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SILICON-ASSISTED SYNTHESIS OF BRIDGED AZABICYCLIC SYSTEMS VIA *N*-ACYLIMINIUM INTERMEDIATES

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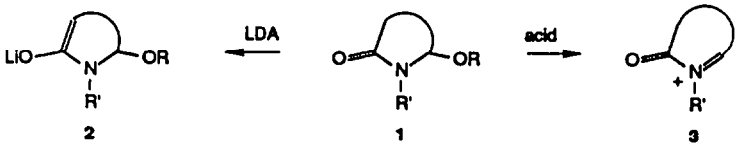
Summary: Intramolecular acid-mediated reactions of 2-propynyl- and allylsilanes with five- and six-membered cyclic *N*-acyliminium ion precursors lead to bridged azabicyclic compounds (Table I). Neat formic acid is the reaction medium of choice in most cases. The cyclization reactions take place with complete regioselectivity. 2-Propynylsilanes are more reactive than allylsilanes. An ordinary olefin reacts poorly. The cyclization products can be useful for the synthesis of γ- and δ-amino acids and derivatives.

INTRODUCTION

Alkoxylactams **1** have been shown to be versatile starting materials for the synthesis of bridged azabicyclic systems (Scheme 1).[1,2] The method used is based on the intrinsic reactivity of **1** as dipolar synthon. Deprotonation using lithium diisopropylamide (LDA) leads to the *nucleophilic* enolate anion **2**, whereas acidic treatment results in formation of the *electrophilic N*-acyliminium ion **3**. Both of these reactive intermediates can be utilized in two consecutive steps for the formation of two C-C bonds. In our procedure, an enolate alkylation is carried out intermolecularly, after which an *N*-acyliminium ion is employed in an intramolecular reaction (Scheme 2).[3]



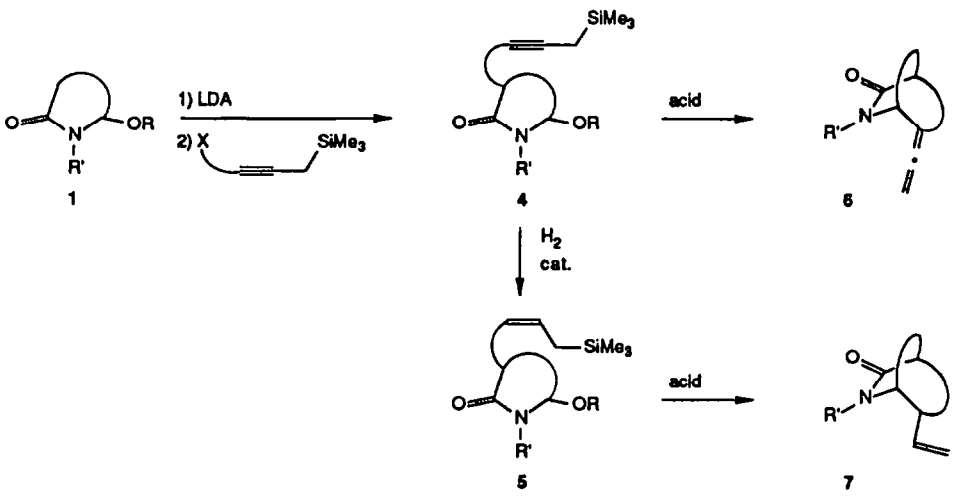
2 **1** **3**

Scheme 1

We have shown in our preliminary communication,[1] that 2-propynylsilanes (**4**) and allylsilanes (**5**) are very suitable π-nucleophiles for the intramolecular reaction with *N*-acyliminium ions. In two subsequent papers[2,4] we have detailed most of our work on the use of 2-propynylsilanes **4**, leading to allenes **6**. This paper deals mainly with the utility of allylsilanes **5** as nucleophilic reaction partners for the *N*-acyliminium ion, producing olefins **7**. The reactivities of 2-propynylsilanes, allylsilanes, and an ordinary olefin are compared. Finally, the amide bond in some cyclization products is cleaved to give access to carbocyclic amino acid derivatives.

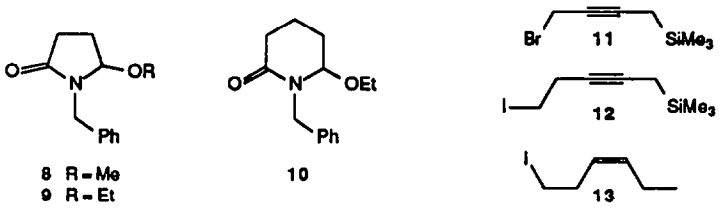
RESULTS

Our experimental results are collected in Table I. The products **14**, **15**, **17**, **19**, and **20** were obtained as isomer mixtures (ca. 60:40 ratio's) through alkylation of the lithium enolates of alkoxylactams **8**-**10**[2,4] with the



Scheme 2

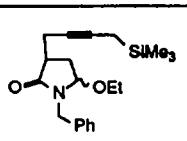
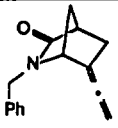
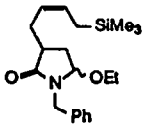
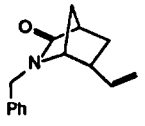
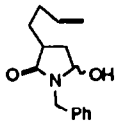
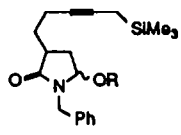
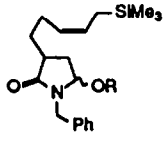
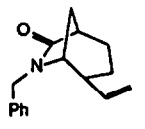
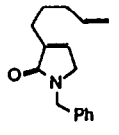
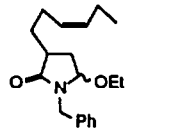
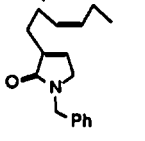
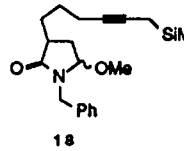
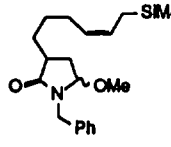
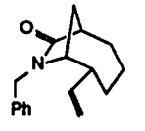
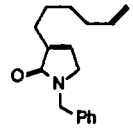
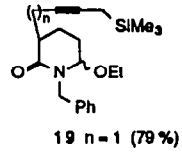
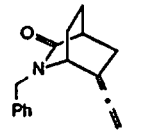
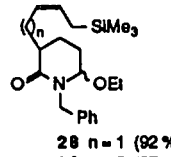
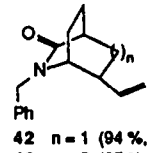
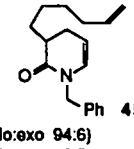
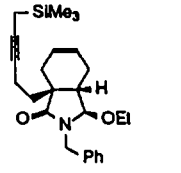
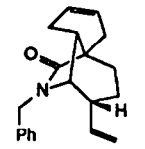
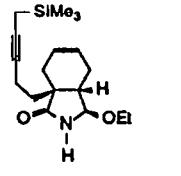
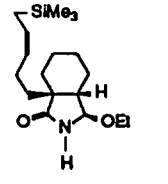
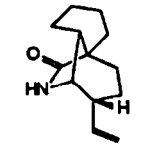
alkyl halides **11**, **12**,[4] and **13**.[5] The bromide **11** was synthesized from the corresponding alcohol via the mesylate.[2] The preparation of the remaining alkylation products was reported before.[2] Partial hydrogenation of the 2-propynylsilanes **14-16** and **18-23**, according to the procedure of Brown,[6,7] gave the correponding allylsilanes **24-32** in excellent yields. Remarkably, the olefinic double bond in **23** was also reduced under these conditions.



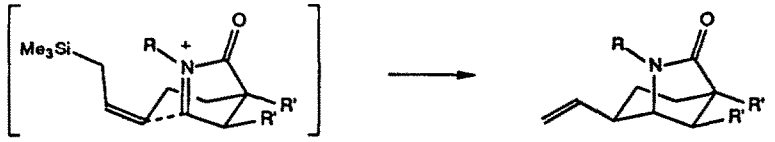
The alkoxylactams containing a π-nucleophilic moiety were then subjected to acidic conditions to bring about the desired cyclization reaction via the intermediacy of the *N*-acyliminium ion. The last column of Table I contains the results of these experiments. Entries 1a and 5a show two additional 2-propynylsilane cyclizations not reported before. The rather strained bicyclic [2.2.1] and [2.2.2] skeletons were formed in excellent yields by using formic acid as reaction medium. The structures of the products were immediately apparent from their characteristic IR-absorptions, i.e. 1970 and 1690 cm^{-1} in **33**, and 1960 and 1650 cm^{-1} in **41**.

The remaining entries of Table 1, except for entry 3, contain the results of cyclization experiments using the allylsilane function as π-nucleophile. Entry 2 shows that neat formic acid is a more favourable reaction medium than trifluoroacetic acid in dichloromethane. The former conditions produced lactam **36** as the only product in 87% yield, whereas the latter conditions gave rise to formation of 10% of **37**, resulting from protodesilylation, elimination of ethanol, and double bond isomerization. These side reactions are typical for systems which are slow to cyclize. This is illustrated by our attempts to prepare eight-membered rings. The 2-propynylsilane corresponding to **30** gave only a trace of cyclization product on dissolution in formic acid.[2] When the reaction was carried out with tin tetrachloride as Lewis acid in dichloromethane, 81% of cyclization product was obtained.[2] However, similar treatment of **30** gave, in addition to byproduct **45**, only about 20% of cyclization product **44**, according to the ^1H NMR spectrum of the crude reaction product. In general, good yields of azabicyclic systems were obtained in those cases, where five- (**34**), six- (**36**, **42**, **46**, **47**), and seven-membered rings (**39**, **43**) were created. Two stereoisomers (endo and exo)

Table I

entry	alkylation product (yield)	hydrogenation product (yield)	acid for cyclization	product(s) (yield)
1				
a	**14** (70 %)		HCOOH	**33** (82 %)
				 
b	**14**	**24** (97 %)	HCOOH	**34** (66 %, endo:exo 36:64) **35** (27 %)
2				 
a	**15** R = Me (63 %)	**25** R = Me (87 %)	CF_3COOH/CH_2Cl_2	**36** (77 %) **37** (10 %)
b	**16** R = Et	**26** R = Et (97 %)	HCOOH	**36** (87 %, endo:exo 95:5)
3				
a	**17** (85 %)		CF_3COOH/CH_2Cl_2	**38** (95 %)
b	**17**		HCOOH	**38** (50 %) + mixture of unknown compounds
4				 
	18	**27** (89 %)	CF_3COOH/CH_2Cl_2	**39** (73 %, endo:exo 8:92) **40** (12 %)
5				
a	**19** n = 1 (79 %)		HCOOH	**41** (98 %)
				 
b	**19** n = 1	**28** n = 1 (92 %)	HCOOH	**42** n = 1 (94 %, endo:exo 94:6)
c	**20** n = 2 (75 %)	**29** n = 2 (97 %)	HCOOH	**43** n = 2 (85 %, endo:exo 42:58)
d	**21** n = 3	**30** n = 3 (98 %)	$SnCl_4/CH_2Cl_2$	**44** n = 3 : **45** = 20:80
6				
	22	**31** (94 %)	HCOOH	**46** (98 %)
7				
	23	**32** (98 %)	HCOOH	**47** (89 %)

were formed, except for the ring closures of **31** and **32**, which gave single products. The stereochemistry of the products was assigned by using the NOE-difference technique in ^{1}H NMR-spectroscopy. The high endo-selectivity, as observed in the cyclizations of **25**, **26**, **31**, **32** can be explained by assuming a chair-like transition state (**48**, Scheme 3) in which the allylsilane moiety occupies an equatorial position.

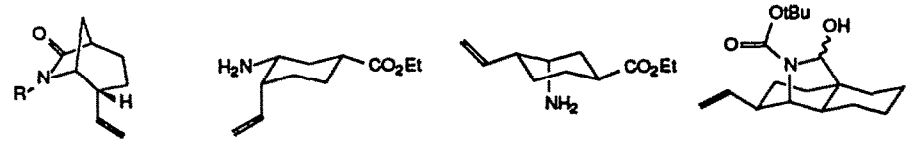


48 **36,45,47**

Scheme 3

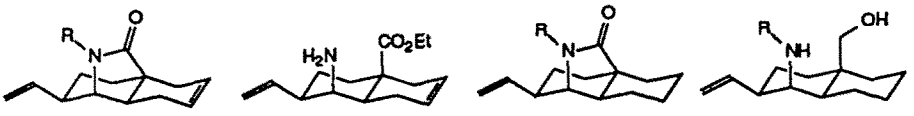
All allyl- and 2-propynylsilane cyclizations take place with complete regioselectivity, in such a manner that C-C bond formation occurs at the γ-carbon atom with respect to the trimethylsilyl function. In this way the reaction takes full advantage of the β-effect of silicon.[8] Comparison of entries **1a** and **1b** shows that cyclization of a 2-propynylsilane is more facile than cyclization of an allylsilane. Compound **14** gave a good yield of a single cyclization product, whereas **24** produced an appreciable amount of protodesilylation product **35** in addition to the desired bicycle **34**. The higher reactivity of 2-propynylsilanes compared to allylsilanes is more generally found (cf the present results with those in reference 2). This difference in reactivity was not detected in the cyclization of **19** and **28**, probably because of the less strained transition state needed for the formation of the azabicyclo[2.2.2]-systems **41** and **42**.

In order to probe the influence of the presence of silicon in the π-nucleophile, the cyclization of olefin **17** (entry 3) was investigated. With trifluoroacetic acid the only product obtained was the elimination product **38**. In formic acid 50% of **38** was formed in addition to a complex mixture of compounds, which possibly contained cyclization products, but was not further investigated. Thus, an ordinary olefinic double bond (as in **17**) is clearly inferior as π-nucleophile to an allylsilane (as in **26**) in this type of reaction.



36 R = CH_2Ph
49 R = H

50a **50b** **54**



46 R = CH_2Ph
51 R = H

52 **47** R = H
53 R = $tBuO_2C$

55 R = $tBuO_2C$
56 R = H

Hydrolysis of the amide bond of the cyclization products would give access to a wide structural variety of γ- and δ-amino acids. To investigate this possibility, lactam **36** was debenzylated through treatment with sodium in ammonia[9] to give **49**. Acidic ethanolysis of **49** produced γ-amino ester **50a**. Upon short-path vacuum distillation

50a partly epimerized to the isomer **50b**. In a similar way **46** was debenzylated to **51** and then treated with ethanolic hydrochloric acid. The desired neutral amino ester **52**, with both the amino and ester substituent rigidly held in axial positions, could not be isolated, as it was probably transformed back into the starting material on neutralization of the reaction mixture. An alternative cleavage procedure was then applied to lactam **47**. After introduction of the *tert*-butoxycarbonyl group onto nitrogen, **53** was reduced with lithium triethylborohydride (2.2 equiv) to give **54** as a mixture of stereoisomers. Further reduction with sodium borohydride, followed by removal of the *tert*-butoxycarbonyl function, furnished the isomerically pure *trans*-fused carbobicyclic aminoalcohol **56**.

In conclusion, 2-propynyl- and allylsilanes are excellent π-nucleophiles for intramolecular reactions with *N*-acyliminium ions. In conjunction with the use of ω-alkoxylactams as dipolar synthons, a variety of azabicyclic systems can now be synthesized. Several of these bicyclic skeletons are not readily accessible by other methods.[10] Finally, hydrolysis or reductive of cleavage of the amide bond in these azabicycles lead to potentially interesting γ- or δ-amino acids[11] or derivatives.

EXPERIMENTAL

General information. Infrared (IR) spectra were obtained from $CHCl_3$ solutions using a Perkin Elmer 298 spectrophotometer and are reported in cm^{-1}. Proton nuclear magnetic resonance (^1H NMR) spectra were determined in $CDCl_3$ as solvent using a Varian XL-100 (100 MHz), a Bruker AC 200 (200 MHz) or a Bruker WM 250 (250 MHz) instrument. The Bruker instruments were also used for the ^{13}C NMR spectra (50.3 or 62.9 MHz) in $CDCl_3$ solution. Chemical shifts are given in ppm downfield from tetramethylsilane. Exact mass measurements were carried out using a Varian MAT 711 or a VG Micromass ZAB-2HF instrument. R_f values were obtained by using thin-layer chromatography (TLC) on silicagel-coated plastic sheets (Merck silica gel 60 F_{254}) with the indicated solvent (mixture). Chromatographic purification refers to flash chromatography using the same solvent as for TLC and Merck silica gel 60 (230-400 mesh). Melting and boiling points are uncorrected.

4-Bromo-1-(trimethylsilyl)-2-butyne (11). To a solution of 5.97 g (42.0 mmol) of 4-(trimethylsilyl)-2-butyn-1-ol[12] in 40 mL of CH_2Cl_2 was added at 0°C 7.00 mL (50.2 mmol) of triethylamine. Subsequently, 3.60 mL (46.5 mmol) of methanesulfonyl chloride was added dropwise with stirring and cooling at 0°C. The mixture was allowed to warm to room temperature, and after 30 min treated with water. The mixture was extracted with CH_2Cl_2 (4 x), and the combined extracts dried (K_2CO_3) and concentrated *in vacuo* to give 8.81 g (40.0 mmol, 95%) of almost pure methanesulfonate as a brown oil. IR 2210 (w, C≡C), 1365 and 1170 (OSO_2), 1250 and 850 (Si-C). ^1H NMR (100 MHz) 0.07 (s, 9 H, $Si(CH_3)_3$), 1.56 (t, *J* 2.5 Hz, 2 H, CH_2Si), 3.10 (s, 3 H, CH_3), 4.86 (t, *J* 2.5 Hz, 2 H, CH_2O). The crude methanesulfonate (8.81 g, 40.0 mmol) was dissolved in 40 mL of DMF and 16.0 g (134 mmol) of potassium bromide was added. The reaction mixture was stirred at 60-70°C for 17 h and poured into 200 mL of water. The aq layer was extracted with pentane (3 x), and the combined extracts dried (K_2CO_3) and concentrated *in vacuo*. The residue was chromatographed to give 6.14 g (29.9 mmol, 75%) of **11** as a colourless oil. R_f 0.80 (pentane). IR 2215 (w, C≡C), 1250 and 845 (Si-C). ^1H NMR (100 MHz) 0.11 (s, 9 H, $Si(CH_3)_3$), 1.51 (t, *J* 3 Hz, 2 H, CH_2Si), 3.93 (t, *J* 3 Hz, 2 H, CH_2Br).

General procedure for the alkylation of alkoxylactams. To a stirred 0.5 M solution of 1.2 equiv of diisopropylamine in THF was added under nitrogen at -78°C, 1.2 equiv of *n*-butyllithium (1.6 M in hexane). After stirring for 15 min, a solution of 1 equiv of alkoxylactam in THF was added dropwise. After stirring the solution for 30 min at -78°C, a solution of 1.3 equiv of iodide in THF was added. The reaction mixture was stirred for 1 h at -78°C, then warmed up to room temperature in 1 h., and diluted with ether and saturated aq NH_4Cl. After extraction with ether (4 x), the combined organic extracts were dried (K_2CO_3) and concentrated *in vacuo*. The residue was chromatographed.

1-Benzyl-5-ethoxy-3-[4-(trimethylsilyl)-2-butynyl]-2-pyrrolidinone (14). Alkoxylactam **9** (0.472 g, 2.15 mmole) was alkylated by using 2.57 mmole of LDA and 0.521 g (2.54 mmole) of bromide **11** to give 0.518 g (1.51 mmole, 70%) of **14** as a yellow oil. R_f 0.43 (EtOAc:hexane 1:2). IR 2215 (w, C≡C), 1680 (CO), 1245 and 845 (Si-C). ^1H NMR (200 MHz) 0.05 and 0.08 (s, 9 H, $Si(CH_3)_3$), 1.17 and 1.18 (t, *J* 7 Hz, 3 H, OCH_2CH_3), 1.37 and 1.42 (t, *J* 2 Hz, 2 H, CH_2Si), 1.80-3.00 (m, 5 H), 3.41 (m, 2 H, OCH_2CH_3), 4.03 and 4.05 (d, *J* 15 Hz, 1 H, CHPh), 4.71 (m,1 H, CHOEt), 4.94 and 4.95 (d, *J* 15 Hz, 1 H, CHPh), 7.27 (m, 5 H, Ph).

1-Benzyl-5-methoxy-3-[5-(trimethylsilyl)-3-pentynyl]-2-pyrrolidinone (15). Alkoxylactam **8** (0.510 g, 2.49 mmole) was alkylated by using 2.99 mmole of LDA and 0.800 g (3.01 mmole) of iodide **12**[4] to give 0.536 g (1.56 mmole, 63%) of **15** as a light yellow oil. R_f 0.28 (EtOAc:hexane 1:2). IR 2220 (w, C≡C), 1685

(CO), 1245 and 850 (Si-C). ^{1}H NMR (100 MHz) 0.08 (s, 9 H, $Si(CH_3)_3$), 1.16-3.00 (m, 7 H), 1.40 (t, *J* 2.5 Hz, 2 H, CH_2Si), 3.21 and 3.24 (s, 3 H, OCH_3), 4.02 (d, *J* 15 Hz, 1 H, CHPh), 4.61 (m, 1 H, CHOMe), 4.98 (d, *J* 15 Hz, 1 H, CHPh), 7.32 (m, 5 H, Ph).

1-Benzyl-5-ethoxy-3-(3-hexenyl)-2-pyrrolidinone (17). Alkoxylactam **9** (0.300 g, 1.37 mmole) was alkylated by using 1.64 mmole of LDA and 0.374 g (1.78 mmole) of iodide **13**[5] to give 0.350 g (1.16 mmole, 85%) of **17** as a light yellow oil. R_f 0.33 (EtOAc:hexane 1:3). IR 1685 (CO). ^{1}H NMR (100 MHz) 0.84-2.84 (m, 9 H), 0.96 (t, *J* 7.5 Hz, 3 H, CH_2CH_3), 1.15 and 1.17 (t, *J* 7 Hz, 3 H, OCH_2CH_3), 3.41 (m, 2 H, OCH_2CH_3), 4.05 (d, *J* 15 Hz, 1 H, CHPh), 4.69 (m,1 H, CHOEt), 4.94 and 4.96 (d, *J* 15 Hz, 1 H, CHPh), 5.16-5.58 (m, 2 H, HC=CH), 7.30 (m, 5 H, Ph).

1-Benzyl-6-ethoxy-3-[4-(trimethylsilyl)-2-butynyl]-2-piperidinone (19). Alkoxylactam **10** (0.480 g, 2.06 mmole) was alkylated by using 2.46 mmole of LDA and 0.515 g (2.51 mmole) of bromide **11** to give 0.580 g (1.62 mmole, 79%) of **19** as a yellow oil. R_f 0.49 (EtOAc:hexane 1:2). IR 2215 (w, C≡C), 1635 (CO), 1250 and 850 (Si-C). ^{1}H NMR (200 MHz) 0.08 and 0.09 (s, 9 H, $Si(CH_3)_3$), 1.20 (t, *J* 7 Hz, 3 H, OCH_2CH_3), 1.43 (t, *J* 2.3 Hz, 2 H, CH_2Si), 1.57-2.99 (m, 7 H), 3.41 (m, 2 H, OCH_2CH_3), 3.97 and 4.04 (d, *J* 15 Hz, 1 H, CHPh), 4.46 (m,1 H, CHOEt), 5.34 (d, *J* 15 Hz, 1 H, CHPh), 7.26 (m, 5 H, Ph).

1-Benzyl-6-ethoxy-3-[5-(trimethylsilyl)-3-pentynyl]-2-piperidinone (20). Alkoxylactam **10** (0.250 g, 1.07 mmole) was alkylated by using 1.29 mmole of LDA and 0.370 g (1.39 mmole) of iodide **12** to give 0.299 g (0.810 mmole, 75%) of **20** as a colourless oil. R_f 0.40 (EtOAc:hexane 1:3). IR 2210 (w, C≡C), 1640 (CO), 1245 and 850 (Si-C). ^{1}H NMR (100 MHz) 0.09 (s, 9 H, $Si(CH_3)_3$),1.09-2.97 (m, 9 H), 1.20 (t, *J* 7 Hz, 3 H, OCH_2CH_3), 1.41 (t, *J* 2.5 Hz, 2 H, CH_2Si), 3.43 (m, 2 H, OCH_2CH_3), 3.98 and 4.03 (d, *J* 15 Hz, 1 H, CHPh), 4.46 (m,1 H, CHOEt), 5.35 (d, *J* 15 Hz, 1 H, CHPh), 7.30 (m, 5 H, Ph).

General procedure for partial hydrogenation of propargylsilanes. According to the procedure of Brown and Ahuja[6,7], to a stirred 0.025 M solution of 0.25 equiv of $Ni(OAc)_2 \cdot 4H_2O$ in EtOH was added at room temperature under a hydrogen atmosphere 1 equiv of a 1 M solution of $NaBH_4$ in EtOH (containing 0.1 M NaOH). After 1 min a few drops of 1,2-diaminoethane were added, followed by a solution of the propargylsilane in EtOH. After stirring for 17 h. under hydrogen, active charcoal was added, followed by filtration over Celite. The reaction flask and the filter were washed with CH_2Cl_2. The combined organic solutions were washed with water (2 x 25 mL), dried (K_2CO_3) and concentrated *in vacuo*. The residue was chromatographed.

1-Benzyl-5-ethoxy-3-[4-(trimethylsilyl)-2-butenyl]-2-pyrrolidinone (24). Propargylsilane **14** (184.7 mg, 0.538 mmole) was hydrogenated by using 0.134 mmole of catalyst and 1 drop of 1,2-diaminoethane, giving 180.8 mg (0.523 mmole, 97%) of **24** as a colourless oil. R_f 0.45 (EtOAc:hexane 1:2). IR 1685 (CO), 1245 and 855 (Si-C). ^{1}H NMR (250 MHz) -0.01 (s, 9 H, $Si(CH_3)_3$), 1.15 and 1.17 (t, *J* 7 Hz, 3 H, OCH_2CH_3), 1.47 (d, *J* 8.7 Hz, 2 H, CH_2Si), 1.71 (m, 1 H), 2.00-2.81 (m, 4 H), 3.34 (m, 2 H, OCH_2CH_3), 4.02 (d, *J* 15 Hz, 1 H, CHPh), 4.65 (m, 1 H, CHOEt), 4.93 and 4.96 (d, *J* 15 Hz, 1 H, CHPh), 5.20 (m, 1 H, HC=CH), 5.51 (m, 1 H, HC=CH), 7.26 (m, 5 H, Ph).

1-Benzyl-5-methoxy-3-[5-(trimethylsilyl)-3-pentenyl]-2-pyrrolidinone (25). Propargylsilane **15** (79 mg, 0.23 mmole) was hydrogenated by using 0.064 mmole of catalyst and 1 drop of 1,2-diaminoethane, giving 69 mg (0.20 mmole, 87%) of **25** as a colourless oil. R_f 0.63 (CH_2Cl_2:acetone 6:1). IR 1685 (CO), 1245 and 855 (Si-C). ^{1}H NMR (100 MHz) 0.00 (s, 9 H, $Si(CH_3)_3$), 1.06-3.02 (m, 7 H), 1.47 (d, *J* 8 Hz, 2 H, CH_2Si), 3.22 and 3.24 (s, 3 H, OCH_3), 4.03 (d, *J* 15 Hz, 1 H, CHPh), 4.65 (m, 1 H, CHOMe), 4.97 (d, *J* 15 Hz, 1 H, CHPh), 5.05-5.62 (m, 2 H, HC=CH), 7.31 (m, 5 H, Ph).

1-Benzyl-5-ethoxy-3-[5-(trimethylsilyl)-3-pentenyl]-2-pyrrolidinone (26). Propargylsilane **16** (2.50 g, 7.01 mmole) was hydrogenated by using 1.40 mmole of catalyst and 3 drops of 1,2-diaminoethane, giving 2.43 g (6.78 mmole, 97%) of **26** as a light yellow oil. R_f 0.42 (EtOAc:hexane 1:2). IR 1685 (CO), 1245 and 855 (Si-C). ^{1}H NMR (100 MHz) 0.00 (s, 9 H, $Si(CH_3)_3$), 1.06-2.82 (m, 7 H), 1.14 and 1.16 (t, *J* 7 Hz, 3 H, OCH_2CH_3), 1.46 (d, *J* 8 Hz, 2 H, CH_2Si), 3.39 (m, 2 H, OCH_2CH_3), 4.03 (d, *J* 15 Hz, 1 H, CHPh), 4.67 (m, 1 H, CHOEt), 4.94 (d, *J* 15 Hz, 1 H, CHPh), 5.10-5.61 (m, 2 H, HC=CH), 7.29 (m, 5 H, Ph).

1-Benzyl-5-methoxy-3-[6-(trimethylsilyl)-4-hexenyl]-2-pyrrolidinone (27). Propargylsilane **18** (0.50 g, 1.40 mmole) was hydrogenated by using 0.35 mmole of catalyst and 2 drops of 1,2-diaminoethane, giving 0.450 g (1.25 mmole, 89%) of **27** as a light yellow oil. R_f 0.34 (EtOAc:hexane 1:2). IR 1685 (CO), 1245 and 855 (Si-C). ^{1}H NMR (100 MHz) 0.00 (s, 9 H, $Si(CH_3)_3$), 1.08-2.72 (m, 9 H), 1.46 (d, *J* 7.5 Hz, 2 H, CH_2Si), 3.22 and 3.24 (s, 3 H, OCH_3), 4.02 (d, *J* 15 Hz, 1 H, CHPh), 4.64 (m, 1 H, CHOMe), 4.97 (d, *J* 15 Hz, 1 H, CHPh), 5.10-5.60 (m, 2 H, HC=CH), 7.32 (m, 5 H, Ph).

1-Benzyl-6-ethoxy-3-[4-(trimethylsilyl)-2-butenyl]-2-piperidinone (28). Propargylsilane **19** (200.0 mg, 0.559 mmole) was hydrogenated by using 0.14 mmole of catalyst and 1 drop of 1,2-diaminoethane, giving 184.3 mg (0.513 mmole, 92%) of **28** as a colourless oil. R_f 0.54 (EtOAc:hexane 1:2). IR 1635 (CO), 1245 and 855

(Si-C). ^{1}H NMR (200 MHz) 0.01 (s, 9 H, $Si(CH_3)_3$), 1.20 and 1.22 (t, *J* 7 Hz, 3 H, $OCH_2\underline{C}H_3$), 1.48 and 1.50 (d, *J* 8.5 Hz, 2 H, CH_2Si), 1.70-2.87 (m, 7 H), 3.44 (m, 2 H, OCH_2CH_3), 3.99 and 4.04 (d, *J* 15 Hz, 1 H, CHPh), 4.46 (m,1 H, CHOEt), 5.20-5.65 (m, 2 H, HC=CH), 5.36 (d, *J* 15 Hz, 1 H, CHPh), 7.27 (m, 5 H, Ph).

1-Benzyl-6-ethoxy-3-[5-(trimethylsilyl)-3-pentenyl]-2-piperidinone (29). Propargylsilane **20** (0.299 g, 0.81 mmole) was hydrogenated by using 0.20 mmole of catalyst and 1 drop of 1,2-diaminoethane, giving 0.291 g (0.78 mmole, 97%) of **29** as a colourless oil. R_f 0.51 (EtOAc:hexane 1:3). IR 1635 (CO), 1240 and 855 (Si-C). ^{1}H NMR (100 MHz) 0.00 (s, 9 H, $Si(CH_3)_3$), 1.07-2.59 (m, 9 H), 1.20 (t, *J* 7 Hz, 3 H, $OCH_2\underline{C}H_3$), 1.47 (d, *J* 7.5 Hz, 2 H, CH_2Si), 3.43 (m, 2 H, OCH_2CH_3), 4.01 (d, *J* 15 Hz, 1 H, CHPh), 4.46 (m,1 H, CHOEt), 5.34 (d, *J* 15 Hz, 1 H, CHPh), 5.13-5.61 (m, 2 H, HC=CH), 7.28 (m, 5 H, Ph).

1-Benzyl-6-ethoxy-3-[6-(trimethylsilyl)-4-hexenyl]-2-piperidinone (30). Propargylsilane **21** (0.151 g, 0.39 mmole) was hydrogenated by using 0.10 mmole of catalyst and 2 drops of 1,2-diaminoethane, giving 0.149 g (0.39 mmole, 98%) of **30** as a colourless oil. R_f 0.37 (EtOAc:hexane 1:3). IR 1640 (CO), 1250 and 860 (Si-C). ^{1}H NMR (100 MHz) 0.00 (s, 9 H, $Si(CH_3)_3$), 1.08-2.56 (m, 11 H), 1.20 (t, *J* 7 Hz, 3 H, $OCH_2\underline{C}H_3$), 1.46 (d, *J* 8 Hz, 2 H, CH_2Si), 3.42 (m, 2 H, OCH_2CH_3), 3.99 and 4.01 (d, *J* 15 Hz, 1 H, CHPh), 4.44 (m,1 H, CHOEt), 5.33 (d, *J* 15 Hz, 1 H, CHPh), 5.12-5.58 (m, 2 H, HC=CH), 7.28 (m, 5 H, Ph).

***rel*-(3*R*,3a*S*,7a*R*)-2-Benzyl-3-ethoxy-2,3,3a,4,7,7a-hexahydro-7a-[5-(trimethylsilyl)-3--pentenyl]-1-isoindolone (31).** Propargylsilane **22** (0.240 g, 0.50 mmole) was hydrogenated by using 0.13 mmole of catalyst and 1 drop of 1,2-diaminoethane, giving 0.192 g (0.47 mmole, 94%) of **31** as a colourless oil. R_f 0.42 (EtOAc:hexane 1:4). IR 1685 (CO), 1245 and 855 (Si-C). ^{1}H NMR (100 MHz) 0.00 (s, 9 H, $Si(CH_3)_3$), 1.03-2.53 (m, 9 H), 1.17 (t, *J* 7 Hz, 3 H, $OCH_2\underline{C}H_3$), 1.46 (d, *J* 7.5 Hz, 2 H, CH_2Si), 3.45 (m, 2 H, OCH_2CH_3), 4.01 (d, *J* 15 Hz, 1 H, CHPh), 4.16 (d, *J* 2.5 Hz, 1 H, CHOEt), 4.95 (d, *J* 15 Hz, 1 H, CHPh), 5.06-5.55 (m, 2 H, $\underline{H}C=C\underline{H}CH_2Si$), 5.55-6.02 (m, 2 H, HC=CH), 7.25 (m, 5 H, Ph).

***rel*-(3*R*,3a*S*,7a*S*)-2-Benzyl-3-ethoxy-2,3,3a,4,5,6,7,7a-octahydro-7a-[5-(trimethylsilyl)-3--pentenyl]-1-isoindolone (32).** Propargylsilane **23** (2.00 g, 6.27 mmole) was hydrogenated by using 1.25 mmole of catalyst and 4 drops of 1,2-diaminoethane, giving 1.99 g (6.16 mmole, 98%) of **32** as a light yellow oil. R_f 0.36 (EtOAc:hexane 1:1). IR 3440 and 3220 (br.) (NH), 1700 (CO), 1245 and 855 (Si-C). ^{1}H NMR (100 MHz) 0.02 (s, 9 H, $Si(CH_3)_3$), 1.10-2.38 (m, 13 H), 1.26 (t, *J* 7 Hz, 3 H, $OCH_2\underline{C}H_3$), 1.50 (d, *J* 8 Hz, 2 H, CH_2Si), 3.57 (m, 2 H, OCH_2CH_3), 4.64 (dd, *J* 1, 4 Hz, 1 H, CHOEt), 5.12-5.60 (m, 2 H, HC=CH), 7.40 (br. s, 1 H, NH).

General procedure for cyclizations in formic acid. A 0.1 M solution of the alkoxylactam in formic acid was stirred for 30 min at room temperature and then concentrated *in vacuo*. The residue was diluted with CH_2Cl_2 and washed with saturated aq $NaHCO_3$ (excess). After extraction of the aq layer with CH_2Cl_2 (3 x), the combined organic extracts were dried (K_2CO_3) and concentrated *in vacuo*. The residue was chromatographed.

General procedure for cyclizations using trifluoroacetic acid. Under a dry nitrogen atmosphere, a solution of the alkoxylactam in CH_2Cl_2 was added at 0°C to a 0.04 M solution of 10 equiv of trifluoroacetic acid (TFA) in CH_2Cl_2. After warming up to room temperature and stirring for 1 h, the reaction mixture was poured out into 100 mL of saturated aq $NaHCO_3$. The aq layer was extracted with CH_2Cl_2 (4 x), and the organic extracts were dried (K_2CO_3) and concentrated *in vacuo*. The residue was chromatographed.

5-Benzyl-3-vinylidene-5-azabicyclo[2.2.1]heptan-6-one (33). Alkoxylactam **14** (108.7 mg, 0.3164 mmol) was cyclized in formic acid to give 58.7 mg (0.260 mmol, 82%) of **33** as a colourless oil. R_f 0.39 (EtOAc:hexane 2:1). IR 1970 (C=C=C), 1690 (CO). ^{1}H NMR (250 MHz) 1.59 (d, *J* 9.5 Hz, 1 H), 1.97 (dd, *J* 1.8, 9.5 Hz, 1 H), 2.34 (dq, *J*d 15.0, *J*q 3.1 Hz, 1 H, $C\underline{H}HC=C$), 2.58 (dq, *J*d 15.0, *J*q 4.2 Hz, 1 H, $CH\underline{H}C=C$), 2.93 (m, 1 H, COCH), 3.88 (d, *J* 15 Hz, 1 H, CHPh), 3.95 (d, *J* 1.6 Hz, 1 H, NCH), 4.68 (d, *J* 15 Hz, 1 H, CHPh), 4.77 (m, 2 H, $C=CH_2$), 7.26 (m, 5 H, Ph). ^{13}C NMR (50 MHz) 30.7 (t, $NCH\underline{C}H_2$), 40.6 (t, $\underline{C}H_2C=C$), 44.7 (t, CH_2Ph), 45.5 (d, $CO\underline{C}H$), 63.8 (d, NCH), 77.9 (t, $C=\underline{C}H_2$), 98.5 (s, $\underline{C}=C=CH_2$), 127.4 (d, Ph), 128.2 (d, Ph), 128.6 (d, Ph), 136.8 (s, Ph), 177.7 (s, CO), 201.8 (s, $\underline{C}=CH_2$). Exact mass 225.1159 (calcd for $C_{15}H_{15}NO$ 225.1154).

5-Benzyl-3-vinyl-5-azabicyclo[2.2.1]heptan-6-one (34) and 1-benzyl-3-(3-butenyl)-5-hydroxy-3--pyrroline-2-one (35). Alkoxylactam **24** (157.9 mg, 0.4569 mmol) was cyclized in formic acid to give 18.2 mg (0.0742 mmol, 16%) of **35** as a colourless oil, 27.4 mg of a mixture of **35** (12.4 mg, 0.0506 mmol, 11%) and **34** (15.0 mg, 0.066 mmol, 14%), and 53.2 mg (0.234 mmol, 51%) of **34** (endo:exo 36:64) as a colourless oil. **34** R_f 0.27 (EtOAc:hexane 2:1). IR 1685 (CO). ^{1}H NMR (250 MHz) exo isomer 1.49 (m, 1 H), 1.63 (m, 1 H), 1.84 (m, 1 H), 2.45 (m, 1 H, $C\underline{H}CH=CH_2$), 2.83 (m, 1 H, COCH), 3.45 (m, 1 H, NCH), 3.98 (d, *J* 15 Hz, 1 H, CHPh), 4.69 (d, *J* 15 Hz, 1 H, CHPh), 4.96 (m, 2 H, $HC=C\underline{H}_2$), 5.63 (m, 1 H, $\underline{H}C=CH_2$), 7.28 (m, 5 H, Ph); endo isomer 1.49 (m, 2 H), 1.84 (m, 1 H), 2.11 (m, 1 H), 2.83 (m, 1 H, COCH), 2.85 (m, 1 H, $C\underline{H}CH=CH_2$), 3.60 (m, 1 H, NCH), 3.78 (d, *J* 15 Hz, 1 H, CHPh), 5.01 (d, *J* 15 Hz, 1 H, CHPh), 5.12 (m, 2 H, $HC=C\underline{H}_2$), 5.71 (m, 1 H, $\underline{H}C=CH_2$), 7.28 (m, 5 H, Ph). ^{13}C NMR (63 MHz) exo isomer 31.6 (t), 37.3 (t), 43.8 (d), 44.2 (t, CH_2Ph), 45.6 (d), 63.6 (d, NCH), 115.4 (t, $HC=\underline{C}H_2$), 127.4 (d, Ph), 127.9 (d, Ph), 128.6 (d, Ph), 137.1 (s, Ph), 139.6 (d, $H\underline{C}=CH_2$), 177.8 (s, CO); endo isomer 30.3 (t), 42.0 (t), 46.0 (d), 46.2 (t, CH_2Ph), 46.4 (d), 63.1 (d, NCH), 116.4

(t, HC=$\underline{C}H_2$), 127.3 (d, Ph), 127.8 (d, Ph), 128.5 (d, Ph), 137.3 (s, Ph), 138.8 (d, H$\underline{C}$=CH_2), 177.1 (s, CO). Exact mass 227.1337 (calcd for $C_{15}H_{17}NO$ 227.1310). **35** R_f 0.33 and 0.43 (EtOAc:hexane 2:1). IR 3370 (br., OH), 1670 (CO). ^{1}H NMR (200 MHz) 1.07-2.84 (m, 7 H), 3.09 (m, 1 H, OH), 4.19 (d, *J* 15 Hz, 1 H, CHPh), 4.82 and 4.83 (d, *J* 15 Hz, 1 H, CHPh), 4.91-5.20 (m, 3 H, HC=CH_2 and C$\underline{H}$OH), 5.80 (m, 1 H, $\underline{H}$C=CH_2), 7.27 (m, 5 H, Ph).

6-Benzyl-4-vinyl-6-azabicyclo[3.2.1]octan-7-one (36). Alkoxylactam **25** (75 mg, 0.23 mmole) was cyclized by using 0.18 mL (2.33 mmole) of TFA, giving 43 mg (0.18 mmole, 77%) of **36** (the crude product contained about 10 % of **37** according to ^{1}H NMR). Alkoxylactam **26** (2.42 g, 6.74 mmole) was cyclized in formic acid to give 1.40 g (5.83 mmole, 87%) of **36** as a white solid, mp 50-52°C (hexane). R_f 0.36 (EtOAc:hexane 2:1). IR 1675 (CO). ^{1}H NMR (100 MHz) 1.35-2.47 (m, 7 H), 2.56 (m, 1 H, COCH), 3.54 (d, *J* 6 Hz, 1 H, NCH), 3.91 (d, *J* 15 Hz, 1 H, CHPh), 4.91-5.31 (m, 2 H, HC=$\underline{C}H_2$), 5.17 (d, *J* 15 Hz, 1 H, CHPh), 5.87 (m, 1 H, $\underline{H}$C=CH_2), 7.30 (m, 5 H, Ph). ^{13}C NMR (63 MHz) 23.1 (t, NCHCH$\underline{C}H_2$), 24.2 (t, NCOCH$\underline{C}H_2$), 37.6 (t, NCH$\underline{C}H_2$), 39.6 (d, CO$\underline{C}$H), 41.4 (d, NCH$\underline{C}$H), 44.6 (t, CH_2Ph), 58.0 (d, NCH), 113.7 (t, HC=$\underline{C}H_2$), 126.4 (d, Ph), 127.0 (d, Ph), 127.6 (d, Ph), 136.3 (s, Ph), 140.4 (d, H$\underline{C}$=CH_2), 175.3 (s, CO). Exact mass 241.1467 (calcd for $C_{16}H_{19}NO$ 241.1467).

Attempted cyclization of **1-benzyl-5-ethoxy-3-(3-hexenyl)-2-pyrrolidinone (17)** leading to **1-benzyl-3-(3-hexenyl)-3-pyrroline-2-one (38).** Alkoxylactam **17** (76.1 mg, 0.25 mmol) was treated with TFA (0.193 mL, 2.50 mmol) to give **38** (60 mg, 0.24 mmol, 95 %) as a yellowish oil. Treatment of **17** with formic acid for 105 h gave a mixture of 50 % of **38** and at least three formates according to ^{1}H NMR. **38** R_f 0.48 (EtOAc:hexane 1:1). IR 1670 (CO). ^{1}H NMR (100 MHz) 0.93 (t, *J* 7.5 Hz, 3 H, $CH_2\underline{C}H_3$), 1.86-2.26 (m, 2 H, $\underline{C}H_2CH_2CH$=CH), 2.27-2.45 (m, 4 H, $\underline{C}H_2$CH=CH$\underline{C}H_2$), 3.69-3.80 (m, 2 H, NC$\underline{H}_2$CH), 4.65 (s, 2 H, CH_2Ph), 5.18-5.59 (m, 2 H, HC=CH), 6.64 (m, 1 H, C=CH), 7.30 (m, 5 H, Ph).

7-Benzyl-5-vinyl-7-azabicyclo[4.2.1]nonan-8-one (39) and 1-benzyl-3-(5-hexenyl)-3-pyrroline--2-one (40). Alkoxylactam **27** (0.449 g, 1.25 mmole) was cyclized by using 0.96 mL (12.5 mmole) of TFA, giving 0.232 g (0.91 mmole, 73%) of **39** as a white solid, mp 75-78°C (hexane) and 37 mg (0.15 mmole, 12%) of **40** as a light yellow oil. **39** R_f 0.29 (EtOAc:hexane 1:1). IR 1665 (CO). ^{1}H NMR (100 MHz) 1.16-2.28 (m, 8 H), 2.38-2.77 (m, 2 H, NCHC$\underline{H}$ and COCH), 3.49 (dd, *J* 1.5, 7 Hz, 1 H, NCH), 3.96 (d, *J* 15 Hz, 1 H, CHPh), 4.85-5.18 (m, 2 H, HC=$\underline{C}H_2$), 5.04 (d, *J* 15 Hz, 1 H, CHPh), 5.70 (m, 1 H, $\underline{H}$C=CH_2), 7.32 (m, 5 H, Ph). ^{13}C NMR (25 MHz) 21.7 (t), 26.5 (t), 29.7 (t), 31.7 (t), 41.2 (d), 42.0 (d), 43.5 (t, CH_2Ph), 60.1 (d, NCH), 114.6 (t, HC=$\underline{C}H_2$), 127.2 (d, Ph), 127.8 (d, Ph), 128.3 (d, Ph), 136.4 (s, Ph), 139.5 (d, H$\underline{C}$=CH_2), 176.9 (s, CO). Exact mass 255.1631 (calcd for $C_{17}H_{21}NO$ 255.1623). **40** R_f 0.44 (EtOAc:hexane 1:1). IR 1670 (CO), 1640 (C=C). ^{1}H NMR (100 MHz) 1.18-2.50 (m, 8 H), 3.74 (m, 2 H, NC$\underline{H}_2$CH), 4.66 (s, 2 H, CH_2Ph), 4.88-5.16 (m, 2 H, HC=$\underline{C}H_2$), 5.84 (m, 1 H, $\underline{H}$C=CH_2), 6.62 (mt, *J*t 1.5 Hz, 1 H, C=CH), 7.32 (m, 5 H, Ph).

5-Benzyl-3-vinylidene-5-azabicyclo[2.2.2]octan-6-one (41). Alkoxylactam **19** (170.4 mg, 0.4766 mmol) was cyclized in formic acid to give 111.7 mg (0.4667 mmol, 98%) of **41** as a white solid, mp 104-106.5°C (EtOAc:hexane 1:1). R_f 0.28 (EtOAc:hexane 2:1). IR 1960 (C=C=C), 1650 (CO). ^{1}H NMR (200 MHz) 1.57-2.09 (m, 4 H), 2.47 (dm, *J*d 16 Hz, 1 H, C$\underline{H}$HC=C), 2.67 (md, *J*d 16 Hz, 1 H, CH$\underline{H}$C=C), 2.78 (m, 1 H, COCH), 3.85 (br. s,1 H, NCH), 4.44 (d, *J* 15 Hz, 1 H, CHPh), 4.64 (m, 2 H, C=$\underline{C}H_2$), 4.72 (d, *J* 15 Hz, 1 H, CHPh), 7.28 (m, 5 H, Ph). ^{13}C NMR (50 MHz) 23.5 (t), 28.0 (t), 30.0 (t), 39.1 (d, CO$\underline{C}$H), 47.8 (t, CH_2Ph), 57.3 (d, NCH), 77.0 (t, C=$\underline{C}H_2$), 98.1 (s, $\underline{C}$=C=CH_2), 127.4 (d, Ph), 128.2 (d, Ph), 128.5 (d, Ph), 137.2 (s, Ph), 174.7 (s, CO), 201.7 (s, $\underline{C}$=CH_2). Exact mass 239.1318 (calcd for $C_{16}H_{17}NO$ 239.1310).

5-Benzyl-3-vinyl-5-azabicyclo[2.2.2]octan-6-one (42). Alkoxylactam **28** (145.2 mg, 0.4038 mmol) was cyclized in formic acid to give 91.8 mg (0.380 mmol, 94%) of **42** (endo:exo 94:6) as a colourless oil. R_f 0.41 (EtOAc). IR 1645 (CO). ^{1}H NMR (200 MHz) endo isomer 1.20-2.13 (m, 6 H), 2.35 (m, 1 H, C$\underline{H}$CH=CH_2), 2.62 (m, 1 H, COCH), 3.33 (m, 1 H, NCH), 3.94 (d, *J* 15 Hz, 1 H, CHPh), 4.79-5.10 (m, 3 H, HC=$\underline{C}H_2$ and CHPh), 5.50 (m, 1 H, $\underline{H}$C=CH_2), 7.24 (m, 5 H, Ph); exo isomer 3.27 (m, 1 H, NCH), 4.44 (d, *J* 15 Hz, 1 H, CHPh), 4.65 (d, *J* 15 Hz, 1 H, CHPh), 5.64 (m, 1 H, $\underline{H}$C=CH_2). ^{13}C NMR (50 MHz) endo isomer 23.4 (t), 27.4 (t), 30.7 (t), 38.2 (d), 42.4 (d), 49.0 (t, CH_2Ph), 57.7 (d, NCH), 114.5 (t, HC=$\underline{C}H_2$), 127.3 (d, Ph), 128.4 (d, Ph), 128.5 (d, Ph), 137.4 (s, Ph), 140.6 (d, H$\underline{C}$=CH_2), 175.0 (s, CO); exo isomer 21.6 (t), 24.6 (t), 30.0 (t), 38.6 (d), 42.3 (d), 47.5 (t, CH_2Ph), 57.1 (d, NCH), 115.9 (t, HC=$\underline{C}H_2$), 127.3 (d, Ph), 128.1 (d, Ph), 128.4 (d, Ph), 137.5 (s, Ph), 139.2 (d, H$\underline{C}$=CH_2), 175.1 (s, CO). Exact mass 241.1472 (calcd for $C_{16}H_{19}NO$ 241.1467).

6-Benzyl-4-vinyl-6-azabicyclo[3.2.2]nonan-7-one (43). Alkoxylactam **29** (0.232 g, 0.623 mmole) was cyclized in formic acid to give 0.135 g (0.529 mmole, 85%, 58:42 mixture of $\mathbf{43}^{exo}$ and $\mathbf{43}^{endo}$) of **43** as a colourless oil. R_f 0.28 (EtOAc:hexane 1:1). IR 1635 (CO). ^{1}H NMR (100 MHz) 1.17-2.51 (m, 9 H), 2.66-2.91 (m, 1 H, COCH), 3.28 (dd, *J* 1, 4.5 Hz, 0.58 H, NCH^{exo}), 3.48 (dd, *J* 3, 7 Hz, 0.42 H, NCH^{endo}), 3.78 (d, *J* 15 Hz, 0.42 H, CHPh^{endo}), 4.38 (d, *J* 15 Hz, 0.58 H, CHPh^{exo}), 4.81 (d, *J* 15 Hz, 0.58 H, CHPh^{exo}), 5.40 (d, *J* 15 Hz, 0.42 H, CHPh^{endo}), 4.89-5.20 (m, 2 H, HC=$\underline{C}H_2$), 5.42-6.04 (m, 1 H, $\underline{H}$C=CH_2), 7.29 (m, 5 H, Ph). Exact mass 255.1616 (calcd for $C_{17}H_{21}NO$ 255.1623).

***rel*-(1*R*,2*S*)-11-Benzyl-10-vinyl-11-azatricyclo[5.3.2.0^{2,7}]-4-dodecen-12-one (46).** Alkoxylactam 31 (0.133 g, 0.324 mmole) was cyclized in formic acid to give 92.9 mg (0.317 mmole, 98%) of 46 as a white solid, mp 89.5-92°C (hexane). R_f 0.35 (EtOAc:hexane 1:3). IR 1675 (CO). ^{1}H NMR (100 MHz) 0.80-2.48 (m, 9 H), 2.66 (md, *J*d 18 Hz, 1 H), 3.13 (s, 1 H, NCH), 3.88 (d, *J* 15 Hz, 1 H, CHPh), 4.94-5.25 (m, 2 H, HC=C$\underline{H}_2$), 5.15 (d, *J* 15 Hz, 1 H, CHPh), 5.40-5.79 (m, 2 H, HC=CH), 5.93 (m, 1 H, $\underline{H}$C=CH$_2$), 7.29 (m, 5 H, Ph). ^{13}C NMR (63 MHz) 24.8 (t), 25.4 (t), 28.4 (t), 33.9 (t), 42.6 (d, NCH$\underline{C}$H), 44.8 (d, NCH$\underline{C}$H), 44.9 (s, CO$\underline{C}$), 46.1 (t, CH$_2$Ph), 63.2 (d, NCH), 114.7 (t, HC=$\underline{C}$H$_2$), 124.6 (d, H$\underline{C}$=CH), 125.3 (d, HC=$\underline{C}$H), 127.4 (d, Ph), 128.3 (d, Ph), 128.9 (d, Ph), 136.8 (s, Ph), 141.2 (d, H$\underline{C}$=CH$_2$), 176.1 (s, CO). Exact mass 293.1788 (calcd for $C_{20}H_{23}NO$ 293.1780).

***rel*-(1*R*,2*S*)-10-Vinyl-11-azatricyclo[5.3.2.0^{2,7}]dodecan-12-one (47).** Alkoxylactam 32 (1.94 g, 6.01 mmole) was cyclized in formic acid to give 1.09 g (5.32 mmole, 89%) of 47 as a white solid, mp 113-114°C (EtOAc). R_f 0.38 (EtOAc:hexane 2:1). IR 3440 (NH), 1695 (CO). ^{1}H NMR (100 MHz) 0.85-2.51 (m, 14 H), 3.17 (br. s, 1 H, NCH), 4.89-5.15 (m, 2 H, HC=C$\underline{H}_2$), 5.73 (m, 1 H, $\underline{H}$C=CH$_2$), 6.34 (br. s, 1 H, NH). ^{13}C NMR (63 MHz) 23.4 (t), 24.3 (t), 24.5 (t), 27.0 (t), 29.5 (t), 33.8 (t), 42.6 (d, NCH$\underline{C}$H), 46.2 (s, CO$\underline{C}$), 50.2 (d, NCH$\underline{C}$H), 58.9 (d, NCH), 114.5 (t, HC=$\underline{C}$H$_2$), 140.5 (d, H$\underline{C}$=CH$_2$), 179.7 (s, CO). Exact mass 205.1446 (calcd for $C_{13}H_{19}NO$ 205.1467).

4-Vinyl-6-azabicyclo[3.2.1]octan-7-one (49). To lactam 36 (0.360 g, 1.49 mmole) was added under nitrogen 25 mL of ammonia and 0.103 g (4.48 mmole) of sodium. After refluxing the solution at -33°C for 1 h, the ammonia was evaporated under atmospheric pressure and 20 mL of saturated aq NH_4Cl was added. The aq layer was extracted with CH_2Cl_2 (4 x 25 mL) and the organic extracts were dried (K_2CO_3) and concentrated *in vacuo*.The residue was chromatographed to yield 0.182 g (1.20 mmole, 81%) of 49 as a white solid, mp 69-72°C (hexane). R_f 0.37 (CH_2Cl_2:acetone 2:1). IR 3430 (NH), 1700 (CO). ^{1}H NMR (100 MHz) 1.42-2.02 (m, 6 H), 2.14-2.50 (m, 3 H), 3.63 (md, *J*d 5 Hz, 1 H, NCH), 4.90-5.15 (m, 2 H, HC=C$\underline{H}_2$), 5.73 (m, 1 H, $\underline{H}$C=CH$_2$), 6.14 (br. s, 1 H, NH).

***rel*-(1*R*,2*R*,4*R*)-2-amino-4-carboethoxy-1-vinyl-cyclohexane (50a).** A solution of 47.2 mg (0.313 mmole) of 49 in 10 mL of a 2 M solution of HCl in EtOH was refluxed for 19 h and then concentrated *in vacuo*. The residue was dissolved in 20 mL of water, and a 25% aq solution of ammonia was added until a pH value of 10 was reached. The aq layer was extracted with CH_2Cl_2 (4 x 25 mL) and the organic extracts were dried (K_2CO_3) and concentrated *in vacuo* to yield 54.1 mg (0.275 mmole, 88%) of 50a as a colourless oil. Distillation of the product (bulb to bulb, bp ± 130°C, 0.1 mm Hg) resulted in partial isomerization to 50b. IR 3365 (NH_2), 1725 (CO). ^{1}H NMR (100 MHz) 1.26 (t, *J* 7 Hz, 3 H, OCH$_2$C$\underline{H}_3$), 1.28 (s, 2 H, NH_2), 1.34-2.02 (m, 6 H), 2.23-2.60 (m, 2 H, COCH and C$\underline{H}$CH=CH$_2$), 2.84 (dt, *J*d 11.5 Hz, *J*t 4 Hz, 1 H, C$\underline{H}$NH$_2$), 4.14 (q, *J* 7 Hz, 2 H, OC$\underline{H}_2$CH$_3$), 5.04-5.30 (m, 2 H, HC=C$\underline{H}_2$), 6.01 (m, 1 H, $\underline{H}$C=CH$_2$). Exact mass 197.1419 (calcd for $C_{11}H_{19}NO_2$ 197.1416).

***rel*-(1*R*,2*S*)-10-Vinyl-11-azatricyclo[5.3.2.0^{2,7}]-4-dodecen-12-one (51).** To lactam 46 (75.5 mg, 0.258 mmole) was added under nitrogen 15 mL of ammonia and 30 mg (1.30 mmole) of sodium. After refluxing the solution at -33°C for 1 h, the ammonia was evaporated under atmospheric pressure and 20 mL of saturated aq NH_4Cl was added. The aq layer was extracted with CH_2Cl_2 (4 x 25 mL) and the organic extracts were dried (K_2CO_3) and concentrated *in vacuo*.The residue was chromatographed to yield 33.0 mg (0.163 mmole, 63%) of 51 as a white solid, mp 102-104°C (hexane). R_f 0.38 (EtOAc:hexane 2:1). IR 3430 (NH), 1690 (CO).
^{1}H NMR (100 MHz) 1.08-2.72 (m, 10 H), 3.25 (br. s, 1 H, NCH), 4.90-5.16 (m, 2 H, HC=C$\underline{H}_2$), 5.50-5.93 (m, 3 H, $\underline{H}$C=CH$_2$ and HC=CH), 6.33 (br. s, 1 H, NH).

***N-tert*-Butoxycarbonylderivative 53.** To a solution of 0.500 g (2.44 mmole) of 47 in 6 mL of CH_2Cl_2 was added under a dry nitrogen atmosphere 0.34 mL (2.44 mmole) of Et_3N, 1.12 mL (4.88 mmole) of di-tbutyldicarbonate and 0.298 g (2.44 mmole) of DMAP. After stirring the solution for 24 h at room temperature, it was concentrated *in vacuo*, and the residue was chromatographed to yield 0.528 g (1.73 mmole, 71%) of 53 as a light yellow viscous oil. R_f 0.36 (EtOAc:hexane 1:3). IR 1780 and 1710 (CO). ^{1}H NMR (100 MHz) 0.85-2.57 (m, 14 H), 1.52 (s, 9 H, OC(C$\underline{H}_3$)$_3$), 3.97 (s, 1 H, NCH), 4.87-5.15 (m, 2 H, HC=C$\underline{H}_2$), 5.77 (m, 1 H, $\underline{H}$C=CH$_2$).

***N-tert*-Butoxycarbonylderivative 55.** To 1.80 mL of a 1 M solution of Et_3LiBH in THF was added at room temperature under nitrogen a solution of 0.251 g (0.82 mmole) of 53 in 2 mL of THF. After stirring for 30 min at room temperature, 1 mL of water was added dropwise, followed by 2 mL of 2 M HCl. The aq layer was extracted with $CHCl_3$ (4 x 15 mL) and the organic extracts were dried (K_2CO_3) and concentrated *in vacuo* to yield 54 as a colourless oil. 54 Was dissolved in 10 mL of EtOH (60%) and after addition of 125 mg (3.29 mmole) of $NaBH_4$, the solution was stirred at 50°C for 2 h and then cooled to 0°C, and 2 mL of 2 M HCl was added dropwise. The mixture was poured out into 10 mL of saturated aq $NaHCO_3$. The aq layer was extracted with $CHCl_3$ (4 x 15 mL) and the organic extracts were dried (K_2CO_3) and concentrated *in vacuo* to yield 156.9 mg (0.508 mmole, 62%) of 55 as a white solid, mp 120-123°C (hexane). R_f 0.31 (EtOAc:hexane 1:2). IR 3450 and 3440 (NH and OH), 1705 (CO). ^{1}H NMR (100 MHz) 0.72-1.58 (m, 15 H), 1.42 (s, 9 H, OC(C$\underline{H}_3$)$_3$), 3.60 (d, *J* 11 Hz, 1 H, C$\underline{H}$OH), 3.78 (m, 1 H, NCH), 3.92 (d, *J* 11 Hz, 1 H, C$\underline{H}$OH), 4.86-5.14 (m, 2 H, HC=C$\underline{H}_2$), 5.66 (br. s, 1 H, NH), 5.84 (m, 1 H, $\underline{H}$C=CH$_2$).

***rel*-(1*R*,2*S*,4a*S*,8a*S*)-1-amino-2-vinyl-4a-hydroxymethyl-perhydronaphthalene (56).** A suspension of 60.1 mg (0.194 mmole) of **55** in 0.5 mL of 30% HCl and 1 mL of EtOAc was stirred at room temperature for 30 min. After evaporation of the EtOAc under reduced pressure, 20 mL of a cold 2 M aq solution of NaOH was added. The aq layer was extracted with $CHCl_3$ (4 x 15 mL) and the organic extracts were dried (K_2CO_3) and concentrated *in vacuo* to give 36.0 mg (0.172 mmole, 89%) of **56** as a white solid, mp 109-111°C (hexane). IR 3380 and 3480-3020 (NH_2 and OH). ^1H NMR (100 MHz) 0.71-1.43 (m, 14 H), 2.99 (m, 1 H, C<u>H</u>NH_2), 3.17 (d, *J* 12 Hz, 1 H, C<u>H</u>OH), 3.46 (br. s, 3 H, NH_2 and OH), 4.14 (dd, *J* 2, 12 Hz, 1 H, C<u>H</u>OH), 4.99-5.27 (m, 2 H, HC=C<u>H</u>$_2$), 5.87 (m, 1 H, <u>H</u>C=CH_2). ^{13}C NMR (50 MHz) 22.0 (t), 22.9 (t), 26.0 (t), 27.4 (t), 37.4 (s, <u>C</u>CH_2OH), 39.5 (t), 41.6 (t), 45.2 (d), 49.7 (d), 52.8 (d), 66.2 (t, CH_2OH), 115.6 (t, HC=<u>C</u>H_2), 140.6 (d, H<u>C</u>=CH_2). Exact mass 209.1809 (calcd for $C_{13}H_{23}NO$ 209.1780).

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