# Transformation of Schiff Bases Derived from α-Naphthaldehyde. Synthesis, Spectral Data and Biological Activity of New-3-Aryl-2-(α-naphtyl)-4-thiazolidinones and *N*-Aryl-*N*-[1-(α-naphthyl)but-3-enyl]amines



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New N-aryl substituted 2-(α-naphthyl)-4-thiazolidinones were prepared by the cyclocondensation of α-mercaptoacetic acid and corresponding *N*-(α-naphthyliden)anilines. The same starting materials were utilized to obtain a new series of *N*-aryl-*N*-[1-(α-naphthyl)but-3-enyl]amines, which was synthesized through an addition of the Grignard reagent (allylmagnesium bromide) to the double bond C=N of the aldimines. The antichagasic and trichomonacidal *in vitro* activity, as well as, the antifungal and cytotoxic properties of some of these compounds were evaluated.

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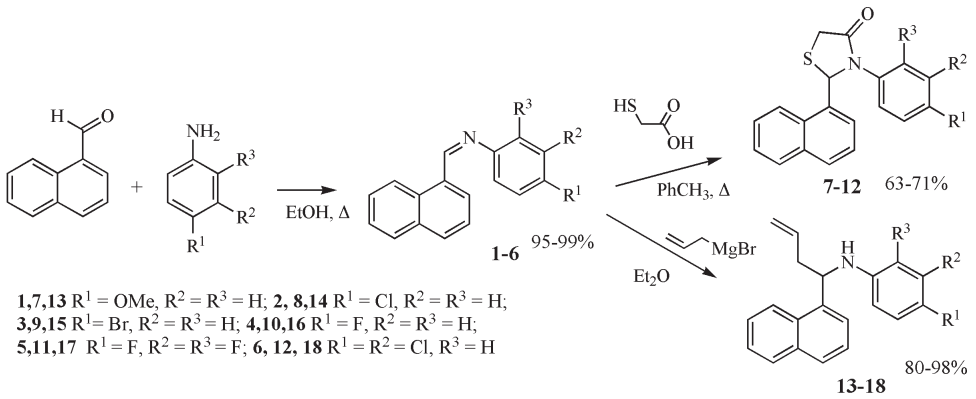
## Introduction.

The aldimines [1,2] are valuable starting materials not only for different N-containing heterocycles [3], but also for diverse functionalized amines [4]. Both classes of compounds are interesting bioactive targets for many organic and medicinal chemists. Among numerous N-containing heterocycles obtained from aldimines, substituted 1,3-thiazolidin-4-ones are of particular interest due to their wide range of biological activities, namely fungicidal, pesticidal, antitubercular, anti-histaminic, antiparasitic, antiinflamatory, anti-nociceptive agents *etc* [5-18]. Different homoallylamines (N-substituted but-3-enylamines) prepared from aldimines *via* allylation reactions are not only useful precursors in the synthesis of new heterocyclic compounds with the biological activity [19], but also are perspective antifungal agents with inhibitory properties of the synthesis of fungal cell wall polymers [20,21]. The biological significance of these kinds of compounds urged us to synthesize a new series of 3-(aryl)-2-(α-naphthyl)-1,3-thiazolidin-4-ones and *N*-aryl-*N*-[1-(α-naphthyl)but-3-enyl]amines. Herein, we wish to report the synthesis, chemical and biological properties of these compounds containing the α-naphthyl nucleus.

## Results and Discussion.

The selected aldimines **1-6** were prepared by refluxing a mixture in dry ethanol of α-naphthylaldehyde and substituted anilines such as *p*-anisidine, *p*-chloroaniline, *p*-bromoaniline, *p*-fluoroaniline, 2,4-difluoroaniline and 2,3-dichloroaniline. The new 3-aryl-2-(α-naphthyl)-1,3-thia-

Scheme 1



zolidin-4-ones **7-12** were obtained similarly to those previously described [22,23] by reacting the corresponding Schiff bases **1-6** with α-mercaptoacetic acid in boiling toluene in good yields as white powder. Using a traditional procedure for the Grignard reaction between the same aldimines and allylmagnesium bromide, prepared from magnesium and allyl bromide in dry ether, we prepared a new series of homoallylamines - *N*-aryl-*N*-[1-(α-naphthyl)but-3-enyl]amines **13-18** that were obtained as viscous reddish or yellow oils and purified by means of a short chromatographic column (Scheme 1).

The IR spectra of the obtained compounds show the presence of an intense and sharp band corresponding to the stretching vibration N-C=O at 1698-1685 $cm^{-1}$ (for **7-12**) or to the stretching N-H at 3425-3403 $cm^{-1}$ (for **13-18**). The mass spectra of the compounds **7-12** contain molecular ion M+· peaks of high abundance, which confirm their molecular formula. The base peak in the mass spectra of N-substituted but-3-enylamines **13-18** results from the loss of 41 mass units (allyl radical). The fragmentation paths of both series of compounds are consistent with literature data for similar ring systems. However, analyzing the GC-MS spectra of the isolated 2-naphtyl thiazolidinones **7-12** we noted the presence of two conformers for only two compounds **11,12**. Studying molecular models of these heterocycles, we concluded that these conformers could arise due to the exceptionally rigid character of these molecules, which imposed a rotational barrier of the $C_{aryl}$-N bond between the aryl and thiazolidine moieties and of the $C_{naphtyl}$-C bond between naphthyl and thiazolidine rings [24]. The $^1H$ NMR spectra of 1,3-substituted thiazolidin-4-ones **7-10** registered the characteristic signals generated by the methylene protons 5-H that appeared as a system AB with a geminal constant of 15.7 - 16.2 Hz in the region from 3.80 to 4.00 ppm, and the signal of the proton 2-H appeared as a singlet approximately in 6.80 ppm. The analogous spectral analysis was made for other series of α-naphthyl aminoderivatives **13-18**.

The thiazolidin-4-ones **7-12** and *N*-[1-(α-naphthyl)-but-3-enyl]amines **13-17** were screened for trypanocidal (anti-epimastigote activity, %AE), trichomonacidal activity (growth inhibition, %GI) and unspecific cytotoxicity (expressed as cytotoxicity percentage - %C) to macrophages as described [25,26]. Its action against epimastigote forms of *Trypanosoma cruzi*, and *Trichomonas vaginalis* are given in Table 1. All compounds tested exhibit a trypanocidal activity ranging from 79.4 to 100% at the higher concentration assayed (100 μg/ml). However, at this concentration compounds also show unspecific cytotoxicity to macrophages. Several compounds **8,9,11** and **12** retain some anti-epimastigote activity at 10 μg/ml, whilst the unspecific cytotoxicity has been dramatically reduced. The activity of these compounds against *T. cruzi* is lower than that shown by Nifurtimox. With respect to the difference between two series of compounds tested, compounds of thiazolidin-4-ones' series possess higher activity than *N*-[1-(α-naphthyl)but-3-enyl]amines. With respect to trichomonacidal activity, none of the compounds tested do possess considerable activity at the non-toxic concentrations (10 and 1 μg/ml) assayed. These series were also screened for antifungal and anticancer activities. Both series were inactive against a panel of standardized dermatophytes [21] (MICs > 250 μg/ml), however some compounds in the series of *N*-[1-(α-naphthyl)but-3-enyl]amines **13-18** were active ($GI_{50}$ 4.5-8.9 mcg/ml) against breast (MCF-7), lung (H-460) and central nervous system (SF-268) human cancer cell lines that make them potential anticancer agents [27].

Table 1
Biological Activity of New Compounds

| Compound | Conc. (μg/ml) | Macrophages %C | T. cruzi %AE | T. vaginalis (%GI) 24 h | 48 h |
|---|---|---|---|---|---|
| **7** | 100 | 68.4 | 97.3 | 86.8 | 4.1 |
| | 10 | 0 | 54.4 | 26.2 | 8.0 |
| | 1 | 0 | 0 | 3.6 | 2.4 |
| **8** | 100 | 90.9 | 100.0 | (96.7) | (100) |
| | 10 | 0 | 73.1 | 29.7 | 32.3 |
| | 1 | 2.7 | 0 | 8.8 | 3.3 |
| **9** | 100 | 63.8 | 89.3 | (91.2) | 85.5 |
| | 10 | 7.4 | 91.4 | 43.9 | 29.5 |
| | 1 | 12.0 | 23.6 | 26.4 | 1.9 |
| **10** | 100 | 100.0 | 94.3 | 84.6 | 84.1 |
| | 10 | 34.0 | 67.6 | 30.8 | 23.9 |
| | 1 | 31.0 | 0 | 13.2 | 0.5 |
| **11** | 100 | 100.0 | 95.3 | 90.6 | 93.0 |
| | 10 | 45.0 | 74.2 | 26.9 | 15.3 |
| | 1 | 22.0 | 15.9 | 9.4 | 0 |
| **12** | 100 | 92.4 | 94.7 | (100) | (100) |
| | 10 | 0 | 86.6 | 36.3 | 0.8 |
| | 1 | 12.6 | 20.2 | 21.0 | 0 |
| **13** | 100 | 75.8 | 100.0 | 75.8 | 84.6 |
| | 10 | 11.7 | 65.5 | 35.1 | 43.5 |
| | 1 | 11.4 | 5.7 | 7.7 | 5.1 |
| **14** | 100 | 100.0 | 100.0 | (96.4) | (100) |
| | 10 | 14.8 | 30.4 | 59.4 | 28.3 |
| | 1 | 0 | 0 | 32.6 | 5.3 |
| **15** | 100 | 96.3 | 79.4 | (97.8) | (100) |
| | 10 | 0 | 19.4 | 68.9 | 28.3 |
| | 1 | 0 | 0 | 13.8 | 2.3 |
| **16** | 100 | 56.0 | 81.5 | 79.0 | (100) |
| | 10 | 13.8 | 14.5 | 42.8 | 11.8 |
| | 1 | 11.0 | 0 | 0.7 | 6.3 |
| **17** | 100 | 97.8 | 100.0 | (100) | (100) |
| | 10 | 32.5 | 48.8 | 49.3 | 20.3 |
| | 1 | 5.2 | 0 | 15.2 | 11.8 |
| Nifurtimox | 10 | | 100 | | |
| | 2.5 | | 88 | | |
| | 0.5 | | 54 | | |
| Metronidazole | 2 | | | 100* | 100* |
| | 1 | | | 97.9* | 100* |
| | 0.5 | | | 83.5 | 94.1* |

*Cytocidal activity (% reduction respect to control).

## EXPERIMENTAL

Melting points were uncorrected and measured in a FISHER-JOHNS melting point apparatus. Infrared spectra were recorded on Nicolet Avatar 360 FT-IR spectrometers as KBr pellets or neat. The $^1H$ and $^{13}C$ nmr spectra were determined on either Inova-400 or Bruker AM-400, in deuterochloroform with tretramethylsilane as internal standard. Data are reported as follows: chemical shifts (multiplicity, number of protons, coupling constants and group). Mass spectra were recorded with a HP 5890 A Series II, link to a network Mass selective detector HP 5972 spectrometer using 70 eV electron impact ionization. The purities of the obtained substance were monitoring by thin layer chromatography on Silufol $UV_{254}$ sheets. Elemental analyses were performed on a Leco CHN-600 analyzer. Solvents and common reagents obtained from Merck and Aldrich were reagent grade.

General Procedure for the Reaction of α-Naphthaldhyde with Anilines.

Equimolar solutions of the anilines (1.00 mol) and α-naphthaldehyde (1.00 mol) in dry ethanol (15 ml) were heated at reflux during 1 h. The ethanol was distilled off and the residual crystallized with petroleum ether. The substituted *N*-(4-aryl)-*N*-(α-naphthyliden)amines **1-6** were isolated as crystalline substances.

*N*-(4-Metoxyphenyl)-*N*-(α-naphthyliden)amine (**1**).

This compound was obtained in 98% yield as a yellow solid, mp 73-74 ºC; ir (potassium bromide): ν =CH 3012, ν C=N 1610 $cm^{-1}$; ms: m/z 261 (molecular ion).

*Anal.* Calcd. for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.97; H, 6.06; N, 5.20.

*N*-(4-Chlorophenyl)-*N*-(α-naphthyliden)amine (**2**).

This compound was obtained in 99% yield as a yellow solid, mp 78-80 ºC; ir (potassium bromide): ν =CH 3060, ν C=N 1610 $cm^{-1}$; ms: m/z 265 (molecular ion).

*Anal.* Calcd. for $C_{17}H_{12}ClN$: C, 76.84; H, 4.55; N, 5.27. Found: C, 76.55; H, 4.87; N, 5.54.

*N*-(4-Bromophenyl)-*N*-(α-naphthyliden)amine (**3**).

This compound was obtained in 99% yield as a yellow solid, mp 84-86 ºC; ir (potassium bromide): ν =CH 3060, ν C=N 1608 $cm^{-1}$; ms: m/z 310 (molecular ion).

*Anal.* Calcd. for $C_{17}H_{12}BrN$: C, 65.83; H, 3.90; N, 4.52. Found: C, 65.58 H, 4.12; N, 4.77.

*N*-(4-Fluorophenyl)-*N*-(α-naphthyliden)amine (**4**).

This compound was obtained in 97% yield as a yellow solid, mp 55-56 ºC; ir (potassium bromide): ν =CH 3043, ν C=N 1610 $cm^{-1}$; ms: m/z 249 (molecular ion).

*Anal.* Calcd. for $C_{17}H_{12}FN$: C, 81.91; H, 4.85; N, 5.62. Found: C, 81.56; H, 5.02 N, 5.45.

*N*-(2,4-Difluorophenyl)-*N*-(α-naphthyliden)amine (**5**).

This compound was obtained in 95% yield as a yellow solid, mp 64-65 ºC; ir (potassium bromide): ν =CH 3052, ν C=N 1612 $cm^{-1}$; ms: m/z 267 (molecular ion).

*Anal.* Calcd. for $C_{17}H_{11}F_2N$: C, 76.39; H, 4.15; N, 5.24. Found: C, 76.11; H, 4.46; N, 5.12.

*N*-(3,4-Dichlorophenyl)-*N*-(α-naphthyliden)amine (**6**).

This compound was obtained in 95% yield as a yellow solid, mp 96-97 ºC; ir (potassium bromide): ν =CH 3089, ν C=N 1610 $cm^{-1}$; ms: m/z 300 (molecular ion).

*Anal.* Calcd. for $C_{17}H_{11}Cl_2N$: C, 68.02; H, 3.69; N, 4.67. Found: C, 67.87; H, 3.98; N, 4.78.

General Procedure for Reaction of Aldimines **1-6** with α-Mercapto Acid [22,23].

A mixture of the appropriate aldimine (**1-6**) (1.00 mmol) and α-mercaptoacetic acid (2.00 mmol) in dry toluene was refluxed on a water bath for 30 h, cooled and poured into water. The organic layer was washed with potassium bicarbonate solution (10 ml, 10%) and then with water, dried with sodium sulfate and the toluene was distilled off. Upon crystallization of the residue from petroleum ether (40-60 ºC)/ethanol (1:1), the thiazolidinones **7-12** were obtained as yellow crystals.

3-(4-Methoxyphenyl)-2-(α-naphthyl)-1,3-thiazolidin-4-one (**7**).

This compound was obtained in 71% yield, mp 106-108 °C; ir (potassium bromide): ν =CH 3050, ν C=O 1685 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 3.68 (s, 3H, $OCH_3$), 3.84 (d, 1H, J = 15.6 Hz, 5-$CH_2$; $H_A$), 3.97 (d, 1H, J = 15.6 Hz, 5-$CH_2$; $H_B$), 6.75 (d, 2H, J = 8.8 Hz, 3-5$H_{ph.}$), 6.79 (s, 1H, 2-CH), 7.24 (br.s, 2H, 2(6)-$H_{ph.}$), 7.38-7.49 (m, 2H, $H_{napht.}$), 7.52 (t, 1H, J = 8.1, 6.8 Hz, $H_{napht.}$), 7.58 (td, 1H, J = 8.4, 6.8, 1.6 Hz, $H_{napht.}$), 7.78 (d, 1H, J = 8.1 Hz, $H_{napht.}$), 7.87 (d, 1H, J = 8.1 Hz, $H_{napht.}$), 7.95 (br.s, 1H, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 171.6 (C=O), 157.8, 114.2 and 114.0 (phenyl carbons), 129.2-121.5 (naphthyl carbons), 62.1 (2-CH), 55.0 ($OCH_3$), 33.1 (5-$CH_2$); gc-ms: $t_R$ = 48.4 min, ms: m/z 335 (molecular ion).

*Anal.* Calcd. for $C_{20}H_{17}NO_2S$: C, 71.62; H, 5.11; N, 4.18. Found: C, 71.45; H, 5.45; N, 4.00.

3-(4-Chlorophenyl)-2-(α-naphthyl)-1,3-thiazolidin-4-one (**8**).

This compound was obtained in 68% yield, mp 138-140 °C; ir (potassium bromide): ν =CH 3056, ν C=O 1695 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 3.82 (d, 1H, J = 15.9 Hz, 5-$CH_2$; $H_A$), 3.92 (d, 1H, J = 15.9 Hz, 5-$CH_2$; $H_B$ ), 6.81 (s, 1H, 2-CH), 7.19 (d, 2H, J = 8.8 Hz, 3-5$H_{ph.}$), 7.28 (br.s, 2H, 2(6)-$H_{ph.}$), 7.36-7.42 (m, 2H, $H_{napht.}$), 7.55 (t, 1H, J = 8.1, 6.8 Hz, $H_{napht.}$), 7.61 (td, 1H, J = 8.4, 6.8, 1.6 Hz, $H_{napht.}$), 7.80 (dd, 1H, J = 6.5, 3.0 Hz, $H_{napht.}$), 7.90 (d, 1H, J = 8.1 Hz, $H_{napht.}$), 7.95 (br.s, 1H, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 171.7 (C=O), 129.4 (3- and 5-$C_{phenyl}$), 129.1-121.3 (naphthyl carbons), 61.1 (2-CH), 33.1 (5-$CH_2$); gc-ms: $t_R$ = 45.8 min, ms: m/z 339 (molecular ion).

*Anal.* Calcd. for $C_{19}H_{14}ClNOS$: C, 67.15; H, 4.15; N, 4.12. Found: C, 66.87; H, 4.36; N, 4.46.

3-(4-Bromophenyl)-2-(α-naphthyl)-1,3-thiazolidin-4-one (**9**).

This compound was obtained in 68% yield, mp 148-150 °C; ir (potassium bromide): ν =CH 3056, ν C=O 1695 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 3.82 (d, 1H, J = 15.9 Hz, 5-$CH_2$; $H_A$), 3.94 (d, 1H, J = 15.9 Hz, 5-$CH_2$; $H_B$ ), 6.81 (s, 1H, 2-CH), 7.25 (br.s, 2H, 2(6)-$H_{ph.}$), 7.31-7.42 (m, 4H, $H_{napht.}$ and 3(5)-$H_{ph.}$), 7.55 (t, 1H, J = 8.1, 6.8 Hz, $H_{napht.}$), 7.61 (td, 1H, J = 8.4, 6.8, 1.3 Hz, $H_{napht.}$), 7.81 (dd, 1H, J = 7.1, 2.0 Hz, $H_{napht.}$), 7.90 (d, 1H, J = 8.1 Hz, $H_{napht.}$), 7.96 (br.s, 1H, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 171.5 (C=O), 131.9, 124.8 (phenyl carbons), 129.4-121.9 (naphthyl carbons), 61.0 (2-CH), 33.1 (5-$CH_2$); gc-ms: $t_R$= 50.7 min, ms: m/z 385 (molecular ion).

*Anal.* Calcd. for $C_{19}H_{14}BrNOS$: C, 59.38; H, 3.67; N, 3.64. Found: C, 59.03; H, 3.94; N, 3.39.

3-(4-Fluorophenyl)-2-(α-naphthyl)-1,3-thiazolidin-4-one (**10**).

This compound was obtained in 65% yield, mp 133-134 °C; ir (potassium bromide): ν =CH 3050, ν C=O 1697 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 3.83 (d, 1H, J = 15.9 Hz, 5-$CH_2$; $H_A$), 3.94 (d, 1H, J = 15.9 Hz, 5-$CH_2$; $H_B$), 6.79 (s, 1H, 2-CH); δ 6.90 (t, 2H, J = 8.4 Hz, 3-5$H_{ph.}$), 7.29 (br.s, 2H, 2(6)-$H_{ph.}$), 7.22-7.40 (m, 2H, $H_{napht.}$), 7.52 (t, 1H, J = 8.1, 6.8 Hz, $H_{napht.}$), 7.58 (t, 1H, J = 8.4, 6.8 Hz, $H_{napht.}$), 7.79 (d, 1H, J = 7.8 Hz, $H_{napht.}$), 7.88 (d, 1H, J = 8.1 Hz, $H_{napht.}$), 7.95 (br.s, 1H, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 171.6 (C=O), 160.5-115.9 (phenyl carbons), 129.3-121.9 (naphthyl carbons), 61.1 (2-CH), 33.1 (5-$CH_2$); gc-ms: $t_R$ = 38.4 min, ms: m/z 323 (molecular ion).

*Anal.* Calcd. for $C_{19}H_{14}FNOS$: C, 70.57; H, 4.36; N, 4.33. Found: C, 70.21; H, 4.59; N, 4.21.

3-(2,4-Difluorophenyl)-2-(α-naphthyl)-1,3-thiazolidin-4-one (**11**).

This compound was obtained in 63% yield, mp 121-123 °C; ir (potassium bromide): ν =CH 3062, ν C=O 1685 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 3.90-4.20 (m, 2H, 5-$CH_2$; $H_A$ and $H_B$), 6.60-6.94 (m, 4H, 2-CH and $H_{ph.}$), 7.38-7.47 (m, 2H, $H_{napht.}$), 7.51 (t, 1H, J = 8.3, 6.8 Hz, $H_{napht.}$), 7.56 (t, 1H, J = 8.6, 6.8 Hz, $H_{napht.}$), 7.79 (d, 1H, J = 7.8 Hz, $H_{napht.}$), 7.86 (d, 1H, J = 8.3 Hz, $H_{napht.}$), 8.04 (br.s, 1H, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 171.6 (C=O), 161.9, 157.8, 111.7 and 105.1 (phenyl carbons), 129.1-121.2 (naphthyl carbons), 59.0 (2-CH), 32.0 (5-$CH_2$); gc-ms: $t_R$ = 35.6 min, ms: m/z 341 (molecular ion).

*Anal.* Calcd. for $C_{19}H_{13}F_2NOS$: C, 66.85; H, 3.84; N, 4.10. Found: C, 66.56; H, 4.07; N, 4.35.

3-(3,4-Dichlorophenyl)-2-(α-naphthyl)-1,3-thiazolidin-4-one (**12**).

This compound was obtained in 63% yield, mp 136-138 °C; ir (potassium bromide): ν =CH 3099, ν C=O 1691 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 3.81 (d, 1H, J = 16.2 Hz, 5-$CH_2$; $H_A$), 3.92 (d, 1H, J = 16.2 Hz, 5-$CH_2$; $H_B$), 6.78 (s, 1H, 2-CH), 7.10 (d, 1H, J = 8.8 Hz, 6-$H_{ph.}$), 7.25 (d, 1H, J = 8.8 Hz, 5-$H_{ph.}$), 7.32 (d, 1H, J = 7.1 Hz, $H_{napht.}$), 7.39 (t, 1H, J = 8.1, 7.1 Hz, $H_{napht.}$), 7.55 (t, 1H, J = 8.1, 7.1 Hz, $H_{napht.}$), 7.61 (t, 1H, J = 8.1, 7.1 Hz, $H_{napht.}$), 7.66 (s, 1H, 2-$H_{ph.}$), 7.81 (d, 1H, J = 8.1 Hz, $H_{napht.}$), 7.90 (d, 1H, J = 8.1 Hz, $H_{napht.}$), 7.94 (br.s, 1H, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 171.6 (C=O), 132.9, 130.4 (phenyl carbons), 129.4, 121.9 (naphthyl carbons), 61.0 (2-CH), 33.1 (5-$CH_2$); gc-ms: $t_R$ = 52.5 min, ms: m/z 373 (molecular ion).

*Anal.* Calcd. for $C_{19}H_{13}Cl_2NOS$: C, 60.97; H, 3.50; N, 3.74. Found: C, 60.68; H, 3.77; N, 3.98.

General procedure for Reaction of Aldimines **1-6** with Allylmagnesium Bromide [22,23].

The appropriate aldimine (**1-6**) (1.00 mmol) in 40 ml of ether was added slowly to 25 ml of a ether solution of allylmagnesium bromide prepared from 6.00 mmol of magnesium and 3.00 mmol of allyl bromide. The mixture was stirred for 8-15 hours at room temperature and then cooled and treated with saturated ammonium chloride solution. The products were extracted with ether (3 x 10 ml). The organic layer was dried (sodium sulfate) and the residue purified by chromatography column (silica gel).

*N*-(4-Methoxyphenyl)-*N*-[1-(α-naphthyl)but-3-enyl]amine (**13**).

This compound was obtained in 80% yield, red oil; ir (neat): ν NH 3403, ν C=C 1513, 919 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 2.49-2.88 (m, 2H, 2-$CH_2$), 3.68 (s, 3H, $OCH_3$), 4.05 (s, 1H, NH), 5.15 (dd, 1H, J = 4.1 Hz, 1-H), 5.81-5.92 (m, 1H, =CH), 5.19, 5.25 (dd, each, $J_{trans}$ = 17.0, $J_{cis}$ = 10.2, $J_{4-4}$ = 1.5 Hz, 2H, =$CH_2$), 6.41, 6.64 (AA´BB´-system, 4H, J = 9.0 Hz, $H_{ph.}$), 7.41 (t, 1H, J = 8.0, 7.3 Hz, $H_{napht.}$), 7.52 (t, 1H, J = 8.0, 7.0 Hz, $H_{napht.}$), 7.58 (td, 1H, J = 9.0, 7.0 Hz, $H_{napht.}$), 7.66 (d, 1H, J = 7.3 Hz, $H_{napht.}$), 7.75 (d, 1H, J = 8.0 Hz, $H_{napht.}$), 7.92 (d, 1H, J = 8.0 Hz, $H_{napht.}$), 8.19 (d, 1H, J = 9.0 Hz, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 151.9 (4-$C_{ph}$), 141.4 (1-$C_{ph}$), 114.7 (3,5-$C_{ph}$) ,114.4 (2,6-$C_{ph}$), 138.3, 134.1, 130.6, 129.2, 127.4, 126.0, 125.7, 125.3, 123.0 and 122.3 (naphthyl carbons), 134.9 (=CH), 118.3 (=$CH_2$), 55.7 ($OCH_3$), 53.5 (1-CH), 41.7 (2-$CH_2$); gc-ms: $t_R$ = 43.0 min, ms: m/z 303 (molecular ion).

*Anal.* Calcd. for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.01; H, 7.13; N, 4.44.

*N*-(4-Chlorophenyl)-*N*-[1-(α-naphthyl)but-3-enyl]amine (**14**).

This compound was obtained in 92% yield, red oil; ir (neat): ν NH 3415, ν C=C 1598, 919 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 2.50-2.90 (m, 2H, 2-$CH_2$), 4.33 (s, 1H, NH), 5.15-5.32 (m, 1H, 1-H and =$CH_2$), 5.78-5.92 (m, 1H, =CH), 6.38, 6.98 (AA´BB´-system, 4H, J = 8.0 Hz, $H_{ph.}$), δ 7.41 (t, 1H, J = 8.3, 7.3 Hz, $H_{napht.}$), 7.50-7.64 (m, 3H, $H_{napht.}$), 7.78 (d, 1H, J = 8.3 Hz, $H_{napht.}$), 7.94 (d, 1H, J = 7.8 Hz, $H_{napht.}$), 8.17 (d, 1H, J = 8.8 Hz, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 145.6 (1-$C_{ph}$), 128.9 (3,5-$C_{ph}$), 121.8 (4-$C_{ph}$) and 114.6 (2,6-$C_{ph}$), 137.3, 134.1, 130.4, 129.3, 127.8, 126.2, 125.7, 125.5, 123.0, 122.1 (naphthyl carbons), 134.4 (=CH), 118.5 (=$CH_2$), 52.9 (1-CH), 41.5 (2-$CH_2$); gc-ms: $t_R$ = 43.0 min, m/z 307 (molecular ion).

*Anal.* Calcd. for $C_{20}H_{18}ClN$: C, 78.04; H, 5.89; N, 4.55. Found: C, 77.85; H, 56.11; N, 4.12.

*N*-(4-Bromophenyl)-*N*-[1-(α-naphthyl)but-3-enyl]amine (**15**).

This compound was obtained in 94% yield, yellow oil; ir (neat): ν NH 3413, ν C=C 1592, 921 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 2.50-2.90 (m, 2H, 2-$CH_2$), 4.33 (s, 1H, NH), 5.14-5.30 (m, 1H, 1-H), 5.76-5.91 (m, 1H, =CH), 5.14-5.30 (m, 2H, =$CH_2$), 6.32, 7.11 (AA´BB´-system, 4H, J = 8.8 Hz, $H_{ph.}$), 7.40 (t, 1H, J = 8.3, 7.3 Hz, $H_{napht.}$), 7.50-7.63 (m, 3H, $H_{napht.}$), 7.77 (d, 1H, J = 8.3 Hz, $H_{napht.}$), 7.94 (d, 1H, J = 7.8 Hz, $H_{napht.}$), 8.16 (d, 1H, J = 8.3 Hz, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 145.9 (1-$C_{ph}$), 131.7 (3,5-$C_{ph}$), 114.9 (2,6-$C_{ph}$) and 108.9 (4-$C_{ph}$), 137.2, 134.1, 130.4, 122.1, 129.2, 127.6, 126.2, 125.6, 125.4 and 123.0 (naphthyl carbons), 134.5 (=CH), 118.6 (=$CH_2$), 52.9 (1-CH), 41.4 (2-$CH_2$); gc-ms: $t_R$ = 46.3 min, ms: m/z 351 (molecular ion).

*Anal.* Calcd. for $C_{20}H_{18}BrN$: C, 68.19; H, 5.15; N, 3.98. Found: C, 68.45; H, 5.04; N, 4.13.

*N*-(4-Fluorophenyl)-*N*-[1-(α-naphthyl)but-3-enyl]amine (**16**).

This compound was obtained in 85% yield, red oil; ir (neat): ν NH 3413, ν C=C 1508, 919 $cm^{-1}$; $^1H$ nmr (deuteriumchloroform): δ 2.49-2.87 (m, 2H, 2-$CH_2$), 4.18 (br.s, 1H, NH), 5.14 (dd, 1H, J = 4.2 Hz, 1-H), 5.79-5.91 (m, 1H, =CH), 5.16, 5.25 (dd, each, 2H, $J_{trans}$ = 17.0, $J_{cis}$ = 10.2, $J_{4-4}$ = 1.5 Hz, =$CH_2$), 6.36 (dd, 2H, J = 4.2 Hz, $H_{ph.}$), 6.73 (t, 2H, J = 8.4, 8.8 Hz, $H_{ph.}$), 7.40 (t, 1H, J = 8.1, 7.8 Hz, $H_{napht.}$), 7.48-7.62 (m, 3H, $H_{napht.}$), 7.75 (d, 1H, J = 8.1 Hz, $H_{napht.}$), 7.92 (d, 1H, J = 7.8 Hz, $H_{napht.}$), 8.16 (d, 1H, J = 8.4 Hz, $H_{napht.}$); $^{13}C$ nmr (100 MHz): δ 156.0 (d, J = 234 Hz, 4-Cph), 143.4 (1-$C_{ph}$), 115.6 (d, J = 22 Hz, 3,5-$C_{ph}$) and 114.1 (d, J = 7.3 Hz, 2,6-$C_{ph}$), 137.7, 134.1, 130.5, 129.3, 127.7, 126.2, 125.7, 125.5, 123.1, 122.1 (naphthyl carbons), 134.7 (=CH), 118.6

(=$CH_2$), 53.4 (1-CH), 41.7 (2-$CH_2$); gc-ms: $t_R$ = 37.8 min, ms: m/z 291 (molecular ion). ms: m/z 291 (molecular ion).

*Anal*. Calcd. for $C_{20}H_{18}FN$: C, 82.45; H, 6.23; N, 4.81. Found: C, 82.12; H, 6.47; N, 4.55.

*N*-(2,4-Difluorophenyl)-*N*-[1-(α-naphthyl)but-3-enyl]amine (**17**).

This compound was obtained in 98% yield, red oil; ir (neat): ν NH 3425, ν C=C 1519, 919 $cm^{-1}$; $^1$H nmr (deuteriumchloroform): δ 2.54-2.90 (m, 2H, 2-$CH_2$), 4.42 (br.s, 1H, NH), 5.14-5.34 (m, 3H, 1-H and =$CH_2$), 5.78-5.93 (m, 1H, =CH), 6.11 (td, 1H, J =9.8, 5.4 Hz, $H_{ph.}$), 6.40-6.48 (m, 1H, $H_{ph.}$), 6.78 (ddd, 1H, J = 2.9 Hz, $H_{ph.}$), 7.41 (t, 1H, J = 7.8, 8.3 Hz, $H_{napht.}$), 7.49-7.63 (m, 3H, $H_{napht.}$), 7.77 (d, 1H, J = 8.3 Hz, $H_{napht.}$), 7.93 (d, 1H, J = 7.8 Hz, $H_{napht.}$), 8.17 (d, 1H, J = 8.3 Hz, $H_{napht.}$); $^{13}$C nmr (100 MHz): δ 154.2 (dd, $^1J_{C-F}$ = 237.0 Hz, $^3J_{C-F}$ = 10.9 Hz, 4-$C_{ph}$), 150.8 (dd, $^1J_{C-F}$ = 241.0 Hz, $^3J_{C-F}$ = 10.9 Hz, 2-$C_{ph}$), 124.8 (1-$C_{ph}$), 112.9 (dd, $^3J_{C-F}$ = 9.2 Hz, 6-$C_{ph}$), 110.4 (dd, $^2J_{C-F}$ = 21.1 Hz, $^4J_{C-F}$ = 3.7 Hz, 5-$C_{ph}$) and 103.2 (dd, $^2J_{C-F}$ = 23.0 Hz, 3-$C_{ph}$), 137.4, 134.1, 130.4, 129.3, 127.7, 126.2, 125.7, 125.5, 123.1, and 122.1 (naphthyl carbons), 134.3 (=CH), 118.7 (=$CH_2$), 53.1 (1-CH), 41.7 (2-$CH_2$); gc-ms: $t_R$ = 36.2 min, ms: m/z 309 (molecular ion).

*Anal*. Calcd. for $C_{20}H_{17}F_2N$: C, 77.65; H, 5.54; N, 4.53. Found: C, 77.49; H, 5.89; N, 4.74.

*N*-(3,4-Dichlorophenyl)-*N*-[1-(α-naphthyl)but-3-enyl]amine (**18**).

This compound was obtained in 81% yield, red oil; ir (neat): ν NH 3415, ν C=C 1594, 919 $cm^{-1}$; $^1$H nmr (deuteriumchloroform): δ 2.55-2.90 (m, 2H, 2-$CH_2$), 4.48 (br.s, 1H, NH), 5.19 (dd, 1H, J = 4.0 Hz, 1-H), 5.20-5.30 (m, 2H, =$CH_2$), 5.77-5.87 (m, 1H, =CH), 6.25 (dd, 1H, J = 9.0, 3.0 Hz, $H_{ph.}$), 6.60 (d, 1H, J = 3.0 Hz, $H_{ph.}$), 7.03 (d, 1H, J = 9.0 Hz, $H_{ph.}$), 7.42 (t, 1H, J = 8.0, 8.0 Hz, $H_{napht.}$), 7.52-7.58 (m, 2H, $H_{napht.}$), 7.62 (t, 1H, J = 9.0, 7.0 Hz, $H_{napht.}$), 7.79 (d, 1H, J = 8.0 Hz, $H_{napht.}$), 7.94 (d, 1H, J = 8.0 Hz, $H_{napht.}$), 8.14 (d, 1H, J = 9.0 Hz, $H_{napht.}$); $^{13}$C nmr (100 MHz): δ 146.5 (1-$C_{ph}$), 132.6 (3-$C_{ph}$), 130.5 (5-$C_{ph}$), 120.1 (4-$C_{ph}$), 114.8 (2-$C_{ph}$), 112.8 (6-$C_{ph}$), 136.8, 134.1, 130.5, 129.3, 127.9, 126.3, 125.6, 125.5, 123.0, 122.1 (naphthyl carbons), 134.2 (=CH), 118.7 (=$CH_2$), 52.9 (1-CH), 41.7 (2-$CH_2$); gc-ms: $t_R$ = 49.1 min, m/z 341 (molecular ion).

*Anal*. Calcd. for $C_{20}H_{17}Cl_2N$: C, 70.18; H, 5.01; N, 4.09. Found: C, 70.36; H, 5.23; N, 4.27.

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[27] These biological results will be published elsewhere.