One-Pot Synthesis of Photochromic 6′-Amino-Substituted Spirooxazines from 1-Nitroso-2-naphthol Zinc Chelate and Indoline Base

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Abstract: A series of spirooxazine derivatives containing nitrogen heterocycles were synthesized through the condensation of 2-methylene-1,3,3-trimethylindoline derivatives with the zinc salt of 1-nitroso-2-naphthol using ethanol as solvent. The method is simple, starts from readily accessible and inexpensive reagents, and leads to the synthesis of 6′-substituted spirooxazines in moderate to good yields. We simplified the workup and found that, for some target compounds, recrystallization can effectively improve efficiency of the separation and purification.

Key words: spirooxazines, heterocycles, condensation, photochromism, one-pot synthesis

In recent years, photochromic organic compounds have been extensively studied because of their application in science and technology.[1,2] In addition to their potential applications utilizing their different absorption properties, the changes in electron delocalization have also been employed for the design of photoswitchable nonlinear optical devices, luminescent devices,[3] host–guest systems[4–7] and enzymatic systems.[8–11] Spirooxazine (SPOs) are one of the most popular classes of photochromic materials, and have been shown to possess high fatigue resistance and excellent photostability.[12] According to our previous report,[13] photochromic spirooxazines containing nitrogen heterocycles at the 6′-position exhibited remarkable fatigue resistance and substantial bathochromic shifts in the absorption spectra of the open forms in both solution and in polymers. Because these properties greatly increase their potential applications, the direct synthesis of these compounds thus assumes great importance.

In recent years, abundant new data on the synthesis of SPOs have become available. The synthesis of this type of compound from aromatic *o*-hydroxynitroso compounds or from 1-amino-2-naphthols and related compounds are commonly used methods.[14] The two fragments that make up the SPO molecule will be referred to as the indoline and oxazine fragments (Figure 1).

Most of the procedures that have been used for structural modification of the oxazine fragment in SPOs are based on the insertion of a substituent into the naphthalene fragment. However, because it is relatively difficult to access 4-substituted 2-naphthols, the 6′-substituted SPOs are less common.[14] Thus, Rickwood and co-workers[15] used various secondary amines as nucleophiles for the preparation of 4-amino-substituted 1,2-naphthoquinones, which were then employed in the synthesis of 6′-amino-substituted SPOs. These authors also developed a simplified (but much less universal) approach to the synthesis of the same compounds based on the reaction of 1-nitroso-2-naphthol, a secondary amine, and Fischer's base, without isolation of the substituted nitrosonaphthol, which partially accounts for the low yield. In 2005, Koshkin et al.[16] reported a one-pot synthesis of 6′-amino-substituted spirooxazines.

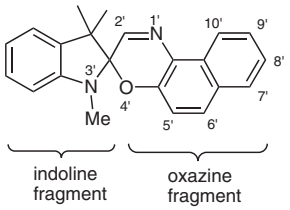
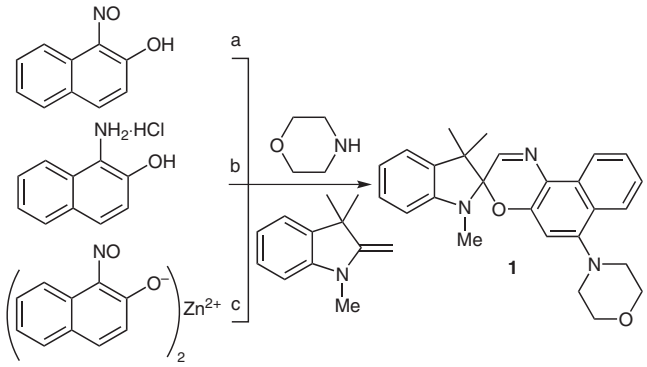


Figure 1



Scheme 1 *Reagents and conditions*: (a) method A: $ClHC{=}CCl_2$; (b) method B: DMSO, Et_3N, MeOH; (c) method C: EtOH.

We used three different methods for the preparation of 1,3,3-trimethyl-6′-morpholinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (**1**; Scheme 1). Our experiments showed that using method A,[13] the synthesis needed a short reaction time, but resulted in a low yield; method B[16] uses expensive 1-aminonaphthol hydrochloride, which can easily be oxidized. We thus designed method C for the synthesis of 6′-substituted SPOs by considering that zinc ions could be effectively chelated with oxygen atoms to form a coordination compound, thus promoting the linkage of the naphthalene fragment with N-heterocycles. During the course of the reaction, the zinc complexes of 1-nitroso-2-naphthol are able to react with secondary

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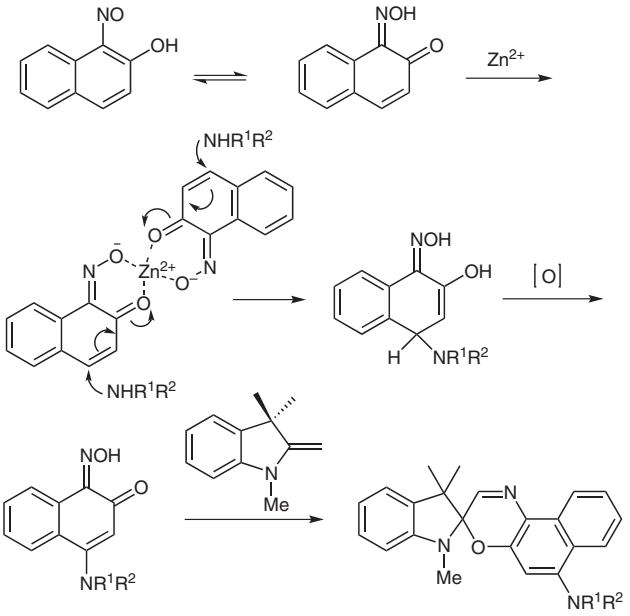


Scheme 2 Reaction mechanism

amines through a Michael addition mechanism (Scheme 2).[14,15] In this process, the zinc chelate of an *ortho*-hydroxynitrosoaromatic compound favors the synthesis of 4-substituted-2-naphthols. On the basis of mechanistic studies, we also optimized the synthetic conditions of a general preparative method. The optimized data are listed in Tables 1 through 3.

Table 1 Effect of Solvent on Reaction Yield[a–d]

2-Methylene-1,3,3-trimethylindoline (mol)	Solvent (40 mL)	Yield (%)
0.001	trichloroethylene	12
0.001	EtOH	70
0.001	MeOH	53

[a] 1-Nitroso-2-naphthol zinc salt (0.006 mol).
[b] Heated at reflux for 20 h.
[c] $NaSO_4$ (0.2 g) added.
[d] Nitrogen atmosphere.

Regarding the data presented in Table 1, it can be concluded that the yield can be improved in polar solvents, presumably because the reactants (zinc chelates) have relatively strong polarities. In addition, the yield obtained in ethanol as solvent was higher than that obtained in methanol; this can be attributed to the fact that ethanol is a more suitable solvent for the hydrophobic part of the reactant. From Table 2, it can be seen that adding desiccant to the reaction significantly increased the yield; anhydrous sodium sulfate was the best, which could be due to the fact that it is a neutral desiccant that can absorb large amounts of water. When activated carbon was added to the reaction the yield decreased, which may be because some product was adsorbed. The data presented in Table 3 show that, under a nitrogen atmosphere, reaction times of 16–20 hours were optimal. Under these conditions, spirooxazine-containing nitrogen heterocycles **1**–**11** were obtained in moderate to good yields (Scheme 3, Table 4).

Table 2 Effect of Additives on Reaction Yield[a–c]

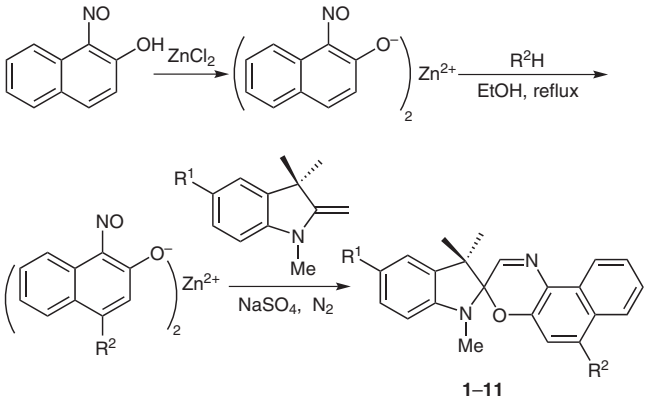
2-Methylene-1,3,3-trimethylindoline (mol)	Additive (0.2 g)	Yield (%)
0.001	–	51
0.001	$MgSO_4$	63
0.001	$NaSO_4$	69
0.001	MS	58
0.001	activated carbon	48

[a] 1-Nitroso-2-naphthol zinc salt (0.006 mol).
[b] Heated at reflux in EtOH (40 mL) for 20 h
[c] Nitrogen atmosphere.

Table 3 Effect of Reaction Time on Yield[a–d]

2-Methylene-1,3,3-trimethylindoline (mol)	Time (h)	Yield (%)
0.001	4	12
0.001	10	42
0.001	16	65
0.001	20	71
0.001	24	62

[a] 1-Nitroso-2-naphthol zinc salt (0.006 mol).
[b] Heated at reflux in EtOH (40 mL).
[c] $NaSO_4$ (0.2 g) added.
[d] Nitrogen atmosphere.



Scheme 3 Optimized synthetic route (R^1 = H, Cl; R^2 = N-heterocycle)

In summary, the condensation of substituted indoline bases with the zinc salt of 1-nitroso-2-naphthols in the presence of cyclic secondary amines can be successfully

Table 4 Prepared 6′-Amino-Substituted Spirooxazines **1–11**

Product	R^1	R^2	Yield (%)
1	H	morpholinyl	74
2	Cl	morpholinyl	68
3	H	piperidyl	68
4	Cl	piperidyl	67
5	H	thiomorpholinyl	52
6	H	indolinyl	65
7	Cl	indolinyl	49
8	H	1,2,3,4-tetrahydroisoquinolinyl	56
9	Cl	1,2,3,4-tetrahydroisoquinolinyl	45
10	H	1,2,3,4-tetrahydroquinolinyl	46
11	H	piperazinyl	65

applied to the synthesis of spirooxazines substituted with secondary cyclic amines at the 6′-position. The yield of the products depends on the nature and structure of the secondary cyclic amines. The method is simple and starts from readily accessible and inexpensive reagents, leading to the synthesis of 6′-substituted spirooxazines in moderate to good yields. In addition, we have optimized the synthetic conditions, simplified the workup, and found that, for some compounds, recrystallization can effectively improve the efficiency of the separation and purification of the products. The synthesis of some compounds (e.g., **1**) may be applied to industrial production after additional optimization of the synthetic conditions.

All starting materials are commercially available. Solvents were used without further purification and dried over molecular sieves, if necessary. Melting points were determined with a Yanagimoto MP-35 melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded with a Bruker AC-P300 spectrometer with TMS as internal standard, as solutions in $CDCl_3$. Mass spectra were recorded with a Thermo Finnigan LCQ Advantage spectrometer in ESI mode-I. Elemental analyses were performed with a Yanaco CHN CORDER MT-3 apparatus. IR spectra were recorded with a Bio-Rad FTS 135 spectrophotometer using KBr disks; wavenumbers are given in cm^{-1}. The identification of previously reported reaction products were made by comparison of their respective ^{1}H NMR spectra and melting points with literature data.

Synthesis of Spirooxazines 1–11; General Procedure

Under stirring, $ZnCl_2$ (1.36 g, 10 mmol) in H_2O (40 mL) was added to a mixture of THF–H_2O (1:1 v/v, 80 mL) containing 1-nitroso-2-naphthol (3.98 g, 23 mmol). The mixture was stirred at r.t. for 20 min. When the reaction was complete, the crude 1-nitroso-2-naphthol zinc salt was filtered, washed with H_2O (3 × 20 mL) and dried under an infrared heat lamp. The zinc salt (96% yield) was used for the next step without further purification.

1-Nitroso-2-naphthol zinc salt (1.0 mmol) and nitrogen heterocycle (3.5 mmol) were added to EtOH (20 mL). The resulting mixture was heated to reflux and stirred for 2 h. Indoline base (1.5 mmol) in EtOH (20 mL) was added to the solution under a nitrogen atmosphere, anhydrous Na_2SO_4 (0.3 g) was then added and the mixture was stirred for an additional 20 h. After removal of the solvent, the residue was purified by column chromatography on silica gel (petroleum ether–EtOAc).

1,3,3-Trimethyl-6′-morpholinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (1)

Mp 192–193 °C (Lit.[15] 196 °C).

IR (KBr): 3066, 2935, 2844, 1610, 1586, 1486, 1448, 1408, 1361, 1302, 1240, 1201, 1138, 1028, 886, 849, 815, 763, 739 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 [s, 6 H, $C(CH_3)_2$], 2.17 (s, 3 H, NCH_3), 3.07 [m, 4 H, $N(CH_2)_2$], 3.94 [m, 4 H, $O(CH_2)_2$], 6.57 (d, *J* = 7.8 Hz, 1 H, H-7), 6.62 (s, 1 H, H-5′), 6.89 (dd, *J* = 7.0, 7.4 Hz, 1 H, H-5), 7.10 (d, *J* = 7.2 Hz, 1 H, H-4), 7.22 (dd, *J* = 8.2, 2.2 Hz, 1 H, H-6), 7.38 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1 H, H-8′), 7.56 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1 H, H-9′), 7.65 (s, 1 H, H-2′), 8.05 (d, *J* = 8.6 Hz, 1 H, H-7′), 8.56 (d, *J* = 7.9 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 (CH_3), 25.3 (CH_3), 29.5 (NCH_3), 51.5 (C-3), 53.3 (2 × C, NCH_2), 67.1 (2 × C, OCH_2), 98.7–151.6 (18 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 414.2 [M + H]$^+$.

Anal. Calcd for $C_{26}H_{27}N_3O_2$: C, 75.52; H, 6.58; N, 10.16. Found: C, 75.57; H, 6.63; N, 10.11.

5-Chloro-1,3,3-trimethyl-6′-morpholinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (2)

Mp 204–206 °C (Lit.[15] 196 °C).

IR (KBr): 3071, 2956, 2846, 1612, 1586, 1481, 1412, 1354, 1293, 1265, 1201, 1185, 1027, 923, 888, 806, 758, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 2.73 (s, 3 H, NCH_3), 3.07 [m, 4 H, $N(CH_2)_2$], 3.95 [m, 4 H, $O(CH_2)_2$], 6.47 (d, *J* = 8.2 Hz, 1 H, H-7), 6.60 (s, 1 H, H-5′), 7.02 (d, *J* = 2.1 Hz, 1 H, H-4), 7.16 (dd, *J* = 8.2, 2.2 Hz, 1 H, H-6), 7.39 (ddd, *J* = 8.2, 8.2, 1.2 Hz, 1 H, H-8′), 7.57 (ddd, *J* = 8.2, 8.2, 1.2 Hz, 1 H, H-9′), 7.62 (s, 1 H, H-2′), 8.06 (d, *J* = 8.3 Hz, 1 H, H-7′), 8.55 (d, *J* = 8.4 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4 (CH_3), 25.2 (CH_3), 29.6 (NCH_3), 51.5 (C-3), 53.3 (2 × C, NCH_2), 67.1 (2 × C, OCH_2), 98.7–162.2 (18 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 448.27 [M + H]$^+$.

Anal. Calcd for $C_{26}H_{26}ClN_3O_2$: C, 69.71; H, 5.85; N, 9.38. Found: C, 69.75; H, 5.89; N, 9.35.

1,3,3-Trimethyl-6′-piperidinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (3)

Mp 228–230 °C (Lit.[15] 238–239 °C).

IR (KBr): 3047, 2954, 2851, 1609, 1586, 1484, 1448, 1408, 1362, 1300, 1267, 1199, 1138, 1027, 891, 858, 831, 763, 731 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.63 (m, 2 H, CH_2), 1.82 (m, 4 H, 2 × CH_2), 2.75 (s, 3 H, NCH_3), 3.02 [m, 4 H, $N(CH_2)_2$], 6.56 (d, *J* = 7.8 Hz, 1 H, H-7), 6.59 (s, 1 H, H-5′), 6.89 (dd, *J* = 7.4, 8.1 Hz, 1 H, H-5), 7.10 (d, *J* = 7.1 Hz, 1 H, H-4), 7.22 (ddd, *J* = 7.7, 7.6, 1.3 Hz, 1 H, H-6), 7.38 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1 H, H-8′), 7.55 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1 H, H-9′), 7.62 (s, 1 H, H-2′), 8.02 (d, *J* = 8.2 Hz, 1 H, H-7′), 8.54 (d, *J* = 8.3 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 (CH_3), 24.4 (CH_3), 25.3 (CH_3), 26.3 (2 × C, CH_2), 29.5 (NCH_3), 51.4 (C-3), 54.4 (2 × C, NCH_2), 98.6–153.3 (18 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 412.47 [M + H]$^+$.

Anal. Calcd for $C_{27}H_{29}N_3O$: C, 78.80; H, 7.10; N, 10.21. Found: C, 78.58; H, 7.13; N, 10.19.

5-Chloro-1,3,3-trimethyl-6′-piperidinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (4)
Mp 229–231 °C (Lit.[15] 220–222 °C).

IR (KBr): 3068, 2930, 2804, 1612, 1566, 1481, 1412, 1352, 1277, 1240, 1202, 1161, 1029, 964, 884, 869, 809, 760, 699 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.64 (m, 2 H, CH_2), 1.85 (m, 4 H, 2 × CH_2), 2.72 (s, 3 H, NCH_3), 3.03 [m, 4 H, $N(CH_2)_2$], 6.47 (d, *J* = 8.2 Hz, 1 H, H-7), 6.58 (s, 1 H, H-5′), 7.02 (d, *J* = 2.1 Hz, 1 H, H-4), 7.15 (dd, *J* = 8.2, 2.1 Hz, 1 H, H-6), 7.39 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1 H, H-8′), 7.55 (ddd, *J* = 8.2, 8.2, 1.2 Hz, 1 H, H-9′), 7.59 (s, 1 H, H-2′), 8.06 (d, *J* = 8.4 Hz, 1 H, H-7′), 8.53 (d, *J* = 8.4 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (CH_3), 24.4 (CH_2), 25.2 (CH_3), 26.3 (2 × C, CH_2), 29.6 (NCH_3), 51.4 (C-3), 54.4 (2 × C, NCH_2), 98.6–153.5 (18 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 446.31 $[M + H]^+$.

Anal. Calcd for $C_{27}H_{28}ClN_3O$: C, 72.71; H, 6.33; N, 9.42; Found: C, 72.75; H, 6.35; N, 9.43.

1,3,3-Trimethyl-6′-thiomorpholinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (5)
Mp 179–181 °C (Lit.[15] 184–185 °C).

IR (KBr): 3060, 2953, 2903, 1610, 1586, 1484, 1448, 1409, 1360, 1297, 1239, 1195, 1116, 1026, 960, 870, 835, 748 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.35 [s, 6 H, $C(CH_3)_2$], 2.75 (s, 3 H, NCH_3), 2.89 [m, 4 H, $N(CH_2)_2$], 3.30 [m, 4 H, $S(CH_2)_2$], 6.57 (d, *J* = 7.8 Hz, 1 H, H-7), 6.62 (s, 1 H, H-5′), 6.89 (dd, *J* = 7.1, 7.2 Hz, 1 H, H-5), 7.09 (d, *J* = 6.6 Hz, 1 H, H-4), 7.22 (ddd, *J* = 7.7, 7.6, 1.3 Hz, 1 H, H-6), 7.38 (ddd, *J* = 7.1, 7.0, 1.3 Hz, 1 H, H-8′), 7.56 (ddd, *J* = 7.1, 7.0, 1.3 Hz, 1 H, H-9′), 7.65 (s, 1 H, H-2′), 7.99 (d, *J* = 8.3 Hz, 1 H, H-7′), 8.55 (d, *J* = 8.2 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 (CH_3), 25.4 (CH_3), 28.3 (2 × C, SCH_2), 29.5 (NCH_3), 51.5 (C-3), 55.4 (2 × C, NCH_2), 98.7–152.7 (18 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 430.41 $[M + H]^+$.

Anal. Calcd for $C_{26}H_{27}N_3OS$: C, 72.69; H, 6.34; N, 9.78. Found: C, 72.69; H, 6.34; N, 9.81.

1,3,3-Trimethyl-6′-indolinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (6)
Mp 251–253 °C (Lit.[15] 231–233 °C).

IR (KBr): 3048, 2965, 2848, 1588, 1481, 1409, 1355, 1300, 1243, 1162, 1138, 1097, 1019, 955, 876, 833, 772, 744, 702 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.36 [s, 6 H, $C(CH_3)_2$], 2.77 (s, 3 H, NCH_3), 3.18 (m, 2 H, CH_2), 3.92 (m, 2 H, NCH_2), 6.28 (d, *J* = 8.0 Hz, 1 H, H-7″), 6.56 (d, *J* = 7.7 Hz, 1 H, H-7), 6.73 (dd, *J* = 7.3, 7.3 Hz, 1 H, H-5″), 6.89 (m, 2 H, H-5, H-4″), 6.93 (s, 1 H, H-5′), 7.07 (d, *J* = 7.0 Hz, 1 H, H-4), 7.18, 7.20 (2 × d, *J* = 8.0, 7.6 Hz, 2 H, H-6, H-6″), 7.34 (ddd, *J* = 8.4, 8.2, 1.3 Hz, 1 H, H-8′), 7.59 (ddd, *J* = 8.1, 8.3, 1.3 Hz, 1 H, H-9′), 7.69 (s, 1 H, H-2′), 7.96 (d, *J* = 8.0 Hz, 1 H, H-7′), 8.61 (d, *J* = 8.4 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (CH_3), 25.4 (CH_3), 28.8 (CH_2), 29.6 (NCH_3), 51.6 (C-3), 55.1 (NCH_2), 98.7–162.2 (24 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 446.51 $[M + H]^+$.

Anal. Calcd for $C_{30}H_{27}N_3O$: C, 80.87; H, 6.11; N, 9.43. Found: C, 80.89; H, 6.14; N, 9.40.

5-Chloro-1,3,3-trimethyl-6′-indolinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (7)
Mp 263–265 °C.

IR (KBr): 3045, 2961, 2842, 1618, 1588, 1482, 1413, 1352, 1292, 1242, 1164, 1026, 959, 878, 831, 818, 769, 747, 705 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 2.74 (s, 3 H, NCH_3), 3.17 (m, 2 H, CH_2), 3.93 (m, 2 H, NCH_2), 6.29 (d, *J* = 7.9 Hz, 1 H, H-7″), 6.47 (d, *J* = 8.2 Hz, 1 H, H-7), 6.74 (dd, *J* = 7.3, 7.3 Hz, 1 H, H-5″), 6.92 (s, 1 H, H-5′), 6.93 (d, *J* = 7.5 Hz, 1 H, H-4″), 7.02 (d, *J* = 1.9 Hz, 1 H, H-4), 7.15, 7.20 (2 × d, *J* = 8.0, 7.6 Hz, 2 H, H-6, H-6″), 7.35 (ddd, *J* = 8.4, 8.2, 1.3 Hz, 1 H, H-8′), 7.60 (ddd, *J* = 7.4, 7.5, 1.3 Hz, 1 H, H-9′), 7.66 (s, 1 H, H-2′), 7.96 (d, *J* = 8.3 Hz, 1 H, H-7′), 8.60 (d, *J* = 8.2 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (CH_3), 25.2 (CH_3), 28.8 (CH_2), 29.7 (NCH_3), 51.6 (C-3), 55.1 (NCH_2), 98.7–162.2 (24 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 480.78 $[M + H]^+$.

Anal. Calcd for $C_{30}H_{26}ClN_3O$: C, 75.07; H, 5.46; N, 8.75. Found: C, 75.04; H, 5.47; N, 8.77.

1,3,3-Trimethyl-6′-1,2,3,4-tetrahydroisoquinolinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (8)
Mp 187–188 °C.

IR (KBr): 3051, 2930, 2875, 1584, 1486, 1408, 1367, 1304, 1266, 1240, 1192, 1102, 1031, 934, 892, 843, 743 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 2.77 (s, 3 H, NCH_3), 3.13 (m, 2 H, CH_2), 3.39 (m, 2 H, CH_2), 4.25 (s, 2 H, CH_2), 6.56 (d, *J* = 7.7 Hz, 1 H, H-7), 6.70 (s, 1 H, H-5′), 6.89 (m, 1 H, H-5), 7.08 (m, 2 H, H-4, H-5″), 7.20 (m, 4 H, H-4″, H-6, H-6″, H-7″), 7.36 (ddd, *J* = 8.2, 8.1, 1.3 Hz, 1 H, H-8′), 7.57 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1 H, H-9′), 7.65 (s, 1 H, H-2′), 8.09 (d, *J* = 8.4 Hz, 1 H, H-7′), 8.58 (d, *J* = 8.1 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 (CH_3), 25.3 (CH_3), 29.5 (CH_2), 29.5 (NCH_3), 51.4 (C-3), 51.5 (CH_2), 54.8 (CH_2), 98.6–151.8 (24 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 460.47 $[M + H]^+$.

Anal. Calcd for $C_{31}H_{29}N_3O$: C, 81.02; H, 6.36; N, 9.14. Found: C, 80.98; H, 6.38; N, 9.15.

5-Chloro-1,3,3-trimethyl-6′-1,2,3,4-tetrahydroisoquinolinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (9)
Mp 216–218 °C.

IR (KBr): 3065, 2978, 2954, 1612, 1581, 1483, 1410, 1365, 1269, 1239, 1161, 1030, 933, 893, 850, 810, 758 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.35 [s, 6 H, $C(CH_3)_2$], 2.74 (s, 3 H, NCH_3), 3.14 (m, 2 H, CH_2), 3.41 (m, 2 H, CH_2), 4.25 (s, 2 H, CH_2), 6.47 (d, *J* = 8.2 Hz, 1 H, H-7), 6.69 (s, 1 H, H-5′), 7.03, 7.07 (2 × d, *J* = 2.1, 6.6 Hz, 2 H, H-4, H-5″), 7.18 (m, 4 H, H-4″, H-6, H-6″, H-7″), 7.37 (ddd, *J* = 8.2, 8.1, 1.3 Hz, 1 H, H-8′), 7.57 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1 H, H-9′), 7.62 (s, 1 H, H-2′), 8.08 (d, *J* = 8.2 Hz, 1 H, H-7′), 8.58 (d, *J* = 8.0 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (CH_3), 25.2 (CH_3), 29.5 (CH_2), 29.7 (NCH_3), 51.5 (C-3), 51.7 (NCH_2), 54.9 (NCH_2), 98.7–162.2 (24 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 494.27 $[M + H]^+$.

Anal. Calcd for $C_{31}H_{28}ClN_3O$: C, 75.37; H, 5.71; N, 8.51. Found: C, 75.26; H, 5.69; N, 8.53.

1,3,3-Trimethyl-6′-1,2,3,4-tetrahydroquinolinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (10)
Mp 182–184 °C.

IR (KBr): 3061, 2960, 2867, 1596, 1487, 1452, 1404, 1357, 1295, 1243, 1194, 1159, 1099, 1027, 960, 857, 818, 745, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 2.12 (m, 2 H, CH_2), 2.77 (s, 3 H, NCH_3), 2.94 (m, 2 H, CH_2), 3.61 (m, 2 H, CH_2), 6.11 (d, *J* = 7.7 Hz, 1 H, H-7″), 6.56 (d, *J* = 7.7 Hz, 1 H, H-7), 6.63 (dd, *J* = 7.3, 7.3 Hz, 1 H, H-5″), 6.78 (dd, *J* = 7.2, 7.2 Hz, 1 H, H-5), 6.87 (dd, *J* = 6.9, 6.9 Hz, 1 H, H-4″), 6.90 (s, 1 H, H-5′), 7.05 (m, 2 H, H-4, H-6), 7.20 (dd, *J* = 7.5, 7.5 Hz, 1 H, H-6″), 7.33 (ddd, *J* = 8.2, 8.1, 1.3 Hz, 1 H, H-8′), 7.57 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1 H, H-9′), 7.72 (s, 1 H, H-2′), 7.86 (d, *J* = 8.4 Hz, 1 H, H-7′), 8.61 (d, *J* = 8.4 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8 (CH_3), 22.5 (CH_2), 25.4 (CH_3), 27.7 (CH_2), 29.6 (NCH_3), 51.5 (C-3), 51.7 (NCH_2), 98.6–150.1 (24 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 460.46 $[M + H]^+$.

Anal. Calcd for $C_{31}H_{29}N_3O$: C, 81.02; H, 6.36; N, 9.14. Found: C, 81.00; H, 6.32; N, 9.18.

1,3,3-Trimethyl-6′-piperazinospiro(indoline-2,3′-naphtho[2,1-*b*][1,4]oxazine) (11)

Mp >300 °C.

IR (KBr): 3056, 2960, 2814, 1612, 1587, 1484, 1453, 1408, 1361, 1298, 1270, 1197, 1137, 1026, 963, 898, 847, 762, 737 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.35 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 2.75 (s, 3 H, NCH_3), 3.05 (m, 4 H, 2 × CH_2), 3.14 (m, 4 H, 2 × CH_2), 6.57 (d, *J* = 7.8 Hz, 1 H, H-7), 6.60 (s, 1 H, H-5′), 6.89 (dd, *J* = 7.3, 7.4 Hz, 1 H, H-5), 7.10 (d, *J* = 7.2 Hz, 1 H, H-4), 7.20 (ddd, *J* = 7.7, 7.6, 1.3 Hz, 1 H, H-6), 7.38 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1 H, H-8′), 7.56 (ddd, *J* = 8.2, 8.2, 1.3 Hz, 1 H, H-9′), 7.63 (s, 1 H, H-2′), 8.04 (d, *J* = 8.4 Hz, 1 H, H-7′), 8.55 (d, *J* = 8.4 Hz, 1 H, H-10′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (CH_3), 25.3 (CH_3), 29.5 (NCH_3), 45.6 (2 × C, CH_2), 54.2 (2 × C, CH_2), 51.4 (C-3), 98.6–152.1 (18 × C, ArC, C-2′).

MS (ESI): *m*/*z* = 413.38 $[M + H]^+$.

Anal. Calcd for $C_{26}H_{28}N_4O$: C, 75.70; H, 6.84; N, 13.58. Found: C, 75.67; H, 6.81; N, 13.63.

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