heterocycles, Vol. 60, No. 60, 2003, pp. 1123 - 1132
Received, 14th January, 2003, Accepted, 14, March, 2003, Published online, 17th March, 2003

EQUILIBRIUM BETWEEN *BIS*(1,3-OXAZOLIDIN-3-YL])METHANES AND 3,8-DIOXA-1,6-DIAZABICYCLO[4.4.1]UNDECANES

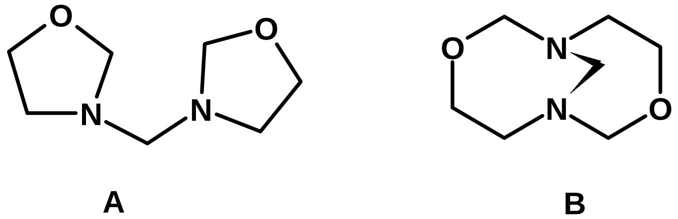
Raúl Salas-Coronado, Juan Carlos Gálvez-Ruiz, Carlos Guadarrama-Pérez, and Angelina Flores-Parra*

Chemistry Department, Centro de Investigación y de Estudios Avanzados, I.P.N. A.P. 14-740, C.P. 07000, México D.F., México Fax: (internat.) + 525555747113. E-mail: aflores@mail.cinvestav.mx

Abstract - The equilibrium between *bis*(1,3-oxazolidin-3-yl])methanes (**A**) and 3,8-dioxa-1,6-diazabicyclo[4.4.1]undecanes (**B**) is reported. **A** and **B** were prepared from formaldehyde and (±)-1-methylethanolamine (**1**), 2,2-dimethyl-ethanolamine (**2**), (1*S*, 2*R*)-1-methyl-2-phenylethanolamine (**3**), ethanolamine (**4**), (*R*)-2-carboxyethanolamine methyl ester (**5**), (*S*)-2-ethylethanolamine (**6**), (*R*)-2-phenylethanolamine (**7**). The equilibrium depends on the substituents. Thermodynamic structures (**A**) derived from **5** and **7** by slow crystallization are completely transformed into undecanes (**B**) by an equilibrium asymmetric transformation. Structures were established by ^{1}H, COSY, HETCOR and NOESY NMR experiments. Preferred conformer of the undecane ring was identified.

Condensation of formaldehyde with primary amines is a versatile reaction that gives different products depending on the ratio of the reagents, reaction conditions, steric demand of the amine and the presence of sulfur salts. Using the condensation of formaldehyde and amines, we have prepared:[1] [*N*,*N'*-dialkyltetrahydro-1,3,5-oxadiazines,[1a] *N*,*N'*,*N''*-trialkylhexahydro-1,3,5-triazines[1b] or *N*-alkyldihydro-1,3,5-dithiazines.[1c,d] The reactions with ethylene-, propylene- or butylenediamines afford bis-dithiazines or bicyclo[1.3]heterononanes.[1c]

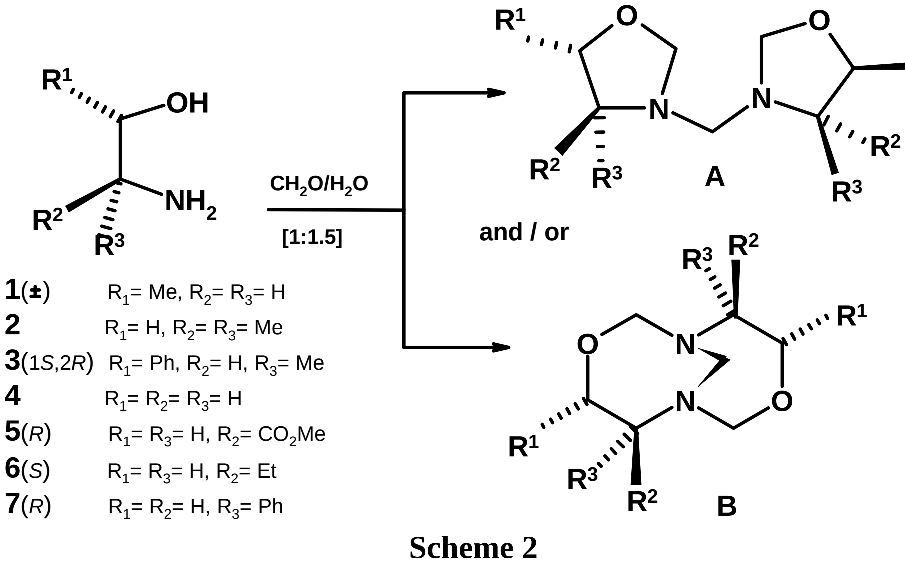
It is reported that the reaction of ethanolamines with formaldehyde in a [1:1.5] ratio provides two different heterocycles,[2] normaly [*bis*(1,3-oxazolidine)methane (**A**) or dioxabicyclo[4.4.1]undecane (**B**)], whereas reactions of formaldehyde with β-functionalized ethyleneamines [$H_2N(CH_2)_2XH$, X = NH or S] give exclusively *bis*(1,3-heterazolidine)methanes (**A**).[3] To our knowledge the presence of an equilibrium between species (**A**) and (**B**) has not been reported, Scheme 1.



Scheme 1

It is also published that the reaction of the (*S*)-1-phenylethanolamine, with an excess of formaldehyde at pH 3 gives the *bis*(oxazolidine)methane,[2c,f] whereas its isomer 2-phenylethanolamine (**7**) affords the dioxabicyclo[4.4.1]undecane under the same conditions.[2d,g]

Related with our interest in the study on these reactions, we have investigated the condensation products of seven ethanolamines [(±)-1-methylethanolamine (**1**), 2,2-dimethylethanolamine (**2**), (1*S*,2*R*)-1-methyl-2-phenylethanolamine (**3**), ethanolamine (**4**), (*R*)-2-carboxyethanolamine methyl ester (**5**), (*S*)-2-ethylethanolamine (**6**), 2-(*R*)-phenylethanolamine (**7**)] and formaldehyde in order to understand the factors determining the route to heterocycles (**A**) or (**B**), Scheme 2.



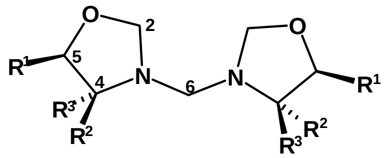
Scheme 2

Compounds (**2A**),[2a] (**3A**)[2b,e] and (**7B**)[2d,f] are already reported. Identification of the structures was performed by ^{1}H and ^{13}C, HETCOR, COSY and NOESY NMR spectral experiments, MS spectra, IR and elemental analyses.

Results and discussion

Ethanolamines and formaldehyde were allowed to react in a 1/1.5 ratio respectively, at two different conditions: a) in THF at -78^{o}C and b) in toluene at 110^{o}C, with the exception of ethanolamine which was reacted in water at 5^{o}C. The reaction products were identified and quantified directly from the reaction mixtures, and in some cases isolated. Mixtures of the isomers (**A** and **B**) were submitted in each case to a detailed NMR spectral analyses, Tables 1- 4.

Table 1 ^{13}C and ^{14}N NMR spectral data of *bis*(oxazolidin-3-yl)methanes (**1A-7A**), in $CDCl_3$



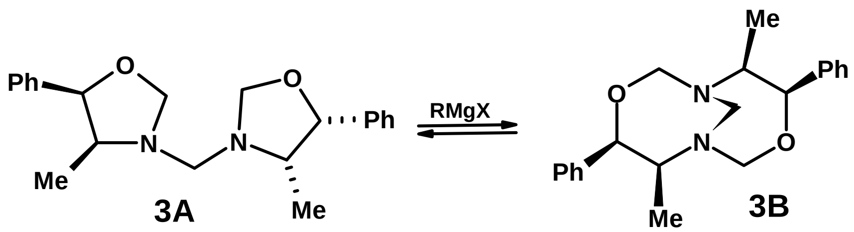
Compds	R[1]	R[2]	R[3]	**C-2**	**C-4**	**C-5**	**C-6**	^{15}**N**	^{14}**N**($h_{1/2,}H_z$)
1A(1)	Me	H	H	84.08 84.07	57.19 57.17	74.84 74.81	70.63 70.62	-314.3	-324(3,167)
2A(2)	H	Me	Me	85.3	58.5	79.0	60.6	-313.3	
3A(3)	Ph	Me	H	85.1	60.0	80.2	72.5	-308.2	
4A	H	H	H	85.4	50.6	63.3	74.6	-315.0	-307(2,127)(4)
5A(5)	H	H	CO_2Me	87.1	64.4	69.5	74.4	-310.8(4)	
5A(6)	H	H	CO_2Me	85.6	62.7	67.7	74.8		
6A(7)	H	H	Et	84.4	63.3	69.4	75.7	-306.9	-300(4,170)
7A(8)	H	H	Ph	86.8	65.3	73.9	71.4	-306.8	

(1) Isomeric mixture; (R^1) ^{13}C δ, 19.7(br s). (2) (R^2 and R^3) ^{13}C δ, 22.0. (3) (R^1) ^{13}C δ, C_i 139.5, C_o 127.1, C_m 127.9, C_p 127.3 and (R^2) δ, 15.2. (4) Measured from a mixture A/B. (5) (R_3) ^{13}C δ, 171.8 and 51.6. (6) In Py-d_5; (R^3) ^{13}C δ, 172.6 and 51.7. (7) (R^2) ^{13}C δ, 26.8. (8) In toluene-d_8 , (R^2 and R^3) ^{13}C δ, C*i* 141.7, C*o* 128.5, C_m 129.3, C_p 128.2. ^{15}N NMR in $CDCl_3$.

1-Methylethanolamine (**1**), 2,2-dimethylethanolamine (**2**), (1*S*,2*R*)-2-methyl-1-phenylethanolamine (**3**) and (*S*)-2-ethylethanolamine (**6**) reacted with formaldehyde in THF at -78^{o}C or in toluene at 110^{o}C to give **A**/**B** mixtures in the ratio (90/10 for **1** and **6** and 80/20 for **2**). Compound (**1A**) was prepared from the racemic ethanolamine and two diasteromers are formed. Compound (**3**) gave exclusively **3A** (98% yield), identified by its ^{1}H NMR spectrum. It has been reported that compound (**3A**) can be prepared from an excess of formaldehyde in water at pH 3 and heated at 75°C.[2e] In our hands the reported reaction lead to a complex mixture of several compounds, which we were unable to separate.

In [1]H NMR, heterocycles (**1A-5A**) present singlets for CH_2-2 and CH_2-6 due to the conformational equilibrium of the oxazolidine rings, Table 1. Whereas **6A** and **7A** are present in a preferred conformation and show a AB coupling pattern.

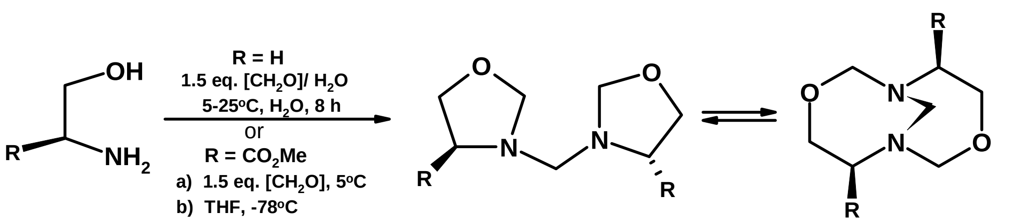
In order to check if there was an equilibrium between heterocycles (**A**) and (**B**), compounds (**1A-3A**) were heated in deuterated toluene at 90°C for one hour. No change was found in the [1]H NMR spectra. But compound (**3A**) in the presence of MeMgCl (0.5 equivalent, THF, 1 h at 0°C) gave slowly an equimolar mixture of **3A**/**3B** as detected by [13]C NMR spectroscopy. Hydrolysis of the Grignard reagent makes the mixture to completely return to compound (**3A**), Scheme 3.



3A 3B

Scheme 3

Ethanolamine (**4**) (in water at 5°C) and ester (**5**) (in THF at -78°C) or both in toluene at 110°C reacted with formaldehyde to afford a mixture of compounds (**A**) and (**B**). These could not be separated by distillation under vacuum and their ratio [**4A**:**4B** (40:60), **5A**:**5B** (50:50)] remained constant in vacuum distillated fractions showing that **A** and **B** are in equilibrium with our another, Scheme 4.



4A R=H **(40%)** **4B** R=H **(60%)**

5A R=CO_2Me **(50%)** **5B** R=CO_2Me **(50%)**

Scheme 4

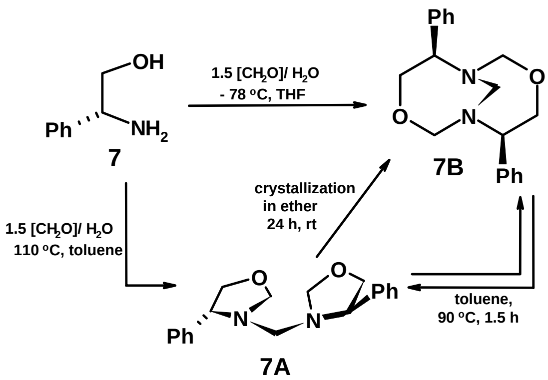
When the equimolar mixture of compounds (**5A**/**5B** [1:1]) ratio is dissolved in ether and hexane is added, compound (**5B**) crystallized and was characterized by its [1]H NMR spectrum.[2h] After separation of **5B** (70%), the residual solution still contained an equimolecular mixture of **5A** and **5B**.

Table 2 ^{1}H NMR spectral data of *bis*(oxazolidin-3-yl)methanes (**1A-7A**), in $CDCl_3$

Compds	**H2**		**H4**		**H5**		**H6**
1A[(1)]	4.26	(s)	2.35; 2.33 3.08, 3.07	(dd; 11.4,7.4) (dd; 11.4,6.4)	3.89	(ddd; 7.4,6.4,6.2)	3.23(s)
2A[(2)]	4.44	(s)		-	3.55	(s)	3.33(s)
3A[(3)]	4.90	(s)	3.44	(dq; 7.5,6.3)	5.10	(d; 7.5)	4.50(s)
4A	4.31	(s)	2.99	(t; 6.9)	3.63	(t; 6.9)	3.22(s)
5A[(4)]	4.44	(s)	3.68	(t; 6.5)	4.03; 3.98	(dd; 15.8,6.5)	3.50(s)
6A[(5)]	4.17 4.49	(d; 5.7) (d; 5.7)	2.85	(m)	3.22 3.85	(dd; 7.7, 5.9) (dd; 7.7, 6.9)	3.23(s)
7A[(6)]	4.21 4.79	(d; 3.7) (d; 3.7)	3.36	(t; 7.7)	3.92; 3.47	(t; 7.7)	3.09(s)

[(1)] Isomeric mixture; (R^1) ^{1}H δ, 1.08 (d, 6.2). [(2)] (R^2 and R^3) ^{1}H δ, 1.10 (s). [(3)] (R^1) ^{1}H δ, Ph 7.2-7.4 (m) and CH_3 0.68 (d; 6.3 Hz). [(4)] (R^3) ^{1}H δ, OCH_3, 3.48 (s). [(5)] (R^2) ^{1}H δ, 1.43 (m, H_A), 1.27 (m, H_B) and 0.84 (t, 6.9 Hz). [(6)] In toluene, (R^3) ^{1}H δ, Ph at 7.2-7.4 (m).

Reaction of formaldehyde with amine (**7**) at low temperature in THF gave only compound of type (**B**) but at 110°C in toluene both isomers, (**A**) and (**B**), were observed in a [90/10] ratio, respectively. Heating pure isomer (**7B**) for 1 h in toluene at 110°C gives a mixture of **7A** (90%) and **7B** (10%), whereas heating the **7A**/**7B** mixture (90/10) for 12 h in toluene at 110°C did not change this ratio. This result indicates that heterocycle (**7A**) thermodynamic whereas **B** is the kinetic product, Scheme 5. In this isomerization, an imine could be an intermediate, and indeed it has been detected in the ^{13}C NMR spectrum (164 ppm).



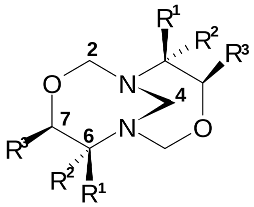
Scheme 5

Slow crystallization of compound (**7A**) in ether totally transformed compound (**7A**) into its constitutional isomer (**7B**). This phenomenon is known as equilibrium asymmetric transformation.[4] It happens when the crystallization is slower than the isomerization rate, in this case, one isomer is completely transformed into the crystalline solid of the second thermodynamically less stable isomer.

Conformational Analysis of Bicyclo[4.4.1]undecanes (B).

Tables 3 and 4 show ^{13}C, ^{15}N, ^{14}N and ^{1}H NMR spectral data of compounds (**1B-7B**). The ^{15}N and some ^{14}N NMR data obtained for compounds of type (**A**) and (**B**) are normal for tertiary amines. (**B**) and (**A**) cycles do not have important differences in ^{13}C NMR spectra.

Table 3 ^{13}C and ^{15}N NMR spectral data of compounds (**1B-7B**), in C_7D_8



Compds	R^1	R^2	R^3	**C-2**	**C-4**	**C-6**	**C-7**	^{15}**N**	^{14}**N**($h_{1/2}$, Hz)
1B(1)	Me	H	H	85.9	72.5	74.3	57.1		
2B(2)	H	Me	Me	83.9	77.1	58.7	78.0		
3B(3)	Me	H	Ph	80.3	(4)	80.0	61.4		
4B	H	H	H	86.9	70.7	51.8	67.6		-307(2,127)(5)
5B (6)	H	H	CO_2Me	85.0	74.4	61.7	66.4	-310.8(5)	-324(3,167)
6B(7)	H	H	Et	86.6	71.8	61.7	67.7		
7B(8)	H	H	Ph	86.2	71.1	66.3	74.6		
7B(9)	H	H	Ph	86.2	71.1	65.8	74.4	-306.8	

(1) ^{13}C δ, (R^1) 20.8. (2) ^{13}C δ, (R^2 and R^3) 22.9. (3) ^{13}C δ, (R^1) 15.0, (R^3) C*i* 137.5, C_o 126.0, C_m 128.0, C_p 127.2. (4) Signal was not assigned. (5) Measured from a mixture **1**A/**1**B. (6) (R^2) ^{13}C δ, 171.9 and 51.4. (7) ^{13}C δ, (R^2) 22.9, 12.0. (8) (R^2) ^{13}C δ, C*i* 142.2, C_o 127.4, C_m 128.1, C_p 127.0. (9) In $CDCl_3$; ^{13}C δ, (R^2) C*i* 140.5, C_o 127.6, C_m 128.7, C_p 127.5.

Table 4 ^{1}H NMR spectral data of **2B-7B** in C_7D_8

Compds	**H-2**		**H-4**	**H-6**		**H-7**	
2B	**H**	4.57 (s)	3.47(s)		-	**H**	4.18(s)
3B(1)	**HA**	5.09 (d)	(2)	**H**	3.13 (dq)	**H**	5.19(d)
	HB	4.52 (d)					
4B	**Heq**	4.25 (d)	4.22(s)	**Heq H**	3.00 (ddd)	**Heq**	3.89(dd)
	Hax	4.05 (d)			3.12 (ddd)	**Hax**	3.59(ddd)
5B(3)	**Heq**	3.88 (d)	4.20(s)	**Hax**	4.02 (dd)	**Heq**	3.80(dd)
	Hax	4.36 (d)				**Hax**	3.59(dd)
6B(4)	**Heq**	3.96 (d)	4.03(s)	**Hax**	3.06 (dd)	**Heq**	3.77(dd)
	Hax	4.27 (d)				**Hax**	3.32(dd)
7B(5)	**Heq**	3.88 (d)	4.48(s)	**Hax**	4.68 (dd)	**Heq**	3.78(dd)
	Hax	4.17 (d)				**Hax**	3.54(dd)
7B(6)	**Heq** **Hax**	4.20 (s)	4.84(s)	**Heq**	4.63(t, 6.0)	**Heq** **Hax**	3.87(d, 6.0)

(1) ^{1}H δ, (R^1) 0.96 (d, 6.7), (R^3) 7.2-7.4. (2) Signal was not assigned. (3) ^{1}H δ, (R^2) 3.69. (4) ^{1}H δ, (R^2) 1.30, 0.90. (5) ^{1}H δ, (R^2) 7.2-7.4 (m). (6) In $CDCl_3$; ^{1}H δ, (R^2) 7.0-7.3 (m).

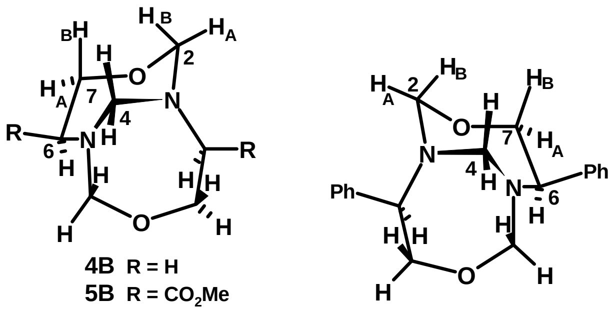
In ^{1}H NMR spectra, the C2 symmetry axis of heterocycles (**B**) makes the two protons of [N-C(4)H_2-N] equivalent, whereas [N-C(2)H_2-O] and [O-C(7)H_2-C] present AB coupling patterns, the values of the geminal couplings > 10.4 Hz reveal an anchored system, Table 5. Analyses of ^{3}J(H/H) coupling constants and the correlation established by NOESY NMR spectra experiments show that heterocycles (**4B**, **5B** and **7B**) are present in the same preferred conformation.

Table 5 Coupling constants and calculated dihedral angle values of **4B**-**7B**

Compds	^{2}J(H2ax/H2eq)	^{2}J(H7ax/H7eq)	^{3}J(H6ax/H7a)	^{3}J(H6ax/H7eq)
4B$^{(*)}$	11.3	13.7	10.7	2.3
5B	11.4	10.2	13.5	3.2
6B	11.0	13.2	9.9	3.0
7B	11.4	13.6	10.5	2.6

$^{(*)}$ ^{2}J(H6ax/H6eq) = 13.1, ^{3}J(6eq/7ax) = 1.6 and ^{3}J(6eq/7eq) = 3.8 Hz

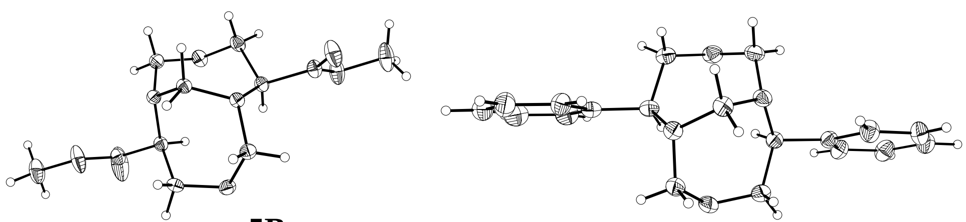
Due to the chirality of the ethanolamines, compound (**7B**) gave the enantiomeric form with respect to compounds (**4B**) and (**5B**), Scheme 6. In isomers of type (**B**), the axial position of H6 is indicated by the values of the coupling constants ^{3}J(H6ax-H7ax) [**4B** 10.7, **7B** 10.5 and **5B** 13.5 Hz] and the small values of ^{3}J(H6ax-H7eq) [from 2.3 to 3.2 Hz].



4B R = H
5B R = CO_2Me
6B R = Et
7B

Scheme 6 Preferred conformation in solution of heterocycles (**B**)

In addition, the conformation of the rings is supported by NOESY experiments which suggest a strong interaction between axial protons H4 with H2B and H7B. The preferred conformation in solution was also found in the X-Ray diffraction structure of compounds (**5B** and **7B**), Figure 1.



5B **7B**

Figure 1. X-Ray diffraction structures of **5B** and **7B** obtained in our laboratory and reported before in references 2b and 2d, respectively.

Conclusion

Condensation reactions of β-ethanolamines with formaldehyde are more complex then reported. Two different heterocycles of type (**A**) and (**B**) can be record, which are in equilibrium. The latter can be shifted completely to **A** or **B** depending on the α-substituents at the nitrogen atom, and it can be modified by the presence of Lewis acids. The **A**/**B** isomer ratios at equilibrium in toluene are shown in Table 6. Compounds (**5**) and (**7**) crystallize in ether respectively to give the kinetic compound of type (**B**) by an equilibrium asymmetric transformation.

Table 6 **A**/**B** ratio at the equilibrium in toluene

Compds	A/B ratio	Compds	A/B ratio	Compds	A/B ratio
1	90/10	**4**	40/60	**6**	90/10
2	80/20	**5**	50/50	**7**	90/10
3	100/0				

EXPERIMENTAL

All solvents were freshly distilled. The ^{1}H, ^{13}C and ^{15}N NMR spectra were recorded at 270, 67.94 and 30.42 MHz, respectively. ^{1}H and ^{13}C chemical shifts are referenced to TMS. Melting points were measured on a Gallenkamp apparatus and are uncorrected. Elemental analyses were performed by Oneida Research Services, Whitesboro, New York. The MS spectra were obtained at 20eV in a HP 5989 spectrometer. $[\alpha]_D$ in Perkin Elmer 241 polarimeter and FT-IR spectra were recorded in a Perkin Elmer 16F spectrometer.

General procedure for reactions at low temperature, Method A. To a solution of the ethanolamine (**1-7**) (0.166 mmol) in THF (80 mL) cooled at -78°C, aqueous formaldehyde (37%, 2.2 mL, 2.5 mmol) was slowly added. The reaction mixture was kept 4 h at -78°C and was then allowed to warm to rt. The mixture was filtered, the solvent evaporated and the residual extracted with $CHCl_3$ (3x30 mL) and washed with water (10 mL). The organic phase was dried with Na_2SO_4 and the solvent evaporated.

General procedure for reactions at high temperature, Method B. To a solution of ethanolamine (**1-7**) (1.66 mmol) in toluene (10 mL) aqueous formaldehyde (37%, 2.2 mL, 2.5 mmol) was slowly added. The reaction mixture was stirred and refluxed for 3 h. Insoluble material was remove by filtration, the solvent evaporated and the residue solid extracted with $CHCl_3$ (3x30 mL) and washed with water (10 mL). The organic phase was dried and the solvent remove in vacuum.

Bis[(5R)-5-methyl-1,3-oxazolidin-3-yl]methane (1A). Preparation of **1A** by the general procedure A gave a colorless liquid that was distilled at 90oC and 0.25 mmHg (2.2 g, 72%). IR ($CHCl_3$) ν (cm^{-1}) = 2988, 1534, 1466, 1240, 1092. Anal. Calcd for $C_9H_{18}N_2O_2·1/2H_2O$: C, 55.36; H, 9.81; N, 14.35. Found: C, 53.81; H, 10.41; N, 15.05. MS *m/z* (20 eV) [%]: 186 (0.6), 142 (1.5), 100 (100), 70 (40), 42 (16).

Bis[4,4-dimethyl-1,3-oxazolidin-3-yl]methane (2A). Compound (**2A**) was prepared by method B. The mixture reaction was distillated at 30°C (0.25 mmHg), and compound (**2A**) was obtained as a colorless liquid (2.4 g, 70%). IR ($CHCl_3$) ν (cm^{-1}) = 2990, 1530, 1466, 1244, 1098. Anal. Calcd for $C_{11}H_{22}N_2O_2$: C, 60.06; H, 10.57; N, 13.79. Found: C, 60.55; H, 10.48; N, 12.77.

Bis[(4R,5S)-4-methyl-5-phenyl-1,3-oxazolidin-3-yl]methane (3A). Procedure A, gave **3A** as a pale yellow solid (1.1 g, 98% yield). mp 86-88°C. $[\alpha]_D$ = +51.3° ($CHCl_3$, c = 0.1). Anal. Calcd for $C_{21}H_{26}N_2O_2$; C, 74.53; H, 7.74; N, 8.28. Found: C, 74.70; H, 7.78; N, 7.94.

(5R,10R,4S,9S)-5,10-Dimethyl-4,9-diphenyl-3,8-dioxa-1,6-diaza-bicyclo[4.4.1]undecane (3B). To a solution of compound (**3A**) (1.3 mmol, 0.2 g), in THF (50 mL) at rt, MeMgCl in THF (1.8 M, 2.6 mmol, 1.4 mL) was slowly added. The mixture was stirred 5 min at 0°C and then analyzed by NMR spectrometry obtaining an equimolecular mixture of compounds (**3A** and **3B**). Then the water (5 mL) was added to the equilibrium mixture. Extraction with $CHCl_3$ yielded only compound (**3A**) was obtained (0.2 g, 90%).

Bis[1,3-oxazolidin-3-yl)methane (4A) and 3,8-dioxa-1,6-diazabicyclo[4.4.1]undecane (4B). Procedure A gave a colorless viscous liquid as a mixture of **4A** and **4B** in a 40/60 ratio (1.8 g, 70%). Anal. Calcd for $C_7H_{14}N_2O_2·1/2H_2O$: C, 50.28; H, 9.04; N, 16.75. Found: C, 49.92; H, 9.00; N, 17.04.

Bis[(4R)-4-methylcarboxylate-1,3-oxazolidin-3-yl]methane (5A) and (5R,10R)-5,10-dimethyl-carboxylate-3,8-dioxa-1,6-diazabicyclo[4.4.1]undecane (5B). Procedure B gave a white solid (95% yield). ^{1}H NMR spectrum show a mixture of **5A/5B** (40/60) which was dissolved in ether. From this solution compound (**5B**) crystallize as white microcrystals by slow addition of hexane (4.1 g, 90%). mp 90-92°C. MS *m/z* (%) 274 [M^+] (1.7), 244 (42), 214 (96), 144 (100), 116 (48), 45 (28). Anal. Calcd for $C_{11}H_{18}N_2O_6$: C, 47.78; H, 6.52; N, 10.87. Found: C, 47.59; H, 6.69; N, 10.24.

(5R,10R)-5,10-Diethyl-3,8-dioxa-1,6-diazabicyclo[4.4.1]undecane (6B). Two compounds was obtained following procedure A as a white solid (3.6 g, 90%). MS *m/z* (20 eV) [%] 240 (0.1), 183 (1.0), 169 (0.3), 114 (100), 84 (6.4), 70 (5.0), 56 (7.5), 42 (20). IR ($CHCl_3$) ν (cm^{-1}) = 2994, 1472, 1454, 1123, 1102. Anal. Calcd for $C_{11}H_{22}N_2O_2·H_2O$: C, 56.87; H, 10.41; N, 12.06. Found: C, 57.07; H, 10.00; N, 10.51.

Bis[(4R)-4-phenyl-1,3-oxazolidin-3-yl]methane (7A). Oxazolidine (**7A**) was prepared following the procedure **A**. It is a white solid (4.4 g, 95%). mp 154-156°C. $[\alpha]_D$= -184.0° ($CHCl_3$, c=0.27). IR ($CHCl_3$) ν (cm^{-1}): 3046, 2976, 1712, 1522, 1424, 1330, 1248, 1188, 1094, 1042, 1006, 928, 850, 818, 704. MS *m/z* (%) 280 [M^+-30] (0.4), 251 (0.3), 162 (100), 118 (8), 42 (48). Anal. Calcd for $C_{19}H_{22}N_2O_2$: C, 73.54; H, 7.09; N, 9.03. Found: C, 73.46; H, 7.07; N, 9.02.

(5R,5'R)-5,5'-Diphenyl-1,6-diaza-3,8-dioxabicyclo[4.4.1]undecane (7B). Compound (**7B**) was prepared following procedure **B** (4.9 g, 95%) as pale yellow crystals. mp 123-125°C. $[\alpha]_D$= -179.5° ($CHCl_3$, c=0.26). IR ($CHCl_3$) ν (cm^{-1}): 3046, 2976, 1710, 1522, 1424, 1330, 1248, 1190, 1094, 1044, 1006, 928, 848, 822, 700. MS *m/z* (%) 310 [M^+] (5), 280 (91), 250 (28), 162 (100), 110 (44), 42 (60). Anal. Calcd for $C_{19}H_{22}N_2O_2$: C, 73.54; H, 7.09; N, 9.03. Found: C, 73.69; H, 7.18; N, 8.88.

ACKNOWLEDGEMENTS

We thank Cinvestav for financial support and Conacyt Mexico for scholarships to R.S.C. and J.C.G.R. Also, we are grateful to Sonia A. Sánchez-Ruiz and Guillermo Uribe for technical assistance.

REFERENCES

1. a) A. Flores-Parra and S. A. Sánchez-Ruiz, *Heterocycles,* 1999, **51**, 2079. b) G. Cadenas-Pliego, M.-J. Rosales-Hoz, R. Contreras, and A. Flores-Parra, *Tetrahedron Asymmetry,* 1994, **5**, 633. c) G. Cadenas-Pliego L. M. R. Martínez-Aguilera, A. M. Bello-Ramírez, M.-J. Rosales-Hoz, R. Contreras, J. C. Daran, S. Halut, and A. Flores-Parra, *Phosphorus, Sulfur, and Silicon,* 1993, **81**, 111. d) G. Cadenas-Pliego, R. Contreras, A. Flores-Parra, J. C. Daran, and S. Haut, *Phosphorus, Sulfur, and Silicon,* 1993, **84**, 9. e) A. Flores-Parra, S. A. Sánchez-Ruiz, C. Guadarrama.Pérez, H. Nöth, and R. Contreras, *J. Eur. J. Inorg. Chem.,* 1999, 2069. f) C. Guadarrama-Pérez, G. Cadenas-Pliego, L. M. R. Martínez-Aguilera, and A. Flores-Parra, *Chem. Ber.,* 1997, **130**, 813. g) L. M. R. Martínez-Aguilera, G. Cadenas-Pliego, R. Contreras, and A. Flores-Parra, *Tetrahedron Asymmetry,* 1995, **6**, 1585. h) A. Flores-Parra, G. Cadenas-Pliego, L. M. R. Martínez-Aguilera, M. L. García-Nares, and R. Contreras, *Chem. Ber.,* 1993, **126**, 863. i) A. Flores-Parra, N. Farfán, A. I. Hernández-Bautista, L. Fernández-Sánchez, and R. Contreras, *Tetrahedron,* 1991, **47**, 6903.
2. a) P. Y. Johnson and D. J. Kerkam, *J. Org. Chem.,* 1976, **41**, 1768. b) von J. Engel, H.-G. Trömer, and W. S. Sheldrick, *Chem. Ztg.,* 1982, **106**, 427. c) P. Pevarello, V. Pinciroli, and M. Varasi, *J. Heterocyclic Chem.,* 1994, **31**, 1089. d) D. J. Aitken, D. Guillaume, H.-P. Husson, and A. Chiaroni, *J. Heterocyclic Chem.,* 1991, **28**, 705. e) D. J. Aitken, A. Chiaroni, C. Riche, and H.-P. Husson, *Arch. Pharm.,* 1995, **328**, 629. f) P. Lemoine, B. Viossat, P.-G. Martin, and D. Aitken, *Acta Cryst.,* 1998, **C54**, 1036. g) C. Bolm, T.-H- Chuang, G. Raabe, and J.-M. Fang, *Synth. Commun.,* 1999, **29**, 43. h) J. Sélambarom, S. Moge, F. Carré, A. Fruchier, J. P. Roque, and A. Pavio, *Carbohyd. Res.,* 2001, **330**, 43.
3. E. L. Eliel, Stereochemistry of Carbon Compounds, ed by McGraw-Hill Kogakusha, LTD, (p. 63, 1962).