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Substituent Effects in the Ring–Chain Tautomerism of 1-Alkyl-3-arylnaphth-[1,2-*e*][1,3]oxazines

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Dedicated to Professor Erich Kleinpeter on the occasion of his 60th birthday

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New 1-(1-aminoalkyl)-2-naphthols **8**–**11** have been synthesised by the condensation of 2-naphthol with aliphatic aldehydes in the presence of ammonia, followed by acidic hydrolysis. The condensation of **7**–**11** with substituted benzaldehydes after microwave irradiation led to 1-alkyl-3-aryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines, which proved to be three-component (r^t-o-r^c) tautomeric mixtures in $CDCl_3$ at 300 K. The electronic effects of the 1-alkyl and 3-aryl groups on the tautomeric ratios could be determined for both the ring^{trans}–chain and the ring^{cis}–chain equilibria with the aid of two-variant linear equations. A significant difference was found between the coefficients of the Meyer parameter V^a, which characterises the volume of the portion of the alkyl substituent within 0.3 nm of the reaction centre, for ring^{trans}–chain and ring^{cis}–chain equilibria, and this is explained in terms of the stereoelectronic effect caused by the alkyl substituent at position 1.

Introduction

The structures and reactivities of numerous five- and six-membered, saturated, 1,3-X,N-heterocycles (X = O, S, NR) can be characterised by the ring–chain tautomeric equilibria of these heterocycles and the corresponding Schiff bases. Oxazolidines and tetrahydro-1,3-oxazines are the saturated 1,3-X,N-heterocycles whose ring–chain tautomerism has been studied most thoroughly. From quantitative studies on their tautomeric equilibria, it has been concluded that the tautomeric ratios for oxazolidines and tetrahydro-1,3-oxazines bearing a substituted phenyl group at position 2 can be characterised by an aromatic substituent dependence [Equation (1)]

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

where K_X is the [ring]/[chain] ratio and σ^+ is the Hammett–Brown parameter (electronic character) of substituent X on the 2-phenyl group.[1,2]

The scope and limitations of Equation (1) have been thoroughly studied from the point of view of the applicability of this equation in the case of complex tautomeric mixtures containing several types of open and/or cyclic forms, and the influence of the steric and/or electronic effects of the substituents at positions other than 2 on the parameters in this equation.[3–8]

Our quantitative investigations on the ring–chain tautomeric equilibria of 1,3-diaryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines have led to the first precise mathematical formulae with which to characterise the effects of substituents situated elsewhere than between the heteroatoms. For example, we have demonstrated that the tautomeric ratio is influenced not only by the aryl substituent at position 3, but also by that at position 1. This additional stabilisation effect was explained as an anomeric effect in the *trans* ring form.[9] When the tautomeric equilibria of 3-alkyl-1-aryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines were analysed, the results of multiple linear regression analysis of the $\log K_R$ values revealed a significant dependence on the inductive effect of substituent Y (σ_F), which was further evidence of the anomeric effect in the *trans* ring form.[9] Systematic quantitative investigations on the ring–chain tautomeric equilibria of 2,4-diarylnaphth[2,1-*e*][1,3]oxazines have demonstrated an analogous inductive influence on the ring^{trans}–chain tautomeric equilibria.[10]

The stereoelectronic effect relating to the relative configurations of C-1 and C-3 in these naphthoxazines could originate from the aryl substituent at position 1. There appears to be no published examples of the study of such effects of an alkyl group at the same position. We therefore set out to synthesise and investigate the substituent effects in a new 1,3-disubstituted naphthoxazine model system bearing an

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alkyl substituent at position 1 and an aryl substituent at position 3.

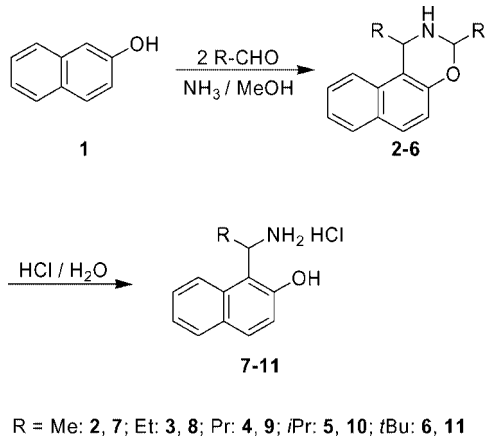
Results and Discussion

One hundred years ago, Betti reported a straightforward synthesis of 1-(α-aminobenzyl)-2-naphthol (the Betti base) from 2-naphthol, benzaldehyde and ammonia.[11] The Betti procedure can be interpreted as an extension of the Mannich condensation, with formaldehyde replaced by an aromatic aldehyde, the secondary amine by ammonia and the C–H acid by an electron-rich aromatic compound, such as 2-naphthol.[11,12] As a consequence of the potential utility of Mannich-type phenolic bases, the aminoalkylation of naphthol derivatives is a subject of current chemical interest.[12]

The classical Betti procedure has generally been confined to the use of aromatic aldehydes (e.g. benzaldehyde) as the aldehyde component,[12] and only a few examples are known where benzaldehyde has been replaced by some other aldehyde. For the synthesis of the desired model compounds, our interest focused on the application of aliphatic aldehydes in the Betti reaction. Formaldehyde was the first aliphatic aldehyde to be used in this three-component reaction.[13,14] For the preparation of 1-(1-aminoethyl)-2-naphthol, the classical Betti procedure was altered: the intermediate naphthoxazine was formed by refluxing 2-naphthol, acetaldehyde and ammonia in benzene to give 1,3-dimethyl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazine. Acidic hydrolysis of this led to 1-(1-aminoethyl)-2-naphthol hydrochloride in an overall yield of 70%.[15] A different synthetic pathway was applied to produce 1-(1-amino-2,2,2-trifluoroethyl)-2-naphthol, namely the preparation of 1-[2,2,2-trifluoro-1-(1-naphth-1-yl-ethylamino)ethyl]-2-naphthol, followed by catalytic hydrogenation.[16,17]

In our experiments, naphthoxazines **2**–**6** were formed by the condensation of 2-naphthol (**1**) and the corresponding aliphatic aldehyde in the presence of methanolic ammonia solution in absolute methanol at 60 °C for 6–72 h (Scheme 1). The acidic hydrolysis of **2**–**6** led to the desired aminonaphthol hydrochlorides **7**–**11** in low yields in a two-step process. The overall yield was improved considerably when the solvent was evaporated off after the formation of the intermediate naphthoxazines (**2**–**6**) and the residue was directly hydrolysed with hydrochloric acid (e.g. for compound **7** the overall yield could be increased from 15% to 95%).

Because of the instability of the Betti base derivatives, compounds **7**–**11** were isolated as hydrochlorides, which in subsequent transformations were basified in situ with triethylamine. The condensation of aminonaphthols **7**–**11** with one equivalent of aromatic aldehyde in absolute methanol in the presence of triethylamine at ambient temperature did not lead to the formation of the desired naphthoxazines. This failure was followed by a more modern attempt to synthesise our target compounds: microwave irradiation treatment[18] was tried, and in this way the preparation of **12**–**16** was successful. After the controlled microwave agitation (CEM microwave reactor, 10 min at 80 °C), the mixture was left to stand at room temperature to crystallise.



R = Me: **2**, **7**; Et: **3**, **8**; Pr: **4**, **9**; *i*Pr: **5**, **10**; *t*Bu: **6**, **11**

Scheme 1.

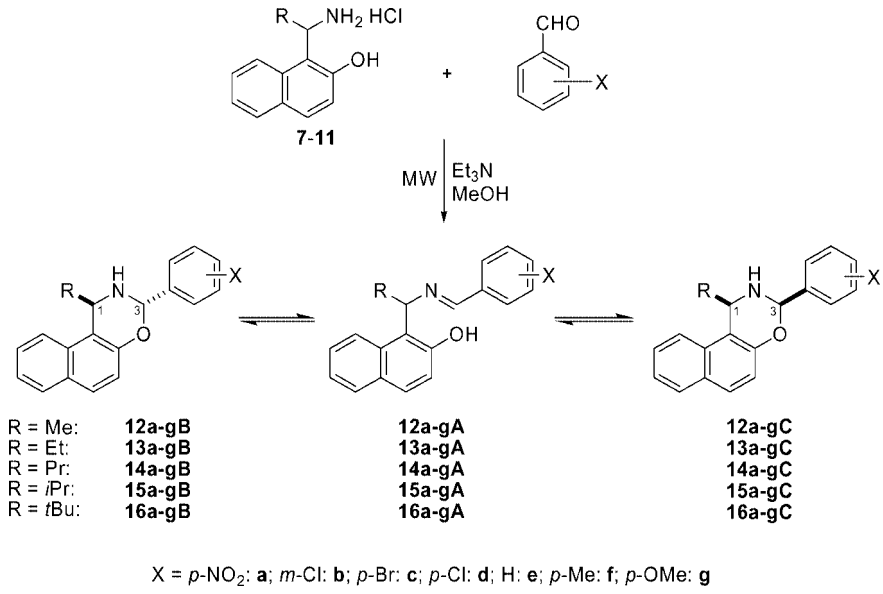
The ^{1}H NMR spectra of **12**–**15** reveal that, in $CDCl_3$ solution at 300 K, the members **a**–**g** of each set of compounds **12**–**15** exist in three-component ring–chain tautomeric mixtures containing the C-3 epimeric naphthoxazines (**B** and **C**) and also the open tautomer (**A**). The proportion of the ring forms decreases as the alkyl substituent at position 1 becomes more bulky. Accordingly, for some 1-isopropyl-3-arylnaphthoxazine derivatives (**15**) the proportions of the ring forms (**B** and **C**) were close to the limiting error and in the case of **16** only the derivatives **16a**, **16e** and **16f** were synthesised. As expected, ring forms **B** and **C** of compounds **16** (Scheme 2) were not found at all in the tautomeric mixture. In order to acquire reliable results, more sample data were needed and the series of compounds was therefore expanded to include naphthoxazines **18**. The tautomeric behaviour of analogues **18** (**18a**, **18d**–**g**) is known from the literature, but compounds **18b** and **18c** were absent and were therefore synthesised according to Scheme 3.[14]

Table 1 shows the proportions of the diastereomeric ring forms (**B** and **C**) from the tautomeric equilibria of **12**–**16** and **18**, as determined by integration of the well-separated O–C*H*Ar–N (ring) and N=C*H*Ar (chain) proton signals in the ^{1}H NMR spectra. As a consequence of the very similar NMR spectroscopic characteristics of 1-alkyl-3-aryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines **12**–**16**, only the data for **12a** were chosen to illustrate the ^{1}H NMR spectra of the prepared tautomeric compounds (see Exp. Sect.).

To study the double substituent dependence of $\log K_B$ and $\log K_C$, the following Hansch-type quantitative structure-properties relationship model equation [Equation (2)] was set up

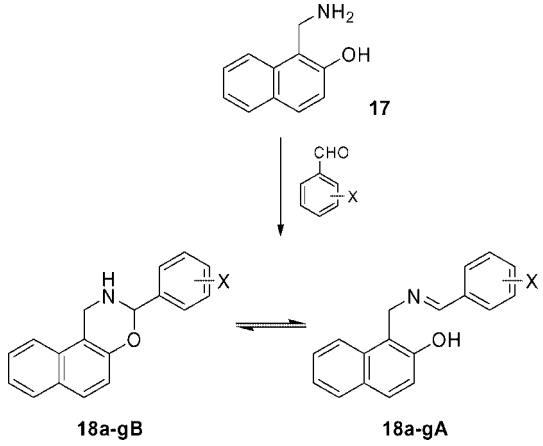
$$\log K_{B/C} = k + \rho^R P^R + \rho^X \sigma^{+X} \quad (2)$$

where K_B = [B]/[A], K_C = [C]/[A], P^R is an alkyl substituent parameter and σ^{+X} is the Hammett–Brown parameter of the aryl substituent at position 3. In order to find the accurate dependence of $\log K_{B/C}$, three different alkyl substituent parameters were studied: E_s (calculated from the hydrolysis



Scheme 2.

or aminolysis of esters)[19] and two other steric parameters that are independent of any kinetic data, namely v, derived from the van der Waals radii,[20,21] and V^a, the volume of the portion of the substituent that is within 0.3 nm of the reaction centre.[22]



Scheme 3.

Multiple linear regression analysis of Equation (2) was performed with the SPSS statistical software, and a value of 0.05 was chosen as the significance level.[23] Good correlations were found for all three alkyl substituent parameters. The linear regression analysis data for the series **12**–**15** and **18** are given in Table 2. The best correlations were observed for the Meyer parameter (V^a) of the alkyl substituents, and this was used for the further examinations.

Table 2. Multiple linear regression analysis of $\log K_B$ and $\log K_C$ values for **12**–**15** and **18**.

		k	ρ^R	ρ^X	r
$P^R = V^a$	**12**–**15**,**18B**⇌**12**–**15**,**18A**	0.605	–0.320	0.848	0.965
	12–**15**,**18C**⇌**12**–**15**,**18A**	0.413	–0.464	0.978	0.994
$P^R = E_s$	**12**–**15**,**18B**⇌**12**–**15**,**18A**	0.609	0.948	0.809	0.938
	12–**15**,**18C**⇌**12**–**15**,**18A**	0.524	1.442	0.881	0.992
$P^R = v$	**12**–**15**,**18B**⇌**12**–**15**,**18A**	0.624	–2.250	0.822	0.946
	12–**15**,**18C**⇌**12**–**15**,**18A**	0.516	–3.356	0.886	0.994

The parameters given in Table 2 indicate that the tautomeric interconversion (e.g. $\log K_B$ and $\log K_C$ values) can be described by using two substituent parameters (V^a and σ^+),

Table 1. Proportions [%] of the ring-closed tautomeric forms (**B** and **C**) in tautomeric equilibria for compounds **12**–**16** and **18** ($CDCl_3$, 300 K).

		R	**18** H	**12** Me		**13** Et		**14** Pr		**15** *i*Pr		**16** *t*Bu	
		V^a	0	2.84		4.31		4.78		5.74		7.16	
Compound	X	σ^+	**B**	**B**	**C**	**B**	**C**	**B**	**C**	**B**	**C**	**B**	**C**
a	*p*-NO_2	0.79	95.2	70.3	10.0	59.4	4.8	60.3	4.4	8.9	≈0	≈0	≈0
b	*m*-Cl	0.40	86.5	52.8	7.7	21.3	6.8	25.3	2.6	3.5	2.5	–	–
c	*p*-Br	0.15	81.1	39.5	6.0	26.5	2.7	23.4	1.5	1.2	0.7	–	–
d	*p*-Cl	0.11	79.4	39.4	6.3	25.2	2.2	24.8	1.5	1.8	1.1	–	–
e	H	0	72.3	30.4	5.2	18.4	1.9	12.8	≈0	≈0	≈0	≈0	≈0
f	*p*-Me	–0.31	58.3	18.0	2.5	11.6	≈0	9.1	≈0	≈0	≈0	≈0	≈0
g	*p*-OMe	–0.78	45.4	10.9	1.7	3.5	≈0	3.9	≈0	≈0	≈0	–	–

which means that, when $\log K_B$ or $\log K_C$ is plotted against the Meyer parameter (V^a) and the Hammett–Brown parameter (σ^+), a plane can be fitted to the data points (Figure 1, a and b).

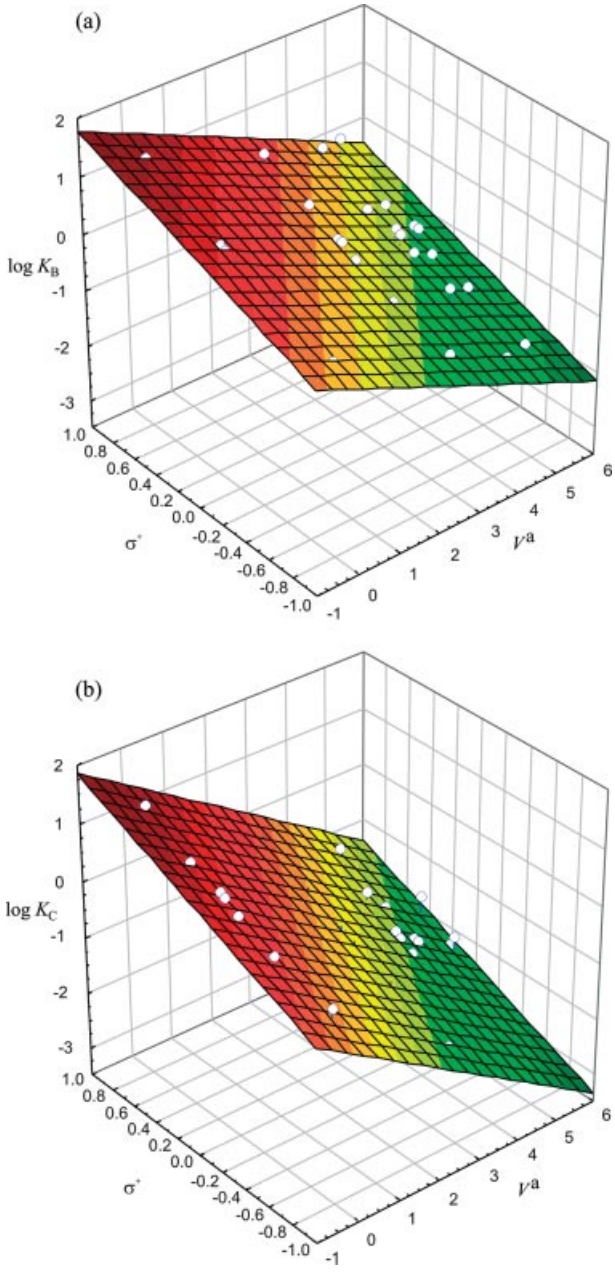


Figure 1. (a) Plots of $\log K_B$ for **12**–**15B** and **18B** vs. Meyer (V^a) and Hammett–Brown parameters (σ^+). (b) Plots of $\log K_C$ for **12**–**15C** and **18C** vs. Meyer (V^a) and Hammett–Brown parameters (σ^+).

The slopes of the alkyl substituent parameters (ρ^R) for the equilibria **B**⇌**A** and **C**⇌**A** exhibit a significant difference (–0.320 vs. –0.464). This difference can be explained by an additional stabilisation effect caused by the alkyl substituents.

Conclusions

New alkyl-substituted Betti base analogue aminonaphthols have been synthesised from aliphatic aldehydes. The reactions of these aminoalkylnaphthol derivatives with substituted benzaldehydes lead to 1-alkyl-3-aryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines, which have proved to be three-component tautomeric mixtures in $CDCl_3$ at 300 K, involving C-3 epimeric naphthoxazines (**B** and **C**) and the open tautomer (**A**). The influence of the alkyl substituent at position 1 on the ring–chain tautomeric equilibria can be described by the Meyer parameter, and that of the aryl substituent at position 3 by the Hammett–Brown parameter (σ^+). Linear equations have been found that describe the double substituent dependence of the equilibrium constants for both the *trans*–chain and *cis*–chain equilibria. The slopes of the Meyer parameter V^a for the *trans* and *cis* forms display a significant difference, which is explained in terms of an alkyl-substituent-controlled stereoelectronic effect in the *trans* ring form. Theoretical examinations of this alkyl substituent effect and its connection with the preferred geometry (relating to the relative configurations of C-1 and C-3) are still in progress.

Experimental Section

Melting points were determined with a Kofler micro melting apparatus and are uncorrected. Elemental analyses were performed with a Perkin–Elmer 2400 CHNS elemental analyser. Merck Kiesegel 60 F_{254} plates were used for TLC. The ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or in [D_6]DMSO solution at 300 K with a Bruker Avance DRX400 spectrometer at 400.13 (^1H) and 100.61 MHz (^{13}C). Chemical shifts are given in δ (ppm) relative to TMS as internal standard. For the equilibria of tautomeric compounds to be established, the samples were dissolved in $CDCl_3$ and the solutions were allowed to stand at ambient temperature for 1 d before the ^1H NMR spectra was run. The number of scans was usually 64.

General Method for the Synthesis of 1-Aminoalkyl-2-naphthols 7–11: The appropriate aliphatic aldehyde (62.5 mmol) and 25% methanolic ammonia solution (20 mL) were added to a solution of 2-naphthol (**1**; 3.6 g, 25 mmol) in absolute MeOH (30 mL). The mixture was then stirred at 60 °C for 4–72 h. The MeOH was removed under reduced pressure and intermediates **2**–**6** were suspended in 10% HCl (210 mL). The mixture was stirred and heated for 3 h at 60 °C, and the solvent was evaporated off. The crystalline hydrochloride of **7**–**11** that separated out from EtOAc (50 mL) was filtered off, washed with $CHCl_3$ and Et_2O, and recrystallised from Et_2O/MeOH (4:1).

1-(1-Aminoethyl)-2-naphthol Hydrochloride (7): Condensation time: 4 h. White crystals, 5.02 g (95%), m.p. 210–212 °C. ^1H NMR ([D_6]-DMSO): δ = 1.62 (d, J = 6.55 Hz, 3 H, CH_3), 5.07–5.17 (m, 1 H, CH_3CH), 7.28–7.36 (m, 2 H, naphthyl), 7.52 (t, J = 7.55 Hz, 1 H, naphthyl), 7.80–7.87 (m, 2 H, naphthyl), 7.98 (d, J = 8.56 Hz, 1 H, naphthyl), 8.28 (s, 3 H, NH_3), 10.84 (s, 1 H, O*H*) ppm. ^{13}C NMR ([D_6]DMSO): δ = 18.4, 44.4, 115.1, 118.6, 121.4, 122.8, 127.0, 128.0, 128.7, 129.9, 131.4, 153.6 ppm. $C_{12}H_{14}ClNO$ (223.70): calcd. C 64.43, H 6.31, N 6.26; found C 64.59, H 6.33, N 6.27.

1-(1-Aminopropyl)-2-naphthol Hydrochloride (8): Condensation time: 3 h. White crystals, 2.37 g (42%), m.p. 191–193 °C. ^1H NMR ([D_6]DMSO): δ = 0.79 (t, J = 7.55 Hz, 3 H, CH_3), 2.07–2.19 (m, 2 H, CH_2), 4.94 (m, 4.83–4.94, 1 H, C*H*), 7.33 (t, J = 7.55 Hz, 1 H, naphthyl), 7.39 (d, J = 8.56 Hz, 1 H, naphthyl), 7.50 (t, J = 7.55 Hz, 1 H, naphthyl), 7.83 (t, J = 8.06 Hz, 2 H, naphthyl), 8.02 (d, J =

8.56 Hz, 1 H, naphthyl), 8.32 (s, 3 H, NH_3), 10.87 (s, 1 H, O*H*) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 10.5, 25.2, 113.6, 118.4, 121.7, 122.6, 126.8, 127.9, 128.7, 130.0, 132.6, 153.8 ppm. $C_{13}H_{16}ClNO$ (237.73): calcd. C 65.68, H 6.78, N 5.89; found C 65.45, H 6.77, N 5.89.

1-(1-Aminobutyl)-2-naphthol Hydrochloride (9): Condensation time: 72 h. White crystals, 1.71 g (27%), m.p. 202–204 °C. ^{1}H NMR ([D$_6$]DMSO): δ = 0.82 (t, J = 7.55 Hz, 3 H, CH_3), 0.98–1.13 (m, 1 H, CH$_3$CH_2), 1.25–1.40 (m, 1 H, CH$_3$CH_2), 1.98–2.18 (m, 2 H, CH_2CH), 4.99 (s, 1 H, CH$_2$C*H*), 7.19–7.52 (m, 3 H, naphthyl), 7.82 (t, J = 9.06 Hz, 2 H, naphthyl), 7.99 (d, J = 8.56 Hz, 1 H, naphthyl), 8.29 (s, 3 H, NH_3), 10.82 (s, 1 H, O*H*) ppm. ^{13}C NMR ([D$_6$]-DMSO): δ = 13.8, 18.9, 34.2, 113.9, 118.5, 121.9, 122.6, 126.9, 127.9, 128.7 129.9, 133.0, 153.9 ppm. $C_{14}H_{18}ClNO$ (251.75): calcd. C 66.79, H 7.21, N 5.56; found C 66.81, H 7.22, N 5.57.

1-(1-Amino-2-methylpropyl)-2-naphthol Hydrochloride (10): Condensation time: 72 h. White crystals, 5.03 g (80%), m.p. 229–232 °C. ^{1}H NMR ([D$_6$]DMSO): δ = 0.65 (d, J = 6.04 Hz, 3 H, CH_3), 1.18 (d, J = 6.56 Hz, 3 H, CH_3), 2.26 (s, 1 H, CH$_3$C*H*), 4.63 (s, 1 H,CH$_3$CHC*H*), 7.31 (t, J = 7.05 Hz, 2 H, naphthyl), 7.41 (s, 1 H, naphthyl), 7.82 (t, J = 9.06 Hz, 2 H, naphthyl), 8.01 (d, J = 8.05 Hz, 1 H, naphthyl) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 19.8, 30.4, 54.1, 114.2, 118.5, 121.8, 122.6, 126.8, 127.8, 128.7, 129.9, 132.9, 153.8 ppm. $C_{14}H_{18}ClNO$ (251.75): calcd. C 66.79, H 7.21, N 5.56; found C 66.31, H 7.19, N 5.55.

1-(1-Amino-2,2-dimethylpropyl)-2-naphthol Hydrochloride (11): 2-Naphthol: 0.56 g (3.88 mmol); condensation time: 72 h. White crystals, 0.39 g (38%), m.p. 236–239 °C. ^{1}H NMR ([D$_6$]DMSO): δ = 1.04 [s, 9 H, (CH_3)$_3$C], 4.86 (d, J = 4.03 Hz, 1 H, CC*H*N), 7.318 (t, J = 7.55 Hz, 1 H, naphthyl), 7.39 (d, J = 9.07 Hz, 1 H, naphthyl), 7.49 (t, J = 7.55 Hz, 1 H, naphthyl), 7.82 (d, J = 9.06 Hz, 2 H, naphthyl), 8.04 (d, J = 8.56 Hz, 1 H, naphthyl), 8.21 (s, 3 H, NH_3), 10.80 (s, 1 H, O*H*) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 28.3, 37.9, 57.7, 113.2, 119.8, 123.4, 123.7, 127.5, 128.8, 129.5, 130.9, 134.3, 154.9 ppm. $C_{15}H_{20}ClNO$ (265.2): calcd. C 67.72, H 7.54, N 5.27; found C 67.49, H 7.53, N 5.28.

General Method for the Synthesis of 1-Alkyl-3-aryl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazines (12–16 and 18): The aminonaphthol (0.39 mmol), one equivalent of X-substituted benzaldehyde, 1.1 equiv. of Et$_3$N and absolute MeOH (7 mL) were mixed in a 10-mL pressurized reaction vial, which was heated for 10 min at 80 °C in a CEM microwave reactor. The crystalline product was filtered off, and washed with MeOH. All of the new compounds **12**–**16** and **18** gave satisfactory elemental analysis data (C, H, N ±0.3%). The compounds were recrystallised from *i*Pr$_2$O. The physical and analytical data for compounds **12**–**16** and **18** are listed in Table 3.

As regards the similarities in the ^{1}H NMR spectroscopic data, a full characterisation is reported only for compound **12a**. The ^{1}H NMR chemical shifts of the characteristic O–C*H*Ar–N protons of

Table 3. Physical, analytical and NMR spectroscopic data for naphth[1,2-*e*][1,3]oxazines **12**–**16** and **18**.

Compd.	M.p. [°C]	Yield [%]	Formula	*MW*	Elemental analysis C found (calcd.)	H found (calcd.)	N found (calcd.)	δ [ppm] N=C*H* (**A**)	N–C*H*–O (**B**)	N–C*H*–O (**C**)
12a	155–158	64	$C_{19}H_{16}N_2O_3$	320.35	71.04 (71.24)	5.04 (5.03)	8.75 (8.74)	8.62	6.15	5.73
12b	135–138	59	$C_{19}H_{16}ClNO$	309.80	73.02 (73.66)	5.21 (5.21)	4.52 (4.52)	8.44	6.03	5.60
12c	176–178	51	$C_{19}H_{16}BrNO$	354.25	64.65 (64.42)	4.53 (4.55)	3.94 (3.95)	8.42	6.01	5.58
12d	178–180	60	$C_{19}H_{16}ClNO$	309.80	73.46 (73.66)	5.22 (5.21)	4.51 (4.52)	8.44	6.03	5.60
12e	119–121	56	$C_{19}H_{17}NO$	275.35	83.05 (82.88)	6.23 (6.22)	5.11 (5.09)	8.46	6.06	5.53
12f	145–148	54	$C_{20}H_{19}NO$	289.38	83.55 (83.01)	6.63 (6.62)	4.85 (4.84)	8.42	6.04	5.59
12g	131–132	67	$C_{20}H_{19}NO_2$	305.38	78.56 (78.66)	6.28 (6.27)	4.58 (4.59)	8.41	6.06	5.62
13a	121–124	71	$C_{20}H_{18}N_2O_3$	334.38	72.01 (71.84)	5.42 (5.43)	8.39 (8.38)	8.56	6.09	5.72
13b	145–149	33	$C_{20}H_{18}ClNO$	323.83	73.90 (74.18)	5.62 (5.60)	4.34 (4.33)	8.38	5.97	5.79
13c	97–100	55	$C_{20}H_{18}BrNO$	368.28	65.32 (65.23)	4.91 (4.93)	3.80 (3.80)	8.37	5.95	5.57
13d	170–172	32	$C_{20}H_{18}ClNO$	323.83	74.42 (74.18)	5.62 (5.60)	4.34 (4.33)	8.37	5.99	5.60
13e	158–160	56	$C_{20}H_{19}NO$	289.38	83.19 (83.01)	6.62 (6.62)	4.83 (4.84)	8.42	6.02	5.62
13f	181–185	15	$C_{21}H_{21}NO$	303.41	82.89 (83.13)	6.88 (6.89)	4.63 (4.62)	8.37	5.98	–
13g	160–163	42	$C_{21}H_{21}NO_2$	319.41	79.13 (78.97)	6.64 (6.63)	4.41 (4.39)	8.32	5.96	–
14a	133–136	76	$C_{21}H_{20}N_2O_3$	348.40	72.16 (72.40)	5.80 (5.79)	8.04 (8.04)	8.52	6.08	5.68
14b	114–116	33	$C_{21}H_{20}ClNO$	337.84	74.82 (74.66)	5.98 (5.97)	4.14 (4.15)	8.38	5.99	5.61
14c	148–150	47	$C_{21}H_{20}BrNO$	382.29	65.98 (66.14)	5.27 (5.28)	3.65 (3.66)	8.36	5.98	5.58
14d	122–125	43	$C_{21}H_{20}ClNO$	337.40	74.80 (74.66)	5.97 (5.97)	4.14 (4.15)	8.38	5.99	5.60
14e	101–103	20	$C_{21}H_{21}NO$	303.40	83.53 (83.13)	6.99 (6.98)	4.62 (4.62)	8.41	6.03	–
14f	129–130	21	$C_{22}H_{23}NO$	317.42	83.74 (83.24)	7.29 (7.30)	4.40 (4.41)	8.35	6.00	–
14g	128–131	38	$C_{22}H_{23}NO_2$	333.42	78.96 (79.25)	6.96 (6.95)	4.21 (4.20)	8.32	5.99	–
15a	139–140	52	$C_{21}H_{20}N_2O_3$	348.41	72.68 (72.40)	5.93 (5.79)	8.01 (8.04)	8.51	6.19	–
15b	153–155	48	$C_{21}H_{20}ClNO$	337.85	74.39 (74.66)	6.09 (5.97)	4.21 (4.15)	8.34	6.10	5.51
15c	121–125	36	$C_{21}H_{20}BrNO$	382.30	65.76 (65.98)	5.07 (5.27)	3.50 (3.66)	8.34	6.08	5.51
15d	139–141	45	$C_{21}H_{20}ClNO$	337.85	74.93 (74.66)	5.83 (5.97)	4.10 (4.15)	8.35	6.10	5.52
15e	125–129	34	$C_{21}H_{21}NO$	303.41	83.11 (83.24)	7.38 (7.30)	4.59 (4.41)	8.36	–	–
15f	120–123	16	$C_{22}H_{23}NO$	289.38	83.41 (83.01)	6.42 (6.62)	4.71 (4.84)	8.33	–	–
15g	106–108	26	$C_{22}H_{23}NO_2$	333.43	79.17 (79.25)	6.79 (6.95)	4.32 (4.20)	8.29	–	–
16a	138–140	61	$C_{22}H_{22}N_2O_3$	362.42	73.16 (72.91)	6.12 (6.11)	7.73 (7.72)	8.51	–	–
16e	164–166	81	$C_{22}H_{23}NO$	317.42	83.41 (83.24)	7.31 (7.30)	4.42 (4.41)	8.39	–	–
16f	145–147	73	$C_{23}H_{25}NO$	331.45	83.19 (83.34)	7.61 (7.60)	4.22 (4.23)	8.29	–	–
18b	109–110	64	$C_{18}H_{14}ClNO$	295.76	72.95 (73.10)	4.76 (4.76)	4.75 (4.74)	8.43	5.84	–
18c	171–172	93	$C_{18}H_{14}BrNO$	340.21	63.66 (63.55)	4.14 (4.15)	4.12 (4.11)	8.46	5.85	–

each tautomeric form for compounds **12**–**16** and **18** are given in Table 3.

1-Methyl-3-*p*-nitrophenyl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazine (12a): A tautomeric mixture of Schiff base **12aA** (19.7%), *cis*-ring form **12aC** (10%) and *trans*-ring form **12aB** (70.3%). Selected signals: ^{1}H NMR ($CDCl_3$, 300 K): δ = 4.72 (q, J = 7.05 Hz, 1 H, CH_3CHN, Schiff base), 5.06 (q, J = 5.04 Hz, 1 H, CH_3CHN, *cis*), 5.58 (q, J = 7.05 Hz, 1 H, CH_3CHNH, Schiff base), 5.73 (s, 1 H, NC*H*O, *cis*), 6.15 (s, 1 H, NC*H*O, *trans*), 8.62 (s, 1 H, NC*H*O, Schiff base) ppm. ^{13}C NMR ($CDCl_3$, 300 K): δ = 22.5 (*trans*), 22.8 (*cis*), 23.1 (Schiff base), 45.8 (*trans*), 47.9 (*cis*), 66.8 (Schiff base), 80.7 (*trans*), 85.5 (*cis*), and 158.8 (Schiff base) ppm. Assignments of the aromatic region could not be made because of the low concentrations of **B** and **C** and the overlapping nature of the signals.

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