



Rational use of substituted *N*-allyl and *N,N*-diallylanilines in the stereoselective synthesis of novel 2-alkenyltetrahydro-1-benzazepines

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ABSTRACT

Two new series of 1,4-epoxy-2-*exo*-vinyl(isopropenyl)tetrahydro-1-benzazepines and *cis*-2-vinyl(isopropenyl)-4-hydroxytetrahydro-1-benzazepines were prepared by an efficient three/four-step route from available substituted *N,N*-diallylanilines and mono *N*-allylanilines. The amino-Claisen rearrangement and the sequential oxidation/intramolecular 1,3-dipolar cycloaddition reactions were used as the key steps in this synthesis. All the synthesized compounds were fully characterized by IR, GC–MS and NMR techniques.

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1. Introduction

The tetrahydro-1-benzazepine ring system is a crucial pharmacophore in drug discovery and many of its derivatives exhibit a broad spectrum of biological activity. Medicinal chemists are often attracted to this type of compounds as a promising therapeutic agents, for instance as renal and cardiovascular agents,¹ potential anti-tumor,² and neuroleptic agents³ as well as promising antihypertensives.⁴ Other tetrahydro-1-benzazepine derivatives have been also reported as orally bioavailable growth hormone secretagogue,⁵ inhibitors of *Trypanosoma cruzi* dihydrofolate reductase,⁶ and potent antagonists of platelet-activating factor⁷ and glycine.⁸

The functionalization of tetrahydro-1-benzazepine ring is an efficient strategy to enhance its pharmacological activity and/or offer more interesting properties. Consequently, it is not surprising that a significant number of synthetic methods have been developed for the synthesis of new derivatives of this heterocyclic system.⁹ For our part, recently we described a simple and efficient synthetic pathway to obtain novel 1,4-epoxy-2-aryl-tetrahydro-1-benzazepines as well as 1,4-epoxy-2-aryl-tetrahydro-naphtho[1,2-*b*]azepines and their reduced tetrahydro-1-benzazepinols starting from available *ortho*-allyl-*N*-benzyl-substituted anilines and

ortho-allyl-*N*-benzyl-substituted α -naphthylamines.¹⁰ Moreover, we have also shown that many of the above mentioned compounds possess remarkable activity in vitro against epimastigote and promastigote forms of *T. cruzi* and *L. chagasi* parasites.¹¹

In order to enhance the utility of our method, and as part of a program to identify structurally novel anti-parasitic compounds against both *T. cruzi* and *L. chagasi* parasites, we are now describing the synthesis and structural elucidation of two new series of 1,4-epoxy-2-vinyl(isopropenyl)tetrahydro-1-benzazepines **5a–e/6a–f** and 4-hydroxy-2-vinyl(isopropenyl)tetrahydro-1-benzazepines **7a–e/8a–f**, using the sequence of selective oxidation and intramolecular 1,3-dipolar cycloaddition of *N*-alkenyl-*ortho*-allylanilines as the key step. To the best of our knowledge, these 2-alkenyl substituted tetrahydro-1-benzazepines have not been yet described in the literature. Nevertheless, two closely related 2-vinyl analogues were prepared by three different research groups, but using another synthetic pathways.¹²

2. Results and discussion

Our synthetic strategy to target compounds is depicted in Schemes 1 and 2. As shown in Scheme 1, the key intermediates **2a–e** and **4a–f** were prepared in one or two steps from the readily available *N,N*-diallylanilines **1a–e** and mono *N*-allylanilines **1f–k**, respectively. Thus, the thermal induced aromatic amino-Claisen

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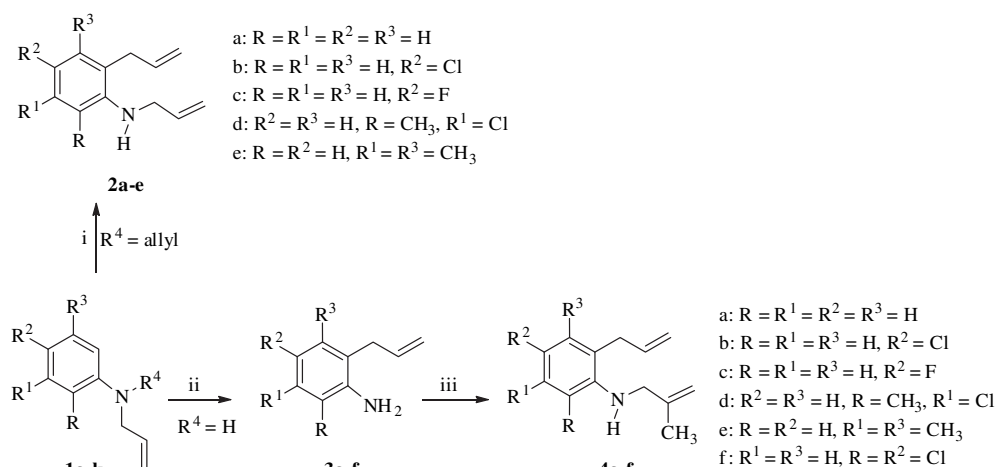
rearrangement of **1a–k** was effectively promoted using **1** or 1.5 equiv of boron trifluoride diethyl ether complex as the catalyst.¹³ After several preliminary experiments, we found that the most suitable reaction times and temperatures to reach the desired rearranged products were 1–4 h and 130–140 °C for the *N,N*-diallylaniline derivatives, and 6–8 h and 120–140 °C for the mono *N*-allylaniline derivatives, respectively. Even though the consumption of the starting substrates were complete as was evidenced by TLC, the isolated yields of **2a–e** and **3a–f** ranged from moderate to good, essentially unaffected by the nature and positions of the substituents on the benzene ring of anilines **1** (Table 1). However, in the conditions employed, the partial isomerization of the formed *ortho*-allylanilines and the formation of the indoline products, two possible side reactions, as well as non-identifiable degradation products, were also observed in the ¹H NMR spectra of the analyzed crude reaction mixtures, thereby reducing the yields of the expected products.

Table 1

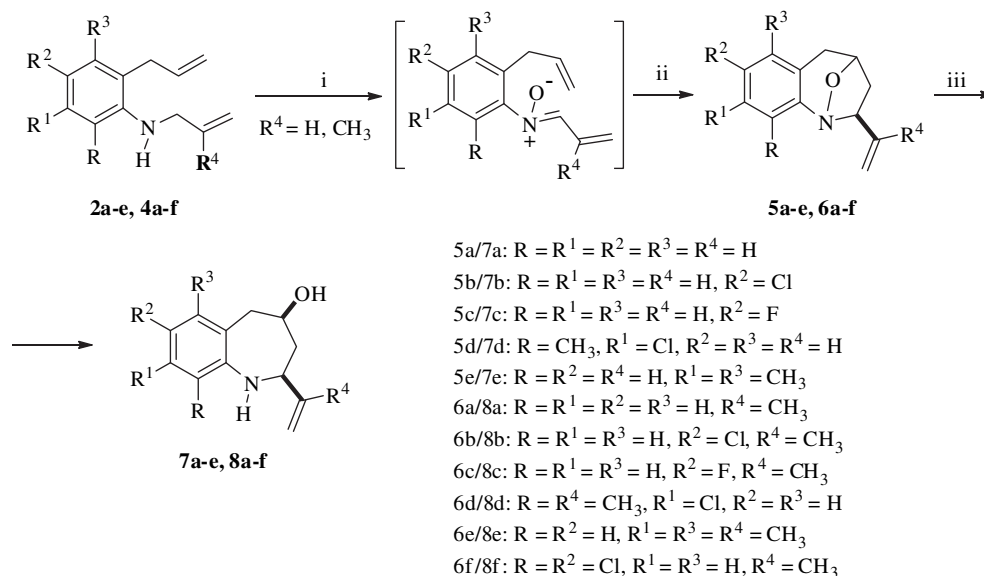
Preparation of *ortho*-allylanilines **2a–e** and **3a–f** by amino-Claisen rearrangement of *N,N*-diallylanilines **1a–e** and mono *N*-allylanilines **1f–k**

1	[BF ₃ ·OEt ₂] equiv	Time (h)	Temperature (°C)	2 and 3 ^a (Yield, %)
1a	1	4	135	2a (62)
1b	1	4	140	2b (66)
1c	1	4	140	2c (63)
1d	1	2	130	2d (65)
1e	1	1	130	2e (70)
1f	1.5	7	135	3a (65)
1g	1.5	8	140	3b (70)
1h	1.5	8	140	3c (68)
1i	1.5	6	130	3d (73)
1j	1.5	6	130	3e (76)
1k	1.5	6	120	3f (58)

^a Yields are for isolated, chromatographically pure products.



Scheme 1. Reagents and reaction conditions: (i) BF₃·OEt₂ (0.01 equiv), 130–140 °C, 1–4 h; (ii) BF₃·OEt₂ (0.015 equiv), 120–140 °C, 6–8 h; (iii) Methallyl chloride (10 mmol), Na₂CO₃ (30 mmol), KI (5 mol %), dry DMF, rt, 12–20 h.



Scheme 2. Reagent and reaction conditions: (i) 30% H₂O₂ (30 mmol), Na₂WO₄·2H₂O (10 mol %), MeOH, 0–25 °C, 6–72 h; (ii) Toluene, 80–110 °C, 4–7 h; (iii) Zn (100 mmol), glacial CH₃CO₂H (70 mmol), 37% HCl (70 mmol), 0 °C, 0.5–2 h.

With the first key precursors **2a–e** in hand, we turned our attention to the *N*-methallylation of the rearranged products **3a–f** in order to obtain the second key precursors, namely *ortho*-allyl-*N*-

methallylanilines **4a–f**. A typical reaction procedure involves the slow addition of an equimolar amount of methallyl chloride to **3a–f** in dry DMF in the presence of sodium carbonate and small amounts

of KI, and stirring the reaction mixtures for 12–20 h at room temperature. In this manner, compounds **4a–f** were obtained as low-viscosity maroon oils in good yields (67–88%), after column chromatography purification.

The preparation of the 1,4-epoxy-cycloadducts **5a–e** and **6a–f** was carried out in the next step of our approach, and involved treating the obtained key intermediates **2a–e** and **4a–f** in methanol with excess of 30% H₂O₂ solution in the presence of 10 mol % of sodium tungstate as the catalyst, according to the methodology reported by Murahashi.¹⁴ The formation of the corresponding nitrones was monitored by TLC by consumption of the starting *ortho*-allylanilines. After completion of the oxidation process, the catalyst and the excess of hydrogen peroxide along with the methanol were removed by extraction from the reaction mixtures, and the remaining organic residues (nitrones) were dissolved in toluene and then heated to promote their intramolecular 1,3-dipolar cycloaddition across the pendant allylic fragment connected to the *ortho* position (Scheme 2).

We have found that the substitution pattern on the benzene ring of both key intermediates **2** and **4** plays a considerable influence on the formation of their nitrones; 5,6- and 4,6-disubstituted *ortho*-allylanilines (**2d**, **4d**, and **4f**) required longer reaction times (72 h) than the 3,5-disubstituted ones (**2e** and **4e**) (8 h), presumably due to steric factors associated with the presence of methyl group or chlorine atom at the C-6 position inhibiting the effective oxidation of the –NH–CH₂– framework. In turn, the oxidation of the non-substituted and 4-substituted *ortho*-allylanilines (R²=H, Cl, F) proceeds more easily than that of their 3,5-disubstituted analogues, giving the corresponding nitrones in 6 h (Table 2). As was also evidenced by TLC, the consumption of all the nitrones generated from **2** and **4** took place after 4–7 h of

heating, yielding the corresponding 1,4-epoxy-cycloadducts **5a–e** and **6a–f**, which were isolated by silica gel column chromatography as maroon oils or crystalline substances in moderate to good yields (Table 2). In all the cases, the formation of only one of the two possible 1,4-epoxy-cycloadducts (*endo* and *exo*) was observed in the ¹H NMR spectra of the crude reaction mixtures along with others non-identifiable degradation products.

Structural elucidation of **5a–e** and **6a–f** was mainly based on NMR studies. In the ¹H NMR spectra of **5a–e**, the signal attributed to tertiary H-2 proton appears at δ 3.89–4.02 as doublets of doublets (ddd) due to coupling with vicinal 3-H_AH_B azepinic protons (³J=7.4–8.3 Hz and ³J=2.1–2.8 Hz) and vicinal 1'-H olefinic proton (³J=6.9–7.5 Hz), while in the spectra of **6a–f** the same proton appears at δ 3.85–3.96 as doublets of doublets (dd) due to coupling with 3-H_AH_B protons (³J=8.3–8.9 Hz and ³J=2.2–2.9 Hz). The signal attributed to 4-H proton in 1,4-epoxy-cycloadducts of type **5** and **6** appears at δ 4.83–4.91 as doublets of doublets (ddd) due to coupling with vicinal 3-H_AH_B (³J=1.4–2.2 Hz and ³J=7.1–7.8 Hz) and 5-H_B (³J=5.3–5.8 Hz) protons. Extensive COSY, DEPT-135, HSQC, and HMBC measurements allowed the assignment of all the signals and correlations to individual H- and C-atoms (see Experimental section). The data derived from these experiments along with the coupling constants values of the six azepinic protons were used to identify the isolated 1,4-epoxy-cycloadducts as the *exo*-isomer in all the cases. In order to provide undoubted structural proof, the X-ray diffraction analysis was carried out for compounds **5a**, **6d**, and **6f**.¹⁵ The X-ray crystal structures of **5a** and **6d** are shown in Fig. 1. Crystallographic data for the structures **5a**, **6d**, and **6f** have been deposited with the Cambridge Crystallographic Data Centre under the numbers CCDC 774910, CCDC 774914, and CCDC 774915, respectively.

All the above information clearly indicates that the stereochemical outcome of the 1,3-dipolar cycloaddition is the consequence of an *exo* approach of the internal olefinic moiety with regard to the transient dipole (nitron) generated from **2a–e** and **4a–f** to produce exclusively the corresponding 2-*exo*-stereoisomer. These results are in full agreement with those obtained previously in our laboratory.¹⁰

In the last step of our synthetic route, the reductive cleavage of the N–O bond of the isolated 1,4-epoxy-cycloadducts to obtain the desired 2-alkenyl-substituted tetrahydro-1-benzazepin-4-ols was examined. We conducted the reductive cleavage of **5a–e** and **6a–f** by treatment with excess of zinc powder in a mixture of glacial acetic acid and concentrated hydrochloric acid at 0 °C, and stirring the reaction mixtures for 0.5–2.0 h. In the conditions employed, the reductive cleavage of the N–O bridged bond proceeded very easy with the formation of the expected *cis*-2-alkenyltetrahydro-1-benzazepinols, which were isolated by silica gel column chromatography in excellent yields (90–95%) as high-viscosity oils or crystalline substances.

Table 2
Preparation of 1,4-epoxy-cycloadducts **5a–e** and **6a–f** from *ortho*-allylanilines **2a–e** and **4a–f**

<i>ortho</i> -Allylaniline	Conditions (temperature, °C/time, h)		5 and 6 ^a (Yield, %)
	Oxidation	1,3-Dipolar cycloaddition	
2a	0–25/6	80/4	5a (58)
2b	0–25/6	80/4	5b (50)
2c	0–25/6	80/4	5c (48)
2d	25/72	110/7	5d (57)
2e	0–25/8	80/5	5e (55)
4a	0–25/6	80/4	6a (49)
4b	0–25/6	80/4	6b (52)
4c	0–25/6	80/4	6c (50)
4d	25/72	110/7	6d (65)
4e	0–25/8	80/7	6e (60)
4f	25/72	110/7	6f (63)

^a Yields are for isolated, chromatographically pure products.

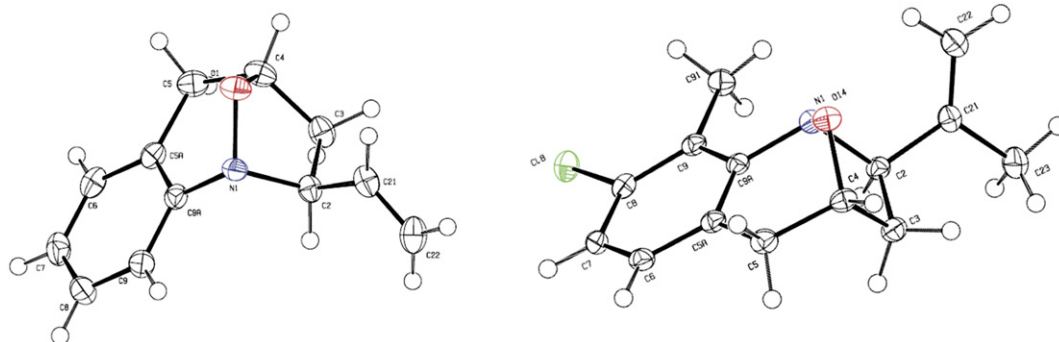
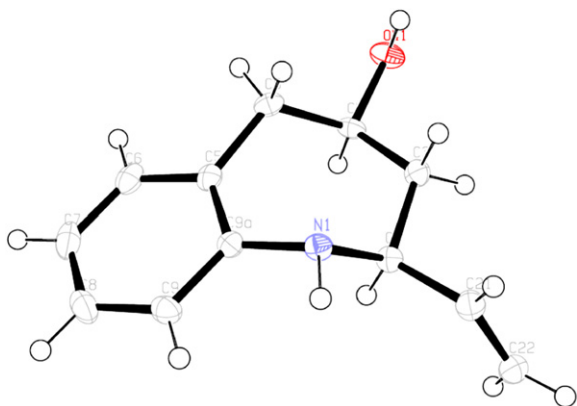


Fig. 1. X-ray crystal structures of 1,4-epoxy-2-*exo*-vinyl-2,3,4,5-tetrahydro-1(1H)-benzazepine **5a** and 8-chloro-9-methyl-1,4-epoxy-2-*exo*-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1(1H)-benzazepine **6d** (ORTEP views).¹⁵

The structures and stereochemistry of these novel compounds were determined by ^1H NMR and ^{13}C NMR spectroscopy. All the signals for each individual H- and C-atoms (see [Experimental](#) section) were also unambiguously assigned on the basis of their COSY, HSQC and HMBC spectra. The *cis* stereochemistry at the stereogenic centers 2-C and 4-C of the tetrahydroazepine ring was established based on its 2D-NOESY spectra, in which the tertiary proton 2-H at 3.39–3.82 ppm (for compounds **7a–e**) and 3.32–3.43 ppm (for compounds **8a–f**) demonstrates unambiguous NOE cross peak with the stereogenic 4-H proton at 3.79–4.15 ppm (for compounds **7a–e**) and 3.77–3.88 ppm (for compounds **8a–f**), indicating that both protons are oriented in the same side of the heterocyclic ring. Consequently, the 2-alkenyl group is oriented equatorially, since the proton 2-H appears as doublets of doublets of doublets (ddd, for compounds **7a–e**) due to coupling with 3- H_{ax} ($^3J=9.9$ – 11.2 Hz), 3- H_{eq} ($^3J=1.9$ – 2.4 Hz) and vicinal olefinic proton $-\text{CH}=\text{}$ ($^3J=7.4$ – 7.5 Hz); in the case of compounds **8a–f**, the proton 2-H appears as doublets of doublets (dd) with $J_1=11$ Hz and $J_2=1.5$ Hz and therefore having exactly one *trans*-axial and one *cis*-equatorial coupling partners, namely 3- H_{ax} and 3- H_{eq} . The 4-hydroxy group is also oriented equatorially, since proton 4-H appears as doublets of doublets of doublets (ddd, for both **7a–e** and **8a–f** compounds) with $J_1=9.5$ Hz, $J_2=4$ Hz, and $J_3=2$ Hz and therefore having two *trans*-axial coupling partners (3- H_{ax} and 5- H_{ax}) and two *cis*-equatorial coupling partners (3- H_{eq} and 5- H_{eq}). The data derived from NOESY experiments along with the coupling constants values of the six azepinic protons were used to identify the isolated 2-aryltetrahydro-1-benzazepin-4-ols as the *cis*-isomer with the tetrahydroazepine ring in the chair conformation and consequently proves that their precursors **5** and **6** are *exo* adducts. The structure assignment of **7a**, **7b**, and **7c** was supported by an X-ray crystallography determination.¹⁶ The X-ray crystal structure of **7a** is shown in [Fig. 2](#). Crystallographic data for the structures **7a**, **7b**, and **7c** have been deposited with the Cambridge Crystallographic Data Centre under the numbers CCDC 728210, CCDC 728212, and CCDC 72821, respectively.



(2-CH₃). MS (EI-70 eV) *m/z* (%): 221 (M⁺, ³⁵Cl, 20), 180 (42), 178 (67), 145 (100), 144 (63), 130 (49), 115 (23). Anal. Calcd for C₁₃H₁₆ClN: C, 70.42; H, 7.27; N, 6.32. Found: C, 70.30; H, 7.15; N, 6.41%.

4.2.2. *N*,2-Diallyl-3,5-dimethylaniline (2e). IR (liquid film) $\nu_{\max}$: 3432 (N–H), 1636 (C=C allyl), 915 (=C–H allyl) cm^{−1}. ¹H NMR (400 MHz, CDCl₃) δ : 6.48 (1H, s, 4-H), 6.38 (1H, s, 6-H), 6.00–5.91 (2H, m, –CH=), 5.28–5.06 (2H, m, N–CH₂–CH=CH₂), 5.17–5.03 (2H, m, –CH₂–CH=CH₂), 3.79 (2H, dt, *J*=5.3, 1.7 Hz, N–CH₂–), 3.34 (2H, dt, *J*=5.7, 1.6 Hz, –CH₂–), 2.29 (3H, s, 5-CH₃), 2.26 (3H, s, 3-CH₃). ¹³C NMR (100 MHz, CDCl₃) δ : 146.6 (1-C), 137.1 (3-C), 136.9 (5-C), 136.1 (CH=), 135.7 (CH=), 121.0 (4-C), 119.4 (2-C), 116.3 (=CH₂), 115.6 (=CH₂), 110.3 (6-C), 47.1 (N–CH₂), 31.6 (–CH₂), 21.9 (5-CH₃), 20.4 (3-CH₃). MS (EI-70 eV) *m/z* (%): 201 (M⁺, 36), 160 (56), 158 (86), 146 (43), 145 (100), 144 (56), 130 (30), 115 (21). Anal. Calcd for C₁₄H₁₉N: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.69; H, 9.42; N, 7.08%.

4.2.3. 6-Allyl-3-chloro-2-methylaniline (3d). IR (liquid film) $\nu_{\max}$: 3482 (N–H), 3399 (N–H), 1622 (C=C allyl), 918 (=C–H allyl) cm^{−1}. ¹H NMR (400 MHz, CDCl₃) δ : 6.86 (1H, d, *J*=8.0 Hz, 3-H), 6.80 (1H, d, *J*=8.0 Hz, 4-H), 5.93 (1H, ddt, *J*=17.1, 10.3, 5.8 Hz, –CH=), 5.16 (1H, dq, *J*=10.3, 1.8 Hz, =CH_AH), 5.12 (1H, dq, *J*=17.1, 1.8 Hz, =CH_BH), 3.29 (2H, dt, *J*=5.8, 1.8 Hz, –CH₂–), 2.27 (3H, s, 6-CH₃). ¹³C NMR (100 MHz, CDCl₃) δ : 144.3 (1-C), 135.6 (CH=), 133.1 (5-C), 128.2 (3-C), 121.9 (2-C), 120.0 (6-C), 118.9 (4-C), 116.5 (=CH₂), 36.6 (–CH₂), 14.0 (6-CH₃). MS (EI-70 eV) *m/z* (%): 181 (M⁺, ³⁵Cl, 100), 166 (39), 146 (48), 131 (83), 130 (46). Anal. Calcd for C₁₀H₁₂ClN: C, 66.12; H, 6.66; N, 7.71. Found: C, 66.00; H, 6.81; N, 7.56%.

4.2.4. 2-Allyl-4,6-dichloroaniline (3f). IR (liquid film) $\nu_{\max}$: 3480 (N–H), 3389 (N–H), 1624 (C=C allyl), 921 (=C–H allyl) cm^{−1}. ¹H NMR (400 MHz, CDCl₃) δ : 7.18 (1H, d, *J*=2.4 Hz, 5-H), 6.95 (1H, d, *J*=2.4 Hz, 3-H), 5.90 (1H, ddt, *J*=17.2, 10.2, 6.1 Hz, –CH=), 5.18 (1H, dq, *J*=10.2, 1.6 Hz, =CH_AH), 5.12 (1H, dq, *J*=17.2, 1.6 Hz, =CH_BH), 4.10 (2H, br s, –NH₂), 3.28 (2H, d, *J*=6.1 Hz, –CH₂–). ¹³C NMR (100 MHz, CDCl₃) δ : 140.3 (1-C), 134.4 (CH=), 128.5 (3-C), 127.2 (5-C), 126.4 (2-C), 122.6 (4-C), 120.2 (6-C), 117.5 (=CH₂), 36.7 (–CH₂). MS (EI-70 eV) *m/z* (%): 201 (M⁺, ³⁵Cl, 93), 186 (74), 151 (80), 131 (100), 130 (80). Anal. Calcd for C₉H₉Cl₂N: C, 53.49; H, 4.49; N, 6.93. Found: C, 53.33; H, 4.38; N, 7.07%.

4.3. General procedure for the synthesis of 2-allyl-*N*-(2-methylallyl)anilines 4

To a mixture of 2-allylanilines **3a–f** (10 mmol) with sodium carbonate (30 mmol, 3.18 g) and potassium iodide (5 mol %) in DMF (25 mL) was slowly added an equimolar amount of methylallyl chloride (10 mmol, 0.97 mL) at room temperature. The reaction mixtures were stirred for 12–20 h (TLC control) and then extracted with CH₂Cl₂ (2×100 mL) and washed with enough water to eliminate DMF. The combined organic layers were dried over anhydrous sodium sulfate, and the solvent removed under reduced pressure. The crude products were purified by silica gel column chromatography (heptane/ethyl acetate; compositions in the range from 90:1 to 60:1 v/v) to give **4a–f** as low-viscosity maroon oils.

4.3.1. 2-Allyl-*N*-(2-methylallyl)aniline (4a). Reaction time: 12 h. Yield: 1.37 g (73%). IR (liquid film) $\nu_{\max}$: 3444 (N–H), 1637 (C=C allyl), 918 (=C–H allyl) cm^{−1}. ¹H NMR (400 MHz, CDCl₃) δ : 7.17 (1H, td, *J*=7.8, 1.3 Hz, 5-H), 7.08 (1H, dd, *J*=7.8, 1.3 Hz, 3-H), 6.73 (1H, t, *J*=7.8 Hz, 4-H), 6.63 (1H, d, *J*=7.8 Hz, 6-H), 5.99 (1H, ddt, *J*=17.4, 10.1, 6.2 Hz, CH= allyl), 5.16 (1H, dq, *J*=10.1, 1.6 Hz, =CH_AH allyl), 5.13 (1H, dq, *J*=17.4, 1.6 Hz, =CH_BH allyl), 4.97 (1H, br s, =CH_AH), 4.91 (1H, br s, =CH_BH), 3.73 (2H, s, N–CH₂–), 3.35 (2H, d, *J*=6.2 Hz, –CH₂– allyl), 1.83 (3H, br s, CH₂=C–CH₃). ¹³C NMR (100 MHz,

CDCl₃) δ : 146.0 (1-C), 142.6 (CH₂=C–), 136.1 (CH= allyl), 129.8 (3-C), 127.6 (5-C), 123.5 (2-C), 117.2 (4-C), 116.2 (=CH₂ allyl), 110.8 (–C=CH₂), 110.8 (6-C), 49.8 (N–CH₂–), 36.6 (–CH₂– allyl), 20.5 (=C–CH₃). MS (EI-70 eV) *m/z* (%): 187 (M⁺, 41), 146 (50), 132 (91), 131 (69), 130 (100), 118 (70). Anal. Calcd for C₁₃H₁₇N: C, 83.37; H, 9.15; N, 7.48. Found: C, 83.51; H, 9.02; N, 7.40%.

4.3.2. 2-Allyl-4-chloro-*N*-(2-methylallyl)aniline (4b). Reaction time: 12 h. Yield: 1.77 g (80%). IR (liquid film) $\nu_{\max}$: 3444 (N–H), 1636 (C=C allyl), 917 (=C–H allyl) cm^{−1}. ¹H NMR (400 MHz, CDCl₃) δ : 7.09 (1H, dd, *J*=8.6, 2.6 Hz, 5-H), 7.04 (1H, d, *J*=2.6 Hz, 3-H), 6.51 (1H, d, *J*=8.6 Hz, 6-H), 5.94 (1H, ddt, *J*=17.0, 10.2, 6.2 Hz, CH= allyl), 5.18 (1H, dq, *J*=10.2, 1.6 Hz, =CH_AH allyl), 5.14 (1H, dq, *J*=17.0, 1.6 Hz, =CH_BH allyl), 4.93 (1H, br s, =CH_AH), 4.90 (1H, br s, =CH_BH), 3.69 (2H, s, N–CH₂–), 3.28 (2H, d, *J*=6.2 Hz, –CH₂– allyl), 1.79 (3H, br s, CH₂=C–CH₃). ¹³C NMR (100 MHz, CDCl₃) δ : 144.6 (1-C), 142.2 (CH₂=C–), 135.1 (CH= allyl), 129.4 (3-C), 127.2 (5-C), 125.0 (2-C), 121.6 (4-C), 116.8 (=CH₂ allyl), 111.7 (6-C), 110.9 (–C=CH₂), 49.7 (N–CH₂–), 36.2 (CH₂– allyl), 20.4 (=C–CH₃). MS (EI-70 eV) *m/z* (%): 221 (M⁺, ³⁵Cl, 36), 180 (36), 166 (59), 165 (30), 164 (53), 131 (100), 130 (78). Anal. Calcd for C₁₃H₁₆ClN: C, 70.42; H, 7.27; N, 6.32. Found: C, 70.35; H, 7.17; N, 6.20%.

4.3.3. 2-Allyl-4-fluoro-*N*-(2-methylallyl)aniline (4c). Reaction time: 14 h. Yield: 1.54 g (75%). IR (liquid film) $\nu_{\max}$: 3440 (N–H), 1637 (C=C allyl), 919 (=C–H allyl) cm^{−1}. ¹H NMR (400 MHz, CDCl₃) δ : 6.85 (1H, dd, *J*=8.3, 3.0 Hz, 3-H), 6.82–6.80 (1H, m, 5-H), 6.54 (1H, dd, *J*=8.3, 4.8 Hz, 6-H), 5.93 (1H, ddt, *J*=17.1, 10.2, 6.2 Hz, CH= allyl), 5.16 (1H, dq, *J*=10.2, 1.5 Hz, =CH_AH allyl), 5.13 (1H, dq, *J*=17.1, 1.5 Hz, =CH_BH allyl), 4.93 (1H, br s, =CH_AH), 4.89 (1H, br s, =CH_BH), 3.68 (2H, d, *J*=6.1 Hz, N–CH₂–), 3.30 (2H, d, *J*=6.2 Hz, –CH₂– allyl), 1.79 (3H, d, *J*=0.4 Hz, CH₂=C–CH₃). ¹³C NMR (100 MHz, CDCl₃) δ : 156.7 (d, *J*=231.0 Hz, 4-C), 142.5 (1-C), 135.4 (CH= allyl), 125.1 (d, *J*=10.1 Hz, 2-C), 117.0 (=CH₂ allyl), 116.6 (d, *J*=22.4 Hz, 3-C), 113.5 (d, *J*=21.5 Hz, 5-C), 111.4 (CH₂=C–), 111.4 (6-C), 110.2 (–C=CH₂), 50.6 (N–CH₂–), 36.4 (–CH₂– allyl), 20.7 (=C–CH₃). MS (EI-70 eV) *m/z* (%): 205 (M⁺, 35), 164 (44), 150 (77), 149 (62), 148 (100), 136 (76), 135 (55). Anal. Calcd for C₁₃H₁₆FN: C, 76.06; H, 7.86; N, 6.82. Found: C, 76.29; H, 8.00; N, 6.71%.

4.3.4. 6-Allyl-3-chloro-2-methyl-*N*-(2-methylallyl)aniline (4d). Reaction time: 20 h. Yield: 1.62 g (69%). IR (liquid film) $\nu_{\max}$: 3372 (N–H), 1637 (C=C allyl), 918 (=C–H allyl) cm^{−1}. ¹H NMR (400 MHz, CDCl₃) δ : 7.02 (1H, d, *J*=8.2 Hz, 4-H), 6.93 (1H, d, *J*=8.2 Hz, 5-H), 5.96 (1H, ddt, *J*=17.1, 10.1, 6.1 Hz, CH= allyl), 5.12 (1H, dq, *J*=10.1, 1.5 Hz, =CH_AH allyl), 5.07 (1H, br s, =CH_AH), 5.05 (1H, dq, *J*=17.1, 1.5 Hz, =CH_BH allyl), 4.92 (1H, br s, =CH_BH), 3.43 (2H, s, N–CH₂–), 3.37 (2H, d, *J*=6.1 Hz, –CH₂– allyl), 2.36 (3H, s, 2-CH₃), 1.83 (3H, s, CH₂=C–CH₃). ¹³C NMR (100 MHz, CDCl₃) δ : 147.9 (1-C), 144.0 (CH₂=C–), 136.9 (CH= allyl), 133.8 (3-C), 130.2 (6-C), 129.3 (2-C), 128.4 (5-C), 123.3 (4-C), 116.3 (=CH₂ allyl), 111.3 (–CH₂=C–), 55.2 (N–CH₂–), 36.5 (CH₂– allyl), 21.0 (=C–CH₃), 15.6 (2-CH₃). MS (EI-70 eV) *m/z* (%): 235 (M⁺, ³⁵Cl, 15), 194 (24), 180 (45), 179 (27), 178 (56), 145 (100), 144 (58), 130 (41), 115 (21). Anal. Calcd for C₁₄H₁₈ClN: C, 71.32; H, 7.70; N, 5.94. Found: C, 71.53; H, 7.57; N, 5.82%.

4.3.5. 2-Allyl-3,5-dimethyl-*N*-(2-methylallyl)aniline (4e). Reaction time: 16 h. Yield: 1.44 g (67%). IR (liquid film) $\nu_{\max}$: 3440 (N–H), 1634 (C=C allyl), 922 (=C–H allyl) cm^{−1}. ¹H NMR (400 MHz, CDCl₃) δ : 6.45 (1H, s, 4-H), 6.31 (1H, s, 6-H), 5.90 (1H, ddt, *J*=17.0, 10.3, 5.7 Hz, CH= allyl), 5.06 (1H, dq, *J*=10.3, 2.0 Hz, =CH_AH allyl), 5.02 (1H, dq, *J*=17.0, 2.0 Hz, =CH_BH allyl), 4.94 (1H, br s, =CH_AH), 4.88 (1H, br s, =CH_BH), 3.67 (2H, s, N–CH₂–), 3.32 (2H, dt, *J*=5.7, 2.0 Hz, –CH₂– allyl), 2.26 (3H, s, 3-CH₃), 2.25 (3H, s, 5-CH₃), 1.79 (3H, s, CH₂=C–CH₃). ¹³C NMR (100 MHz, CDCl₃) δ : 145.4 (1-C),

143.0 (CH₂=C–), 136.8 (3-C), 136.6 (5-C), 135.5 (CH= allyl), 120.5 (4-C), 118.9 (2-C), 115.4 (=CH₂ allyl), 110.8 (–CH₂=C–), 109.8 (6-C), 50.1 (N–CH₂–), 31.6 (CH₂– allyl), 21.6 (3H, 5-CH₃), 20.8 (3H, 3-CH₃), 20.2 (=C–CH₃). MS (EI-70 eV) *m/z* (%): 215 (M⁺, 42), 174 (36), 160 (83), 159 (59), 158 (94), 146 (79), 145 (100), 144 (55), 130 (33), 115 (21). Anal. Calcd for C₁₅H₂₁N: C, 83.67; H, 9.83; N, 6.50. Found: C, 83.80; H, 9.69; N, 6.38%.

4.3.6. 2-Allyl-4,6-dichloro-N-(2-methylallyl)aniline (4f). Reaction time: 20 h. Yield: 2.24 g (88%). IR (liquid film) ν_{max} : 3386 (N–H), 1640 (C=C allyl), 920 (=C–H allyl) cm^{–1}. ¹H NMR (400 MHz, CDCl₃) δ : 7.22 (1H, d, *J*=2.4 Hz, 5-H), 7.04 (1H, d, *J*=2.4 Hz, 3-H), 5.93 (1H, ddt, *J*=17.1, 10.1, 6.3 Hz, CH= allyl), 5.16 (1H, dq, *J*=10.1, 1.6 Hz, =CH_AH allyl), 5.10 (1H, dq, *J*=17.1, 1.6 Hz, =CH_BH allyl), 5.02 (1H, br s, =CH_AH), 4.89 (1H, br s, =CH_BH), 3.54 (2H, s, N–CH₂–), 3.40 (2H, d, *J*=6.3 Hz, –CH₂– allyl), 1.80 (3H, s, CH₂=C–CH₃). ¹³C NMR (100 MHz, CDCl₃) δ : 143.6 (CH₂=C–), 143.1 (1-C), 136.1 (CH= allyl), 134.7 (2-C), 129.3 (3-C), 127.7 (4-C), 127.4 (5-C), 126.9 (6-C), 117.2 (=CH₂ allyl), 111.8 (–CH₂=C–), 54.9 (N–CH₂–), 36.2 (CH₂– allyl), 20.8 (=C–CH₃). MS (EI-70 eV) *m/z* (%): 255 (M⁺, ³⁵Cl, 12), 214 (42), 200 (65), 199 (48), 198 (70), 165 (100), 164 (69), 151 (36), 130 (70), 115 (24). Anal. Calcd for C₁₃H₁₅Cl₂N: C, 60.95; H, 5.90; N, 5.47. Found: C, 60.73; H, 6.07; N, 5.33%.

4.4. General procedure for the synthesis of 2-exo-vinyltetrahydro-1,4-epoxybenzo[b]azepines 5 and 2-exo-(prop-1-en-2-yl)tetrahydro-1,4-epoxy-benzo[b]azepines 6

For the preparation of compounds **5** and **6**, sodium tungstate dihydrate (10 mol % Na₂WO₄·2H₂O, 0.33 g), followed by 30% aqueous hydrogen peroxide solution (30 mmol, 10.2 mL), were added to a stirred and cooled (ice-bath) solution of the appropriately substituted 2-allyl-N-alkenylaniline **2** or **4** (10 mmol) in methanol (30 mL). The resulting mixtures were stirred at 0 °C for 2 h and then at ambient temperature for additionally 4–70 h. Each mixture was filtered and then extracted with ethyl acetate and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and toluene (30 mL) was added to the organic black residue. The resulting solution was heated at 80–110 °C for 4–7 h. After cooling each solution to ambient temperature, the solvent was removed under reduced pressure and the crude product was purified by chromatography on silica gel using heptane/ethyl acetate (compositions in the range from 60:1 to 10:1 v/v) as eluent.

4.4.1. 2-Exo-Vinyl-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (5a). Yield: 1.08 g (58%). Colorless crystals, mp 62 °C (heptane). *R*_f: 0.32 (7% ethyl acetate/heptane). IR (KBr) ν_{max} : 1640 (C=C vinyl), 1261 (C–N), 1049 (C–O), 992 (N–O), 920 (=C–H vinyl) cm^{–1}. ¹H NMR (400 MHz, CDCl₃) δ : 7.15 (1H, td, *J*=8.0, 2.0 Hz, 8-H), 7.09 (1H, td, *J*=8.0, 2.0 Hz, 7-H), 7.07 (1H, dd, *J*=8.0, 2.0 Hz, 6-H), 7.05 (1H, dd, *J*=8.0, 2.0 Hz, 9-H), 6.01 (1H, ddd, *J*=17.2, 10.4, 7.1 Hz, –CH=), 5.22 (1H, dt, *J*=17.2, 1.1 Hz, =CH_AH), 5.12 (1H, dt, *J*=10.4, 1.1 Hz, =CH_BH), 4.87 (1H, ddd, *J*=7.1, 5.3, 2.2 Hz, 4-H), 4.01 (1H, ddd, *J*=7.9, 7.1, 2.1 Hz, 2-H), 3.36 (1H, br dd, *J*=16.4, 5.3 Hz, 5-H_B), 2.47 (1H, br d, *J*=16.4 Hz, 5-H_A), 2.33 (1H, dddd, *J*=12.2, 7.1, 2.1, 1.1 Hz, 3-H_B), 2.28 (1H, ddd, *J*=12.2, 7.9, 2.2 Hz, 3-H_A). ¹³C NMR (100 MHz, CDCl₃) δ : 150.2 (9a-C), 140.1 (–CH=), 129.8 (6-C), 126.6 (8-C), 126.0 (7-C), 125.3 (5a-C), 122.0 (9-C), 114.6 (=CH₂), 74.8 (2-C, 4-C), 40.1 (3-C), 39.8 (5-C). MS (EI-70 eV) *m/z* (%): 187 (M⁺, 44), 170 (28), 157 (10), 130 (22), 105 (41), 104 (100), 78 (25). Anal. Calcd for C₁₂H₁₃NO: C, 76.98; H, 7.00; N, 7.48. Found: C, 76.39; H, 7.12; N, 7.21%.

4.4.2. 7-Chloro-2-exo-vinyl-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (5b). Yield: 1.11 g (50%). Pale yellow oil. *R*_f: 0.32 (7% ethyl acetate/heptane). IR (liquid film) ν_{max} : 1632 (C=C vinyl), 1250

(C–N), 1048 (C–O), 985 (N–O), 924 (=C–H vinyl) cm^{–1}. ¹H NMR (400 MHz, CDCl₃) δ : 7.11 (1H, dd, *J*=8.4, 2.4 Hz, 8-H), 7.07 (1H, d, *J*=2.4 Hz, 6-H), 6.97 (1H, d, *J*=8.4 Hz, 9-H), 5.97 (1H, ddd, *J*=17.1, 10.4, 7.1 Hz, –CH=), 5.21 (1H, dt, *J*=17.1, 1.2 Hz, =CH_AH), 5.11 (1H, dt, *J*=10.4, 1.2 Hz, =CH_BH), 4.84 (1H, ddd, *J*=7.5, 5.4, 2.1 Hz, 4-H), 3.96 (1H, ddd, *J*=7.4, 7.1, 2.4 Hz, 2-H), 3.41 (1H, br dd, *J*=16.7, 5.4 Hz, 5-H_B), 2.44 (1H, br d, *J*=16.7 Hz, 5-H_A), 2.33 (1H, dddd, *J*=12.5, 7.5, 2.4, 1.1 Hz, 3-H_B), 2.25 (1H, ddd, *J*=12.5, 7.4, 2.1 Hz, 3-H_A). ¹³C NMR (100 MHz, CDCl₃) δ : 148.8 (9a-C), 139.7 (–CH=), 131.2 (7-C), 129.7 (6-C), 127.3 (5a-C), 126.8 (8-C), 123.4 (9-C), 114.9 (=CH₂), 74.8 (2-C), 74.3 (4-C), 40.1 (3-C), 34.7 (5-C). MS (EI-70 eV) *m/z* (%): 221 (M⁺, ³⁵Cl, 46), 204 (15), 191 (6), 164 (12), 139 (62), 138 (100), 112 (23). Anal. Calcd for C₁₂H₁₂ClNO: C, 65.02; H, 5.46; N, 6.32. Found: C, 65.52; H, 5.28; N, 6.52%.

4.4.3. 7-Fluoro-2-exo-vinyl-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (5c). Yield: 0.98 g (48%). Pale yellow oil. *R*_f: 0.29 (7% ethyl acetate/heptane). IR (liquid film) ν_{max} : 1642 (C=C vinyl), 1253 (C–N), 1049 (C–O), 996 (N–O), 923 (=C–H vinyl) cm^{–1}. ¹H NMR (400 MHz, CDCl₃) δ : 7.03 (1H, dd, *J*=8.0, 7.0 Hz, 9-H), 6.88 (1H, td, *J*=8.0, 3.0 Hz, 8-H), 6.84 (1H, dd, *J*=8.0, 2.0 Hz, 6-H), 5.98 (1H, ddd, *J*=17.3, 10.3, 7.5 Hz, –CH=), 5.21 (1H, dt, *J*=17.3, 1.2 Hz, =CH_AH), 5.11 (1H, dt, *J*=10.3, 1.2 Hz, =CH_BH), 4.84 (1H, ddd, *J*=7.5, 5.5, 2.2 Hz, 4-H), 3.95 (1H, ddd, *J*=8.1, 7.5, 2.8 Hz, 2-H), 3.32 (1H, br dd, *J*=16.9, 5.5 Hz, 5-H_B), 2.60 (1H, dddd, *J*=12.5, 7.5, 2.8, 1.2 Hz, 3-H_B), 2.45 (1H, br d, *J*=16.9 Hz, 5-H_A), 2.33 (1H, ddd, *J*=12.5, 8.1, 2.2 Hz, 3-H_A). ¹³C NMR (100 MHz, CDCl₃) δ : 160.5 (d, *J*=234.0 Hz, 7-C), 145.9 (9a-C), 139.7 (–CH=), 127.1 (d, *J*=8.2 Hz, 5a-C), 123.3 (d, *J*=8.5 Hz, 9-C), 116.0 (d, *J*=22.3 Hz, 6-C), 114.6 (=CH₂), 113.3 (d, *J*=22.4 Hz, 8-C), 74.6 (2-C), 74.0 (4-C), 39.9 (3-C), 34.8 (5-C). MS (EI-70 eV) *m/z* (%): 205 (M⁺, 35), 188 (13), 175 (7), 148 (17), 123 (46), 122 (100), 96 (33). Anal. Calcd for C₁₂H₁₂FNO: C, 70.23; H, 5.89; N, 6.82. Found: C, 70.59; H, 5.73; N, 6.69%.

4.4.4. 8-Chloro-9-methyl-2-exo-vinyl-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (5d). Yield: 1.34 g (57%). Pale yellow oil. *R*_f: 0.39 (7% ethyl acetate/heptane). IR (liquid film) ν_{max} : 1638 (C=C vinyl), 1267 (C–N), 1052 (C–O), 975 (N–O), 925 (=C–H vinyl) cm^{–1}. ¹H NMR (400 MHz, CDCl₃) δ : 7.10 (1H, d, *J*=8.1 Hz, 7-H), 6.85 (1H, d, *J*=8.1 Hz, 6-H), 5.97 (1H, ddd, *J*=17.2, 10.3, 6.9 Hz, –CH=), 5.26 (1H, dt, *J*=17.2, 1.3 Hz, =CH_AH), 5.13 (1H, dt, *J*=10.3, 1.3 Hz, =CH_BH), 4.87 (1H, ddd, *J*=7.6, 5.3, 2.0 Hz, 4-H), 3.89 (1H, ddd, *J*=8.3, 6.9, 2.4 Hz, 2-H), 3.30 (1H, dd, *J*=16.7, 5.3 Hz, 5-H_B), 2.40 (1H, br d, *J*=16.7 Hz, 5-H_A), 2.36 (3H, s, 9-CH₃), 2.33 (1H, dddd, *J*=12.6, 7.6, 2.4, 1.3 Hz, 3-H_B), 2.23 (1H, ddd, *J*=12.6, 8.3, 2.0 Hz, 3-H_A). ¹³C NMR (100 MHz, CDCl₃) δ : 149.4 (9a-C), 139.4 (–CH=), 132.3 (9-C), 128.9 (8-C), 127.8 (6-C), 126.0 (7-C), 123.4 (5a-C), 114.7 (=CH₂), 74.6 (4-C), 73.1 (2-C), 40.1 (3-C), 34.4 (5-C), 13.7 (9-CH₃). MS (EI-70 eV) *m/z* (%): 235 (M⁺, ³⁵Cl, 51), 218 (18), 205 (9), 178 (9), 153 (100), 152 (54), 126 (9). Anal. Calcd for C₁₃H₁₄ClNO: C, 66.24; H, 5.99; N, 5.94. Found: C, 66.55; H, 6.07; N, 5.88%.

4.4.5. 6,8-Dimethyl-2-exo-vinyl-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (5e). Yield: 1.18 g (55%). Pale yellow oil. *R*_f: 0.31 (7% ethyl acetate/heptane). IR (liquid film) ν_{max} : 1641 (C=C vinyl), 1272 (C–N), 1053 (C–O), 990 (N–O), 919 (=C–H vinyl) cm^{–1}. ¹H NMR (400 MHz, CDCl₃) δ : 6.84 (1H, s, 7-H), 6.76 (1H, s, 9-H), 6.03 (1H, ddd, *J*=17.2, 10.3, 7.1 Hz, –CH=), 5.23 (1H, dt, *J*=17.2, 1.9 Hz, =CH_AH), 5.15 (1H, dt, *J*=10.3, 1.9 Hz, =CH_BH), 4.91 (1H, ddd, *J*=7.5, 5.5, 2.0 Hz, 4-H), 4.02 (1H, ddd, *J*=8.3, 7.1, 2.4 Hz, 2-H), 3.11 (1H, br dd, *J*=16.7, 5.5 Hz, 5-H_B), 2.54 (1H, br d, *J*=16.7 Hz, 5-H_A), 2.33 (1H, dddd, *J*=12.6, 7.5, 2.4, 1.1 Hz, 3-H_B), 2.27 (3H, s, 8-CH₃), 2.23 (1H, ddd, *J*=12.6, 8.3, 2.0 Hz, 3-H_A), 2.13 (3H, s, 6-CH₃). ¹³C NMR (100 MHz, CDCl₃) δ : 149.9 (9a-C), 140.2 (–CH=), 137.5 (6-C), 136.0 (8-C), 128.0 (7-C), 120.3 (5a-C), 120.1 (9-C), 114.5 (=CH₂), 74.8 (4-C), 74.7 (2-C), 40.5 (3-C), 33.1 (5-C), 20.9 (8-CH₃), 18.5 (6-CH₃). MS

(EI-70 eV) m/z (%): 215 (M^+ , 49), 198 (23), 185 (9), 158 (9), 133 (100), 132 (60), 106 (14). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.86; H, 8.05; N, 6.33%.

4.4.6. 2-exo-(Prop-1-en-2-yl)-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (6a). Yield: 0.98 g (49%). Yellow viscous oil. R_f : 0.45 (7% ethyl acetate/heptane). IR (liquid film) ν_{max} : 1648 (C=C isopropenyl), 1259 (C–N), 1055 (C–O), 980 (N–O), 913 (C–H isopropenyl) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 7.11 (1H, td, $J=8.3$, 2.2 Hz, 8-H), 7.10 (1H, td, $J=8.3$, 1.4 Hz, 7-H), 7.09 (1H, dd, $J=8.3$, 2.2 Hz, 6-H), 7.04 (1H, dd, $J=8.3$, 1.4 Hz, 9-H), 5.04 (1H, d, $J=0.7$ Hz, $=CH_AH$), 4.86 (1H, ddd, $J=7.6$, 5.4, 1.7 Hz, 4-H), 4.84 (1H, d, $J=0.7$ Hz, $=CH_BH$), 3.96 (1H, dd, $J=8.7$, 2.7 Hz, 2-H), 3.36 (1H, br dd, $J=16.6$, 5.4 Hz, 5- H_B), 2.48 (1H, br d, $J=16.6$ Hz, 5- H_A), 2.44 (1H, dddd, $J=12.6$, 7.6, 2.7, 1.2 Hz, 3- H_B), 2.25 (1H, ddd, $J=12.6$, 8.7, 1.7 Hz, 3- H_A), 1.86 (3H, s, $CH_2=C-CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 150.9 (9a-C), 145.6 (C=), 129.7 (6-C), 126.4 (8-C), 125.7 (7-C), 125.2 (5a-C), 121.7 (9-C), 111.1 ($=CH_2$), 76.7 (2-C), 74.8 (4-C), 38.6 (3-C), 34.5 (5-C), 19.6 ($CH_2=C-CH_3$). MS (EI-70 eV) m/z (%): 201 (M^+ , 63), 184 (8), 171 (3), 130 (15), 105 (45), 104 (100), 78 (31). Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.91; H, 7.26; N, 6.72%.

4.4.7. 7-Chloro-2-exo-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (6b). Yield: 1.22 g (52%). Pale yellow viscous oil. R_f : 0.49 (7% ethyl acetate/heptane). IR (liquid film) ν_{max} : 1650 (C=C isopropenyl), 1259 (C–N), 1080 (C–O), 980 (N–O), 913 (C–H isopropenyl) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 7.10 (1H, dd, $J=8.4$, 2.9 Hz, 8-H), 7.07 (1H, br s, 6-H), 6.98 (1H, d, $J=8.4$ Hz, 9-H), 5.02 (1H, s, $=CH_AH$), 4.86 (1H, s, $=CH_BH$), 4.84 (1H, ddd, $J=7.6$, 5.4, 1.7 Hz, 4-H), 3.90 (1H, dd, $J=8.6$, 2.4 Hz, 2-H), 3.32 (1H, br dd, $J=16.8$, 5.4 Hz, 5- H_B), 2.46 (1H, br d, $J=16.8$ Hz, 5- H_A), 2.44 (1H, dddd, $J=12.6$, 7.6, 2.4, 1.3 Hz, 3- H_B), 2.21 (1H, ddd, $J=12.6$, 8.6, 1.7 Hz, 3- H_A), 1.89 (3H, s, $CH_2=C-CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 149.3 (9a-C), 145.1 (C=), 131.0 (7-C), 129.6 (6-C), 127.2 (5a-C), 126.6 (8-C), 123.1 (9-C), 111.4 ($=CH_2$), 77.0 (2-C), 74.3 (4-C), 38.6 (3-C), 34.4 (5-C), 19.6 ($CH_2=C-CH_3$). MS (EI-70 eV) m/z (%): 235 (M^+ , ^{35}Cl , 64), 218 (52), 205 (3), 164 (10), 139 (66), 138 (100), 112 (21). Anal. Calcd for $C_{13}H_{14}ClNO$: C, 66.24; H, 5.99; N, 5.94. Found: C, 66.02; H, 5.82; N, 6.16%.

4.4.8. 7-Fluoro-2-exo-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (6c). Yield: 1.10 g (50%). Pale yellow viscous oil. R_f : 0.45 (7% ethyl acetate/heptane). IR (liquid film) ν_{max} : 1647 (C=C isopropenyl), 1249 (C–N), 1098 (C–O), 979 (N–O), 915 (C–H isopropenyl) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 6.99 (1H, dd, $J=8.6$, 5.3 Hz, 9-H), 6.84 (1H, dd, $J=8.6$, 2.8 Hz, 8-H), 6.79 (1H, dd, $J=8.4$, 2.8 Hz, 6-H), 5.03 (1H, d, $J=0.7$ Hz, $=CH_AH$), 4.86 (1H, d, $J=1.3$ Hz, $=CH_BH$), 4.83 (1H, ddd, $J=7.8$, 5.5, 1.7 Hz, 4-H), 3.89 (1H, dd, $J=8.7$, 2.2 Hz, 2-H), 3.33 (1H, br dd, $J=16.8$, 5.5 Hz, 5- H_B), 2.47 (1H, br d, $J=16.8$ Hz, 5- H_A), 2.44 (1H, dddd, $J=12.7$, 7.8, 2.2, 1.3 Hz, 3- H_B), 2.23 (1H, ddd, $J=12.7$, 8.7, 1.7 Hz, 3- H_A), 1.84 (3H, s, $CH_2=C-CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 160.6 (d, $J=242.4$ Hz, 7-C), 147.0 (d, $J=2.7$ Hz, 9a-C), 145.6 (C=), 127.5 (d, $J=8.1$ Hz, 5a-C), 123.4 (d, $J=8.5$ Hz, 9-C), 116.2 (d, $J=22.3$ Hz, 6-C), 113.4 (d, $J=22.4$ Hz, 8-C), 111.3 ($=CH_2$), 76.9 (2-C), 74.4 (4-C), 38.9 (3-C), 34.9 (5-C), 19.8 ($CH_2=C-CH_3$). MS (EI-70 eV) m/z (%): 219 (M^+ , 58), 148 (15), 123 (49), 122 (100), 96 (23). Anal. Calcd for $C_{13}H_{14}FNO$: C, 71.21; H, 6.44; N, 6.39. Found: C, 70.98; H, 6.21; N, 6.53%.

4.4.9. 8-Chloro-9-methyl-2-exo-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (6d). Yield: 1.62 g (65%). Colorless crystals, mp 94 °C (heptane). R_f : 0.52 (7% ethyl acetate/heptane). IR (KBr) ν_{max} : 1650 (C=C isopropenyl), 1274 (C–N), 1095 (C–O), 970 (N–O), 918 (C–H isopropenyl) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 7.10 (1H, d, $J=8.2$ Hz, 7-H), 6.86 (1H, d, $J=8.2$ Hz, 6-H), 5.11 (1H, d,

$J=0.6$ Hz, $=CH_AH$), 4.87 (1H, br s, $=CH_BH$), 4.84 (1H, ddd, $J=7.4$, 5.6, 1.4 Hz, 4-H), 3.85 (1H, dd, $J=8.8$, 2.4 Hz, 2-H), 3.31 (1H, br dd, $J=16.6$, 5.6 Hz, 5- H_B), 2.43 (1H, br d, $J=16.6$ Hz, 5- H_A), 2.42 (1H, dddd, $J=12.5$, 7.4, 2.4, 1.0 Hz, 3- H_B), 2.35 (3H, s, 9- CH_3), 2.22 (1H, ddd, $J=12.5$, 8.8, 1.4 Hz, 3- H_A), 1.83 (3H, s, $CH_2=C-CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 150.5 (9a-C), 145.3 (C=), 132.5 (8-C), 129.2 (9-C), 127.9 (6-C), 126.0 (7-C), 123.7 (5a-C), 111.3 ($=CH_2$), 75.6 (2-C), 74.7 (4-C), 39.3 (3-C), 34.5 (5-C), 19.4 ($CH_2=C-CH_3$), 14.0 (9- CH_3). MS (EI-70 eV) m/z (%): 249 (M^+ , ^{35}Cl , 53), 232 (16), 219 (3), 192 (6), 153 (100), 152 (53), 126 (9). Anal. Calcd for $C_{14}H_{16}ClNO$: C, 67.33; H, 6.46; N, 5.61. Found: C, 67.76; H, 6.29; N, 5.42%.

4.4.10. 6,8-Dimethyl-2-exo-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (6e). Yield: 1.37 g (60%). Pale yellow viscous oil. R_f : 0.40 (7% ethyl acetate/heptane). IR (liquid film) ν_{max} : 1650 (C=C isopropenyl), 1272 (C–N), 1065 (C–O), 922 (C–H isopropenyl), 912 (N–O) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 6.83 (1H, s, 7-H), 6.73 (1H, s, 9-H), 5.04 (1H, dd, $J=1.8$, 0.9 Hz, $=CH_AH$), 4.90 (1H, ddd, $J=7.5$, 5.4, 1.6 Hz, 4-H), 4.86 (1H, d, $J=1.4$ Hz, $=CH_BH$), 3.94 (1H, dd, $J=8.9$, 2.9 Hz, 2-H), 3.12 (1H, br dd, $J=16.5$, 5.4 Hz, 5- H_B), 2.43 (1H, dddd, $J=12.5$, 7.5, 2.9, 1.3 Hz, 3- H_B), 2.29 (1H, br d, $J=16.5$ Hz, 5- H_A), 2.27 (3H, s, 6- CH_3), 2.22 (1H, ddd, $J=12.5$, 8.9, 1.6 Hz, 3- H_A), 2.15 (3H, s, 8- CH_3), 1.86 (3H, s, $CH_2=C-CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 150.7 (9a-C), 145.9 (C=), 137.4 (6-C), 136.0 (8-C), 128.0 (7-C), 120.4 (5a-C), 119.9 (9-C), 111.0 ($=CH_2$), 77.0 (2-C), 74.9 (4-C), 39.2 (3-C), 32.9 (5-C), 21.0 (8- CH_3), 19.7 ($CH_2=C-CH_3$), 18.5 (6- CH_3). MS (EI-70 eV) m/z (%): 229 (M^+ , 56), 212 (9), 199 (3), 158 (9), 133 (100), 132 (53), 106 (12). Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.93; H, 8.16; N, 5.89%.

4.4.11. 7,9-Dichloro-2-exo-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1,4-epoxybenzo[b]azepine (6f). Yield: 1.69 g (63%). Colorless crystals, mp 97 °C (heptane). R_f : 0.45 (7% ethyl acetate/heptane). IR (KBr) ν_{max} : 1648 (C=C isopropenyl), 1279 (C–N), 1060 (C–O), 927 (C–H isopropenyl), 915 (N–O) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 7.22 (1H, d, $J=2.1$ Hz, 8-H), 7.01 (1H, d, $J=2.1$ Hz, 6-H), 5.09 (1H, br s, $=CH_AH$), 4.92 (1H, br s, $=CH_BH$), 4.86 (1H, ddd, $J=7.5$, 5.8, 1.6 Hz, 4-H), 3.95 (1H, dd, $J=8.3$, 2.7 Hz, 2-H), 3.33 (1H, br dd, $J=16.9$, 5.8 Hz, 5- H_B), 2.50 (1H, dddd, $J=12.8$, 7.5, 2.7, 1.2 Hz, 3- H_B), 2.44 (1H, br d, $J=16.9$ Hz, 5- H_A), 2.15 (1H, ddd, $J=12.8$, 8.3, 1.6 Hz, 3- H_A), 1.89 (3H, s, $CH_2=C-CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 146.1 (9a-C), 144.9 (C=), 130.9 (7-C), 129.1 (5a-C), 128.3 (6-C), 127.9 (9-C), 127.4 (8-C), 111.9 ($=CH_2$), 75.5 (2-C), 74.6 (4-C), 38.4 (3-C), 34.6 (5-C), 20.0 ($CH_2=C-CH_3$). MS (EI-70 eV) m/z (%): 269 (M^+ , ^{35}Cl , 59), 252 (6), 239 (3), 198 (17), 173 (76), 172 (100), 145 (9). Anal. Calcd for $C_{13}H_{13}Cl_2NO$: C, 57.80; H, 4.85; N, 5.18. Found: C, 58.02; H, 4.93; N, 5.35%.

4.5. General procedure for the synthesis of *cis*-2-vinyltetrahydro-1H-benzo[b]azepinols 7 and *cis*-2-(prop-1-en-2-yl)-tetrahydro-1H-benzo[b]azepinols 8

To a stirred and cooled (ice-bath) solutions of 1,4-epoxy-cycloadducts **5a–e** or **6a–f** (10 mmol) in MeOH (25 mL), were added glacial acetic acid (70 mmol, 4 mL), zinc powder (100 mmol, 6.54 g), and hydrochloric acid (37% HCl, 70 mmol, 6.81 mL). The resulting reaction mixtures were then stirred at 0 °C for additional 0.5–2 h (TLC control). Each mixture was filtered and the filtrate was neutralized with a 25% ammonium hydroxide solution to pH=8, and then extracted with ethyl acetate (3×50 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and then concentrated under reduced pressure. The remaining crude material was purified by column chromatography on silica gel using heptane/ethyl acetate (compositions ranged from 10:1 to 1:1 v/v) as eluent to give **7a–e** and **8a–f**.

4.5.1. cis-2-Vinyl-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (7a). Reaction time: 0.5 h. Yield: 1.76 g (93%). Colorless crystals, mp 103 °C (heptane). *R*_f: 0.28 (33% ethyl acetate/heptane). IR (KBr) ν_{max} : 3287 (NH/OH), 1241 (C–N), 1095 (C–O), 935 (C–H vinyl) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 7.16 (1H, d, *J*=7.4 Hz, 6-H), 7.09 (1H, td, *J*=7.4, 1.2 Hz, 8-H), 6.89 (1H, td, *J*=7.4, 1.0 Hz, 7-H), 6.75 (1H, d, *J*=7.4 Hz, 9-H), 5.99 (1H, ddd, *J*=17.4, 10.3, 7.4 Hz, =CH), 5.27 (1H, d, *J*=17.4 Hz, =CH_AH), 5.16 (1H, d, *J*=10.3 Hz, =CHH_B), 3.80 (1H, ddd, *J*=9.5, 3.9, 1.6 Hz, 4-H_{ax}), 3.47 (1H, ddd, *J*=10.3, 7.4, 2.0 Hz, 2-H_{ax}), 3.02 (1H, dd, *J*=12.8, 9.5 Hz, 5-H_{ax}), 2.96 (1H, dt, *J*=12.8, 1.6 Hz, 5-H_{eq}), 2.13 (1H, ddd, *J*=12.8, 3.9, 2.0 Hz, 3-H_{eq}), 1.80 (1H, ddd, *J*=12.8, 10.3, 10.0 Hz, 3-H_{ax}). ^{13}C NMR (100 MHz, CDCl_3) δ : 148.5 (9a-C), 140.6 (–CH=), 131.5 (6-C), 128.1 (5a-C), 127.4 (8-C), 121.8 (7-C), 120.2 (9-C), 115.4 (=CH₂), 69.7 (4-C), 58.9 (2-C), 46.1 (3-C), 44.3 (5-C). MS (EI-70 eV) *m/z* (%): 189 (M^+ , 91), 172 (11), 170 (33), 162 (8), 146 (26), 145 (28), 144 (100), 130 (65), 118 (92), 117 (54), 107 (11), 106 (46). Anal. Calcd for $\text{C}_{12}\text{H}_{15}\text{NO}$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.93; H, 7.80; N, 7.53%.

4.5.2. 7-Chloro-cis-2-vinyl-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (7b). Reaction time: 0.5 h. Yield: 2.07 g (95%). Colorless crystals, mp 118 °C (heptane). *R*_f: 0.28 (33% ethyl acetate/heptane). IR (KBr) ν_{max} : 3298 (NH/OH), 1252 (C–N), 1090 (C–O), 928 (C–H vinyl) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 7.10 (1H, d, *J*=2.4 Hz, 6-H), 7.02 (1H, dd, *J*=8.3, 2.4 Hz, 8-H), 6.68 (1H, d, *J*=8.3 Hz, 9-H), 5.96 (1H, ddd, *J*=17.5, 10.3, 7.4 Hz, =CH), 5.27 (1H, d, *J*=17.5 Hz, =CH_AH), 5.16 (1H, d, *J*=10.3 Hz, =CHH_B), 3.79 (1H, ddd, *J*=9.5, 3.9, 2.2 Hz, 4-H_{ax}), 3.43 (1H, ddd, *J*=10.2, 7.4, 2.0 Hz, 2-H_{ax}), 2.96 (1H, dd, *J*=12.6, 9.5 Hz, 5-H_{ax}), 2.90 (1H, dt, *J*=12.6, 2.2 Hz, 5-H_{eq}), 2.12 (1H, ddd, *J*=13.0, 3.9, 2.0 Hz, 3-H_{eq}), 1.78 (1H, ddd, *J*=13.0, 10.2, 10.0 Hz, 3-H_{ax}). ^{13}C NMR (100 MHz, CDCl_3) δ : 146.9 (9a-C), 140.2 (–CH=), 132.1 (6-C), 129.8 (5a-C), 127.1 (8-C), 126.6 (7-C), 121.4 (9-C), 115.8 (=CH₂), 69.3 (4-C), 59.1 (2-C), 45.8 (3-C), 44.0 (5-C). MS (EI-70 eV) *m/z* (%): 223 (M^+ , ^{35}Cl , 100), 206 (21), 204 (30), 196 (7), 180 (58), 179 (37), 178 (94), 164 (57), 152 (68), 151 (46), 141 (11), 140 (44). Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{ClNO}$: C, 64.43; H, 6.31; N, 6.26. Found: C, 64.02; H, 6.15; N, 6.50%.

4.5.3. 7-Fluoro-cis-2-vinyl-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (7c). Reaction time: 0.5 h. Yield: 1.93 g (93%). Colorless crystals, mp 127 °C (heptane). *R*_f: 0.26 (33% ethyl acetate/heptane). IR (KBr) ν_{max} : 3289 (NH/OH), 1253 (C–N), 1092 (C–O), 932 (C–H vinyl) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 6.89 (1H, dd, *J*=8.0, 2.4 Hz, 6-H), 6.82 (1H, td, *J*=7.6, 2.4 Hz, 8-H), 6.75 (1H, dd, *J*=7.6, 4.8 Hz, 9-H), 6.11 (1H, ddd, *J*=16.4, 10.0, 7.5 Hz, =CH), 5.48 (1H, dt, *J*=16.4, 1.0 Hz, =CH_AH), 5.38 (1H, dd, *J*=10.0, 1.0 Hz, =CHH_B), 4.15 (1H, ddd, *J*=9.2, 4.0, 2.0 Hz, 4-H_{ax}), 3.82 (1H, ddd, *J*=10.4, 7.5, 2.0 Hz, 2-H_{ax}), 3.46 (1H, dd, *J*=12.0, 9.2 Hz, 5-H_{ax}), 3.36 (1H, dt, *J*=12.0, 2.0 Hz, 5-H_{eq}), 2.67 (1H, ddd, *J*=11.6, 4.0, 2.0 Hz, 3-H_{eq}), 2.38 (1H, ddd, *J*=11.6, 10.4, 10.4 Hz, 3-H_{ax}). ^{13}C NMR (100 MHz, CDCl_3) δ : 158.3 (d, *J*=230.0 Hz, 7-C), 144.6 (9a-C), 140.5 (–CH=), 130.4 (d, *J*=8.0 Hz, 5a-C), 121.4 (d, *J*=10.0 Hz, 9-C), 117.9 (d, *J*=20.0 Hz, 6-C), 115.7 (=CH₂), 113.7 (d, *J*=20.0 Hz, 8-C), 69.5 (4-C), 59.3 (2-C), 46.2 (3-C), 44.2 (5-C). MS (EI-70 eV) *m/z* (%): 207 (M^+ , 60), 190 (7), 188 (21), 180 (7), 164 (27), 163 (27), 162 (90), 148 (67), 136 (100), 135 (55), 125 (13), 124 (45). Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{FNO}$: C, 69.55; H, 6.81; N, 6.76. Found: C, 69.91; H, 6.60; N, 6.53%.

4.5.4. 8-Chloro-9-methyl-cis-2-vinyl-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (7d). Reaction time: 2 h. Yield: 2.23 g (94%). Colorless crystals, mp 63 °C (heptane). *R*_f: 0.33 (33% ethyl acetate/heptane). IR (KBr) ν_{max} : 3397 (NH/OH), 1250 (C–N), 1103 (C–O), 928 (C–H vinyl) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 6.91 (2H, br s, 6-H, 7-H), 6.01 (1H, ddd, *J*=17.4, 10.3, 7.5 Hz, =CH), 5.28 (1H, d, *J*=17.4 Hz, =CH_AH), 5.17 (1H, d, *J*=10.3 Hz, =CHH_B), 3.79 (1H,

ddd, *J*=9.4, 4.5, 2.0 Hz, 4-H_{ax}), 3.39 (1H, ddd, *J*=9.9, 7.5, 1.9 Hz, 2-H_{ax}), 2.94 (1H, dd, *J*=12.0, 9.4 Hz, 5-H_{ax}), 2.90 (1H, dt, *J*=12.0, 2.0 Hz, 5-H_{eq}), 2.27 (3H, s, 9-CH₃), 2.10 (1H, ddd, *J*=12.7, 4.5, 1.9 Hz, 3-H_{eq}), 1.75 (1H, ddd, *J*=12.7, 9.9, 9.4 Hz, 3-H_{ax}). ^{13}C NMR (100 MHz, CDCl_3) δ : 148.4 (9a-C), 140.4 (–CH=), 132.9 (8-C), 129.4 (6-C), 127.1 (5a-C), 124.4 (9-C), 122.1 (7-C), 115.7 (=CH₂), 69.5 (4-C), 58.5 (2-C), 45.5 (3-C), 43.4 (5-C), 14.4 (9-CH₃). MS (EI-70 eV) *m/z* (%): 237 (M^+ , ^{35}Cl , 100), 220 (21), 218 (33), 210 (12), 194 (48), 193 (27), 192 (70), 178 (70), 166 (85), 165 (48), 155 (12), 154 (58). Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{ClNO}$: C, 65.68; H, 6.78; N, 5.89. Found: C, 65.96; H, 6.60; N, 6.05%.

4.5.5. 6,8-Dimethyl-cis-2-vinyl-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (7e). Reaction time: 1 h. Yield: 2.04 g (94%). Colorless crystals, mp 99 °C (heptane). *R*_f: 0.30 (33% ethyl acetate/heptane). IR (KBr) ν_{max} : 3274 (NH/OH), 1294 (C–N), 1072 (C–O), 930 (C–H vinyl) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 6.66 (1H, s, 6-H), 6.46 (1H, s, 9-H), 5.98 (1H, ddd, *J*=17.4, 10.3, 7.4 Hz, =CH), 5.26 (1H, dt, *J*=17.4, 1.1 Hz, =CH_AH), 5.15 (1H, dd, *J*=10.3, 1.1 Hz, =CHH_B), 3.80 (1H, ddd, *J*=9.3, 4.1, 2.2 Hz, 4-H_{ax}), 3.48 (1H, ddd, *J*=11.2, 7.4, 2.4 Hz, 2-H_{ax}), 3.11 (1H, dt, *J*=13.8, 2.2 Hz, 5-H_{eq}), 2.86 (1H, dd, *J*=13.8, 9.3 Hz, 5-H_{ax}), 2.33 (3H, s, 6-CH₃), 2.24 (3H, s, 8-CH₃), 2.10 (1H, dddd, *J*=12.9, 4.1, 2.4, 1.8 Hz, 3-H_{eq}), 1.79 (1H, ddd, *J*=12.9, 11.2, 9.3 Hz, 3-H_{ax}). ^{13}C NMR (100 MHz, CDCl_3) δ : 149.0 (9a-C), 140.9 (–CH=), 137.6 (6-C), 136.3 (8-C), 125.0 (7-C), 123.9 (5a-C), 119.0 (9-C), 115.2 (=CH₂), 69.4 (4-C), 59.2 (2-C), 45.5 (3-C), 37.8 (5-C), 20.8 (6-CH₃), 20.8 (8-CH₃). MS (EI-70 eV) *m/z* (%): 217 (M^+ , 57), 198 (14), 184 (9), 172 (68), 158 (78), 146 (100), 145 (59), 134 (49), 91 (37). Anal. Calcd for $\text{C}_{14}\text{H}_{19}\text{NO}$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.59; H, 8.36; N, 6.25%.

4.5.6. cis-2-(Prop-1-en-2-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (8a). Reaction time: 0.5 h. Yield: 1.83 g (90%). Viscous maroon oil. *R*_f: 0.32 (33% ethyl acetate/heptane). IR (liquid film) ν_{max} : 3352 (NH/OH), 1253 (C–N), 1097 (C–O), 906 (C–H isopropenyl) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 7.12 (1H, d, *J*=7.4 Hz, 6-H), 7.08 (1H, td, *J*=7.6, 1.4 Hz, 8-H), 6.88 (1H, td, *J*=7.4, 1.0 Hz, 7-H), 6.72 (1H, d, *J*=7.6 Hz, 9-H), 5.02 (1H, br s, =CH_AH), 4.88 (1H, d, *J*=2.8 Hz, =CHH_B), 3.79 (1H, ddd, *J*=9.6, 3.7, 2.1 Hz, 4-H_{ax}), 3.38 (1H, dd, *J*=11.2, 2.1 Hz, 2-H_{ax}), 2.99 (1H, dd, *J*=13.6, 9.2 Hz, 5-H_{ax}), 2.92 (1H, dt, *J*=13.6, 2.1 Hz, 5-H_{eq}), 2.10 (1H, ddd, *J*=12.7, 3.7, 2.1 Hz, 3-H_{eq}), 1.88 (1H, ddd, *J*=12.7, 11.2, 10.0 Hz, 3-H_{ax}), 1.86 (3H, s, CH₂=C–CH₃). ^{13}C NMR (100 MHz, CDCl_3) δ : 149.1 (9a-C), 148.0 (–C=), 131.5 (6-C), 127.8 (5a-C), 127.4 (8-C), 121.6 (7-C), 119.9 (9-C), 111.4 (=CH₂), 69.8 (4-C), 61.9 (2-C), 45.0 (3-C), 44.4 (5-C), 19.3 (CH₂=C–CH₃). MS (EI-70 eV) *m/z* (%): 203 (M^+ , 55), 188 (4), 186 (5), 184 (6), 162 (31), 160 (11), 159 (14), 144 (38), 130 (17), 118 (100), 117 (23), 107 (5), 106 (24). Anal. Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}$: C, 76.81; H, 8.43; N, 6.89. Found: C, 77.13; H, 8.25; N, 6.68%.

4.5.7. 7-Chloro-cis-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (8b). Reaction time: 0.5 h. Yield: 2.18 g (92%). Viscous maroon oil. *R*_f: 0.35 (33% ethyl acetate/heptane). IR (liquid film) ν_{max} : 3344 (NH/OH), 1253 (C–N), 1100 (C–O), 903 (C–H isopropenyl) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ : 7.10 (1H, d, *J*=2.4 Hz, 6-H), 7.02 (1H, dd, *J*=8.3, 2.4 Hz, 8-H), 6.69 (1H, d, *J*=8.3 Hz, 9-H), 5.04 (1H, br s, =CH_AH), 4.89 (1H, t, *J*=1.4 Hz, =CHH_B), 3.77 (1H, ddd, *J*=9.4, 3.4, 2.1 Hz, 4-H_{ax}), 3.43 (1H, dd, *J*=11.3, 2.0 Hz, 2-H_{ax}), 2.98 (1H, dd, *J*=11.3, 9.4 Hz, 5-H_{ax}), 2.92 (1H, dt, *J*=11.3, 2.1 Hz, 5-H_{eq}), 2.10 (1H, ddd, *J*=12.9, 3.4, 2.0 Hz, 3-H_{eq}), 1.85 (1H, ddd, *J*=12.9, 11.3, 9.4 Hz, 3-H_{ax}), 1.83 (3H, s, CH₂=C–CH₃). ^{13}C NMR (100 MHz, CDCl_3) δ : 147.5 (–C=), 147.0 (9a-C), 131.1 (6-C), 129.7 (5a-C), 129.6 (7-C), 127.1 (8-C), 121.3 (9-C), 111.8 (=CH₂), 69.5 (4-C), 62.1 (2-C), 44.7 (3-C), 44.0 (5-C), 19.2 (CH₂=C–CH₃). MS (EI-70 eV) *m/z* (%): 237 (M^+ , ^{35}Cl , 87), 222 (8), 220 (8), 218 (7), 196 (55), 194 (20), 193 (23), 178 (32), 164 (17), 152 (100), 151 (10), 141 (12),

140 (32). Anal. Calcd for $C_{13}H_{16}ClNO$: C, 65.68; H, 6.78; N, 5.89. Found: C, 65.17; H, 7.03; N, 5.68%.

4.5.8. 7-Fluoro-cis-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (8c). Reaction time: 0.5 h. Yield: 2.06 g (93%). Viscous maroon oil. R_f : 0.32 (33% ethyl acetate/heptane). IR (liquid film) $\nu_{\max}$: 3350 (NH/OH), 1258 (C–N), 1112 (C–O), 904 (C–H isopropenyl) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 6.84 (1H, dd, $J=9.1$, 2.8 Hz, 6-H), 6.76 (1H, td, $J=8.4$, 2.8 Hz, 8-H), 6.65 (1H, dd, $J=8.4$, 5.0 Hz, 9-H), 5.03 (1H, br s, $=CH_AH$), 4.88 (1H, t, $J=1.4$ Hz, $=CH_BH$), 3.77 (1H, ddd, $J=10.0$, 3.9, 2.2 Hz, 4- H_{ax}), 3.32 (1H, dd, $J=11.3$, 1.2 Hz, 2- H_{ax}), 2.99 (1H, dd, $J=13.6$, 10.0 Hz, 5- H_{ax}), 2.89 (1H, dt, $J=13.6$, 2.2 Hz, 5- H_{eq}), 2.10 (1H, ddd, $J=12.8$, 3.9, 2.0 Hz, 3- H_{eq}), 1.85 (1H, ddd, $J=12.8$, 11.3, 10.0 Hz, 3- H_{ax}), 1.84 (3H, s, $CH_2=C-CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 158.1 (d, $J=238.0$ Hz, 7-C), 148.1 (C=), 145.5 (9a-C), 130.0 (d, $J=8.0$ Hz, 5a-C), 121.1 (d, $J=8.0$ Hz, 9-C), 117.9 (d, $J=22.0$ Hz, 6-C), 113.7 (d, $J=22.0$ Hz, 8-C), 111.6 ($=CH_2$), 69.8 (4-C), 62.3 (2-C), 45.3 (3-C), 44.4 (5-C), 19.5 ($CH_2=C-CH_3$). MS (EI-70 eV) m/z (%): 221 (M^+ , 49), 206 (3), 204 (3), 202 (3), 180 (31), 178 (9), 177 (14), 162 (37), 149 (6), 136 (100), 135 (20), 125 (6), 124 (26). Anal. Calcd for $C_{13}H_{16}FNO$: C, 70.56; H, 7.29; N, 6.33. Found: C, 70.26; H, 7.45; N, 6.43%.

4.5.9. 8-Chloro-9-methyl-cis-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (8d). Reaction time: 2 h. Yield: 2.26 g (90%). Colorless crystals, mp 101 °C (heptane). R_f : 0.33 (33% ethyl acetate/heptane). IR (KBr) $\nu_{\max}$: 3396 (NH/OH), 1257 (C–N), 1106 (C–O), 905 (C–H isopropenyl) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 6.91 (1H, d, $J=8.2$ Hz, 6-H), 6.88 (1H, d, $J=8.2$ Hz, 7-H), 5.07 (1H, br s, $=CH_AH$), 4.91 (1H, t, $J=1.4$ Hz, $=CH_BH$), 3.79 (1H, ddd, $J=9.5$, 4.1, 2.2 Hz, 4- H_{ax}), 3.35 (1H, dd, $J=11.3$, 1.3 Hz, 2- H_{ax}), 2.99 (1H, dd, $J=13.6$, 10.1 Hz, 5- H_{ax}), 2.89 (1H, dt, $J=13.6$, 2.2 Hz, 5- H_{eq}), 2.26 (3H, s, 9- CH_3), 2.08 (1H, ddd, $J=12.7$, 4.1, 1.3 Hz, 3- H_{eq}), 1.84 (1H, ddd, $J=12.7$, 11.3, 9.5 Hz, 3- H_{ax}), 1.86 (3H, s, $CH_2=C-CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 148.9 (9a-C), 148.1 (C=), 133.1 (8-C), 129.6 (6-C), 126.9 (5a-C), 124.3 (9-C), 121.9 (7-C), 111.9 ($=CH_2$), 69.8 (4-C), 61.6 (2-C), 44.5 (3-C), 44.1 (5-C), 19.5 ($CH_2=C-CH_3$), 14.4 (9- CH_3). MS (EI-70 eV) m/z (%): 251 (M^+ , ^{35}Cl , 54), 236 (3), 234 (3), 232 (3), 210 (31), 208 (11), 207 (9), 192 (30), 178 (14), 166 (100), 165 (14), 155 (31), 154 (6). Anal. Calcd for $C_{14}H_{18}ClNO$: C, 66.79; H, 7.21; N, 5.56. Found: C, 67.01; H, 7.45; N, 5.39%.

4.5.10. 6,8-Dimethyl-cis-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (8e). Reaction time: 1 h. Yield: 2.19 g (95%). Viscous maroon oil. R_f : 0.37 (33% ethyl acetate/heptane). IR (liquid film) $\nu_{\max}$: 3346 (NH/OH), 1264 (C–N), 1106 (C–O), 906 (C–H isopropenyl) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 6.63 (1H, s, 7-H), 6.43 (1H, s, 9-H), 5.02 (1H, br s, $=CH_AH$), 4.86 (1H, t, $J=1.4$ Hz, $=CH_BH$), 3.81 (1H, ddd, $J=9.2$, 3.9, 2.0 Hz, 4- H_{ax}), 3.43 (1H, dd, $J=11.3$, 2.0 Hz, 2- H_{ax}), 3.09 (1H, dt, $J=13.9$, 2.0 Hz, 5- H_{eq}), 2.86 (1H, dd, $J=13.9$, 9.0 Hz, 5- H_{ax}), 2.31 (3H, s, 6- CH_3), 2.22 (3H, s, 8- CH_3), 2.06 (1H, ddd, $J=13.1$, 3.9, 2.0 Hz, 3- H_{eq}), 1.85 (1H, ddd, $J=13.1$, 11.3, 9.4 Hz, 3- H_{ax}), 1.83 (3H, s, $CH_2=C-CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 149.3 (9a-C), 148.2 (C=), 137.7 (6-C), 136.3 (8-C), 124.6 (7-C), 123.7 (5a-C), 118.6 (9-C), 111.2 ($=CH_2$), 69.8 (4-C), 61.9 (2-C), 44.0 (3-C), 37.7 (5-C), 20.8 (8- CH_3), 19.3 (6- CH_3), 19.3 ($CH_2=C-CH_3$). MS (EI-70 eV) m/z (%): 231 (M^+ , 35), 190 (20), 172 (34), 158 (20), 146 (100), 131 (26), 91 (27). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.99; H, 9.05; N, 5.97%.

4.5.11. 7,9-Dichloro-cis-2-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-ol (8f). Reaction time: 2 h. Yield: 2.44 g (90%). Viscous maroon oil. R_f : 0.44 (33% ethyl acetate/heptane). IR (liquid film) $\nu_{\max}$: 3360 (NH/OH), 1267 (C–N), 1104 (C–O), 906 (C–H isopropenyl) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ : 7.21 (1H, d, $J=2.4$ Hz, 8-H), 7.01 (1H, d, $J=2.4$ Hz, 6-H), 5.09 (1H, br s, $=CH_AH$), 4.92 (1H, t, $J=1.4$ Hz, $=CH_BH$), 3.88 (1H, ddd, $J=9.7$, 4.0, 2.5 Hz,

4- H_{ax}), 3.41 (1H, dd, $J=11.2$, 1.2 Hz, 2- H_{ax}), 3.00 (1H, dt, $J=13.6$, 2.5 Hz, 5- H_{eq}), 2.91 (1H, dd, $J=13.6$, 8.8 Hz, 5- H_{ax}), 2.10 (1H, ddd, $J=13.2$, 4.0, 1.2 Hz, 3- H_{eq}), 1.86 (3H, s, $CH_2=C-CH_3$), 1.84 (1H, ddd, $J=13.2$, 11.2, 9.7 Hz, 3- H_{ax}). ^{13}C NMR (100 MHz, $CDCl_3$) δ : 147.1 (C=), 144.1 (9a-C), 130.3 (5a-C), 129.8 (6-C), 127.1 (8-C), 125.0 (7-C), 124.3 (9-C), 112.2 ($=CH_2$), 69.2 (4-C), 61.0 (2-C), 43.8 (3-C), 43.7 (5-C), 19.3 ($CH_2=C-CH_3$). MS (EI-70 eV) m/z (%): 271 (M^+ , ^{35}Cl , 40), 256 (9), 254 (6), 252 (6), 230 (49), 228 (17), 227 (9), 212 (40), 198 (17), 186 (100), 185 (17), 175 (17), 174 (34). Anal. Calcd for $C_{13}H_{15}Cl_2NO$: C, 57.37; H, 5.56; N, 5.15. Found: C, 57.25; H, 5.63; N, 5.29%.

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Supplementary data

Selected 1H , ^{13}C and NOESY NMR spectra as well as GC–MS spectra of compounds **5–8** are provided. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.08.067. These data include MOL files and InChIKeys of the most important compounds described in this article.

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