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Reduction of 4*H*-chromen-4-ylidene amines: synthesis of 2-[(1-aminoalkyl)-3-aryl-2-propenyl] phenols

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Abstract—A procedure for the reduction of 4*H*-chromen-4-ylidene amines **1** is described, which affords to 2-[(1-aminoalkyl)-3-aryl-2-propenyl] phenols **2**, previously unknown in literature. The efficacy of the procedure is compared with alternative synthetic routes.

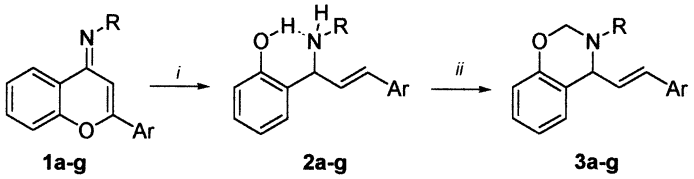
1. Introduction

4*H*-Chromen-4-ylidene amines **1** are a restricted group of derivatives of flavones, almost absent from the literature, that have awoken a new interest because the most simple of them, (2-phenyl-4*H*-chromen-4-imine), has been the subject of patents[1,2] for treatment of cell proliferative diseases and for its anti hypoxic, hypotensive, and anti-allergic properties. During the course of our studies we have developed a new synthetic methodology to access this class of compounds.[3] Moreover preliminary experiments showed that the reduction of **1** gave aminoalkyl phenols **2**, widely studied compounds as chiral auxiliaries in important stereoselective reactions,[4,5] that we have applied mainly as pre-catalysts in the enantioselective addition of dialkylzinc reagents to aldehydes.[6,7] In addition, the aminoalkyl phenols **2** are intermediate in the synthesis of 3,4-dihydro-2*H*-1,3-benzoxazines, which show very important biological and pharmacological activities.[8–10] Thus in the aim to explore the reactivity of 4*H*-chromen-4-ylidene amines **1**, we have extended our attention to the reduction of a series of these substrates.

2. Results

When 4*H*-chromen-4-ylidene amines **1** are dissolved in methanol and treated with sodium borohydride, an immediate fading of the general original yellow coloration is observed. After workup a single product is isolated, that proved to be aminoalkyl phenol **2**, deriving from a double process of reduction and ring opening. Products **2** were then treated with formaldehyde to form the corresponding benzoxazine **3** (Scheme 1).

A reduction mechanism in two steps is proposed in Scheme 2, on the basis of pre-existing literature.[6] The transfer of an hydride atom from the trimethoxyborohydride species, formed in methanolic solution, to C-2 atom of chromenylidene amines **1** takes place with the formation of the anion **4**. A subsequent opening of the pyran ring takes place, favoured from a second trimethoxyborohydride species, with the formation of the intermediate **6**. Then the imine bond in the species **6** is intramolecularly reduced affording **2**. All the aminoalkyl phenols **2** contains a *trans* C=C bond geometry.



1a-g **2a-g** **3a-g**

Scheme 1. *i*: $NaBH_4$, 2.5 mol, MeOH, r.t., 15–60 min; *ii*: 37% aq. CH_2O, THF, r.t., 2h.

Keywords: chromenes; reduction; allylamines; benzoxazines; aldol condensation.
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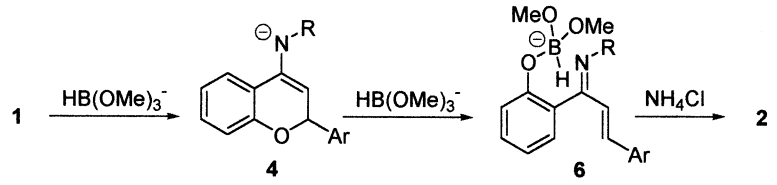


Scheme 2.

Table 1. Reduction of 4*H*-chromen-4-ylideneamine **1** and cyclization of aminoallylphenol **2** to benzoxazine **3**

Entry	1	R	Ar	2	Yield (%)[a]	3	Yield (%)[a]
1	**1a**	Me	Ph	**2a**	50	**3a**	80
2	**1b**	Pr^i	Ph	**2b**	66	**3b**	78
3	**1c**	Bn	Ph	**2c**	87	**3c**	81
4	**1d**	Ph	Ph	**2d**	0		
5	**1e**	R*[b]	Ph	(*R*,*R*)-**2e**	89[c]	(4*S*,1′*R*)-**3e**	76
6	**1f**	Me	*p*-MeO–Ph	**2f**	92	**3f**	92
7	**1g**	Pr^i	*p*-MeO–Ph	**2g**	73	**3g**	88

[a] Chromatographic isolated yields.
[b] R*-NH_2=(*R*)-(+)-1-phenylethylamine (99% ee).
[c] $NaBH_4$/MeOH, rt 0.5 h dr=62/38; $NaBH(MeO)_3$/THF, 0°C, 1 h, dr=76/24.

All reactions gave good overall yields, as reported in Table 1 except chromylidene amine **1d** (R=Ar=Ph, entry 4) which was recovered after a prolonged reaction time (24 h).

Semiempirical calculations[11] (see Fig. 1) show that the intermediate (1,4)-**4d**, deriving from 1,4-addition, is at lower energies with respect to (1,2)-**4d** resulting from 1,2-addition and this may be an indirect confirmation of the proposed mechanism hypothesis. Calculations also show that in **1d** both the phenyl groups bonded to the nitrogen atom and to C-2 are not coplanar with respect to the plane containing the conjugate O–C=C–C=N unsaturated system, but have a dihedral angle of +65 and +45°, respectively. Moreover in **1d** the phenyl rings exert a steric effect that prevents C-2 from attack by trimethoxyborohydride, although the resulting intermediate (1,4)-**4d** is stabilized by the presence of the phenyl ring with respect to the corresponding intermediate (1,4)-**4a**.

The reduction of starting material **1e** (R=(*R*)-α-phenylethyl, Ar=Ph, entry 5) results in a moderate diastereoselectivity (dr=62/38) if performed in the same conditions of the other. The diastereoselectivity increases by pre-forming a stoichiometric amount of sodium trimethoxyborohydride in THF at 0°C (dr=76/24, see Section 4).

The synthesis of aminoallylphenol **2** has been compared to an alternative pathway to evaluate its synthetic utility. Based on our previous experience[6] product **2** should be obtained by reduction of the corresponding imidoyl phenol **7**. The synthesis of imidoyl phenol **7c** was tried, but, despite its simple structure **7c** was not obtained, as reported in Scheme 3.

The synthesis of **7c** has been attempted in different ways. First of all the classical direct condensation of benzylamine with chalcone **8** in the presence of acid catalyst and with

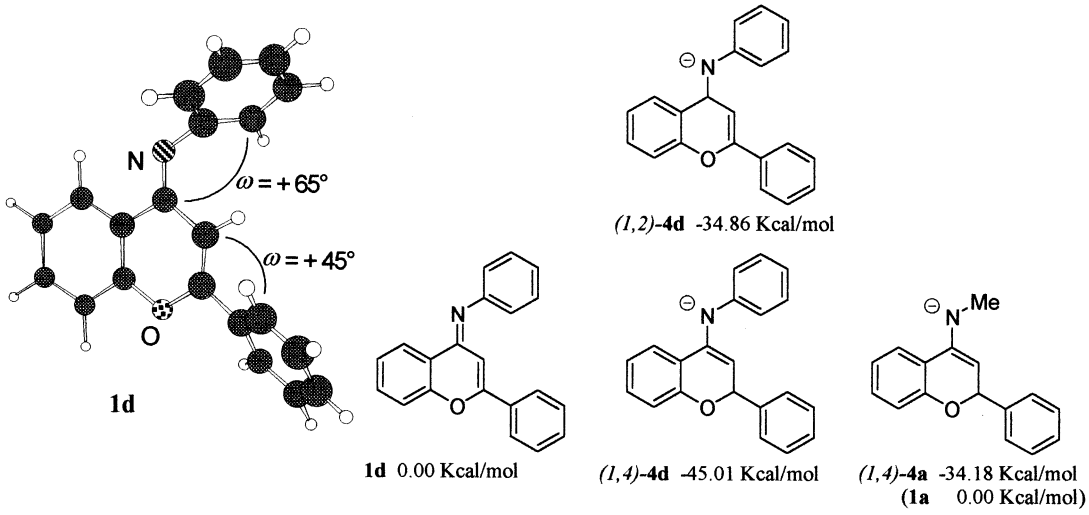
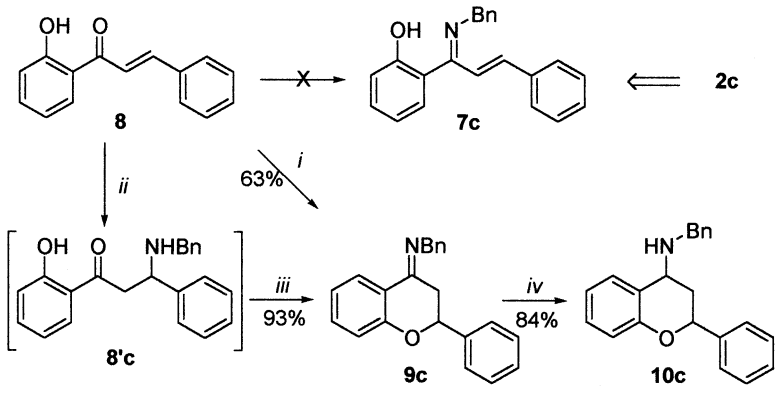


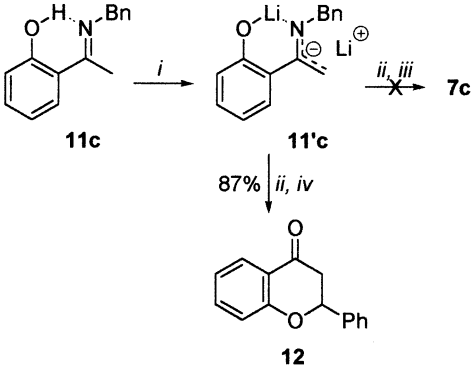
Figure 1. The calculated (PM3 semiempirical minimization) preferred conformations for the chromenylideneamine **1d** and the relative stability of the ipotized intermediates (1,2)- and (1,4)-**4a**,**d**.



Scheme 3. *i*: H_2N-Bn, 1.5 mol, H^+, C_6H_6, reflux; *ii*: H_2N-Bn, 1.1 mol, r.t., 3 h; *iii*: MeOH, r.t.; *iv*: $NaBH_4$, 1.5 mol, MeOH, r.t.

azeotropic removal of the water was tried[12–14] (Scheme 3, reaction conditions (i)). This reaction resulted only in 63% yield of product **9c**; no trace of **7c** was found. A second attempt was made using our direct solventless procedure[15] of preparation of imidoyl phenols (Scheme 3, reaction conditions (ii)). In this case, after 3 h, ^{1}H-NMR of the crude mixture revealed the presence of a major product probably due to 1,4 attack of amine on chalcone (**8′c**), but all attempts to isolate and attribute a defined structure to it failed. When the crude oil obtained in this way was dissolved in methanol an orange crystalline solid precipitated, showing a different ^{1}H NMR spectrum, to which structure **9c** was attributed and confirmed through reduction of **9c** with $NaBH_4$ in methanol to amine **10c**.

As product **10c** has been prepared only once in literature[16] and in poor yield (24%) too, several attempts to make this route more general were made, but the reaction performed with amines other than benzylamine failed. The solventless mixing of chalcone **8** with isopropylamine, α-methylbenzylamine, *n*-butyl- and *n*-pentylamine, either at room temperature or at the amine refluxing temperature, does not result in a major product, but only in mixtures of iminoflavones **9** and α,β-unsaturated imidoyl phenols **7** in proportions depending on the amine used, varying from **9/7**=37/63 to **9/7**=54/46. Moreover in all the reaction mixtures some 18–32% of flavanone **12** was found. The chromatographic separation on silica gel of these products resulted in their decomposition and afforded to flavanone **12** and chalcone **8** mixtures in poor yields.



Scheme 4. *i*: LiTMP, 2.5 mol, THF, 0°C, 1h; *ii*: PhCHO, 1.5 mol; *iii*: aq NH_4Cl, pH 6; *iv*: 2M HCl, pH 2.

Finally we tried the synthesis of **7c** by an aldol type condensation between benzaldehyde and imidoyl phenol **11c** through the lithium dianion (**11′c**), but this resulted in the recovery of unreacted starting material or in the production of flavanone **12** depending on the pH of the quenching solution, as shown in Scheme 4.

3. Conclusion

These experimental results show that 4*H*-chromen-4-ylideneamines **1** are useful precursors for the synthesis of aminoallylphenols **2**, through a classical reduction procedure with sodium borohydride in methanol. Although this sequence might seem complex, here is demonstrated that aminoallylphenols **2** cannot be obtained through simpler synthetic pathways. The reaction yields to *trans* double bonds products only and is a practical access to aminoallyl phenols **2**, previously unknown in literature.

Moreover during an alternative synthesis of products **2**, imino flavone **9c**, previously unknown in literature, was obtained selectively and in high yields by an isomerization process favored by its spontaneous crystallization in methanol.

4. Experimental

4.1. General methods

^{1}H- and ^{13}C NMR spectra were recorded with a Varian VXR 300 instrument. Chemical shifts are given in ppm downfield from Me_4Si in $CDCl_3$ solution. Coupling constants are given in Hertz. IR spectra were recorded with a Perkin–Elmer 257 spectrometer. GC–MS analyses were performed with an HP 59970 workstation formed by an HP-5890 gas chromatograph equipped with a methyl silicone capillary column and by an HP-5970 mass detector. All melting points are uncorrected. THF was dried by refluxing over sodium wire until the blue color of benzophenone ketyl persisted and then distilled into a dry receiver under a nitrogen atmosphere. All reagents and solvents were distilled prior to use or were of commercial quality.

Starting materials **1a–g** were prepared as previously

reported[3] using lithium tetramethylpiperidide instead of LDA as base. Spectral data of starting material **1e** follows:

4.1.1. (1*R*)-1-Phenyl-*N*-(2-phenyl-4*H*-chromen-4-ylidene)-ethan-1-amine (1e). Oil; [Found: C, 84.74; H, 5.81; N, 4.31%. $C_{23}H_{19}NO$ requires: C, 84.89; H, 5.89; N, 4.30%]. ν_{max} (liquid film) 1638, 1569, 1427, 1361, 1043, 819, 760 cm^{-1}: δ_H (300 MHz, $CDCl_3$) 1.67 (d, 3H, *J*=6.6 Hz, *Me*), 5.00 (q, 1H, *J*=6.6 Hz, C*H*Me), 6.80 (s, 1H, C*H*=), 7.25–8.60 (m, 14H, *Ar*); δ_C (300 MHz, $CDCl_3$) 25.73, 58.44, 97.36, 117.86, 125.18, 125.38, 126.27, 126.35, 126.93, 127.17, 127.69, 128.79, 128.90, 129.24, 130.92, 131.45, 131.64, 153.81, 189.84; MS (EI, 70 eV) *m/z* (%) 325 (M^+, 16), 310 (100), 248 (12), 206 (11), 105 (14), 77 (15).

4.2. General procedure for the reduction of 4*H*-chromen-4-ylidene amines 1 to aminoallyl phenols 2

In a 50 mL round bottom reaction flask, equipped with magnetic stirring, the orange–yellow starting materials **1a–g** (2 mmol) were dissolved in methanol (5 mL) at 0°C. Sodium borohydride (0.151 g, 4 mmol) was then added in portions to the solution over 5 min. Immediate hydrogen evolution and heating of the mixture are observed, with a simultaneous fading of the original coloration of the solution, until a pale yellow color was reached. The reaction was monitored by TLC (ethyl acetate/*n*-hexane=50/50) and after a variable time (15–60 min) the starting material was consumed. The reaction mixture was treated with 1 mL of saturated aqueous ammonium chloride and the solvent evaporated under reduced pressure then the residue was dissolved in water and extracted with CH_2Cl_2 (2×50 mL). The organic fractions were then mixed, dried with anhydrous sodium sulfate and evaporated under reduced pressure. Chromatographic separation of the crude oil obtained, using cyclohexane/ethyl acetate=60/40 as eluent, afforded to the aminoalkyl phenols **2a–c,e–g** in 50–92% yields.

Reduction of **1e** was also performed by an alternative procedure: sodium borohydride (0.151 g, 4 mmol) was added to a mixture of methanol (0.5 mL, 12 mmol) and THF (5 mL). Starting material **1e** was then added and the reaction monitored by TLC until it was consumed. Workup was as reported above. Diastereoselectivity of reduction of **1e** was determined on the basis of ^1H NMR spectra of the crude mixtures obtained as reported above.

4.2.1. 2-[(*E*)-2-(1-Methylamino)-3-phenylprop-2-enyl]-phenol (2a). Oil; [Found: C, 80.44; H, 7.35; N, 5.68%. $C_{16}H_{17}NO$ requires: C, 80.30; H, 7.16; N, 5.85%]; ν_{max} (liquid film) 3031, 1400, 1259, 965, 755, 693 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 2.01 (br s, 1H, N*H*), 2.50 (s, 3H, *Me*), 4.40 (d, 1H, *J*=8.0 Hz, C*H*N), 6.42 (dd, 1H, *J*=15.8, 8.0 Hz, CHC*H*=), 6.62 (d, 1H, *J*=15.8 Hz, =C*H*Ph), 6.80–7.50 (m, 9H, *Ar*), 11.43 (br s, 1H, O*H*). δ_C (300 MHz, $CDCl_3$) 34.08, 68.34, 117.45, 119.83, 124.70, 127.16, 128.49, 128.91, 129.17, 129.22, 129.45, 136.88, 132.73, 158.14. MS (EI, 70 eV) *m/z* (%) 208 (M^+, 72), 207 (100), 178 (17), 131 (58).

4.2.2. 2-[(*E*)-2-(1-Isopropylamino)-3-phenylprop-2-enyl]-phenol (2b). Oil; [Found: C, 80.78H, 7.75; N, 5.48% $C_{18}H_{21}NO$ requires: C, 80.86; H, 7.92; N, 5.24%.] ν_{max} (liquid film) 2966, 1628, 1466, 1371, 1340, 1258, 966, 755, 694 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 1.17 (d, 3H, *J*=6.3 Hz, Me_a), 1.19 (d, 3H, *J*=6.3 Hz, Me_b), 1.35 (br s, 1H, N*H*), 2.98 (sept, 1H, *J*=6.3 Hz, C*H*$(Me)_2$), 4.65 (d, 1H, *J*=8.0 Hz, C*H*N), 6.38 (dd, 1H, *J*=15.8, 8.0 Hz, CHC*H*=), 6.59 (d, 1H, *J*=15.8 Hz, =C*H*Ph), 6.68–7.60 (m, 9H, *Ar*), 10.78 (br s, 1H). δ_C (300 MHz, $CDCl_3$) 22.98, 23.28, 46.51, 63.64, 117.51, 119.70, 126.09, 126.84, 127.08, 128.82, 129.10, 129.29, 129.57, 132.36, 136.85, 158.35.

4.2.3. 2-[(*E*)-2-(1-Benzylamino)-3-phenylprop-2-enyl]-phenol (2c). Oil; [Found: C, 83.64; H, 6.64; N, 4.68% $C_{22}H_{21}NO$ requires: C, 83.78; H, 6.71; N, 4.44%]. ν_{max} (liquid film) 3027, 1256, 1028, 961, 768, 692 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 2.25 (br s, 1H, N*H*), 3.82, (d, 1H, *J*=13.1 Hz, CH_aH_bPh), 3.92 (d, 1H, *J*=13.1 Hz, CH_aH_bPh), 4.58 (d, 1H, *J*=7.7 Hz, C*H*N), 6.45 (dd, 1H, *J*=15.8, 7.7 Hz, CHC*H*=), 6.60 (d, 1H, *J*=15.8 Hz, =C*H*Ph), 6.85–7.65 (m, 14H, *Ar*, 11.43 (br s, 1H, O*H*); δ_C (300 MHz, $CDCl_3$) 51.59, 65.83, 117.50, 119.92, 124.51, 127.06, 128.10, 128.43, 128.95, 129.06, 129.11, 129.18, 129.23, 129.48, 132.75, 136.73, 138.78, 157.87; MS (EI, 70 eV) *m/z* (%) 208 (67), 207 (100), 178 (12), 131 (55).

4.2.4. 2-((1*R*,2*E*)-3-Phenyl-1-{[(1′*R*)-1′-phenylethyl]amino}-prop-2-enyl)phenol [(*R*,*R*)-2e]. White crystals mp 93–95°C (hexane); [Found: C, 83.78; H, 6.97; N, 4.31%. $C_{23}H_{23}NO$ requires: C, 83.85; H, 7.04; N, 4.25%]. ν_{max} (Nujol) 3027, 1588, 1493, 1256, 1098, 964, 832, 757, 700 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 1.48 (d, 3H, *J*=6.7 Hz, *Me*), 2.15 (br s, 1H, N*H*), 3.82 (br q, 1H, *J*=6.7 Hz, C*H*Me), 4.23–4.30 (m, 1H, C*H*N), 6.31–6.40 (m, 1H, CHC*H*=), 6.43 (d, 1H, *J*=12.9 Hz, =C*H*Ph), 6.76–7.46 (m, 14H, *Ar*), 11.70 (br s, 1H, O*H*); δ_C (300 MHz, $CDCl_3$) 23.40, 54.99, 63.33, 116.95, 119.45, 123.94, 126.40, 126.55, 127.60, 127.88, 128.54, 128.59, 128.85, 128.90, 129.07, 131.49, 136.26, 143.39, 157.70. $[\alpha]^D_{20}=-151.5$ (*c*=1.18, $CHCl_3$).

4.2.5. 2-((1*S*,2*E*)-3-Phenyl-1-{[(1′*R*)-1′-phenylethyl]amino}-prop-2-enyl)phenol [(1*S*,1′*R*)-2e]. Spectral data of this product are obtained from enriched chromatographic fraction spectra. ν_{max} (Nujol) 3031, 1583, 1502, 1248, 1092, 963, 828, 757, 700 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 1.49 (d, 3H, *J*=6.7 Hz, *Me*), 2.15 (br s, 1H, N*H*), 4.04 (q, 1H, *J*=6.7 Hz, C*H*Me), 4.42 (d, 1H, *J*=8.5 Hz, C*H*N), 6.30 (dd, 1H, *J*=15.9, 8.5 Hz, CHC*H*=), 6.43 (d, 1H, *J*=15.9 Hz, =C*H*Ph), 6.70–7.50 (m, 14H, *Ar*), 11.70 (br s, 1H, O*H*); δ_C (300 MHz, $CDCl_3$) 23.93, 55.48, 62.71, 117.43, 119.69, 119.92, 126.86, 127.02, 127.26, 127.37, 128.08, 128.35, 128.48, 129.00, 129.36, 134.04, 136.76, 143.88, 158.16.

4.2.6. 2-[(*E*)-2-(4-Methoxyphenyl)-(1-methylamino)-prop-2-enyl]phenol (2f). Oil; [Found: C, 75.59; H, 7.08; N, 5.02%. $C_{17}H_{19}NO_2$ requires: C, 75.81; H, 7.11; N, 5.20%] ν_{max} (liquid film) 3013, 1315, 1211, 756, 648 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 2.47 (s, 3H, *Me*), 3.80 (s, 3H, O*Me*), 3.84 (br s, 1H, N*H*), 4.35 (d, 1H, *J*=8.1 Hz, C*H*N), 6.24 (dd, 1H, *J*=15.7, 8.1 Hz, CHC*H*=), 6.53 (d, 1H, *J*=15.7 Hz, =C*H*Ph), 6.70–7.40 (m, 8H, *Ar*) 11.80 (br s, 1H,

O*H*); δ_C (300 MHz, $CDCl_3$) 33.57, 55.30, 68.03, 113.98, 116.85, 119.17, 125.86, 126.50, 127.79, 128.62, 128.66, 128.79, 131.71, 157.80, 159.75.

4.2.7. 2-[(*E*)-2-(1-Isopropylamino)-3-(4-methoxyphenyl)-prop-2-enyl]phenol (2g). Oil; [Found: C, 76.48; H, 7.61; N, 4.68%. $C_{19}H_{23}NO_2$ requires: C, 76.73; H, 7.80; N, 4.71%]. ν_{max} (liquid film) 3021, 1348, 1232, 756, 681 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 1.14 (d, 3H, *J*=6.3 Hz, Me_a), 1.17 (d, 3H, *J*=6.3 Hz, Me_b), 2.94 (sept, 1H, *J*=6.3 Hz, C*H*$(Me)_2$), 3.52 (br s, 1H, N*H*), 3.80 (s, 3H, O*Me*), 4.60 (d, 1H, *J*=8.2 Hz, C*H*N), 6.22 (dd, 1H, *J*=15.7, 8.2 Hz, CHC*H*=), 6.51 (d, 1H, *J*=15.7 Hz, =C*H*C_6H_4OMe), 6.70–7.40 (m, 8H, *Ar*), 11.15 (br s, 1H, O*H*); δ_C (300 MHz, $CDCl_3$) 22.49, 22.79, 43.36, 63.26, 66.27, 113.98, 119.12, 126.55, 126.75, 127.75, 128.23, 128.36, 128.53, 128.67, 142.56, 159.41, 171.49.

4.3. General procedure for the synthesis of benzoxazine 3

Aminoalkyl phenols **2a**–**c** and **e**–**g** (2 mmol) were dissolved in THF (5 mL), and then 37% wt aqueous formaldehyde (0.30 mL, 4 mmol) was added. The reaction was monitored by TLC until the starting material **2** was consumed (1–2 h). The reaction mixture was added to 50 mL of CH_2Cl_2, the organic layer was dried with anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The residue was filtered on a thin pad of silica gel (cyclohexane/ethyl acetate=70/30). Benzoxazines **3** were obtained in 76–92% yield.

4.3.1. 3-Methyl-4-[(*E*)-2-phenylethenyl]-3,4-dihydro-2*H*-1,3-benzoxazine (3a). Oil; [Found C, 81.18; H, 6.98; N, 5.68%. $C_{17}H_{17}NO$ requires: C, 81.24; H, 6.82; N, 5.57%]. ν_{max} (liquid film) 3026, 1581, 1487, 1453, 1230, 935, 755, 693 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.65 (s, 3H, *Me*), 4.31 (br d, 1H, *J*=2.9 Hz, C*H*N), 4.65 (dd, 1H, J_{ab}=9.7, $J_{1,5}$=1.3 Hz, CH_aH_b), 4.94 (d, 1H, J_{ab}=9.7 Hz, CH_aH_b), 6.32–6.48 (m, 2H, C*H*=C*H*), 6.77–7.50 (m, 9H, *Ar*); δ_C (300 MHz, $CDCl_3$) 40.35, 62.20, 80.54, 117.15, 120.90, 127.02, 127.51, 128.21, 128.69, 129.05, 129.95, 131.67, 133.66, 137.10, 154.00.

4.3.2. 3-Isopropyl-4-[(*E*)-2-phenylethenyl]-3,4-dihydro-2*H*-1,3-benzoxazine (3b). Oil; [Found: C, 81.41; H, 7.52; N, 4.97%. $C_{19}H_{21}NO$ requires: C, 81.68; H, 7.58; N, 5.01%]. ν_{max} (liquid film) 2966, 1582, 1487, 1450, 1231, 1178, 930, 754, 692 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 1.22 (d, 3H, *J*=6.4 Hz, Me_a), 1.27 (d, 3H, *J*=6.4 Hz, Me_b), 3.22 (sept, 1H, *J*=6.4 Hz, C*H*Me_aMe_b), 4.59 (d, 1H, *J*=4.0 Hz, C*H*N), 4.96–5.00 (m, 2H, CH_2), 6.39 (d, 1H, *J*=15.0 Hz, =C*H*Ph), 6.49 (dd, 1H, *J*=4.0, 15.0 Hz, CHC*H*=), 6.80–7.50 (m, 9H, *Ar*); δ_C (300 MHz, $CDCl_3$) 21.84, 22.62, 51.96, 56.74, 77.09, 117.39, 120.58, 122.93, 127.02, 128.05, 128.41, 129.04, 129.61, 132.33, 132.83, 137.38, 155.57.

4.3.3. 3-Benzyl-4-[(*E*)-2-phenylethenyl]-3,4-dihydro-2*H*-1,3-benzoxazine (3c). Oil; [Found: C, 84.25; H, 6.31; N, 4.24%. $C_{23}H_{21}NO$ requires: C, 84.37; H, 6.46; N, 4.28%] ν_{max} (liquid film) 3027, 1487, 1453, 1219, 942, 831, 756, 694 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 3.94 (d, 1H, J_{cd}=13.8 Hz, CH_cH_dPh), 4.12 (d, 1H, J_{cd}=13.8 Hz, CH_cH_dPh), 4.41 (br d, 1H, *J*=4.3 Hz, C*H*N), 4.77 (dd, 1H, J_{ab}=10.1, $J_{1,5}$=1.6 Hz, OCH_aCH_b), 5.07 (d, 1H, J_{ab}=10.1 Hz, OCH_aCH_b), 6.33 (d, 1H, *J*=16.8 Hz, =C*H*Ph), 6.47 (dd, 1H, *J*=4.3, 16.8 Hz, CHC*H*=), 6.90–7.50 (m, 14H, *Ar*); δ_C (300 MHz, $CDCl_3$) 56.00, 58.46, 78.32, 116.83, 120.42, 120.64, 126.55, 127.43, 127.67, 128.27, 128.52, 128.57, 128.82, 129.76, 131.92, 132.69, 136.79, 138.37, 154.02.

4.3.4. (4*S*)-4-[(*E*)-2-Phenylethenyl]-3-[(1′*R*)-1′-phenylethyl]-3,4-dihydro-2*H*-1,3-benzoxazine [(4*S*,1′*R*)-3e]. Oil. [Found: C, 84.38; H, 6.62; N, 4.03%. $C_{24}H_{23}NO$ requires: C, 84.42; H, 6.79; N, 4.10%].%]. ν_{max} (liquid film) 3050, 1461, 1453, 1225, 938, 847, 748, 688 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 1.54 (d, 3H, *J*=6.6 Hz, *Me*), 4.03 (q, 1H, *J*=6.6 Hz, C*H*Me), 4.31 (br d, 1H, *J*=4.2 Hz, C*H*N), 5.08 (d, 1H, J_{ab}=10.3 Hz, OCH_aCH_b), 5.19 (dd, 1H, $J_{1,5}$=1.8, J_{ab}=10.3 Hz, OCH_aCH_b), 6.23 (d, 1H, *J*=16.0 Hz, =C*H*Ph), 6.37 (dd, 1H, *J*=4.2, 16.0 Hz, CHC*H*=), 6.85–7.50 (m, 14H, *Ar*); δ_C (300 MHz, $CDCl_3$) 22.66, 58.27, 59.00, 75.43, 117.12, 120.73, 121.38, 126.97, 127.64, 127.75, 128.03, 128.50, 129.01, 129.13, 130.38, 132.67, 132.81, 137.36, 145.85, 155.39.

4.3.5. 4-[(*E*)-2-(4-Methoxyphenyl)ethenyl]-3-methyl-3,4-dihydro-2*H*-1,3-benzoxazine (3f). Oil; [Found C, 76.83; H, 6.83; N, 5.01%. $C_{18}H_{19}NO_2$ requires: C, 76.84; H, 6.81; N, 4.98%]. ν_{max} (liquid film) 3015, 1471, 1452, 1232, 950, 741, 694 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 2.65 (s, 3H, N*Me*), 3.80 (s, 3H, O*Me*), 4.28 (br d, 1H, *J*=4.3 Hz, C*H*N), 4.63 (dd, 1H, $J_{1,5}$=1.3, J_{ab}=9.7 Hz, CH_aH_b), 4.94 (d, 1H, *J*=9.7 Hz, CH_aH_b), 6.30 (m, 2H, C*H*=C*H*), 6.80–7.30 (m, 8H, *Ar*); δ_C (300 MHz, $CDCl_3$) 30.20, 40.28, 55.78, 62.28, 80.53, 114.44, 117.09, 120.83, 121.36, 128.19, 128.61, 129.38, 129.88, 129.98, 133.16, 160.00.

4.3.6. 3-Isopropyl-4-[(*E*)-2-(4-methoxyphenyl)ethenyl]-3,4-dihydro-2*H*-1,3-benzoxazine (3g). Oil; [Found: C, 77.70; H, 38; N, 4.61%. $C_{20}H_{23}NO_2$ requires: C, 77.64; H, 7.49; N, 4.53%]. ν_{max} (liquid film) 3002, 1478, 1225, 937, 831, 687 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 1.17 (d, 3H, *J*=6.4 Hz, Me_a), 1.21 (d, 3H, *J*=6.4 Hz, Me_b), 3.16 (sept, 1H, *J*=6.4 Hz, C*H*$(Me)_2$), 3.80 (s, 3H, O*Me*), 4.53 (br s, 1H, C*H*N), 4.90–4.96 (m, 2H, CH_2), 6.28 (m, 2H, C*H*=C*H*), 6.80–7.40 (m, 8H, *Ar*); δ_C (300 MHz, $CDCl_3$) 21.74, 22.56, 51.77, 55.78, 56.80, 114.39, 117.26, 120.47, 123.04, 128.12, 128.26, 129.14, 129.62, 130.13, 130.59, 131.82, 155.49, 159.63.

4.4. Synthesis of 4*H*-chromen-4-ylidene amine 9c

The reaction was performed by mixing chalcone **8** (1.041 g, 5 mmol) with benzylamine (0.589 g, 5.5 mmol) in a round bottom reaction flask, equipped with magnetic stirring, in the absence of solvent, at room temperature until **8** was consumed.[15] The reaction mixture was then dissolved in *n*-hexane (50 mL) and washed with water (2×50 mL). The organic layer was separated, dried with Na_2SO_4 and evaporated under reduced pressure. The crude orange oil obtained after workup was dissolved in methanol (10 mL) and allowed to stand at room temperature. After 15 min the formation of orange crystals was observed, these were filtered and recrystallized from ethyl acetate giving **9c** in 93% yield (1.457 g). Reduction of **9c** (0.313 g, 1 mmol)

with $NaBH_4$ (0.057 g, 1.5 mmol) in methanol (5 mL) afforded **10c**.[16] Spectral data of **9c** follows.

4.4.1. *N*-Benzyl-*N*-(2-phenyl-2,3-dihydro-4*H*-chromen-4-ylidene)amine (9c). Yellow crystals mp 106–109°C (hexane); [Found: C, 84.58; H, 6.02; N, 4.22%. $C_{22}H_{19}NO$ requires C, 84.31; H, 6.11; N, 4.47%]. ν_{max} (Nujol) 2924, 1602, 1306, 1222, 1009, 762, 699 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.75 (dd, 1H, *J*=12.4, 16.5 Hz, CH_cH$_d$CHPh), 3.23 (dd, 1H, *J*=2.9, 16.5 Hz, CH$_c$$H_d$CHPh), 4.66 (d, 1H, *J*=16.1 Hz, CH_aH$_b$Ph), 4.80 (d, 1H, *J*=16.1 Hz, CH$_a$$H_b$Ph), 5.22 (dd, 1H, *J*=2.9, 12.4 Hz, C*H*Ph), 6.70–7.60 (m, 13H, *Ar*), 8.20–8.30 (m, 1H, *Ar*); δ_C (300 MHz, $CDCl_3$) 35.48, 54.87, 78.51, 118.11, 122.05, 126.34, 126.66, 127.54, 127.64, 128.05, 129.02, 129.28, 129.48, 132.54, 133.07, 139.50, 158.45, 160.13; MS (EI, 70 eV) *m*/*z* (%) 313 (M^+, 100), 236 (21), 222 (60), 209 (88), 180 (37), 91 (69).

4.5. Aldol condensation of imidoyl phenol 11c dianion with benzaldehyde

In a three necked round bottom reaction flask, equipped with magnetic stirring bar and under inert atmosphere, imidoylphenol **11c** (0.450 g, 2 mmol) was dissolved in THF (5 mL).A solution previously prepared by mixing buthyllithium (2.5 M in hexane, 5 mmol) with tetramethylpiperidine (0.706 g, 5 mmol) in 2 mL THF was added dropwise at 0°C. After 1 h the mixture was cooled to −70°C and added of benzaldehyde (0.318 g, 3 mmol in 2 mL THF). The reaction was monitored by TLC until starting material was consumed (2 h) and then treated with 0.2 mL of water dissolved in 1 mL of THF. The mixture was then quenched with aqueous ammonium chloride (until pH 6 was reached) and extracted with CH_2Cl_2 (2×30 mL), dried with sodium sulfate, filtered and the solvent evaporated under reduced pressure. The crude oil was then submitted to ^{1}H NMR analysis, and starting material **11c** was found. Alternatively quenching was made with 6 M hydrochloric acid (until pH 2 was reached) and after workup and ^{1}H NMR analysis flavanone **12** was found (see Scheme 4).

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