*Tetrahedron* Vol 45, No 7, pp 2193 to 2200, 1989
Printed in Great Britain

0040-4020/89 $3 00+ 00


# 2-AMINO IMIDAZOLE ALKALOIDS FROM THE MARINE SPONGE *LEUCETTA CHAGOSENSIS*

Shmuel Carmely[a], Micha Ilan[b] and Yoel Kashman[a]*

[a]School of Chemistry, Sackler Faculty of Exact Sciences, [b]Department of Zoology, Tel-Aviv University, Ramat Aviv, 69978 Tel Aviv, ISRAEL.

(*Received in UK* 24 *January* 1989)

**ABSTRACT**

Nine new 2-amino imidazole alkaloids belonging to four different groups have been isolated from a Red Sea sponge. The structures of all compounds were elucidated from spectral data, mainly by 1D and 2D NMR techniques, by mass spectra and in case of naamidine A also by chemical transformations. A nudibranch, *Notodoris citrina* feeding on the *L. chagosensis* sponge was found to concentrate the new imidazole alkaloids.

The antifungal activity of the MeOH-Toluene (3:1) extract of the small bright yellow calcareous sponge *Leucetta chagosensis* brought us to investigate the secondary metabolites of this sponge. *L. chagosensis* collected in the Gulf of Eilat, The Red Sea, belongs to the class Calcisponginae (Calcarea) which is relatively, to the Demospongiae class, unexplored.

The 5-10% methanolic chloroform extract of the freeze-dried organism was found by us to be rich in nitrogen containing metabolites. Repeated chromatographies on Sephadex LH-20 and RP-18 columns separated between a mixture of nucleosides and a complex mixture of imidazole alkaloids. Out of the latter mixture we separated and purified nine new 2-amino imidazoles belonging to four closely related groups of compounds. The structures of four compounds designated naamidine A(1), naamine A(2), isonaamidine A(3) and isonaamine A(4)# - representatives of the four types of the novel alkaloids (Figure 1) were reported by us most recently[1]. It is the aim of this report to describe the structure of five additional new compounds belonging to these 2-amino imidazoles and the full spectral data of all the nine alkaloids.

The structure of naamidine A(1) $C_{23}H_{23}N_5O_4$, one of the two major alkaloids of the sponge, was determined on the basis of NMR studies [$^1$H&$^{13}$C(Table 1) and 2D COSY[2], HETCOSY[3] and NOE experiments] mass fragmentations as well as its reduction and degradation[1]. The COSY experiment suggested two para-substituted benzyl groups which were further confirmed by the hetero nuclear correlation experiment (HETCOSY)[3], namely by, $^3J_{CH}$ correlations in the benzene rings and correlations from H-7 and 14 to C-9(13) and 16(20) respectively. The latter experiment also determined the position of the two benzyls on the imidazole ring (due to $^2$J and $^3$J correlations of H-7 and 14 to C-4 and 5) as well as the locations of two methyl groups, one at N(3) of the imidazole and the second at N(1') of the imidazoledione (by correlations of the $CH_3$-N(3) to C-2&4, and the $CH_3$-N(1') to C-4'&5'). Sodium borohydride reduction of 1 reduced the latter ring to give two tetrahydro naamidine A derivatives, compounds 10 and 11, in a ratio of ca. 20:1 (Fig.2). The $^1$H NMR of 10 (an additional aminal

#The compounds were named after the Bay of Naama where the sponge was first collected.

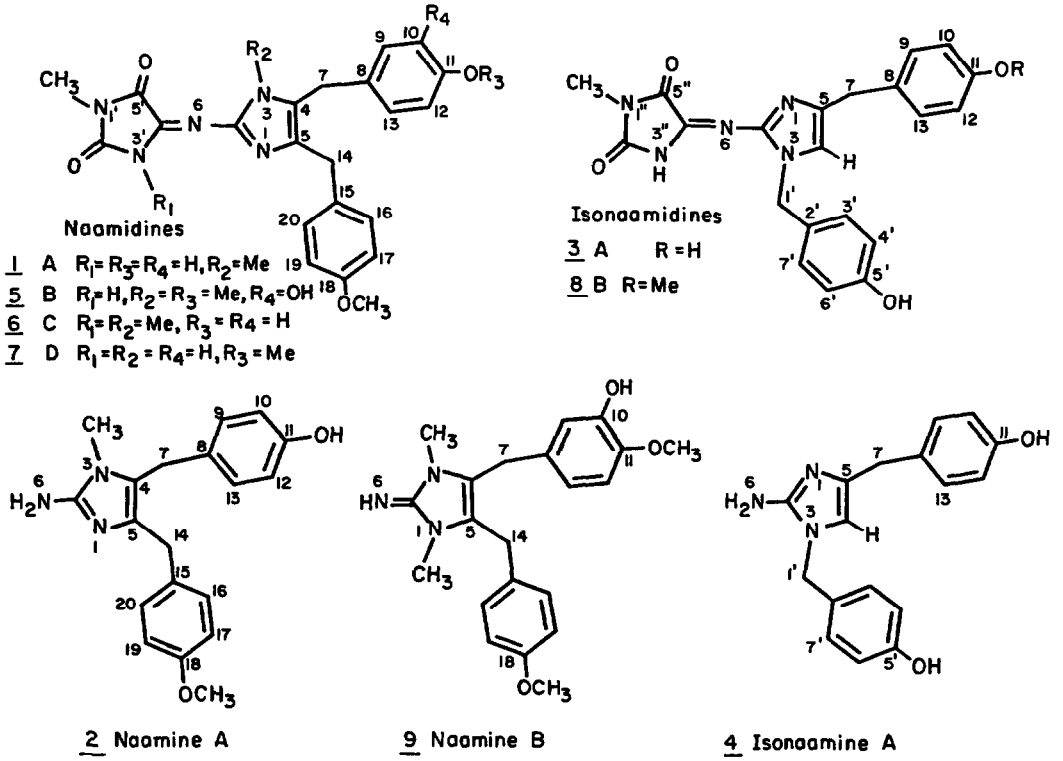



Figure 1. 2-Aminoimidazole alkaloids of L. chagosensis

(In all naamidines and isonaamidines, except for 6, two tautomers of the -NH(6)C=N(3'or3")-moiety are possible).

proton-signal at $\delta$ 4.72, H-5' as part of the $N^{5'}CH(OH)^{4'}CH(NH)(NH)$ group; $\delta$ 4.86dt,H-4',$\delta$ 6.11brd & 6.84brs) confirmed the 4-amino-imidazole-2,5-dione functionality of 1[1]. The mass spectra of 1 and 10 were in full agreement with the suggested structure[1] (cleavages of the C(4')-N(6), N(6)-C(2), C(4)-C(7) and C(5)-C(14) bonds). Acid treatment of 1 (HBr in MeOH) afforded compound 2 which was identical with a second natural product named naamine A(2)(Fig.1).

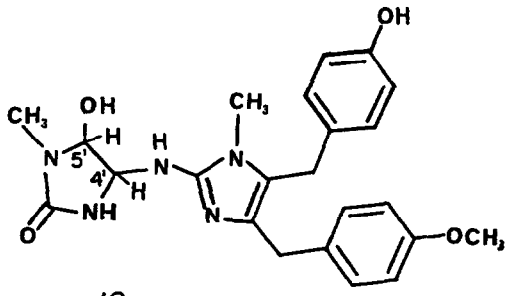
The $^{1}H$ and $^{13}C$ NMR data of 2 (Table 3) are in full agreement with the suggested 2-amino-3-methyl-4,5-dibenzyl structure. The resonance-lines assignments of 2 are based on the $^{1}J_{CH}$ to $^{3}J_{CH}$ correlations; particularly the $N(3)C\underline{H}_3$ to C-2 & 4, the 2H-7 to C-4,8 & 9, the 2H-14 to C-5, 15 & 16, the $OC\underline{H}_3(18)$ to C-18 and the $^{3}J_{CH}$ phenyl rings correlations observed in a HETCOSY experiment and confirmed by NOE enhancements measured between 2H-7 and $N(3)CH_3$&H-9, and between 2H-14 and H-16.

Table 1 NMR data of naamidines A-D ($CDCl_3$+$CD_3OD$)

| | Naamidine-A(1) | | Naamidine-B(5) | Naamidine-C(6) | | Naaminine-D(7) | |
|---|---|---|---|---|---|---|---|
| No. | $\delta_C$# | $\delta_H$ | $\delta_H$ | $\delta_C$ | $\delta_H$ | $\delta_C$ | $\delta_H$ |
| 2 | 146.2s | | | 146.0s | | 146.3s | |
| 4 | 126.7s | | | 126.6s | | 126.7s | |
| 5 | 132.9s | | | 133.0s | | 126.7s | |
| 7 | 28.2t | 3.88brs | 3.87brs | 27.9t | 3.84brs | 29.4t | 3.85brs |
| 8 | 127.4s | | | 128.1s | | 129.4s | |
| 9 | 128.7d | 6.84d,8.6 | 6.58d,2.0 | 128.7d | 6.88d,8.3 | 128.9d | 7.05d,8.5 |
| 10 | 115.6d | 6.72d,8.6 | | 115.9d | 6.73d,8.3 | 113.9d | 6.82d,8.5 |
| 11 | 155.6s | | | 155.9s | | 158.2s | |
| 12 | 115.6d | 6.72d,8.6 | 6.85d,8.4 | 115.9d | 6.73d,8.3 | 113.9d | 6.82d,8.5 |
| 13 | 128.7d | 6.84d,8.6 | 6.46dd,8.4,2.0 | 128.7d | 6.88d,8.3 | 128.9d | 7.05d,8.5 |
| 14 | 31.3t | 3.91brs | 3.92brs | 29.9t | 3.89brs | 29.4t | 3.85brs |
| 15 | 130.7s | | | 132.0s | | 129.4s | |
| 16 | 129.1d | 7.11d,8.6 | 7.13d,8.6 | 129.6d | 7.10d,8.6 | 128.9d | 7.05d,8.5 |
| 17 | 113.9d | 6.81d,8.6 | 6.75d,8.6 | 114.3d | 6.81d,8.6 | 113.9d | 6.82d,8.5 |
| 18 | 158.3s | | | 158.6s | | 158.2s | |
| 19 | 113.9d | 6.81d,8.6 | 6.75d,8.6 | 114.3d | 6.81d,8.6 | 113.9d | 6.82d,8.5 |
| 20 | 129.1d | 7.11d,8.6 | 7.13d,8.6 | 129.6d | 7.10d,8.6 | 128.9d | 7.05d,8.5 |
| 3-$NCH_3$ | 29.6q | 3.48brs | 3.51s | 29.4q | 3.40brs | | + |
| 11-OR | | * | 3.85s | | * | 54.8q | 3.78s |
| 18-$OCH_3$ | 55.0q | 3.77s | 3.79s | 55.0q | 3.72s | 54.8q | 3.78s |
| 2' | 158.3s | | | 158.9s | | 156.5s | |
| 4' | 148.4s | | | 147.2s | | 147.8s | |
| 5' | 163.3s | | | 164.6s | | 163.3s | |
| 1'-$NCH_3$ | 24.4q | 3.13s | 3.14s | 25.2q | 2.98s | | 3.12s |
| 3'-NR | | + | + | 33.7q | 3.08s | | + |

* OH; + NH; # $\delta_C$(mult.), $\delta_H$(mult., J in Hz).

Together with naamidine A (1) we have isolated in smaller amounts three additional closely related compounds designated naamidines B(5), C(6) and D(7). Comparison of the NMR data of these compounds with that of naamidine A(1) - Table 1, pointed clearly to the same skeleton for all four. Naamidines B-D(5-7) (Figure 1) differ from 1 only in the N,O-substituents [an 11-$OCH_3$ for 5, a N(3')$CH_3$ for 6, a N(3)H and 11-$OCH_3$ for 7] and in case of 5 also in an additional hydroxylic phenol (10-OH). As with 1 the two phenyl substitution patterns of compounds 5-7 were established by COSY experiments which were further confirmed by NOE measurements. In case of naamidine D(7), isolated only once in minute amounts, the $^1J_{CH}$ correlations were established by a HMQC experiment[4], and for 6 we have measured the HETCOSY[3] spectrum. In the latter spectrum, in addition to the same correlations which were observed for 1[1](*vide supra*), two new correlations could have been seen between the extra




IO

Figure 2.
The major reduction product of naamine A.

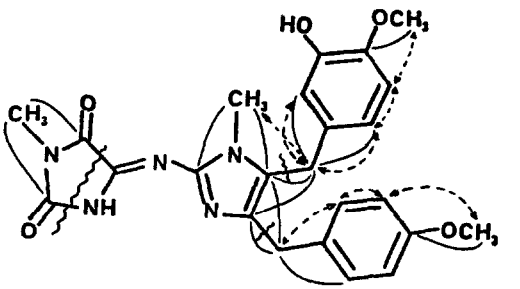



Figure 3. CH correlations(—),NOE's(---) and characteristic mass fragmentations(~~)of 5.

Table 2 NMR data of isonaamidine A & B and isonaamine A.

| | isonaamidine A(3) | | isonaamidine B(8)($CDCl_3$+$CD_3OD$) | | isonaamine A(4)($d_6$-DMSO) | |
|---|---|---|---|---|---|---|
| No. | $\delta_C$(mult) | $\delta_H$(mult,J inHz | $\delta_C$(mult) | $\delta_H$(mult,J inHz) | $\delta_C$(mult) | $\delta_H$(mult,J inHz) |
| 2 | 145.9s | | | | 146.1s | |
| 4 | 116.0d(195Hz) | 6.89brs | 115.8d | 6.49brs | 112.3d | 6.55brs |
| 5 | 137.5s | | | | 125.6s | |
| 7 | 32.5t | 3.75brs | 32.6t | 3.86brs | 29.5t | 3.61brs |
| 8 | 129.4s | | | | 126.8s | |
| 9 | 125.6d | 7.04d,8.6 | 129.6d | 7.15d,8.6 | 129.6d | 7.00d,8.5 |
| 10 | 115.2d | 6.66d,8.6 | 114.0d | 6.85d,8.6 | 115.5d | 6.69d,8.5 |
| 11 | 155.8s | | | | 156.3s | |
| 12 | 115.2d | 6.66d,8.6 | | 6.85d,8.6 | 115.5d | 6.69d,8.5 |
| 13 | 125.6d | 7.04d,8.6 | | 7.15d,8.6 | 129.6d | 7.00d,8.5 |
| 11-OR | | * | 55.2q | 3.80s(6-$NCH_3$) | | 7.73brs |
| 1' | 47.5t | 5.09brs | 50.2t | 5.18brs | 47.3t | 4.91brs |
| 2' | 127.4s | | | | 127.6s | |
| 3' | 129.3d | 7.09d,8.6 | 129.5d | 7.11d,8.6 | 129.5d | 7.13d,8.6 |
| 4' | 115.4d | 6.69d,8.6 | 115.6d | 6.78d,8.6 | 115.7d | 6.75d,8.6 |
| 5' | 157.1s | | | | 157.6s | |
| 6' | 115.4d | 6.69d,8.6 | 115.6d | 6.78d,8.6 | 115.7d | 6.75d,8.6 |
| 7' | 129.3d | 7.09d,8.6 | 129.5d | 7.11d,8.6 | 129.5d | 7.13d,8.6 |
| 2" | 157.2s | | | | | |
| 4" | 148.6s | | | | | |
| 5" | 162.5s | | | | | |
| 1"$NCH_3$ | 24.5q | 2.95brs | 24.6q | 3.17brs | | |

* OH

N(3')C$\underline{H}_3$ and its neighbors C-2' and 4'. The CI mass spectra of **4**-**7** (Experimental), which include the imidazoledione fragment $C_3H_3NO_2$ (85mu), the substituted benzyls (107,121,137 mu) and the M-imidazoledione fragments (324mu for **1**,**6**, **7** and 354mu for **5**), are in full agreement with the suggested structures. For a summary of the CH-correlations, NOE's and mass fragmentations of **5** see Fig.3).

The second major metabolite isonaamidine A(**3**) resembled compound **1** in its functionalities. Compound **3** possesses two benzyls (both p-hydroxy substituted as confirmed by homo and hetero, $^3J_{CH}$ correlations), a N-methyl imidazoledione (exhibiting the N(1")C$\underline{H}_3$ correlation with C-2" and -5" as in the naamidines) and according to the $^{13}C$ NMR data (Table 2) and mass fragmentations (the above mentioned benzyls, 85mu, and cleavages of C(4")-N(6) and N(6)-C(2), Experimental) also a 2-amino-imidazole ring[1]. Standing out in the NMR spectrum of **3** was the down-field shift of one of the two benzyl-methylenes (shifting from 3.88ppm in **1** to 5.08ppm in **3**) and the appearance of a new vinyl proton at 6.84ppm - suggesting the migration of the 5-benzyl, of **1**, to N(1). The proposed structure (Figure 1) is in full agreement with the COSY, HETCOSY, NOE and mass spectrum measurements[1].

Under acidic conditions compound **3** degrades to afford compound **4** which is the N-benzyl isomer of naamine A (Figure 1) and was also found to be a natural product named isonaamine A (**4**, Table 2). Characteristic in the NMR spectra of **4**, as in **3**, is the =C(4)H-N(3) group (Table 2; $\delta_H$ 6.55brs, $\delta_C$ 112.3d & $J_{CH}$=195Hz) and its correlations with C-5 & 7.

Another metabolite of the sponge is the 11-methoxy derivative of compound **3**, named isonaamidine-B (**8**, Figure 1 and Table 2). The location of the newly introduced methoxyl was established by CH-correlations[5] observed between the latter OMe protons and C-11 and between 2H-7 and C-5, 8 & 9, connectivities which came in addition to the same correlations as were observed for isonaamidine A(**3**).

The final dibenzyl imidazole isolated from the sponge, compound **9**, is close in its structure to naamine A(**2**).

Compound **9**, $C_{21}H_{25}N_3O_3$, designated naamine B possesses, on the one hand, the same skeleton as naamine A(**2**) and, on the other hand, carries the same two substituted benzyls as in naamidine B(**2**) (see Tables 1 and 3). From the $^1H$ NMR it was clear that in addition to the two OMe-groups compound **9** contains two NMe's. The 1,3 location of the latter two methyls was determined on the basis of CH correlations between these N(1) and N(3) methyls and the neighbor C-2 & 4 and C-2 & 5 atoms respectively. The 313($MH^+$-$C_2N_2H_3$), 231($MH^+$-137), 137(hydroxy, methoxybenzyl), 121(pOMe benzyl) and 85mu[$(MeN)_2C$=$NH^+$] fragments observed in the mass spectrum of **9** are in full agreement with the suggested structure.

Of interest from the biogenetic point of view is the question whether the naamidines (and naamines) are the precursors of the isonaamidines (and isonaamines) or <u>vice versa</u>, or whether the two are synthesized in separate routes. Thus, it can be suggested that the 4,5-disubstituted imidazoles of the former compounds result from a coupling of two phenethylamines and that the iso-compounds are obtained either by a 1,2-migration of a benzyl from a carbon to the neighbour nitrogen or alternatively from two $C_6$-$C_3$ and $C_6$-$C_1$ units.

**Table 3 NMR data of naamines A AND B.**

| | Naamine A(2) ($d_6$-DMSO) | | Naamine B(9) ($CDCl_3$+$CD_3OD$) | |
|---|---|---|---|---|
| | $\delta_C$(mult) | $\delta_H$(mult J,Hz) | $\delta_C$(mult) | $\delta_H$(mult J,Hz) |
| 2 | 146.4s | | 146.3s | |
| 4 | 122.4s | | 122.9s | |
| 5 | 121.9s | | 122.9s | |
| 6 | | 7.60brs | | * |
| 7 | 26.9t | 3.84brs | 27.7t | 3.87brs |
| 8 | 127.3s | | 128.5s | |
| 9 | 129.1d | 6.89d,8.6 | 114.3d | 6.64d,1.9 |
| 10 | 115.0d | 6.70d,8.6 | 146.4s | |
| 11 | 156.3s | | 146.5s | |
| 12 | 115.7d | 6.70d,8.6 | 111.6d | 6.81d,8.4 |
| 13 | 129.1d | 6.89d,8.6 | 118.7d | 6.57dd,8.4,1.9 |
| 14 | 28.2t | 3.79brs | 27.6t | 3,92brs |
| 15 | 130.3s | | 127.5s | |
| 16 | 129.6d | 7.16d,8.6 | 128.6d | 7.05d,8.6 |
| 17 | 114.1d | 6.83d,8.6 | 114.3d | 6.87d,8.6 |
| 18 | 158.2s | | 158.6s | |
| 19 | 114.1d | 6.83d,8.6 | 114.3d | 6.87d,8.6 |
| 20 | 129.6d | 7.16d,8.6 | 128.6d | 7.05d,8.6 |
| 1-$NCH_3$ | | | 29.9q | 3.29brs |
| 3-$NCH_3$ | 29.7q | 3.15brs | 29.9q | 3.30brs |
| 11-$OCH_3$ | | | 55.0q | 3.80s |
| 18-$OCH_3$ | 55.3q | 3.69s | 55.7q | 3.86s |

* NH

One of us (M.I) succeeded in the collection of the nudibranch *Notodoris citrina (Family Aegiridae)*. (a small animal with a dark green back and bright yellow belly - same colour as the sponge) feeding on the *L. chagosensis* and it could be shown that this animal concentrates the above mentioned new imidazole alkaloids. Whether these compounds serve as antimicrobial and antifungal agents and/or do have other activities has to be explored. .pa

## EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer Model 177 spectrophotometer. UV spectra were recorded on a Perkin-Elmer Model 257 spectrophotometer. Low-resolution mass spectra were recorded on a Finnigan-4021 mass spectrometer; source temperature 220-230°C; pressure of reagent gases for CI spectra: $CH_4$,0.28 Torr, and $NH_3$,0.15-0.20 Torr; the electron energies in EI mode were 25-35eV. $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker AM-360 spectrometer, equipped with an Aspect 3000 computer and operating at 360.1 and 90.5

MHz for $^{1}H$ and $^{13}C$, respectively. All chemical shifts are reported with respect to $Me_4Si(\delta = 0)$.

The 2D NMR experiments were measured on samples in $CDCl_3$ at 298°K. The H-H shift correlation experiments were performed with a COSY 45 sequence[2]. The two-dimensional maps were composed of 512 x 2K data point spectra. A 1-s recycle delay was allowed between each pulse sequence. Quadrature detection was applied in both dimensions by using the 16-step phase cycling for N-type peak selection. Data were multiplied with sine bell shaping function, zero filled to 1K x 2K and then Fourier transformed and symmetrized.

The sponge speciments were collected at the Bay of Naama (and other locations) in the Gulf of Eilat in July 1980. The samples were deep-frozen immediately after collection, freeze-dried and then extracted with chloroform and 5-10% methanol in chloroform. The latter extract was separated by a Sephadex LH-20 column prepared and eluted with a mixture of chloroform-methanol 1:1 followed by a column of RP-18 eluted with increasing percents of MeOH in water. From repeated chromatographies we have obtained ( % dry wt.) naamidine A(1)-0.15, isonaamidine A(3)-0.15, naamine A(2)-0.10, isonaamine A(4)-0.08, naamidines B and C(5 & 6) and iso naamidine B(8)-0.01 each and naamidine D(7)-0.001. All compounds were obtained as foaming oils or amorphous powders. A typical amount of dry sponge to start with was 25gr.

Naamidine A(1): for $^{1}H$ & $^{13}C$ NMR see Table 1. HR EI MS: m/e/433.1783 ($M^+$, calc. for $C_{23}H_{23}N_5O_4$, 433.1750); CI MS (isobutane) m/z (relative intensity); 434($MH^+$, 23), and 324(100); UV $\lambda_{max}(CHCl_3)$; 240(1160); 281(4330); 366(10460); 392(13500) and 416(10650); IR $\nu_{max}$(KBr) 3650-3100br, 2930, 1707, 1570, 1510, 1440, 1250, 1170 and 1025 $cm^{-1}$.

Naamidine B(5): for $^{1}H$ NMR see Table 1. HR EI MS m/e 463.1926($M^+$,calc. for $C_{24}H_{25}N_5O_5$: 463.1856); CI MS(methane)m/z(relative intensity); 492($MC_2H_5^+$,6), 478($MCH_3^+$,6), 464($MH^+$,51), 368(2), 354(6), 137(5), 121(10), 109(9) and 85(100). IR $\nu_{max}$(KBr)3500br,2930,1705$cm^{-1}$.

Naamidine C(6): for $^{1}H$ & $^{13}C$ NMR see Table 1. CI MS (methane) m/z (relative intensity); 448($MH^+$,16), 447($M^+$,100), 446($M^+$-H,7), 434($MH^+$-$CH_3$,15), 324(4) and 107(3); IR $\nu_{max}$(KBr)3400br, 2930, 1705$cm^{-1}$; (Found: C,64.20; H,5.55. $C_{24}H_{25}N_5O_4$ requires: C,64.42;H,5.63%).

Naamidine D(7): for $^{1}H$ & $^{13}C$ NMR see Table 1; CI MS (isobutane) m/z (relative intensity); 434($MH^+$,41), 324(100), 309(53) and 121(16); UV $\lambda_{max}$($CHCl_3$/MeOH 1:1): 240(8800),268(305) and 386(6500)nm; IR $\nu_{max}$(KBr) 3700-3120br, 2922, 2855, 1705, 1645, 1620, 1570, 1510, 1445, 1390, 1247, 1165 and 1030$cm^{-1}$.

Isonaamidine A(3): for $^{1}H$ & $^{13}C$ NMR see Table 2; CI MS(isobutane)m/z(relative intensity): 406($MH^+$,42), 300(100), 243(40), 190(26), 127(65), 107(28) and 85(47); UV $\lambda_{max}$(dioxane): 227(20000); 264(540), 358(6000), 366(6800) and 380(590)nm; IR $\nu_{max}$(KBr) 3600-3000br, 2930, 1710, 1670, 1616, 1565, 1515, 1445 and 1245$cm^{-1}$.

Isonaamidine B (8): for $^{1}H$ & $^{13}C$ NMR see Table 2; CI MS(methane) m/z(relative intensity): 448($MC_2H_5^+$,12), 434($MCH_3^+$,9), 420($MH^+$,99), 419($M^+$,25), 314(36), 121(16), 107(100) and 85(60); IR $\nu_{max}$(KBr)3400br, 2930, 1708$cm^{-1}$. (Found: C,62.91;H,5.19.$C_{22}H_{21}N_5O_4$, requires: C,63.00,H,5.05%).

Naamine A(2): for $^{1}H$ & $^{13}C$ NMR see Table 3; CI MS(isobutane) m/z (relative intensity):

324($M^+$,100) and 107(7); UV $\lambda_{max}$(dioxane); 226(17000), 260(11000), 282(6000), 290(5500), 302(4700)nm; $\nu_{max}$(KBr)3500br, 2930, 1670, 1615cm$^{-1}$.

Naamine B (9): for $^1H$ & $^{13}C$ NMR see Table 3; CI MS(methane) m/z (relative intensity): 368($MH^+$,40), 313(40), 231(10), 137(20), 121(26) and 85(100); $\nu_{max}$(KBr) 3500br, 2920, 1670, 1615cm$^{-1}$. (Found: C,68.78;H,6.58,$C_{21}H_{25}N_3O_3$, requires: C,68.64,H,6.86%)

Isonaamine A (4): for $^1H$ & $^{13}C$ NMR see Table 2; EI MS m/e(relative intensity); 295($M^+$,7), 200(7), 188(8), 106(61) and 78(100); $\nu_{max}$(KBr)3500br, 2920, 1670, 1615cm$^{-1}$.

Reduction of Naamidine A (1): Naamidine A(10mg) in MeOH(5ml) was treated with $NaBH_4$(10mg) for 1/2h, the excess of reagent was then destroyed with dil. HOAc and the solvent evaporated. Chromathography of the residue on a silica gel H column afforded two tetrahydro derivatives of 1 in a ratio of 20:1: the major product (10): $^1H$ MNR($d_6$-DMSO) 9.15brs(1H), 7.13d(J=8.7Hz,2H), 6.84brs(1H), 6.81d(J=8.5Hz,2H), 6.78d(J=8.7Hz,2H), 6.61d(J=8.5Hz,2H), 6.11brd(J=8.7,1H), 4.86dt(J=8.7,1.7Hz,2H), 4.72brd(J=1.7Hz,1H), 3.70brs(2H), 3.69brs(3H), 3.63brs(2H), 3.00s(3H), 2.65s(3H); EI MS m/e(relative intensity): 406($M^+$-MeOH,100), 324(35)and 264(84) and the minor product (11): $^1H$ NMR($d_6$-DMSO); 9.12brs(1H), 7.13d(J=8.7Hz,2H), 6.82d(J=8.5Hz,2H), 6.74brs(1H), 6.79d(J=8.7Hz,2H), 6.60d(J=8.5Hz,2H), 5.52d(J=8.3Hz,1H), 5.24ddd(J=8.7,8.3,1.8 Hz,1H), 4.97d(J=8.7Hz,1H), 3.71brs(2H), 3.69brs(3H), 3.63brs(2H), 3.01s(3H) and 2.68s(3H), EI MS m/e 406($M^+$-MeOH,100).

Hydrolisis of Naamidine A and Isonamidine A: Naamidine A(1), or isonamidine A(4), (10mg) in a 5% HBr-MeOH solution (10ml) was left at room temperature overnight. The acid was then neutralized with $NaHCO_3$, the solvent removed under vacuum and the residue chromatographed on a SepPack RP-18 column to give compounds 2 and 4 respectively.

## REFERENCES

1. S. Carmely and Y. Kashman, Tet. Letters 28, 3003 (1987).
2. A. Bax and R. Freeman, J. Magn. Reson. 44, 542 (1981).
3. Y. Sato, M. Geckle and S.J. Gould, Tet. Letters 26, 4019 (1985).
4a. A. Bax, M.F.J. Summers, J. Am. Chem. Soc. 108, 2093 (1986).
b. A. Bax, A. Aszalos, Z. Dinya, K. Sudo, ibid, 8056 (1986).
5. A. Bax and G. Morris, J. Magn. Reson 42, 501 (1981).