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Synthesis of complex fused polycyclic heterocycles utilizing IMDAF reactions of allylamino- or allyloxy-furyl(hetero)arenes

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ABSTRACT

Arenes and heteroarenes carrying a halogen and an amino- or hydroxy group have been converted to allylamino- or allyloxy-furyl-(hetero)arenes. These compounds underwent IMDAF reactions to give complex fused polycyclic heterocycles. The reactivity of the substrates was highly dependent on the detailed substitution pattern, however cyclizations occurred with high stereoselectivity in most cases. Experimental findings regarding reactivity and stereoselectivity were supported by calculations.

1. Introduction

Despite their aromaticity, furan derivatives may participate as dienes in Diels–Alder cycloadditions. The intramolecular Diels–Alder reaction on furans (IMDAF) is a versatile reaction where two or more rings can be formed in a single step often with high regio- and stereochemical control, and where the oxanorbornene ring system initially formed, can easily be converted into other cyclic structures.[1] The IMDAF reaction is often applied in synthesis directed toward natural products[2] and numerous other polycyclic systems. There is a continuous need for efficient and selective protocols for the construction of complex polycyclic heterocycles found as components in natural products and other bioactive molecules. We have previously formed the tetrahydrodiazepinopurine heterocyclic core in asmarines with ring closing metathesis as the key step,[3] and studied cyclization processes leading to indolizines.[4] We envisaged that the IMDAF reaction could be applied in the construction in a variety of novel polycyclic heterocycles, and we herein present our results from a study of reactivity and diastereoselectivity in cyclizations between furans and allylamines or allyl ethers both attached to an arene or heteroarene as depicted in Fig. 1.

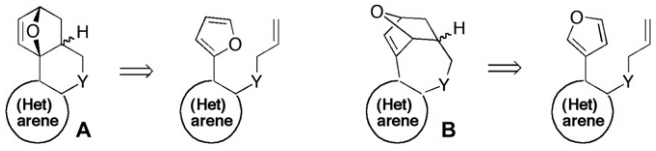

Fig. 1. An overview of the ring systems **A** and **B** constructed by IMDAF reactions.

2. Results and discussion

The furylbenzenes **3** and **4** for the IMDAF reaction leading to type **A** adducts (Fig. 1) were synthesized as shown in Scheme 1. The furyl group was introduced by a Pd-catalyzed coupling on the halides **1**. The Suzuki–Miyaura cross-coupling reaction of potassium furyltrifluoroborate was found to be an efficient way to synthesize most furan derivatives described in this paper.[5] The products **2** were *N*- or *O*-allylated to give compounds **3**. The allylation could be achieved in the presence of Hünig's base and a catalytic amount of hydrochloric acid at 80 °C, however under these conditions some of the more reactive products also partly underwent the Diels–Alder reaction. In these cases the allylation was performed under milder conditions employing an alkali metal hydride and a suitable crown ether at ambient temperature. When NaH was found to react too slowly or not at all, most likely due to the lack of acidity for the proton in question, KH was used. The *N*,*N*-disubstituted anilines **4** were formed as a by-product in the synthesis of compounds **3** or by further transformation of the mono-*N*-allylated anilines **3**.

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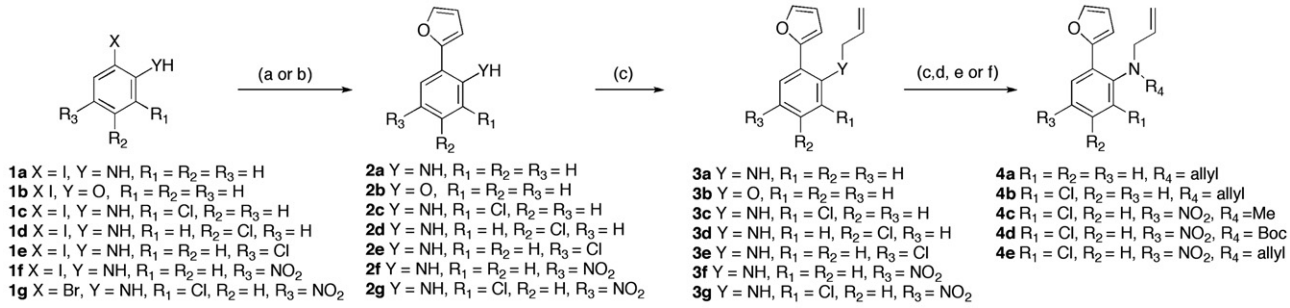
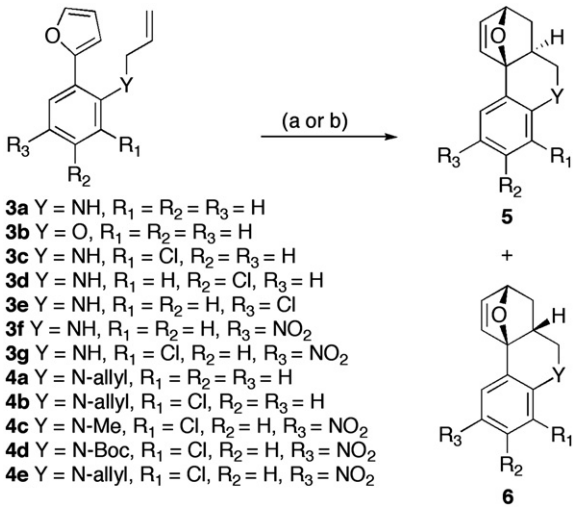


Scheme 1. (a) 2-FurylB(OH)$_2$ or 2-furylBF$_3$K, Pd(OAc)$_2$, PPh$_3$, EtOH, 80 °C; (b) 2-furylSnBu$_3$, Pd(PPh$_3$)$_2$Cl$_2$, DMF, 60–100 °C; (c) allyl-Br, for detailed reaction conditions, see Experimental section; (d) MeI, K$_2$CO$_3$, DMF; (e) (Boc)$_2$O, DMAP, K$_2$CO$_3$, THF; (f) formed as a by-product in the synthesis of **3**.

Compounds **3** and **4** were heated in an inert solvent in order to affect IMDAF cyclization (Scheme 2) and the results are summarized in Table 1.



Scheme 2. (a) PhMe, 100 °C; (b) xylene, 150 °C.

N-Allyl(furyl)aniline **3a** did not react at all in toluene at 100 °C for 24 h. Extended reaction time (7 days) or increased temperature (150 °C in xylene) did not have any positive effect on the reaction. Also the phenol derivative **3b** was unreactive at 100 °C, but cyclization was observed when the reaction was carried out at 150 °C. Only the *exo* isomer **5** was observed and isolated, and the stereochemistry was determined by NOESY NMR spectroscopy (Fig. 2). No Claisen rearrangement product **7** (Fig. 2) of this aryl allyl ether was observed. Calculations at the DFT level (PBE/def2-SVP, see Computational details) showed that the barrier for the rearrangement is higher (6 kcal/mol) than for the Diels–Alder reaction. Interestingly, however, the product of the Claisen rearrangement is more stable (9 kcal/mol) than the Diels–Alder product. The cycloaddition product is thus the kinetically preferred product, whereas the Claisen rearrangement product is the thermodynamically preferred one. The conversion in the reaction appeared to be ca. 75%, but the isolated yield of the Diels–Alder adduct **5b** was reduced due to low stability on both silica and alumina chromatography columns. The same was observed for several other adducts **5** and **6**.

A chloride *ortho* to the *N*-allyl substituent (compounds **3c** and **3g**) has a positive effect on the cyclization. In both cases a mixture of compounds **5** and **6** was formed with the *exo* adducts **5** as the major isomer. Introduction of substituents *meta* or *para* to the *N*-allyl substituent (compounds **3d**–**f**) did not result in compounds with significantly higher reactivity compared to the aniline derivative **3a**.

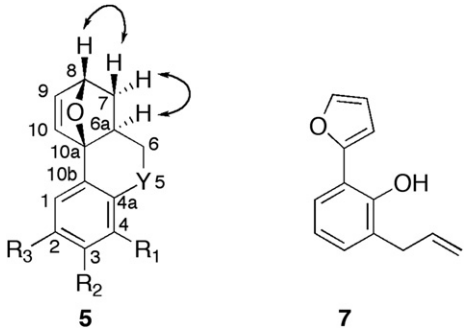


Fig. 2. Important NOESY correlations for structure elucidation of the major isomer **5** and the numbering of the ring atoms in compounds **5**, **6**, **13**, and **14**. Potential Claisen rearrangement product **7** from the allyloxybenzene **3b**.

Table 1
IMDAF cyclization of compounds **3** and **4**

Starting material	Y	R_1	R_2	R_3	Solvent	Temp (°C)	Ratio **5**/**6**[a]	Unreacted starting material (%)[a]	Isolated yields **5** and **6** (%)
3a	NH	H	H	H	Toluene	100	—	>99	—
3b	O	H	H	H	Toluene	100	—	>99	—
3b	O	H	H	H	Xylene	150	>99:1	23	28, **5b**
3c	NH	Cl	H	H	Toluene	100	9:1	27	33, **5c** and **6c**
3d	NH	H	Cl	H	Toluene	100	—	>99	—
3e	NH	H	H	Cl	Toluene	100	—	>99	—
3f	NH	H	H	NO_2	Toluene	100	—	>99	—
3f	NH	H	H	NO_2	Xylene	150	6:1	22	13, **5f** and **6f**
3g	NH	Cl	H	NO_2	Toluene	100	9:1	<1	88, **5g** and **6g**
4a	*N*-Allyl	H	H	H	Toluene	100	10:3	<1	—[b] **5h** and **6h**
4b	*N*-Allyl	Cl	H	H	Toluene	100	7:1	38	—[b] **5i** and **6i**
4c	*N*-Me	Cl	H	NO_2	Toluene	100	7:3	2	66, **5j** and 24, **6j**
4d	*N*-Boc	Cl	H	NO_2	Toluene	100	—	—	—
4e	*N*-Allyl	Cl	H	NO_2	Toluene	100	4:1	<1	76, **5l** and **6l**

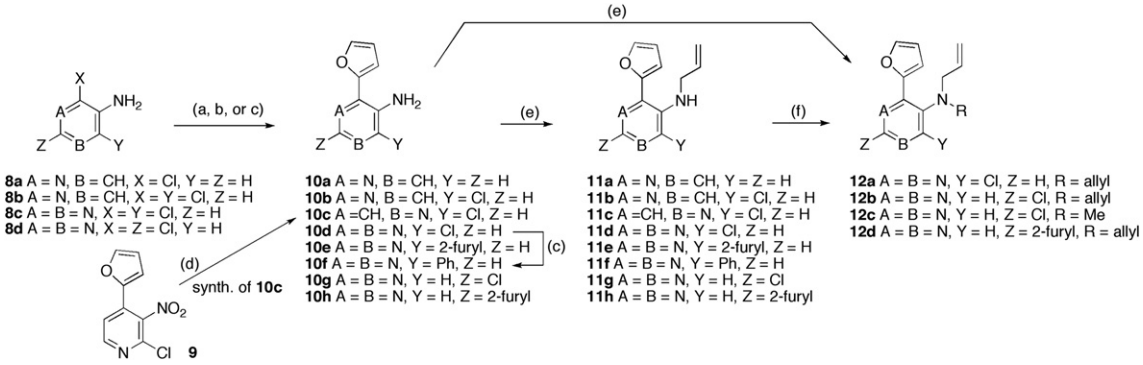
[a] From ^{1}H NMR of the crude product.
[b] Not isolated in pure form.

The *N*,*N*-dialkylated anilines **4a**–**c** and **4e** were all prone to cyclization at 100 °C, and in all cases the *exo* adducts **5** were the major isomers, but the *N*-Boc derivative **4d** did not react under the same set of reaction conditions.

We then studied the IMDAF reaction on substrates where the benzene ring in compounds **3** and **4** were exchanged with a pyridine or pyrimidine ring. The syntheses of these starting materials **11** and **12**, following the same strategy as for the synthesis of **3** and **4**, are shown in Scheme 3. Compound **10c** is not available by a regioselective coupling on dichloropyridine **8a**.[6] Instead this intermediate was synthesized by reduction of the nitropyridine **9**.

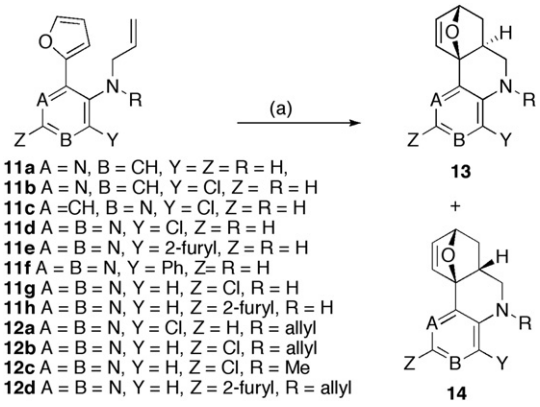
Pyridine **11a** did not react at all under standard conditions. Increased reaction time had no effect, and when the reaction was attempted at higher temperatures, decomposition took place.

The results shown in Tables 1 and 2 show that in all cases examined the *exo* compounds **5** and **13** are the preferred diastereomers in the cyclization of the 2-furyl derivatives **3**, **4**, **11**, and **12**. This is consistent with former studies of IMDAF reactions on simpler furans carrying an allylamino substituent in the 2-position,[7] and in our cases the diastereoselective outcome is also supported by theoretical calculations at the PBE/def2-SVP level of theory. Fig. 3 illustrates the situation for the cyclization of allyl-



Scheme 3. (a) 2-FurylB(OH)$_2$, Pd(*t*-Bu$_3$P)$_4$, KF, dioxane, Δ; (b) 2-furylSnBu$_3$, Pd(PPh$_3$)$_2$Cl$_2$ or [(Furyl)$_3$]$_4$Pd DMF, 60 °C; (c) PhBF$_3$K or 2-FurylBF$_3$K, Pd(OAc)$_2$, PPh$_3$, K$_2$CO$_3$, EtOH, 80 °C; (d) H$_2$, Raney-Ni, MeOH; (e) allyl-Br, for detailed reaction conditions, see Experimental section; (f) allyl halide or MeI, KH, 18-crown-6, toluene.

Compounds **11** and **12** were heated in an inert solvent in order to affect IMDAF cyclization (Scheme 4) and the results are summarized in Table 2.



Scheme 4. (a) Toluene, 100 °C.

amine **3a**; both the active conformation leading to cyclization, the transition state and the product is higher in energy for the *endo* compound.

Both a substituent on the allylic amine nitrogen in compounds **4** and **12**, and a substituent *ortho* to the allylic side chain in all substrates **3**, **4**, **11**, and **12** appears to have a very positive influence on reactivity in the cyclization. At least when it comes to the *ortho* substituent the experimental results indicate that this effect is steric rather than electronic. Effects of *N*-substituents on IMDAF reactions of allylic amides have also been discussed before.[8] Our theoretical studies revealed that the increased reactivity of *ortho* substituted compounds is mainly due to a steric effect, which destabilizes the minimum conformation of the reactant compared to the active conformations. The transition states and the products are not influenced significantly by the *ortho* substituents. The same effect is observed for the compounds bearing an additional *N*-substituent. This is schematically shown in Fig. 4.

The activation barrier out of the active conformation $\Delta E^{\ddagger}_{\text{active}}$ is relatively constant as is the reaction energy out of the active conformation ΔE_{active}. When looking, however, at the real activation barrier $\Delta E^{\ddagger}$ from the minimum conformation the barrier becomes

Table 2
IMDAF cyclization of compounds **11** and **12**

Starting material	A	B	Y	Z	R	Ratio **13**/**14**[a]	Unreacted starting material (%)[a]	Isolated yields **13** and **14** (%)
11a	N	CH	H	H	H	—	>99	—
11b	N	CH	Cl	H	H	25:1[b]	<1	49, **13b** and **14b**
11c	CH	N	Cl	H	H	10:1	<1	88, **13c** and **14c**
11d	N	N	Cl	H	H	16:1	<1	55, **13d**
11e	N	N	2-Fur	H	H	6:1	<1	66, **13e** and **14e**
11f	N	N	Ph	H	H	15:1	25[c]	58, **13f** and **14f**
11g	N	N	H	Cl	H	—	>99	—
11h	N	N	H	2-Fur	H	—	>99	—
12a	N	N	Cl	H	Allyl	4:1	47	38, **13i** and 10, **14i**
12b	N	N	H	Cl	Allyl	4:1	<1	80, **13j** and 20, **14j**
12c	N	N	H	Cl	Me	4:1	13	54, **13k** and 14, **14k**
12d	N	N	H	2-Fur	Allyl	8:1	<1	78, **13l** and 15, **14l**

[a] From ^{1}H NMR of the crude product.
[b] From ^{1}H NMR of the isolated product.
[c] Recovered starting material.

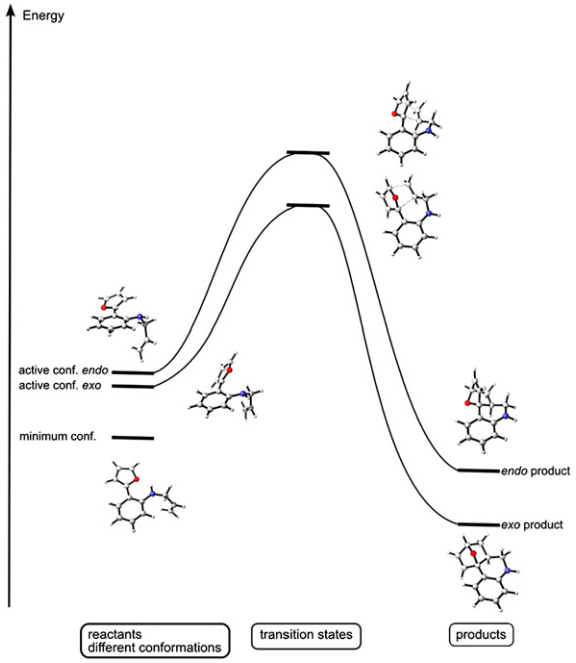


Fig. 3. Schematic representation of the reaction mechanism of the IMDAF reaction for compound **3a** based on PBE/def2-SVP calculations (see text and Table 3 for details).

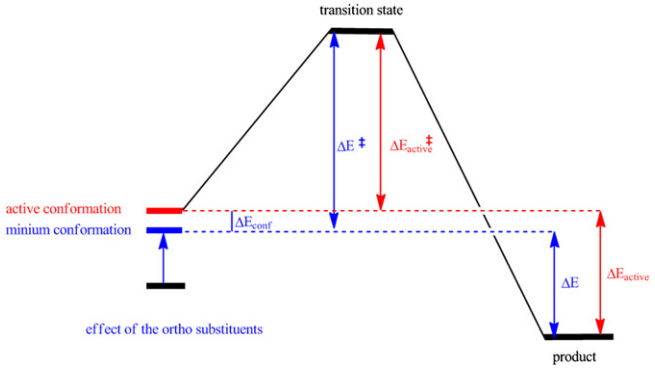


Fig. 4. Effect of the *ortho* substituents R_1 in compounds **3** and **4** and Y in compounds **11** and **12**≠H in blue.

lower for sterically more demanding substituents. The reaction energy ΔE, however, increases. This means that sterically demanding substituents lead to a faster reaction and are subject to an increased thermodynamic driving force. For the parent compound **3a** the energy difference between the active conformation and the minimum conformation is 8 kcal/mol (for *exo*). This means that at 100 °C and assuming thermal equilibrium in the reaction mixture the ratio between the populations of the two conformations is 0.00003, which explains the lack of reactivity for this substrate. In the case of the more reactive *ortho* substituted substrate **3c**, the energy difference between the conformers is only 2 kcal/mol, which means that the ratio of the two conformers at 100 °C is 0.09. Tables 3 and 4 summarize relative energies for selected reactions.

After seeing the dramatic effect on the *N*-substituent and the '*ortho* to *N*'-substituent on reactivity, we found it interesting to study the cyclization of substrates where these two substituents are combined to form an additional ring and hence we synthesized the *N*-allyl-furyl(aza)indoles **17** and examined their reactivity in the IMDAF reaction. The furyl group was introduced by a Suzuki-coupling employing potassium trifluoro(2-furyl)borate, and N-allylation was achieved when compounds **16a** and **16b** were reacted with an allyl halide in the presence of alkali metal hydride and a crown ether. N-Alkylation of purines normally results in the *N*-9 substituted isomer as the major product. Hence, purine **16c** was allylated in the presence of methylaquacobaloxime, which is known to facilitate a selective reaction at *N*-7.[3,9]

Compounds **17** were heated in toluene (Scheme 5, Table 5), and the indole **17a** was cyclized to the IMDAF product **18a**, which was isolated in 69% yield. The numbering system used in the interpretation of the NMR spectra of compounds **18** is shown in Scheme 5. Also the pyrrolopyrimidine **17b** cyclized with complete stereoselectivity to *exo* product **18b**, but the conversion was moderate under standard conditions. The purine **17c** did not cyclize at all after heating for 24 h at 100 °C (toluene) or 24 h at 150 °C (xylene). It can be seen from the calculated energies presented in Tables 3–5, that the ring nitrogen(s) in the starting materials destabilize mainly the product and the transition state. Nevertheless, several pyridines and pyrimidines **11** and **12** gave Diels–Alder adducts in good yields (Table 2). In the case of the bicyclic system (compounds **17**), the overall reaction energy (Table 5) is less favorable compared to the monocyclic systems. This is probably again a ring strain effect. Therefore, additional nitrogen atoms in the ring led to overall unstable compounds. For the purine **17c** the reaction is thermodynamically unfavorable and will not take place. For the reaction on the pyrrolopyrimidine **17b**, only the *exo* isomer is predicted to be stable, whereas for the indole **17a** both isomers should be isolable. However, we could only detect formation of the *exo* isomer.

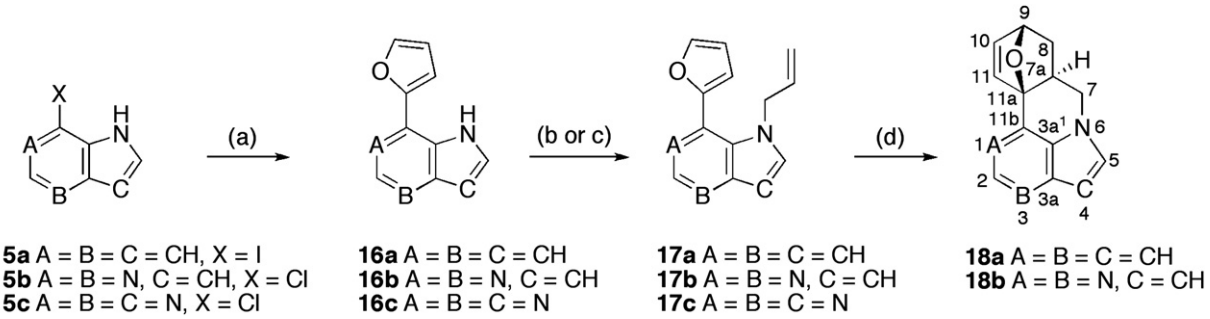
Finally we examined the possibility of carrying out the IMDAF reaction on 3-furylarenes in order to form polycyclic products containing a seven-membered ring. The 3-furylarene **19** was formed from a Suzuki coupling on compound **1g** and the amine was mono- or diallylated to give the allylamines **20** or **22** depending on the detailed reaction conditions (Scheme 6). Both compounds **20** and **22** cyclized to give IMDAF products **21** and **23**. Compound **22** gave only the *endo* product **23** (structure shown) according to the ^{1}H NMR spectra of the crude product, and for compound **21** a 6:1

Table 3
Reaction energies ΔE, activation barriers for Diels–Alder reaction $\Delta E^{\ddagger}$ and energy difference between the active and the minimum conformation of the reactant ΔE_{conf} for the *endo* and *exo* isomers formed from selected starting materials **3**. For the *exo* isomer reaction energies ΔE_{active} and activation barriers for Diels–Alder reaction $\Delta E^{\ddagger}_{active}$ relative to the active conformer of the reactant is also shown. All energies at the PBE/def2-SVP level, given in kcal/mol. See also Figs. 3 and 4 for illustration

Compound	R^1	*exo*					*endo*		
		ΔE	$\Delta E^{\ddagger}$	ΔE_{conf}	ΔE_{active}	$\Delta E^{\ddagger}_{active}$	ΔE	$\Delta E^{\ddagger}$	ΔE_{conf}
3a	H	−4.4	23.8	7.1	−11.5	16.7	1.0	25.9	5.7
3c	Cl	−10.8	17.4	1.4	−12.4	16	−5.8	19.2	0.0

Table 4
Reaction energies ΔE, activation barriers for Diels–Alder reaction $\Delta E^{\ddagger}$ and energy difference between the active and the minimum conformation of the reactant ΔE_{conf} for the *endo* and *exo* isomers formed from selected starting materials **11**. For the *exo* isomer reaction energies ΔE_{active} and activation barriers for Diels–Alder reaction $\Delta E^{\ddagger}_{active}$ relative to the active conformer of the reactant is also shown. All energies at the PBE/def2-SVP level, given in kcal/mol. See also Figs. 3 and 4 for illustration

Compound	A	B	Y	*exo*					*endo*		
				ΔE	$\Delta E^{\ddagger}$	ΔE_{conf}	ΔE_{active}	$\Delta E^{\ddagger}_{active}$	ΔE	$\Delta E^{\ddagger}$	ΔE_{conf}
11a	N	CH	H	−1.6	26.8	8.8	−10.4	18.0	5.3	29.3	9.6
11b	N	CH	Cl	−8.3	20.0	2.3	−10.6	17.3	−1.6	22.4	3.0
11d	N	N	Cl	−7.4	20.5	1.8	−9.2	18.7	−1.1	22.7	2.8
11e	N	N	2-fur	−10.6	18.1	0.0	−10.6	18.1	−4.3	20.0	0.8
11f	N	N	Ph	−5.8	23.4	6.0	−11.8	17.4	1.3	26.0	6.9



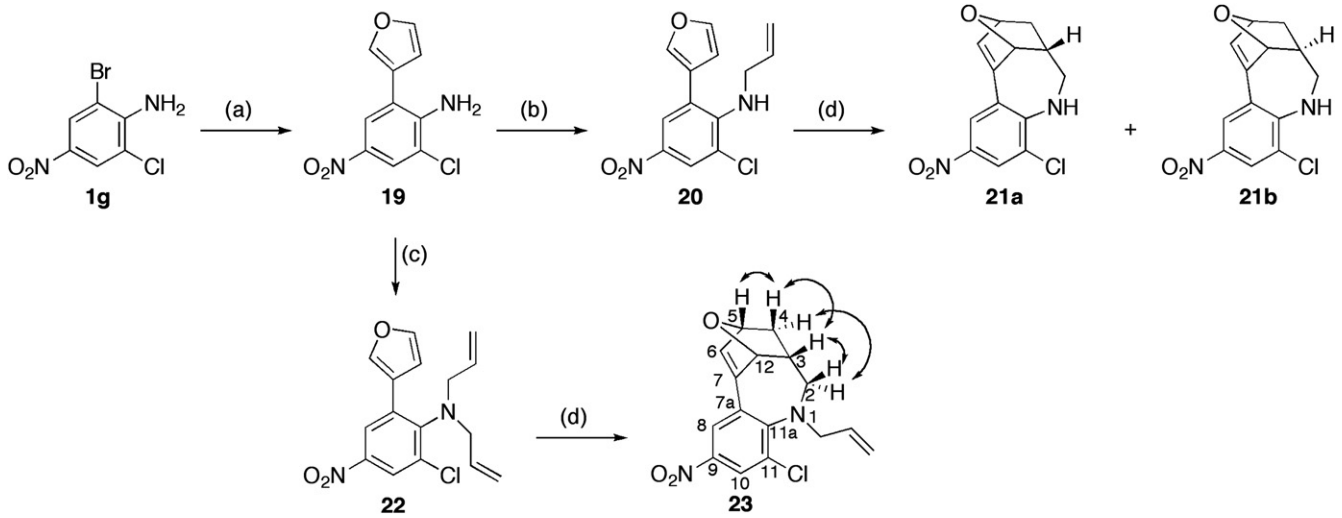
Scheme 5. (a) 2-FurylBF_3K, $Pd(OAc)_2$, PPh_3, K_2CO_3, EtOH, 60–80 °C; (b) allyl-Br, KH, 18-crown-6, toluene; (c) allyl-I, methylaquacobaloxime, K_2CO_3, MeCN; (d) toluene 100 °C.

Table 5
IMDAF cyclization of compounds **17**; Experimental outcome and calculated energies at PBE/def2-SVP in kcal/mol

A	B	B	Unreacted starting material **17** (%)[a]	Isolated yield **18** (%)	Energies compounds **18**			
					exo		*endo*	
					ΔE	$\Delta E^{\ddagger}$	ΔE	$\Delta E^{\ddagger}$
CH	CH	CH	<1	69, **18a**	−6.8	18.2	−2.7	21.2
N	N	CH	56	33, **18b**	−1.8	22.0	3.2	25.5
N	N	N	>99	—, **18c**	2.0	24.2	6.7	28.0

[a] From ^{1}H NMR of the crude product.

to the allylic side chain are shown to have very positive influence on reactivity in the cyclization. Our theoretical studies revealed that the increased reactivity of *ortho* substituted compounds is mainly due to a steric effect, which destabilizes the minimum conformation of the reactant compared to the active conformations. The cyclizations occur with high stereoselectivity in most cases; 2-furyl derivatives led mainly to *exo* adducts and 3-furyls to the *endo* isomer. These findings were supported by calculations. The Diels–Alder adducts formed contain several functional groups that may be manipulated further in syntheses of complex heterocyclic systems.



Scheme 6. (a) 3-Furyl$B(OH)_2$, $Pd(OAc)_2$, PPh_3, EtOH, 85 °C; (b) allyl-Br, NaH, 15-crown-5, toluene; (c) allyl-I, KH, 16-crown-8, toluene, 40 °C; (d) toluene, 40 °C.

endo/*exo* ratio was observed. Isomers **21a** and **21b** could be separated and were isolated in 59 and 11% yields, respectively. In both cases no unreacted starting material could be seen in the crude product. Important NOESY correlations used in structure elucidation of the *endo* adduct **23** are shown in Scheme 6. Calculations showed the *endo* product **21a** to be considerably more stable than **21b** (by 30 kcal/mol). Furthermore the *exo* product **21b** was found to be thermodynamically unstable, whereas the *endo* product **21a** was predicted to be stable (by 6 kcal/mol).

In conclusion, we have shown that several complex polycyclic heterocycles can be constructed with an IMDAF reaction on allylamino- or allyloxy-furyl-(hetero)arenes as the key step. Both a substituent on the allylic amine nitrogen and a substituent *ortho*

3. Experimental

3.1. General

^{1}H NMR spectra were recorded at 600 MHz on a Bruker AV 600 instrument, at 500 MHz on a Bruker DRX 500 instrument, at 400 MHz on a Bruker AVII 400 instrument, at 300 MHz on a Bruker Avance DPX 300 instrument, or at 200 MHz on a Bruker Avance DPX 200 instrument. The decoupled ^{13}C NMR spectra were recorded at 150, 125, 100, 75 or 50 MHz using the instruments mentioned above. Mass spectra under electron impact conditions were recorded on a VG Prospec instrument at 70 eV ionizing voltage, and are presented as *m*/*z* (% rel int.). Melting points were determined on

a Büchi Melting Point B-545 apparatus and are uncorrected. Dry DMF, MeCN, and DMF were obtained from a solvent purification system, MB SPS-800 from MBraun, Garching, Germany. Toluene, xylene (isomeric mixture), and Hünig's base were distilled from CaH_2 and dioxane from sodium/benzophenone. MeCN (HPLC quality) was used without further purification in the synthesis of **3b**. All other reagents were commercially available and used as received. Silica gel for flash chromatography was purchased from Merck, Darmstadt, Germany (Merck No. 09385). Compounds available by literature methods: Methylaquacobaloxime,[10] **2a**,[11] **8d**,[12] **9**,[6] **10b**,[6] **11d**.[13]

*3.1.1. 2-(2-Furyl)phenol (**2b**).* A mixture of $Pd(OAc)_2$ (51 mg, 0.23 mmol), PPh_3 (300 mg, 1.15 mmol), 2-furylboronic acid (1.00 g, 8.80 mmol), K_2CO_3 (1.25 g, 9.00 mmol), and 2-iodophenol (**1b**) (1.00 g, 4.54 mmol) in EtOH (96%, 100 mL) were stirred under Ar for 16 h at 80 °C. The solvent was removed in vacuo and the product purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (2:3); yield 672 mg, (93%) colorless oil. The spectroscopic data were in good agreement with those reported before.[14]

*3.1.2. 2-Chloro-6-(2-furyl)aniline (**2c**).* (2-Furyl)tributyltin (0.13 mL, 0.40 mmol) was added to a stirring solution of $(Ph_3P)_2PdCl_2$ (15 mg, 0.020 mmol) and 2-chloro-6-iodoaniline (**1c**) (100 mg, 0.400 mmol) in DMF (19 mL) and the mixture was stirred at 60 °C under N_2 for 16 h, and evaporated in vacuo. The residue was dissolved in satd KF in THF (20 mL), stirred at ambient temperature for 16 h, and evaporated in vacuo. The residue was placed on top of a flash chromatography column and the product purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (3:7); yield 70 mg (90%), mp 59–61 °C, pale yellow crystals. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.50 (dd, J=1.8, 0.7 Hz, 1H, H-5 in furyl), 7.36 (dd, J=7.9, 1.5 Hz, 1H, H-3 or H-5), 7.22 (dd, J=7.9, 1.5 Hz, 1H, H-3 or H-5), 6.70 (t, J=7.9 Hz, 1H, H-4), 6.60 (dd, J=3.4, 0.7 Hz, 1H, H-3 in furyl), 6.51 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 4.81 (s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.8 (C-2 in furyl), 141.9 (C-5 in furyl), 139.9 (C-1), 128.9 (C-3 or C-5), 126.4 (C-3 or C-5), 120.7 (C-2), 118.4 (C-4), 117.5 (C-6), 111.7 (C-4 in furyl), 107.4 (C-3 in furyl); MS EI m/z (rel %) 195/193 (32/100, M^+), 166/164 (30/91), 71 (1); HRMS (EI) calcd for $C_{10}H_8ClNO$: 193.0294. Found 193.0292.

*3.1.3. 5-Chloro-2-(2-furyl)aniline (**2d**).* A mixture of $Pd(OAc)_2$ (25 mg, 0.11 mmol), PPh_3 (110 mg, 0.420 mmol), potassium 2-furyltrifluoroborate (420 mg, 2.40 mmol), K_2CO_3 (450 mg, 3.26 mmol), and 5-chloro-2-iodoaniline (**1d**) (400 mg, 1.60 mmol) in EtOH (96%, 100 mL) was stirred under Ar for 5 h at 80 °C. The solvent was removed in vacuo and the product purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:4); yield 245 mg (84%), yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48 (d, J=1.8 Hz, 1H, H-5 in furyl), 7.35 (d, J=7.9 Hz, 1H, H-3), 6.73 (m, 2H, H-4 and H-6), 6.53 (dd, J=3.4, 0.7 Hz, 1H, H-3 in furyl), 6.48 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 4.30 (br s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.5 (C-2 in furyl), 144.2 (C-1), 141.4 (C-5 in furyl), 134.1 (C-5), 128.6 (C-3), 118.4 (C-4), 116.1 (C-6), 114.6 (C-2), 111.4 (C-4 in furyl), 106.6 (C-3 in furyl); MS EI m/z (rel %) 195/193 (34/100, M^+), 166/164 (27/81), 158 (5), 130 (23); HRMS (EI) calcd for $C_{10}H_8ClNO$: 193.0294. Found 193.0293.

*3.1.4. 4-Chloro-2-(2-furyl)aniline (**2e**).* The title compound was synthesized from 4-chloro-2-iodoanile (**1e**) (400 mg, 1.60 mmol) as described for the synthesis of compound **2d** above and purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:4); yield 245 mg (79%), yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48 (d, J=1.8 Hz, 1H, H-5 in furyl), 7.43 (d, J=2.5 Hz, 1H, H-3), 7.02 (dd, 1H, J=8.6, 2.5 Hz, H-5), 6.65 (d, 1H, J=8.6 Hz, 1H, H-6), 6.57 (d, J=3.4 Hz, 1H, H-3 in furyl), 6.48 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 4.38 (br s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.0 (C-2 in furyl), 141.7 (C-1), 141.6 (C-5 in furyl), 128.4 (C-5), 126.9 (C-3), 123.0 (C-4), 117.9 (C-6), 117.3 (C-2), 111.4 (C-4 in furyl), 107.2 (C-3 in furyl); MS EI m/z (rel %) 195/193 (36/100, M^+), 166/164 (29/85), 158 (5), 130 (25); HRMS (EI) calcd for $C_{10}H_8ClNO$: 193.0294. Found 193.02884.

*3.1.5. 2-(2-Furyl)-4-nitroaniline (**2f**).* The title compound was synthesized from 2-iodo-4-nitroaniline (**1f**) (200 mg, 0.750 mmol) as described for the synthesis of compound **2c** above. The reaction temperature was 100 °C and reaction time 16 h. The product was purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:1); yield 125 mg (80%), mp 125–127 °C, yellow solid. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.35 (d, J=2.6 Hz, 1H, H-3), 7.98 (dd, J=9.0, 2.6 Hz, 1H, H-5), 7.53 (d, J=1.9 Hz, 1H, H-5 in furyl), 6.69 (m, 2H, H-3 in furyl and H-6), 6.54 (dd, J=3.4, 1.9 Hz, 1H, H-4 in furyl), 5.17 (s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.4 (C-2 in furyl), 148.9 (C-1), 142.1 (C-5 in furyl), 138.9 (C-4), 124.8 (C-5), 124.1 (C-3), 115.4 (C-6), 114.7 (C-2), 111.7 (C-4 in furyl), 107.8 (C-3 in furyl); MS EI m/z (rel %) 204 (100, M^+), 188 (2), 158 (16); HRMS (EI) calcd for $C_{10}H_8N_2O_3$: 204.0535. Found 204.0529.

*3.1.6. 2-Chloro-6-(2-furyl)-4-nitroaniline (**2g**).* The title compound was synthesized from 2-bromo-6-chloro-4-nitroaniline (**1g**) (1.00 g, 4.00 mmol) as described for the synthesis of compound **2d** above and purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (3:7); yield 665 mg (70%), mp 180–182 °C, yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.27 (d, J=2.5 Hz, 1H, H-5), 8.16 (d, J=2.5 Hz, 1H, H-3), 7.55 (br s, 1H, H-5 in furyl), 6.73 (d, J=3.4 Hz, 1H, H-3 in furyl), 6.56 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 5.66 (br s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.7 (C-2 in furyl), 145.1 (C-1), 142.5 (C-5 in furyl), 138.1 (C-4), 124.4 (C-3), 122.2 (C-5), 119.2 (C-2), 115.3 (C-6), 111.9 (C-4 in furyl), 108.6 (C-3 in furyl); MS EI m/z (rel %) 240/238 (33/100, M^+), 164 (25), 128 (21), 102 (15); HRMS (EI) calcd for $C_{10}H_7N_2O_3Cl$: 238.0145. Found 238.0146.

*3.1.7. N-Allyl-2-(2-furyl)aniline (**3a**). Method A.* HCl (2 drops, 37% in water) was added to a mixture of 2-(2-furyl)aniline (**2a**) (400 mg, 2.52 mmol), allyl bromide (0.22 mL, 2.5 mmol), and $(i\text{-Pr})_2NEt$ (0.44 mL, 2.5 mmol) and the resulting mixture was stirred at 80 °C for 3 h. Satd aq $NaHCO_3$ (5 mL) was added and the mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic extracts were dried ($MgSO_2$), evaporated and the product isolated by flash chromatography on silica gel eluting with EtOAc/hexane (1:19); yield 360 mg (72%), yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56 (d, J=1.8 Hz, 1H, H-5 in furyl), 7.52 (dd, J=7.7, 1.6 Hz, 1H, H-3), 7.27 (m, 1H, H-5), 6.86–6.76 (m, 2H, H-4 and H-6), 6.64 (dd, J=3.4, 0.7 Hz, 1H, H-3 in furyl), 6.57 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 6.05 (m, 1H, CH=), 5.42–5.23 (m, 3H, CH_2= and NH), 3.90 (m, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.1 (C-2 in furyl), 145.1 (C-1), 141.7 (C-5 in furyl), 135.7 (CH=), 129.6 (C-3), 128.6 (C-5), 117.4 (C-4), 116.5 (CH_2=), 116.4 (C-2), 112.0 (C-6), 111.8 (C-4 in furyl), 107.1 (C-3 in furyl), 46.8 (NCH_2); MS EI m/z (rel %) 199 (100, M^+), 172 (14), 143 (46), 130 (53); HRMS (EI) calcd for $C_{13}H_{13}NO$: 199.0997. Found 199.1004.

Method B. A solution of 2-(2-furyl)aniline (**2a**) (475 mg, 3.00 mmol) and 18-crown-6-ether (950 mg, 3.60 mmol) in dry toluene (50 mL) at 0 °C was treated with KH (700 mg, ca. 6.00 mmol, ca. 35% in mineral oil) and stirred for 10 min under Ar. Allyl bromide (0.30 mL, 3.6 mmol) was added and the resulting mixture was stirred at ambient temperature for 16 h. Water (10 mL) was added and the mixture was extracted with EtOAc (3×50 mL). The combined organic extracts were dried ($MgSO_2$), evaporated and the products isolated by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:4); yield 240 mg (40%) of *N*-allyl-2-(2-furyl)aniline (**3a**) and 72 mg (10%) of *N*,*N*-diallyl-2-(2-furyl)aniline (**4a**), data below.

*3.1.8. 2-[2-(Allyloxy)phenyl]furan (**3b**).* A mixture of 2-(2-furyl) phenol (**2b**) (750 mg, 4.70 mmol), allyl bromide (0.80 mL, 9.4 mmol), and K_2CO_3 (1.30 g, 9.40 mmol) in MeCN (100 mL) was stirred at ambient temperature for 48 h, concentrated in vacuo and the product was purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:9); yield 730 mg (78%), colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.86 (dd, J=7.8, 1.7 Hz, 1H, H-3), 7.46 (dd, J=1.8, 0.7 Hz, 1H, H-5 in furyl), 7.25–7.14 (m, 1H, H-4), 7.07–6.88 (m, 3H, H-5 and H-6, H-3 in furyl), 6.49 (dd, J=3.3, 1.8 Hz, 1H, H-4 in furyl), 6.14 (ddt, J=17.2, 10.6, 5.4 Hz, 1H, CH=), 5.52–5.23 (m, 2H, CH_2=), 4.65 (dt, J=5.4, 1.4 Hz, 2H, OCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.5 (C-1), 150.4 (C-2 in furyl), 141.3 (C-5 in furyl), 133.4 (CH=), 128.1 (C-4), 126.3 (C-3), 121.1 (C-5 or C-6), 120.4 (C-2), 118.2 (CH_2=), 112.5 (C-5 or C-6), 111.9 (C-4 in furyl), 110.2 (C-3 in furyl), 69.5 (OCH_2). MS EI m/z (rel %) 200 (74, M^+), 160 (48), 131 (100); HRMS (EI) calcd for $C_{13}H_{12}O_2$: 200.0837. Found 200.0830.

*3.1.9. N-Allyl-2-chloro-6-(2-furyl)aniline (**3c**).* The title compound was synthesized from 2-chloro-6-(2-furyl)aniline (**2c**) (120 mg, 0.620 mmol) and allyl bromide (0.07 mL, 0.72 mmol) at 35 °C otherwise as described for the synthesis of compound **3a** (Method B) above and purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:3:15); yield 100 mg (69%), colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.50–7.40 (m, 2H, H-5 in furyl and H-3 or H-5), 7.27 (dd, J=7.9, 1.3 Hz, 1H, H-3 or H-5), 6.89 (m, 1H, H-4), 6.77 (d, J=3.2 Hz, 1H, H-3 in furyl), 6.48 (dd, J=3.2, 1.8 Hz, 1H, H-4 in furyl), 5.87 (m, 1H, CH=), 5.38–4.79 (m, 2H, CH_2=), 4.20 (br s, 1H, NH), 3.52 (d, J=5.7 Hz, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 151.8 (C-2 in furyl), 142.5 (C-1), 141.9 (C-5 in furyl), 136.1 (CH=), 129 (C-3 or C-5), 127.6 (C-3 or C-5), 127.2 (C-2 or C-6), 124.1 (C-2 or C-6), 122.1 (C-4), 116.2 (CH_2=), 111.8 (C-4 in furyl), 108.9 (C-3 in furyl), 50.1 (NCH_2); MS EI m/z (rel %) 235/233 (33/98, M^+), 192 (19), 177 (100), 166 (36), 164 (96); HRMS (EI) calcd for $C_{13}H_{12}ClNO$: 233.0607. Found 233.0604.

*3.1.10. N-Allyl-5-chloro-2-(2-furyl)aniline (**3d**).* The title compound was synthesized from 5-chloro-2-(2-furyl)aniline (**2d**) (520 mg, 2.69 mmol) and allyl bromide (0.23 mL, 2.7 mmol) as described for the synthesis of compound **3a** (Method A) above and purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:9); yield 410 mg (65%), yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49 (m, 1H, H-5 in furyl), 7.34 (d, J=8.2 Hz, 1H, H-3), 6.71–6.65 (m, 2H, H-4 and H-6), 6.54 (d, J=3.3 Hz, 1H, H-3 in furyl), 6.50 (dd, J=3.3, 1.8 Hz, 1H, H-4 in furyl), 6.00–5.91 (m, 1H, CH=), 5.34–5.19 (m, 3H, CH_2= and NH), 3.80 (m, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.7 (C-2 in furyl), 145.5 (C-1), 141.4 (C-5 in furyl), 134.8 (C-5), 134.4 (CH=), 128.8 (C-3), 116.7 (CH_2=), 116.4 (C-6), 114.4 (C-2), 111.3 (C-4 in furyl), 111.3 (C-4) 106.8 (C-3 in furyl), 46.1 (NCH_2); MS EI m/z (rel %) 235/233 (35/100, M^+), 206 (17), 192 (8), 177 (39), 166 (13); HRMS (EI) calcd for $C_{13}H_{12}ClNO$: 233.0607. Found 233.0605.

*3.1.11. N-Allyl-4-chloro-2-(2-furyl)aniline (**3e**).* The title compound was synthesized from 4-chloro-2-(2-furyl)aniline (**2e**) (520 mg, 2.59 mmol) and allyl bromide (0.23 mL, 2.6 mmol) as described for the synthesis of compound **3a** (Method A) above and purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:9); yield 385 mg (64%), yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49 (br s, 1H, H-5 in furyl), 7.41 (d, J=2.5 Hz, 1H, H-3), 7.10 (dd, J=8.6, 2.5 Hz, 1H, H-5), 6.58 (d, J=8.6 Hz, 1H, H-6), 6.57 (d, J=3.4 Hz, 1H, H-3 in furyl), 6.50 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 6.01–5.89 (m, 1H, CH=), 5.31–5.17 (m, 3H, CH_2= and NH), 3.80 (m, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.7 (C-2 in furyl), 143.5 (C-1), 142.3 (C-5 in furyl), 135.1 (CH=), 129.0 (C-3), 127.7 (C-5), 122.1 (C-4), 117.7 (C-2), 117.7 (CH_2=), 113.3 (C-6), 111.8 (C-4 in furyl), 107.8 (C-3 in furyl), 46.8 (NCH_2); MS EI m/z (rel %) 235/233 (34/100, M^+), 206 (19), 192 (11), 177 (36), 166 (21); HRMS (EI) calcd for $C_{13}H_{12}ClNO$: 233.0607. Found 233.0603.

*3.1.12. N-Allyl-2-(2-furyl)-4-nitroaniline (**3f**).* NaH (20 mg, ca. 0.65 mmol, ca. 65% in mineral oil) was added to a stirring solution of 2-(2-furyl)-4-nitroaniline (**2f**) (100 mg, 0.500 mmol) in dry THF (20 mL) at 0 °C under N_2 and the resulting mixture was allowed to warm to ambient temperature with stirring over 10 min. Allyl bromide (0.04 mL, 0.6 mmol) and Bu_4NBr (160 mg, 0.500 mmol) were added. The mixture was stirred at ambient temperature for 3 h, concentrated in vacuo and purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:3) followed by CH_2Cl_2; yield 50 mg (40%), yellow oil. *N*,*N*-Diallyl-2-(2-furyl)-4-nitroaniline 43 mg (30%) was also isolated. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.30 (d, J=2.5 Hz, 1H, H-3), 8.04 (dd, J=9.2, 2.5 Hz, 1H, H-5), 7.52 (d, J=1.2 Hz, 1H, H-5 in furyl), 6.70–6.48 (m, 3H, H-3, H-4 in furyl and H-6 in Ar), 6.17 (s, 1H, NH), 5.93 (ddt, J=17.2, 10.2, 5.1 Hz, 1H, CH=), 5.37–5.16 (m, 2H, CH_2=), 3.99–3.86 (m, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.9 (C-2 in furyl), 149.9 (C-1), 142.6 (C-5 in furyl), 138.1 (C-4), 133.6 (CH=), 125.9 (C-5), 124.6 (C-3), 117.6 (CH_2=), 115.4 (C-2), 112.1 (C-3 or C-4 in furyl), 110.6 (C-6), 108.5 (C-3 or C-4 in furyl), 46.2 (NCH_2); MS EI m/z (rel %) 244 (100, M^+), 207 (3), 198 (7), 188 (30); HRMS (EI) calcd for $C_{13}H_{12}N_2O_3$: 244.0848. Found 244.0843.

*3.1.13. N-Allyl-2-chloro-6-(2-furyl)-4-nitroaniline (**3g**).* NaH (125 mg, ca. 3.36 mmol, ca. 65% in mineral oil) was added to a stirring solution of 2-chloro-6-(2-furyl)-4-nitroaniline (**2g**) (800 mg, 3.36 mmol) in dry THF (20 mL) at 0 °C under N_2 and the resulting mixture was allowed to warm to ambient temperature with stirring over 10 min. Allyl bromide (3.0 mL, 3.6 mmol) and Bu_4NBr (1.00 g, 3.36 mmol) were added. The mixture was stirred at ambient temperature for 3 h, concentrated in vacuo and purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:3:15); yield 612 mg (66%), yellow oil. ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 8.18 (m, 2H, H-3 and H-5), 7.56 (br s, 1H, H-5 in furyl), 6.64 (d, J=3.4 Hz, 1H, H-3 in furyl), 6.56 (dd, J=3.4 and 1.8 Hz, 1H, H-4 in furyl), 5.82 (m, 1H, CH=), 5.32–5.10 (m, 3H, CH_2= and NH), 3.60 (m, 2H, NCH_2); ^{13}C NMR (CD_2Cl_2, 75 MHz) δ 150.4 (C-2 in furyl), 148.5 (C-1), 143.0 (C-5 in furyl), 139.0 (C-4), 135.0 (CH=), 125.9 (C-3), 125.2 (C-5), 123.0 (C-2), 119.1 (C-6), 117.1 (CH_2=), 112.1 (C-4 in furyl), 110.4 (C-3 in furyl), 48.7 (NCH_2); MS EI m/z (rel %) 280/278 (33/100, M^+), 222 (74), 163 (81), 128 (68); HRMS (EI) calcd for $C_{13}H_{11}N_2O_3Cl$: 278.0458. Found 278.0455.

*3.1.14. N,N-Diallyl-2-(2-furyl)aniline (**4a**).* The title compound was formed as a by-product in the synthesis of compound **3a** (Method B). Colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J=7.7 Hz, 1H, H-3), 7.48 (br s, 1H, H-5 in furyl), 7.23–7.10 (m, 4H, H-3 in furyl and H-4, H-5 and H-6), 6.54–6.45 (m, 1H, H-4 in furyl), 5.81 (m, 2H, 2× CH=), 5.14 (m, 4H, 2× CH_2=), 3.63 (d, J=6.3 Hz, 4H, 2× NCH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.0 (C-2 in furyl), 147.5 (C-1), 141.0 (C-5 in furyl), 134.8 (2× CH=), 127.4 (C-4, C-5 or C-6), 127.2 (C-3), 126.4 (C-2), 123.5 (C-4, C-5 or C-6), 123.0 (C-4, C-5 or C-6), 117.7 (2× CH_2=), 111.6 (C-4 in furyl), 109.0 (C-3 in furyl), 55.2 (2× NCH_2); MS EI m/z (rel %) 239 (100, M^+), 212 (28), 198 (14), 172 (4), 143 (29); HRMS (EI) calcd for $C_{16}H_{17}NO$: 239.1310. Found 239.1307.

*3.1.15. N,N-Diallyl-2-chloro-6-(2-furyl)aniline (**4b**).* A solution of *N*-allyl-2-chloro-6-(2-furyl)aniline (**3c**) (190 mg, 0.820 mmol) and 18-crown-6-ether (430 mg, 1.60 mmol) in dry toluene (20 mL) at 0 °C was treated with KH (280 mg, ca. 2.40 mmol, ca. 35% in mineral oil) and stirred for 10 min under Ar. Allyl iodide (0.15 mL, 1.6 mmol) was added and the resulting mixture was stirred at ambient temperature for 5 h. Water (10 mL) was added and the mixture was extracted with EtOAc (3×20 mL). The combined organic extracts

were dried ($MgSO_2$), evaporated and the products isolated by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:9); yield 135 mg (60%), colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64 (dd, J=7.8, 1.4 Hz, 1H, H-5), 7.46 (br s, 1H, H-5 in furyl), 7.29–7.20 (m, 1H, H-3), 7.09 (m, 1H, H-4), 7.01 (d, J=3.3 Hz, 1H, H-3 in furyl), 6.48 (dd, J=3.3, 1.8 Hz, 1H, H-4 in furyl), 5.83 (m, 2H, 2× CH=), 5.20–4.90 (m, 4H, 2× CH_2=), 3.70 (d, J=6.7 Hz, 4H, 2× NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.9 (C-2 in furyl), 143.6 (C-1), 141.9 (C-5 in furyl), 136.1 (2× CH=), 133.1 (C-2), 129.8 (C-3), 126.4 (C-4 or C-5), 126.1 (C-4 or C-5), 117.3 (2× CH_2=), 111.9 (C-4 in furyl), 110.2 (C-3 in furyl), 100.2 (C-6), 55.8 (2× NCH_2); MS ESI m/z (rel %) 275/273 (33/100, M^+), 246 (32), 238 (20), 206 (26), 177 (24); HRMS (ESI) calcd for $C_{16}H_{16}ClNO$: 273.0920. Found 273.0916.

*3.1.16. N-Allyl-2-chloro-6-(2-furyl)-N-methyl-4-nitroaniline (**4c**).* To a solution of *N*-allyl-2-chloro-6-(2-furyl)-4-nitroaniline (**3g**) (410 mg, 1.47 mmol) in dry DMF (10 mL) were subsequently added K_2CO_3 (405 mg, 2.94 mmol) and methyl iodide (0.10 mL, 1.5 mmol). The reaction mixture was stirred at ambient temperature for 18 h under Ar and extracted with EtOAc (3×30 mL). The combined organic layers were washed with water (5×30 mL), dried ($MgSO_4$), and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with hexane; yield 200 mg (46%), yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.40 (d, J=2.7 Hz, 1H, H-5), 8.10 (d, J=2.7 Hz, 1H, H-3), 7.52 (br s, 1H, H-5 in furyl), 6.87 (d, J=3.4 Hz, 1H, H-3 in furyl), 6.52 (ddd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 5.80 (m, 1H, CH=), 5.10 (m, 2H, CH_2=), 3.63 (d, J=6.6 Hz, 2H, NCH_2), 2.75 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.8 (C-1), 149.8 (C-2 in furyl), 143.8 (C-4), 142.8 (C-5 in furyl), 134.8 (CH=), 131.1 (C-2), 124.8 (C-6), 124.4 (C-3), 122.1 (C-5), 118.2 (CH_2=), 112.0 (C-4 in furyl), 110.8 (C-3 in furyl), 57.7 (NCH_2), 38.9 (CH_3); MS EI m/z (rel %) 294/292 (34/100, M^+), 236 (85), 223 (68), 177 (43); HRMS (EI) calcd for $C_{14}H_{13}N_2O_3Cl$: 292.0615. Found 292.0607.

*3.1.17. tert-Butyl-allyl[2-chloro-6-(2-furyl)-4-nitrophenyl]carbamate (**4d**).* To a solution of *N*-allyl-2-chloro-6-(2-furyl)-4-nitroaniline (**3g**) (480 mg, 1.72 mmol) in dry THF (50 mL) were subsequently added Boc_2O (380 mg, 1.72 mmol), K_2CO_3 (475 mg, 3.44 mmol), and DMAP (105 mg, 0.860 mmol). The reaction was stirred at ambient temperature for 20 h under Ar, and extracted with EtOAc (3×20 mL). The combined organic layers were washed with water (5×30 mL), dried ($MgSO_4$), and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:4:7); yield 370 mg (57%), yellow oil. NMR data for the major rotamer is reported. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.55 (d, J=2.7 Hz, 1H, H-5), 8.15 (d, J=2.7 Hz, 1H, H-3), 7.56 (dd, J=1.8, 0.5 Hz, 1H, H-5 in furyl), 6.72 (d, J=3.5 Hz, 1H, H-3 in furyl), 6.53 (dd, J=3.5, 1.8 Hz, 1H, H-4 in furyl), 5.74 (m, 1H, CH=), 4.94 (m, 2H, CH_2=), 4.30 (m, 1H, H_A in NCH_2), 3.88 (m, 1H, H_B in NCH_2), 1.28 (s, 9H, *t*-Bu); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.2 (CO), 148.6 (C-2 in furyl), 146.7 (C-4), 143.7 (C-5 in furyl), 139.7 (C-1), 136.7 (C-6 and C-2), 132.0 (CH=), 122.7 (C-5), 120.2 (C-3), 119.3 (CH_2=), 112.5 (C-4 in furyl), 111.3 (C-3 in furyl), 81.3 (C in *t*-Bu), 50.7 (NCH_2), 27.9 (CH_3 in *t*-Bu); MS CI m/z (rel %) 381/379 (23/65, M+1), 351 (18), 325 (38), 323 (100), 281 (28), 279 (80).

*3.1.18. N,N-Diallyl-2-chloro-6-(2-furyl)-4-nitroaniline (**4e**).* To a stirring solution of 2-chloro-6-(2-furyl)-4-nitroaniline (**2g**) (175 mg, 0.750 mmol) in THF (20 mL) at 0 °C, NaH (90 mg, ca. 2.3 mmol, ca. 60% in mineral oil) was added. The reaction mixture was allowed to warm to ambient temperature over 10 min. Allyl bromide (0.18 mL, 0.80 mmol) was added, the reaction mixture was stirred at ambient temperature for 16 h and evaporated in vacuo. The resulting solid was dissolved in $CHCl_3$ (50 mL) and the mixture subsequently washed with water (3×50 mL), dried ($MgSO_4$), and evaporated in vacuo. The product was purified by flash chromatography on silica eluting with EtOAc/CH_2Cl_2/hexane (1:4:16); yield 100 mg (42%), yellow oil. *N*-Allyl-2-chloro-6-(2-furyl)-4-nitroaniline (**3g**) (53 mg, 25%) was also isolated. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.46 (d, J=2.8 Hz, 1H, H-3 or H-5), 8.10 (d, J=2.8 Hz, 1H, H-3 or H-5), 7.53 (dd, J=1.8, 0.7 Hz, 1H, H-5 in furyl), 6.97 (dd, J=3.4, 0.7 Hz, 1H, H-3 in furyl), 6.53 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 5.79 (ddt, J=16.7, 9.9, 6.7 Hz, 2H, 2× CH=), 5.25–4.97 (m, 4H, 2× CH_2=), 3.70 (d, J=6.7 Hz, 4H, 2× NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.9 (C-2 in furyl or C-6), 149.5 (C-2 in furyl or C-6), 144.3 (C-4), 143.0 (C-5 in furyl), 135.6 (C-1), 134.8 (CH=), 132.1 (C-2), 124.6 (C-3 or C-5), 121.9 (C-3 or C-5), 118.5 (CH_2=), 112.3 (C-4 in furyl), 111.2 (C-3 in furyl), 55.3 (NCH_2); MS EI m/z (rel %) 320/318 (26/75, M^+), 293/291 (11/36), 277 (20), 41 (100); HRMS (EI) calcd for $C_{16}H_{15}ClN_2O_3$: 318.0771. Found 318.0762.

*3.1.19. (±) (6aS,8S)-6a,7,8,10a-Tetrahydro-8,10a-epoxy-6H-benzo[c]chromene (**5b**).* A stirring solution of 2-[2-(allyloxy)phenyl]furan (**3b**) (150 mg, 0.750 mmol) in dry xylene (15 mL) was heated at 150 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:9); yield 42 mg (28%), colorless oil, 35 mg (23%) starting material was recovered. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.48 (dd, J=7.6, 1.4 Hz, 1H, H-1), 7.37–7.28 (m, 1H, H-3), 7.09–6.93 (m, 1H, H-2), 6.97 (d, J=8.3 Hz, 1H, H-4), 6.58 (dd, J=5.7, 1.6 Hz, 1H, H-9), 6.29 (d, J=5.7 Hz, 1H, H-10), 5.11–4.90 (m, 1H, H-8), 4.48 (dd, J=10.7, 5.0 Hz, 1H, H-6_A), 3.77 (m, 1H, H-6_B), 2.05 (dddd, J=10.7, 5.0, 3.7, 1.7 Hz, 1H, H-6a), 1.72–1.58 (m, 1H, H-7_A), 1.48 (dd, J=11.5, 3.7 Hz, 1H, H-7_B); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 156.4 (C-4a), 138.4 (C-9), 136.6 (C-10), 130.8 (C-1), 130.2 (C-3), 121.0 (C-2), 120.1 (C-10b), 116.9 (C-4), 82.6 (C-10a), 77.9 (C-8), 69.9 (C-6), 33.9 (C-6a), 29.7 (C-7); MS EI m/z (rel %) 200 (88, M^+), 158 (100), 131 (54), 115 (20), 77 (11); HRMS (EI) calcd for $C_{13}H_{12}O_2$: 200.0837. Found 200.0833.

*3.1.20. (±) (6aS,8S)-4-Chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxyphenanthridine (**5c**).* A stirring solution of *N*-allyl-2-chloro-6-(2-furyl)aniline (**3c**) (300 mg, 1.30 mmol) in dry toluene (7 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:4:15); yield 100 mg (33%, ratio **5c**/**6c**, 15:1), mp 98–100 °C, colorless solid. NMR data presented are for the major isomer **5c**. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.33 (dd, J=7.6, 1.7 Hz, 1H, H-1), 7.28 (br d, J=7.6 Hz, 1H, H-3), 6.72 (m, 1H, H-2), 6.56 (dd, J=5.7, 1.6 Hz, 1H, H-9), 6.25 (d, J=5.7 Hz, 1H, H-10), 5.00 (dd, J=4.6, 1.6 Hz, 1H, H-8), 4.82 (br s, 1H, NH), 3.60 (ddd, J=11.3, 5.3, 3.8 Hz, 1H, H-6_A), 3.04–2.93 (m, 1H, H-6_B), 1.94–1.89 (m, 1H, H-6a), 1.69 (dd, J=11.4, 7.6 Hz, 1H, H-7_A), 1.54 (ddd, J=11.4, 4.6, 3.0 Hz, 1H, H-7_B); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 143.0 (C-4a), 138.4 (C-9), 137.1 (C-10), 129.8 (C-1), 129.4 (C-3), 120.1 (C-10b), 118.8 (C-4), 117.5 (C-2), 84.3 (C-10a), 77.7 (C-8), 46.1 (C-6), 33.8 (C-6a), 31.8 (C-7); MS EI m/z (rel %) 235/233 (35/100, M^+), 214 (77), 190 (94), 177 (27), 164 (35); HRMS (EI) calcd for $C_{13}H_{12}ClNO$: 233.0607. Found 233.0607.

*3.1.21. (±) (6aS,8S)-5,6,6a,7,8,10a-Hexahydro-2-nitro-8,10a-epoxyphenanthridine (**5f**).* A stirring solution of *N*-allyl-2-(2-furyl)-4-nitroaniline (**3f**) (78 mg, 0.32 mmol) in dry xylene (10 mL) was heated at 150 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with acetone/hexane (1:4); yield 10 mg (13%, ratio **5f**/**6f**; 14:1), yellow oil. NMR data presented are for the major isomer **5f**. ^{1}H NMR (DMSO-d_6, 600 MHz) δ 8.03 (d, J=2.6 Hz, 1H, H-1), 7.99 (dd, J=9.1, 2.6 Hz, 1H, H-3), 7.84 (d, J=3.9 Hz, 1H, NH), 6.76 (d, J=9.1 Hz, 1H, H-4), 6.66 (dd, J=5.6, 1.6 Hz, 1H, H-9), 6.33 (d, J=5.6 Hz, 1H, H-10), 4.97 (dd, J=4.6, 1.6 Hz, 1H, H-8), 3.57 (dt, J=12.0, 5.0 Hz, 1H, H-6_A), 2.73 (t, J=12.0 Hz, 1H, H-6_B), 1.72–1.66

(m, 1H, H-6a), 1.58 (dd, *J*=11.4, 7.5 Hz, 1H, H-7_A), 1.43 (ddd, *J*=11.4, 4.6, 2.9 Hz, 1H, H-7_B); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 153.2 (C-4a), 140.0 (C-9), 136.5 (C-10), 136.1 (C-2), 128.4 (C-1), 126.2 (C-3), 116.7 (C-10b), 114.2 (C-4), 83.8 (C-10a), 77.6 (C-8), 45.0 (C-6), 32.2 (C-6a or C-7), 32.2 (C-6a or C-7); MS EI *m*/*z* (rel %) 244 (100, M^+), 232 (31), 201 (69), 175 (28), 129 (13); HRMS (EI) calcd for $C_{13}H_{12}N_2O_3$: 244.0848. Found 244.0852.

*3.1.22. (±) (6aS,8S)-2-Chloro-5,6,6a,7,8,10a-hexahydro-2-nitro-8,10a-epoxyphenanthridine (**5g**).* A stirring solution of *N*-allyl-2-chloro-6-(2-furyl)-4-nitroaniline (**3g**) (90 mg, 0.33 mmol) in dry toluene (5 mL) was heated at 100 °C for 16 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (3:17); yield 80 mg (88%, ratio **5g**/**6g**; 9:1), waxy yellow solid. NMR data presented are for the major isomer **5g**. ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 8.19 (br s, 2H, H-1 and H-3), 6.61 (dd, *J*=5.7, 1.7 Hz, 1H, H-9), 6.24 (d, *J*=5.7 Hz, 1H, H-10), 5.65 (br s, 1H, NH), 5.00 (dd, *J*=4.5, 1.7 Hz, 1H, H-8), 3.70 (m, 1H, H-6_A), 3.03 (dd, *J*=12.0, 0.5 Hz, 1H, H-6_B), 1.86 (m, 1H, H-6a), 1.68 (dd, *J*=11.5, 7.4 Hz, 1H, H-7_A), 1.55 (m, 1H, H-7_B); ^{13}C NMR (CD_2Cl_2, 75 MHz) δ 148.3 (C-4a), 139.8 (C-9), 137.5 (C-2), 136.1 (C-10), 126.8 (C-1), 125.5 (C-3), 118.9 (C-10b), 118.1 (C-4), 84.0 (C-10a), 78.4 (C-8), 45.9 (C-6), 33.1 (C-6a), 32.3 (C-7); MS EI *m*/*z* (rel %) 280/278 (32/100, M^+), 235 (56), 222 (41); HRMS (EI) calcd for $C_{13}H_{11}N_2O_3Cl$: 278.0458. Found 278.0466.

*3.1.23. (±) (6aS,8S)-5-Allyl-4-chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxyphenanthridine (**5i**).* A stirring solution of *N*,*N*-diallyl-2-chloro-6-(2-furyl)aniline (**4b**) (130 mg, 0.480 mmol) in dry toluene (10 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The residue was dissolved in EtOAc (200 mL), washed with water (2×100 mL), dried ($MgSO_4$), and evaporated in vacuo; crude yield 112 mg (ratio of **5i**, **6i** and unconverted **4b**: 7:1:5), colorless oil. Attempts to purify by chromatography were not successful. NMR data presented are for the major isomer **5i**. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.41–7.35 (m, 1H, H-1 or H-3), 7.27 (dd, *J*=8.0, 1.7 Hz, 1H, H-1 or H-3), 6.99 (t, *J*=7.7 Hz, 1H, H-2), 6.54 (dd, *J*=5.7, 1.7 Hz, 1H, H-9), 6.27 (d, *J*=5.7 Hz, 1H, H-10), 6.14–6.06 (m, 1H, CH=), 5.30 (ddd, *J*=13.7, 10.9, 0.9 Hz, 2H, CH_2=), 4.99 (dd, *J*=4.5, 1.7 Hz, 1H, H-8), 3.98 (ddd, *J*=15.3, 3.9, 1.9 Hz, 1H, H_A in NCH_2), 3.55 (dd, *J*=15.3, 7.9 Hz, 1H, H_B in NCH_2), 3.44 (dd, *J*=13.7, 4.3 Hz, 1H, H-6_A), 2.87–2.72 (m, 1H, H-6_B), 1.97 (ddd, *J*=12.2, 7.6, 3.7 Hz, 1H, H-6a), 1.64 (dd, *J*=11.4, 7.7 Hz, 1H, H-7_A), 1.45 (ddd, *J*=11.4, 4.3, 3.5 Hz, 1H, H-7_B); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 146.5 (C-10b), 137.9 (C-9), 137.2 (C-10), 136.0 (CH=), 135.9 (C-4a), 131.0 (C-1 or C-3), 129.4 (C-1 or C-3), 128.5 (C-4), 122.5 (C-2), 117.3 (CH_2=), 84.8 (C-10a), 77.8 (C-8), 56.2 (NCH_2), 50.4 (C-6), 31.0 (C-7), 29.2 (C-6a); MS EI *m*/*z* (rel %) 275/273 (33/100, M^+), 246 (21), 238 (37), 232 (20); HRMS (EI) calcd for $C_{16}H_{16}NOCl$: 273.0920. Found 273.0919.

*3.1.24. (±) (6aS,8S)-2-Chloro-5,6,6a,7,8,10a-hexahydro-2-nitro-5-methyl-8,10a-epoxyphenanthridine (**5j**) and (±) (6aR,8S)-2-chloro-5,6,6a,7,8,10a-hexahydro-2-nitro-5-methyl-8,10a-epoxyphenanthridine (**6j**).* A stirring solution of *N*-allyl-2-chloro-6-(2-furyl)-*N*-methyl-4-nitroaniline (**4c**) (150 mg, 0.512 mmol) in dry toluene (10 mL) was heated at 100 °C for 16 h under Ar, cooled to ambient temperature and concentrated in vacuo. The products were separated by flash chromatography on silica gel eluting with EtOAc/hexane (3:7); yield 100 mg (66%) **5j** and 35 mg (24%) **6j**.

*3.1.24.1. (±) (6aS,8S)-2-Chloro-5,6,6a,7,8,10a-hexahydro-2-nitro-5-methyl-8,10a-epoxyphenanthridine (**5j**).* Yellow oil. ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 8.20 (m, 2H, H-1 and H-3), 6.57 (dd, *J*=5.7, 1.7 Hz, 1H, H-9), 6.20 (d, *J*=5.7 Hz, 1H, H-10), 4.98 (dd, *J*=4.5, 1.7 Hz, 1H, H-8), 3.34 (dd, *J*=13.4, 4.5 Hz, 1H, H-6_A), 3.18 (s, 3H, CH_3), 2.96 (m, 1H, H-6_B), 1.90 (m, 1H, H-6a), 1.64 (dd, *J*=11.6, 7.5 Hz, 1H, H-7_A), 1.47 (m, 1H, H-7_B); ^{13}C NMR (CD_2Cl_2, 75 MHz) δ 152.4 (C-4a), 140.5 (C-2), 138.9 (C-9), 136.1 (C-10), 126.9 (C-1), 126.7 (C-10b), 125.7 (C-3), 125.2 (C-4), 84.4 (C-10a), 77.9 (C-8), 55.8 (C-6), 42.6 (CH_3), 30.9 (C-7), 30.3 (C-6a); MS EI *m*/*z* (rel %) 294/292 (34/100, M^+), 275 (34), 265 (25), 263 (22), 249 (24), 236 (45); HRMS (EI) calcd for $C_{14}H_{13}N_2O_3Cl$: 292.0615. Found 292.0614.

*3.1.24.2. (±) (6aR,8S)-2-Chloro-5,6,6a,7,8,10a-hexahydro-2-nitro-5-methyl-8,10a-epoxyphenanthridine (**6j**).* Yellow oil. ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 8.15 (d, *J*=2.7 Hz, 1H, H-3), 8.02 (d, *J*=2.7 Hz, 1H, H-1), 6.71 (dd, *J*=5.6, 1.8 Hz, 1H, H-9), 5.98 (d, *J*=5.6 Hz, 1H, H-10), 5.15 (dd, *J*=4.5, 1.8 Hz, 1H, H-8), 3.62 (dd, *J*=11.2, 5.8 Hz, 1H, H-6_A), 3.25 (s, 3H, CH_3), 2.59 (t, *J*=11.2 Hz, 1H, H-6_B), 2.27 (m, 1H, H-7_A), 2.08 (m, 1H, H-6a), 1.09 (dd, *J*=11.3, 5.0 Hz, 1H, H-7_B); ^{13}C NMR (CD_2Cl_2, 75 MHz) δ 152.4 (C-4a), 139.7 (C-9), 138.5 (C-2), 134.4 (C-10), 128.9 (C-10a), 127.5 (C-3), 120.4 (C-4), 117.4 (C-1), 84.4 (C-10b), 80.4 (C-8), 56.6 (C-6), 43.1 (CH_3), 39.1 (C-6a), 30.6 (C-7); MS EI *m*/*z* (rel %) 294/292 (33/100, M^+), 275 (31), 265 (35), 263 (28), 236 (55), 223 (40); HRMS (EI) calcd for $C_{14}H_{13}N_2O_3Cl$: 292.0615. Found 292.0616.

*3.1.25. (±) (6aS,8S)-5-Allyl-4-chloro-5,6,6a,7,8,10a-hexahydro-2-nitro-8,10a-epoxyphenanthridine (**5l**).* A stirring solution of *N*,*N*-diallyl-2-chloro-6-(2-furyl)-4-nitroaniline (**4e**) (620 mg, 1.95 mmol) in dry toluene (10 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), washed with water (2×50 mL), dried ($MgSO_4$), and evaporated in vacuo; yield 470 mg (76%, ratio **5l**/**6l**; 4:1), yellow oil. NMR data presented are for the major isomer **5l**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.22 (q, *J*=2.7 Hz, 2H, H-1 and H-3), 6.57 (dd, *J*=5.7, 1.7 Hz, 1H, H-9), 6.21 (d, *J*=5.7 Hz, 1H, H-10), 6.07–5.95 (m, 1H, CH=), 5.38–5.21 (m, 2H, CH_2=), 4.99 (dd, *J*=4.5, 1.7 Hz, 1H, H-8), 4.16 (ddd, *J*=15.9, 3.9, 1.8 Hz, 1H, H_A in NCH_2), 3.68 (dd, *J*=15.9, 7.3 Hz, 1H, H_B in NCH_2), 3.44 (dd, *J*=13.6, 4.5 Hz, 1H, H-6_A), 2.83–2.74 (m, 1H, H-6_B), 1.84 (m, 1H, H-6a), 1.64 (dd, *J*=11.5, 7.6 Hz, 1H, H-7_A), 1.46 (ddd, *J*=11.6, 4.5, 3.2 Hz, 1H, H-7_B); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 152.1 (C-4a), 140.7 (C-2 or C-4), 139.1 (C-9), 136.4 (C-10), 134.8 (CH=), 127.5 (C-2 or C-4), 127.3 (C-10b), 126.9 (C-1 or C-3), 125.9 (C-1 or C-3), 118.4 (CH_2=), 84.7 (C-10a), 78.1 (C-8), 56.6 (NCH_2), 51.5 (C-6), 31.2 (C-7), 30.8 (C-6a); MS EI *m*/*z* (rel %) 320/318 (34/100, M^+), 301 (35), 277 (11), 203 (22); HRMS (EI) calcd for $C_{16}H_{15}ClN_2O_3$: 318.0771. Found 318.0765.

*3.1.26. 2-(2-Furyl)pyridin-3-amine (**10a**).* Dry KF (150 mg, 2.57 mmol) and Pd(*t*-$Bu_3P)_4$ (12 mg, 0.023 mmol) were added to a solution of 3-amino-2-chloropyridine (**8a**) (100 mg, 0.780 mmol) and 2-furylboronic acid (175 mg, 1.56 mmol) in dry dioxane. The reaction mixture was heated at reflux for 18 h. After cooling, the mixture was extracted with EtOAc (3×40 mL), the combined organic layers were washed with water (5×20 mL), dried ($MgSO_4$), and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:2); yield 110 mg (88%), yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.02 (s, 1H, H-5), 7.50 (s, 1H, H-5 in furyl), 7.01–6.92 (m, 3H, H-3 in furyl, H-4 and H-6), 6.51 (dd, *J*=3.5, 1.8 Hz, 1H, H-4 in furyl), 4.62 (br s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.2 (C-2 in furyl), 141.8 (C-5 in furyl), 139.2 (C-3), 139.1 (C-6), 133.9 (C-2), 123.9 (C-5), 122.8 (C-4), 111.6 (C-4 in furyl), 108.8 (C-3 in furyl); MS EI *m*/*z* (rel %) 160 (100, M^+), 131 (65), 104 (15); HRMS (EI) calcd for $C_9H_8N_2O$: 160.0637. Found 160.0632.

*3.1.27. 2-Chloro-4-(2-furyl)pyridin-3-amine (**10c**).* 2-Chloro-4-(2-furyl)-3-nitropyridine (**9**) (330 mg, 1.47 mmol cont. ca. 10% of the regioisomer 4-chloro-2-(2-furyl)-3-nitropyridine) and Raney nickel (250 mg) were added to a flask containing methanol (25 mL).

The mixture was stirred under H_2-atm for 16 h at ambient temperature, filtered through a short plug of Celite, and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:3:6); yield 230 mg [81%, cont. ca. 20% of the regioisomer 4-chloro-2-(2-furyl)pyridin-3-amine], yellow oil. Data for the title compound are given. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.77 (d, J=5.1 Hz, 1H, H-6), 7.59 (d, J=1.1 Hz, 1H, H-5 in furyl), 7.29 (d, J=5.1 Hz, 1H, H-5), 6.81 (d, J=3.4 Hz, 1H, H-3 in furyl), 6.57 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 4.93 (s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 150.9 (C-2 in furyl), 143.1 (C-5 in furyl), 139.2 (C-2 or C-3), 137.6 (C-6), 135.5 (C-2 or C-3), 122.8 (C-4), 120.0 (C-5), 112.1 (C-4 in furyl), 109.8 (C-3 in furyl); MS EI m/z (rel %) 196/194 (33/100, M^+), 167 (16), 165 (49), 129 (49); HRMS (EI) calcd for $C_9H_7ClN_2O$: 194.0247. Found 194.0243.

*3.1.28. 4,6-Di(2-furyl)-pyrimidin-5-amine (**10e**).* The title compound was formed as a by-product in the synthesis of compound **10d**;[6] yield 200 mg (36%), mp 91–92 °C, yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.54 (s, 1H, H-2), 7.61 (dd, J=1.7, 0.7 Hz, 2H, H-5 in furyl), 7.29 (dd, J=5.5, 0.7 Hz, 2H, H-3 in furyl), 6.59 (dd, J=3.5, 1.7, 2H, H-4 in furyl), 5.73 (s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.2 (C-2 in furyl), 147.4 (C-2), 143.6 (C-5 in furyl), 140.4 (C-4), 132.3 (C-5), 112.5 (C-3 in furyl), 112.1 (C-4 in furyl); MS EI m/z (rel %) 227 (100, M^+), 198 (39), 170 (18), 78 (7); HRMS (EI) calcd for $C_{12}H_9N_3O_2$: 227.0695. Found 227.0699.

*3.1.29. 4-(2-Furyl)-6-phenyl-pyrimidin-5-amine (**10f**).* A mixture of $Pd(OAc)_2$ (7 mg, 0.03 mmol), PPh_3 (30 mg, 0.11 mmol), potassium phenyltrifluoroborate (200 mg, 1.10 mmol), K_2CO_3 (300 mg, 2.20 mmol), and 4-chloro-6-(2-furyl)pyrimidin-5-amine (**10d**) (140 mg, 0.700 mmol) in EtOH (10 mL, 96%) was stirred at 60 °C for 1 h under Ar, before CH_2Cl_2 (50 mL) was added to the reaction mixture, and the resulting mixture subjected to dry flash chromatography on a short plug of silica. The column was washed with acetone (50 mL) and the solution was evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:5:5); yield 156 mg (94%), mp 122–125 °C, yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.66 (s, 1H, H-2), 7.77–7.67 (m, 2H, Ph), 7.62 (br s, 1H, H-5 in furyl), 7.57–7.40 (m, 3H, Ph), 7.30 (d, J=3.4 Hz, 1H, H-3 in furyl), 6.61 (dd, J=3.4, 1.7 Hz, 1H, H-4 in furyl), 4.85 (s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.5 (C-2 in furyl), 153.2 (C-4), 148.6 (C-2), 143.8 (C-5 in furyl), 139.4 (C-5 or C-6), 136.6 (C-1 in Ph), 133.8 (C-5 or C-6), 129.8 (C-3 or C-4 in Ph), 129.3 (C-3 or C-4 in Ph), 128.6 (C-2 in Ph), 112.5 (C-3 or C-4 in furyl), 112.4 (C-3 or C-4 in furyl); MS EI m/z (rel %) 237 (100, M^+), 236 (91), 208 (14), 104 (7), 77 (5); HRMS (EI) calcd for $C_{14}H_{11}N_3O$: 237.0902. Found 237.0894.

*3.1.30. 2-Chloro-4-(2-furyl)-pyrimidin-5-amine (**10g**).* Tri(2-furyl) phosphine (36 mg, 0.16 mmol) and $Pd_2(dba)_3$ (20 mg, 0.020 mmol) were added to DMF (10 mL) under N_2 at ambient temperature and stirred for 10 min. Subsequently, 2,4-dichloropyrimidine-5-amine (**8d**) (100 mg, 0.600 mmol) and (2-furyl)tributyltin (0.2 mL, 0.6 mmol) were added. The mixture was stirred at 60 °C for 16 h, and evaporated in vacuo. The residue was dissolved in satd KF in THF (20 mL), stirred at ambient temperature for 16 h, and evaporated in vacuo. The residue was placed on top of a flash chromatography column and the product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (5:8:12); yield 73 mg (61%), mp 169–170 °C, yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.08 (s, 1H, H-4), 7.61 (dd, J=1.8, 0.7 Hz, 1H, H-5 in furyl), 7.31 (dd, J=3.6, 0.7 Hz, 1H, H-3 in furyl), 6.59 (dd, J=3.6, 1.8 Hz, 1H, H-4 in furyl), 4.71 (s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.4 (C-2 in furyl), 149.6 (C-2), 148.2 (C-4), 144.6 (C-5 in furyl), 141.3 (C-6), 135.1 (C-1), 113.9 (C-3 in furyl), 112.8 (C-4 in furyl); MS EI m/z (rel %) 197/195 (38/100, M^+), 168 (19), 166 (49), 67 (3); HRMS (EI) calcd for $C_8H_6ClN_3O$: 195.0199. Found 195.0197.

*3.1.31. 2,4-Di(2-furyl)-pyrimidin-5-amine (**10h**).* A mixture of $Pd(OAc)_2$ (20 mg, 0.070 mmol), PPh_3 (80 mg, 0.30 mmol), potassium (2-furyl)trifluoroborate (530 mg, 3.00 mmol), K_2CO_3 (340 mg, 2.46 mmol), and 2,4-dichloropyrimidine-5-amine (**8d**) (200 mg, 1.20 mmol) in EtOH (50 mL, 96%) was stirred at 80 °C for 16 h under Ar, and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:5:5); yield 220 mg (80%), mp 173–175 °C (dec), yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.28 (s, 1H, H-4), 7.62 (dd, J=1.7, 0.8 Hz, 1H, H-5 in furyl), 7.53 (dd, J=1.7, 0.8 Hz, 1H, H-5 in furyl), 7.37 (dd, J=3.5, 0.8 Hz, 1H, H-3 in furyl), 7.12 (dd, J=3.5, 0.8 Hz, 1H, H-3 in furyl), 6.61 (dd, J=3.5, 1.7 Hz, 1H, H-4 in furyl), 6.50 (dd, J=3.5, 1.7 Hz, 1H, H-4 in furyl), 3.86 (br s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.3 (C-2 in furyl), 152.5 (C-2 in furyl), 148.7 (C-2, C-5, or C-6), 145.8 (C-4), 144.0 (C-5 in furyl), 143.8 (C-5 in furyl), 139.1 (C-2, C-5, or C-6), 134.1 (C-2, C-5, or C-6), 112.8 (C-3 in furyl), 112.4 (C-4 in furyl), 112.0 (C-4 in furyl), 110.4 (C-3 in furyl); MS EI m/z (rel %) 227 (100, M^+), 198 (37), 171 (7), 114 (6), 78 (6); HRMS (EI) calcd for $C_{12}H_9N_3O_2$: 227.0695. Found 227.0694.

*3.1.32. N-Allyl-2-(2-furyl)pyridin-3-amine (**11a**).* A solution of 2-(2-furyl)pyridine-3-amine (**10a**) (70 mg, 0.44 mmol) in THF (10 mL) was treated with NaH (18 mg, ca. 0.44 mmol, ca. 65% in mineral oil) and stirred at ambient temperature for 20 min under N_2. Allyl bromide (0.2 mL, 2 mmol) and Bu_4NBr (283 mg, 0.878 mmol) were added. The mixture was heated at 80 °C for 12 h, and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (2:3); yield 60 mg (68%), yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.96 (dd, J=4.4, 1.4 Hz, 1H, H-6), 7.60 (s, 1H, H-5 in furyl), 7.11–6.99 (m, 3H, H-5 and H-6, H-3 in furyl), 6.60 (ddd, J=3.5, 1.8 Hz, 1H, H-4 in furyl), 6.03 (m, 1H, CH=), 5.94 (br s, 1H, NH), 5.38–5.22 (m, 2H, CH_2=), 3.92 (m, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.6 (C-2 in furyl), 142.0 (C-5 in furyl), 141.1 (C-3), 137.7 (C-6), 135.1 (CH=), 135.4 (C-2), 123.7 (CH_2=), 111.9 (C-4 in furyl), 109.1 (C-3 in furyl), 45.9 (NCH_2); MS EI m/z (rel %) 200 (100, M^+), 171 (44), 131 (53); HRMS (EI) calcd for $C_{12}H_{12}N_2O$: 200.0950. Found 200.0942.

*3.1.33. N-Allyl-4-chloro-2-(2-furyl)pyridin-3-amine (**11b**). Method A*: A solution of 4-chloro-2-(2-furyl)pyridin-3-amine (**10b**) (150 mg, 0.770 mmol) in THF (15 mL) at 0 °C was treated with NaH (35 mg, ca. 0.95 mmol, ca. 60% in mineral oil) and stirred at ambient temperature for 20 min under N_2. Allyl bromide (0.07 mL, 0.8 mmol) was added and the mixture was heated at 80 °C for 3 h, and concentrated in vacuo. The residue was dissolved in $CHCl_3$ (50 mL), washed with water (3×50 mL), dried ($MgSO_4$), and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc; yield 45 mg (39%), yellow oil. (±) (6a*S*,8*S*)-4-Chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxybenzo[*c*][1,5]naphthyridine (**13b**) and isomer **14b**; 28 mg (16%; 12:1 ratio) were also isolated (data see below).

Method B: A solution of 4-chloro-2-(2-furyl)pyridin-3-amine (**10b**) (810 mg, 4.17 mmol) and 15-crown-5-ether (1.65 mL, 8.40 mmol) in dry toluene (100 mL) at 0 °C was treated with NaH (330 mg, ca. 8.40 mmol, ca. 60% in mineral oil) and stirred for 10 min under N_2. Allyl bromide (0.75 mL, 4.80 mmol) was added and the mixture was stirred at 45 °C for 16 h before water (50 mL) was added. The resulting mixture was extracted with EtOAc (3×50 mL), dried ($MgSO_4$), and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:3:6); yield 760 mg (78%), yellow oil. ^{1}H NMR (CD_2Cl_2, 600 MHz) δ 8.08 (d, J=5.0 Hz, 1H, H-6), 7.63–7.53 (m, 1H, H-5 in furyl), 7.19 (d, J=5.0 Hz, 1H, H-5), 7.09 (d, J=3.4 Hz, 1H, H-

3 in furyl), 6.57 (dd, *J*=3.4, 1.8 Hz, 1H, H-4 in furyl), 5.91 (ddt, *J*=16.3, 10.3, 5.9 Hz, 1H, CH=), 5.25–5.05 (m, 2H, CH_2=), 4.60 (s, 1H, NH), 3.72 (d, *J*=6.1 Hz, 2H, NCH_2); ^{13}C NMR (CD_2Cl_2, 150 MHz) δ 153.2 (C-2), 143.3 (C-5 in furyl), 142.7 (C-6), 142.3 (C-2), 139.7 (C-3), 136.3 (CH=), 124.1 (C-5), 117.9 (C-4), 116.7 (CH_2=), 112.2 (C-4 in furyl), 111.9 (C-3 in furyl), 50.7 (NCH_2); MS EI *m*/*z* (rel %) 236/234 (33/100, M^+), 217 (44), 205 (96), 193 (13), 178 (29), 165 (80); HRMS (EI) calcd for $C_{12}H_{11}ClN_2O$: 234.0560. Found 234.0553.

*3.1.34. N-Allyl-2-chloro-4-(2-furyl)pyridin-3-amine (**11c**).* NaH (150 mg, ca. 2.60 mmol, ca. 60% in mineral oil) was added to a solution of 2-chloro-4-(2-furyl)pyridin-3-amine (**10c**) [230 mg, ca. 1.19 mmol, cont. ca. 20% of the regioisomer 4-chloro-2-(2-furyl) pyridin-3-amine] and 15-crown-5-ether (0.5 mL, 3 mmol) in dry toluene (40 mL) at ambient temperature, and the resulting mixture was stirred under Ar for 10 min. Allyl bromide (0.13 mL, 1.4 mmol) was added and the mixture was stirred for 16 h. Water (10 mL) was added and the resulting mixture was extracted with EtOAc (3×20 mL). The combined organic extracts were dried and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:4:14); yield 120 mg (43%), colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.89 (d, *J*=5.1 Hz, 1H, H-6), 7.46 (dd, *J*=1.8, 0.5 Hz, 1H, H-5 in furyl), 7.40 (d, *J*=5.1 Hz, 1H, H-5), 6.98 (dd, *J*=3.4, 0.5 Hz, 1H, C-3 in furyl), 6.47 (dd, *J*=3.4, 1.8 Hz, 1H, H-4 in furyl), 5.82 (ddt, *J*=16.9, 10.3, 5.8 Hz, 1H, CH=), 5.10 (m, 2H, CH_2=), 3.96 (br s, 1H, NH), 3.48 (dd, *J*=6.7, 5.8 Hz, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.5 (C-2 in furyl), 146.0 (C-4), 143.5 (C-5 in furyl), 142.1 (C-6), 137.7 (C-2), 135.7 (CH=), 131.3 (C-3), 121.1 (C-5), 117.0 (CH_2=), 112.6 (C-3 or C-4 in furyl), 112.5 (C-3 or C-4 in furyl), 49.9 (NCH_2); MS EI *m*/*z* (rel %) 236/234 (36/100, M^+), 205 (29), 178 (54), 165 (45), 129 (42), 102 (19); HRMS (EI) calcd for $C_{12}H_{11}ClN_2O$: 234.0560. Found 234.0556.

*3.1.35. N-Allyl-4-chloro-6-(2-furyl)-pyrimidin-5-amine (**11d**).* A solution of 4-chloro-6-(2-furyl)-pyrimidin-5-amine (**10d**) (420 mg, 2.15 mmol) and 15-crown-5-ether (0.85 mL, 4.3 mmol) in dry toluene (50 mL) at 0 °C under Ar was treated with NaH (160 mg, ca. 4.30 mmol, ca. 60% in mineral oil) and stirred for 10 min. Allyl bromine (0.17 mL, 1.9 mmol) was added and the reaction mixture stirred for 30 min at 0 °C and without cooling for a further 30 min. Water (50 mL) was added, the mixture was extracted with EtOAc (2×50 mL), the combined organic extracts were washed with satd aq NaCl (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (2:3:16); yield 360 mg (71%), colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.51 (s, 1H, H-2), 7.63 (dd, *J*=1.8, 0.7 Hz, 1H, H-5 in furyl), 7.36 (dd, *J*=3.5, 0.7 Hz, 1H, H-3 in furyl), 6.60 (dd, *J*=3.5, 1.8 Hz, 1H, H-4 in furyl), 6.05–5.85 (m, 1H, CH=), 5.18 (ddd, *J*=13.7, 11.5, 1.4 Hz, 2H, CH_2=), 4.22 (br s, 1H, NH), 3.76 (d, *J*=5.8 Hz, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.4 (C-4), 150.4 (C-2 in furyl), 150.4 (C-2), 146.0 (C-6), 144.7 (C-5 in furyl), 135.7 (C-5), 134.9 (CH=), 117.2 (CH_2=), 115.3 (C-3 in furyl), 112.5 (C-4 in furyl), 49.7 (NCH_2); MS EI *m*/*z* (rel %) 237/235 (34/100, M^+), 208 (32), 194 (12), 179 (16), 168 (15); HRMS (EI) calcd for $C_{11}H_{10}ClN_3O$: 235.0512. Found. 235.0510.

*3.1.36. N-Allyl-4,6-di(2-furyl)-pyrimidin-5-amine (**11e**).* A solution of 2,4-di(2-furyl)-pyrimidin-5-amine (**10h**) (540 mg, 2.40 mmol) and 16-crown-8-ether (1.27 g, 4.80 mmol) in dry toluene (100 mL) at 0 °C under Ar was treated with KH (540 mg, ca. 4.80 mmol, ca. 35% in mineral oil) and stirred for 10 min. Allyl bromine (0.20 mL, 2.4 mmol) was added and the reaction mixture stirred for 90 min at 0 °C. Water (50 mL) was added, the mixture was extracted with EtOAc (2×50 mL), the combined organic extracts were washed with satd aq NaCl (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with CH_2Cl_2/EtOAc/hexane (4:1:5); yield 265 mg (41%), colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H, H-2), 7.66 (d, *J*=1.8 Hz, 2H, H-5 in furyl), 7.42 (d, *J*=3.5 Hz, 2H, H-3 in furyl), 6.64 (dd, *J*=3.5, 1.8 Hz, 2H, H-4 in furyl), 5.99–5.75 (m, 1H, CH=), 5.31–5.00 (m, 3H, CH_2= and NH), 3.59 (d, *J*=5.7 Hz, 2H, NCH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7 (C-2 in furyl or C-2), 151.6 (C-2 in furyl or C-2), 147.9 (C-4), 144.3 (C-5 in furyl), 135.4 (CH=), 134.5 (C-5), 116.4 (CH_2=), 114.5 (C-3 in furyl), 112.3 (C-4 in furyl), 50.5 (NCH_2); MS EI *m*/*z* (rel %) 267 (100, M^+), 240 (7), 211 (15); HRMS (EI) calcd for $C_{15}H_{13}N_3O_2$: 267.1008. Found. 267.1012.

*3.1.37. N-Allyl-4-(2-furyl)-6-phenyl-pyrimidin-5-amine (**11f**).* NaH (30 mg, ca. 0.77 mmol, ca. 60% in mineral oil) was added to a solution of 4-(2-furyl)-6-phenyl-pyrimidin-5-amine (**10f**) (130 mg, 0.550 mmol) and 15-crown-5-ether (0.22 mL, 1.1 mmol) in dry toluene (10 mL) at 0 °C, and the resulting mixture was stirred under N_2 for 10 min. Allyl bromide (0.06 mL, 0.7 mmol) was added and the mixture was stirred for 4 h at ambient temperature. Water (10 mL) was added and the resulting mixture was extracted with EtOAc (3×20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (2:5:5); yield 90 mg (60%), yellow oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.70 (s, 1H, H-2), 7.85–7.72 (m, 2H, H-2, H-6 in Ph), 7.57 (dd, *J*=1.8, 0.8 Hz, 1H, H-5 in furyl), 7.46–7.32 (m, 3H, H-3 and H-4, H-5 in Ph), 7.28 (dd, *J*=3.5, 0.8 Hz, 1H, H-3 in furyl), 6.55 (dd, *J*=3.5, 1.8 Hz, 1H, H-4 in furyl), 5.59 (ddt, *J*=17.4, 10.0, 5.8 Hz, 1H, CH=), 5.21–4.60 (m, 3H, CH_2= and NH), 3.25 (d, *J*=5.8 Hz, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.0 (C-6), 152.9 (C-2 in furyl), 150.6 (C-2), 145.0 (C-4), 144.3 (C-5 in furyl), 138.8 (C-1 in Ph), 136.9 (C-5), 135.7 (CH=), 129.8 (C-4 in Ph), 129.1 (C-3 in Ph), 128.6 (C-2 in Ph), 116.8 (CH_2=), 113.9 (C-3 in furyl), 112.7 (C-4 in furyl), 50.6 (NCH_2); MS EI *m*/*z* (rel %) 277 (100, M^+), 236 (6), 221 (10), 77 (10); HRMS (EI) calcd for $C_{17}H_{15}N_3O$: 277.1215. Found 277.1211.

*3.1.38. N-Allyl-2-chloro-4-(2-furyl)-pyrimidin-5-amine (**11g**).* A solution of 2-chloro-4-(2-furyl)-pyrimidin-5-amine (**10g**) (150 mg, 0.770 mmol) in THF (15 mL) at 0 °C was treated with NaH (35 mg, ca. 0.95 mmol, ca. 60% in mineral oil) and stirred at ambient temperature for 10 min under N_2. Allyl bromide (0.07 mL, 0.8 mmol) was added and the mixture was heated at 50 °C for 2.5 h, and concentrated in vacuo. The residue was dissolved in $CHCl_3$ (50 mL), washed with water (3×50 mL), dried ($MgSO_4$), and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:4); yield 42 mg (23%), yellow oil. *N*,*N*-Diallyl-2-chloro-4-(2-furyl)pyrimidin-5-amine (**12b**) 58 mg (55%) was also formed (data see below). ^1H NMR (CD_2Cl_2, 500 MHz) δ 8.01 (s, 1H, H-6), 7.67 (dd, *J*=1.8, 0.8 Hz, 1H, H-5 in furyl), 7.31 (dd, *J*=3.6, 0.8 Hz, 1H, H-3 in furyl), 6.64 (dd, *J*=3.6, 1.8 Hz, 1H, H-4 in furyl), 6.07–5.84 (m, 2H, NH and CH=), 5.37–5.18 (m, 2H, CH_2=), 4.00–3.78 (m, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 153.0 (C-2 in furyl), 148.1 (C-4), 144.8 (C-5 in furyl), 143.7 (C-2), 141.4 (C-6), 136.4 (C-1), 134.2 (CH=), 117.1 (CH_2=), 113.7 (C-3 in furyl), 112.9 (C-4 in furyl), 46.0 (NCH_2); MS EI *m*/*z* (rel %) 237/235 (33/100, M^+), 208 (18), 208 (44), 144 (9); HRMS (EI) calcd for $C_{11}H_{10}ClN_3O$: 235.0512. Found 235.0511.

*3.1.39. N-Allyl-2,4-di(2-furyl)-pyrimidin-5-amine (**11h**).* A solution of 2,4-di(2-furyl)pyrimidin-5-amine (**10h**) (55 mg, 0.24 mmol) and 18-crown-6-ether (126 mg, 0.480 mmol) in dry toluene (10 mL) was treated with KH (40 mg, ca. 0.29 mmol, ca. 35% in mineral oil) and stirred at ambient temperature for 10 min under Ar. Allyl bromide (0.03 mL, 0.6 mmol) was added and the mixture was stirred for 3 h. Water (10 mL) was added and the mixture was extracted with EtOAc (3×20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The product was

purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:4:4); yield 30 mg (47%), yellow wax. *N,N*-Diallyl-2,4-di(2-furyl)pyrimidin-5-amine (**12d**) 30 mg (41%) was also isolated (data, see below). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.20 (s, 1H, H-4), 7.60 (dd, J=1.8, 0.8 Hz, 1H, H-5 in furyl), 7.52 (dd, J=1.8, 0.8 Hz, 1H, H-5 in furyl), 7.37 (dd, J=3.5, 0.8 Hz, 1H, H-3 in furyl), 7.06 (dd, J=3.4, 0.8 Hz, 1H, H-3 in furyl), 6.60 (dd, J=3.5, 1.8 Hz, 1H, H-4 in furyl), 6.49 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 5.95 (ddt, J=17.2, 10.2, 5.1 Hz, 1H, CH=), 5.83 (br s, 1H, NH), 5.28 (m, 2H, CH_2=), 3.99–3.89 (m, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.7 (C-2 in furyl), 152.9 (C-2 in furyl), 147.7 (C-2 or C-6), 143.7 (C-5 in furyl), 143.5 (C-5 in furyl), 141.2 (C-4), 139.1 (C-2 or C-6), 135.1 (C-5), 134.0 (CH=), 117.3 (CH_2=), 112.7 (C-3 in furyl), 112.4 (C-4 in furyl), 111.9 (C-4 in furyl), 109.7 (C-3 in furyl), 45.7 (NCH_2); MS EI *m*/*z* (rel %) 267 (100, M^+), 238 (9), 226 (26), 198 (34), 133 (5), 106 (15); HRMS (EI) calcd for $C_{15}H_{13}N_3O_2$: 267.1008. Found 267.1007.

*3.1.40. N,N-Diallyl-4-chloro-6-(2-furyl)-pyrimidin-5-amine (**12a**).* A solution of *N*-allyl-4-chloro-6-(2-furyl)-pyrimidin-5-amine (**11d**) (250 mg, 1.30 mmol), allyl bromine (0.33 mL, 3.9 mmol), and 18-crown-6-ether (410 mg, 1.55 mmol) in dry toluene (20 mL) was treated with KH (300 mg, ca. 2.60 mmol, ca. 35% in mineral oil) and stirred at ambient temperature for 5 h under Ar. Water (10 mL) was added and the mixture was extracted with EtOAc (3×20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:9); yield 260 mg (72%), colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.75 (s, 1H, H-2), 7.69 (d, J=1.8 Hz, 1H, H-5 in furyl), 7.63 (d, J=3.5 Hz, 1H, H-3 in furyl), 6.61 (dd, J=3.5, 1.8 Hz, 1H, H-4 in furyl), 5.82 (ddt, J=16.9, 9.8, 6.9 Hz, 2H, 2× CH=), 5.11 (m, 4H, 2× CH_2=), 3.76 (d, J=6.9 Hz, 4H, 2× NCH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.1 (C-4 or C-6), 156.2 (C-4 or C-6), 154.4 (C-2), 149.3 (C-1 in furyl), 145.4 (C-5 in furyl), 136.4 (C-5), 134.2 (2× CH=), 118.8 (2× CH_2=), 118.0 (C-3 in furyl), 112.5 (C-4 in furyl), 55.2 (2× NCH_2); MS EI *m*/*z* (rel %) 277/275 (23/83 M^+), 248 (36), 234 (57), 179 (11), 41 (100); HRMS (EI) calcd for $C_{14}H_{14}ClN_3O$: 275.0825. Found 275.0828.

*3.1.41. N,N-Diallyl-2-chloro-4-(2-furyl)-pyrimidin-5-amine (**12b**).* The title compound was formed as a by-product in the synthesis of compound **11g**. Yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.24 (s, 1H, H-2), 7.67 (dd, J=1.7, 0.7 Hz, 1H, H-5 in furyl), 7.58 (dd, J=3.5, 0.7 Hz, 1H, H-3 in furyl), 6.58 (dd, J=3.5, 1.7 Hz, 1H, H-4 in furyl), 5.74 (ddt, J=16.8, 10.4, 6.4 Hz, 2H, 2× CH=), 5.25–5.07 (m, 4H, 2× CH_2=), 3.65 (d, J=6.4 Hz, 4H, 2× NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.3 (C-2), 154.9 (C-2 in furyl), 152.6 (C-2), 148.9 (C-6), 146.0 (C-5 in furyl), 138.8 (C-1), 133.2 (2× CH=), 120.1 (2× CH_2=), 118.0 (C-3 in furyl), 112.9 (C-4 in furyl), 55.1 (2× NCH_2); MS EI *m*/*z* (rel %) 277/275 (34/98 M^+), 246 (60), 179 (14), 41 (100); HRMS (EI) calcd for $C_{14}H_{14}ClN_3O$: 275.0825. Found 275.0824.

*3.1.42. N-Allyl-2-chloro-4-(2-furyl)-N-methyl-pyrimidin-5-amine (**12c**).* A solution of *N*-allyl-2-chloro-4-(2-furyl)-pyrimidin-5-amine (**11g**) (65 mg, 0.28 mmol) and 18-crown-6-ether (150 mg, 0.560 mmol) in dry toluene (10 mL) was treated with KH (64 mg, ca. 0.56 mmol, ca. 35% in mineral oil) and stirred at ambient temperature for 10 min under Ar. Methyl iodide (0.04 mL, 0.6 mmol) was added and the mixture was stirred at 40 °C for 30 min. Water (10 mL) was added and the mixture was extracted with EtOAc (3×20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (2:3:16); yield 52 mg (75%), colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.28 (s, 1H, H-4), 7.64 (dd, J=1.8, 0.8 Hz, 1H, H-5 in furyl), 7.49 (dd, J=3.5, 0.8 Hz, 1H, H-3 in furyl), 6.55 (dd, J=3.5, 1.8 Hz, 1H, H-4 in furyl), 5.89–5.65 (m, 1H, CH=), 5.28–5.09 (m, 2H, CH_2=), 3.58 (d, J=6.4 Hz, 2H, NCH_2), 2.71 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.4 (C-2 or C-6), 152.3 (C-4), 151.3 (C-2 or C-6), 148.8 (C-2 in furyl), 145.7 (C-5 in furyl), 140.7 (C-5), 133.4 (CH=), 119.6 (CH_2=), 117.5 (C-3 in furyl), 112.6 (C-4 in furyl), 58.2 (NCH_2), 40.5 (CH_3); MS EI *m*/*z* (rel %) 251/249 (22/67, M^+), 234 (12), 222/220 (43/100), 208 (11), 182 (10), 179 (9); HRMS (EI) calcd for $C_{12}H_{12}ClN_3O$: 249.0669. Found 249.0674.

*3.1.43. N,N-Diallyl-2,4-di(2-furyl)pyrimidin-5-amine (**12d**).* A solution of 2,4-di(2-furyl)pyrimidin-5-amine (**10h**) (315 mg, 1.39 mmol) and 18-crown-6-ether (730 mg, 2.80 mmol) in dry toluene (50 mL) was treated with KH (500 mg, ca. 4.20 mmol, ca. 35% in mineral oil) and stirred at ambient temperature for 10 min under Ar. Allyl iodide (0.40 mL, 4.20 mmol) was added and the mixture was stirred at 40 °C for 3 h. Water (50 mL) was added and the mixture was extracted with EtOAc (3×50 mL). The combined organic extracts were washed with satd aq NaCl (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:1:2); yield 332 mg (78%), mp 73–75 °C, yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.41 (s, 1H, H-4), 7.67 (dd, J=1.7, 0.8 Hz, 1H, H-5 in furyl), 7.58 (dd, J=1.7, 0.8 Hz, 1H, H-5 in furyl), 7.55 (dd, J=3.5, 0.7 Hz, 1H, H-3 in furyl), 7.28–7.21 (m, 1H, H-3 in furyl), 6.56 (dd, J=3.5, 1.8 Hz, 1H, H-4 in furyl), 6.52 (dd, J=3.4, 1.8 Hz, 1H, H-4 in furyl), 5.88–5.65 (m, 2H, 2× CH=), 5.14 (ddd, J=6.6, 4.2, 1.0 Hz, 4H, 2× CH_2=), 3.68 (d, J=6.4 Hz, 4H, 2× NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.7 (C-2 in furyl, C-2, or C-6), 152.6 (C-4), 152.4 (C-2 in furyl, C-2, or C-6), 150.2 (C-2 in furyl, C-2, or C-6), 149.8 (C-2 in furyl, C-2, or C-6), 145.1 (C-5 in furyl), 144.7 (C-5 in furyl), 137.7 (C-5), 133.5 (2× CH=), 119.4 (2× CH_2=), 116.6 (C-3 in furyl), 112.4 (C-3 in furyl or C-4 in furyl), 112.3 (C-3 in furyl or C-4 in furyl), 112.2 (C-3 in furyl or C-4 in furyl), 55.2 (2× NCH_2); MS EI *m*/*z* (rel %) 307 (100, M^+), 280 (9), 266 (18), 236 (37), 211 (13), 199 (14); HRMS (EI) calcd for $C_{18}H_{17}N_3O_2$: 307.1321. Found 307.1321. The title compound was also formed as a by-product in the synthesis of compound **11h**.

*3.1.44. (±) (6aS,8S)-4-Chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxybenzo[c][1,5]naphthyridine (**13b**).* *N*-Allyl-4-chloro-(2-furyl)pyridine-3-amine (**11b**) (85 mg, 0.36 mmol) was dissolved in dry toluene (10 mL). The reaction mixture was heated at 100 °C for 24 h under Ar, allowed to cool to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (2:3:3); yield 41 mg (49%, ratio **13b**/**14b**; 25:1), colorless wax. NMR data presented are for the major isomer **13b**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.95 (d, J=5.0 Hz, 1H, H-2), 7.15 (d, J=5.0 Hz, 1H, H-3), 6.52 (dd, J=5.7, 1.7 Hz, 1H, H-9), 6.35 (d, J=5.7 Hz, 1H, H-10), 4.99 (dd, J=4.5, 1.7 Hz, 1H, H-8), 4.69 (s, 1H, NH), 3.56 (ddd, J=11.4, 5.2, 4.0 Hz, 1H, H-6_A), 2.96 (m, 1H, H-6_B), 2.00–1.90 (m, 1H, H-6a), 1.68 (dd, J=11.4, 7.6 Hz, 1H, H-7_A), 1.52 (ddd, J=11.4, 4.5, 3.2 Hz, 1H, H-7_B); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 140.0 (C-4a), 139.4 (C-10b), 138.9 (C-2), 137.7 (C-9), 136.1 (C-10), 127.4 (C-4), 124.0 (C-3), 85.2 (C-10a), 78.0 (C-8), 45.7 (C-6), 34.1 (C-6a), 32.2 (C-7); MS EI *m*/*z* (rel %) 236/234 (32/100 M^+), 217 (8), 205 (20), 191 (47), 178 (29), 165 (28); HRMS (EI) calcd for $C_{12}H_{11}ClN_2O$: 234.0560. Found 234.0558.

*3.1.45. (±) (6aS,8S)-4-Chloro-6,6a,7,8,-tetrahydro-5H-8,10a-epoxybenzo[c][1,7]naphthyridine (**13c**).* A stirring solution of *N*-allyl-2-chloro-4-(2-furyl)pyridin-3-amine (**11c**) (120 mg, 0.510 mmol) in dry toluene (20 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:1:3); yield 105 mg (88%, ratio **13c**/**14c**; 10:1), mp 156–159 °C, colorless solid. NMR data presented are for the major isomer **13c**. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.75 (d, J=4.8 Hz, 1H, H-2), 7.21 (d, J=4.8 Hz, 1H, H-1), 6.56 (dd, J=5.7, 1.6 Hz, 1H, H-9), 6.18 (d, J=5.7 Hz, 1H, H-10), 4.99 (dd, J=4.5, 1.6 Hz, 1H, H-8), 4.84 (s,

1H, NH), 3.59 (ddd, J=11.6, 5.3, 4.1 Hz, 1H, H-6$_A$), 2.91 (m, 1H, H-6$_B$), 1.90–1.77 (m, 1H, H-6a), 1.66 (dd, J=11.5, 7.6 Hz, 1H, H-7$_A$), 1.50 (ddd, J=11.5, 4.5, 3.1 Hz, 1H, H-7$_B$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 139.7 (C-4a), 139.1 (C-9), 136.8 (C-10b), 136.5 (C-2), 135.9 (C-10), 127.0 (C-4), 124.4 (C-1), 83.0 (C-10a), 78.0 (C-8), 45.7 (C-6), 33.4 (C-6a), 31.6 (C-7); MS EI m/z (rel %) 236/234 (32/100 M^+), 217 (8), 205 (20), 191 (47), 178 (29), 165 (28); HRMS (EI) calcd for $C_{12}H_{11}ClN_2O$: 234.0560. Found 234.0558.

*3.1.46. (±) (6aS,8S)-4-Chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13d**).* A stirring solution of *N*-allyl-4-chloro-6-(2-furyl)-pyrimidin-5-amine (**11d**) (100 mg, 0.430 mmol) in dry toluene (10 mL) was heated at 100 °C for 16 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (2:3); yield 55 mg (55%, only isomer **13d**), mp 156–159 °C, colorless solid. ^{1}H NMR (CD_2Cl_2, 600 MHz) δ 8.36 (s, 1H, H-2), 6.55 (dd, J=5.7, 1.7 Hz, 1H, H-9), 6.31 (d, J=5.7 Hz, 1H, H-10), 5.01 (dd, J=4.5, 1.7 Hz, 1H, H-8), 4.80 (s, 1H, NH), 3.64 (ddd, J=11.8, 5.3, 4.1 Hz, 1H, H-6$_A$), 2.94 (t, J=11.8 Hz, 1H, H-6$_B$), 1.95–1.89 (m, 1H, H-6a), 1.71 (dd, J=11.5, 7.6 Hz, 1H, H-7$_A$), 1.53 (ddd, J=11.5, 4.5, 3.1 Hz, 1H, H-7$_B$); ^{13}C NMR (CD_2Cl_2, 150 MHz) δ 146.3 (C-2), 145.2 (C-4), 144.9 (C-10b), 138.4 (C-9), 137.9 (C-4a), 135.4 (C-10), 84.2 (C-10a), 78.4 (C-8), 45.4 (C-6), 33.7 (C-6a), 31.9 (C-7); MS EI m/z (rel %) 235 (100, M^+), 218 (25), 206 (47), 192 (60), 166 (20); HRMS (EI) calcd for $C_{11}H_{10}ClN_3O$: 235.0512. Found 235.0518.

*3.1.47. (±) (6aS,8S)-5,6,6a,7,8,10a-4-(2-Furyl)-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13e**).* A stirring solution of *N*-allyl-4,6-di(2-furyl)-pyrimidin-5-amine (**11e**) (265 mg, 0.990 mmol) in dry toluene (80 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2 (3:7); yield 174 mg (66%, ratio **13e**/**14e**; 8:1) mp 167–172 °C (dec), orange solid. NMR data presented are for the major isomer **13e**. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (s, 1H, H-2), 7.59 (dd, J=1.8, 0.8 Hz, 1H, H-5 in furyl), 7.27 (dd, J=3.6, 0.8 Hz, 1H, H-3 in furyl), 6.58 (dd, J=3.6, 1.8 Hz, 1H, H-4 in furyl), 6.53 (dd, J=5.7, 1.7 Hz, 1H, H-9), 6.34 (d, J=5.7 Hz, 1H, H-10), 6.00 (s, 1H, NH), 5.00 (dd, J=4.4, 1.7 Hz, 1H, H-8), 3.60 (dd, J=11.6, 5.1 Hz, 1H, H-6$_A$), 2.97 (t, J=11.9 Hz, 1H, H-6$_B$), 2.00–1.86 (m, 1H, H-6a), 1.69 (dd, J=11.4, 7.5 Hz, 1H, H-7$_A$), 1.53 (ddd, J=11.5, 4.3, 3.2 Hz, 1H, H-7$_B$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.4 (C-2 in furyl), 147.7 (C-2), 146.5 (C-10b or C-4), 143.8 (C-5 in furyl), 139.4 (C-10b or C-4), 138.1 (C-4 in furyl), 136.6 (C-4a), 135.8 (C-10), 112.4 (C-3 in furyl), 112.4 (C-9), 84.6 (C-10a), 78.3 (C-8), 45.6 (C-6), 33.7 (C-6a), 32.2 (C-7); MS EI m/z (rel %) 267 (100, M^+), 250 (8), 238 (26), 224 (57), 210 (9), 198 (15); HRMS (EI) calcd for $C_{15}H_{13}N_3O_2$: 267.1008. Found 267.1002.

*3.1.48. (±) (6aS,8S)-5,6,6a,7,8,10a-Hexahydro-4-phenyl-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13f**).* A stirring solution of *N*-allyl-4-(2-furyl)-6-phenyl-pyrimidin-5-amine (**11f**) (90 mg, 0.32 mmol) in dry toluene (10 mL) was heated at 100 °C for 16 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (2:5:5); yield 52 mg (58%, ratio **13f**/**14f**; 22:1), yellow oil. NMR data presented are for the major isomer **13f**. ^{1}H NMR (CD_2Cl_2, 600 MHz) δ 8.65 (d, J=4.7 Hz, 1H, H-2), 7.76–7.67 (m, 2H, H-2 in Ph), 7.56–7.45 (m, 3H, H-3 and H-4 in Ph), 6.64–6.50 (m, 1H, H-10), 6.38 (d, J=5.7 Hz, 1H, H-9), 4.99 (dd, J=4.5, 1.7 Hz, 1H, H-8), 4.76 (s, 1H, NH), 3.47 (ddd, J=11.5, 5.0, 4.2 Hz, 1H, H-6$_A$), 2.81 (t, J=11.5 Hz, 1H, H-6$_B$), 1.99–1.89 (m, 1H, H-6a), 1.69 (dd, J=11.4, 7.6 Hz, 1H, H-7$_A$), 1.50 (ddd, J=11.4, 4.3, 3.3 Hz, 1H, H-7$_B$); ^{13}C NMR (CD_2Cl_2, 150 MHz) δ 151.8 (C-4), 148.6 (C-2), 145.6 (C-10b), 139.2 (C-4a), 138.1 (C-10), 136.7 (C-1 in Ph), 136.5 (C-9), 130.0 (C-3 or C-4 in Ph), 129.5 (C-3 or C-4 in Ph), 128.7 (C-2 in Ph), 85.3 (C-10a), 78.7 (C-8), 46.2 (C-6), 34.6 (C-6a), 32.5 (C-7); MS EI m/z (rel %) 277 (100, M^+), 260 (15), 248 (38), 234 (59), 208 (13), 77 (9); HRMS (EI) calcd for $C_{17}H_{15}N_3O$: 277.1215. Found 277.1210.

*3.1.49. (±) (6aS,8S)-5-Allyl-4-chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13i**) and (±) (6aR,8S)-5-allyl-4-chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**14i**).* A stirring solution of *N*,*N*-diallyl-4-chloro-6-(2-furyl)-pyrimidin-5-amine (**12a**) (250 mg, 0.900 mmol) in dry toluene (60 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (3:2); yield 95 mg (38%) of **13i**, and 24 mg (10%) of **14i**. Starting material **12a** was recovered (44%).

*3.1.49.1. (±) (6aS,8S)-5-Allyl-4-chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13i**).* Mp 99–101 °C, colorless solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.60 (s, 1H, H-2), 6.56 (dd, J=5.8, 1.6 Hz, 1H, H-9), 6.35 (d, J=5.8 Hz, 1H, H-10), 5.98 (m, 1H, CH=), 5.29 (ddd, J=13.7, 10.8, 0.8 Hz, 2H, CH_2=), 5.03 (dd, J=4.1, 1.6 Hz, 1H, H-8), 4.02 (dd, J=15.7, 2.5 Hz, 1H, H$_A$ in NCH_2), 3.68 (dd, J=15.7, 7.3 Hz, 1H, H$_B$ in NCH_2), 3.43 (dd, J=13.1, 4.5 Hz, 1H, H-6$_A$), 2.80 (m, 1H, H-6$_B$), 1.98 (ddd, J=12.2, 7.6, 4.5 Hz, 1H, H-6a), 1.68 (dd, J=11.5, 7.6 Hz, 1H, H-7$_A$), 1.53–1.43 (m, 1H, H-7$_B$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 153.3 (C-10b or C-4), 152.9 (C-10b or C-4), 150.2 (C-2), 141.3 (C-4a), 138.0 (C-9), 135.2 (C-10), 134.4 (CH=), 118.1 (CH_2=), 84.3 (C-10a), 78.5 (C-8), 55.7 (NCH_2), 50.9 (C-6), 31.3 (C-7), 31.0 (C-6a); MS EI m/z (rel %) 277/275 (35/100, M^+), 258 (25), 234 (25), 206 (26), 192 (22), 170 (11); HRMS (EI) calcd for $C_{14}H_{14}ClN_3O$: 275.0825. Found 275.0819.

*3.1.49.2. (±) (6aR,8S)-5-Allyl-4-chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**14i**).* Colorless oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.44 (s, 1H, H-2), 6.77 (dd, J=5.6, 1.8 Hz, 1H, H-9), 6.11 (d, J=5.6 Hz, 1H, H-10), 5.92 (dddd, J=17.3, 10.1, 7.3, 5.1 Hz, 1H, CH=), 5.35–5.15 (m, 3H, CH_2= and H-8), 4.29–4.10 (m, 1H, H$_A$ in NCH_2), 3.86 (dd, J=15.6, 7.3 Hz, 1H, H$_B$ in NCH_2), 3.61 (dd, J=11.0, 5.4 Hz, 1H, H-6$_A$), 2.48 (dd, J=13.2, 11.0 Hz, 1H, H-6$_B$), 2.33 (ddd, J=11.3, 9.0, 4.6 Hz, 1H, H-7$_A$), 2.22 (ddd, J=8.8, 7.7, 4.5 Hz, 1H, H-6a), 1.09 (dd, J=11.3, 5.1 Hz, 1H, H-7$_B$); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 155.6 (C-10b), 148.1 (C-4), 148.0 (C-2), 139.9 (C-9), 137.4 (C-4a), 133.8 (CH=), 133.3 (C-10), 118.7 (CH_2=), 84.6 (C-10a), 80.8 (C-8), 57.0 (NCH_2), 53.0 (C-6), 38.7 (C-6a), 29.4 (C-6); MS EI m/z (rel %) 277/275 (33/100, M^+) 248 (38), 240 (37), 234 (58), 206 (63); HRMS (EI) calcd for $C_{14}H_{14}ClN_3O$: 275.0825. Found 275.0821.

*3.1.50. (±) (6aS,8S)-5-Allyl-2-chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13j**) and (±) (6aR,8S)-5-allyl-2-chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**14j**).* A stirring solution of *N*,*N*-diallyl-2-chloro-4-(2-furyl)-pyrimidin-5-amine (**12b**) (58 mg, 0.20 mmol) in dry toluene (10 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:1); yield 46 mg (80%) of **13j**, and 12 mg (20%) of **14j**.

*3.1.50.1. (±) (6aS,8S)-5-Allyl-2-chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13j**).* Waxy yellow solid. ^{1}H NMR (CD_2Cl_2, 500 MHz) δ 8.06 (s, 1H, H-4), 6.53 (dd, J=5.7, 1.7 Hz, 1H, H-9), 6.30 (d, J=5.7 Hz, 1H, H-10), 5.81 (ddt, J=17.2, 10.3, 5.0 Hz, 1H, CH=), 5.25–5.16 (m, 2H, CH_2=), 4.98 (dd, J=4.5, 1.7 Hz, 1H, H-8), 4.10–3.82 (m, 2H, NCH_2), 3.37 (dd, J=12.0, 5.3 Hz, 1H, H-6$_A$), 3.01 (t, J=12.1 Hz, 1H, H-6$_B$), 1.98–1.86 (m, 1H, H-6a), 1.68 (dd, J=11.5, 7.5 Hz, 1H, H-7$_A$), 1.49 (ddd, J=11.5, 4.5, 3.0 Hz, 1H, H-7$_B$); ^{13}C NMR (CD_2Cl_2, 125 MHz) δ 148.6 (C-10b), 148.0 (C-2), 144.0 (C-4), 140.5 (C-4a), 138.5 (C-9), 135.8 (C-10), 131.9 (CH=), 117.9 (CH_2=), 84.4 (C-10a), 78.9 (C-8), 53.8 (NCH_2 or C-6), 53.5 (NCH_2 or C-6), 33.7 (C-6a), 32.5 (C-7); MS

EI *m*/*z* (rel %) 277/275 (37/100, M^+), 248 (21), 234 (42); HRMS (EI) calcd for $C_{14}H_{14}ClN_3O$: 275.0825. Found 275.0828.

*3.1.50.2. (±) (6aR,8S)-5-Allyl-2-chloro-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**14j**).* Yellow oil. ^1H NMR (CD_2Cl_2, 500 MHz) δ 7.84 (s, 1H, H-4), 6.73 (dd, *J*=5.6, 1.9 Hz, 1H, H-9), 6.06 (d, *J*=5.6 Hz, 1H, H-10), 5.80 (ddt, *J*=17.2, 10.4, 4.6 Hz, 1H, CH=), 5.29–5.08 (m, 3H, CH_2= and H-8), 4.00–3.79 (m, 2H, NCH_2), 3.49 (dd, *J*=11.3, 5.2 Hz, 1H, H-6_A), 2.96–2.85 (m, 1H, H-6_B), 2.35–2.20 (m, 2H, H-6a and H-7_A), 1.11–0.97 (m, 1H, H-7_B); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 151.5 (C-10b), 146.8 (C-2), 140.5 (C-4), 139.8 (C-9), 137.5 (C-4a), 133.6 (C-10), 131.1 (CH=), 116.8 (CH_2=), 84.4 (C-10a), 81.1 (C-8), 53.2 (C-6), 52.3 (NCH_2), 37.2 (C-6a), 29.7 (C-7); MS EI *m*/*z* (rel %) 277/275 (35/100, M^+), 248 (30), 234 (43); HRMS (EI) calcd for $C_{14}H_{14}ClN_3O$: 275.0825. Found 275.0828.

*3.1.51. (±) (6aS,8S)-2-Chloro-5,6,6a,7,8,10a-hexahydro-5-methyl-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13k**) and (±) (6aR,8S)-2-chloro-5,6,6a,7,8,10a-hexahydro-5-methyl-8,10a-epoxypyrimido[5,4-c]isoquinoline (**14k**).* A stirring solution of *N*-allyl-2-chloro-4-(2-furyl)-*N*-methyl-pyrimidin-5-amine (**12c**) (50 mg, 0.20 mmol) in dry toluene (10 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:1); yield 27 mg (54%) of **13k**, and 7 mg (14%) of **14k**.

*3.1.51.1. (±)(6aS,8S)-2-Chloro-5,6,6a,7,8,10a-hexahydro-5-methyl-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13k**).* Mp 160–162 °C, colorless solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.06 (s, 1H, H-4), 6.54 (dd, *J*=5.8, 1.7 Hz, 1H, H-9), 6.34 (d, *J*=5.8 Hz, 1H, H-10), 5.01 (dd, *J*=4.5, 1.7 Hz, 1H, H-8), 3.32 (dd, *J*=11.7, 5.3 Hz, 1H, H-6_A), 3.05–2.84 (m, 4H, CH_3 and H-6_B), 2.05–1.88 (m, 1H, H-6a), 1.69 (dd, *J*=11.5, 7.5 Hz, 1H, H-7_A), 1.51 (m, 1H, H-7_B); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.8 (C-2 or C-4a), 148.7 (C-2 or C-4a), 143 (C-4), 141.2 (C-10b), 138.5 (C-9), 135.2 (C-10), 84 (C-10a), 78.6 (C-8), 55.0 (C-6), 38.6 (CH_3), 33.7 (C-6a), 32.2 (C-7); MS EI *m*/*z* (rel %) 251/249 (35/100, M^+), 248 (22), 220 (62), 206 (70), 180 (29); HRMS (EI) calcd for $C_{12}H_{12}ClN_3O$: 249.0669. Found 249.0676.

*3.1.51.2. (±) (6aR,8S)-2-Chloro-5,6,6a,7,8,10a-hexahydro-5-methyl-8,10a-epoxypyrimido[5,4-c]isoquinoline (**14k**).* Waxy colorless solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.87 (s, 1H, H-4), 6.71 (dd, *J*=5.6, 1.9 Hz, 1H, H-9), 6.04 (d, *J*=5.7 Hz, 1H, H-10), 5.19 (dd, *J*=4.0, 1.7 Hz, 1H, H-8), 3.43 (dd, *J*=11.2, 5.3 Hz, 1H, H-6_A), 3.07–2.82 (m, 4H, H-6_B and CH_3), 2.39–2.20 (m, 2H, H-6a and H-7_A), 1.02 (d, *J*=6.2 Hz, 1H, H-7_B); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.1 (C-10b), 147.3 (C-2), 139.7 (C-9), 139.1 (C-4), 137.9 (C-4a), 133.3 (C-10), 84.2 (C-10a), 81.1 (C-8), 54.8 (C-6), 37.6 (CH_3), 37.2 (C-6a), 29.9 (C-7); MS EI *m*/*z* (rel %) 251/249 (34/100, M^+), 248 (16), 220 (62), 206 (74), 180 (29); HRMS (EI) calcd for $C_{12}H_{12}ClN_3O$: 249.0669. Found 249.0674.

*3.1.52. (±) (6aS,8S)-5-Allyl-2-(2-furyl)-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (13l) and (±) (6aR,8S)-5-allyl-2-(2-furyl)-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**14l**).* A stirring solution of *N*,*N*-diallyl-2,4-di(2-furyl)pyrimidin-5-amine (**12d**) (100 mg, 0.330 mmol) in dry toluene (10 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (2:5:5); yield 78 mg (78%) of **13l**, and 15 mg (15%) of **14l**.

*3.1.52.1. (±) (6aS,8S)-5-Allyl-2-(2-furyl)-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**13l**).* Mp 125–127 °C, colorless solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.21 (s, 1H, H-4), 7.47 (dd, *J*=1.7, 0.8 Hz, 1H, H-5 in furyl), 7.07 (dd, *J*=3.4, 0.8 Hz, 1H, H-3 in furyl), 6.53 (dd, *J*=5.7, 1.7 Hz, 1H, H-9), 6.44 (dd, *J*=3.4, 1.7 Hz, 1H, H-4 in furyl), 6.39 (d, *J*=5.7 Hz, 1H, H-10), 5.89–5.67 (m, 1H, CH=), 5.24–5.10 (m, 2H, CH_2=), 5.01 (dd, *J*=5.3, 1.7 Hz, 1H, H-8), 4.13–3.76 (m, 2H, NCH_2), 3.33 (dd, *J*=12.0, 4.4 Hz, 1H, H-6_A), 3.07 (t, *J*=12.0 Hz, 1H, H-6_B), 2.04–1.84 (m, 1H, H-6a), 1.67 (dd, *J*=11.4, 7.5 Hz, 1H, H-7_A), 1.55–1.40 (m, 1H, H-7_B); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.9 (C-2 in furyl), 148.1 (C-2), 146.1 (C-4a), 143.7 (C-5 in furyl), 141.4 (C-4), 139.2 (C-10b), 138.2 (C-9), 136.2 (C-10), 131.9 (CH=), 118.2 (CH_2=), 112.1 (C-4 in furyl), 110.2 (C-3 in furyl), 84.7 (C-10a), 78.8 (C-8), 53.6 (NCH_2 or C-6), 53.3 (NCH_2 or C-6), 34.0 (C-6a), 32.5 (C-7); MS EI *m*/*z* (rel %) 307 (100, M^+), 280 (6), 277 (19), 238 (15), 224 (20); HRMS (EI) calcd for $C_{18}H_{17}N_3O_2$: 307.1321. Found 307.1320.

*3.1.52.2. (±) (6aR,8S)-5-Allyl-2-(2-furyl)-5,6,6a,7,8,10a-hexahydro-8,10a-epoxypyrimido[5,4-c]isoquinoline (**14l**).* Yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.07 (s, 1H, H-2), 7.51 (dd, *J*=1.8, 0.8 Hz, 1H, H-5 in furyl), 7.14 (d, *J*=3.4, 0.8 Hz, 1H, H-3 in furyl), 6.75 (dd, *J*=5.6, 1.8 Hz, 1H, H-9), 6.48 (dd, *J*=3.4, 1.8 Hz, 1H, H-4 in furyl), 6.15 (d, *J*=5.6 Hz, 1H, H-10), 5.83 (ddt, *J*=17.2, 10.4, 4.8 Hz 1H, =CH), 5.37–5.08 (m, 3H, H-8 and =CH_2), 4.09–3.82 (m, 2H, NCH_2), 3.53 (dd, *J*=11.0, 5.4 Hz, 1H, H-6), 2.96 (dd, *J*=12.5, 11.0 Hz, 1H, H-6), 2.49–2.21 (m, 2H, H-6a and H-7), 1.06 (dd, *J*=10.5, 4.3 Hz, 1H, H-7); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.6 (C-2 in furyl), 148.9 (C-2 or C-10b), 146.8 (C-2 or C-10b), 143.2 (C-5 in furyl), 139.3 (C-9), 138.1 (C-4), 135.9 (C-4a), 133.6 (C-10), 130.9 (=CH), 117.1 (=CH_2), 111.7 (C-4 in furyl), 109.7 (C-3 in furyl), 84.4 (C-10a), 80.8 (C-8), 53.0 (C-6), 52.0 (NCH_2), 37.2 (C-6a), 29.7 (C-7); MS EI *m*/*z* (rel %) 307 (100, M^+), 280 (7), 278 (13), 238 (16), 224 (3); HRMS (EI) calcd for $C_{18}H_{17}N_3O_2$: 307.1321. Found 307.134.

*3.1.53. 7-(2-Furyl)-1H-indole (**16a**).* A mixture of $Pd(OAc)_2$ (12 mg, 0.050 mmol), PPh_3 (60 mg, 0.25 mmol), potassium 2-furyltrifluoroborate (210 mg, 1.20 mmol), K_2CO_3 (280 mg, 2.00 mmol), and 7-iodo-1*H*-indole (**15a**) (250 mg, 1.00 mmol) in EtOH (20 mL, 96%) was stirred at 60 °C for 4 h under Ar, and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (3:17); yield 145 mg (79%), colorless oil. ^1H NMR ($CDCl_3$, 300 MHz) δ 9.37 (s, 1H, NH), 7.78 (d, *J*=7.9 Hz, 1H, H-5 or H-6), 7.62 (d, *J*=8.5 Hz, 2H, H-3 in furyl and H-4 or H-6), 7.39–7.25 (m, 2H, H-2 and H-5), 6.86 (d, *J*=3.2 Hz, 1H, H-3 in furyl), 6.79–6.70 (m, 1H, H-3), 6.64 (dd, *J*=3.2, 1.8 Hz, 1H, H-4 in furyl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.4 (C-2 in furyl), 141.5 (C-5 in furyl), 131.6 (C-3a or C-7a), 129.2 (C-3a or C-7a), 124.8 (C-2 or C-5), 120.5 (C-4 or C-6), 120.0 (C-2 or C-5), 118.0 (C-4 or C-6), 114.7 (C-7), 111.8 (C-4 in furyl), 105.2 (C-3 in furyl), 102.6 (C-3); MS EI *m*/*z* (rel %) 183 (100, M^+), 154 (76), 127 (9), 92 (7), 77 (8); HRMS (EI) calcd for $C_{12}H_9NO$: 183.0684. Found 183.0679.

*3.1.54. 4-(2-Furyl)-5H-pyrrolo[3,2-d]pyrimidine (**16b**).* A mixture of $Pd(OAc)_2$ (20 mg, 0.10 mmol), PPh_3 (100 mg, 0.250 mmol), potassium 2-furyltrifluoroborate (390 mg, 2.13 mmol), K_2CO_3 (450 mg, 3.20 mmol), and 4-chloro-5*H*-pyrrolo[3,2-*d*]pyrimidine (280 mg, 1.83 mmol) (**15b**) in EtOH (50 mL, 96%) was stirred at 80 °C for 3 h under Ar, and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with acetone/hexane (2:3); yield 260 mg (78%), mp 160–162 °C, colorless solid. ^1H NMR (DMSO-d_6, 300 MHz) δ 11.86 (s, 1H, NH), 8.80 (s, 1H, H-2), 8.04 (dd, *J*=1.8, 0.8 Hz, 1H, H-5 in furyl), 7.90 (d, *J*=3.1 Hz, 1H, H-6), 7.47 (dd, *J*=3.5, 0.8 Hz, 1H, H-3 in furyl), 6.82 (dd, *J*=3.5, 1.8 Hz, 1H, H-4 in furyl), 6.67 (dd, *J*=3.1, 1.7 Hz, 1H, H-7); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 152.2 (C-2 in furyl or C-3a), 152.0 (C-2 in furyl or C-3a), 150.8 (C-2), 146.7 (C-5 in furyl), 138.9 (C-4), 135.0 (C-6), 121.4 (C-3b), 113.5 (C-4 in furyl), 113.2 (C-3 in furyl), 102.3 (C-7); MS EI *m*/*z* (rel %) 185 (100, M^+), 157 (27), 129 (9), 118 (7), 103 (6); HRMS (EI) calcd for $C_{10}H_7N_3O$: 185.0589. Found 185.0589.

*3.1.55. 6-(2-Furyl)-1H-purine (**16c**).* A mixture of $Pd(OAc)_2$ (30 mg, 0.15 mmol), PPh_3 (120 mg, 0.46 mmol), potassium 2-furyltrifluoroborate (410 mg, 2.36 mmol), K_2CO_3 (750 mg,

5.40 mmol), and 6-chloro-1*H*-purine (300 mg, 1.95 mmol) (**15c**) in EtOH (50 mL, 96%) was stirred at 80 °C for 16 h under N_2, and the reaction mixture was, after cooling to ambient temperature, subjected to dry flash chromatography on a short plug of silica. The column was washed with EtOH (100 mL) and the solution was evaporated in vacuo. The residue was dissolved in a minimum of EtOH and water was added until the product precipitated. The product was isolated by filtration, washed with cold hexane, and dried; yield 340 mg (94%) off-white powder. The spectral data were in good agreement with those reported before.[15]

*3.1.56. 1-Allyl-7-(2-furyl)-1H-indole (**17a**).* A solution of 7-(2-furyl)-1*H*-indole (**16a**) (130 mg, 0.750 mmol) and 18-crown-6-ether (370 mg, 1.50 mmol) in dry toluene (10 mL) at 0 °C was treated with KH (103 mg, ca. 0.900 mmol, ca. 35% in mineral oil) and stirred for 10 min under Ar, before allyl bromide (0.08 mL, 0.8 mmol) was added and the mixture was stirred at ambient temperature for 3 h. Water (10 mL) was added and the mixture was extracted with EtOAc (3×20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:49); yield 74 mg (44%), colorless oil. ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 7.70 (dd, *J*=7.7, 1.4 Hz, 1H, H-6), 7.59 (dd, *J*=1.9, 0.9 Hz, 1H, H-5 in furyl), 7.21 (dd, *J*=7.3, 1.5 Hz, 1H, H-4 or H-5), 7.17–7.10 (m, 2H, H-2 and H-4 or H-5), 6.62 (d, *J*=3.2 Hz, 1H, H-3), 6.58 (dd, *J*=3.2, 1.9 Hz, 1H, H-4 in furyl), 6.50 (dd, *J*=3.2, 0.9 Hz, 1H, H-3 in furyl), 5.80 (m, 1H, CH=), 5.02 (dd, *J*=17.1, 1.5 Hz, 1H, H_A in CH_2=), 4.81 (dd, *J*=17.1, 1.5 Hz, 1H, H_B in CH_2=), 4.45 (d, *J*=5.5 Hz, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.3 (C-2 in furyl), 142.4 (C-5 in furyl), 135.2 (CH=), 134.4 (C-7a or C-3a), 130.9 (C-7a or C-3a), 130.5 (C-2), 125.6 (C-6), 122.6 (C-4 or C-5), 119.5 (C-4 or C-5), 116.6 (CH_2=), 116.1 (C-7), 111.9 (C-4 in furyl), 109.7 (C-3 in furyl), 102.6 (C-3), 50.6 (NCH_2); MS EI *m*/*z* (rel %) 223 (100, M^+), 206 (15), 194 (50), 154 (60), 127 (9); HRMS (EI) calcd for $C_{15}H_{13}NO$: 223.0997. Found 223.0992.

*3.1.57. 5-Allyl-4-(2-furyl)-5H-pyrrolo[3,2-d]pyrimidine (**17b**).* A solution of 4-(2-furyl)-5*H*-pyrrolo[3,2-*d*]pyrimidine (**16b**) (870 mg, 4.70 mmol) and 15-crown-5-ether (1.5 mL, 9.4 mmol) in dry acetonitrile (100 mL) at ambient temperature was treated with NaH (370 mg, ca.9.4 mmol, ca. 60% in oil) and stirred for 5 min under Ar before allyl iodide (790 mg, 4.70 mmol) was added. The mixture was stirred at ambient temperature for 1 h. Water was added (50 mL), and the resulting mixture was extracted with Et_2O (3×100 mL). The combined organic phases were washed with brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (1:1); yield 520 mg (49%), colorless oil. ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 8.87 (s, 1H, H-2), 7.69 (d, *J*=0.9 Hz, 1H, H-5 in furyl), 7.53 (d, *J*=3.2 Hz, 1H, H-6), 7.18 (d, *J*=3.4 Hz, 1H, H-3 in furyl), 6.71 (d, *J*=3.2 Hz, 1H, H-7), 6.65 (dd, *J*=3.4, 1.8 Hz, 1H, H-4 in furyl), 5.96–5.77 (m, 1H, CH=), 5.12–4.75 (m, 4H, CH_2= and NCH_2); ^{13}C NMR (CD_2Cl_2, 75 MHz) δ 154.0 (C-3a), 152.0 (C-2 in furyl), 150.5 (C-2), 144.7 (C-5 in furyl), 140.1 (C-4), 137.8 (C-6), 134.4 (CH=), 124.1 (C-3b), 117.3 (CH_2=), 113.6 (C-3 in furyl), 112.8 (C-4 in furyl), 102.9 (C-7), 52.6 (NCH_2); MS EI *m*/*z* (rel %) 225 (100, M^+), 208 (26), 196 (69), 170 (21), 157 (27); HRMS (EI) calcd for $C_{13}H_{11}N_3O$: 225.0902. Found 225.0898.

*3.1.58. 7-Allyl-6-(2-furyl)-7H-purine (**17c**).* 6-(2-Furyl)-9*H*-purine (**16c**) (450 mg, 2.42 mmol) and methylaquacobaloxime (800 mg, 2.66 mmol) in dry MeCN (50 mL) was stirred at ambient temperature under N_2 for 5 min, before K_2CO_3 (370 mg 2.66 mmol) was added and the mixture was stirred for another 30 min. Allyl iodide (0.50 mL, 4.8 mmol) was added and the mixture was stirred in the dark. More allyl iodide (0.25 mmol) was added after 24 hand 48 h. After stirring in the dark for a total of 96 h, the mixture was evaporated in vacuo and the residue transferred to a separatory funnel using $CHCl_3$ (100 mL) and aq NaOH (2 M, 200 mL). The phases were separated and the aqueous phase was extracted with $CHCl_3$ (3×100 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with acetone/hexane (1:9); yield 201 mg (37%), yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.02 (s, 1H, H-2), 8.27 (s, 1H, H-8), 7.69 (dd, *J*=1.8, 0.8 Hz, 1H, H-5 in furyl), 7.38 (dd, *J*=3.5, 0.8 Hz, 1H, H-3 in furyl), 6.67 (dd, *J*=3.5, 1.8 Hz, 1H, H-4 in furyl), 6.02–5.80 (m, 1H, CH=), 5.20 (dt, *J*=5.4, 1.5 Hz, 2H, CH_2=), 5.06 (ddd, *J*=17.6, 13.8, 0.5 Hz, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.2 (C-4), 152.9 (C-2), 151.2 (C-2 in furyl), 150.1 (C-8), 145.2 (C-3 in furyl), 141.6 (C-6), 132.7 (CH=), 120.9 (C-5), 118.7 (CH_2=), 114.8 (C-3 in furyl), 113.3 (C-4 in furyl), 51.3 (NCH_2); MS EI *m*/*z* (rel %) 226 (100, M^+), 199 (6), 185 (7), 159 (2); HRMS (EI) calcd for $C_{12}H_{10}N_4O$: 226.0855. Found 226.0855.

*3.1.59. (±) (7aS,9S)-7a,8,9,11a-Tetrahydro-9,11a-epoxy-7H-pyrrolo[3,2,1-de]phenanthridine (**18a**).* A stirring solution of 1-allyl-7-(2-furyl)-1*H*-indole (**17a**) (160 mg, 0.72 mmol) in dry toluene (50 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with acetone/CH_2Cl_2/hexane (1:2:9); yield 110 mg (69%), colorless waxy material. ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 7.63 (d, *J*=7.9 Hz, 1H, H-1 or H-3), 7.31 (d, *J*=7.1 Hz, 1H, H-1 or H-3), 7.15 (m, 2H, H-4 or H-5 and H-2), 6.68 (dd, *J*=5.7, 1.7 Hz, 1H, H-10), 6.51 (d, *J*=3.0 Hz, 1H, H-4 or H-5), 6.40 (d, *J*=5.7 Hz, 1H, H-11), 5.11 (dd, *J*=4.5, 1.6 Hz, 1H, H-9), 4.45 (dd, *J*=12.0, 6.1 Hz, 1H, H-7_A), 3.67 (t, *J*=11.8 Hz, 1H, H-7_B), 2.39–2.18 (m, 1H, H-7a), 1.77 (dd, *J*=11.5, 7.5 Hz, 1H, H-8_A), 1.71–1.60 (m, 1H, H-8_B); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 140.3 (C-10), 136.9 (C-11), 136.1 (C-11b), 127.3 (C-2, C-4 or C-5), 121.5 (C-1 or C-3), 121.4 (C-1 or C-3), 120.4 (C-2, C-4 or C-5), 118.6 (C-3a), 101.7 (C-4 or C-5), 84.4 (C-11a), 80.7 (C-3a[1]), 79.4 (C-9), 48.9 (C-7), 35.8 (C-7a), 32.8 (C-8); MS EI *m*/*z* (rel %) 223 (100, M^+), 206 (10), 194 (42), 180 (36), 167 (12), 154 (35); HRMS (EI) calcd for $C_{15}H_{13}NO$: 223.0997. Found 223.0992.

*3.1.60. (±) (7aS,9S)-7a,8,9,11a-Tetrahydro-9,11a-epoxy-7H-benzo[f]pyrimido[4,5,6-hi]indolizine (**18b**).* A stirring solution of 5-allyl-4-(2-furyl)-5*H*-pyrrolo[3,2-*d*]pyrimidine (**17b**) (60 mg, 0.27 mmol) in dry toluene (10 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with acetone/hexane (1:1); yield 20 mg (33%), mp 200–202 °C (dec), colorless solid. ^{1}H NMR (CD_2Cl_2, 300 MHz) δ 9.02 (s, 1H, H-2), 7.52 (d, *J*=3.0 Hz, 1H, H-5), 6.71 (dd, *J*=5.8, 1.6 Hz, 1H, H-10), 6.65 (d, *J*=3.0 Hz, 1H, H-4), 6.51 (d, *J*=5.8 Hz, 1H, H-11), 5.23 (dd, *J*=4.4, 1.5 Hz, 1H, H-9), 4.53 (dd, *J*=12.2, 6.3 Hz, 1H, H-7_A), 3.79 (m, 1H, H-7_B), 2.59–2.35 (m, 1H, H-7a), 1.82 (m, 1H, H-8_A), 1.77–1.66 (m, 1H, H-8_B); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.8 (C-2), 149.7 (C-3a), 145.3 (C-11b), 140.2 (C-10), 134.8 (C-11), 133.8 (C-5), 127.8 (C-3a[1]), 102.4 (C-4), 84.6 (C-11a), 80.6 (C-9), 48.9 (C-7), 37.9 (C-7a), 32.6 (C-8); MS EI *m*/*z* (rel %) 225 (100, M^+), 208 (29), 196 (56), 182 (12), 170 (10), 157 (12); HRMS (EI) calcd for $C_{13}H_{11}N_3O$: 225.0902. Found 225.0904.

*3.1.61. 2-Chloro-6-(3-furyl)-4-nitroaniline (**19**).* A mixture of $Pd(OAc)_2$ (24 mg, 0.10 mmol), PPh_3 (130 mg, 0.500 mmol), 3-furylboronic acid (270 mg, 2.40 mmol), K_2CO_3 (800 mg, 5.97 mmol), and 2-bromo-6-chloro-4-nitroaniline (**1g**) (500 mg, 2.00 mmol) in EtOH (100 mL, 96%) was stirred at 85 °C for 16 h under Ar, and evaporated in vacuo. The product was purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (2:3); yield 385 mg (81%), yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz)

δ 8.21 (d, J=2.4 Hz, 1H, H-3), 8.03 (d, J=2.4 Hz, 1H, H-5), 7.71 (s, 1H, H-2 in furyl), 7.62 (s, 1H, H-5 in furyl), 6.75–6.49 (m, 1H, H-4 in furyl), 5.01 (s, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 146.8 (C-4), 144.4 (C-5 in furyl), 140.6 (C-2 in furyl), 138.4 (C-2), 124.7 (C-3), 124.4 (C-5), 121.3 (C-3 in furyl), 118.2 (C-1 or C-6), 118.2 (C-1 or C-6), 110.3 (C-4 in furyl); MS EI m/z (rel %) 240/238 (33/100, M^+), 221 (36), 192 (21); HRMS (EI) calcd for $C_{10}H_7ClN_2O_3$: 238.0145. Found 238.0139.

*3.1.62. N-Allyl-2-chloro-6-(3-furyl)-4-nitroaniline (**20**).* A solution of 2-chloro-6-(3-furyl)-4-nitroaniline (**19**) (360 mg, 1.50 mmol) and 15-crown-5-ether (0.60 mL, 3.0 mmol) in dry toluene (50 mL) at 0 °C was treated with NaH (120 mg, ca. 3.0 mmol, ca. 60% in mineral oil) and stirred for 10 min under Ar. Allyl bromide (0.19 mL, 2.3 mmol) was added and the mixture was stirred at ambient temperature for 5 h before water (50 mL) was added. The resulting mixture was extracted with EtOAc (2×50 mL), dried ($MgSO_4$), and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:1); yield 115 mg (28%), yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.19 (d, J=2.6 Hz, 1H, H-3 or H-5), 8.00 (d, J=2.6 Hz, 1H, H-3 or H-5), 7.70–7.63 (m, 1H, H-2 in furyl), 7.54 (d, J=1.7 Hz, 1H, H-5 in furyl), 6.64 (dd, J=1.7, 0.8 Hz, 1H, H-4 in furyl), 5.80–5.75 (m, 1H, CH=), 5.28–4.95 (m, 2H, CH_2=), 4.79 (s, 1H, NH), 3.80–3.44 (m, 2H, NCH_2); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 148.8 (C-1), 143.6 (C-5 in furyl), 140.6 (C-3 in furyl), 139.2 (C-4), 134.6 (CH=), 126.2 (C-3 or C-5), 124.5 (C-3 or C-5), 123.1 (C-3 in furyl), 122.7 (C-2 or C-6), 121.4 (C-2 or C-6), 117.0 (CH_2=), 110.9 (C-4 in furyl), 49.1 (NCH_2); MS EI m/z (rel %) 280/278 (33/100, M^+), 251 (36), 237 (13), 232 (14), 222 (8), 211 (7); HRMS (EI) calcd for $C_{13}H_{11}ClN_2O_3$: 278.0458. Found 278.0455.

*3.1.63. (±) (3S,5S)-11-Chloro-2,3,4,5-tetrahydro-9-nitro-5,12-epoxy-7,3-methano-1H-benzo[b]azonine (**21a**) and (±) (3R,5S)-11-chloro-2,3,4,5-tetrahydro-9-nitro-5,12-epoxy-7,3-methano-1H-benzo[b]azonine (**21b**).* A stirring solution of *N*-allyl-2-chloro-6-(3-furyl)-4-nitroaniline (**20**) (90 mg, 0.32 mmol) in dry toluene (20 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with EtOAc/CH_2Cl_2/hexane (1:2:7) followed by EtOAc/CH_2Cl_2/hexane (1:4:5); yield 53 mg (59%) of **21a**, and 10 mg (11%) of **21b**.

*3.1.63.1. (±) (3S,5S) 11-Chloro-2,3,4,5-tetrahydro-9-nitro-5,12-epoxy-7,3-methano-1H-benzo[b]azonine (**21a**).* Mp 220–221 °C, yellow solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.11 (d, J=2.5 Hz, 1H, H-10), 8.01 (d, J=2.5 Hz, 1H, H-8), 6.22 (d, J=1.0 Hz, 1H, H-6), 5.24 (s, 1H, NH), 5.22 (d, J=5.2 Hz, 1H, H-12), 5.15 (d, J=4.2 Hz, 1H, H-5) 3.70 (m, 1H, H-2_A), 2.97 (ddd, J=10.5, 5.2, 2.0 Hz, 1H, H-3), 2.78–2.46 (m, 1H, H-2_B), 2.13 (ddd, J=11.6, 7.9, 4.2 Hz, 1H, H-4_A), 1.07 (dd, J=11.6, 2.0 Hz, 1H, H-4_B); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 148.9 (C-11a), 143.4 (C-7), 139.1 (C-9), 129.1 (C-5), 123.5 (C-10), 123.1 (C-11), 122.0 (C-8), 119.7 (C-7a), 82.8 (C-12), 79.5 (C-5), 50.5 (C-2), 39.0 (C-3), 32.4 (C-4); MS EI m/z (rel %) 280/278 (31/100, M^+), 249 (48), 232 (13), 203 (32) HRMS (EI) calcd for $C_{13}H_{11}ClN_2O_3$: 278.0458. Found 278.0463.

*3.1.63.2. (±) (3R,5S)-11-Chloro-2,3,4,5-tetrahydro-9-nitro-5,12-epoxy-7,3-methano-1H-benzo[b]azonine (**21b**).* Yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.28 (d, J=2.6 Hz, 1H, H-8 or H-10), 8.18 (d, J=2.6 Hz, 1H, H-8 or H-10), 5.28 (s, 1H, NH), 4.69 (d, J=5.2 Hz, 1H, H-5), 4.67 (d, J=5.2 Hz, 1H, H-6), 3.88–3.66 (m, 1H, H-2_A), 3.61 (s, 1H, H-12), 3.32–3.11 (m, 1H, H-2_B), 2.98–2.79 (m, 1H, H-3), 2.20–1.87 (m, 1H, H-4_A), 1.42 (dd, J=12.3, 3.4 Hz, 1H, H-4_B); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 150.6 (C-11a), 139.6 (C-9), 124.3 (C-8), 123.1 (C-10), 121.5 (C-7a or 11), 120.5 (C-7a or 11), 78.1 (C-6), 75.8 (C-5), 60.3 (C-12), 59.0 (C-7), 49.2 (C-2), 43.0 (C-3), 31.8 (C-4); MS EI m/z 280/278 (rel %) (30/100, M^+), 249 (48), 232 (11), 203 (33); HRMS (EI) calcd for $C_{13}H_{11}ClN_2O_3$: 278.0458. Found 278.0460.

*3.1.64. N,N-Diallyl-2-chloro-6-(3-furyl)-4-nitroaniline (**22**).* A solution of 2-chloro-6-(3-furyl)-4-nitroaniline (**19**) (160 mg, 0.670 mmol) and 16-crown-8-ether (350 mg, 1.34 mmol) in dry toluene (100 mL) at ambient temperature under Ar was treated with KH (300 mg, ca. 2.60 mmol, ca. 35% in mineral oil) and stirred for 10 min. Allyl iodide (0.25 mL, 2.6 mmol) was added and the reaction mixture stirred for 5 h at 40 °C. Water (50 mL) was added, the mixture was extracted with EtOAc (2×50 mL), the combined organic extracts were washed with satd aq NaCl (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (1:3); yield 160 mg (75%), yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.16 (d, J=2.7 Hz, 1H, H-3 or H-5), 8.12 (d, J=2.7 Hz, 1H, H-3 or H-5), 7.89–7.84 (m, 1H, H-2 in furyl), 7.54 (d, J=1.8 Hz, 1H, H-5 in furyl), 6.73 (d, J=2.3 Hz, 1H, H-4 in furyl), 5.79 (ddt, J=16.9, 10.0, 6.8 Hz, 2H, CH=), 5.30–4.95 (m, 4H, CH_2=), 3.71 (d, J=6.8 Hz, 4H, NCH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.1 (C-1), 143.8 (C-4), 143.3 (C-5 in furyl), 141.4 (C-2 in furyl), 134.5 (C-2 or C-3 in furyl), 134.3 (CH=), 134.0 (C-2 or C-3 in furyl), 124.8 (C-3 or C-5), 123.6 (C-3 or C-5), 123.1 (C-6), 118.4 (CH_2=), 110.5 (C-4 in furyl), 55.1 (NCH_2); MS EI m/z (rel %) 320/318 (26/80, M^+), 291 (25), 283 (13), 277 (89), 251 (14), 41 (100); HRMS (EI) calcd for $C_{16}H_{15}ClN_2O_3$: 318.0771. Found 318.0768.

*3.1.65. (±) (3S,5S) 1-Allyl-11-chloro-2,3,4,5-tetrahydro-9-nitro-5,12-epoxy-7,3-methano-1H-benzo[b]azonine (**23**).* A stirring solution of *N*,*N*-diallyl-2-chloro-6-(3-furyl)-4-nitroaniline (**22**) (77 mg, 0.27 mmol) in dry toluene (30 mL) was heated at 100 °C for 24 h under Ar, cooled to ambient temperature and concentrated in vacuo. The product was purified by flash chromatography on silica gel eluting with CH_2Cl_2/hexane (3:7) followed by EtOAc/CH_2Cl_2/hexane (1:7:12); yield 60 mg (86%), yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.15 (d, J=2.7 Hz, 1H, H-10), 8.02 (d, J=2.7 Hz, 1H, H-8), 6.28 (d, J=1.0 Hz, 1H, H-6), 6.21–5.95 (m, 1H, CH=), 5.45–5.33 (m, 2H, CH_2=), 5.19 (d, J=4.2 Hz, 1H, H-5), 5.04 (d, J=5.0 Hz, 1H, H-12), 4.26–4.09 (m, 1H, NCH_2), 3.78 (dd, J=15.2, 8.7 Hz, 1H, CH_2), 3.62 (dd, J=14.7, 7.2 Hz, 1H, H-2_A), 2.97 (ddd, J=10.2, 5.3, 2.6 Hz, 1H, H-3), 2.28 (dd, J=14.7, 11.0 Hz, 1H, H-2_B), 2.12 (ddd, J=11.6, 8.0, 4.3 Hz, 1H, H-4_A), 1.04 (dd, J=11.6, 2.0 Hz, 1H, H-4_B); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.7 (C-11a), 144.3 (C-7), 141.7 (C-9), 134.5 (CH=), 132.0 (C-7a), 130.6 (C-6), 128.2 (C-11), 125.0 (C-10), 121.3 (C-8), 119.3 (CH_2=), 83.3 (C-12), 79.7 (C-5), 55.3 (NCH_2), 52.2 (C-2), 36.8 (C-3), 32.2 (C-4); MS EI m/z (rel %) 320/318 (33/100, M^+), 291 (23), 283 (12), 277 (100); HRMS (EI) calcd for $C_{16}H_{15}ClN_2O_3$: 318.0771. Found 318.0768.

3.2. Computational details

All structures (minima and transition states) were fully optimized at the gradient corrected density functional theory (DFT) level using the exchange-correlation functional of Perdew, Burke, and Ernzerhof[16] making use of the resolution of the identity approximation.[17] The basis sets that were used were the Weigend–Ahlrichs basis sets denoted def2-SVP and def2-TZVPP[18] and the corresponding fitting basis.[19] The influence of the basis set size on the structures and relative energies for significant steps in the mechanism was tested and it was found that the influence was minor. Therefore all structures presented were obtained using the def2-SVP basis set in combination with the PBE functional (denoted as PBE/def2-SVP). This methodology was also found to be reliable for the given purpose in comparison to RI-MP2/def2-TZVPP for the basic mechanism.[20] Analytic Hessians were used to characterize the nature of the stationary points on the potential energy surface.[21] All energy, gradient, and hessian calculations were performed using

the Turbomole program package.[22] All computations were performed on the Stallo supercomputer located at the University of Tromsø, Norway.

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References and notes

1. See for instance: Kappe, C. O.; Murphree, S. S.; Padwa, A. *Tetrahedron* **1997**, *53*, 14179–14233 and references sited therein.
2. Selected recent examples: (a) Li, C.-C.; Liang, S.; Zhang, X.-H.; Xie, Z.-X.; Chen, J.-H.; Wu, Y.-D.; Yang, Z. *Org. Lett.* **2005**, *7*, 3709–3712; (b) Wang, Q.; Padwa, A. *Org. Lett.* **2006**, *8*, 601–604; (c) Lauchli, R.; Shea, K. J. *Org. Lett.* **2006**, *8*, 5287–5289; (d) Sarang, P. S.; Yadav, A. A.; Patil, P. S.; Krishna, U. M.; Trivedi, G. K.; Salunkhe, M. M. *Synthesis* **2007**, 1091–1095; (e) Jung, M. E.; Min, S.-J. *Tetrahedron* **2007**, *63*, 3682–3701; (f) Bobeck, D. R.; France, S.; Leverett, C. A.; Sanchez-Cantalejo, F.; Padwa, A. *Tetrahedron Lett.* **2009**, *50*, 3145–3147; (g) Zubkov, F. I.; Ershova, J. D.; Zaytsev, V. P.; Obushak, M. D.; Matiychuck, V. S.; Sokolova, E. A.; Khrustalev, V. N.; Varlamov, A. V. *Tetrahedron Lett.* **2010**, *51*, 6822–6824.
3. Vik, A.; Gundersen, L.-L. *Tetrahedron Lett.* **2007**, *48*, 1931–1934.
4. (a) Østby, O. B.; Dalhus, B.; Gundersen, L.-L.; Rise, F.; Bast, A.; Haenen, G. R. M. M. *Eur. J. Org. Chem.* **2000**, *9*, 3763–3770.
5. See for instance: Molander, G. A.; Canturk, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 9240–9261 and references sited therein.
6. Khoje, A. D.; Gundersen, L.-L. *Tetrahedron Lett.* **2011**, *52*, 523–525.
7. For a recent example, see for instance: Dadwal, M.; Kesharwani, M. K.; Danayak, V.; Ganguly, B.; Mobin, S. M.; Muruganantham, R.; Namboothiri, I. N. N. *Eur. J. Org. Chem.* **2008**, 6106–6118 and references sited therein.
8. For a recent example, see for instance: Nakamura, M.; Takahashi, I.; Yamada, S.; Dobashi, Y.; Kitagawa, O. *Tetrahedron Lett.* **2011**, *52*, 53–55 and references sited therein.
9. Jähne, G.; Kroha, H.; Müller, A.; Helsberg, M.; Winkler, I.; Gross, G.; Scholl, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 562–563.
10. Schrauzer, G. N. *Inorg. Synth.* **1968**, *11*, 61–70.
11. Youn, S. W.; Bihn, J. H. *Tetrahedron Lett.* **2009**, *50*, 4598–4601.
12. Whittaker, N.; Jones, T. S. G. *J. Chem. Soc.* **1951**, 1565–1570.
13. Read, M. L.; Brændvang, M.; Miranda, P. O.; Gundersen, L.-L. *Bioorg. Med. Chem.* **2010**, *18*, 3885–3897.
14. Nielsen, L. B.; Slamet, R.; Wege, D. *Tetrahedron* **2009**, *65*, 4569–4577.
15. Gundersen, L.-L.; Nissen-Meyer, J.; Spilsberg, B. *J. Med. Chem.* **2002**, *45*, 1383–1386.
16. Perdew, P.; Burke, K.; Ernzerhof, M. *Phys. Rev. Lett.* **1996**, *77*, 3865–3868.
17. Eichkorn, K.; Treutler, O.; Oehm, H.; Haeser, M.; Ahlrichs, R. *Chem. Phys. Lett.* **1995**, *242*, 652–660.
18. Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305.
19. Weigend, F. *Phys. Chem. Chem. Phys.* **2006**, *8*, 1057–1065.
20. (a) Weigend, F.; Häser, M. *Theor. Chem. Acc.* **1997**, *97*, 331–340; (b) Weigend, F.; Häser, M.; Patzelt, H.; Ahlrichs, R. *Chem. Phys. Lett.* **1998**, *294*, 143–152.
21. Deglmann, P.; Furche, F.; Ahlrichs, R. *Chem. Phys. Lett.* **2002**, *362*, 511–518.
22. TURBOMOLE V6.2, a development of University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, 1989–2007, TURBO MOLE GmbH; available from: http://www.turbomole.com.