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Substituent effects in the ring-chain tautomerism of 1,3-diaryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines

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Abstract—Condensation of Betti base analogue amino naphthols with substituted benzaldehydes led to 1,3-diaryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines (**3**–**9**) which proved to be three-component (r^1–o–r^2) tautomeric mixtures in $CDCl_3$ at 300 K. The electronic effects of the 3-aryl groups on the ratios of the ring-chain tautomeric forms at equilibrium could be described by the equation $\log K_X=\rho\sigma^+ + \log K_{X=H}$. The value of the intercept was found to be strongly influenced by the steric arrangement of the 1,3-diaryl substituents.

1. Introduction

The structures and reactivities of numerous five- and six-membered, saturated, *N*-unsubstituted 1,3-*X*,*N* heterocycles (X=O, S, NR) can be characterized by the ring-chain tautomeric equilibria of the 1,3-*X*,*N* heterocycles and the corresponding Schiff bases.[1] The oxazolidines and tetrahydro-1,3-oxazines are the saturated 1,3-*X*,*N* heterocycles whose ring-chain tautomerism has been studied most thoroughly.[2] The tautomeric character of 1,3-*O*,*N* heterocycles offers a great number of synthetic possibilities, e.g. they can be used as intermediates in the synthesis of *N*-substituted amino alcohols[3] or nitrogen-bridged heterocyclic systems[4] and they serve as aldehyde sources in carbon transfer reactions.[5]

For the tautomeric equilibria of oxazolidines and tetrahydro-1,3-oxazines bearing a substituted phenyl group at position 2, a Hammett-type linear correlation was found between the $\log K (K = [\text{ring}]/[\text{chain}])$ values of the equilibria and the electronic character (σ^+) of the substituents *X* on the 2-phenyl group (Eq. (1)), in both the liquid and the gas phase. The value of ρ in Eq. (1) proved to be characteristic of the ring system and dependent on temperature and the nature of the solvent:[1]

$$\log K_X = \rho\sigma^+ + \log K_{X=H} \quad (1)$$

In contrast with the great number of studies on the dependence of the tautomeric equilibria of tetrahydro-1,3-oxazines on the aromatic substituent at position 2, less is known on the effects of such substituents at other positions. The investigation of ring-chain tautomeric 2-aryltetrahydro-1,3-oxazines bearing a substituted phenyl group at position 4 or 6 showed that the substituent on the 4/6-phenyl group does not exert a significant influence on the parameters in Eq. (1). However, the presence of the aryl group itself stabilized the cyclic tautomer, more significantly at position 4 than at position 6.[6] The influence of the electronic character of a substituted phenyl group attached at a position other than 2 was found to be more pronounced in the ring-chain tautomeric equilibria of analogous 1,3,4-*O*,*N*,*N* or-1,3-*N*,*N* ring systems. For 4-aryl-2,2-dialkyl-substituted 1,3,4-oxadiazines, the electron-withdrawing groups on the 4-phenyl ring increased the proportions of the ring-closed tautomers.[7] In the ring-chain equilibria of 1,2-diarylimidazolidines, the 2-aryl substituent dependence of which was observed to follow Eq. (1), electron-donating substituents on the 1-phenyl ring produced higher values of ρ.[8]

Our present aim was to study the substituent effects on the ring-chain tautomerism of naphthalene-condensed 1,3-oxazine derivatives bearing aryl groups at positions 2 and 4, with the aims of a refinement of the scope and limitations of application of Eq. (1) among six-membered 1,3-*O*,*N* heterocycles, and a quantitative characterization of the effects of both aryl substituents on the ring-chain equilibria.

2. Results and discussion

Betti's classical procedure, a Mannich-type aminoalkylation reaction of 2-naphthol,[9] was applied to prepare the starting materials for the synthesis of the present target compounds. Condensation of 2-naphthol (**1**) and benzaldehyde or substituted benzaldehydes in the presence of ammonia,

Keywords: amino alcohols; oxazines; substituent effects; tautomerism.

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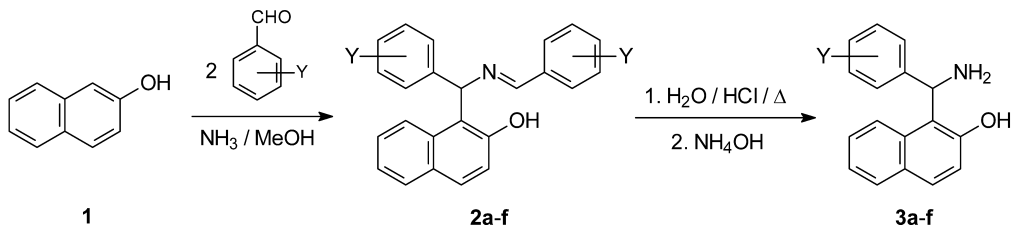


Y = NO_2(*m*): (57%) **a**, Br(*m*): (47%) **b**, Cl(*p*): (53%) **c**, H: (56%) **d**, Me(*p*): (71%) **e**, OMe(*p*): (45%) **f**

Scheme 1.

and subsequent acidic hydrolysis, gave amino naphthols **3a–f** in good yields (Scheme 1). The potential utility of the Mannich-type phenolic bases makes the aminoalkylation reaction of naphthol derivatives a subject of current chemical interest.[10] For example, the enantiomers of Betti base **3d** and its *N*-substituted derivatives were found to be potent chiral catalysts in additions of dialkylzincs to aldehydes,[11] and this contributed to the enhanced attention recently paid to the preparation of chiral *N*-substituted amino naphthol derivatives.[12]

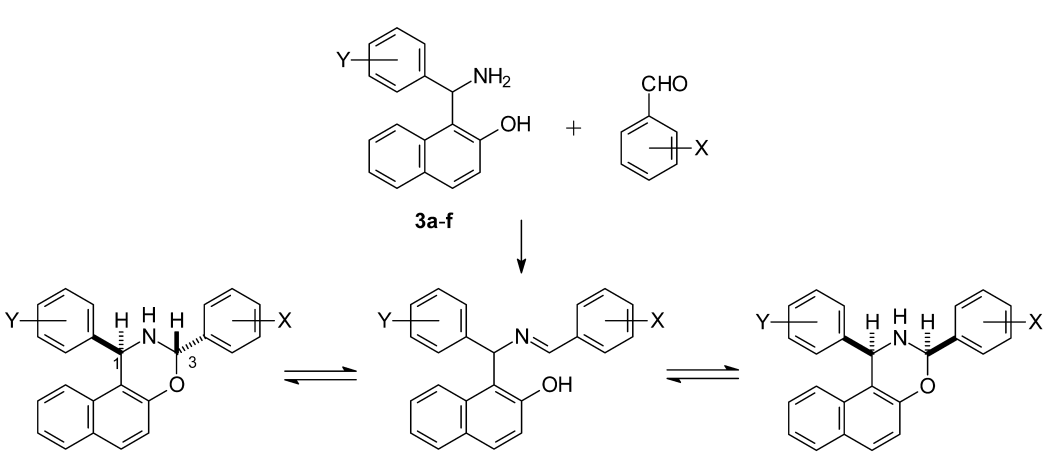
Condensations of amino naphthols **3a–f** with equivalent amounts of aromatic aldehydes resulted in naphthoxazine model compounds **4–9** as crystalline products (Scheme 2). The ^{1}H NMR spectra of **4–9** revealed that, in $CDCl_3$ solution at 300 K, the **a–f** members of each set of compounds **4–9** participated in three-component ring-chain tautomeric equilibria containing C-3 epimeric naphthoxazines (**B** and **C**) besides the open tautomer (**A**). For the 3-(*p*-dimethylaminophenyl)-substituted derivatives (**4g–9g**), the tautomeric equilibria contained only one ring-closed form (**B**).

The intermediate of the Betti reaction was earlier presumed to have a ring-chain tautomeric character.[13] By condensation of the Betti base with aromatic aldehydes, Smith and Cooper prepared 1-phenyl-3-aryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines, and studied their ring-chain tautomeric equilibria by means of 60 MHz ^{1}H NMR.[13a] They made the assumption that 1,3-diaryl groups prefer pseudoequatorial and therefore a *cis* arrangement in the *major* ring-closed tautomer. In contrast with this assumption, and the *cis* position of the diaryl groups found for the *major* ring-closed tautomers in both 2,4- and 2,6-diarylperhydro-1,3-oxazines,[6] the NOESY spectra of **6a** unequivocally showed that the *major* ring forms in all tautomeric equilibria (**4–9**) contain the 1,3-diaryl substituents in the *trans* position (**B**).

To characterize the effects of the aryl substituent at position 1 on the tautomeric character of this ring system, 1-unsubstituted 3-aryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines (**11**) were also prepared from the readily available[14] 1-aminomethyl-2-naphthol (**10**) and aromatic aldehydes. In $CDCl_3$ at 300 K, **11a–g** proved to participate in ring-chain tautomeric equilibria (Scheme 3).

The proportions of the chain (**A**) and diastereomeric ring forms (**B** and **C**) of the tautomeric equilibria of **4–9** and **11** (K_X) were determined by integration of the well-separated O–C*H*Ar-N (ring) and N=C*H*Ar (chain) proton singlets or doublets (Table 3) in the ^{1}H NMR spectra (Table 1).

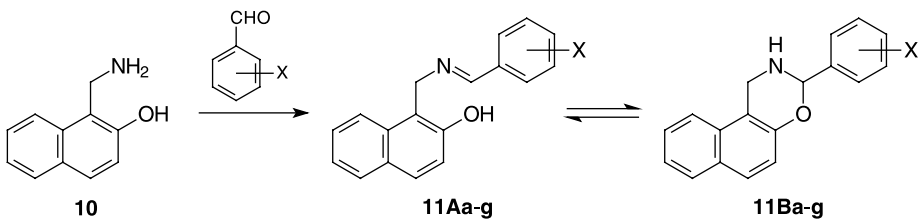
In consequence of the very similar NMR spectroscopic



Y = NO_2(*m*):	**4Ba-g**	**4Aa-g**	**4Ca-g** (69-90%)
Y = Br(*m*):	**5Ba-g**	**5Aa-g**	**5Ca-g** (67-85%)
Y = Cl(*p*):	**6Ba-g**	**6Aa-g**	**6Ca-g** (73-88%)
Y = H:	**7Ba-g**	**7Aa-g**	**7Ca-g** (74-90%)
Y = Me(*p*):	**8Ba-g**	**8Aa-g**	**8Ca-g** (75-92%)
Y = OMe(*p*):	**9Ba-g**	**9Aa-g**	**9Ca-g** (76-93%)

X = NO_2(*p*): **a**, Br(*m*): **b**, Cl(*p*): **c**, H: **d**, Me(*p*): **e**, OMe(*p*): **f**, NMe_2(*p*): **g**

Scheme 2.



X = NO_2(*p*): (72%) **a**, Br(*m*): (83%) **b**, Cl(*p*): (78%) **c**, H: (85%) **d**, Me(*p*): (75%) **e**, OMe(*p*): (80%) **f**, NMe_2(*p*): (77%) **g**

Scheme 3.

Table 1. Proportions (%) of the ring-closed tautomeric forms (**B** and **C**) in tautomeric equilibria for compounds **4**–**9** and **11** ($CDCl_3$, 300 K)

Compound	X	σ^+	**4** (Y=*m*NO_2), 0.73		**5** (Y=*m*Br), 0.405		**6** (Y=*p*Cl), 0.114		**7** (Y=H), 0		**8** (Y=*p*Me), −0.311		**9** (Y=*p*OMe), −0.778		**11**, –
			B	**C**	**B**	**C**	**B**	**C**	**B**	**C**	**B**	**C**	**B**	**C**	**B**
a	*p*NO_2	0.79	89.0	8.3	90.9	7.0	93.6	3.6	86.1	10.8	89.0	7.6	88.5	8.3	95.2
b	*m*Br	0.405	85.2	8.1	82.0	9.5	82.0	9.4	79.5	10.6	76.7	11.3	79.5	10.0	88.0
c	*p*Cl	0.114	80.1	7.5	77.3	8.6	76.6	8.4	72.4	9.7	71.7	9.3	72.8	9.1	79.4
d	H	0	73.6	7.9	68.0	8.4	70.1	7.8	64.4	9.3	63.6	8.7	62.2	8.2	72.3
e	*p*Me	−0.311	63.6	6.3	57.3	6.6	60.0	6.1	52.6	7.7	50.9	6.8	53.2	6.6	58.3
f	*p*OMe	−0.778	47.7	3.7	42.1	5.4	43.5	4.6	37.8	5.9	36.6	4.7	38.1	5.4	45.4
g	*p*NMe_2	−1.7	13.3	~0	9.8	~0	10.2	~0	10.4	~0	9.0	~0	8.6	~0	10.3

characteristics of 1,3-diaryl-2,3-dihydro-2*H*-naphth[1,2-*e*]-[1,3]oxazines **4**–**9**, determination of the relative configurations of the *major* and *minor* ring-closed tautomers was performed only for **6a**. Data on **6a**, **9g** and **11f** were chosen to illustrate the ^{1}H NMR spectra of the prepared tautomeric compounds (see Experimental). 1,2-Diaryl substituents did not change the sequence of the chemical shifts of the characteristic O–C*H*Ar-N and N=C*H*Ar protons. The configuration of the azomethine double bond was found to be *E*, according to the NOE interaction observed between the Nph–C*H*Ar-N and N=C*H*Ar protons.

When Eq. (1) was applied to the log K_X values, good linear correlations were obtained vs the Hammett–Brown parameter σ^+ of the substituent X on the 3-phenyl group for **4**–**9** and **11** (Figure 1 and Table 2).

The linear regression analysis data in Table 2 show that, as is customary among 2-aryl-1,3-*O*,*N* heterocycles,[1,2] the value of ρ is positive in each case, i.e. electron-withdrawing substituents on the 3-phenyl ring favour the ring-closed tautomer. While the value of ρ for 1-unsubstituted 3-aryl-2,3-dihydro-2*H*-naphth[1,2-*e*][1,3]oxazines (**11**: 0.81) is the same (within experimental error) as that for the parent 2-arylperhydro-1,3-oxazines (**12**: 0.76), the values of ρ for 1,3-diaryl-2,3-dihydro-2*H*-naphth[1,2-*e*][1,3]oxazines (**4**–**9**: 0.81–1.05) are somewhat higher. The *cis* or *trans* arrangement of the 1,3-diaryl substituents in the ring forms

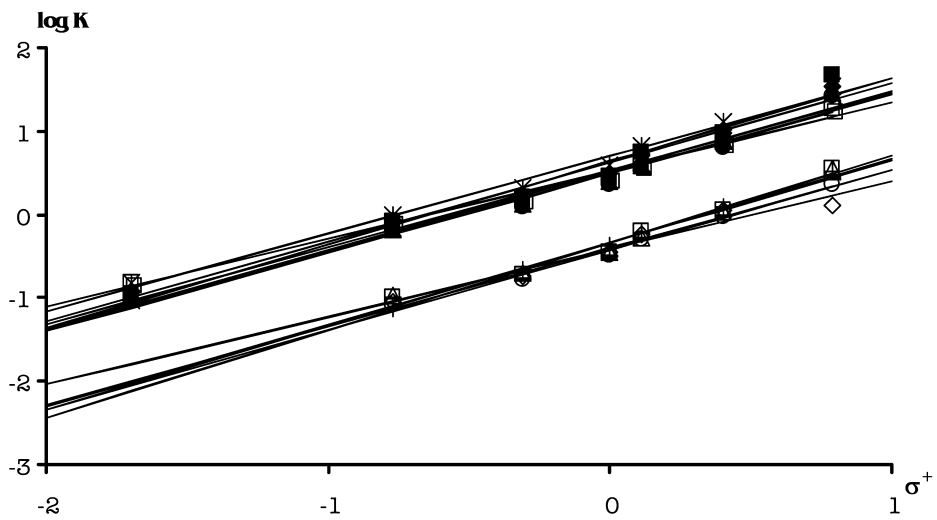
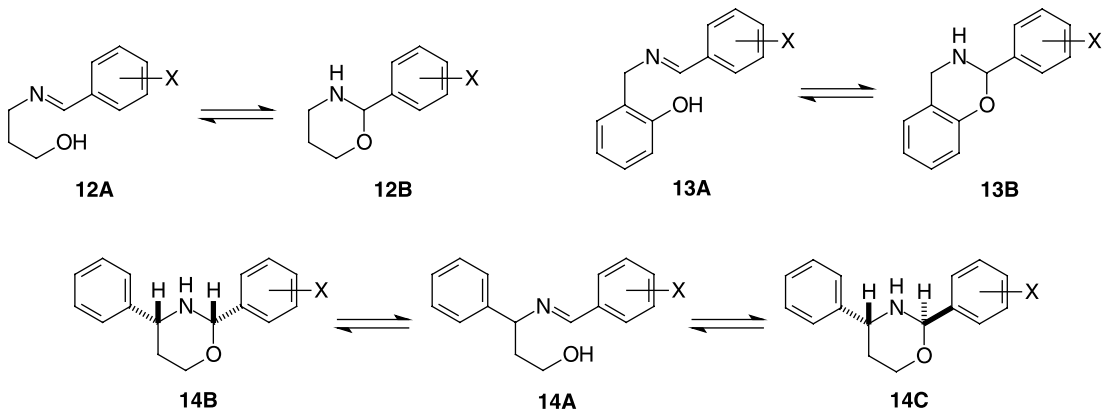


Figure 1. Plots of log K_X (in $CDCl_3$) for **4B** (X), **4C** (+), **5B** (■), **5C** (□), **6B** (◆), **6C** (◇), **7B** (▲), **7C** (△), **8B** (●), **8C** (○), **9B** (×), **9C** (−), **11B** (▯) vs Hammett–Brown parameter σ^+.

Table 2. Linear regression data on compounds **4**–**9**, **11**, 2-aryl-3,4,5,6-tetrahydro-2*H*-1,3-oxazines (**12**), 2-aryl-3,4-dihydro-2*H*-1,3-benzoxazines (**13**) and 2-aryl-4-phenyl-3,4,5,6-tetrahydro-2*H*-1,3-oxazines (**14**)



X = NO_2(*p*), NO_2(*m*), Cl(*m*), Cl(*p*), H, Me(*p*), OMe(*p*), NMe_2(*p*)

Equilibrium	No. of points	Slope[a] (ρ)	Intercept[a]	Correlation coefficient	c[b]
4A⇌**4B**	7	0.93 (4)	0.70 (8)	0.995	0.85
4A⇌**4C**	6	1.04 (2)	−0.33 (2)	0.999	−0.18
5A⇌**5B**	7	1.00 (8)	0.64 (15)	0.985	0.79
5A⇌**5C**	6	1.01 (9)	−0.33 (10)	0.985	−0.18
6A⇌**6B**	7	0.96 (5)	0.62 (10)	0.993	0.77
6A⇌**6C**	6	0.81 (8)	−0.42 (10)	0.979	−0.27
7A⇌**7B**	7	0.92 (6)	0.53 (13)	0.988	0.68
7A⇌**7C**	6	0.98 (9)	−0.34 (10)	0.983	−0.19
8A⇌**8B**	7	0.95 (6)	0.49 (12)	0.989	0.64
8A⇌**8C**	6	0.95 (5)	−0.42 (6)	0.993	−0.27
9A⇌**9B**	7	0.95 (6)	0.52 (11)	0.991	0.67
9A⇌**9C**	6	0.94 (8)	−0.40 (9)	0.986	−0.25
11A⇌**11B**	7	0.81 (4)	0.52 (8)	0.994	0.67
12A⇌**12B**[c]	7	0.74 (6)	−0.15 (5)	0.984	–
13A⇌**13B**[c]	7	0.82 (4)	−0.66 (3)	0.995	−0.51
14A⇌**14B**[d]	6	0.72 (2)	0.42 (5)	0.997	0.57
14A⇌**14C**[d]	6	0.99 (4)	−1.12 (8)	0.996	−0.97

[a] Standard deviations are given in parentheses.
[b] Relative ring stability constant: see the text.
[c] Data from Ref. 2b.
[d] For compounds **14** (Ref. 6), tautomeric ratios were remeasured and the linear regression analysis was performed separately for the equilibria involving C-2 epimeric ring forms.

of 1,3-diaryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines does not seem to influence the value of ρ; the plots for the equilibria containing C-2 epimeric ring forms of **4**–**9** (**B**–**A** and **C**–**A**) are practically parallel.

To characterize the effects of the substituents and the presence of an annelated ring on the stability of the ring forms, a substitution effect parameter (c_s) was calculated as the difference in the intercepts for the given naphthoxazine derivative (**4**–**9**, **11**) and the parent 2-arylperhydro-1,3-oxazine (**12**: $\log K_0=-0.15$): $c_s=\log K_{X=H}-\log K_0$. This kind of relative ring stability constant was introduced earlier for the saturated 2-aryl-1,3-*O*,*N* heterocycles bearing substituents at positions 4–6.[1b,2b] A positive value of c_s means a more stable ring form relative to the corresponding parent 2-arylperhydro-1,3-*O*,*N* heterocycle.

While an annelated benzene ring considerably decreased the stability of the ring form of 2-arylperhydro-1,3-oxazine (**13**: $c_s=-0.66$),[2b] an annelated naphthalene ring caused a dramatic increase in ring stability (**11**: $c_s=0.67$). This increased stability of the ring form was observed for all naphthoxazines having *trans* diaryl substituents (**4**–**9 B**: $c_s=0.63-0.85$), while the negative c_s values for the *cis* isomers of these compounds (**4**–**9 C**: $c_s=-0.18--0.27$) indicates that the stabilizing effect of the naphthalene ring is diminished by the unfavourable steric arrangement of the aryl substituents.

3. Conclusions

Some new Betti base analogue amino naphthols were obtained by the Mannich-type aminoalkylation of 2-naphthol. The reactions of substituted amino naphthols and substituted benzaldehydes led to 1,3-diaryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines which at 300 K proved to be three-component tautomeric mixtures in $CDCl_3$ containing C-3 epimeric naphthoxazines (**B** and **C**) besides the open tautomer (**A**). The influence of aryl substituents at position 3 on the ring-chain tautomeric equilibria could be described by the Hammett equation. Study of the influence of aryl substituents at position 1 is still in progress.

4. Experimental

^{1}H NMR spectra (400 MHz) were recorded at 300 K. Chemical shifts are given in δ (ppm) relative to TMS ($CDCl_3$) as internal standard. For the equilibria to be established in tautomeric compounds,[2] the samples were dissolved in $CDCl_3$ and the solutions were allowed to stand at ambient temperature for 1 day before the ^{1}H NMR spectra were run. The number of scans was usually 32.

4.1. General method for the synthesis of 1-(α-amino-*Y*-substituted-benzyl)-2-naphthols (3a–f)

To a solution of 2-naphthol (**1**, 14.42 g, 0.1 mol) in absolute MeOH (50 mL) was added the appropriate aromatic aldehyde (0.2 mol; for liquid aldehydes, a freshly distilled sample was used) and 25% methanolic ammonia solution (20 mL). The mixture was left to stand at ambient temperature for 2 days, during which a crystalline product (**2a–f**) separated out. The crystals were filtered off and washed with cool MeOH (2×20 mL), dried and suspended in 20% HCl (200 mL). The mixture was stirred and refluxed for 3 h, and the crystalline hydrochloride of **3a–f** that separated out was filtered off and washed with EtOAc (2×25 mL). The hydrochloride was suspended in H_2O (30 mL), and the mixture was treated with conc. NH_4OH (30 mL) and extracted with EtOAc (3×50 mL). After drying (Na_2SO_4) and evaporation, crystalline **3a–f** was obtained, which was recrystallized from iPr$_2$O.

4.1.1. Compound 3a. Beige crystals. Yield: 16.76 g (57%), mp 111–113°C. ^{1}H NMR ($CDCl_3$) δ 6.27 (s, 1H, NC*H*(Ar)NPh), 7.16 (d, 1H, *J*=9.0 Hz, Nph-H3), 7.27 (t, 1H, *J*=7.0 Hz, Nph-H6), 7.40 (t, 1H, *J*=7.0 Hz, Nph-H7), 7.40 (t, 1H, *J*=8.0 Hz, Ar), 7.70 (d, 1H, *J*=9.0 Hz, Nph-H8), 7.71–7.76 (m, 2H, Nph-H4, Nph-H5), 7.77 (d, 1H, *J*=8.0 Hz, Ar), 8.10 (d, 1H, *J*=8.0 Hz, Ar), 8.38 (s, 1H, Ar), ^{13}C NMR ($CDCl_3$) δ 55.2, 114.5, 121.3, 121.5, 122.9, 123.6, 123.8, 127.9, 129.0, 129.9, 131.0, 131.2, 132.1, 134.5, 144.8, 148.9, 157.2. Anal. Calcd for $C_{17}H_{14}N_2O_3$: C, 69.38; H, 4.79; N, 9.52. Found: C, 69.51; H, 4.75; N, 9.64. IR ν_{max} 3361, 1521, 1347, 730 cm^{-1}.

4.1.2. Compound 3b. White crystals. Yield: 15.42 g (47%), mp 118–120°C. ^{1}H NMR ($CDCl_3$) δ 6.10 (s, 1H, NC*H*(Ar)NPh), 7.14–7.17 (m, 2H, Nph-H3, Ar), 7.25 (t, 1H, *J*=8.5 Hz, Nph-H6), 7.34–7.38 (m, 3H, Nph-H7, Ar), 7.62 (s, 1H, Ar), 7.66 (d, 1H, *J*=8.5 Hz, Nph-H8), 7.71 (d, 1H, *J*=8.5 Hz, Nph-H4), 7.73 (d, 1H, *J*=8.0 Hz, Nph-H5), ^{13}C NMR ($CDCl_3$) δ 55.9, 115.1, 121.1, 121.5, 123.2, 123.5, 126.7, 126.8, 127.2, 129.5, 130.6, 131.1, 131.1, 131.7, 132.5, 145.3, 157.7. Anal. Calcd for $C_{17}H_{14}BrNO$: C, 62.21; H, 4.30; N, 4.27. Found: C, 62.39; H, 4.17; N, 4.35. IR ν_{max} 3353, 1436, 1284, 810 cm^{-1}.

4.1.3. Compound 3c. Light beige crystals. Yield: 15.03 g (53%), mp 109–111°C (lit.,[15] mp 120°C). ^{1}H NMR ($CDCl_3$) δ 6.11 (s, 1H, NC*H*(Ar)NPh), 7.15 (d, 1H, *J*=9.0 Hz, Nph-H3), 7.23–7.28 (m, 3H, Nph-H6, Ar), 7.34 (t, 1H, *J*=8.0 Hz, Nph-H7), 7.39 (d, 2H, *J*=8.5 Hz, Ar), 7.66 (d, 1H, *J*=8.5 Hz, Nph-H8), 7.71 (d, 1H, *J*=9.0 Hz, Nph-H4), 7.73 (d, 1H, *J*=8.0 Hz, Nph-H5), ^{13}C NMR ($CDCl_3$) δ 55.8, 115.4, 121.0, 121.4, 123.0, 127.1, 129.2, 129.3, 129.3, 129.7, 130.4, 132.4, 134.4, 141.4, 157.5. IR ν_{max} 3345, 1623, 1237, 829 cm^{-1}.

4.1.4. Compound 3d. Beige crystals. Yield: 13.94 g (56%), mp 116–118°C (lit.,[9] mp 124–125°C). ^{1}H NMR ($CDCl_3$) δ 6.11 (s, 1H, NC*H*(Ar)NPh), 7.17 (d, 1H, *J*=9.0 Hz, Nph-H3), 7.20–7.24 (m, 2H, Nph-H6, Ar), 7.29 (d, 2H, *J*=7.5 Hz, Ar), 7.33 (t, 1H, *J*=7.5 Hz, Nph-H7), 7.44 (d, 2H, *J*=7.5 Hz, Ar), 7.67–7.71 (m, 3H, Nph-H4, Nph-H5, Nph-H8), ^{13}C NMR ($CDCl_3$) δ 56.6, 115.9, 121.0, 121.7, 122.9, 127.1, 127.9, 128.4, 129.1, 129.3, 129.5, 130.8, 132.8, 143.2, 157.8. IR ν_{max} 3296, 1622, 1238, 770 cm^{-1}.

4.1.5. Compound 3e. Pale yellow crystals. Yield: 18.67 g (71%), mp 103–104°C (lit.,[16] mp 109.5°C). ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 3H, C*H*$_3$), 6.08 (s, 1H, NC*H*(Ar)NPh), 7.09 (d, 2H, *J*=8.0 Hz, Ar), 7.14 (d, 1H, *J*=9.0 Hz, Nph-H3), 7.21 (t, 1H, *J*=9.0 Hz, Nph-H6), 7.31–7.35 (m, 3H, Nph-H7, Ar), 7.69–7.73 (m, 3H, Nph-H4, Nph-H8, Nph-H5), ^{13}C NMR ($CDCl_3$) δ 21.6, 56.1, 115.9, 121.0, 121.7, 122.9, 127.0, 127.6, 129.2, 129.2, 130.0, 130.2, 132.6, 138.2, 140.0, 157.6. IR ν_{max} 3347, 1468, 1235, 814 cm^{-1}.

4.1.6. Compound 3f. Beige crystals. Yield: 12.55 g (45%), mp 117–118°C. ^{1}H NMR ($CDCl_3$) δ 3.71 (s, 3H, OC*H*$_3$), 6.06 (s, 1H, NC*H*(Ar)NPh), 6.80 (d, 2H, *J*=8.5 Hz, Ar), 7.15 (d, 1H, *J*=9.0 Hz, Nph-H3), 7.22 (t, 1H, *J*=7.5 Hz, Nph-H6), 7.32 (t, 1H, *J*=7.5 Hz, Nph-H7), 7.35 (d, 2H, *J*=8.5 Hz, Ar), 7.65–7.72 (m, 3H, Nph-H4, Nph-H5, Nph-H8), ^{13}C NMR ($CDCl_3$) δ 55.6, 55.7, 114.5, 115.7, 120.8, 121.5, 122.8, 126.8, 128.8, 128.9, 129.2, 130.0, 132.3, 135.0, 157.1, 159.5. Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.4; H, 6.13; N, 5.01. Found: C, 77.32; H, 6.23; N, 5.11. IR ν_{max} 3287, 1510, 1249, 824 cm^{-1}.

4.2. 1-Aminomethyl-2-naphthol (10)

Compound **10** was prepared from 2-naphthol (11.44 g, 0.08 mol) and hexamethylenetetramine (11.20 g, 0.08 mol) according to Ref. 14a.

4.2.1. Compound 10. Yellow crystals. Yield: 8.52 g (62%), mp 131–133°C (lit.,[17] mp 135–138°C). ^{1}H NMR (DMSO) δ 4.30 (s, 2H, NC*H*$_2$NPh), 7.07 (d, 1H, *J*=9.0 Hz, Nph-H3), 7.24 (t, 1H, *J*=7.5 Hz, Nph-H6), 7.37 (t, 1H, *J*=7.5 Hz, Nph-H7), 7.68 (d, 1H, *J*=9.0 Hz, Nph-H4), 7.75 (d, 1H, *J*=8.5 Hz, Nph-H5), 7.87 (d, 1H, *J*=8.5 Hz, Nph-H8), ^{13}C NMR (DMSO) δ 45.0, 115.6, 119.5, 122.9, 123.0, 127.1, 129.0, 129.2, 129.5, 134.0, 156.1. IR ν_{max} 1268, 1238, 813, 741 cm^{-1}.

4.3. General method for the synthesis of 3-aryl- and 1,3-diaryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines (4–9 and 11)

To a solution of the appropriate amino naphthol (**3a–f** or **10**, 1 mmol) in absolute MeOH (20 mL), an equivalent amount of aromatic aldehyde was added (for liquid aldehydes, a freshly distilled sample was used), and the mixture was left to stand at ambient temperature for 24 h. The crystalline products were filtered off, washed with Et_2O and

Table 3. Physical and analytical data on naphth[1,2-*e*][1,3]oxazines **4**–**9** and **11**

Compound	Mp (°C)	Yield (%)	Formula	M.W.	C% Found (calculated)	H% Found (calculated)	N% Found (calculated)
4a	207–208[a]	78	$C_{24}H_{17}N_3O_5$	427.41	67.38 (67.44)	4.02 (4.01)	9.81 (9.83)
4b	173–175[b]	81	$C_{24}H_{17}BrN_2O_3$	461.31	62.51 (62.49)	3.70 (3.71)	6.06 (6.07)
4c	167–168[b]	69	$C_{24}H_{17}ClN_2O_3$	416.86	69.12 (69.15)	4.12 (4.11)	6.72 (6.72)
4d	146–147[a]	83	$C_{24}H_{18}N_2O_3$	382.41	75.43 (75.38)	4.75 (4.74)	7.33 (7.33)
4e	161–163[a]	75	$C_{25}H_{20}N_2O_3$	396.44	75.61 (75.74)	5.09 (5.08)	7.08 (7.07)
4f	126–128[b]	86	$C_{25}H_{20}N_2O_4$	412.44	72.68 (72.80)	4.89 (4.89)	6.78 (6.79)
4g	201–202[b]	90	$C_{26}H_{23}N_3O_3$	425.48	73.37 (73.40)	5.46 (5.45)	9.88 (9.88)
5a	193–195[b]	72	$C_{24}H_{17}BrN_2O_3$	461.31	62.58 (62.49)	3.70 (3.71)	6.08 (6.07)
5b	123–125[b]	67	$C_{24}H_{17}Br_2NO$	495.21	58.30 (58.21)	6.45 (6.46)	2.84 (2.83)
5c	163–164[b]	80	$C_{24}H_{17}BrClNO$	450.76	63.88 (63.95)	3.81 (3.80)	3.12 (3.11)
5d	132–134[a]	75	$C_{24}H_{18}BrNO$	416.31	69.17 (69.24)	4.37 (4.36)	3.35 (3.36)
5e	143–145[a]	82	$C_{25}H_{20}BrNO$	430.34	69.85 (69.78)	4.67 (4.68)	3.24 (3.25)
5f	108–110[a]	85	$C_{25}H_{20}BrNO_2$	446.34	67.17 (67.27)	4.51 (4.52)	3.13 (3.14)
5g	161–164[a]	70	$C_{26}H_{23}BrN_2O$	459.38	67.88 (67.98)	5.06 (5.05)	3.11 (6.10)
6a	181–182[b]	81	$C_{24}H_{17}ClN_2O_3$	416.86	69.09 (69.15)	4.11 (4.11)	6.73 (6.72)
6b	147–148[a]	75	$C_{24}H_{17}BrClNO$	450.76	64.02 (63.95)	3.81 (3.80)	3.11 (3.11)
6c	155–156[b,c]	78	$C_{24}H_{17}Cl_2NO$	406.31	70.93 (70.95)	4.23 (4.22)	3.46 (3.45)
6d	154–156[a]	85	$C_{24}H_{18}ClNO$	371.86	77.48 (77.52)	4.89 (4.88)	3.78 (3.77)
6e	163–165[a]	73	$C_{25}H_{20}ClNO$	385.89	77.78 (77.81)	5.21 (5.22)	3.64 (3.63)
6f	163–164[b]	86	$C_{25}H_{20}ClNO_2$	401.89	74.69 (74.72)	5.01 (5.02)	3.48 (3.49)
6g	177–178[b]	88	$C_{26}H_{23}ClN_2O$	414.93	75.31 (75.26)	5.58 (5.59)	3.76 (6.75)
7a	176–178[a,d]	74	$C_{24}H_{18}N_2O_3$	382.41	75.42 (75.38)	4.74 (4.74)	7.34 (7.33)
7b	153–155[a]	81	$C_{24}H_{18}BrNO$	416.31	69.33 (69.24)	4.36 (4.36)	3.35 (3.36)
7c	171–173[b,e]	86	$C_{24}H_{18}ClNO$	371.86	77.45 (77.52)	4.87 (4.88)	3.76 (3.77)
7d	146–148[a,f]	90	$C_{24}H_{19}NO$	337.42	85.39 (85.43)	5.67 (5.68)	4.15 (4.15)
7e	155–157[a,g]	77	$C_{25}H_{21}NO$	351.44	85.51 (85.44)	6.03 (6.02)	3.98 (3.99)
7f	143–146[a,h]	81	$C_{25}H_{21}NO_2$	367.44	81.84 (81.72)	5.75 (5.76)	3.82 (3.81)
7g	225–227[a,i]	78	$C_{26}H_{24}N_2O$	380.48	82.19 (82.07)	6.37 (6.36)	7.35 (7.36)
8a	181–183[b]	75	$C_{25}H_{20}N_2O_3$	396.44	75.69 (75.74)	5.09 (5.08)	7.07 (7.07)
8b	116–117[b]	92	$C_{25}H_{20}BrNO$	430.34	69.71 (69.78)	5.68 (4.68)	3.26 (3.25)
8c	137–138[b]	83	$C_{25}H_{20}ClNO$	385.89	77.92 (77.81)	5.21 (5.22)	3.64 (3.63)
8d	131–133[b]	89	$C_{25}H_{21}NO$	351.44	85.39 (85.44)	6.02 (6.02)	3.98 (3.99)
8e	148–149[b,j]	77	$C_{26}H_{23}NO$	365.47	85.52 (85.45)	6.33 (6.34)	3.83 (3.83)
8f	128–132[b]	85	$C_{26}H_{23}NO_2$	381.47	82.02 (81.86)	6.07 (6.08)	3.68 (3.67)
8g	197–198[b]	76	$C_{27}H_{26}N_2O$	394.51	82.11 (82.20)	6.65 (6.64)	7.08 (7.10)
9a	157–159[b]	84	$C_{25}H_{20}N_2O_4$	412.44	72.75 (72.80)	4.88 (4.89)	6.78 (6.79)
9b	177–178[b]	77	$C_{25}H_{20}BrNO_2$	446.34	67.36 (67.27)	4.52 (4.52)	3.13 (3.14)
9c	180–182[a]	84	$C_{25}H_{20}ClNO_2$	401.89	74.89 (74.72)	5.01 (5.02)	3.50 (3.49)
9d	156–159[a]	93	$C_{25}H_{21}NO_2$	367.44	81.68 (81.72)	5.76 (5.76)	3.82 (3.81)
9e	177–178[a]	88	$C_{26}H_{23}NO_2$	381.47	81.71 (81.86)	6.07 (6.08)	3.66 (3.67)
9f	182–184[a,k]	76	$C_{26}H_{23}NO_3$	397.47	78.66 (78.57)	5.84 (5.83)	3.52 (3.52)
9g	177–179[a]	79	$C_{27}H_{26}N_2O_2$	410.51	79.11 (79.00)	6.39 (6.38)	6.83 (6.82)
11a	161–162[b]	72	$C_{18}H_{14}N_2O_3$	306.32	70.65 (70.58)	4.62 (4.61)	9.16 (9.15)
11b	154–156[b]	83	$C_{18}H_{14}BrNO$	340.21	63.44 (63.55)	4.15 (4.15)	4.13 (4.12)
11c	155–157[a]	78	$C_{18}H_{14}ClNO$	295.76	72.97 (73.10)	4.76 (4.77)	4.74 (4.74)
11d	109–111[a]	85	$C_{18}H_{15}NO$	261.32	82.81 (82.73)	5.78 (5.79)	5.36 (5.36)
11e	125–126[a]	75	$C_{19}H_{17}NO$	275.35	82.72 (82.88)	6.23 (6.22)	5.08 (5.09)
11f	146–147[a]	80	$C_{19}H_{17}NO_2$	291.34	78.48 (78.33)	5.88 (5.88)	4.82 (4.81)
11g	152–154[a]	77	$C_{20}H_{20}N_2O$	304.39	78.88 (78.92)	6.63 (6.62)	9.21 (9.20)

[a] Recrystallized from *i*Pr_2O.
[b] Recrystallized from *i*Pr_2O-EtOAc.
[c] Lit.,[15] mp 150°C.
[d] Lit.,[13a] mp 174–175°C.
[e] Lit.,[13a] mp 173°C.
[f] Lit.,[13a] mp 144–145°C.
[g] Lit.,[18] mp 169°C.
[h] Lit.,[18] mp 95°C.
[i] Lit.,[13a] mp 192–193°C.
[j] Lit.,[16] mp 149°C.
[k] Lit.,[16] mp 181°C.

recrystallized. All of the recrystallized new compounds (**4a**–**g**, **5a**–**g**, **6a**, **6b**, **6d**–**g**, **7b**, **8a**–**d**, **8f**, **8g**, **9a**–**e**, **9g**, **11a**–**g**) gave satisfactory data on elemental analysis (C, H, N±0.3%). The physical and analytical data for compounds **4**–**9** and **11** are listed in Table 3.

With regard to the similarities in the ^{1}H NMR data, full spectra are described only for three representatives of the prepared compounds (**6a**, **9g** and **11f**). In a consequence of the very low relative concentrations and the extensive signal overlaps in the aromatic region, a full NMR characterization of the *minor* ring closed tautomers **C** was not possible. The ^{1}H NMR chemical shifts of the characteristic O–C*H*Ar-N and N=C*H*Ar protons of each tautomer and the characteristic IR wavenumbers for compounds **4**–**9** and **11** are given in Table 4.

Table 4. NMR and IR spectroscopical data on naphth[1,2-*e*][1,3]oxazines **4**–**9** and **11**

Compound	δN=C*H* (**A**)	δN–C*H*–O (**B**)	δN–C*H*–O (**C**)	$\nu_{max.}$ (cm^{-1})
4a	8.80(s)	5.75(s)	6.04(s)	3854, 1598, 1343, 1233
4b	8.61(s)	5.68(s)	5.96(d)	3332, 1527, 1352, 1238
4c	8.64(s)	5.69(s)	5.99(s)	3332, 1527, 1345, 1234
4d	8.68(s)	5.72(s)	6.03(s)	3332, 1525, 1349, 1233
4e	8.62(s)	5.70(s)	6.02(s)	1525, 1468, 1347, 1232
4f	8.55(s)	5.66(s)	5.98(s)	3338, 1526, 1348, 1232
4g	8.43(s)	5.66(s)	–	1601, 1344, 1181, 741
5a	8.32(s)	5.69(d)	5.91(d)	1518, 1339, 1232, 753
5b	8.55(s)	5.62(s)	5.87(d)	3322, 1234, 989, 774
5c	8.57(s)	5.63(s)	5.88(d)	33316, 1233, 986, 957
5d	8.61(s)	5.65(d)	5.91(d)	3317, 1467, 1233, 704
5e	8.55(s)	5.62(s)	5.90(d)	3321, 1238, 986, 931
5f	8.50(s)	5.60(s)	5.89(s)	1515, 1251, 1234, 985
5g	8.39(s)	5.60(s)	–	3308, 1365, 1233, 955
6a	8.73(s)	5.68(s)	5.91(d)	3320, 1519, 1339, 814
6b	8.56(s)	5.61(s)	5.89(d)	3307, 1233, 990, 825
6c	8.57(s)	5.60(s)	5.90(d)	3320, 1233, 984, 745
6d	8.60(s)	5.64(s)	5.92(d)	3320, 1236, 825, 747
6e	8.51(s)	5.57(s)	5.88(d)	3314, 1233, 985, 745
6f	8.50(s)	5.60(s)	5.91(s)	1515, 1231, 930, 749
6g	8.39(s)	5.59(s)	–	3850, 1597, 1367, 1182
7a	8.73(s)	5.73(s)	5.94(s)	3307, 1518, 1340, 1231
7b	8.55(s)	5.63(s)	5.91(d)	3308, 1229, 924, 750
7c	8.62(s)	5.65(s)	5.93(d)	3320, 1235, 984, 750
7d	8.63(s)	5.71(s)	5.97(s)	1236, 932, 743, 698
7e	8.56(s)	5.65(s)	5.94(d)	3320, 1237, 834, 749
7f	8.53(s)	5.66(s)	5.94(d)	3320, 1512, 1169, 983
7g	8.43(s)	5.65(d)	–	1602, 1455, 1366, 1181
8a	8.65(s)	5.72(s)	5.88(s)	3311, 1521, 1341, 1233
8b	8.55(s)	5.67(s)	5.89(d)	3317, 1232, 989, 789
8c	8.53(s)	5.64(s)	5.88(d)	3850, 1231, 987, 807
8d	8.54(s)	5.68(s)	5.89(s)	1233, 985, 808, 746
8e	8.52(s)	5.66(s)	5.90(s)	3302, 1233, 987, 746
8f	8.51(s)	5.66(s)	5.90(s)	1450, 1248, 1229, 903
8g	8.39(s)	5.63(s)	–	1604, 1365, 1182, 812
9a	8.69(s)	5.72(s)	5.87(s)	3292, 1510, 1342, 1229
9b	8.50(s)	5.63(s)	5.86(d)	3313, 1508, 1247, 1233
9c	8.54(s)	5.64(s)	5.87(d)	3316, 1511, 1247, 1233
9d	8.55(s)	5.68(s)	5.89(d)	3850, 1505, 1454, 942
9e	8.51(s)	5.65(s)	5.88(s)	3320, 1510, 1170, 747
9f	8.50(s)	5.65(s)	5.89(s)	1607, 1511, 1253, 831
9g	8.40(s)	5.62(s)	–	1605, 1509, 1251, 811
11a	8.58(s)	5.93(d)	–	3314, 1510, 1338, 1224
11b	8.43(s)	5.84(s)	–	3308, 1245, 1231, 811
11c	8.46(s)	5.85(s)	–	3253, 1225, 951, 818
11d	8.50(s)	5.89(s)	–	3248, 1227, 740, 695
11e	8.47(s)	5.87(s)	–	1225, 996, 910, 811
11f	8.39(s)	5.83(s)	–	3266, 1248, 1227, 813
11g	8.29(s)	5.81(s)	–	1601, 1368, 1181, 815

4.4. ^{1}H NMR spectroscopic data on 6a, 9g and 11f in $CDCl_3$

The protons of the open form (**A**) are numbered according to the corresponding protons of the naphth[1,2-*e*][1,3]oxazine ring form (**B**, **C**) (δ in ppm, in brackets the multiplicity, couplings in Hz and assignment, respectively).

4.4.1. Compound 6aB. ^{1}H NMR ($CDCl_3$) δ 5.63 (s, 1H, NC*H*(Ar)NPh), 5.68 (s, 1H, NC*H*(Ar)O), 7.24 (d, 1H, *J*=9.0 Hz, H5), 7.27–7.32 (m, 4H, Ar), 7.32–7.35 (m, 3H, H7, H8, H9), 7.78 (d, 2H, *J*=9.0 Hz, Ar), 7.79–7.83 (m, 2H, H6, H10), ^{13}C NMR ($CDCl_3$) δ 53.6, 81.6, 114.6, 119.4, 123.1, 123.8, 124.1, 127.3, 127.8, 129.0, 129.3, 129.5, 130.1, 131.1, 131.2, 131.4, 141.2, 146.1, 148.4, 152.5.

4.4.2. Compound 9gA. ^{1}H NMR ($CDCl_3$) δ 3.03 (s, 6H, *p*-N(CH_3)*2*), 3.73 (s, 3H, *p*-OCH_3), 6.31 (s, 1H, NC*H*(Ar)NPh), 6.68 (d, 2H, *J*=8.5 Hz, Ar), 6.78 (d, 2H, *J*=8.5 Hz, Ar), 7.22 (d, 1H, *J*=9.0 Hz, Nph-H3), 7.23–7.39 (m, 3H, Ar, Nph-H6), 7.37 (t, 1H, *J*=7.5 Hz, Nph-H7), 7.63 (d, 2H, *J*=8.5 Hz, Ar), 7.72 (d, 1H, *J*=9.0 Hz, Nph-H4), 7.74 (d, 1H, *J*=8.0 Hz, Nph-H5), 7.83 (d, 1H, *J*=8.5 Hz, Nph-H8), 8.40 (s, 1H, C*H*=N), ^{13}C NMR ($CDCl_3$) δ 40.6, 55.7, 74.3, 112.1, 114.6, 120.8, 117.5, 122.2, 122.8, 123.0, 127.6, 129.2, 129.3, 129.4, 129.9, 131.1, 132.5, 134.5, 153.5, 156.3, 159.6, 161.7.

4.4.3. Compound 11fA. ^{1}H NMR ($CDCl_3$) δ 3.86 (s, 3H, OCH_3), 5.36 (s, 2H, H1), 6.96 (d, 2H, *J*=7.0 Hz, Ar), 7.15 (d, 1H, *J*=8.5 Hz, Nph-H3), 7.31 (t, 1H, *J*=8.0 Hz, Nph-H6), 7.48 (t, 1H, *J*=8.0 Hz, Nph-H7), 7.68 (d, 1H, *J*=8.5 Hz, Nph-H4), 7.71 (d, 2H, *J*=7.0 Hz, Ar), 7.77 (d, 1H, *J*=8.5 Hz, Nph-H5), 7.79 (d, 1H, *J*=9.0 Hz, Nph-H8), 8.39

(s, 1H, C*H*=N), ^{13}C NMR ($CDCl_3$) δ 55.9, 60.3, 112.9, 114.7, 120.5, 121.4, 121.5, 123.1, 126.9, 128.0, 128.9, 129.1, 130.8, 132.2, 155.6, 162.3, 163.0.

4.4.4. Compound 11fB. ^{1}H NMR ($CDCl_3$) δ 3.82 (s, 3H, OCH_3), 4.37 (d, 1H, J=17.0 Hz, H1), 4.53 (d, 1H, J=17.0 Hz, H1), 5.83 (s, 1H, NC*H*(Ar)NPh), 6.94 (d, 2H, J=7.0 Hz, Ar), 7.14 (d, 1H, J=9.0 Hz, H5), 7.35 (t, 1H, J=8.0 Hz, H8), 7.47 (t, 1H, J=8.0 Hz, H9), 7.57 (d, 2H, J=8.0 Hz, Ar), 7.64 (d, 1H, J=9.0 Hz, H10), 7.67 (d, 1H, J=9.0 Hz, H6), 7.77 (d, 1H, J=8.5 Hz, H7), ^{13}C NMR ($CDCl_3$) δ 42.7, 55.7, 87.3, 114.0, 114.3, 119.9, 121.6, 121.7, 123.9, 126.9, 128.0, 129.3, 129.4, 131.6, 131.9, 152.7, 160.2.

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