INTRAMOLECULAR CYCLIZATION OF ALLYLSILYL SUBSTITUTED *N*-ACYLIMINIUM IONS. ACCESS TO 1- AND 2-AZABICYCLO[X.Y.0]-ALKANES. TOTAL SYNTHESIS OF (±)-MESEMBRINE

Yvonne Gelas-Mialhe, Jean-Claude Gramain, Hassane Hajouji, and Roland Remuson*

Laboratoire de Chimie des Substances Naturelles, URA CNRS 485, Université Blaise Pascal (Clermont-II), 63177 Aubière Cedex, France

Abstract - Access to 1- and 2-azabicyclo[x.y.0]alkanes by intramolecular cyclization of allylsilanes on α-acyliminium ions is described. This methodology is also used to achieve a highly stereoselective total synthesis of (±)- mesembrine.

N-Acyliminium ions have been shown to be highly important intermediates in organic synthesis.[1] *N*-Acyliminium ion - olefin cyclization revealed in several cases high regio- and stereoselectivities which were exploited with success in the total synthesis of several alkaloids such as histrionicotoxin,[2] gephyrotoxin,[3] lupinine[4] and isoretronecanol.[5]

Allylsilanes have been recently used as π-nucleophiles in organic synthesis.[6] These very reactive compounds are known to react with electrophiles with high regioselectivity due to the β effect of silicon.[7]

Intermolecular reactions of allylsilanes with *N*-acyliminium ions were described.[8] Intramolecular version with vinylsilanes,[9] allylsilanes[10] and propargylsilanes[11] was also observed, as well as allylsilanes-iminium ions cyclizations which generate substituted piperidines.[12]

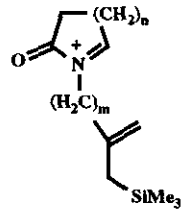
Azabicycloalkanes constitute important intermediates in alkaloid synthesis.[5] We wish to report here the access to 1-azabicyclo[x.y.0]alkane derivatives where the nitrogen atom is in the bridgehead position, 2-azabicyclo-[4.3.0]nonanes where the nitrogen atom is next to the ring junction and mesembrine which is a 7-azabicyclo-[4.3.0]nonane with the nitrogen atom in the α position of the ring junction. The route to these compounds we anticipated was based on an intramolecular cyclization of acyliminium ions substituted by an allylsilyl side chain as an internal π-nucleophile. α–Hydroxylactams and α-ethoxylactams produced from cyclic imides could serve as precursors to these intermediates.[13]

RESULTS AND DISCUSSION

1 - Synthesis of 1-azabicyclo[x.y.0]alkanes.

Access to 1-azabicyclo[x.y.0]alkanes was expected from *N*-acyliminium ions (**1**), (**2**) and (**3**) (Scheme 1). Ring closure of *N*-acyliminium intermediates (**1a**) and (**1b**) is an example of a 5-endo-trig process which is known to be disfavoured according to Baldwin's rules.[14] However, some exceptions have been encountered with this process[15] and we envisaged that this cyclization might be allowed due to the cation stabilizing β-effect of the

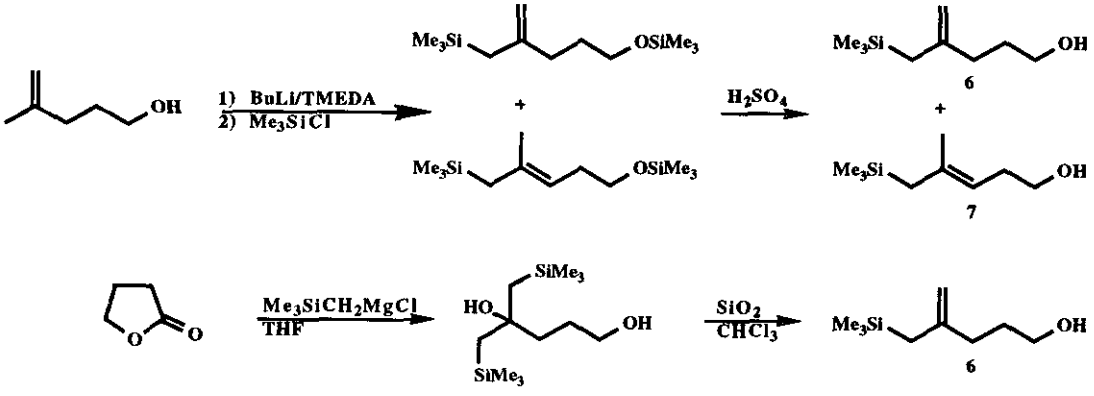
silicon atom. Ring forming reactions from **2** and **3** are 6- or 7-endo-trig cyclizations which are favoured.



1 a	**m=1**	**n=1**
1 b	**m=1**	**n=2**
2 a	**m=2**	**n=1**
2 b	**m=2**	**n=2**
3	**m=3**	**n=1**

Scheme 1

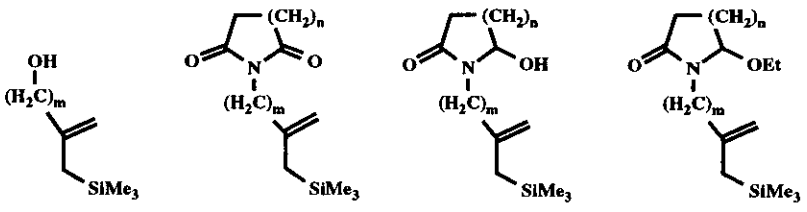
The synthesis of α-hydroxylactams or α–ethoxylactams precursors of intermediates (**1-3**) began with the preparation of alcohols (**4**), (**5**) and (**6**) (Scheme 3). Alcohol (**4**) was previously described by Trost.[16] Alcohol (**5**) was simultaneously synthesized by Japanese authors[17] and by us,[10] following the same procedure. Analogous reaction sequences with 4-methyl-4-penten-1-ol provided a 1:1 mixture of isomeric allylsilanes (**6**) and (**7**). They were separated by silica gel column chromatography (Scheme 2).



Scheme 2

This reaction leading to a mixture of isomeric products, we developed an alternative route to the required alcohol (**6**). Treatment of γ-butyrolactone with trimethylsilylmethylmagnesium chloride followed by treatment of the disilylated intermediate by silica gel, according to a described procedure,[18] afforded pure **6**. Synthesis of imides (**8**), (**9**) and (**10**) was accomplished from alcohols and succinimide or glutarimide *via* the Mitsunobu reaction.[19] Reduction of imides (**8-10**) with $NaBH_4$, by the method of Speckamp[20] and Chamberlin,[4] gave α-hydroxylactams (**11-13**). Hydroxylactams (**11a**) and (**12a**) were converted to ethoxylactams (**14**) and (**15**).
Five-membered ring forming reactions were attempted with α-hydroxylactams (**11a**) and (**11b**) and α-ethoxylactam (**14**). Treatment of **11a** and **11b** with trifluoroacetic acid (4 equiv.) in dichloromethane at room

temperature led exclusively to protodesylilated products. Cyclization also failed from **14** by treatment with Lewis acids ($TiCl_4$, $SnCl_4$ or BF_3 . Et_2O).[8,21]

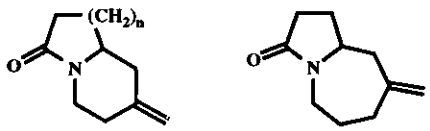


4 m=1 **5** m=2 **6** m=3

8a m=1 n=1 **8b** m=1 n=2 **9a** m=2 n=1 **9b** m=2 n=2 **10** m=3 n=1

11a m=1 n=1 **11b** m=1 n=2 **12a** m=2 n=1 **12b** m=2 n=2 **13** m=3 n=1

14 m=1 n=1 **15** m=2 n=1



16a n=1 **16b** n=2 **17**

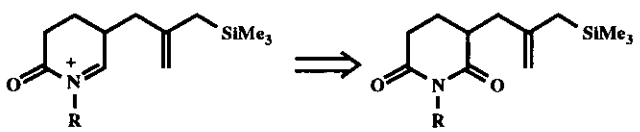
Scheme 3

Reactions of **12a**, **12b** and **13** with trifluoroacetic acid gave the cyclized products (**16a**), (**16b**) and (**17**) in respectively 70, 94 and 78 % yields. Compound (**16a**) was also obtained by treatment of **15** with $TiCl_4$ in dichloromethane.

Contrary to our expectations, our attempts at obtaining five-membered rings *via* a 5-endo-trig cyclization were unsuccessful. On the other hand, these reactions constitute excellent routes to functionalized indolizidines, quinolizidines and 1-azabicyclo[5.3.0]decanes.

2 - Synthesis of 2-azabicyclo[4.3.0]nonanes.

These compounds were assumed to be obtained from *N*-acyliminium ion (**18**) with the allylsilyl side chain α to the imide function (Scheme 4).



R = H, Me

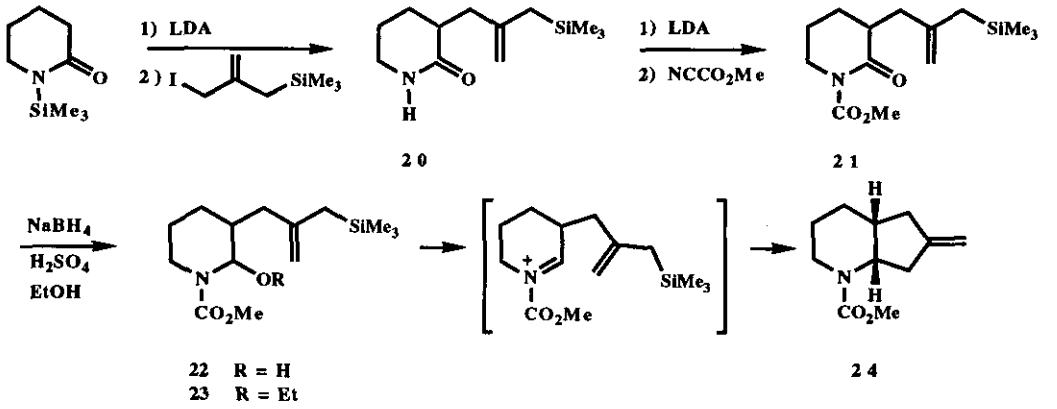
18 **19**

Scheme 4

Cyclization of **18** is a 5-exo-trig reaction which is a favoured process. Precursor of intermediate (**18**) was

thought to be the α-hydroxylactam produced from cyclic imide (**19**) coming from alkylation of glutarimide with 1-iodo-2-trimethylsilyl-2-propene. Introduction of a side chain in the position 3 of glutarimide has been described using sodium amide in liquid ammonia[22] or LDA in THF/HMPA.[23] Under these conditions we were not able to introduce the allylsilyl side chain at the α-carbon of glutarimide or *N*-methylglutarimide.

Because of the failure of this strategy, we considered an alternative method (Scheme 5). The key feature in this approach was based upon introduction of the allylsilyl side chain in the α-position of a lactam moiety, then *N*-methoxycarbonylation of the lactam in order to stabilize the iminium ion which would be formed during the cyclization step. We already used this strategy for the synthesis of azacarboprostacyclines.[24] This kind of cyclization is probably kinetically controlled and the stereochemistry of the isolated product is determined by the transition state of lowest energy. A careful examination of molecular models shows that the transition state which ensures a good orbital overlap should lead to the bicyclic compound with a *cis* stereochemistry of the ring junction.

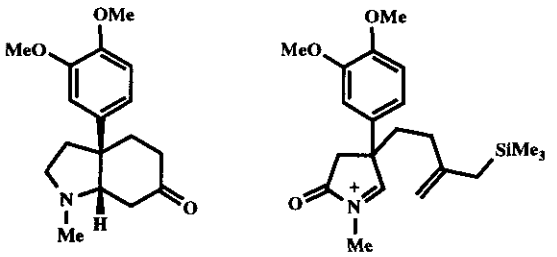


Scheme 5

Alkylation of *N*-trimethylsilylpiperidin-2-one at -78°C in THF using LDA as base with 1-iodo-2-trimethylsilylmethyl-2-propene led to the expected lactam (**20**) in 76% yield. *N*-Methoxycarbonylation of **20** gave **21** in 89 % yield. Either hydroxylactam (**22**) ($NaBH_4$, H_2SO_4, EtOH) or ethoxylactam (**23**) ($NaBH_4$, excess H_2SO_4, EtOH) were prepared by reduction of **21** according to Hiemstra's procedure.[25] Treatment of hydroxylactam (**22**) with CF_3CO_2H or ethoxylactam (**23**) with $TiCl_4$ led to a mixture of products resulting from cyclization and isomerization of the double bond. Therefore, we generated the acyliminium ion in a nonacidic medium; the reaction was carried out with methanesulfonyl chloride and triethylamine in dichloromethane. Under these conditions, hydroxylactam (**22**) led to a single bicyclic compound which was assigned structure (**24**). Although the stereochemistry of this compound has not yet been demonstrated (in particular, the H-1 and H-6 resonances in the nmr spectrum are too complex to allow the determination of coupling constants), it is supposed to be *cis* in view of stereoelectronic considerations (*vide infra*).

3 - Synthesis of (±)-Mesembrine.

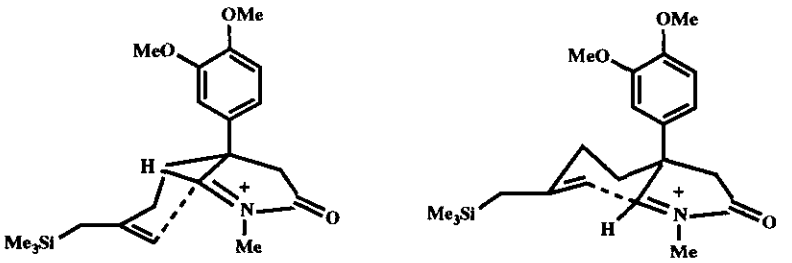
Mesembrine (**25**) is an alkaloid of considerable interest due to its CNS activity.[26] We planed to prepare this 7-azabicyclo[4.3.0]nonane *via* intramolecular cyclization of cyclic acyliminium ion (**26**) (Scheme 6).



25 26

Scheme 6

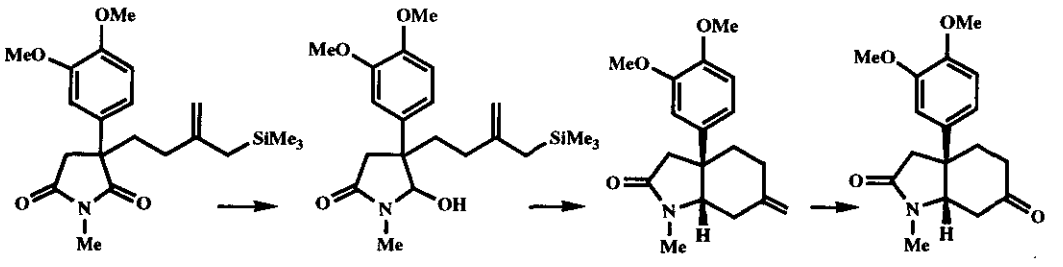
An important stereochemical issue concerns the ring junction stereochemistry which is established in the cyclization step. It was anticipated that this reaction would be highly stereoselective from considerations of the transition states. Among the two possible chair-like transition states (**A** and **B**), **A**, leading to the *cis* stereochemistry, would be predominant over **B**, leading to a *trans* ring junction, to avoid the steric repulsion between the aryl substituent and the π-nucleophile. Furthermore, p orbitals overlapping is possible in **A**, which is not the case in **B** (Scheme 7).



A B

Scheme 7

The requisite precursors of intermediate (**26**) were prepared according to Scheme 8.



27 28 29 30

Scheme 8

Alkylation of *N*-methyl-3-arylsuccinimide with tosylate of alcohol (**5**) is possible due to the presence of the aryl

substituent which increases the acidic character in α-position of the imide function. It gave imide (**27**) in 60 % yield. It seemed possible to carry out the regioselective reduction of the more sterically hindered carbonyl group of **27**, based on work with geminally disubstituted succinimides.[13] As expected, reduction of **27** exclusively afforded hydroxyamide (**28**) as a mixture of diastereoisomers which were not separated. Cyclization of **28** under usual acidic conditions (trifluoroacetic acid in dichloromethane) led to a mixture of isomeric compounds resulting from isomerization of the exocyclic double bond to the more stable endocyclic position. Therefore, the acyliminium ion was generated in a nonacidic medium (MsCl, Et_3N, CH_2Cl_2); it gave **29** as a single isomer, which was ozonized (O_3, then Me_2S) to give **30**. The ^{1}H-nmr spectrum of **30** was in excellent agreement with that of *cis*-1-methyl-3a-(3,4-dimethoxyphenyl)octahydroindole-2,6-dione depicted in the literature,[27] thereby establishing the *cis* stereochemistry of **29**.

As was anticipated, the reaction is highly stereoselective, we isolated a single isomer with a *cis* ring junction. As **30** has been shown to be a precursor of mesembrine (**25**),[27] this strategy constitutes a new formal total synthesis of (±)-mesembrine (**25**) in a highly stereoselective manner.

In conclusion, intramolecular nucleophilic attack of allylsilanes on acyliminium intermediates has been found to give methylene substituted azabicycloalkanes in good yields. Access to 5, 6 and 7 membered rings was possible by varying the size of the starting imide or the length of the allylsilyl chain. These cyclizations offer the opportunity of introducing an exocyclic methylene group as a useful functionality for further structural elaborations. Moreover, they proceed in a highly stereoselective manner. They are potentially very useful for the total synthesis of alkaloids, as was shown here with the synthesis of (±)-mesembrine. Studies of other applications of these reactions toward the synthesis of alkaloids are in progress.

EXPERIMENTAL

Proton nuclear magnetic resonance spectra were recorded on JEOL C 60 H and Bruker MSL 300 spectrometers. Carbon 13 nuclear magnetic resonance spectra were run on JEOL FX 60 and Bruker MSL 300 spectrometers. Chemical shifts are recorded as δ values (ppm) relative to tetramethylsilane as the internal reference standard. A Perkin-Elmer 377 instrument was used to determine ir spectra. Mass spectra were recorded on a Varian CH 5 spectrometer. Merck Kieselgel 60 PF_{254} plates were used for analytical chromatography. Products were purified by flash column chromatography using silica gel.

4-Trimethylsilylmethyl-4-penten-1-ol (**6**)

a) A procedure described by Ochiai[17] was followed. To a solution of *N,N,N',N'*-tetramethylethylenediamine (20 g, 0.17 mol) in hexane (160 ml) was added dropwise a hexane solution of n-butyllithium (1.5 M, 113 ml, 0.17 mol) followed by 4-methyl-4-penten-1-ol[28] (8.6 g, 0.086 mol), under nitrogen. The mixture was heated at 60°C for 6 h. The resulting red mixture was cooled to -78°C and trimethylchlorosilane (28 g, 0.26 mol) was added. The reaction mixture was stirred for 4 h at room temperature, then diluted with water and the products were extracted with ether and dried ($MgSO_4$). Evaporation of the solvent left a syrup which was purified by distillation (bp 95-110°C/15 mm Hg) to give a mixture (1:1) of disilylated compounds (14 g, 67 % yield), ^{1}H-nmr ($CDCl_3$) δ 5.00 (1H, m), 4.60 (2H, m), 3.40-3.70 (4H, m), 1.90-2.40 (6H, m), 1.60 (3H, s), 1.50 (4H, s), 0.01 (18H, s), 0.00 (18H, s); ^{13}C-nmr ($CDCl_3$) δ 147.3 (s), 135.3 (s), 118,3 (d), 107.5 (t), 63.0 (t), 62.6

(t), 34.8 (t), 32.7 (t), 31.3 (t), 27.3 (t), 26.7 (t), 23.8 (q), 0.0 .

The preceding mixture (14.7 g, 0.06 mol) in THF (110 ml) was treated with a 1N aqueous solution of H_2SO_4 (30 ml) for 20 min at 0°C. Solid anhydrous potassium carbonate was then added and the organic products were extracted with ether. After usual work-up, the crude product was distilled (bp 70-87°C/4 mm Hg) to give a mixture of alcohols (**6**) and (**7**) (6.5 g, 63 % yield; ir (CCl_4, cm^{-1}) 3350 and 1640); they were separated by flash column chromatography (Hexane-AcOEt 8:2). Alcohol **6** : spectral data identical with that reported.[29] Alcohol **7** : ^{1}H-nmr ($CDCl_3$) δ 5.20 (2H, t, J = 6.8 Hz), 3.75 (2H, t, J = 6.6 Hz), 3.40 (1H, s), 2.30-2.60 (2H, m), 1.90 (3H, broad s), 1.70 (2H, s), 0.20 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 135.9 (s), 118.0 (d), 62.5 (t), 32.4 (t), 26.5 (q), 23.6 (t), 0.0. Anal. Calcd for $C_9H_{20}OSi$: C, 62.79; H, 11.63. Found : C, 62.30; H, 11.91.

b) A procedure described by Ochiai[18] was followed. γ-Butyrolactone (4.4 g, 0.051 mol) in ether (15 ml) was added to a solution of trimethylsilylmethylmagnesium chloride (0.204 mol) in anhydrous ether (100 ml), at 0°C. The mixture was stirred for 2 h under reflux, then saturated aqueous NH_4Cl (50 ml) was added and the layers were separated. The aqueous phase was extracted with ether and the combined organic phases were dried ($MgSO_4$). The solvent was then removed and the crude product in $CHCl_3$ (200 ml) was stirred with silica gel for 24 h at room temperature. After filtration then concentration, the crude product was subjected to flash column chromatography (Hexane-AcOEt 8:2) to yield alcohol (**6**) (2.2 g, 25 %).

N-[2-(Trimethylsilylmethyl)prop-2-en-1-yl]succinimide (**8a**)

Diethyl azodicarboxylate (DEAD, 0.09 g, 0.5 mmol) was added dropwise to a solution of succinimide (0.05 g, 0.5 mmol), 1-hydroxy-2-trimethylsilylmethylpropene[16] (0.15 g, 1 mmol) and triphenylphosphine (0.13 g, 0.5 mmol) in anhydrous THF (2.5 ml). The resulting reaction mixture was stirred at room temperature for 8 h. After evaporation to dryness, the residue was purified by flash chromatography (Hexane-AcOEt 1:1) to afford **8a** as an oil (0.10 g, 89 %); ir (CCl_4, cm^{-1}) 1710 and 1780; ^{1}H-nmr ($CDCl_3$) δ 4.60 (2H, d, J = 6 Hz), 3.90 (2H, s), 2.75 (4H,s), 1.50 (2H, s), 0.00 (9H, s, $SiMe_3$). Anal. Calcd for $C_{11}H_{19}NO_2Si$: C, 58.63; H, 8.51; N, 6.22; Si, 12.43. Found : C, 58.63; H, 8.52; N, 6.22; Si, 11.90.

N-[2-(Trimethylsilylmethyl)prop-2-en-1-yl]glutarimide (**8b**)

According to the previous procedure we obtained **8b** as an oil in 46 % yield after purification by flash chromatography (Hexane-AcOEt 1:1); ir (CCl_4, cm^{-1}) 1650 and 1740; ^{1}H-nmr ($CDCl_3$) δ 4.40 (2H, d, J = 6 Hz), 4.10 (2H, s), 2.50 (4H, t, J=6 Hz), 1.10 (2H, m), 1.50 (2H, s), 0.00(9H, s, $SiMe_3$). Anal. Calcd for $C_{12}H_{21}NO_2Si$: C, 60.22; H, 8.85; N, 5.86; Si, 11.70. Found : C, 60.14; H, 8.65; N, 5.76; Si, 11.62.

N-[3-(Trimethylsilylmethyl)but-3-en-1-yl]succinimide (**9a**)

According to the previous procedure we obtained **9a** as an oil in 71 % yield after purification by flash chromatography (Hexane-AcOEt 1:1); ir (CCl_4, cm^{-1}) 1680 and 1730; ^{1}H-nmr ($CDCl_3$) δ 4.60 (2H, s), 3.60 (2H, t, J = 6 Hz), 2.65 (4H, s), 2.20 (2H, t, J = 6 Hz), 1.55 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 178.5, 145.3, 110.9, 38.6, 37.1, 29.6, 27.7, 0.0; exact mass calcd for $C_{12}H_{21}NO_2Si$ 239.1336; found 239.1346. Anal. Calcd for $C_{12}H_{21}NO_2Si$: C, 60.22; H, 8.85; N, 5.86; Si, 11.70. Found : C, 60.19; H, 8.88; N, 6.12; Si, 11.52.

N-[3-(Trimethylsilylmethyl)but-3-en-1-yl]glutarimide (**9b**)

According to the previous procedure we obtained **9b** as an oil in 46 % yield after purification by flash chromatography (Hexane-AcOEt 1:1); ir (CCl_4, cm^{-1}) 1680 and 1730; ^{1}H-nmr ($CDCl_3$) δ 4.55 (2H, s), 3.85 (2H, t, J = 7 Hz), 2.55 (4H, m), 2.10 (4H, m), 1.50 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 173.7, 146.1,

110.5, 39.5, 37.7, 34.3, 27.9, 18.6, 0.0. Anal. Calcd for $C_{13}H_{23}NO_2Si$: C, 61.62; H, 9.16; N, 5.53; Si, 11.05. Found : C, 61.48; H, 9.02; N, 5.80; Si, 10.71.

N-[4-(Trimethylsilylmethyl)pent-4-en-1-yl]succinimide (**10**)

According to the previous procedure we obtained **10** as an oil in 54 % yield after purification by flash chromatography (Hexane-AcOEt 6:4); ^{1}H-nmr ($CDCl_3$) δ 4.55 (2H, m), 3.48 (2H, t, J = 7 Hz), 2.70 (4H, m), 1.60-2.40 (4H, m), 1.50 (2H, s), 0.00 (9H, s); ^{13}C-nmr δ 177.0 (s), 145.9 (s), 107.3 (t), 38.4 (t), 35.1 (t), 28.0 (t), 26.6 (t), 25.5 (t), 0.0. Anal. Calcd for $C_{13}H_{23}NO_2Si$: C, 61.62; H, 9.16; N, 5.53; Si, 11.05. Found : C, 61.59; H, 9.25; N, 5.53; Si, 10.84.

1-[2-(Trimethylsilylmethyl)prop-2-en-1-yl]-5-hydroxy-2-pyrrolidone (**11a**)

A solution of **8a** (0.04 g, 0.16 mmol) and $NaBH_4$ (0.02 g, 0.5 mmol) in anhydrous methanol (3 ml) was stirred at - 5°C for 5 h. Water was added then extraction with $CHCl_3$ (3 x 3 ml), drying ($MgSO_4$), removal of the solvent and purification by flash chromatography (Hexane-AcOEt 3:7) gave **11a** as an oil (0.04 g, 94 %); ir (CCl_4, cm^{-1}) 1690; ^{1}H-nmr ($CDCl_3$) δ 5.10 (2H, d, J = 5 Hz), 4.60 (1H, broad s), 4.10 (1H, broad s, exch. with D_2O), 3.80 (2H, AB spectrum, J_{AB} = 15 Hz), 2.10 (4H, m), 1.50 (2H, s), 0.00 (9H, s). Anal. Calcd for $C_{11}H_{21}NO_2Si$: C, 58.12; H, 9.32; N, 6.16; Si, 12.32. Found : C, 58.27; H, 9.33; N, 6.07; Si, 12.02.

1-[2-(Trimethylsilylmethyl)prop-2-en-1-yl]-6-hydroxy-2-piperidone (**11b**)

According to the previous procedure we obtained **11b** as an oil in 67 % yield after purification by flash chromatography (Hexane-AcOEt 3:7); ir (CCl_4, cm^{-1}) 3300 and 1640; ^{1}H-nmr ($CDCl_3$) δ 4.90 (2H, broad s), 4.60 (2H, broad s with 1H exch. with D_2O), 3.90 (2H, AB spectrum, J_{AB} = 15 Hz), 2.40-1.50 (6H, m), 1.50 (2H, s), 0.00 (9H, s). Anal. Calcd for $C_{12}H_{23}NO_2Si$: C, 59.71; H, 9.61; N, 5.81; Si, 11.60. Found : C, 59.77; H, 9.56; N, 5.93; Si, 11.42.

1-[3-(Trimethylsilylmethyl)but-3-en-1-yl]-5-hydroxy-2-pyrrolidone (**12a**)

According to the previous procedure we obtained **12a** as an oil in 95 % yield after purification by flash chromatography (Hexane-AcOEt 3:7); ir (CCl_4, cm^{-1}) 3350 and 1670; ^{1}H-nmr ($CDCl_3$) δ 5.20 (1H, m), 4.60 (3H with 1H exch. with D_2O, m), 3.70-3.10 (2H, m), 2.40-2.00 (6H, m), 1.50 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 176.5, 145.9, 110.3, 84.5, 39.7, 37.3, 30.4, 29.5, 27.9, 0.0; exact mass calcd for $C_{12}H_{23}NO_2Si$ 241.1492; found 241.1493. Anal. Calcd for $C_{12}H_{23}NO_2Si$: C, 59.71; H, 9.61; N, 5.81; Si, 11.60. Found : C, 59.59; H, 9.66; N, 5.77; Si, 11.26.

1-[3-(Trimethylsilylmethyl)but-3-en-1-yl]-6-hydroxy-2-piperidone (**12b**)

According to the previous procedure we obtained **12b** as an oil in 67 % yield after purification by flash chromatography (Hexane-AcOEt 3:7); ir (CCl_4, cm^{-1}) 3300 and 1650; ^{1}H-nmr ($CDCl_3$) δ 6.40 (1H, t, J = 6 Hz), 4.55 (2H, s), 4.20 (1H exch. with D_2O, broad s), 3.70-3.10 (4H, m), 2.20-2.00 (4H, m), 1.60 (2H, m), 1.45 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 174.9, 145.9, 110.4, 63.0, 39.1, 38.8, 37.5, 33.4, 27.8, 23.4, 0.0; exact mass calcd for $C_{13}H_{25}NO_2Si$ 255.1448; found 255.1455. Anal. Calcd for $C_{13}H_{25}NO_2Si$: C, 61.14; H, 9.87; N, 5.49; Si, 10.96. Found : C, 61.03; H, 10.11; N, 5.13; Si, 10.76.

1-[4-(Trimethylsilylmethyl)pent-4-en-1-yl]-5-hydroxy-2-pyrrolidone (**13**)

According to the previous procedure we obtained **13** as an oil in 62 % yield after purification by flash chromatography (AcOEt); ir (CCl_4, cm^{-1}) 3320 and 1680; ^{1}H-nmr ($CDCl_3$) δ 5.95 (1H, d, J = 7.5 Hz), 5.40-5.00 (1H, m), 4.58 (1H, broad s), 4.52 (1H, broad s), 3.65-3.10 (2H, m), 2.55-1.65 (8H, m), 1.52 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 176.6, 147.8, 108.6, 84.3, 41.0, 36.8, 30.4, 29.4, 28.0, 26.9, 0.6. Anal.

Calcd for $C_{13}H_{25}NO_2Si$: C, 61.14; H, 9.87; N, 5.49. Found : C, 61.16; H, 10.20; N, 5.41.

1-[2-(Trimethylsilylmethyl)prop-2-en-1-yl]-5-ethoxy-2-pyrrolidone (**14**)

To a suspension of NaH (0.06 g, 2.5 mmol) in anhydrous THF (1.5 ml), EtI (0.47 g, 3 mmol) was added at 50°C. Then, **11a** (0.5 g, 2.2 mmol) in anhydrous THF (1 ml) was added dropwise over 15 min; the resulting solution was stirred for 2 h at 50°C then cooled and hydrolysed with H_2O. Extraction, drying ($MgSO_4$) and removal of the solvent afforded **14** as an oil (0.45 g, 80 %) after purification by flash chromatography (Hexane-AcOEt 1:1); ir (CCl_4, cm^{-1}) 1700; ^{1}H-nmr ($CDCl_3$) δ 4.90-4.70 (1H, m), 4.60 (2H, s), 3.60-3.20 (4H, m), 2.60-2.10 (4H, m), 1.60 (2H, s), 1.20 (3H, t, J = 6 Hz), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 174.9, 146.7, 108.9, 88.2, 61.9, 45.9, 28.9, 24.9, 84.0, 15.3, 0.0; exact mass calcd for $C_{13}H_{25}NO_2Si$ 255.1648; found 255.1648. Anal. Calcd for $C_{13}H_{25}NO_2Si$: C, 61.14; H, 9.87; N, 5.49. Found : C, 61.54; H, 9.73; N, 5.15.

1-[3-(Trimethylsilylmethy)but-3-en-1-yl]-5-ethoxy-2-pyrrolidone (**15**)

According to the previous procedure we obtained **15** as an oil in a 80% yield; ir (CCl_4, cm^{-1}) 1700; ^{1}H-nmr ($CDCl_3$) δ 5.10-4.90 (1H, m), 4.65 (2H, s), 3.80-3.20 (4H, m), 2.40-2.20 (6H, m), 1.60 (2H, s), 1.20 (3H, t, J = 6 Hz), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 176.0, 146.0, 110.1, 90.6, 62.8, 40.3, 37.4, 30.3, 27.9, 26.2, 16.7, 0.0; exact mass calcd for $C_{14}H_{27}NO_2Si$ 269.1804; found 269.1804. Anal. Calcd for $C_{14}H_{27}NO_2Si$: C, 62.42; H, 10.11; N, 5.49; Si, 10.96. Found : C, 61.54; H, 9.73; N, 5.15; Si, 10.86.

1-Aza-2-oxo-7-methylenbicyclo[3.4.0]nonane (**16a**)

To a solution of **12a** (0.24 g, 1 mmol) in anhydrous CH_2Cl_2 (3 ml) stirred to 0°C was added dropwise CF_3CO_2H (0.45 g, 4 mmol); the resulting mixture was stirred at 0°C for 4h then washed with saturated $NaHCO_3$, water and dried ($MgSO_4$). The solvent was removed and purification by flash chromatography (Hexane-AcOEt 1:9) afforded **16a** as an oil (0.1 g, 70 %); ir (CCl_4, cm^{-1}) 1690 and 1650; ^{1}H-nmr ($CDCl_3$) δ 4.83 (2H, s), 4.22 (1H, ddd, J = 13.0, 6.0, 1.5 Hz), 3.70-3.30 (1H, m), 2.70-1.50 (9H, m); ^{13}C-nmr ($CDCl_3$) δ 173.7, 143.65, 110.0, 58.3, 42.3, 40.7, 33.3, 30.2, 24.9; exact mass calcd for $C_9H_{13}NO$ 151.0994; found 151.0990. Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found : C, 71.38; H, 8.58; N, 9.15.

1-Aza-2-oxo-8-methylenbicyclo[4.4.0]decane (**16b**)

According to the previous procedure we obtained **16b** as an oil in 94 % yield after purification by flash chromatography (Hexane-AcOEt 1:9); ir (CCl_4, cm^{-1}) 1650; ^{1}H-nmr ($CDCl_3$) δ 5.10-4.80 (1H, m), 4.70 (2H, s), 3.50-3.00 (1H, m), 2.70-1.50 (11H, m); ^{13}C-nmr ($CDCl_3$) δ 169.4, 144.6, 109.5, 57.3, 43.1, 42.3, 34.0, 33.0, 30.0, 19.0; exact mass calcd for $C_{10}H_{15}NO$ 165.1150; found 165.1147. Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found : C, 72.48; H, 9.65; N, 8.38.

1-Aza-2-oxo-7-methylenbicyclo[3.5.0]decane (**17**)

According to the previous procedure we obtained **17** as an oil in 78 % yield after purification by flash chromatography (C_6H_6-MeOH 95:5); ir (CCl_4, cm^{-1}) 1670; ^{1}H-nmr ($CDCl_3$) δ 4.82 (1H, s), 4.71 (1H, s), 3.93 (1H, ddd, J = 2.5, 6.0, 14.0 Hz), 3.70-3.58 (1H, m), 2.85 (1H, ddd, J = 2.5, 11.0, 14.0 Hz), 2.46 (1H, dd, J = 4.3, 14.0 Hz), 2.90-2.70 (3H, m), 2.65-2.40 (2H, m), 1.80-1.50 (4H, m); ^{13}C-nmr ($CDCl_3$) δ 174.8, 145.7, 114.6, 59.2, 43.0, 41.7, 37.0, 30.9, 27.1, 25.3; ms (m/z) 165 (65), 150 (24), 137 (19), 122 (12), 110 (100), 97 (48), 96 (36), 84 (52), 82 (33), 81 (27). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.68; H, 9.16; N, 9.69. Found : C, 72.97; H, 9.20; N, 8.79.

3-[2-(Trimethylsilylmethyl)prop-2-en-1-yl]-2-piperidone (**20**)

To a solution of LDA obtained from $(iPr)_2NH$ (0.96g, 9.6 mmol) and nBuLi (6.6 ml, c = 1.5 M) in anhydrous

THF (5 ml) a solution of 1-trimethylsilyl-2-piperidone[30] (1.58 g, 9.2 mmol) in THF (5 ml) was added dropwise. The mixture was stirred at -78°C for 45 min. A solution of 1-iodo-2-(trimethylsilylmethyl)propene (2.4 g, 9.4 mmol) was then added and the resulting mixture was stirred overnight then allowed to warm to room temperature for 2 h. The mixture was poured into water and extracted with CH_2Cl_2. The combined organic layers were washed with 5 % NaOH, then water and dried ($MgSO_4$). After removal of the solvent and purification by flash chromatography (AcOEt) we obtained **20** as an oil (1.44 g, 72 %); ir (CCl_4, cm^{-1}) 1660; ^{1}H-nmr ($CDCl_3$) δ 7.50 (1H, broad s, exch. with D_2O), 4.60 (2H, s), 3.30-3.00 (2H, m), 2.60-1.40 (7H, m), 1.50 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 175.9, 145.5, 109.8, 42.8, 40.8, 39.5, 26.3, 26.0, 21.5, 0.0; exact mass calcd for $C_{12}H_{23}NOSi$ 225.1548; found 225.1547. Anal. Calcd for $C_{12}H_{23}NOSi$: C, 63.96; H, 10.29; N, 6.22; Si, 12.43. Found : C, 63.89; H, 10.11; N, 6.29; Si, 12.52.

1-Methoxycarbonyl-3-[2-(trimethylsilylmethyl)prop-2-en-1-yl)-2-piperidone (**21**)

To a solution of LDA (5 mmol) in anhydrous THF (10 ml) cooled to -78°C was added dropwise a solution of **20** (1 g, 4.5 mmol) in THF (50 ml); the mixture was stirred at -78°C for 45 min then neat methyl cyanoformate (0.4 g, 4.8 mmol) was added dropwise. The resulting mixture was stirred at -78°C overnight and allowed to warm to room temperature for 2 h. The mixture was poured into water and extracted with $CHCl_3$. Organic layers were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (AcOEt) afforded **21** as an oil (1.13 g, 89 %); ir (CCl_4, cm^{-1}) 1780 and 1710; ^{1}H-nmr ($CDCl_3$) δ 4.60 (2H, s), 3.90-3.70 (5H, m), 2.90-1.60 (7H, m), 1.50 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 174.3, 173.6, 144.9, 110.1, 54.0, 46.6, 42.4, 40.2, 26.3, 25.9, 21.8, 0.0; exact mass calcd for $C_{14}H_{25}NO_3Si$ 283.1598; found 283.1599.Anal. Calcd for $C_{14}H_{25}NO_3Si$: C, 59.33; H, 8.90; N, 4.94; Si, 9.88. Found : C, 59.51; H, 8.79; N, 4.89; Si, 9.75.

1-Methoxycarbonyl-2-hydroxy-3-[2-(trimethylsilylmethyl)prop-2-en-1-yl]piperidine (**22**)

To a solution of imide (**21**) (0.1 g, 0.35 mmol) in absolute ethanol (3 ml), cooled to 0°C, $NaBH_4$ (0.1 g, 2.6 mmol) was added. The mixture was stirred at 0°C while six drops of 2M H_2SO_4 were added each 15 min. After completion of the reaction, the mixture was poured into saturated $NaHCO_3$ and extracted with $CHCl_3$; the combined organic layers were washed with brine and dried (K_2CO_3). Removal of the solvent and purification by flash chromatography (AcOEt) gave **22** (0.07 g, 70 %) as an oil; ir (CCl_4, cm^{-1}) 3400 and 1700; ^{1}H-nmr ($CDCl_3$) δ 5.50 (1H, broad s), 4.60 (2H, s), 3.70-3.60 (5H, m), 3.20 (1H, broad s, exch. with D_2O), 2.20-1.40 (7H, m), 1.50 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 157.1, 146.9, 146.2, 110.8, 109.4, 90.3, 89.3, 53.2, 46.5, 45.4, 43.3, 40.9, 38.7, 28.0, 27.2, 16.0, 0.0. Anal. Calcd for $C_{14}H_{27}NO_3Si$: C, 58.91; H, 9.54; N, 4.91; Si, 9.81. Found : C, 58.67; H, 9.26; N, 4.87; Si, 10.13.

1-Methoxycarbonyl-2-ethoxy-3-[2-(trimethylsilylmethyl)prop-2-en-1-yl]piperidine (**23**)

To a solution of the imide (**21**) (1g, 3.5 mmol) in absolute ethanol (20 ml) cooled to -20°C, $NaBH_4$ (0.94 g, 25 mmol) was added. Then, each 15 min, 2M H_2SO_4 (six drops) was added. After completion of the reaction (1h), the mixture was treated with 6M H_2SO_4 until pH 2. The mixture was poured into saturated $NaHCO_3$ and extracted with $CHCl_3$; the combined organic layers were washed with brine, dried (K_2CO_3) and concentrated. Purification by flash chromatography (AcOEt) afforded **23** (1g, 90 %) as an oil; ir (CCl_4, cm^{-1}) 1700; ^{1}H-nmr ($CDCl_3$) δ 5.40 (1H, s), 4.60 (2H, s), 3.80 (3H, s), 3.70-3.40 (4H, m), 2.10-1.40 (7H, m), 1.50 (2H, s), 1.20 (3H, t, J = 7.0 Hz), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 157.7, 146.9, 146.1, 110.8, 109.2, 89.2, 89.0, 65.2, 53.2, 46.3, 45.4, 43.2, 41.0, 38.4, 28.2, 27.9, 27.4, 16.2, 0.0; exact mass calcd for $C_{16}H_{31}NO_3Si$ 312.9847; found 312.9846. Anal. Calcd for $C_{16}H_{31}NO_3Si$: C, 61.30; H, 9.97; N, 4.47; Si, 8.93. Found : C,

61.46; H, 10.05; N, 4.38; Si, 8.76.

2-Aza-2-methoxycarbonyl-8-methylenbicyclo[4.3.0]nonane (**24**)

To a solution of the hydroxycabamate (**22**) (0.16 g, 1.6 mmol) in anhydrous CH_2Cl_2 (0.6 ml) cooled to -20°C, NEt_3 (0.17 g, 1.7 mmol) and MsCl (0.19 g, 1.17 mmol) were added. The resulting solution was stirred at room temperature for 16 h, then washed with aqueous $NaHCO_3$, saturated NaCl and dried ($MgSO_4$). After removal of the solvent and purification by flash chromatography (AcOEt) we obtained **24** (0.14 g, 45 %) as an oil; ir (CCl_4, cm^{-1}) 1710 and 1670; ^{1}H-nmr ($CDCl_3$) δ 4.75 (2H, d, J = 16 Hz), 3.80–3.70 (4H, m), 3.60–3.40 (2H, m), 2.60 (2H, d, J = 7.5 Hz), 1.90–1.70 (4H, m), 1.70–1.50 (3H, m); ^{13}C-nmr ($CDCl_3$) δ 154.3, 143.7, 111.9, 52.9, 44.3, 42.1, 42.0, 24.7, 24.4, 21.7; exact mass calcd for $C_{11}H_{17}NO_2$ 195.1255; found 195.1258. Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found : C, 67.48; H, 8.86; N, 7.08.

N-methyl-3-(3,4-dimethoxyphenyl)-3-[3-(trimethylsilylmethyl)but-3-en-1-yl]succinimide (**27**)

To a solution of NaH (0.18g, 7.5 mmol) in dry DME (19 ml) under N_2 cooled to 0°C, was added a solution of *N*-methyl-3-(3,4-dimethoxyphenyl)succinimide[31] (0.8 g, 3.2 mmol) in dry DME (19 ml). To the stirred mixture, DMSO (19 ml) was quickly added and stirring was continued for 15 min at 0°C. Then, a solution of tosylate[32] (0.2 g, 6.4 mmol) of the alcohol (**5**) in DME (3 ml) was added dropwise over 5 min and, after addition was complete, the mixture was stirred at 50°C for 1 h. The mixture was then poured into H_2O (70 ml) and extracted with ether (3 x 20 ml). The combined extracts were washed with brine, dried ($MgSO_4$) and concentrated. After purification by flash chromatography (Hexane-AcOEt 7:3) we obtained **27** (0.74 g, 60 %) as an oil; ir (CCl_4, cm^{-1}) 1780 and 1710; ^{1}H-nmr ($CDCl_3$) δ 7.20-6.80 (3H, m), 4.60 (2H, s), 3.92 (3H, s), 3.90 (3H, s), 3.06-3.02 (2H, m), 3.05 (3H, s), 2.50-2.00 (4H, m), 1.55 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 181.7, 176.9, 150.5, 149.8, 147.5, 133.9, 119.8, 112.5, 111.2, 108.9, 57.3, 52.6, 42.7, 39.8, 34.4, 28.3, 26.3, 0.0; exact mass calcd for $C_{21}H_{31}NO_4Si$ 389.2014; found 389.2015. Anal. Calcd for $C_{21}H_{31}NO_4Si$: C, 64.75; H, 8.03; N, 3.60; Si, 7.19. Found : C, 64.81; H, 8.04; N, 7.08; Si, 7.33.

1-Methyl-4-(3,4-dimethoxyphenyl)-4-[3-(trimethylsilylmethyl)but-3-en-1-yl]-5-hydroxy-2-pyrrolidone (**28**)

A mixture of **27** (0.17 g, 0.45 mmol) and $NaBH_4$ (0.12 g, 3.2 mmol) in EtOH (8 ml) was stirred at 0°C while at regular intervals (15 min) 3-4 drops of 2N HCl in EtOH were added. Stirring was continued for 24 h then the solution was poured into H_2O and extracted with $CHCl_3$. The extract was dried ($MgSO_4$), the solvent was removed and purification by flash chromatography (AcOEt) afforded **28** (0.1 g, 67 %) as an oil; ir (CCl_4, cm^{-1}) 3350, 1710 and 1685; ^{1}H-nmr ($CDCl_3$) δ 7.10-6.80 (3H, m), 6.50-6.00 (1H, m), 5.30-5.10 (1H, m), 4.70-4.50 (2H, m), 3.90 (6H, s), 2.90 (5H, m), 2.10-1.30 (4H, m), 1.50 (2H, s), 0.00 (9H, s); ^{13}C-nmr ($CDCl_3$) δ 175.8, 149.2, 142.7, 140.8, 138.2, 110.1, 96.8, 94.7, 90.1, 85.2, 50.1, 28.2, 0.0; exact mass calcd for $C_{21}H_{33}NO_4Si$ 391.2170; found 391.2171. Anal. Calcd for $C_{21}H_{33}NO_4Si$: C, 64.41; H, 5.94; N, 3.58; Si, 7.15. Found : C, 64.09; H, 5.82; N, 3.92; Si, 7.08.

7-Aza-7-methyl-8-oxo-1-(3,4-dimethoxyphenyl)-4-methylenbicyclo[3.4.0]nonane (**29**)

To a solution of **28** (0.12 g, 0.3 mmol) in anhydrous CH_2Cl_2 (0.2 ml) cooled to - 20°C, NEt_3 (0.03 g, 0.32 mmol) and MsCl (0.036 g, 0.32 mmol) were added. The resulting solution was stirred overnight at room temperature. The reaction was quenched with sat. $NaHCO_3$, extracted with CH_2Cl_2 (3 x 1 ml) and the extract was washed with sat. NaCl and dried ($MgSO_4$). After removal of the solvent and purification by flash chromatography (AcOEt) we obtained **29** (0.07 g, 80 %) as an oil; ir (CCl_4, cm^{-1}) 1680 and 1650; ^{1}H-nmr ($CDCl_3$) δ 6.90 (3H, s), 4.80 (2H, s), 4.00 (1H, t, J = 4.5 Hz), 3.90 (6H, s), 2.80 (3H, s), 2.60-2.40 (2H,

m), 2.20-1.90 (6H, m); ^{13}C-nmr ($CDCl_3$) δ 173.7, 150.4, 149.7, 143.0, 133.8, 118.4, 112.4, 111.3, 110.2, 64.4, 56.0, 47.2, 42.6, 35.9, 35.5, 29.7, 26.9; exact mass calcd for $C_{18}H_{23}NO_3$ 301.1672; found 301.1675. Anal. Calcd for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.65. Found : C, 71.86; H, 7.68; N, 4.35.

7-Aza-7-methyl-4,8-dioxo-1-(3,4-dimethoxyphenyl)bicyclo[3.4.0]nonane (**30**)

To a solution of **29** (0.03 g, 0.11 mmol) in CH_2Cl_2-MeOH (1:1) (2 ml) was added 0.1 ml of 0.1 % sudan red 7B/methylene chloride solution. The red solution was cooled to -78°C and ozonized until the red color began to lighten. The solution was rapidly purged with N_2 for 10 min. then treated with dimethyl sulfide (0.1 ml) and allowed to warm to room temperature. The solution was washed twice with water, once with brine and dried ($MgSO_4$). After removal of the solvent and purification by flash chromatography (AcOEt) we obtained **30** (0.032 g, 95 %) as an oil; the spectral data are identical with that reported;[27] ir (CCl_4, cm^{-1}) 1720 and 1690; ^{1}H-nmr ($CDCl_3$) δ 6.90-6.80 (3H, m), 4.40 (1H, t, J = 7.0 Hz), 3.90 (6H, s), 2.90-2.70 (7H, m), 2.40-2.30 (4H, m); ^{13}C-nmr ($CDCl_3$) δ 216.7, 175.4, 149.6, 147.2, 118.4, 112.4, 111.4, 110.0, 64.8, 55.2, 46.4, 41.5, 36.2, 31.2, 29.0, 25.2.

REFERENCES

1. H. E. Zaug, Synthesis, 1984, **85**, 181; W. N. Speckamp and H. Hiemstra, Tetrahedron, 1985, **41**, 4367; W. N. Speckamp, Rec. Trav. Chim. Pays Bas, 1981, **100**, 345.
2. H. E. Schoemaker and W. N. Speckamp, Tetrahedron, 1980, **36**, 951.
3. D. J. Hart and K. J. Kamai, J. Am. Chem. Soc., 1983, **105**, 1255.
4. A. R. Chamberlin, H. D. Nguyen, and J. Y. L. Chung, J. Org. Chem., 1984, **49**, 1682.
5. H. Hiemstra, M. H. A. M. Sno, R. J. Vijn, and W. N. Speckamp, J. Org. Chem., 1985, **50**, 4014.
6. T. N. Danks, S. E. Thomas, and T. Gallagher, "Specialist Periodical Report, Organic and Synthetic Methods", Vol. 12, The Royal Society of Chemistry, Burlington House, London 1990, pp. 365-370; H. H. Mooiweer, H. Hiemstra, and W. N. Speckamp, Tetrahedron, 1989, **45**, 4627; G. Majetich, J. Defauw, and C. Ringold, J. Org. Chem., 1988, **53**, 50.
7. I. Fleming, "Comprehensive Organic Chemistry", ed. by D. Barton and W. D. Ollis, Pergamon Press, 1979, 539.
8. G. A. Kraus and K. Neuenschwander, J. Chem. Soc., Chem. Commun., 1982, 134.
9. L. E. Overman, T. C. Malone, and G. P. Meier, J. Am. Chem. Soc., 1983, **105**, 6993.
10. J.-C. Gramain and R. Remuson, Tetrahedron Lett., 1985, **26**, 327.
11. H. Hiemstra and W. N. Speckamp, Tetrahedron Lett., 1983, **24**, 1407.
12. P. A. Grieco and W. F. Fabre, Tetrahedron Lett., 1986, **17**, 5067.
13. J. B. P. A. Wijnberg, H. E. Schoemaker, and W. N. Speckamp, Tetrahedron, 1978, **34**, 179.
14. J. E. Baldwin, J. Chem. Soc., Chem. Commun., 1976, 734.
15. B. Tarnchompoo, C. Thebtaranonth, and Y. Thebtaranonth, Tetrahedron Lett., 1987, **28**, 6675; A. Padwa and B. H. Norman, Tetrahedron Lett., 1988, **29**, 3041; H. Ishibashi, N. Nakamura, T. Sato, M. Takeuchi, and M. Ikeda, Tetrahedron Lett., 1991, **32**, 1725.
16. B. M. Trost and D. M. T. Chan, J. Am. Chem. Soc., 1983, **105**, 2315; B. M. Trost, D. M. T. Chan, and T.N. Nanninga, Org. Synth., 1984, **62**, 58.

17. M. Ochiai, E. Fujita, M. Arimoto, and H. Yamaguchi, Chem. Pharm. Bull., 1983, **31**, 86.
18. M. Ochiai, E. Fujita, M. Arimoto, and H. Yamaguchi, J. Chem. Soc., Chem. Commun., 1982, 1108.
19. O. Mitsunobu, Synthesis, 1981, 1.
20. J. C. Hubert, J. B. P. A. Wynberg, and W. N. Speckamp, Tetrahedron, 1975, **31**, 1437.
21. D. J. Hart and Y. M. Tsai, Tetrahedron Lett., 1981, **22**, 1567.
22. J. F. Wolfe and T. G.Rogers, J. Org. Chem., 1970, **35**, 3600.
23. R. Schlecker and D. Seebach, Helv. Chim. Acta, 1977, **60**, 1459.
24. J.-C. Gramain and R. Remuson, Heterocycles, 1989, **29**, 1263.
25. K. H. Melching, H. Hiemstra, W. J. Klaver, and W. N. Speckamp, Tetrahedron Lett., 1986, **27**, 4799.
26 J.-C. Gramain and R. Remuson, Tetrahedron Lett., 1985, **26**, 4083 and references cited therein.
27. H. Taguchi, T. Oh-Ishi, and H. Kugita, Chem. Pharm. Bull., 1970, **18**, 299.
28. M. C. Pirrung, J. Am. Chem. Soc., 1981, **103**, 82.
29. R. Ahmed-Schofield and P. S. Mariano, J. Org. Chem., 1985, **50**, 5667.
30. T. Nagasaka, S. Esumi, N. Ozawa, Y. Kosugi, and F. Hamaguchi, Heterocycles, 1981, **16**, 1987.
31. G. N. Walker, J. Am. Chem. Soc., 1956, **78**, 3698.
32. Tosylate was prepared from the corresponding alcohol **5** using standard conditions (TsCl, pyridine, 0°C, overnight).

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