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By means of simple or domino ring-closure reactions of 1-(α-aminobenzyl)-2-naphthol (Betti base: **1**), 1-aminomethyl-2-naphthol (**2**) and 2-(α-aminobenzyl)-1-naphthol (reverse Betti base: **3**) with phosgene, ethyl benzimidate, 2-carboxybenzaldehyde, levulinic acid, salicylaldehyde/formalin or salicylaldehyde/acetaldehyde, naphth[1,2-*e*][1,3]oxazine and naphth[2,1-*e*][1,3]oxazine derivatives were prepared. All of the nitrogen-bridged polycyclic derivatives of **1** and **3** containing a number of centers of asymmetry were formed with nearly complete diastereoselectivity. Considerable differences were observed in the ring-closing abilities of the unsubstituted and phenyl-substituted aminonaphthols **1** and **2** and of the regioisomeric compounds **1** and **3**.

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Introduction.

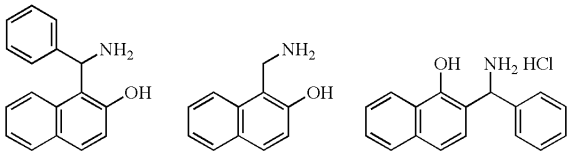
Although Betti's classical procedure for the preparation of 1-(α-aminobenzyl)-2-naphthol (**1**: Betti base) was published more than a century ago [1], the possibilities of the application of this versatile synthon in the ring-closure reactions to give naphthalene-condensed heterocyclic derivatives have not been thoroughly investigated. The few publications that have appeared on this topic focus on the reactions of **1** with aldehydes. Condensation products of **1** and substituted benzaldehydes proved to participate in ring-chain tautomeric equilibria involving two diastereomeric naphthoxazines and an open imine form, the ratios of which were strongly influenced by the electronic effects of the substituents on the aromatic aldehyde [2-5]. The ring-chain tautomeric character of these condensation products of **1** and substituted benzaldehydes was utilized by Desai *et al*. to prepare 4-thiazolidone derivatives with antibacterial activity by the addition of mercaptoacetic acid to the imine forms [6].

Since Naso *et al*. first reported the application of the enantiomers of **1** in asymmetric transformations [7,8], a number of transformation reactions of the enantiopure Betti base, including ring closures to afford heterocyclic intermediates have been published. The *N*-butyl derivative of (*S*)-**1** was prepared by reductive alkylation *via* the corresponding ring-chain tautomeric naphthoxazine intermediate [8]. Nonracemic 1-[α-(1-azacycloalkyl)benzyl]-2-naphthols were synthetized by Hu *et al*. *via* nitrogen-bridged tetracyclic naphthoxazine derivatives obtained by reductive cyclization of the enantiomers of **1** with dials in the presence of $NaBH_3CN$ [9, 10].

Our present aim was to extend the synthetic applicability of aminonaphthol **1** for the preparation of new heterocyclic derivatives. To investigate the effects of the phenyl substituent and the chemical behavior of the regioisomeric structures **1** and **3**, these transformations were also performed by starting from aminonaphthols **2** and **3**.

Results and Discussion.

The starting aminonaphthols **1-3** were prepared by known procedures [11-13]. Phenyl-substituted regioisomeric compounds **1** and **3** were synthesized by Mannich aminoalkylation of the corresponding 1- or 2-naphthol with benzaldehyde in the presence of ammonia [11,12]. Acidic hydrolysis of the naphthoxazine intermediates leads to aminonaphthol **1** or **3**, respectively. In consequence of the facile decomposition of the free base, compound **3** was used in further transformations as the hydrochloride. Aminonaphthol **2** was obtained by the reaction of 2-naphthol and hexamethylenetetramine in acetic acid, followed by acidic hydrolysis of the intermediate condensation product [12].



1 **2** **3**

In the first stage of the transformation reactions of compounds **1-3** to yield heterocyclic derivatives, a one-carbon segment with sp^2 configuration was inserted between the hydroxy and amino groups.

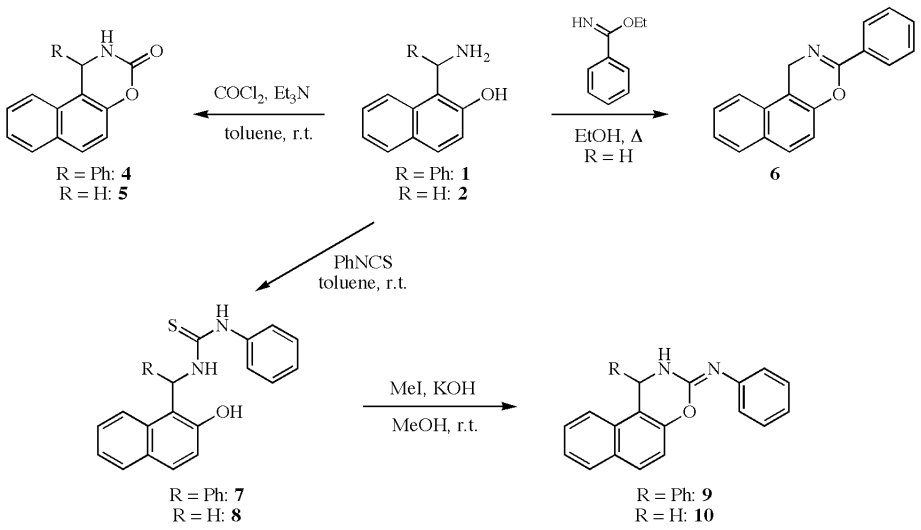
When aminonaphthols **1-3** were treated with phosgene in the presence of Et_3N, the corresponding naphthalene-condensed 1,3-oxazin-2-ones **4**, **5** and **18** were formed in each case (Schemes 1 and 4). Similar ring closures of the analogous 2-aminomethylphenol were recently investigated [14]. The reactions of **1-3** with ethyl benzimidate in boiling EtOH gave the desired 1,3-oxazine derivative **6** only in the case of the unsubstituted aminophenol **2**; with the phenyl-substituted regioisomers **1** and **3**, only decomposition of the starting aminonaphthols was observed (Scheme 1). Whereas the preparation of dihydro-1,3-oxazine derivatives by the ring closure of aminoalcohols with imidates is well known in the literature [15], compound **2** was the first aminophenol for which this transformation was successfully accomplished.

For the preparation of 2-phenylimino-substituted 1,3-oxazines, aminonaphthols **1**-**3** were reacted with phenyl isothiocyanate. In the cases of 1-substituted 2-naphthols **1** and **2**, the corresponding thiourea derivatives **7** and **8** were formed in good yields. Thioureas **7** and **8** were converted to the corresponding *S*-methyl isothiourea derivatives with methyl iodide, and subsequent treatment with methanolic KOH gave the corresponding 2-arylimino-substituted 1,3-oxazines **9** and **10** *via* methyl mercaptan elimination (Scheme 1). This type of ring closure is well known among *N*-thiocarbamoyl-substituted aminoalcohols [16], but as far as we are aware compounds **9** and **10** are the first 2-arylimino-substituted 1,3-oxazine derivatives formed from *N*-thiocarbamoyl-substituted aminophenols. Endocyclic-exocyclic tautomerism of the C=N bond was not investigated.

capable of reacting with the amino group of the naphthoxazine formed, the tautomeric equilibrium can be shifted completely toward the ring-closed form by this second ring closure, resulting in nitrogen-bridged heterocycles. This principle was successfully applied earlier in the domino ring-closure reactions of *N*-unsubstituted aminoalcohols or aminophenols with γ- or δ-oxoacids [17, 18].

The reactions of aminonaphthols **1**-**3** with 2-carboxybenzaldehyde under mild conditions (r.t.) gave the corresponding isoindole-condensed naphthoxazines **11**, **12** and **19** (Schemes 2 and 4). NMR measurements indicated that pentacycles **11** and **19** were formed with practically complete stereoselectivity, with the relative configurations depicted in the Schemes; no minor diastereomers were detected even in the crude products. Similarly high diastereoselectivity is often observed in the analogous ring

Scheme 1

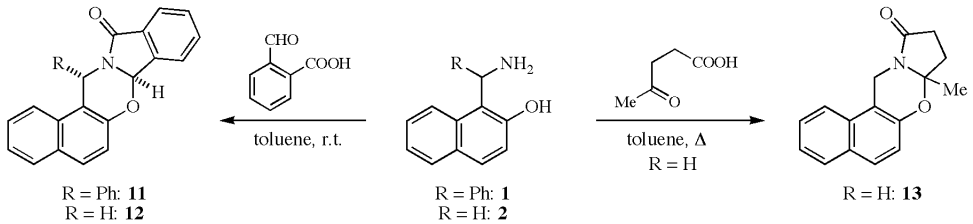


As mentioned above, the ring closures of *N*-unsubstituted aminonaphthols **1**-**3** with oxo compounds (*i.e.* the insertion of a one-carbon segment with sp^3 configuration) result in naphthalene-condensed 1,3-oxazines with a ring-chain tautomeric character [2-5]. If the oxo compound used in this reaction contains another functional group

closures of aminoalcohols and is explained as a result of the kinetic control governing the second ring closures of the cyclic tautomeric intermediates [19,20].

The analogous reactions of **1**-**3** with levulinic acid could not be accomplished under mild conditions, the corresponding pyrrolo-naphthoxazine **13** being produced only

Scheme 2



in the case of the unsubstituted aminonaphthol **2** (Scheme 2). Elevated temperature again caused the decomposition of aminonaphthols **1** and **3** instead of cyclization.

A complete shift of the ring-chain tautomeric equilibrium of 1,3-*O*,*N*-heterocycles can be achieved by means of another transformation. If the oxo compound contains another functional group (*e.g.* OH) capable of coupling with the amino group of the ring-closed tautomers *via* an appropriate agent, this reaction can be a second ring closure with another aldehyde. This type of transformation was exploited earlier in the preparation of 1,3-*O*,*N*-heterocycle-condensed 1,3-oxazines by subsequent cyclization of the aminoalcohols with salicylaldehyde and another aldehyde [21-23].

When aminonaphthols **1** and **2** were reacted with salicylaldehyde, crystalline condensation products **14** and **15** were formed. NMR measurements revealed that the tautomeric equilibrium of **15** in $CDCl_3$ at 300 K was practically totally shifted toward the open form **15A**, while the phenyl-substituted compound **14** was found to participate under similar conditions in a three-component tautomeric equilibrium involving the *trans* (**14B**: 56.7%) and the *cis* (**14C**: 8.5%) cyclic diastereomers besides the Schiff base (**14A**: 34.8%). These data are in accordance with earlier observations on the predominance of the open form in the tautomeric equilibria of the condensation products of 1,2- and 1,3-aminoalcohols and salicylaldehyde, which is explained by the stabilization caused by the strong intramolecular hydrogen bonds [21,22].

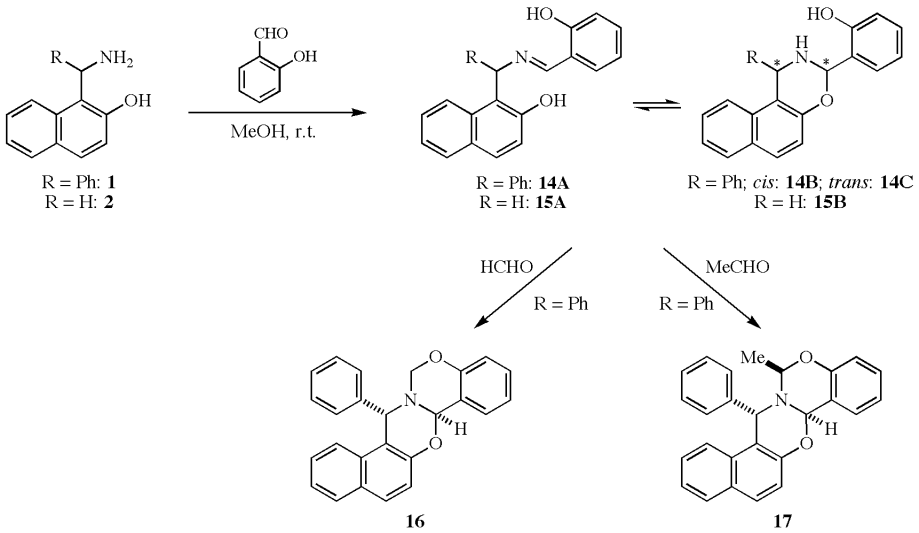
17 as crystalline products, whereas the similar transformations of **15** failed. The difference in cyclization behavior between **14** and **15** can be explained on the basis of the better crystallization ability of the pentacyclic products **16** and **17** formed from **14**, which causes a continuous shift of the tautomeric equilibrium toward the predominant cyclic tautomer **14B** [21,22]. In contrast, Stankevich *et al*. related the successful formation of oxazolobenzoxazines in analogous reactions to the increased ratio of the cyclic form in the tautomeric equilibria of the 2-(*o*-hydroxyphenyl)-oxazolidine intermediates [23]. According to the NMR data, pentacycles **16** and **17** were formed with high stereoselectivity (*de* ~100%), with the relative configurations depicted in Scheme 3.

Structures.

In the NMR spectra of the products **4**-**19**, proton and carbon chemical shifts can be assigned by using COSY, HSQC and HMBC experiments. The relative configurations of the diastereomers for **11**, **14**, **16**, **17** and **19** were deduced from the NOESY spectra, in which the cross-peak for the protons of the chiral C atoms proved their *trans* arrangement for all these compounds.

The structures were also confirmed by molecular modeling. The conformational protocol comprised a stochastic search *via* the Merck Molecular Force Field (MMFF94), and a subsequent minimization of the resulting low-energy conformations at the *ab initio* level, using the HF/3-21G* basis set for **11**, **14**, **16**, **17** and **19**. The resulting structures

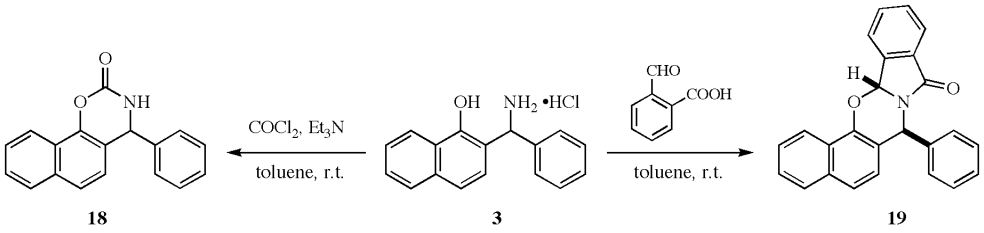
Scheme 3



Treatment of compound **14** with 40% formalin or ethanolic acetaldehyde solution resulted in the formation of phenyl-substituted naphthoxazino-benzoxazines **16** and

proved to be rigid, since no minor conformation was found within the 6 kcal/mol energy window. The final conformations for **11**, **16**, **17** and **19** are shown in Figure 1.

Scheme 4



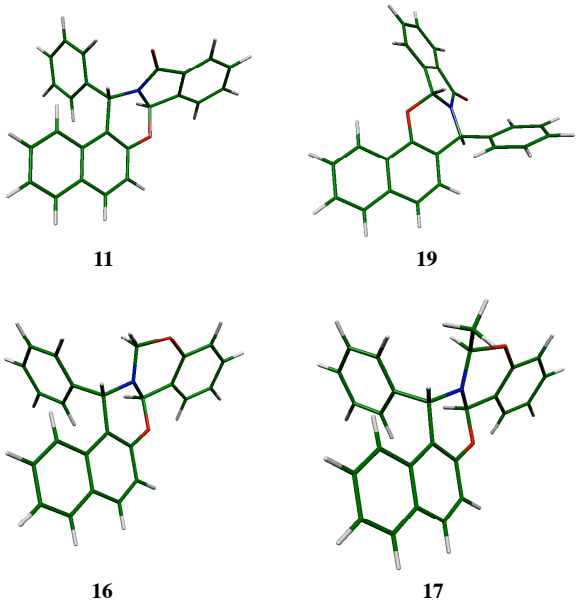


Figure 1. Final predominant minimum energy molecular structures for **11**, **16**, **17** and **19**, obtained by using *ab initio* HF/3-21G* calculations.

Our results prove that the Betti base **1** and its aminonaphthol analogs **2** and **3** are useful starting materials for the preparation of naphthalene-condensed tri-, tetra- or pentacyclic 1,3-oxazine derivatives. The ring closures of **1** and **3** to furnish tetra- and pentacycles were found to be characterized by virtually complete diastereoselectivity. Probably as a result of the different chemical stabilities of **1**-**3**, considerable differences were observed in the cyclization abilities of the unsubstituted and phenyl-substituted aminonaphthols **1** and **2** and of the regioisomeric compounds **1** and **3**.

EXPERIMENTAL

Melting points were determined on a Kofler micro melting apparatus and are uncorrected. Elemental analyses were performed with a Perkin-Elmer 2400 CHNS elemental analyzer. Merck Kieselgel $60F_{254}$ plates were used for TLC: the eluent was toluene-methanol 4:1. The ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ solution in 5 mm tubes, at room temperature, on a Bruker *Avance* DRX400 spectrometer at 400.13 (^{1}H) and 100.61 (^{13}C) MHz, with the deuterium signal of the solvent as the lock and TMS as internal standard. Compounds **1** and **2** were prepared by following literature methods [18]. For the equilibria to be established in the tautomeric compounds samples were dissolved in $CDCl_3$ and the solutions were allowed to stand at ambient temperature for 1 day before the VT-NMR spectra were run at 300 K.

1-Phenyl-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazin-3-one (**4**).

Aminonaphthol **1** (0.30 g, 1.20 mmol) was dissolved in abs. toluene (10 mL), and Et_3N (0.24 g, 2.41 mmol) and phosgene (0.63 mL; 20% in toluene, 1.20 mmol) were added. The mixture was stirred at r.t. for 3 h and then H_2O (40 mL) and EtOAc (40 mL) were added. The organic layer was separated, dried (Na_2SO_4) and evaporated. The oily residue crystallized on treatment with Et_2O (20 mL). The crystalline product was collected by filtration and recrystallized from *i*Pr_2O (30 mL). Yield: 0.18 g (54%), mp: 210-211 °C; ^{1}H-NMR (deuteriochloroform): δ 6.08 (1H, d, J = 2.0 Hz, 1-H), 5.96 (1H, bs, NH), 7.24-7.36 (6H, m, 5H, Ph), 7.38-7.44 (2H, m, 8-H, 9-H), 7.54-7.59 (1H, m, 6-H), 7.81-7.89 (2H, m, 7-H, 10-H); ^{13}C-NMR (deuteriochloroform): δ 56.6 (1-C), 113.2 (10b-C), 117.4 (5-C), 123.0 (10-C), 125.4 (4'-C), 127.2 (2'-C, 6'-C), 127.4 (6a-C), 127.7 (8-C), 129.0 (9-C), 129.1 (6-C), 129.7 (3'-C, 5'-C), 130.9 (7-C), 131.2 (10a-C), 141.9 (1'-C), 148.4 (4a-C), 150.4 (3-C).

Anal. Calcd. for $C_{18}H_{13}NO_2$ (275.31): C, 78.53; H, 4.76; N, 5.09. Found: C, 78.75; H, 4.75; N, 5.09.

2,3-Dihydro-1*H*-naphth[1,2-*e*][1,3]oxazin-3-one (**5**).

Aminonaphthol **2** (0.30 g, 1.73 mmol) was dissolved in abs. toluene (10 mL) and Et_3N (0.35 g, 3.47 mmol) and phosgene (20% in toluene, 0.90 mL; 1.73 mmol) were added. The mixture was stirred at r.t. for 4 h and then H_2O (40 mL) and EtOAc (40 mL) were added. The organic layer was separated, dried (Na_2SO_4) and evaporated. The oily residue crystallized on treatment with *n*-hexane (20 mL). The crystalline product was collected by filtration and recrystallized from *n*-hexane-*i*Pr_2O (4:1, 50 mL). Yield: 0.11 g (32%), mp: 166-168 °C; ^{1}H-NMR (deuteriochloroform): δ 4.94 (2H, s, 2 x 1-H), 5.72 (1H, bs, NH), 7.22 (1H, d, J = 9.1 Hz, 5-H), 7.46-7.60 (3H, m, 8-H, 9-H, 10-H), 7.81 (1H, d, J = 8.8 Hz, 6-H), 7.87 (1H, d, J = 8.1 Hz, 7-H); ^{13}C-NMR (deuteriochloroform): δ 41.5 (1-C), 108.7 (10b-C), 117.3 (5-C), 121.8 (10-C), 125.6 (8-C), 127.8 (9-C), 129.1 (7-C), 129.3 (6a-C), 130.1 (6-C), 133.2 (10a-C), 147.4 (4a-C), 150.6 (3-C).

Anal. Calcd. for $C_{12}H_9NO_2$ (199.21): C, 72.35; H, 4.55; N, 7.03. Found: C, 72.19; H, 4.54; N, 7.01.

3-Phenyl-1*H*-naphth[1,2-*e*][1,3]oxazine (**6**).

A mixture of aminonaphthol **2** (0.40 g, 2.31 mmol) and ethyl

benzimidate (0.31 g, 2.31 mmol) was refluxed in EtOH (20 mL) for 8 h. After evaporation, the residue crystallized on treatment with Et_2O (20 mL). The crystalline product was collected by filtration and recrystallized from iPr_2O (30 mL). Yield: 0.22 g (37%), mp: 161-162 °C; ^{1}H-NMR (deuteriochloroform): δ 5.13 (2H, s, 2 x 1-H), 7.21 (1H, d, J = 8.8 Hz, 5-H), 7.39-7.51 (4H, m, 8-H, 3'-H, 4'-H, 5'-H), 7.55 (1H, t, J = 7.8 Hz, 9-H), 7.67 (1H, d, J = 8.8 Hz, 6-H), 7.75 (1H, d, J = 8.8 Hz, 7-H), 7.82 (1H, d, J = 8.1 Hz, 8-H), 8.10-8.15 (2H, m, 2'-H, 6'-H); ^{13}C-NMR (deuteriochloroform): δ 43.5 (1-C), 110.9 (10b-C), 116.7 (5-C), 122.3 (10-C), 125.1 (8-C), 127.2 (9-C), 127.5 (3'-C, 5'-C), 128.5 (2'-C, 6'-C), 128.8 (6-C), 128.9 (7-C), 130.1 (6a-C), 131.3 (4'-C), 132.3 (10a-C), 146.6 (1'-C), 152.6 (4a-C), 154.4 (3-C).

Anal. Calcd. for $C_{18}H_{13}NO$ (259.31): C, 83.38; H, 5.05; N, 5.40. Found: C, 83.61; H, 5.04; N, 5.41.

N^1-[α-(2-Hydroxy-1-naphthyl)benzyl]-N^2-phenylthiourea (**7**).

A mixture of aminonaphthol **1** (0.50 g, 2.00 mmol) and phenyl isothiocyanate (0.35 mL, 2.93 mmol) in abs. toluene (20 mL) was stirred for 1 day. The crystals that separated out were collected by filtration and washed with toluene (2 x 20 mL) and used in the next step without further purification. Yield: 0.35 g (45%), mp: 177-179 °C; ^{1}H-NMR (deuteriochloroform): δ 6.11 (1H, bs, C*H*-NH), 7.07-7.47 (10H, m, 3-H, 2'-H, 3'-H, 5'-H, 6'-H, NH-*Ph*), 7.54 (1H, t, J = 7.3 Hz, 4'-H), 7.60-7.69 (1H, m, 6-H), 7.69-7.94 (4H, m, 4-H, 5-H, 7-H, 8-H); ^{13}C-NMR (deuteriochloroform): δ 55.8 (*C*H-NH), 109.7 (3-C), 118.0 (8-C), 118.9 (1-C), 123.9 (4''-C), 125.3 (2''-C, 6''-C), 126.3 (3''-C, 5''-C), 126.7 (6-C), 128.0 (7-C), 128.7 (2'-C, 6'-C), 129.2 (4-C), 130.0 (4'-C), 130.3 (3'-C, 5'-C), 132.3 (4a-C), 134.7 (5-C), 135.8 (8a-C), 136.5 (1''-C), 152.0 (1'-C), 153.4 (2-C), 192.3 (NH-*C*=S-NH).

Anal. Calcd. for $C_{24}H_{20}N_2OS$ (384.50): C, 74.97; H, 5.24; N, 7.29. Found: C, 74.76; H, 5.22; N, 7.31.

N^1-(2-Hydroxy-1-naphthyl)methyl-N^2-phenylthiourea (**8**)

A mixture of aminonaphthol **2** (0.50 g, 2.89 mmol) and phenyl isothiocyanate (0.40 mL, 3.34 mmol) in abs. toluene (20 mL) was stirred for 1 day. The crystals that separated out were filtered off and washed with toluene (2 x 20 mL) and used in the next step without further purification. Yield: 0.42 g (47%), mp: 152-155 °C; ^{1}H-NMR (deuteriochloroform): δ 4.80 (1H, bs, NH), 5.27 (2H, d, J = 4.3 Hz, C*H*$_2$-NH), 6.88 (1H, bs, NH), 7.12 (2H, d, J = 7.8 Hz, 2'-H, 6'-H), 7.19 (1H, d, J = 8.8 Hz, 3-H), 7.23-7.40 (4H, m, 6-H, 7-H, 3'-H, 5'-H), 7.44 (1H, t, J = 8.1 Hz, 4'-H), 7.67 (1H, d, J = 5.3 Hz, 4-H), 7.69 (1H, d, J = 6.0 Hz, 5-H), 7.75 (1H, d, J = 8.1 Hz, 8-H); ^{13}C-NMR (deuteriochloroform): δ 40.8 (*C*H$_2$-NH), 115.0 (1-C), 120.5 (3-C), 121.2 (8-C), 123.4 (6-C), 125.4 (2'-C, 6'-C), 127.3 (4'-C), 128.0 (7-C), 129.3 (5-C), 129.4 (4a-C), 130.5 (4-C), 130.6 (3'-C, 5'-C), 133.3 (8a-C), 135.6 (1'-C), 153.7 (2-C), 180.3 (NH-*C*=S-NH).

Anal. Calcd. for $C_{18}H_{16}N_2OS$ (308.41): C, 70.10; H, 5.23; N, 9.08. Found: C, 69.92; H, 5.23; N, 9.06.

1-Phenyl-3-phenylimino-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]-oxazine (**9**).

To a solution of thiourea **7** (0.30 g, 0.78 mmol) in MeOH (10 mL), MeI (0.40 mL, 6.43 mmol) was added and the solution was stirred for 2 h. After evaporation of the solvent, the residue was stirred in 3 *M* methanolic KOH (20 mL) for 4 h. Following evaporation, H_2O (30 mL) was added to the residue and the mixture was extracted with $CHCl_3$ (3 x 20 mL). After drying (Na_2SO_4) and evaporation of the solvent, the crystalline oxazine was obtained on treatment with *n*-hexane (20 mL); it was collected by filtration and recrystallized from *n*-hexane-iPr_2O (5:1, 36 mL). Yield: 0.15 g (55%), mp: 156-158 °C; ^{1}H-NMR (deuteriochloroform): δ 6.27 (1H, bs, 1-H), 7.01 (1H, t, J = 7.3 Hz, 4'-H), 7.16-7.47 (12H, m, 5-H, 8-H, 9-H, 2'-H, 3'-H, 5'-H, 6'-H, N-*Ph*), 7.67-7.71 (1H, m, 6-H), 7.79-7.84 (2H, m, 7-H, 10-H); ^{13}C-NMR (deuteriochloroform): δ 56.0 (1-C), 114.7 (10b-C), 116.4 (5-C), 119.4 (5-C), 122.7 (10-C), 123.1 (8-C), 123.3 (6-C), 124.5 (7-C), 125.1 (2''-C, 6''-C), 127.4 (4''-C), 127.6 (3''-C, 5''-C), 128.8 (4'-C), 129.0 (2'-C, 6'-C), 129.2 (3'-C, 5'-C), 129.6 (6a-C), 131.3 (10a-C), 139.7 (1'-C), 143.8 (N-*C*(Ph)), 144.7 (4a-C), 147.0 (*C*=N).

Anal. Calcd. for $C_{24}H_{18}N_2O$ (350.42): C, 82.26; H, 5.18; N, 7.99. Found: C, 82.48; H, 5.17; N, 7.97.

3-Phenylimino-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazine (**10**).

To a solution of thiourea **8** (0.40 g, 1.30 mmol) in MeOH (10 mL), MeI (0.50 mL, 8.03 mmol) was added and the solution was stirred for 2 h. After evaporation of the solvent, the residue was stirred in 3 *M* methanolic KOH (20 mL) for 4 h. Following evaporation, H_2O (30 mL) was added to the residue and the mixture was extracted with $CHCl_3$ (3 x 20 mL). After drying (Na_2SO_4) and evaporation of the solvent, the crystalline oxazine was obtained on treatment with *n*-hexane (20 mL); it was collected by filtration and recrystallized from *n*-hexane-iPr_2O (3:1, 40 mL). Yield: 0.20 g (56%), mp: 158-160 °C; ^{1}H-NMR (deuteriochloroform): δ 4.97 (2H, s, 2 x 1H), 5.12 (1H, bs, NH), 7.05 (1H, t, J = 7.3 Hz, 4'-H), 7.10 (1H, d, J = 9.3 Hz, 5-H), 7.33 (2H, t, J = 7.8 Hz, 2'-H, 6'-H), 7.41-7.50 (3H, m, 8-H, 3'-H, 5'-H), 7.55 (1H, t, J = 7.8 Hz, 9-H), 7.66 (1H, d, J = 8.3 Hz, 6-H), 7.73 (1H, d, 9.1 Hz, 7-H), 7.82 (1H, d, J = 8.3 Hz, 10-H); ^{13}C-NMR (deuteriochloroform): δ 42.2 (1-C), 112.3 (10b-C), 116.4 (5-C), 119.7 (10-C), 122.3 (8-C), 122.8 (9-C), 125.0 (4'-C), 127.2 (6-C), 128.8 (2'-C, 6'-C), 129.2 (3'-C, 5'-C), 130.2 (6a-C), 130.9 (10a-C), 139.0 (7-C), 145.7 (1'-C), 146.9 (4a-C), 185.2 (3-C)

Anal. Calcd. for $C_{18}H_{14}N_2O$ (274.33): C, 78.81; H, 5.14; N, 10.21. Found: C, 78.70; H, 5.14; N, 10.16.

(7a*R**,14*S**)-14-Phenyl-7a*H*,12*H*,14*H*-naphth[1',2':5,6][1,3]-oxazino[2,3-*a*]isoindol-12-one (**11**).

To a solution of aminonaphthol **1** (0.50 g, 2.00 mmol) in abs. toluene (20 mL), 2-carboxybenzaldehyde (0.30 g, 2.01 mmol) was added. The mixture was stirred at r.t. for 5 days, during which a white solid separated out. The solvent was evaporated off and the residue crystallized on treatment with Et_2O (20 mL). The crystalline product was collected by filtration and recrystallized from iPr_2O (30 mL). Yield: 0.45 g (62%), mp: 221-222 °C; ^{1}H-NMR (deuteriochloroform): δ 6.09 (1H, s, 14-H), 6.95 (1H, s, 7a-H), 7.19 (1H, d, J = 9.1 Hz, 6-H), 7.22-7.33 (5H, m, Ph), 7.42-7.47 (2H, m, 2-H, 3-H), 7.48-7.61 (3H, m, 8-H, 9-H, 10-H), 7.70 (1H, d, J = 7.3 Hz, 5-H), 7.73-7.79 (2H, m, 4-H, 1-H), 7.87 (1H, d, J = 7.1 Hz, 11-H); ^{13}C-NMR (deuteriochloroform): δ 50.7 (14-C), 79.2 (7a-C), 111.9 (14a-C), 118.7 (6-C), 123.8 (1-C), 124.0 (3-C), 124.3 (4'-C), 124.4 (2-C), 127.2 (10-C), 128.3 (11-C), 128.6 (5-C), 128.7 (2'-C, 6'-C), 129.1 (3'-C, 5'-C), 129.9 (4a-C), 130.2 (8-C), 130.6 (4-C), 131.5 (14b-C), 132.5 (9-C), 132.6 (11a-C), 140.7 (7b-C), 141.9 (1'-C), 151.4 (6a-C), 165.4 (12-C).

Anal. Calcd. for $C_{25}H_{17}NO_2$ (363.42): C, 82.63; H, 4.72; N, 3.85. Found: C, 82.45; H, 4.72; N, 3.84.

7a*H*,12*H*,14*H*-Naphth[1',2':5,6][1,3]oxazino[2,3-*a*]isoindol-12-one (**12**).

To a solution of aminonaphthol **2** (0.30 g, 1.73 mmol) in abs. toluene (20 mL), 2-carboxybenzaldehyde (0.26 g, 1.73 mmol) was added. The mixture was stirred at r.t. for 1 day, during which white solid separated out. The solvent was evaporated off and the residue crystallized on treatment with Et_2O (20 mL). The crystalline product was collected by filtration and recrystallized twice from *i*Pr_2O-EtOAc (3:1, 40 mL). Yield: 0.18 g (36%), mp: 176-178 °C; ^{1}H-NMR (deuteriochloroform): δ 4.90 (1H, d, J = 16.9 Hz, 14-H), 5.52 (1H, d, J = 16.9 Hz, 14-H), 6.08 (1H, s, 7a-H), 7.17 (1H, d, J = 9.1 Hz, 6-H), 7.45 (1H, t, J = 7.3 Hz, 10-H), 7.54-7.86 (7H, m, 1-H, 2-H, 3-H, 4-H, 5-H, 8-H, 9-H), 7.94 (1H, d, J = 7.3 Hz, 11-H); ^{13}C-NMR (deuteriochloroform): δ 38.0 (14-C), 82.2 (7a-C), 111.1 (14a-C), 119.0 (6-C), 121.6 (1-C), 124.1 (3-C), 124.2 (2-C), 124.8 (10-C), 127.5 (11-C), 128.9 (5-C), 129.3 (8-C), 130.8 (4-C), 132.5 (9-C), 135.8 (4a-C), 140.7 (14b-C), 143.2 (11a-C), 149.6 (7b-C), 149.9 (6a-C), 168.6 (12-C).

Anal. Calcd. for $C_{19}H_{13}NO_2$ (287.32): C, 79.43; H, 4.56; N, 4.87. Found: C, 79.58; H, 4.55; N, 4.87%

7a-Methyl-8,9-dihydro-7a*H*,10*H*,12*H*-naphth[1,2-*e*]pyrrolo[2,1-*b*]-[1,3]oxazin-10-one (**13**).

To a solution of aminonaphthol **2** (0.40 g, 2.31 mmol) in abs. toluene (10 mL), levulinic acid (0.27 g, 2.31 mmol) was added. The mixture was refluxed for 3 h, and the solvent was evaporated off. The product was purified by column chromatography (silica gel, eluent: toluene-MeOH, 14:1). Yield: 0.09 g (17%), mp: 104-106 °C; ^{1}H-NMR (deuteriochloroform): δ 1.62 (3H, s, Me), 2.17-2.28 (1H, m, 9-H), 2.43-2.67 (3H, m, 9-H, 2 x 8-H), 4.43 (1H, d, J = 16.6 Hz, 12-H), 5.41 (1H, d, J = 16.6 Hz, 12-H), 6.99 (1H, d, J = 8.8 Hz, 6-H), 7.37 (1H, t, J = 7.3 Hz, 3-H), 7.50 (1H, t, J = 7.6 Hz, 2-H), 7.65 (1H, d, J = 9.1 Hz, 5-H), 7.70 (1H, d, J = 8.3 Hz, 4-H), 7.76 (1H, d, J = 8.3 Hz, 1-H); ^{13}C-NMR (deuteriochloroform): δ 22.8 (Me), 29.3 (9-C), 31.8 (8-C), 36.2 (12-C), 91.1 (7a-C), 109.9 (12a-C), 119.4 (6-C), 121.4 (1-C), 124.2 (3-C), 127.1 (2-C), 128.7 (4-C), 129.0 (5-C), 129.2 (4a-C), 131.0 (12b-C), 149.9 (6a-C), 174.8 (10-C).

Anal. Calcd. for $C_{16}H_{15}NO_2$ (253.30): C, 75.87; H, 5.97; N, 5.53. Found: C, 76.08; H, 5.96; N, 5.54.

3-(2-Hydroxyphenyl)-1-phenyl-2,3-dihydro-1*H*-naphth[1,2-*e*]-[1,3]oxazine (**14**).

A solution of aminonaphthol **1** (1.50 g, 6.03 mmol) and salicylaldehyde (0.74 g, 6.03 mmol) in MeOH (40 mL) was stirred at r.t. for 1 h. The solvent was evaporated off and the residue crystallized on treatment with Et_2O (40 mL). The crystalline product was collected by filtration and recrystallized from *i*Pr_2O-EtOAc (3:1, 80 mL). Yield: 1.83 g (86%), mp: 180-181 °C; ^{1}H-NMR (deuteriochloroform): δ 5.68 and 5.78 (*trans* diastereomer, major compound), 5.88 and 5.95 (*cis* diastereomer, minor compound), 8.60 (Schiff base)**;** ^{13}C-NMR (deuteriochloroform): δ 54.2 and 79.0 for the *trans* diastereomer, 57.0 and 83.7 for *cis* diastereomer, and 166.9 for the Schiff base.

3-(2-Hydroxyphenyl)-2,3-dihydro-1*H*-naphth[1,2-*e*][1,3]oxazine (**15**).

A solution of aminonaphthol **2** (1.50 g, 8.67 mmol) and salicylaldehyde (1.06 g, 8.67 mmol) in MeOH (40 mL) was stirred at r.t. for 1 h. The solvent was evaporated off and the residue crystallized on treatment with Et_2O (40 mL). The crystalline product was collected by filtration and recrystallized from *i*Pr_2O-EtOAc (6:1, 70 mL). Yield: 1.45 g (67%), mp: 175-177 °C; ^{1}H-NMR (deuteriochloroform): δ 5.30 (2H, s, CH_2-N=CH), 6.79 (1H, t, J = 7.6 Hz, 3'-H), 6.90 (1H, d, J = 8.1 Hz, 3-H), 7.00 (1H, t, J = 8.1 Hz, 4'-H), 7.08 (1H, d, J = 8.6 Hz, 5'-H), 7.10 (1H, d, J = 8.1 Hz, 4-H), 7.36 (1H, t, J = 7.8 Hz, 6-H), 7.52 (1H, t, J = 8.6 Hz, 7-H), 7.72 (1H, d, J = 8.8 Hz, 6'-H), 7.79 (1H, d, J = 7.8 Hz, 5-H), 7.99 (1H, d, J = 8.6 Hz, 8-H), 8.37 (1H, s, N=C*H*); ^{13}C-NMR (deuteriochloroform): δ 51.8 (*C*H_2-N=CH), 114.9 (1-C), 115.5 (1'-C), 117.5 (5'-C), 118.0 (3-C), 118.4 (3'-C), 122.9 (8-C), 123.7 (6-C), 127.5 (7-C), 128.9 (4-C), 130.2 (5-C), 131.8 (2'-C), 132.7 (4'-C), 133.2 (4a-C), 135.6 (8a-C), 151.9 (2-C), 163.0 (6'-C), 166.4 (N=*C*H).

Anal. Calcd. for $C_{18}H_{15}NO_2$ (277.33): C, 77.96; H, 5.45; N, 5.05. Found: C, 78.14; H, 5.45; N, 5.06%

(7a*R**,15*S**)-15-Phenyl-7a*H*,13*H*,15*H*-naphth[1',2':5,6][1,3]-oxazino[3,2-*c*][1,3]benzoxazine (**16**).

To a solution of **14** (0.30 g, 0.85 mmol) in EtOH (20 mL), 40% aqueous formaldehyde (2.5 mL) was added. The mixture was stirred at r.t. for 30 min., during which white crystals separated out. The crystalline product was collected by filtration, and recrystallized from *i*Pr_2O-EtOAc (3:1, 40 mL). Yield: 0.29 g (93%), mp: 214-216 °C; ^{1}H-NMR (deuteriochloroform): δ 4.91 (1H, d, J = 6.8 Hz, 13-H), 4.96 (1H, d, J = 6.8 Hz, 13-H), 5.53 (1H, s, 15-H), 5.61 (1H, s, 7a-H), 6.92-7.01 (2H, m, 11-H, 9-H), 7.13 (1H, d, J = 9.0 Hz, 6-H), 7.22-7.36 (9H, m, 2-H, 3-H, 8-H, 10-H, Ph), 7.38-7.42 (1H, m, 5-H), 7.74-7.81 (2H, m, 1-H, 4-H); ^{13}C-NMR (deuteriochloroform): δ 57.9 (15-C), 77.9 (13-C), 78.7 (7a-C), 111.3 (15a-C), 117.2 (11-C), 119.1 (6-C), 120.3 (7b-C), 121.3 (9-C), 122.8 (1-C), 123.8 (3-C), 127.1 (2-C), 128.0 (5-C), 128.7 (2'-C, 6'-C), 128.9 (4'-C), 129.3 (10-C), 129.4 (3'-C, 5'-C), 130.0 (4-C), 130.8 (8-C), 132.0 (4a-C), 2 x 141.5 (15b-C, 1'-C), 150.7 (6a-C), 153.3 (11a-C).

Anal. Calcd. for $C_{25}H_{19}NO_2$ (365.44): C, 82.17; H, 5.24; N, 3.83. Found: C, 82.39; H, 5.25; N, 3.82%

(7a*R**,13*R**,15*S**)-13-Methyl-15-phenyl-7a*H*,13*H*,15*H*-naphth-[1',2':5,6][1,3]oxazino[3,2-*c*][1,3]benzoxazine (**17**).

A mixture of compound **14** (0.30 g, 0.85 mmol), EtOH (20 mL) and acetaldehyde (2 mL) was stirred at r.t. until the TLC showed no more starting material (for *ca*. 10 h). The solvent was evaporated off and the residue crystallized on treatment with Et_2O (30 mL). The crystalline product was collected by filtration and recrystallized from *i*Pr_2O-EtOAc (4:1, 50 mL). Yield: 0.25 g (78%), mp: 226-228 °C; ^{1}H-NMR (deuteriochloroform): δ 1.78 (3H, d, J = 5.5 Hz, Me), 5.15 (1H, q, J = 5.5 Hz, 13-H), 5.70 (1H, s, 15-H), 5.89 (1H, s, 7a-H), 6.94-7.07 (2H, m, 9-H, 11-H), 7.19 (1H, d, J = 9.1 Hz, 6-H), 7.27-7.41 (9H, m, 2-H, 3-H, 8-H, 10-H, Ph), 7.44-7.49 (1H, m, 5-H), 7.80-7.86 (2H, m, 3-H, 4-H); ^{13}C-NMR (deuteriochloroform): δ 19.8 (Me), 54.7 (15-C), 79.4 (13-C), 81.1 (7a-C), 111.0 (15a-C), 116.8 (11-C), 119.1 (6-C), 120.3 (7b-C), 121.0 (9-C), 122.3 (1-C), 123.7 (3-C), 128.6 (2-C), 128.7 (5-C), 128.9 (2'-C, 6'-C), 129.0 (4'-C), 129.4 (10-C), 129.5 (3'-C, 5'-C), 130.0 (4-C), 130.6 (8-C), 132.1 (4a-C), 2 x 141.9 (15b-C, 1'-C), 151.5 (6a-C), 153.7 (11a-C).

Anal. Calcd. for $C_{26}H_{21}NO_2$ (379.46): C, 82.30; H, 5.58; N, 3.69. Found: C, 82.49; H, 5.56; N, 3.70.

4-Phenyl-3,4-dihydro-2*H*-naphth[2,1-*e*][1,3]oxazin-2-one (**18**).

Aminonaphthol hydrochloride **3** (0.30 g, 1.05 mmol) was suspended in abs. toluene (10 mL), and Et_3N (0.34 g, 3.15 mmol) and phosgene (0.55 mL; 20% in toluene, 1.05 mmol) were added. The

mixture was stirred at r.t. for 4 h and then EtOAc (40 mL) and H_2O (40 mL) were added. The organic layer was separated, dried (Na_2SO_4) and evaporated. The oily residue crystallized on treatment with *n*-hexane (20 mL). The crystalline product was filtered off and recrystallized from *n*-hexane-*i*Pr_2O (40-10 mL). Yield: 0.09 g (31%), mp: 196-198 °C; ^{1}H-NMR (deuteriochloroform): δ 5.78 (1H, s, 4-H), 5.97 (1H, bs, NH), 6.93 (1H, d, J = 8.6 Hz, 5-H), 7.31-7.41 (5H, m, Ph), 7.49-7.62 (3H, m, 6-H, 8-H, 9-H), 7.78 (1H, d, J = 7.8 Hz, 7-H), 8.36 (1H, d, J = 8.6 Hz, 10-H); ^{13}C-NMR (deuteriochloroform): δ 58.6 (4-C), 114.8 (4a-C), 121.7 (6-C), 123.5 (10-C), 124.6 (8-C), 127.1 (9-C), 127.4 (7-C), 127.7 (4'-C), 127.8 (2'-C, 6'-C), 129.1 (5-C), 129.5 (3'-C, 5'-C), 133.9 (10a-C), 141.8 (6a-C), 142.9 (1'-C), 144.4 (10b-C), 150.3 (2-C)

Anal. Calcd. for $C_{18}H_{13}NO_2$ (275.31): C, 78.53; H, 4.76; N, 5.09. Found: C, 78.32; H, 4.75; N, 5.08%

(7*S**,13b*R**)-7-Phenyl-7*H*,9*H*,13b*H*-naphth[2',1':5,6][1,3]-oxazino[2,3-*a*]isoindol-9-one (**19**).

To a suspension of aminonaphthol hydrochloride **3** (0.50 g, 1.75 mmol) in abs. toluene (20 mL), 2-carboxybenzaldehyde (0.27 g, 1.73 mmol) and Et_3N (0.20 g, 1.98 mmol) were added. The mixture was stirred at r.t. for 8 days and then was washed consecutively with H_2O (50 mL) and with 2 *M* HCl solution (50 mL) after adding of EtOAc (50 mL). The organic layer was separated, dried (Na_2SO_4) and evaporated. The oily residue crystallized on treatment with *n*-hexane (20 mL). The crystalline product was collected by filtration and recrystallized from *n*-hexane-*i*Pr_2O (8:1, 45 mL). Yield: 0.27 g (42%), mp: 156-158 °C; ^{1}H-NMR (deuteriochloroform): δ 6.17 (1H, s, 7-H), 6.51 (1H, s, 13b-H), 7.10 (1H, d, J = 8.6 Hz, 6-H), 7.25-7.37 (3H, m, 2'-H, 4'-H, 6'-H), 7.42-7.58 (7H, m, 2-H, 3-H, 5-H, 13-H, 3'-H, 5'-H), 7.63 (1H, t, J = 7.6 Hz, 11-H), 7.76-7.89 (3H, m, 4-H, 10-H, 12-H), 8.24-8.30 (1H, m, 1-H); ^{13}C-NMR (deuteriochloroform): δ 52.9 (7-C), 80.2 (13b-C), 114.6 (6a-C), 121.7 (5-C), 121.9 (1-C), 124.0 (2-C), 124.2 (3-C), 125.2 (14b-C), 126.0 (4'-C), 126.2 (11-C), 127.0 (10-C), 127.8 (4-C), 128.4 (6-C), 129.0 (13-C), 129.1 (2'-C, 6'-C), 130.7 (3'-C, 5'-C), 132.5 (12-C), 132.8 (4a-C), 133.9 (9a-C), 140.7 (13a-C), 142.0 (1'-C), 148.5 (14a-C), 166.1 (9-C).

Anal. Calcd. for $C_{25}H_{17}NO_2$ (363.42): C, 82.63; H, 4.72; N, 3.85. Found: C, 82.86; H, 4.73; N, 3.86.

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