Tetrahedron 66 (2010) 8392–8401

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

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

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ARTICLE INFO

Article history:
Received 2 June 2010
Received in revised form 24 August 2010
Accepted 27 August 2010
Available online 16 September 2010

Keywords:
1,4-Epoxy-2-alkenyltetrahydro-1-benzazepines
2-Alkenyl-4-hydroxytetrahydro-1-benzazepines
Intramolecular 1,3-dipolar cycloaddition
ortho-Allylanilines
N-Allylanilines

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.

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 agents[3] 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 factor[7] 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-aryltetrahydro-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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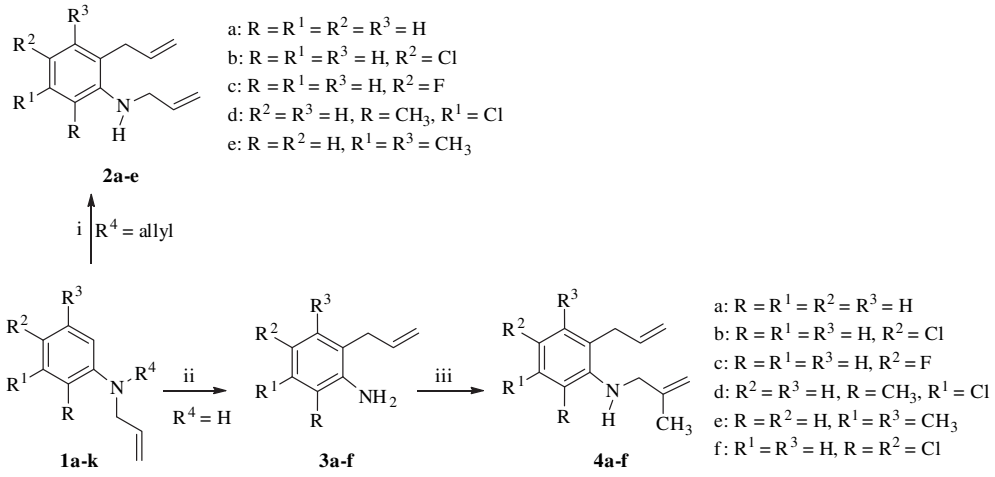
0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.08.067

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 ^{1}H NMR spectra of the analyzed crude reaction mixtures, thereby reducing the yields of the expected products.

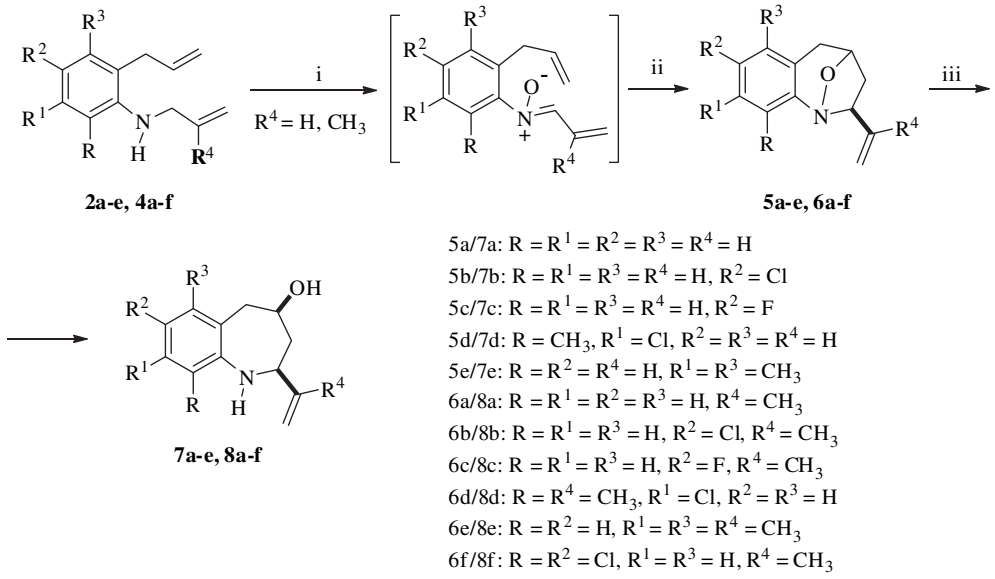
Table 1
Preparation of *ortho*-allylanilines **2a**–**e** and **3a**–**f** by amino-Claisen rearrangement of *N*,*N*-diallylanilines **1a**–**e** and mono *N*-allylanilines **1f**–**k**

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) BF_3·OEt_2 (0.01 equiv), 130–140 °C, 1–4 h; (ii) BF_3·OEt_2 (0.015 equiv), 120–140 °C, 6–8 h; (iii) Methallyl chloride (10 mmol), Na_2CO_3 (30 mmol), KI (5 mol %), dry DMF, rt, 12–20 h.



Scheme 2. Reagent and reaction conditions: (i) 30% H_2O_2 (30 mmol), Na_2WO_4·$2H_2O$ (10 mol %), MeOH, 0–25 °C, 6–72 h; (ii) Toluene, 80–110 °C, 4–7 h; (iii) Zn (100 mmol), glacial CH_3CO_2H (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% H_2O_2 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 $-NH-CH_2-$ framework. In turn, the oxidation of the non-substituted and 4-substituted *ortho*-allylanilines (R^2=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 ^{1}H NMR spectra of the crude reaction mixtures along with others non-identifiable degradation products.

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

ortho-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.

Structural elucidation of **5a**–**e** and **6a**–**f** was mainly based on NMR studies. In the ^{1}H NMR spectra of **5a**–**e**, the signal attributed to tertiary H-2 proton appears at δ 3.89–4.02 as doublets of 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=6.9–75 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 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 (nitrone) 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.

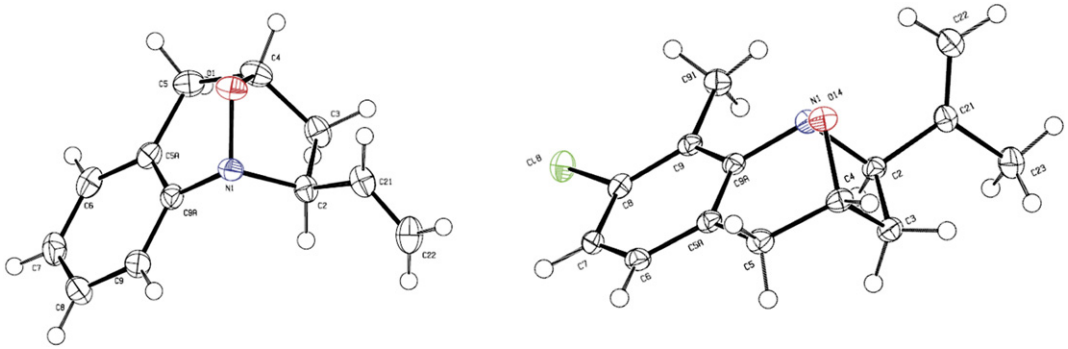


Fig. 1. X-ray crystal structures of 1,4-epoxy-2-*exo*-vinyl-2,3,4,5-tetrahydro-1(1*H*)-benzazepine **5a** and 8-chloro-9-methyl-1,4-epoxy-2-*exo*-(prop-1-en-2-yl)-2,3,4,5-tetrahydro-1(1*H*)-benzazepine **6d** (ORTEP views).[15]

The structures and stereochemistry of these novel compounds were determined by ^{1}H 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} (^{3}J=9.9–11.2 Hz), 3-H_{eq} (^{3}J=1.9–2.4 Hz) and vicinal olefinic proton –CH= (^{3}J=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.

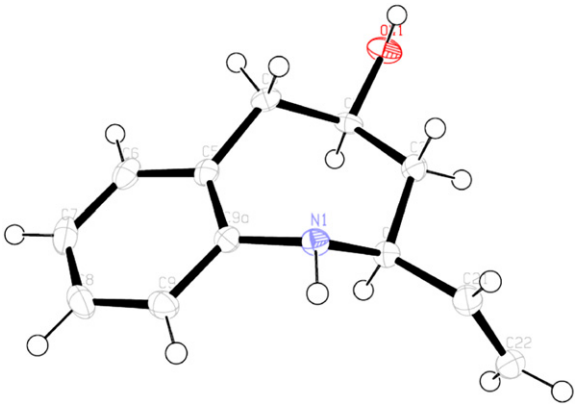


Fig. 2. X-ray crystal structure of *cis*-4-hydroxy-2-vinyl-2,3,4,5-tetrahydro-1(1*H*)-benzazepine **7a** (ORTEP view).[16]

3. Conclusion

In summary, the present work describes a simple and efficient stereoselective synthesis of novel 1,4-epoxy-2-*exo*-vinyl(isopropenyl) tetrahydro-1-benzazepines and *cis*-2-vinyl(isopropenyl)-4-hydroxy-tetrahydro-1-benzazepines; compounds that are not otherwise readily accessible. We believe the method is flexible enough to allow the synthesis of many analogues, simply by varying the alkenylic substituent on the nitrogen atom. These compounds are of special interest in medicinal chemistry, especially as anti-parasitic agents. In line with this purpose, preliminary results obtained clearly indicate they exhibit remarkable activity against the epimastigote and amastigote forms of *T. cruzi* as well as against promastigote form of *L. chagasi* parasite. Detailed results from this biological study will be reported in the near future elsewhere.

4. Experimental

4.1. General

All the reagents and solvents were purchased from Sigma–Aldrich or Merck companies, and used without further purification. Monitoring of the reactions was performed using silica gel TLC plates (silica Merck 60 F_{254}). Spots were visualized by UV light at 254 and 365 nm. Column chromatography was performed on Merck Kieselgel 60–230 mesh (ASTM). All the chromatographic solvent proportions were volume to volume. Melting points were determined with a MEL-TEMP 1201D capillary apparatus and are uncorrected. IR spectra were recorded on a Nicolet Avatar 360-FTIR spectrometer and referenced to polystyrene standard, using cells equipped with potassium bromide windows. ^{1}H and ^{13}C NMR spectra were measured on a Bruker AM-400 and Bruker Ultrashield 400 spectrometers, using $CDCl_3$ as the solvent. Chemical shifts (δ) and coupling constants (J) values are reported in parts per million and hertz, respectively. Chemical shifts are relative to the solvent peaks used as reference [$CDCl_3$: δ_H=7.26, and δ_C=77.0]. For ^{1}H NMR, the assignments are: q=quartet, t=triplet, d=doublet, s=singlet, br=broad, and m=multiplet. Multiplet refers to unresolved resonances from one or more protons having intractable ^{1}H–^{1}H coupling constants. A Hewlett–Packard (HP) 5890 A series II Gas Chromatograph interfaced to an HP 5972 Mass Selective Detector with an HP MS ChemStation Data system was used for MS identification. Elemental analyses (C, H, N) were performed on a Perkin–Elmer 2400 Series II analyzer.

The following *ortho*-allylanilines are known compounds and have physical and spectral data in agreement with those reported in the literature: **2a**–**c**[17] and **3a**–**c**,**e**.[18]

4.2. General procedure for the synthesis of rearranged products 2 and 3

A mixture of the appropriately substituted *N*,*N*-diallylanilines **1a**–**e** (10 mmol) or mono *N*-allylanilines **1f**–**k** and boron trifluoride diethyl ether complex (10 mmol, 1.25 mL for **1a**–**e** derivatives, and 15 mmol, 1.88 mL for **1f**–**k** derivatives) was heated at 120–140 °C for 1–8 h. The reaction mixtures were neutralized with saturated sodium carbonate solution and then extracted with CH_2Cl_2 (2×100 mL). The organic layers were dried over anhydrous sodium sulfate and the solvent removed under reduced pressure. The crude products were purified by column chromatography on silica gel, eluting with mixtures of heptane and ethyl acetate (compositions in the range from 100:1 to 70:1 v/v for **3a**–**e**, and 50:1 to 10:1 v/v for **3f**–**k**) to obtain rearranged products as low-viscosity maroon oils. Spectral data and elemental analysis for previously unreported *ortho*-allylanilines **2d**, **2e**, **3d**, and **3f** are listed below:

*4.2.1. N,6-Diallyl-3-chloro-2-methylaniline (**2d**).* IR (liquid film) ν_{max}: 3380 (N–H), 1638 (C=C allyl), 917 (=C–H allyl) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.03 (1H, d, J=8.2 Hz, 4-H), 6.94 (1H, d, J=8.2 Hz, 3-H), 6.04–5.91 (2H, m, –CH=), 5.31–5.14 (2H, m, N–CH_2–CH=CH_2), 5.14–5.02 (2H, m, –CH_2–CH=CH_2), 3.54 (2H, dt, J=5.9, 1.3 Hz, N–CH_2), 3.37 (2H, d, J=6.1 Hz, –CH_2–), 2.37 (s, 2-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.7 (1-C), 136.8 (CH=), 136.3 (CH=), 133.9 (5-C), 130.2 (2-C), 129.3 (6-C), 128.4 (3-C), 123.4, (4-C), 116.4 (=CH_2), 116.3 (=CH_2), 52.1 (N–CH_2), 36.7 (–CH_2), 15.4

(2-CH_3). MS (EI-70 eV) *m*/*z* (%): 221 (M^+, ^{35}Cl, 20), 180 (42), 178 (67), 145 (100), 144 (63), 130 (49), 115 (23). Anal. Calcd for $C_{13}H_{16}ClN$: 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) ν_{max}: 3432 (N–H), 1636 (C=C allyl), 915 (=C–H allyl) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 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–CH_2–CH=CH_2), 5.17–5.03 (2H, m, –CH_2–CH=CH_2), 3.79 (2H, dt, *J*=5.3, 1.7 Hz, N–CH_2–), 3.34 (2H, dt, *J*=5.7, 1.6 Hz, –CH_2–), 2.29 (3H, s, 5-CH_3), 2.26 (3H, s, 3-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) 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 (=CH_2), 115.6 (=CH_2), 110.3 (6-C), 47.1 (N–CH_2), 31.6 (–CH_2), 21.9 (5-CH_3), 20.4 (3-CH_3). 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 $C_{14}H_{19}N$: 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) ν_{max}: 3482 (N–H), 3399 (N–H), 1622 (C=C allyl), 918 (=C–H allyl) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 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, =CHH_B), 3.29 (2H, dt, *J*=5.8, 1.8 Hz, –CH_2–), 2.27 (3H, s, 6-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) 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 (=CH_2), 36.6 (–CH_2), 14.0 (6-CH_3). MS (EI-70 eV) *m*/*z* (%): 181 (M^+, ^{35}Cl, 100), 166 (39), 146 (48), 131 (83), 130 (46). Anal. Calcd for $C_{10}H_{12}ClN$: 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) ν_{max}: 3480 (N–H), 3389 (N–H), 1624 (C=C allyl), 921 (=C–H allyl) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 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, =CHH_B), 4.10 (2H, br s, -NH_2), 3.28 (2H, d, *J*=6.1 Hz, –CH_2–). ^{13}C NMR (100 MHz, $CDCl_3$) 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 (=CH_2), 36.7 (–CH_2). MS (EI-70 eV) *m*/*z* (%): 201 (M^+, ^{35}Cl, 93), 186 (74), 151 (80), 131 (100), 130 (80). Anal. Calcd for $C_9H_9Cl_2N$: 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 methallyl chloride (10 mmol, 0.97 mL) at room temperature. The reaction mixtures were stirred for 12–20 h (TLC control) and then extracted with CH_2Cl_2 (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) ν_{max}: 3444 (N–H), 1637 (C=C allyl), 918 (=C–H allyl) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 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, C*H*= allyl), 5.16 (1H, dq, *J*=10.1, 1.6 Hz, =CH_AH allyl), 5.13 (1H, dq, *J*=17.4, 1.6 Hz, =CHH_B allyl), 4.97 (1H, br s, =CH_AH), 4.91 (1H, br s, =CHH_B), 3.73 (2H, s, N–CH_2–), 3.35 (2H, d, *J*=6.2 Hz, –CH_2– allyl), 1.83 (3H, br s, CH_2=C–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.0 (1-C), 142.6 (CH_2=C–), 136.1 (CH= allyl), 129.8 (3-C), 127.6 (5-C), 123.5 (2-C), 117.2 (4-C), 116.2 (=CH_2 allyl), 110.8 (–C=CH_2), 110.8 (6-C), 49.8 (N–CH_2–), 36.6 (–CH_2– allyl), 20.5 (=C–CH_3). MS (EI-70 eV) *m*/*z* (%): 187 (M^+, 41), 146 (50), 132 (91), 131 (69), 130 (100), 118 (70). Anal. Calcd for $C_{13}H_{17}N$: 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) ν_{max}: 3444 (N–H), 1636 (C=C allyl), 917 (=C–H allyl) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 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, C*H*= allyl), 5.18 (1H, dq, *J*=10.2, 1.6 Hz, =CH_AH allyl), 5.14 (1H, dq, *J*=17.0, 1.6 Hz, =CHH_B allyl), 4.93 (1H, br s, =CH_AH), 4.90 (1H, br s, =CHH_B), 3.69 (2H, s, N–CH_2–), 3.28 (2H, d, *J*=6.2 Hz, –CH_2– allyl), 1.79 (3H, br s, CH_2=C–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.6 (1-C), 142.2 (CH_2=C–), 135.1 (CH= allyl), 129.4 (3-C), 127.2 (5-C), 125.0 (2-C), 121.6 (4-C), 116.8 (=CH_2 allyl), 111.7 (6-C), 110.9 (–C=CH_2), 49.7 (N–CH_2–), 36.2 (CH_2– allyl), 20.4 (=C–CH_3). MS (EI-70 eV) *m*/*z* (%): 221(M^+, ^{35}Cl, 36), 180 (36), 166 (59), 165 (30), 164 (53), 131 (100), 130 (78). Anal. Calcd for $C_{13}H_{16}ClN$: 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) ν_{max}: 3440 (N–H), 1637 (C=C allyl), 919 (=C–H allyl) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 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, C*H*= allyl), 5.16 (1H, dq, *J*=10.2, 1.5 Hz, =CH_AH allyl), 5.13 (1H, dq, *J*=17.1, 1.5 Hz, =CHH_B allyl), 4.93 (1H, br s, =CH_AH), 4.89 (1H, br s, =CHH_B), 3.68 (2H, d, *J*=6.1 Hz, N–CH_2–), 3.30 (2H, d, *J*=6.2 Hz, –CH_2– allyl), 1.79 (3H, d, *J*=0.4 Hz, CH_2=C–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) 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 (=CH_2 allyl), 116.6 (d, *J*=22.4 Hz, 3-C), 113.5 (d, *J*=21.5 Hz, 5-C), 111.4 (CH_2=C–), 111.4 (6-C), 110.2 (–C=CH_2), 50.6 (N–CH_2–), 36.4 (–CH_2– allyl), 20.7 (=C–CH_3). MS (EI-70 eV) *m*/*z* (%): 205(M^+, 35), 164 (44), 150 (77), 149 (62), 148 (100), 136 (76), 135 (55). Anal. Calcd for $C_{13}H_{16}FN$: 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) ν_{max}: 3372 (N–H), 1637 (C=C allyl), 918 (=C–H allyl) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 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, C*H*= 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, =CHH_B allyl), 4.92 (1H, br s, =CHH_B), 3.43 (2H, s, N–CH_2–), 3.37 (2H, d, *J*=6.1 Hz, –CH_2– allyl), 2.36 (3H, s, 2-CH_3), 1.83 (3H, s, CH_2=C–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.9 (1-C), 144.0 (CH_2=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 (=CH_2 allyl), 111.3 (–CH_2=C–), 55.2 (N–CH_2–), 36.5 (CH_2– allyl), 21.0 (=C–CH_3), 15.6 (2-CH_3). MS (EI-70 eV) *m*/*z* (%): 235 (M^+, ^{35}Cl, 15), 194 (24), 180 (45), 179 (27), 178 (56), 145 (100), 144 (58), 130 (41), 115 (21). Anal. Calcd for $C_{14}H_{18}ClN$: 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) ν_{max}: 3440 (N–H), 1634 (C=C allyl), 922 (=C–H allyl) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 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, C*H*= allyl), 5.06 (1H, dq, *J*=10.3, 2.0 Hz, =CH_AH allyl), 5.02 (1H, dq, *J*=17.0, 2.0 Hz, =CHH_B allyl), 4.94 (1H, br s, =CH_AH), 4.88 (1H, br s, =CHH_B), 3.67 (2H, s, N–CH_2–), 3.32 (2H, dt, *J*=5.7, 2.0 Hz, –CH_2– allyl), 2.26 (3H, s, 3-CH_3), 2.25 (3H, s, 5-CH_3), 1.79 (3H, s, CH_2=C–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.4 (1-C),

143.0 (CH_2=*C*–), 136.8 (3-C), 136.6 (5-C), 135.5 (CH= allyl), 120.5 (4-C), 118.9 (2-C), 115.4 (=CH_2 allyl), 110.8 (–*C*H_2=C–), 109.8 (6-C), 50.1 (N–CH_2–), 31.6 (CH_2– allyl), 21.6 (3H, 5-CH_3), 20.8 (3H, 3-CH_3), 20.2 (=C–CH_3). 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 $C_{15}H_{21}N$: 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, $CDCl_3$) 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, C*H*= allyl), 5.16 (1H, dq, *J*=10.1, 1.6 Hz, =CH_AH allyl), 5.10 (1H, dq, *J*=17.1, 1.6 Hz, =CHH_B allyl), 5.02 (1H, br s, =CH_AH), 4.89 (1H, br s, =CHH_B), 3.54 (2H, s, N–CH_2–), 3.40 (2H, d, *J*=6.3 Hz, –*C*H_2– allyl), 1.80 (3H, s, CH_2=C–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.6 (CH_2=*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 (=CH_2 allyl), 111.8 (–*C*H_2=C–), 54.9 (N–CH_2–), 36.2 (CH_2– allyl), 20.8 (=C–*C*H_3). MS (EI-70 eV) *m*/*z* (%): 255 (M^+, ^{35}Cl, 12), 214 (42), 200 (65), 199 (48), 198 (70), 165 (100), 164 (69), 151 (36), 130 (70), 115 (24). Anal. Calcd for $C_{13}H_{15}Cl_2N$: 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 % $Na_2WO_4 \cdot 2H_2O$, 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, $CDCl_3$) 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, –C*H*=), 5.22 (1H, dt, *J*=17.2, 1.1 Hz, =CH_AH), 5.12 (1H, dt, *J*=10.4, 1.1 Hz, =CHH_B), 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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 (=CH_2), 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 $C_{12}H_{13}NO$: 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, $CDCl_3$) 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, –C*H*=), 5.21 (1H, dt, *J*=17.1, 1.2 Hz, =CH_AH), 5.11 (1H, dt, *J*=10.4, 1.2 Hz, =CHH_B), 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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 (=CH_2), 74.8 (2-C), 74.3 (4-C), 40.1 (3-C), 34.7 (5-C). MS (EI-70 eV) *m*/*z* (%): 221 (M^+, ^{35}Cl, 46), 204 (15), 191 (6), 164 (12), 139 (62), 138 (100), 112 (23). Anal. Calcd for $C_{12}H_{12}ClNO$: 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, $CDCl_3$) 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, –C*H*=), 5.21 (1H, dt, *J*=17.3, 1.2 Hz, =CH_AH), 5.11 (1H, dt, *J*=10.3, 1.2 Hz, =CHH_B), 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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 (=CH_2), 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 $C_{12}H_{12}FNO$: 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, $CDCl_3$) 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, –C*H*=), 5.26 (1H, dt, *J*=17.2, 1.3 Hz, =CH_AH), 5.13 (1H, dt, *J*=10.3, 1.3 Hz, =CHH_B), 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-CH_3), 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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 (=CH_2), 74.6 (4-C), 73.1 (2-C), 40.1 (3-C), 34.4 (5-C), 13.7 (9-CH_3). MS (EI-70 eV) *m*/*z* (%): 235 (M^+, ^{35}Cl, 51), 218 (18), 205 (9), 178 (9), 153 (100), 152 (54), 126 (9). Anal. Calcd for $C_{13}H_{14}ClNO$: 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, $CDCl_3$) 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, –C*H*=), 5.23 (1H, dt, *J*=17.2, 1.9 Hz, =CH_AH), 5.15 (1H, dt, *J*=10.3, 1.9 Hz, =CHH_B), 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-CH_3), 2.23 (1H, ddd, *J*=12.6, 8.3, 2.0 Hz, 3-H_A), 2.13 (3H, s, 6-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) 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 (=CH_2), 74.8 (4-C), 74.7 (2-C), 40.5 (3-C), 33.1 (5-C), 20.9 (8-CH_3), 18.5 (6-CH_3). 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, =CHH_B), 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, =CHH_B), 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, =CHH_B), 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, =CHH_B), 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, =CHH_B), 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, =CHH_B), 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-1*H*-benzo[*b*]azepinols 7 and *cis*-2-(prop-1-en-2-yl)-tetrahydro-1*H*-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, =C*H*), 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 (=CH_2), 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 $C_{12}H_{15}NO$: 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, =C*H*), 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 (=CH_2), 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 $C_{12}H_{14}ClNO$: 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, =C*H*), 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 (=CH_2), 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 $C_{12}H_{14}FNO$: 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, =C*H*), 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-CH_3), 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 (=CH_2), 69.5 (4-C), 58.5 (2-C), 45.5 (3-C), 43.4 (5-C), 14.4 (9-CH_3). 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 $C_{13}H_{16}ClNO$: 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, =C*H*), 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-CH_3), 2.24 (3H, s, 8-CH_3), 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 (=CH_2), 69.4 (4-C), 59.2 (2-C), 45.5 (3-C), 37.8 (5-C), 20.8 (6-CH_3), 20.8 (8-CH_3). 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 $C_{14}H_{19}NO$: 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, CH_2=C–CH_3). ^{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 (=CH_2), 69.8 (4-C), 61.9 (2-C), 45.0 (3-C), 44.4 (5-C), 19.3 (CH_2=C–CH_3). 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 $C_{13}H_{17}NO$: 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, CH_2=C–CH_3). ^{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 (=CH_2), 69.5 (4-C), 62.1 (2-C), 44.7 (3-C), 44.0 (5-C), 19.2 (CH_2=C–CH_3). 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) ν_{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, =CHH_B), 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) ν_{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, =CHH_B), 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) ν_{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, =CHH_B), 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) ν_{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, =CHH_B), 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%.

Acknowledgements

The authors would like to acknowledge for the financial support due by the Colombian Institute for Science and Research (COLCIENCIAS, grant No 1102–408-20563), and the Research Center of Excellence CENIVAM (contract No 432). A. P. also thanks Dr. E. Stashenko (Laboratory of Chromatography, School of Chemistry, Industrial University of Santander) for providing GC–MS spectra.

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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