 52.2 (CH_2), 41.8 (CH_3), 38.7 (CH_2); *m*/*z* (EI) 139.0998 ($M^+ - N_2$. $C_8H_{13}NO$ requires 139.0997).

4-(*N,N*-Diallylamino)-1-diazobutan-2-one 2b. Diazabicyclo-[4.3.0]non-5-ene (0.74 cm^3, 6.0 mmol) was added dropwise to a vigorously stirred solution of 4-bromo-1-diazobutan-2-one (**1**) (1.06 g, 5.99 mmol) and hydroquinone (50 mg, 0.45 mmol) in dry diethyl ether (50 cm^3) at −10 °C. The resulting mixture was stirred at −10 °C for a further 7 min and then filtered through a sinter into a solution of diallylamine (2.33 g, 24.0 mmol) in dry diethyl ether (10 cm^3) at 0 °C. The mixture was stirred at room temperature for a further 2 h and the solvent removed *in vacuo*. The residue was purified by flash column chromatography on silica gel (1% triethylamine in diethyl ether–hexane, 4 : 1) to give the *α-diazo ketone* **2b** (0.85 g, 73%) as a green liquid; ν_{max}(film)/cm^{-1} 3080, 2978, 2925, 2809, 2105, 1641, 998, 922; δ_H (250 MHz, $CDCl_3$) 5.83 (2H, ddt, *J* 17.1, 10.3, 6.5, 2 × C*H*=CH_2), 5.39 (1H, br s, CHN_2), 5.22–5.18 (2H, m, 2 × *trans* CH=CH_2), 5.18–5.11 (2H, m, 2 × *cis* CH=CH_2), 3.09 (4H, d, *J* 6.5, 2 × CH_2CH=CH_2), 2.79 (2H, t, *J* 7.2, NCH_2CH_2), 2.47 (2H, t, *J* 7.2, CH_2CO); δ_C (67.8 MHz, $CDCl_3$) 193.8 (CO), 135.1 (CH), 117.5 (CH_2), 56.6 (CH_2), 54.5 (CH), 48.6 (CH_2), 38.5 (CH_2); *m*/*z* (EI) 165.1147 ($M^+ - N_2$. $C_{10}H_{15}NO$ requires 165.1154).

General procedure for trifluoroacetyl protection of amino acids

Ethyl trifluoroacetate was added dropwise to a solution of the amino acid and triethylamine in dry methanol. The resulting solution was stirred at room temperature and the solvent was then removed *in vacuo*. The residue was diluted with 2 M hydrochloric acid and extracted with diethyl ether, and the aqueous layer was then saturated with solid sodium chloride and extracted with further diethyl ether. The combined organic extracts were dried over anhydrous magnesium sulfate and the solvent removed *in vacuo*. The product was purified by flash column chromatography on silica gel or by recrystallisation.

4-[*N*-(Trifluoroacetyl)amino]butanoic acid 3a. Following the general protection procedure, 4-aminobutanoic acid (4.12 g, 40.0 mmol) was treated with ethyl trifluoroacetate (6.00 cm^3, 50.4 mmol) and triethylamine (5.60 cm^3, 40.2 mmol) in dry methanol (20 cm^3), and the resulting solution was stirred at room temperature for 19 h. The crude product was diluted with 2 M hydrochloric acid (100 cm^3) and extracted with diethyl ether (2 × 100 cm^3). After addition of sodium chloride, the aqueous layer was extracted with diethyl ether (2 × 100 cm^3). The product was purified by recrystallisation (diethyl ether–hexane) to give the *protected amino acid* **3a** (7.06 g, 89%) as a white solid; mp 81–83 °C [lit.,[20] 81–82 °C]; ν_{max}($CHCl_3$)/cm^{-1} 3517, 3438, 3268, 2991, 2947, 1716; δ_H (250 MHz, $CDCl_3$) 6.78 (1H, br s, NH), 3.46 (2H, t, *J* 6.4, NCH_2), 2.36 (2H, t, *J* 6.8, CH_2CO), 1.86 (2H, tt, *J* 6.8, 6.4, NCH_2CH_2); δ_C (67.8 MHz, CD_3OD) 177.1 (CO_2H), 159.6 (CON, q, $^2J_{FC}$ 37), 118.0 (CF_3, q, $^1J_{FC}$ 287), 40.6 (CH_2), 32.4 (CH_2), 25.6 (CH_2) (Found C, 36.25; H, 4.2; N, 7.1. $C_6H_8F_3NO_3$ requires C, 36.2; H, 4.0; N, 7.0%).

5-[*N*-(Trifluoroacetyl)amino]pentanoic acid 4a. Following the general protection procedure, 5-aminopentanoic acid (2.34 g, 20.0 mmol) was treated with ethyl trifluoroacetate (3.00 cm^3, 25.2 mmol) and triethylamine (2.80 cm^3, 20.1 mmol) in dry methanol (10 cm^3), and the resulting solution was stirred at room temperature for 18 h. The crude product was diluted with 2 M hydrochloric acid (50 cm^3) and extracted with diethyl ether (3 × 60 cm^3). After addition of sodium chloride, the aqueous layer was extracted with diethyl ether (60 cm^3). The product was purified by recrystallisation (diethyl ether–hexane) to give the *protected amino acid* **4a** (3.84 g, 90%) as a white solid; mp 96–98 °C [lit.,[20] 94–96 °C]; ν_{max}($CHCl_3$)/cm^{-1} 3437, 2955, 1723; δ_H (250 MHz, $CDCl_3$) 6.51 (1H, br s, NH), 3.44–3.36 (2H, m, NCH_2), 2.43 (2H, t, *J* 6.7, CH_2CO), 1.74–1.63 (4H, m, NCH_2CH_2 and CH_2CH_2CO); δ_C (67.8 MHz, CD_3OD) 177.2 (CO_2H), 159.0 (CON, q, $^2J_{FC}$ 37), 117.5 (CF_3, q, $^1J_{FC}$ 287), 40.3 (CH_2), 34.2 (CH_2), 29.2 (CH_2), 23.1 (CH_2) (Found C, 39.5; H, 4.8; N, 6.5. $C_7H_{10}F_3NO_3$ requires C, 39.4; H, 4.7; N, 6.6%).

5-[*N*-Methyl-*N*-(trifluoroacetyl)amino]pentanoic acid 4b. Following the general protection procedure, 5-(*N*-methylamino)-pentanoic acid hydrochloride salt (0.35 g, 2.1 mmol) was treated with ethyl trifluoroacetate (0.31 cm^3, 2.6 mmol) and triethylamine (0.63 cm^3, 4.5 mmol) in dry methanol (5 cm^3), and the resulting solution was stirred at room temperature for 29 h. The crude product was diluted with 1 M hydrochloric acid (10 cm^3) and extracted with diethyl ether (4 × 10 cm^3). The product was purified by flash column chromatography on silica gel (diethyl ether–hexane, 3 : 2) to give the *protected amino acid* **4b** (0.30 g, 63%) as a colourless liquid; ν_{max}($CHCl_3$)/cm^{-1} 3179, 2948, 2828, 1694; δ_H (400 MHz, $[CD_3]_2SO$, 393 K) 2.86 (2H, t, *J* 7.3, NCH_2), 2.50 (3H, s, NCH_3), 2.26 (2H, t, *J* 7.1, CH_2CO), 1.75–1.68 (2H, m, NCH_2CH_2), 1.66–1.58 (2H, m, CH_2CH_2CO); δ_C (100 MHz, $[CD_3]_2SO$, 393 K) 173.9 (CO_2H), 156.4 (CON, q, $^2J_{FC}$ 35), 116.8 (CF_3, q, $^1J_{FC}$ 289), 48.8 (CH_2), 34.1 (CH_3), 33.3 (CH_2), 25.8 (CH_2), 21.8 (CH_2); *m*/*z* (EI) 227.0768 (M^+. $C_8H_{12}F_3NO_3$ requires 227.0769).

6-[*N*-(Trifluoroacetyl)amino]hexanoic acid 5a. Following the general protection procedure, 6-aminohexanoic acid (5.25 g, 40.0 mmol) was treated with ethyl trifluoroacetate (6.00 cm^3, 50.4 mmol) and triethylamine (5.60 cm^3, 40.2 mmol) in dry methanol (20 cm^3), and the resulting solution was stirred at room temperature for 17 h. The crude product was diluted with a 2 M hydrochloric acid (100 cm^3) and the resulting precipitate collected by filtration and dissolved in diethyl ether (100 cm^3). The aqueous layer was extracted with diethyl ether (2 × 80 cm^3) and sodium chloride added. The aqueous layer was extracted with diethyl ether (2 × 80 cm^3). The product was purified by recrystallisation (diethyl ether–hexane) to give the *protected amino acid* **5a** (6.90 g, 76%) as a white solid; mp 88–90 °C [lit.,[20] 89–91 °C]; ν_{max}($CHCl_3$)/cm^{-1} 3436, 2925, 2848, 1722, 1602; δ_H (250 MHz, CD_3OD) 3.29 (2H, t, *J* 7.1, NCH_2), 2.31 (2H, t, *J* 7.3, CH_2CO), 1.69–1.53 (4H, m, NCH_2CH_2 and CH_2-CH_2CO), 1.43–1.31 (2H, m, $NCH_2CH_2CH_2$); δ_C (67.8 MHz, CD_3OD) 177.5 (CO_2H), 158.9 (CON, q, $^2J_{FC}$ 37), 117.5 (CF_3, q, $^1J_{FC}$ 287), 40.5 (CH_2), 34.7 (CH_2), 29.5 (CH_2), 27.2 (CH_2), 25.5 (CH_2) (Found C, 42.4; H, 5.5; N, 6.4. $C_8H_{12}F_3NO_3$ requires C, 42.3; H, 5.3; N, 6.2%).

1-Diazo-5-[*N*-(trifluoroacetyl)amino]pentan-2-one 6a. Following the general procedure, the acid chloride was prepared by the reaction of the *N*-protected amino acid **3a** (4.98 g, 25.0 mmol) with oxalyl chloride (10.9 cm^3, 125 mmol) and dry dimethylformamide (five drops) in dry dichloromethane (125 cm^3) at 0 °C for 1 h and then at room temperature for 5 h. The acid chloride was dissolved in dry dichloromethane (30 cm^3) and added to a solution of diazomethane (~150 mmol) in diethyl ether (350 cm^3) at 0 °C, and the mixture was stirred at 0 °C for 2 h. The remaining diazomethane was consumed with glacial acetic acid (12.9 cm^3, 225 mmol). Purification by flash column chromatography on silica gel (diethyl ether–hexane, 1 : 1) afforded the *α-diazo ketone* **6a** (4.46 g, 80%) as a yellow solid; mp 39–41 °C; ν_{max}($CHCl_3$)/cm^{-1} 3436, 3274, 2940, 2112, 1723,

1634; δ_H (250 MHz, $CDCl_3$) 7.68 (1H, br s, NH), 5.36 (1H, br s, CHN_2), 3.40 (2H, q, *J* 6.3, NCH_2), 2.46 (2H, t, *J* 6.3, CH_2CO), 1.94 (2H, tt, *J* 6.3 and 6.3, NCH_2CH_2); δ_C (67.8 MHz, $CDCl_3$) 194.9 (CO), 157.4 (CON, q, $^2J_{FC}$ 36), 115.8 (CF_3, q, $^1J_{FC}$ 288), 55.1 (CH), 39.5 (CH_2), 37.6 (CH_2), 23.3 (CH_2); *m*/*z* (EI) 182.0397 ($M^+ - CHN_2$. $C_6H_7F_3NO_2$ requires 182.0429).

1-Diazo-6-[*N*-(trifluoroacetyl)amino]hexan-2-one 7a. Following the general procedure, the acid chloride was prepared by the reaction of the *N*-protected amino acid **4a** (2.13 g, 10.0 mmol) with oxalyl chloride (4.40 cm^3, 50.4 mmol) and dry dimethylformamide (one drop) in dry dichloromethane (50 cm^3) at 0 °C for 1 h and then at room temperature for 2 h. The acid chloride was dissolved in dry dichloromethane (40 cm^3) and added to a solution of diazomethane (~60 mmol) in diethyl ether (180 cm^3) at 0 °C, and the mixture was stirred at 0 °C for 2 h and at room temperature for 1 h. The remaining diazomethane was consumed with glacial acetic acid (6.80 cm^3, 119 mmol). Purification by flash column chromatography on silica gel (diethyl ether–hexane, 2 : 1) afforded the *α-diazo ketone* **7a** (1.96 g, 83%) as a yellow liquid; $\nu_{max}(CHCl_3)/cm^{-1}$ 3440, 3272, 3118, 2947, 2864, 2111, 1722, 1636; δ_H (400 MHz, $CDCl_3$) 7.03 (1H, br s, NH), 5.29 (1H, br s, CHN_2), 3.36 (2H, q, *J* 6.4, NCH_2), 2.39 (2H, br, CH_2CO), 1.73–1.59 (4H, m, NCH_2CH_2 and CH_2CH_2CO); δ_C (67.8 MHz, $CDCl_3$) 195.1 (CO), 157.3 (CON, q, $^2J_{FC}$ 37), 115.8 (CF_3, q, $^1J_{FC}$ 288), 54.6 (CH), 39.6 (CH_2), 39.2 (CH_2), 27.8 (CH_2), 21.6 (CH_2).

1-Diazo-6-[*N*-methyl-*N*-(trifluoroacetyl)amino]hexan-2-one 7b. Following the general procedure, the acid chloride was prepared by the reaction of the *N*-protected amino acid **4b** (1.93 g, 8.50 mmol) with oxalyl chloride (3.70 cm^3, 42.4 mmol) and dry dimethylformamide (seven drops) in dry dichloromethane (50 cm^3) at 0 °C for 1 h and then at room temperature for 2 h 40 min. The acid chloride was dissolved in dry dichloromethane (50 cm^3) and added to a solution of diazomethane (~60 mmol) in diethyl ether (350 cm^3) at 0 °C, and the mixture was stirred at 0 °C for 1 h 50 min and then at room temperature for 1 h. The remaining diazomethane was consumed with glacial acetic acid (5.20 cm^3, 90.8 mmol). Purification by flash column chromatography on silica gel (diethyl ether–hexane, 2 : 1) afforded the *α-diazo ketone* **7b** (1.69 g, 79%) as a yellow liquid (mixture of amide rotamers); ν_{max}(film)/cm^{-1} 3092, 2948, 2104, 1695, 1642; δ_H (250 MHz, $CDCl_3$) 5.32 (1H, br s, CHN_2), 3.47–3.38 (2H, m, NCH_2), 3.12 (2.1H, q, *J* 1.5, 0.7 × CH_3), 3.02 (0.9H, m, 0.3 × CH_3), 2.38 (2H, s, CH_2CO), 1.72–1.62 (4H, m, NCH_2CH_2 and CH_2CH_2CO); δ_C (100 MHz, $CDCl_3$) 194.2 (CO), 193.8 (CO), 156.7 (CON, q, $^2J_{FC}$ 36), 156.6 (CON, q, $^2J_{FC}$ 36), 116.4 (CF_3, q, $^1J_{FC}$ 288), 116.3 (CF_3, q, $^1J_{FC}$ 288), 54.3 (CH), 49.0 (CH_2), 48.7 (CH_2), 39.7 (CH_2), 34.5 (CH_3), 34.1 (CH_3), 27.5 (CH_2), 25.6 (CH_2), 21.6 (CH_2), 21.4 (CH_2); *m*/*z* (EI) 223.0824 ($M^+ - N_2$. $C_9H_{12}F_3NO_2$ requires 223.0820).

1-Diazo-7-[*N*-(trifluoroacetyl)amino]heptan-2-one 8a. Following the general procedure, the acid chloride was prepared by the reaction of the *N*-protected amino acid **5a** (5.86 g, 25.8 mmol) with oxalyl chloride (10.9 cm^3, 125 mmol) and dry dimethylformamide (seven drops) in dry dichloromethane (125 cm^3) at 0 °C for 2 h and then at room temperature for 2 h 15 min. The acid chloride was dissolved in dry dichloromethane (70 cm^3) and added to a solution of diazomethane (~150 mmol) in diethyl ether (350 cm^3) at 0 °C, and the mixture was allowed to warm to room temperature for 16 h. The remaining diazomethane was consumed with glacial acetic acid (12.9 cm^3, 225 mmol). Purification by flash column chromatography on silica gel (diethyl ether–hexane, 2 : 1) afforded the *α-diazo ketone* **8a** (5.34 g, 82%) as a yellow solid; mp 48–50 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3439, 3297, 3116, 2945, 2862, 2109, 1722, 1634; δ_H (250 MHz, $CDCl_3$) 7.35 (1H, br s, NH), 5.33 (1H, br s, CHN_2), 3.36 (2H, t, *J* 6.7, NCH_2), 2.50–2.23 (2H, m, CH_2CO), 1.71–1.55 (4H, m, NCH_2CH_2 and CH_2CH_2CO), 1.43–1.30 (2H, m, $NCH_2CH_2CH_2$); δ_C (67.8 MHz, $CDCl_3$) 195.1 (CO), 157.3 (CON, q, $^2J_{FC}$ 37), 115.8 (CF_3, q, $^1J_{FC}$ 287), 54.6 (CH), 40.3 (CH_2), 39.5 (CH_2), 28.3 (CH_2), 25.9 (CH_2), 24.2 (CH_2); *m*/*z* (EI) 210.0743 ($M^+ - CHN_2$. $C_8H_{11}F_3NO_2$ requires 210.0742).

1-Diazo-5-(*N*,*N*-diallylamino)pentan-2-one 9. The α-diazo ketone **6a** (1.00 g, 4.48 mmol) was dissolved in a saturated aqueous solution of barium hydroxide (30.0 cm^3) and the solution stirred at room temperature for 18 min. The solution was then extracted with ethyl acetate (3 × 30 cm^3). The aqueous phase was evaporated to dryness *in vacuo* and the solid residue washed with ethyl acetate (2 × 30 cm^3). The combined organic phases were then dried over anhydrous potassium carbonate the solvent removed *in vacuo*. Allyl bromide (1.16 cm^3, 13.4 mmol) was then added to a suspension of the residue and potassium carbonate (1.86 g, 13.5 mmol) in dry tetrahydrofuran (30 cm^3). The resulting suspension was stirred at room temperature for 24 h and the solvent was removed *in vacuo*. The residue was diluted with water (45 cm^3) and extracted with diethyl ether (5 × 30 cm^3), and the combined organic extracts were dried over anhydrous potassium carbonate. The solvent was removed *in vacuo* and the residue was purified by flash column chromatography on silica gel (1% triethylamine in diethyl ether) to give the *α-diazo ketone* **9** (0.45 g, 48%) as a green liquid; ν_{max}(film)/cm^{-1} 3078, 3007, 2977, 2930, 2806, 2104, 1641, 997, 920; δ_H (250 MHz, $CDCl_3$) 5.82 (2H, ddt, *J* 17.1, 10.2, 6.5, 2 × CH=CH_2), 5.25 (1H, br s, CHN_2), 5.18 (2H, dtd, *J* 17.1, 1.2, 0.5, 2 × *trans* CH=CH_2), 5.13 (2H, dtd, *J* 10.2, 1.2 and 0.5, 2 × *cis* CH=CH_2), 3.07 (4H, dt, *J* 6.5, 1.2, 2 × CH_2CH=CH_2), 2.47–2.40 (2H, m, NCH_2CH_2), 2.34 (2H, t, *J* 6.8, CH_2CO), 1.84–1.72 (2H, m, NCH_2CH_2); δ_C (67.8 MHz, $CDCl_3$) 194.8 (CO), 135.5 (CH), 117.2 (CH_2), 56.5 (CH_2), 54.1 (CH), 52.0 (CH_2), 38.4 (CH_2), 22.3 (CH_2); *m*/*z* (EI) 171.1313 ($M^+ - N_2$. $C_{11}H_{17}NO$ requires 171.1310).

6-(*N*-Allyl-*N*-methylamino)-1-diazohexan-2-one 11. The α-diazo ketone **7b** (136 mg, 0.573 mmol) was dissolved in a 0.05 M aqueous solution of sodium hydroxide (5.40 cm^3) and the resulting solution stirred at room temperature for 2 h 10 min. After this time, the aqueous phase was extracted with ethyl acetate (3 × 15 cm^3). The aqueous extracts were evaporated *in vacuo* and the resulting residue dissolved in dry tetrahydrofuran (8 cm^3). Potassium carbonate (180 mg, 1.30 mmol) and allyl bromide (0.10 cm^3, 1.2 mmol) were added and the mixture stirred at room temperature for 6 h 30 min. The solvent was then removed *in vacuo* and the residue was purified by flash column chromatography on silica gel (1% triethylamine in ethyl acetate) to give the *α-diazo ketone* **11** (17.9 mg, 17%) as a green liquid.

The combined organic extracts were dried over anhydrous potassium carbonate and concentrated *in vacuo*. The residue and potassium carbonate (150 mg, 1.09 mmol) were suspended in dry tetrahydrofuran (5 cm^3) and allyl bromide (0.10 cm^3, 1.2 mmol) was added. The resulting suspension was stirred at room temperature for 3 h and the solvent was then removed *in vacuo*. The residue was purified by column chromatography (1% triethylamine in ethyl acetate) to give the *α-diazo ketone* **11** (21.1 mg, 20%) as a green liquid (combined yield 38.9 mg, 37%); $\nu_{max}(CHCl_3)/cm^{-1}$ 2937, 2855, 2109, 1643; δ_H (250 MHz, $CDCl_3$) 5.82 (1H, m, dddd, *J* 17.0, 10.2, 6.5, 6.5, CH=CH_2), 5.24 (1H, br s, CHN_2), 5.18–5.10 (1H, m, *trans* CH=CH_2), 5.13–5.07 (1H, m, *cis* CH=CH_2), 2.96 (2H, d, *J* 6.5, CH_2CH=CH_2), 2.34–2.28 (4H, m, NCH_2 and CH_2CO), 2.17 (3H, s, NCH_3), 1.68–1.42 (4H, m, NCH_2CH_2 and CH_2CH_2CO); δ_C (67.8 MHz, $CDCl_3$) 194.8 (CO), 135.6 (CH), 117.2 (CH_2), 60.8 (CH_2), 56.6 (CH_2), 54.1 (CH), 41.8 (CH_3), 40.6 (CH_2), 26.7 (CH_2), 22.9 (CH_2); *m*/*z* (EI) 167.1323 ($M^+ - N_2$. $C_{10}H_{17}NO$ requires 167.1310).

7-(*N,N*-Diallylamino)-1-diazoheptan-2-one 12. The α-diazo ketone **8a** (1.45 g, 5.77 mmol) was dissolved in a saturated aqueous solution of barium hydroxide (40 cm^3) and stirred at room temperature for 20 min. After this time, further saturated aqueous barium hydroxide solution (10 cm^3) was added. The reaction was then stirred for 10 min and the solution was extracted with ethyl acetate (3 × 50 cm^3). The aqueous phase was evaporated to dryness *in vacuo* and the solid residue washed with ethyl acetate (2 × 50 cm^3). The combined organic phases were dried over anhydrous potassium carbonate and the solvent was removed *in vacuo*. The residue and potassium carbonate (2.48 g, 17.9 mmol) were suspended in dry tetrahydrofuran (40 cm^3) and allyl bromide (1.55 cm^3, 17.9 mmol) was added in one portion. The resulting suspension was stirred at room temperature for 20 h and the solvent was then removed *in vacuo*. The residue was diluted with water (80 cm^3) and extracted with diethyl ether (4 × 80 cm^3). The combined organic extracts were dried over anhydrous potassium carbonate and the solvent removed *in vacuo*. The residue was purified by flash column chromatography on silica gel (1% triethylamine in diethyl ether) to give the *α-diazo ketone* **12** (0.73 g, 54%) as a green liquid; ν_{max}(film)/cm^{-1} 3078, 3007, 2977, 2934, 2861, 2801, 2104, 1641, 996, 919; δ_H (250 MHz, $CDCl_3$) 5.84 (2H, ddt, *J* 16.9, 10.3, 6.5, 2 × C*H*=CH_2), 5.25 (1H, br s, CHN_2), 5.16 (2H, dddd, *J* 16.9, 1.3, 1.3, 0.6, 2 × *trans* CH=CH_2), 5.12 (2H, dddd, *J* 10.3, 1.3, 1.3, 0.6, 2 × *cis* CH=CH_2), 3.07 (4H, dt, *J* 6.5, 1.3, 2 × CH_2CH=CH_2), 2.43–2.35 (2H, m, NCH_2CH_2), 2.31 (2H, t, *J* 7.4, CH_2CO), 1.63 (2H, tt, *J* 7.4, 7.4, CH_2CH_2CO), 1.53–1.26 (4H, m, NCH_2CH_2 and $NCH_2CH_2CH_2$); δ_C (67.8 MHz, $CDCl_3$) 195.0 (CO), 135.6 (CH), 117.1 (CH_2), 56.7 (CH_2), 54.1 (CH), 52.9 (CH_2), 40.8 (CH_2), 26.9 (CH_2), 26.5 (CH_2), 24.9 (CH_2); *m*/*z* (EI) 194.1302 ($M^+ - C_3H_5$. $C_{10}H_{16}N_3O$ requires 194.1293).

4,5,6,7-Tetrahydro-[1,2,3]triazolo[1,5-*a*]pyridine 14. The α-diazo ketone **7a** (46.0 mg, 0.19 mmol) was dissolved in a 0.18 M aqueous solution of sodium hydroxide (4.6 cm^3) and the mixture was stirred at room temperature for 96 h. The mixture was extracted with diethyl ether (3 × 10 cm^3) and the combined organic extracts were dried over anhydrous magnesium sulfate. The solvent was removed *in vacuo* and the residue was purified by flash column chromatography on silica gel (diethyl ether) to give the *triazole* **14** (16.0 mg, 67%) as a colourless liquid; ν_{max}($CHCl_3$)/cm^{-1} 2992, 2948, 2853, 1629; δ_H (250 MHz, $CDCl_3$) 7.43 (1H, s, CH=C), 4.36 (2H, t, *J* 6.1, NCH_2), 2.84 (2H, t, *J* 6.3, CH_2CH=C), 2.13–2.00 (2H, m, NCH_2CH_2), 1.99–1.86 (2H, m, CH_2CH_2C=C); δ_C (67.8 MHz, $CDCl_3$) 133.1 (C), 130.4 (CH), 45.8 (CH_2), 22.6 (CH_2), 19.9 (CH_2), 19.9 (CH_2); *m*/*z* (EI) 123.0801 (M^+. $C_6H_9N_3$ requires 123.0797).

2-(2-Aminoethyl)benzoic acid hydrochloride salt 16. The lactam **15** (1.03 g, 7.00 mmol) and concentrated hydrochloric acid (13.0 cm^3) were heated in a sealed tube at 165 °C for 42 h. The reaction mixture was cooled to room temperature and the contents of the tube were diluted with water (50 cm^3) and extracted with diethyl ether (3 × 50 cm^3). The aqueous phase was concentrated *in vacuo* and the residue recrystallised (methanol–diethyl ether) to give the *amino acid hydrochloride salt* **16** (0.83 g, 59%) as a white solid; mp 191–194 °C [lit.,[21] 199–200 °C]; ν_{max}(KBr)/cm^{-1} 3028, 1708, 1603, 770, 759, 749; δ_H (250 MHz, D_2O) 7.93 (1H, dd, *J* 7.2, 1.4, ArH), 7.62 (1H, dt, *J* 7.6 and 1.4, ArH), 7.48–7.41 (2H, m, 2 × ArH), 3.29 (4H, s, NCH_2CH_2 and NCH_2CH_2); δ_C (67.8 MHz, D_2O) 171.6 (CO), 138.7 (C), 134.0 (CH), 132.6 (CH), 132.0 (CH), 130.3 (C), 128.5 (CH), 41.5 (CH_2), 32.5 (CH_2) (Found C, 53.5; H, 6.2; N, 7.1. $C_9H_{12}ClNO_2$ requires C, 53.6; H, 6.0; N, 6.9%).

2-[2-(*N*-(Trifluoroacetyl)amino)ethyl]benzoic acid 17. The amino acid hydrochloride salt **16** (55.2 mg, 0.274 mmol) was dissolved in dry methanol (5 cm^3) and triethylamine (84 μl, 0.60 mmol) was added dropwise over 30 s. The resulting solution was stirred at room temperature for 15 min and then ethyl trifluoroacetate (40 μl, 0.34 mmol) was added dropwise over 15 s. The reaction mixture was stirred at room temperature for 17 h and further portions of triethylamine (80 μl, 0.57 mmol) and ethyl trifluoroacetate (40 μl, 0.34 mmol) were then added. The resulting solution was stirred at room temperature for a further 3.5 h and the solvent was then removed *in vacuo*. The residue was diluted with a 2 M hydrochloric acid (7.0 cm^3) and extracted with diethyl ether (3 × 10 cm^3). The combined organic extracts were dried over anhydrous magnesium sulfate and the solvent removed *in vacuo*. The residue was recrystallised (diethyl ether–hexane) to give the *protected amino acid* **17** (49.4 mg, 69%) as a white solid; mp 178–179 °C; ν_{max}($CHCl_3$)/cm^{-1} 3699, 3273, 2927, 2853, 1716, 1602; δ_H (250 MHz, CD_3OD) 7.95 (1H, dd, *J* 7.6, 1.2, ArH), 7.47 (1H, td, *J* 7.5, 1.4, ArH), 7.35–7.26 (2H, m, 2 × ArH), 3.57 (2H, t, *J* 6.9, NCH_2CH_2), 3.23 (2H, t, *J* 6.9, NCH_2CH_2); δ_C (67.8 MHz, CD_3OD) 171.1 (CO_2H), 159.2 (CON, q, *J* 37), 141.8 (C), 133.5 (CH), 133.1 (CH), 132.5 (CH), 131.8 (s), 128.1 (CH), 117.8 (CF_3, q, *J* 287), 42.5 (CH_2), 34.5 (CH_2); *m*/*z* (EI) 261.0590 (M^+. $C_{11}H_{10}F_3NO_3$ requires 261.0612) (Found C, 50.6; H, 3.85; N, 5.35. $C_{11}H_{10}F_3NO_3$ requires C, 50.6; H, 3.9; N, 5.4%).

[2-(*N*-Trifluoroacetylamino)ethyl]diazoacetophenone 18. Following the general procedure, the acid chloride was prepared by the reaction of the *N*-protected amino acid **17** (0.39 g, 1.5 mmol) with oxalyl chloride (0.65 cm^3, 7.5 mmol) and dry dimethylformamide (five drops) in dry dichloromethane (20 cm^3) at 0 °C for 35 min and then at room temperature for 2 h 10 min. The acid chloride was dissolved in dry dichloromethane (10 cm^3) and added to a solution of diazomethane (~9 mmol) in diethyl ether (30 cm^3) at 0 °C, and the mixture was stirred at 0 °C for 1 h 30 min and at room temperature for 2 h. The remaining diazomethane was consumed with glacial acetic acid (1.00 cm^3, 17.5 mmol). Purification by flash column chromatography on silica gel (diethyl ether–hexane, 2 : 1) afforded the *α-diazo ketone* **18** (0.35 g, 82%) as a yellow solid; mp 85–87 °C; ν_{max}($CHCl_3$)/cm^{-1} 3242, 2108, 1714, 1614, 1558; δ_H (250 MHz, $CDC1_3$) 9.02 (1H, br s, NH), 7.39–7.16 (4H, m, 4 × ArH), 5.66 (1H, br s, CHN_2), 3.55–3.47 (2H, m, NCH_2CH_2), 2.95–2.89 (2H, m, NCH_2CH_2); δ_C (67.8 MHz, $CDCl_3$) 191.0 (CO), 157.4 (CON, q, $^2J_{FC}$ 37), 137.3 (C), 137.2 (C), 131.7 (CH), 131.1 (CH), 127.3 (CH), 126.8 (d), 115.8 (CF_3, q, $^1J_{FC}$ 288), 57.6 (CH), 42.1 (CH_2), 30.5 (CH_2); *m*/*z* (EI) 257.0664 ($M^+ - N_2$. $C_{12}H_{10}F_3NO_2$ requires 257.0664).

5,6-Dihydro-[1,2,3]triazolo[5,1-*a*]isoquinoline 19. The α-diazo ketone **18** (100 mg, 0.351 mmol) was dissolved in a saturated aqueous solution of barium hydroxide (3.70 cm^3). The solution was stirred at room temperature for 18 min and then extracted with ethyl acetate (3 × 7 cm^3). The combined organic extracts were dried over anhydrous potassium carbonate and the solvent removed *in vacuo*. The residue and potassium carbonate (145 mg, 1.05 mmol) were suspended in dry tetrahydrofuran (5 ml) and allyl bromide (0.11 cm^3, 1.3 mmol) was added in one portion. The resulting suspension was stirred at room temperature for 18 h and the solvent was then removed *in vacuo*. The residue was diluted with water (10 cm^3) and extracted with diethyl ether (3 × 10 cm^3), and the combined organic extracts were then dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* and the residue was purified by flash column chromatography on silica gel (diethyl ether–hexane, 3 : 1) to give the *triazole* **19** (34.1 mg, 57%) as a colourless solid; mp 102–104 °C; ν_{max}($CHCl_3$)/cm^{-1} 2993, 2952, 2841, 1651, 985, 908, 830; δ_H (250 MHz, $CDCl_3$) 7.96 (1H, s, NCH=C), 7.61–7.55 (1H, m, ArH), 7.40–7.32 (3H, m, 3 × ArH), 4.61 (2H, t, *J* 7.0, NCH_2CH_2), 3.25 (2H, t, *J* 7.0, NCH_2CH_2); δ_C (67.8 MHz, $CDCl_3$) 133.6 (C), 131.8 (C), 129.1 (CH), 128.3 (CH), 128.3 (CH), 127.7 (CH), 124.4 (CH), 124.1 (C), 44.4 (CH_2), 28.5 (CH_2); *m*/*z* (EI) 171.0790 (M^+. $C_{10}H_9N_3$ requires 171.0797).

General procedure for carbenoid generation, ylide formation and rearrangement

A solution of the α-diazo ketone in dry solvent was added dropwise from a pressure-equalising addition funnel through the condenser to a solution of the appropriate copper(II) or rhodium(II) complex in the same solvent at reflux. The resulting solution was stirred at reflux and the solvent was then removed *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the rearrangement product.

2-Allyl-1-methylpyrrolidin-3-one 20. According to the general procedure, a solution of the α-diazo ketone **2a** (177 mg, 1.06 mmol) in dry benzene (80 cm^3) was added to a solution of $Cu(acac)_2$ (5.2 mg, 0.020 mmol) in dry benzene (20 cm^3) at reflux, over a period of 2 h 55 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (diethyl ether) gave the pyrrolidin-3-one **20** (107 mg, 73%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **2a** (83.8 mg, 0.501 mmol) in dry benzene (40 cm^3) was added to a solution of $Rh_2(OAc)_4$ (4.5 mg, 0.010 mmol) in dry benzene (20 cm^3) at reflux, over a period of 52 min. The resulting solution was stirred at reflux for a further 8 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *pyrrolidinone* **20** (40.3 mg, 58%) as a colourless liquid; ν_{max}(film)/cm^{-1} (liquid film) 3077, 2944, 2844, 2785, 1757, 1642, 996, 916; δ_H (250 MHz, $CDCl_3$) 5.75 (1H, dddd, *J* 17.1, 10.1, 7.0, 7.0, *trans* C*H*=CH_2), 5.16–5.05 (1H, m, *cis* CH=CH_2), 5.09–5.02 (1H, m, CH=CH_2), 3.38–3.31 (1H, m, 1 × NCH_2), 2.54–2.31 (6H, m, 1 × NCH_2, NCHCO, CH_2CO and CH_2CH=CH_2), 2.45 (3H, s, CH_3); δ_C (67.8 MHz, $CDCl_3$) 214.9 (CO), 134.1 (CH), 117.1 (CH_2), 71.2 (CH), 51.9 (CH_2), 41.4 (CH_3), 37.1 (CH_2), 32.7 (CH_2); *m*/*z* (EI) 139.1004 (M^+. $C_8H_{13}NO$ requires 139.0997).

1,2-Diallylpyrrolidin-3-one 21. According to the general procedure, a solution of the α-diazo ketone **2b** (70.0 mg, 0.362 mmol) in dry dichloromethane (20 cm^3) was added to a solution of $Cu(acac)_2$ (5.2 mg, 0.020 mmol) in dry dichloromethane (20 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 14 h. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *pyrrolidinone* **21** (18.0 mg, 30%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **2b** (194 mg, 1.00 mmol) in dry tetrahydrofuran (80 cm^3) was added to a solution of $Cu(acac)_2$ (5.2 mg, 0.020 mmol) in dry tetrahydrofuran (40 cm^3) at reflux, over a period of 2 h 15 min. The resulting solution was stirred at reflux for a further 12 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the pyrrolidin-3-one **21** (115 mg, 70%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **2b** (186 mg, 0.960 mmol) in dry benzene (80 cm^3) was added to a solution of $Cu(acac)_2$ (5.2 mg, 0.020 mmol) in dry benzene (40 cm^3) at reflux, over a period of 2 h 15 min. The resulting solution was stirred at reflux for a further 20 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 1 : 1) gave the *pyrrolidinone* **21** (120 mg, 76%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **2b** (194 mg, 1.00 mmol) in dry dichloromethane (80 cm^3) was added to a solution of $Rh_2(OAc)_4$ (8.5 mg, 0.019 mmol) in dry dichloromethane (40 cm^3) at room temperature, over a period of 1 h 55 min. The resulting solution was stirred at room temperature for a further 1 h 30 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *pyrrolidinone* **21** (86.0 mg, 52%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **2b** (196 mg, 1.02 mmol) in dry tetrahydrofuran (80 cm^3) was added to a solution of $Rh_2(OAc)_4$ (8.8 mg, 0.020 mmol) in dry tetrahydrofuran (40 cm^3) at room temperature, over a period of 2 h 15 min. The resulting solution was stirred at room temperature for a further 30 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *pyrrolidinone* **21** (105 mg, 63%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **2b** (197 mg, 1.02 mmol) in dry benzene (80 cm^3) was added to a solution of $Rh_2(OAc)_4$ (8.8 mg, 0.020 mmol) in dry benzene (40 cm^3) at room temperature, over a period of 2 h. The resulting solution was stirred at room temperature for a further 30 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *pyrrolidinone* **21** (118 mg, 70%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **2b** (98.0 mg, 0.507 mmol) in dry dichloromethane (20 cm^3) was added to a solution of $Rh_2(OAc)_4$ (4.4 mg, 0.010 mmol) in dry dichloromethane (20 cm^3) at reflux, over a period of 2 h. The resulting solution was stirred at reflux for a further 5 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 1 : 1) gave the *pyrrolidinone* **21** (39.8 mg, 47%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **2b** (191 mg, 0.988 mmol) in dry tetrahydrofuran (80 cm^3) was added to a solution of $Rh_2(OAc)_4$ (8.8 mg, 0.020 mmol) in dry tetrahydrofuran (40 cm^3) at reflux, over a period of 2 h 45 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *pyrrolidinone* **21** (111 mg, 68%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **2b** (195 mg, 1.01 mmol) in dry benzene (80 cm^3) was added to a solution of $Rh_2(OAc)_4$ (8.8 mg, 0.020 mmol) in dry benzene (40 cm^3) at reflux, over a period of 1 h 55 min. The resulting solution was stirred at reflux for a further 45 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *pyrrolidinone* **21** (117 mg, 70%) as a colourless liquid; ν_{max}(film)/cm^{-1} 3078, 2979, 2917, 2799, 1757, 1642, 996, 919; δ_H (250 MHz, $CDCl_3$) 5.91 (1H, dddd, *J* 17.1, 10.1, 7.8, 5.4, NCH_2C*H*=CH_2), 5.77 (1H, dddd, *J* 17.1, 10.1, 7.0, 7.0, $CHCH_2C$*H*=CH_2), 5.31–5.02 (4H, m, NCH_2CH=CH_2 and $CHCH_2CH$=CH_2), 3.57 (1H, ddt, *J* 13.5, 5.4, 1.5, 1 × NCH_2CH=CH_2), 3.39–3.32 (1H, m, 1 × NCH_2CH_2), 2.95 (1H, ddd, *J* 13.5, 7.8, 0.7, 1 × NCH_2-CH=CH_2), 2.60 (1H, t, *J* 4.7, NCHCO), 2.51–2.28 (5H, m, 1 × NCH_2CH_2, CH_2CO and NCHCH_2); δ_C (100 MHz, $CDCl_3$) 215.1 (CO), 134.3 (CH), 134.1 (CH), 118.2 (CH_2), 117.2 (CH_2), 69.0 (CH), 57.2 (CH_2), 48.8 (CH_2), 36.9 (CH_2), 33.1 (CH_2); *m*/*z* (FAB) 166.1236 (M^+ + H. $C_{10}H_{16}NO$ requires 166.1232).

1,2-Diallylpiperidin-3-one 22. According to the general procedure, a solution of the α-diazo ketone **9** (73.0 mg, 0.352 mmol) in dry benzene (35 cm^3) was added to a solution of $Cu(acac)_2$ (2.0 mg, 0.0076 mmol) in dry benzene (5 cm^3) at reflux, over a period of 40 min. The resulting solution was stirred at reflux for a further 20 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *piperidinone* **22** (49.7 mg, 79%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **9** (99.6 mg, 0.481 mmol) in dry benzene (48 cm^3) was added to a solution of $Cu(hfacac)_2$ (4.8 mg, 0.097 mmol) in dry benzene (5 cm^3) at reflux, over a period of 50 min. The resulting solution was stirred at reflux for a further 10 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *piperidinone* **22** (63.3 mg, 73%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **9** (104 mg, 0.500 mmol) in dry benzene (45 cm^3) was added to a solution of $Rh_2(OAc)_4$ (4.3 mg, 0.0097 mmol) in dry benzene (5 cm^3) at reflux, over a period of 42 min. The resulting solution was stirred at reflux for a further 18 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *piperidinone* **22** (66.0 mg, 74%) as a colourless liquid; ν_{max}(film)/cm^{-1} 3077, 3007, 2946, 2868, 2811, 1718, 1642, 996, 919; δ_H (250 MHz, $CDCl_3$) 5.90–5.65 (2H, m, $NCH_2CH{=}CH_2$ and $CHCH_2CH{=}CH_2$), 5.26–5.14 (2H, m, $NCH_2CH{=}CH_2$), 5.13–5.01 (2H, m, $CHCH_2CH{=}CH_2$), 3.29 (1H, ddt, *J* 13.9, 6.2, 1.3, 1 × $NCH_2CH{=}CH_2$), 3.21–2.99 (3H, m, 1 × $NCH_2CH{=}CH_2$, NCHCO and 1 × NCH_2CH_2), 2.73–2.27 (5H, m, 1 × NCH_2CH_2, CH_2CO, $CHCH_2CH{=}CH_2$), 2.04–1.25 (2H, m, NCH_2CH_2); δ_C (67.8 MHz, $CDCl_3$) 209.6 (CO), 134.6 (CH), 134.3 (CH), 117.9 (CH_2), 116.8 (CH_2), 69.8 (CH), 56.1 (CH_2), 47.0 (CH_2), 38.0 (CH_2), 31.1 (CH_2), 24.0 (CH_2); *m*/*z* (EI) 179.1329 (M^+. $C_{11}H_{17}NO$ requires 179.1310).

2-Allyl-1-methylhexahydroazepin-3-one 23. According to the general procedure, a solution of the α-diazo ketone **11** (196 mg, 1.00 mmol) in dry benzene (50 cm^3) was added to a solution of $Cu(acac)_2$ (5.7 mg, 0.022 mmol) in dry benzene (5 cm^3) at reflux, over a period of 48 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 3 : 1) gave the *azepinone* **23** (140 mg, 84%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **11** (93.0 mg, 0.476 mmol) in dry benzene (43 cm^3) was added to a solution of $Cu(hfacac)_2$ (4.8 mg, 0.0097 mmol) in dry benzene (5 cm^3) at reflux, over a period of 41 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 1 : 1) gave the *azepinone* **23** (46.5 mg, 58%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **11** (45.9 mg, 0.235 mmol) in dry benzene (20 cm^3) was added to a solution of $Rh_2(OAc)_4$ (2.1 mg, 0.0048 mmol) in dry benzene (4 cm^3) at reflux, over a period of 20 min. The resulting solution was stirred at reflux for a further 10 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 2 : 1) gave the *azepinone* **23** (22.2 mg, 56%) as a colourless liquid; ν_{max}(film)/cm^{-1} 3075, 2931, 2849, 2799, 1698, 1640, 997, 913; δ_H (250 MHz, $CDCl_3$) 5.79 (1H, m, dddd, *J* 17.1, 10.1, 6.9, 6.9, $CH{=}CH_2$), 5.07–5.04 (1H, m, *trans* $CH{=}CH_2$),5.01–4.94 (1H, m, *cis* $CH{=}CH_2$), 3.30 (1H, t, *J* 7.0, NCHCO), 3.08–2.96 (1H, m, 1 × NCH_2), 2.83–2.71 (1H, m, 1 × NCH_2), 2.56–2.20 (4H, m, $NCHCH_2$ and CH_2CO), 2.29 (3H, s, NCH_3), 1.83–1.56 (4H, m, NCH_2CH_2 and CH_2CH_2CO); δ_C (67.8 MHz, $CDCl_3$) 212.9 (CO), 135.5 (CH), 116.3 (CH_2), 71.5 (CH), 57.4 (CH_2), 43.0 (CH_2), 37.6 (CH_3), 33.1 (CH_2), 26.7 (CH_2), 23.5 (CH_2); *m*/*z* (EI) 167.1293 (M^+. $C_{10}H_{17}NO$ requires 167.1310) (Found C, 72.1; H, 10.6; N, 8.4. $C_{10}H_{17}NO$ requires C, 71.8; H, 10.2; N, 8.4%).

1,2-Diallyloctahydroazocin-3-one 24. According to the general procedure, a solution of the α-diazo ketone **12** (158 mg, 0.673 mmol) in dry benzene (60 cm^3) was added to a solution of $Cu(acac)_2$ (3.5 mg, 0.013 mmol) in dry benzene (7 cm^3) at reflux, over a period of 52 min. The resulting solution was stirred at reflux for a further 10 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 3 : 1) gave the *azocinone* **24** (54.4 mg, 39%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **12** (159 mg, 0.676 mmol) in dry benzene (60 cm^3) was added to a solution of $Cu(hfacac)_2$ (6.6 mg, 0.013 mmol) in dry benzene (7 cm^3) at reflux, over a period of 50 min. The resulting solution was stirred at reflux for a further 10 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 1 : 1) gave the *azocinone* **24** (18.5 mg, 13%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **12** (160 mg, 0.678 mmol) in dry benzene (60 cm^3) was added to a solution of $Rh_2(OAc)_4$ (6.8 mg, 0.015 mmol) in dry benzene (9 cm^3) at reflux, over a period of 58 min. The resulting solution was stirred at reflux for a further 10 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 1 : 1) gave the *azocinone* **24** (7.7 mg, 5%) as a colourless liquid; ν_{max}(film)/cm^{-1} 3076, 3025, 2927, 2859, 2820, 1708, 1640, 996, 915; δ_H (250 MHz, $CDCl_3$) 6.03–5.83 (2H, m, $NCH_2CH{=}CH_2$ and $CHCH_2CH{=}CH_2$), 5.24–4.95 (4H, m, $NCH_2CH{=}CH_2$ and $CHCH_2CH{=}CH_2$), 3.40–3.12 (4H, m, NCHCO, $NCH_2CH{=}CH_2$ and 1 × CH_2CO), 2.75 (1H, ddd, *J* 12.6, 4.1, 2.9, 1 × NCH_2CH_2), 2.63–2.37 (2H, m, 1 × NCH_2CH_2 and 1 × $CHCH_2CH{=}CH_2$), 2.33–2.20 (1H, m, 1 × $CHCH_2CH{=}CH_2$), 2.12–2.03 (1H, m, 1 × CH_2CO), 1.98–1.89 (1H, m, 1 × CH_2CH_2CO), 1.85–1.38 (4H, m, 1 × CH_2CH_2CO, NCH_2CH_2 and 1 × $NCH_2CH_2CH_2$), 1.02–0.86 (1H, m, 1 × $NCH_2CH_2CH_2$); δ_C (67.8 MHz, $CDCl_3$) 218.7 (CO), 137.4 (CH), 136.6 (CH), 117.6 (CH_2), 115.8 (CH_2), 70.2 (CH), 60.2 (CH_2), 51.9 (CH_2), 38.9 (CH_2), 30.9 (CH_2), 27.6 (CH_2), 26.6 (CH_2), 26.1 (CH_2); *m*/*z* (EI) 207.1623 (M^+. $C_{13}H_{21}NO$ requires 207.1623).

1-Diazopent-3-en-2-one 26. *n*-Butyllithium (7.25 cm^3 of 1.60 M solution in hexane, 11.6 mmol) was rapidly added to a solution of hexamethyldisilylamine (1.87 g, 11.6 mmol) at 0 °C. The mixture was stirred at 0 °C for 30 min and then cooled to −78 °C. A solution of pent-3-en-2-one (0.88 g, 10 mmol) was added dropwise over a period of 30 min and the mixture was stirred for 1 h. 2,2,2-Trifluoroethyl trifluoroacetate (2.47 g, 12.7 mmol) was added in one portion and the mixture was stirred for 30 min then poured into a separatory funnel containing a mixture of 5% hydrochloric acid (100 cm^3) and diethyl ether (75 cm^3). The aqueous phase was extracted with diethyl ether (2 × 75 cm^3) and the combined organic extracts were dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was dissolved in acetonitrile (30 cm^3), and water (1.8 cm^3) and triethylamine (2.0 cm^3, 14.3 mmol) were added. This was followed by the addition of a solution of methanesulfonyl azide (1.85 g, 15.3 mmol) in acetonitrile (30 cm^3) over a period of 30 min. The mixture was stirred at room temperature for 4 h and then concentrated (~30 cm^3), and diluted with diethyl ether (75 cm^3), then washed with a 10% aqueous solution of sodium hydroxide (2 × 100 cm^3) and brine (100 cm^3). The organic phase was dried over anhydrous magnesium sulfate and then concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (diethyl ether–hexane, 2 : 1) to give the *α-diazo ketone* **26** (0.89 g, 77%) as a yellow liquid; ν_{max}(film)/cm^{-1} 3081, 2970, 2941, 2914, 2850, 2105, 1657, 1604, 966, 917; δ_H (250 MHz, $CDCl_3$) 6.82 (1H, dq, *J* 15.3, 6.9, $CHCH_3$), 6.03 (1H, dd, *J* 15.3, 1.6, CHCO), 5.43 (1H, s, CHN_2), 1.88 (3H, dd, *J* 6.9, 1.6, CH_3CH); δ_C (67.8 MHz, $CDCl_3$) 184.4 (CO), 139.7 (CH), 128.5 (CH), 54.5 (CH), 17.5 (CH_3).

1-Diazo-4-(*N*-allyl-*N*-methylamino)pentan-2-one 27. *N*-Methylallylamine (1.32 g, 18.6 mmol) was added to a solution of the α-diazo ketone **26** (1.0 g, 9.1 mmol) in dry diethyl ether (30 cm^3) and the mixture stirred at room temperature for 48 h. The solvent was removed *in vacuo* and the residue purified by flash column chromatography on silica gel (diethyl ether) to give the *amine* **27** (1.4 g, 85%) as a yellow liquid; ν_{max}(film)/cm^{-1} 3078, 2969, 2876, 2846, 2791, 2104, 1637, 997, 965, 919; δ_H (250 MHz, $CDCl_3$) δ 5.77 (1H, dddd, *J* 16.9, 10.4, 6.3, 6.3, $CH{=}CH_2$), 5.32 (1H, br s, CHN_2), 5.17–5.03 (2H, m, $CH{=}CH_2$), 3.25–3.17 (1H, m, CH_3CH), 2.97 (2H, d, *J* 6.3, $CH_2CH{=}CH_2$), 2.56–2.48 (1H, m, 1 × CH_2CO), 2.20–2.13 (1H, m, 1 × CH_2CO), 2.13 (3H, s, CH_3N), 0.98 (3H, d, *J* 6.6, CH_3CH); δ_C (67.8 MHz, $CDCl_3$) 194.0 (CO), 136.3 (CH), 116.8 (CH_2), 56.7 (CH_2), 54.8 (CH), 54.8 (CH), 44.2 (CH_2), 36.2 (CH_3), 14.4 (CH_3); *m*/*z* (CI, CH_4)

182.1297 (M^+ + H. $C_9H_{16}N_3O$ requires 182.1293), 182 (M^+ + H, 85%), 181 (M^+, 5%), 153 (14), 140 (5), 111 (19), 70 (38).

4-Diallylamino-1-diazopentan-2-one 28. Diallylamine (3.6 g, 37 mmol) was added to a solution of the α-diazo ketone **26** (1.0 g, 9.1 mmol) in dry diethyl ether (30 cm^3) and the mixture stirred at room temperature for 48 h. The solvent was removed *in vacuo* and the residue purified by flash column chromatography on silica gel (diethyl ether–petroleum ether 40–60, 2 : 1) to give the *amine* **28** (1.2 g, 64%) as a yellow liquid; ν_{max}(film)/cm^{-1} 3078, 3006, 2968, 2930, 2809, 2101, 1640, 993, 965, 919; δ_H (250 MHz, $CDCl_3$) 5.80 (2H, dddd, *J* 17.1, 10.3, 6.7, 5.6, 2 × C*H*=CH_2), 5.30 (1H, br s, CHN_2), 5.18 (2H, dd, *J* 17.1, 1.6, 2 × *trans* CH=C*H*$_2$), 5.13–5.08 (2H, m, 2 × *cis* CH=C*H*$_2$), 3.37 (1H, m, CH_3CH), 3.10 (2H, dd, *J* 14.3, 5.6, 2 × C*H*$_A$H$_B$CH=CH_2), 2.98 (2H, dd, *J* 14.3, 6.7, 2 × CH_AH_BCH=CH_2), 2.56 (1H, dd, *J* 13.8, 6.6, 1 × CH_2CO), 2.2 (1H, dd, *J* 13.8, 7.5, 1 × CH_2CO), 1.0 (3H, d, *J* 6.7, CH_3); δ_C (67.8 MHz, $CDCl_3$) 194.0 (CO), 136.8 (CH), 116.6 (CH_2), 54.8 (CH), 52.4 (CH_2), 51.8 (CH), 44.9 (CH_2), 14.6 (CH_3); *m*/*z* (EI) 179.1318 ($M^+ - N_2$. $C_{11}H_{17}NO$ requires 179.1310).

4-Aminopentanoic acid 30. 5-Methylpyrrolidin-2-one **29** (5.0 g, 50 mmol) was dissolved in 6 M hydrochloric acid and the mixture heated at reflux for 8 h. The mixture was then concentrated *in vacuo* and the residue was purified by flash column chromatography on Amberlite® IR 120B (120 mL), which was washed with water and eluted with 2 M ammonium hydroxide. The ninhydrin-positive fractions were collected and concentrated *in vacuo* to give a colourless solid, which was purified by recrystallisation (methanol) to give the *amino acid* **30** (4.5 g, 76%) as colourless prisms; mp 216–218 °C [lit.,[15] 212 °C]. ν_{max}(KBr)/cm^{-1} 3048, 2975, 1642; δ_H (250 MHz, CD_3OD) 3.37–3.24 (1H, m, CH_3CH), 2.28–2.21 (2H, m, CH_2CO), 1.95–1.66 (2H, m, C*H*$_2$CH$_2$CO), 1.24 (3H, d, *J* 6.7, CH_3); δ_C (67.8, CD_3OD) 182.5 (CO_2H), 48.6 (CH), 34.4 (CH_2), 31.5 (CH_2), 18.4 (CH_3); *m*/*z* (EI) 117.0790 (M^+. $C_5H_{11}NO_2$ requires 117.0785), 117 (M^+, 2%), 102 (14), 101 (0.3), 73 (0.8), 44 (100).

4-(Trifluoroacetylamino)pentanoic acid 31. Following the general protection procedure, 4-aminopentanoic acid **30** (4.0 g, 34 mmol) was treated with ethyl trifluoroacetate (9.7 g, 68 mmol) and triethylamine (3.5 g, 35 mmol) in dry methanol (20 cm^3), and the resulting solution was stirred at room temperature for 18 h. The crude product was diluted with 2 M hydrochloric acid (100 cm^3) and extracted with diethyl ether (3 × 100 cm^3). After the addition of sodium chloride, the aqueous layer was extracted with diethyl ether (100 cm^3). The product was purified by recrystallisation (diethyl ether–hexane) to give the *protected amino acid* **31** (6.5 g, 89%) as a white solid; mp 101–103 °C; ν_{max}(KBr)/cm^{-1} 3301, 1692; δ_H (250 MHz, CD_3OD) 4.05–3.95 (1H, m, CH_3CH), 2.33 (2H, t, *J* 7.5, C*H*$_2$CO$_2$H), 1.92–1.74 (2H, m, C*H*$_2$CH$_2$CO$_2$H), 1.21 (3H, d, *J* 6.7, C*H*$_3$CH); δ_C (67.8 MHz, CD_3OD), 177.8 (CO_2H), 159.6 (CON, q, $^2J_{FC}$ 37), 118.6 (CF_3, q, $^1J_{FC}$ 287), 48.1 (CH), 32.9 (CH_2), 32.6 (CH_2), 21.3 (CH_3); *m*/*z* (EI) 213.0610 (M^+. $C_7H_{10}NO_3F_3$ requires 213.0613), 213 (M^+, 3%), 195 (13), 180 (4), 154 (10), 140 (100) (Found C, 39.4; H, 4.7; N, 6.4. $C_7H_{10}F_3NO_3$ requires C, 39.4; H, 4.7; N, 6.6%).

1-Diazo-5-[*N*-(trifluoroacetyl)amino]hexan-2-one 32. Following the general procedure, the acid chloride was prepared by the reaction of the *N*-protected amino acid **31** (2.1 g, 9.9 mmol) with oxalyl chloride (6.0 g, 47 mmol) and dry dimethylformamide (two drops) in dry dichloromethane (50 cm^3) at 0 °C. The mixture was warmed to room temperature and stirred for 3 h. The acid chloride was dissolved in dry dichloromethane (20 cm^3) and added to a solution of diazomethane (~33 mmol) in diethyl ether (100 cm^3) at 0 °C, and the mixture was allowed to warm to room temperature over 2 h. The remaining diazomethane was consumed with glacial acetic acid (2.80 cm^3, 48.9 mmol). Purification by flash column chromatography on silica gel (diethyl ether–hexane, 2 : 1) afforded the *α-diazo ketone* **32** (1.6 g, 68%) as a yellow solid; mp 80–81 °C; ν_{max}($CHCl_3$)/cm^{-1} 2934, 2111, 1716, 1633; δ_H (250 MHz, $CDCl_3$) 7.53 (1H, br s, NH), 5.37 (1H, br s, CHN_2), 4.06–3.92 (1H, m, CH_3CH), 2.52–2.32 (2H, m, CH_2CO), 2.00–1.78 (2H, m, C*H*$_2$CH$_2$CO), 1.25 (3H, d, *J* 6.6, C*H*$_3$CH); δ_C (67.8 MHz, $CDCl_3$) 194.8 (CO), 156.8 (CON, q, $^2J_{FC}$ 37), 115.8 (CF_3, q, $^1J_{FC}$ 288), 55.1 (CH), 46.4 (CH), 36.8 (CH_2), 30.2 (CH_2), 20.1 (CH_3); *m*/*z* (FAB) 238.0804 (M^+ + H. $C_8H_{11}F_3N_3O_2$ requires 238.0803), 238 (M^+ + H, 100%), 210 (12), 154 (36).

5-(*N*,*N*-Diallylamino)-1-diazohexan-2-one 33. The α-diazo ketone **32** (1.2 g, 5.1 mmol) was dissolved in a saturated aqueous solution of barium hydroxide (20 cm^3) and the mixture stirred at room temperature for 1 h. The solution was then extracted with ethyl acetate (2 × 50 cm^3) and the aqueous phase was evaporated to dryness *in vacuo*. The residue washed with ethyl acetate (2 × 30 cm^3) and the combined organic extracts were dried over anhydrous potassium carbonate then concentrated *in vacuo*. The residue was dissolved in dry tetrahydrofuran (30 cm^3), potassium carbonate (1.8 g, 13 mmol) and allyl bromide (1.57 g, 13.0 mmol) were added, and the mixture was stirred at room temperature for 24 h. The solvent was removed *in vacuo* and the residue diluted with a saturated aqueous solution of sodium bicarbonate (30 cm^3) and extracted with ethyl acetate (3 × 30 cm^3). The combined organic extracts were dried over anhydrous potassium carbonate and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (diethyl ether–hexane, 2 : 1) to give the *amine* **33** (0.35 g, 31%) as a yellow liquid; ν_{max}(film)/cm^{-1} 3077, 3005, 2962, 2930, 2809, 2101, 1641, 993, 965, 916; δ_H (250 MHz, $CDCl_3$) 5.76 (2H, dddd, *J* 17.2, 10.0, 7.4, 4.8, C*H*=CH_2), 5.30 (1H, br s, CHN_2), 5.23–5.04 (4H, m, CH=C*H*$_2$), 3.21–3.12 (2H, m, C*H*$_A$H$_B$CH=CH_2), 2.88–2.72 (3H, m, CH_3CH and 2 × CH_AH_BCH=CH_2), 2.46–2.39 (2H, m, CH_2CO), 1.83–1.55 (2H, m, C*H*$_2$CH$_2$CO), 0.91 (3H, d, *J* 6.5, C*H*$_3$CH); δ_C (67.8 MHz, $CDCl_3$) 196.0 (CO), 137.9 (C), 116.7 (CH_2), 54.0 (CH), 53.6 (CH), 52.6 (CH_2), 38.8 (CH_2), 29.8 (CH_2), 13.7 (CH_3); *m*/*z* (FAB) 222.1604 (M^+ + H. $C_{12}H_{20}N_3O$ requires 222.1606), 222 (M^+ + H, 23%), 193 (2), 180 (5), 152 (8).

2-Allyl-1,5-dimethylpyrrolidin-3-one 34a–b. According to the general procedure, a solution of the α-diazo ketone **27** (0.18 g, 0.99 mmol) in dry benzene (70 cm^3) was added to a solution of $Cu(acac)_2$ (5.2 mg, 0.020 mmol) in dry benzene (30 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Analysis of the crude reaction mixture by ^{1}H NMR indicated a 1 : 1 mixture of diastereoisomers. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 5 : 1) gave a mixture of the *pyrrolidinones* **34a**–**b** (106 mg, 70%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **27** (0.18 g, 0.99 mmol) in dry benzene (70 cm^3) was added to a solution of $Rh_2(OAc)_4$ (8.8 mg, 0.020 mmol) in dry benzene (30 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Analysis of the crude reaction mixture by ^{1}H NMR indicated a 1 : 1 mixture of diastereoisomers. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 5 : 1) an inseparable mixture (1 : 1) of the *pyrrolidinones* **34a**–**b** (95 mg, 62%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **27** (0.18 g, 0.99 mmol) in dry benzene (70 cm^3) was added to a solution of $Cu(hfacac)_2$ (9.9 mg, 0.020 mmol) in dry benzene (30 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel

(hexane–diethyl ether, 5 : 1) gave a mixture (1 : 1) of the *pyrrolidinones* **34a**–**b** (38 mg, 25%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **27** (0.18 g, 0.99 mmol) in dry benzene (70 cm^3) was added to a solution of copper(II) trifluoroacetylacetonate [Cu(tfacac)$_2$] (5.7 mg, 0.015 mmol) in dry benzene (30 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Analysis of the crude reaction mixture by ^{1}H NMR indicated a 1 : 1.7 mixture of diastereoisomers. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 5 : 1) gave a mixture (1 : 1) of the *pyrrolidinones* **34a**–**b** (53 mg, 35%) as a colourless liquid.

The mixture of isomers was converted into a single isomer by dissolution in diethyl ether (25 mL per mmol) and addition of silica gel (1 g per mmol) followed by stirring at room temperature for 24–48 h. Data for product obtained after epimerisation: ν_{max}(film)/cm^{-1} 3077, 2971, 1756, 1641, 998, 915; δ_H (250 MHz, $CDCl_3$) δ 5.81 (1H, dddd, *J* 17.1, 10.3, 6.9, 6.9, C*H*=CH_2), 5.14–5.00 (2H, m, CH=CH_2), 2.61–2.41 (5H, m, 1 × CH_2CO, CH_3CH, NC*H*CO, CH_2CH=CH_2), 1.95 (1H, dd, *J* 17.8, 10.6, 1 × CH_2CO), 1.26 (3H, d, *J* 5.8, CH_3CH); δ_C (67.8 MHz, $CDCl_3$) δ 214.4 (CO), 134.5 (CH), 116.8 (CH_2), 72.8 (CH), 57.6 (CH), 45.0 (CH_2), 38.5 (CH_3), 33.4 (CH_2), 18.5 (CH_3); *m*/*z* (EI) 153.1152 (M^+. $C_9H_{15}NO$ requires 153.1154), 153 (M^+, 1%), 112 (100).

1,2-Diallyl-5-methylpyrrolidin-3-one 35a–b. According to the general procedure, a solution of the α-diazo ketone **28** (0.10 g, 0.48 mmol) in dry benzene (50 cm^3) was added to a solution of Cu(acac)$_2$ (2.6 mg, 0.010 mmol) in dry benzene (10 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 5 : 1) gave a mixture (1.7 : 1) of the *pyrrolidinones* **35a**–**b** (73 mg, 84%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **28** (0.10 g, 0.48 mmol) in dry benzene (50 cm^3) was added to a solution of $Rh_2(OAc)_4$ (4.4 mg, 0.010 mmol) in dry benzene (10 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 5 : 1) gave a mixture (2 : 1) of the *pyrrolidinones* **35a**–**b** (72 mg, 83%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **28** (0.10 g, 0.48 mmol) in dry benzene (50 cm^3) was added to a solution of Cu(hfacac)$_2$ (5 mg, 0.01 mmol) in dry benzene (10 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 5 : 1) gave a mixture (1.5 : 1) of the *pyrrolidinones* **35a**–**b** (63 mg, 73%) as a colourless liquid.

A solution of the pyrrolidinones **35a**–**b** (0.20 g, 1.1 mmol) and silica gel (1 g) in diethyl ether (25 cm^3) was stirred at room temperature for 24 h. The mixture was then filtered and the solution concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give a mixture (8 : 1) of the *pyrrolidinones* **35a**–**b** (0.18 g, 90%) as a colourless liquid. Data for major isomer after epimerisation: ν_{max}(film)/cm^{-1} 3075, 2972, 2929, 2812, 1755, 1640, 997, 918; δ_H (250 MHz, $CDCl_3$) 6.00–5.72 (2H, m, NCH_2CH=CH_2 and $CHCH_2CH$=CH_2), 5.33–5.01 (4H, m, NCH_2CH=CH_2 and $CHCH_2CH$=CH_2), 3.43–3.40 (2H, m, CH_3CH and NCHCO), 3.01–2.89 (2H, m, NCH_2CH=CH_2), 2.49–2.39 (3H, m, CHCH_2CH=CH_2 and 1 × CH_2CO), 1.92 (1H, dd, *J* 17.9, 10.7, CH_2CO), 1.25 (3H, d, *J* 6.0, CH_3CH).

1,2-Diallyl-6-methylpiperidin-3-one 36a–b. According to the general procedure, a solution of the α-diazo ketone **33** (0.19 g, 0.86 mmol) in dry benzene (70 cm^3) was added to a solution of Cu(acac)$_2$ (5.2 mg, 0.020 mmol) in dry benzene (30 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 5 : 1) gave an inseparable mixture (1 : 1) of the *piperidinones* **36a**–**b** (0.12 g, 72%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **31** (0.18 g, 0.81 mmol) in dry benzene (70 cm^3) was added to a solution of $Rh_2(OAc)_4$ (8.8 mg, 0.020 mmol) in dry benzene (30 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 5 : 1) gave an inseparable mixture (1 : 1) of the *piperidinones* **36a**–**b** (0.11 g, 70%) as a colourless liquid.

According to the general procedure, a solution of the α-diazo ketone **33** (0.12 g, 0.54 mmol) in dry benzene (50 cm^3) was added to a solution of Cu(hfacac)$_2$ (5.4 mg, 0.011 mmol) in dry benzene (50 cm^3) at reflux, over a period of 30 min. The resulting solution was stirred at reflux for a further 15 min. Purification by flash column chromatography on silica gel (hexane–diethyl ether, 5 : 1) gave an inseparable mixture (1 : 1) of the *piperidinones* **36a**–**b** (70 mg, 67%) as a colourless liquid.

A solution of the piperidinones **36a**–**b** (0.1 g, 0.5 mmol) and silica gel (1 g) in diethyl ether (20 cm^3) was stirred at room temperature for 24 h. The mixture was then filtered and the solution concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give an inseparable mixture (2 : 1) of the *piperidinones* **36a**–**b** (80 mg, 80%) as a colourless liquid; ν_{max}(film)/cm^{-1} 3076, 2968, 1716, 1641, 996, 917; δ_H (250 MHz, $CDCl_3$) 5.93–5.64 (2H, m, NCHC*H*=CH_2 and $CHCH_2CH$=CH_2), 5.23–5.00 (4H, m, NCH_2CH=CH_2 and $CHCH_2CH$=CH_2), 3.38–2.94 (4H, m, CH_3CH, NCHCO and NCH_2CH=CH_2), 2.55–2.32 (4H, m, CH_2CO and CHCH_2CH=CH_2), 2.19–1.71 (2H, m, NCHCH_2), 1.18 (3H, d, *J* 6.4, CH_3CH minor isomer), 1.15 (3H, d, *J* 6.6, CH_3CH major isomer); δ_C (67.8 MHz, $CDCl_3$) 211.6 (CO), 210.3 (CO), 136.1 (CH), 135.1 (CH), 134.5 (CH), 134.4 (CH), 117.3 (CH_2), 116.9 (CH_2), 116.6 (CH_2), 116.5 (CH_2), 68.8 (CH), 66.5 (CH), 53.5 (CH), 51.7 (CH_2), 50.9 (CH_2), 48.4 (CH), 38.1 (CH_2), 36.4 (CH_2), 34.4 (CH_2), 31.8 (CH_2), 31.2 (CH_2), 30.7 (CH_2), 20.5 (CH_3), 17.9 (CH_3); *m*/*z* (EI) 192.1387 (M^+. $C_{12}H_{18}NO$ requires 192.1388), 192 (M^+, 1%), 152 (100).

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