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# SYNTHESIS OF NAPHTHOTHIAZOLIUM SALTS FROM BINOL

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**Abstract** – Naphthothiazolium salts with axial chirality were prepared from (*S*)-BINOL through introduction of a thiol group in place of the hydroxyl group by the Newmann-Kwart rearrangement and construction of the thiazolium ring by treatment of the air-sensitive *N*-alkylated aminothionaphthol with triethyl orthoformate in the presence of hydrogen chloride.

Organocatalysis has been shown to be an expedient and environmentally benign procedure for a variety of transformations and recent examples using chiral organocatalysts have demonstrated their crucial role in asymmetric synthesis, for example, asymmetric aldol reaction catalyzed with proline, asymmetric Diels- Alder reaction and 1,3-dipolar cycloaddition catalyzed with chiral imidazolidinones, and so on.[1] Recently, our interest has focused on development of new organocatalysis for the benzoin reaction and the Stetter reaction.[2] An asymmetric version of these reactions by use of chiral tetrazolium salts has been demonstrated.[3] Generally, these reactions are catalyzed by a nucleophilic carbene species generated from azolium salts and a base. Although thiazolium salts are a pioneer of organocatalysts, there have so far been no efficient chiral thiazolium salts in terms of chemical yield and enantiomeric excess in the benzoin reaction and the Stetter reaction.[4] Recently, Enders and coworkers screened a number of thiazolium salts with an extended conjugate system and observed that in the formoin reaction catalyzed by thiazolium salts like the benzoin reaction,[5] the thiazolium salt derived from benzothiazole with a conjugate system was an especially excellent catalyst better than that of thiazole itself.[6] These results led us to develop a new chiral thiazolium salt with an extended conjugate system. We envisioned that chiral thiazolium salt (**1**) from BINOL depicted in Figure 1 should have both the reactivity reported by Enders and the enantioselectivity by the shielding effect of the bottom aryl group. To date, there are no chiral thiazolium

salts derived from BINOL as a chiral template.[7] Herein we report the synthesis of new chiral naphthothiazolium salts from (*S*)-BINOL.

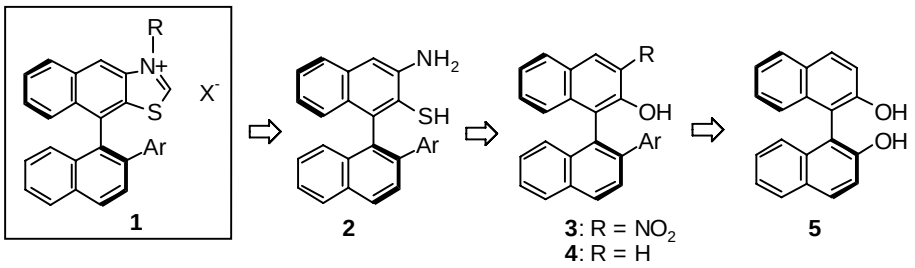
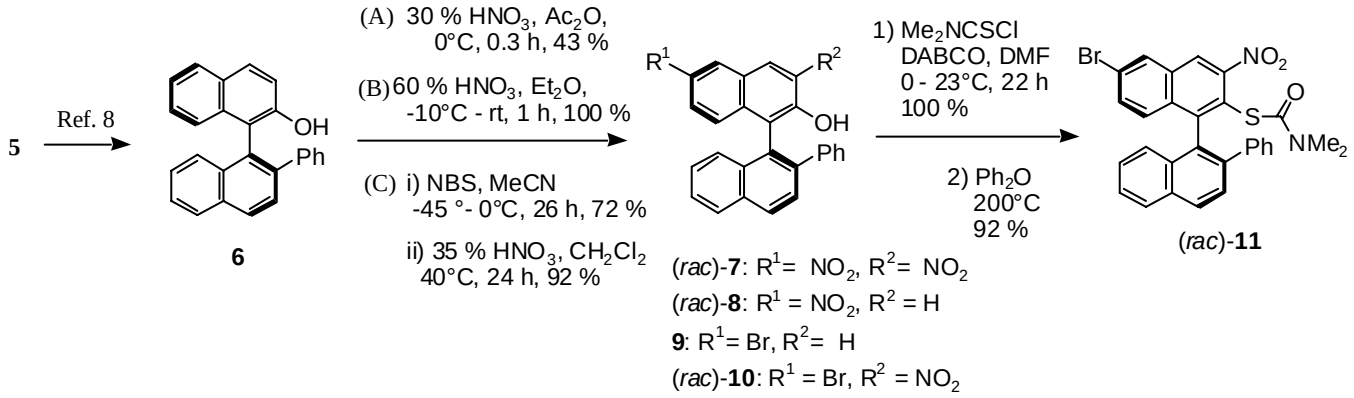



Figure 1

Our synthetic plan for the new thiazolium salts is shown in Figure 1. The thiazolium salts can be constructed from the corresponding aminothiophenol (**2**), which should be obtained from the nitrophenol (**3**) through the Newmann-Kwart rearrangement and reduction. The nitrophenol (**3**) can be derived from the corresponding phenol (**4**), which would be constructed from (*S*)-BINOL (**5**) through monoactivation of two phenol functions and palladium-catalyzed cross-coupling reaction with an organometallic reagent.

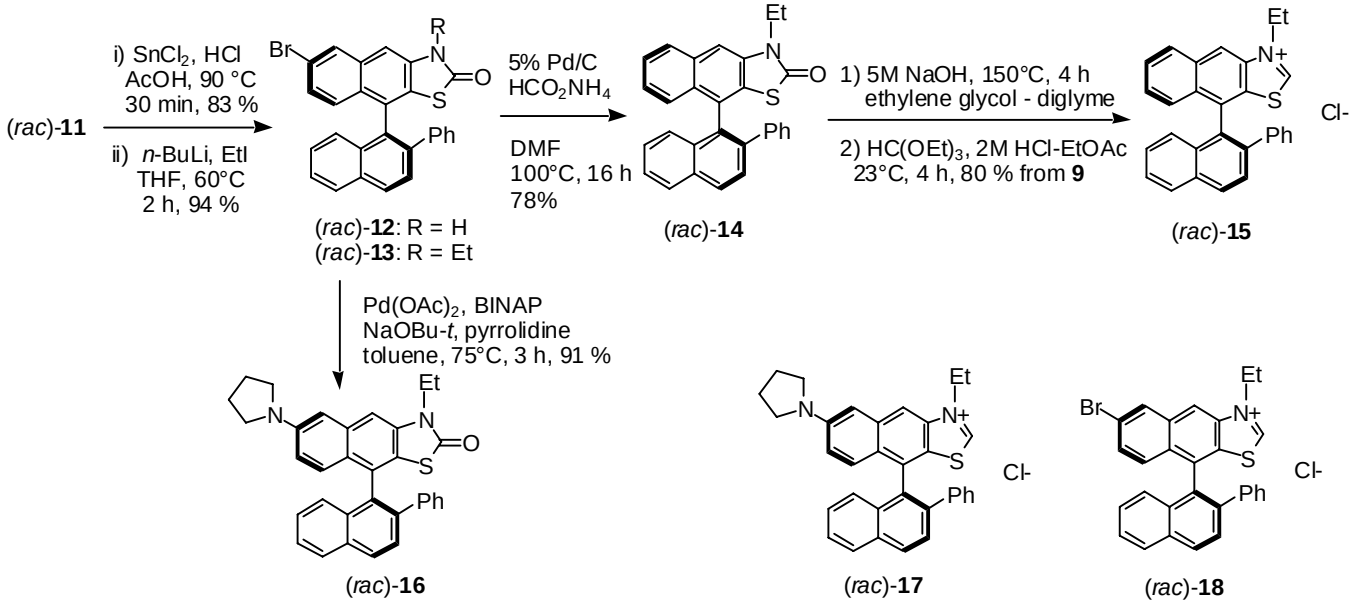
Synthesis of **1** started with palladium-catalyzed cross-coupling reaction of the known (*S*)-BINOL monotriflate[8] with phenylmagnesium bromide according to the literature method as shown in Scheme 1.




**Scheme 1**

With large quantities of binaphthol (**6**) in hand, the regioselective nitration of **6** was attempted. When this reaction was carried out with treatment of 30% nitric acid in acetic anhydride (method A), overreacted 3,6-dinitro derivative (**7**) was generated in 43% yield. Careful treatment of **6** with 1 equivalent of 60% nitric acid at –10 to 23°C in ether (method B) again resulted in undesired 6-nitro derivative (**8**) in quantitative yield. Since the attempts for *ortho*-selective nitration failed, we turned our attention to protection against electrophiles at the C6-reactive position of **6**. Selective protection at the C6 position was carried out by treatment with 1 equivalent of *N*-bromosuccinimide (NBS) at -40°C to 23°C in acetonitrile to afford the 6-bromo derivative (**9**) in 72% yield (method C). Introduction of a bromide group is very useful for the synthesis of naphthothiazolium analogues because of not only the easy removal by hydrogenolysis but also the conversion to other function groups through palladium-catalyzed

cross-coupling reaction. The bromide (**9**) was reacted with 1.2 equivalent of 30% nitric acid at 40°C in methylene chloride to furnish the desired 3-nitro derivative (**10**) in 92% yield. The thus-obtained **10**, however, was found to completely racemize on the axial chirality.[9] Although this was a serious problem, we decided to synthesize **1** as a racemic compound and examine its reactivity. Conversion of the hydroxy group to a thiol group in (*rac*)-**10** was carried out by the Newmann-Kwart rearrangement. Thus, (*rac*)-**10** was coupled with dimethylthiocarbamoyl chloride ($Me_2NCSCl$) in the presence of diazabicyclo[2.2.2]octane (DABCO) in dimethylformamide (DMF) to give the *O*-thiocarbamate in quantitative yield. The rearrangement of the *O*-thiocarbamate was performed at 200°C in diphenyl ether to afford the desired *S*-thiocarbamate [(*rac*)-**11**] in 92% yield.[10] Deprotection of the *S*-dimethylcarbamoyl group, however, was unexpectedly difficult. After some trials and errors, we were pleased to find chemoselective reduction of the 3-nitro group in (*rac*)-**11** with stannous chloride in the presence of hydrochloric acid and acetic acid and spontaneous conversion to thiazolinone [(*rac*)-**12**] through intramolecular attack of the resulting amine to the *S*-dimethylcarbamoyl group in 83% yield. Since (*rac*)-**12** resisted alkaline hydrolysis and reductive cleavage, the thiazolinone [(*rac*)-**12**] was first *N*-ethylated with *n*-butyllithium and iodoethane at 60°C for 24 h in THF to give *N*-ethylthiazolinone [(*rac*)-**13**] in 94% yield. Removal of the 6-bromo group was performed under transfer hydrogenolysis conditions to give (*rac*)-**14** in 78% yield. Cleavage of the *N*-ethylthiazolinone ring in (*rac*)-**14** was accomplished by alkaline hydrolysis with 5M sodium hydroxide in ethylene glycol-diglyme to give the aminothiophenol derivative. Unsurprisingly, this product was very sensitive to air or oxygen. Therefore, this step was carried out under oxygen-free conditions and the product was used for the next step without any purification. The crude aminothiophenol was treated with triethyl orthoformate in ethyl acetate in the presence of hydrogen chloride at 23°C for 4 h to produce the desired thiazolium salt [(*rac*)-**15**] in 80%




**Scheme 2**

yield.[11] For demonstration of the utility concerning the C6-bromo protection in (*rac*)-**13**, Buchwald's amination reaction[12] with Pd catalyst in the presence of BINAP was applied to the bromide [(*rac*)-**13**] to provide the corresponding amine [(*rac*)-**16**] in 91% yield. Finally, these compounds (*rac*)-**13** and (*rac*)-**16** were converted to the corresponding thiazolium salts (*rac*)-**18** and (*rac*)-**17**, respectively, by a similar procedure. The thus-obtained chiral naphthothiazolium salts (*rac*)-**15**, (*rac*)-**17**, and (*rac*)-**18** were applied to the asymmetric benzoin reaction as a bench-mark reaction. Unfortunately, the reaction failed to afford the desired compound.

In summary, we have demonstrated the first synthetic approach to new chiral naphthothiazolium salts with axial chirality from BINOL. Although the reactivity of these new naphthothiazolium salts remains to be improved, the present method described here will be useful for synthesis of other new thiazolium salts with a conjugate system. Further modification of naphthothiazolium salts is currently under way.

## EXPERIMENTAL

### General.

Melting points were determined on a Yamato MP-21 apparatus and are uncorrected. IR spectra were measured with a Perkin-Elmer 1600 FTIR spectrophotometer. $^{1}$H-NMR and $^{13}$C-NMR spectra were recorded on a JEOL JNM-ALPHA 400 or JEOL JNM-AL 400 spectrometer with tetramethylsilane or $CHCl_3$ as an internal standard. Optical rotations were measured with a JASCO DIP-1000 digital polarimeter. TLC was performed using precoated (0.25 mm) Merck silica gel F-254 plates. Column chromatography was performed using silica gel (FL-100D; Fuji Silysia Chemical Ltd.).

### 6-Nitro-2'-phenyl-1,1'-binaphthalen-2-ol (8)

To a solution of **6** (346.4 mg, 1.00 mmol) in ether (9.5 mL), aqueous $HNO_3$ (60%, 76 μL, 1.00 mmol) was added at –10°C under nitrogen atmosphere. After stirring the mixture for 1 h at 0°C, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with ether. The organic extract was washed with water and saturated aqueous brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 1/0 then 9/1) to give **8** (396 mg, 100%) as yellow crystals: mp 96°C (EtOAc/*n*-hexane); IR (KBr) 1637, 1654, 1685, 1735, 3433 cm$^{-1}$; $^{1}$H-NMR (400 MHz, $CDCl_3$) δ 5.64 (1H, s), 7.00-7.09 (5H, m), 7.14 (1H, d, *J* = 9.2 Hz), 7.22 (1H, d, *J* = 8.6 Hz), 7.27-7.36 (2H, m), 7.51 (1H, dd, *J* = 6.6, 8.4 Hz), 7.65 (1H, d, *J* = 8.4 Hz), 7.89-7.92 (2H, m), 7.97 (1H, d, *J* = 8.6 Hz), 8.16 (1H, d, *J* = 8.3 Hz), 8.68 (1H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 118.6, 119.5, 120.1, 125.0, 125.6, 126.2, 126.7, 126.8, 127.1, 127.3, 127.6, 127.9, 128.4, 128.5, 128.6, 130.1, 132.7, 133.3, 136.9, 140.3, 142.0, 143.6, 154.5. HRMS (FAB) calcd for $C_{26}H_{17}NO_3$: 391.1208 ($M+H^+$). Found: 391.1213.

**(*S*)-6-Bromo-2'-phenyl-1,1'-binaphthalen-2-ol (9)**

To a solution of **6** (3.74 g, 10.8 mmol) in MeCN (75 mL) at –45°C under nitrogen atmosphere, NBS (2.02 g, 11.3 mmol) was added and the mixture was gradually warmed to 0°C for 26 h. The reaction was quenched with water and extracted with EtOAc. The organic extract was washed with water and saturated aqueous brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* and the resulting residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 1/0 then 97/3) to give **9** (3.30 g, 72%) as pale yellow amorphous powder: mp 85°C (EtOAc/*n*-hexane); $[\alpha]^{20}_{D}$ –48.1° (*c* 1.01, $CHCl_3$); IR (KBr) 763, 820, 874, 934, 1045, 1242, 1373, 1494, 1588, 1731 $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$) δ 4.89 (1H, bs), 6.95 (1H, d, *J* = 9.0 Hz), 7.03-7.11 (5H, m), 7.14 (1H, d, *J* = 8.8 Hz), 7.23-7.26 (2H, m), 7.33 (1H, ddd, *J* = 12.0, 6.8, 1.2 Hz), 7.51 (1H, ddd, *J* = 8.1, 6.8, 1.2 Hz), 7.66 (1H, d, *J* = 9.0 Hz), 7.68 (1H, d, *J* = 8.3 Hz), 7.90 (1H, d, *J* = 2.0 Hz), 7.97 (1H, d, *J* = 8.1 Hz), 8.07 (1H, d, *J* = 8.5 Hz); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 117.0, 118.0,118.3, 126.0, 126.5, 126.8, 127.1, 127.3, 127.8, 128.3, 128.5, 128.6, 128.9, 129.6, 129.79, 129.84, 130.0, 132.6, 132.9, 133.2, 140.6, 141.7, 151.3. HRMS (FAB) calcd for $C_{26}H_{17}OBr$: 424.0463 ($M+H^+$). Found: 424.0498.

**6-Bromo-3-nitro-2'-phenyl-1,1'-binaphthalen-2-ol (10)**

To a solution of **9** (1.30 g, 3.07 mmol) in $CH_2Cl_2$ (5.2 mL), aqueous $HNO_3$ (35%, 0.82 mL, 3.68 mmol) was added at 23°C under nitrogen atmosphere and the mixture was heated at 40°C for 24 h. Heptane (24 mL) was added to the mixture and the resulting precipitates were collected by filtration to give **10** (1.32 g, 92%) as orange crystals: mp 294°C (EtOAc/*n*-hexane); IR (KBr) 762, 822, 938, 1066, 1192, 1313, 1353, 1443, 1489, 1520, 1598, 1622 $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.01 (1H, d, *J* = 9.1 Hz), 7.04-7.08 (3H, m), 7.13-7.16 (3H, m), 7.33 (1H, ddd, *J* = 1.2, 6.8, 8.3 Hz), 7.38 (1H, dd, *J* = 2.0, 9.0 Hz), 7.50 (1H, ddd, *J* = 1.0, 6.8, 8.1 Hz), 7.65 (1H, d, *J* = 8.5 Hz), 7.99 (1H, d, *J* = 8.5 Hz), 8.00 (1H, d, *J* = 2.0 Hz), 8.07 (1H, d, *J* = 8.3 Hz), 8.67 (1H, s), 10.13 (1H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 119.2, 124.9, 125.5, 125.7, 126.1, 126.9, 126.96, 127.02, 127.2, 127.7, 128.3, 128.4, 128.7, 129.1, 131.6, 132.3, 132.9, 134.0, 134.6, 136.4, 140.8, 141.3, 147.5. HRMS (FAB) calcd for $C_{26}H_{16}NO_3Br$: 469.0313 ($M+H^+$). Found: 469.0297.

***O*-(6-Bromo-3-nitro-2'-phenyl-1,1'-binaphthalene-2-yl)dimethylthiocarbamate**

To a solution of **10** (0.97 g, 2.07 mmol) in DMF (10 mL), DABCO (0.46 g, 4.14 mmol) and *N*, *N*-dimethylthiocarbamoyl chloride (0.51 g, 4.14 mmol) were added at 0°C under nitrogen atmosphere and the mixture was stirred at 23°C for 24 h. Water (20 mL) was added and the resulting precipitates were collected by filtration to give pure *O*-thiocarbamate (1.15 g, 100%) as pale yellow crystals: mp 293°C (EtOAc/*n*-hexane); IR (KBr) 762, 822, 914, 1112, 1172, 1227, 1283, 1346, 1396, 1527, 1592 $cm^{-1}$; $^1$H-NMR (The spectrum could not be assigned for the presence of the rotational isomers); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 38.3, 38.7, 43.1, 43.2, 121.6, 124.6, 126.4, 126.5, 126.9, 127.0, 127.1, 127.5, 127.7,

127.8, 127.9, 128.2, 128.38, 128.41, 128.5, 128.7, 129.2, 129.5, 130.2, 130.3, 131.6, 132.1, 132.5, 133.3, 134.6, 140.2, 141.00, 141.02, 142.5, 184.8. *Anal*. Calcd for $C_{29}H_{21}N_2O_3BrS$: C, 62.48; H 3.80; N 5.03. Found: C, 62.29; H, 3.93; N, 5.03.

**_S_-(6-Bromo-3-nitro-2'-phenyl-1,1'-binaphthalene-2-yl)dimethylthiocarbamate (11)**

A suspension of *O*-thiocarbamate (1.11 g, 1.99 mmol) in diphenyl ether (11 mL) was heated to 200°C under nitrogen atmosphere for 7.5 h. After cooling the mixture, the resulting residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 95/5) to give **11** (1.02 g, 92%) as colorless crystals: mp 263°C (EtOAc/*n*-hexane); IR (KBr) 764, 822, 924, 1097, 1255, 1364, 1534, 1560, 1671 $cm^{-1}$; $^1$H-NMR (400 MHz, DMSO-$d_6$) δ 2.64 (6H, s), 6.96 (1H, dd, *J* = 0.6, 8.4 Hz), 7.00-7.09 (6H, m), 7.31 (1H, ddd, *J* = 1.2, 6.8, 8.4 Hz), 7.52 (1H, ddd, *J* = 1.2, 6.8, 8.0 Hz), 7.62 (1H, dd, *J* = 2.0, 8.8 Hz), 7.64 (1H, d, *J* = 8.0 Hz), 8.06 (1H, d, *J* = 8.4 Hz), 8.18 (1H, d, *J* = 8.4 Hz), 8.46 (1H, d, *J* = 2.0 Hz), 8.67 (1H, s); $^{13}$C-NMR (100 MHz, DMSO-$d_6$) δ 35.9, 121.5, 121.6, 123.6, 123.7, 125.1, 125.6, 126.3, 126.4, 127.0, 127.4, 127.6, 127.9, 128.4, 128.6, 128.7, 130.8, 130.9, 131.4, 131.8, 132.0, 138.9, 139.9, 144.3, 150.2, 162.4. *Anal*. Calcd for $C_{29}H_{21}N_2O_3BrS$: C, 62.48; H 3.80; N 5.03. Found: C, 62.10; H, 3.93; N, 5.04.

**6-Bromo-9-(2-phenyl-1-naphthyl)naphtho[2,3-*d*]thiazol-2(3*H*)-one (12)**

To a suspension of **11** (1.02 g, 1.84 mmol) in acetic acid (28 mL) at 23°C were added concd HCl (4.0 mL, 47.7 mmol, 10.0 equiv) and $SnCl_2$•$H_2O$ (3.49 g, 10.8 mmol). After stirring the mixture at 90°C for 30 min, the reaction mixture was cooled to 0°C and the resulting precipitates were collected by filtration to give **12** (0.73 g, 83%) as colorless crystals: mp >300°C (EtOAc); IR (KBr) 760, 818, 886, 930, 1028, 1073, 1217, 1415, 1493, 1619, 1683 $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$) δ 6.99-7.10 (7H, m), 7.20 (1H, d, *J* = 9.2 Hz), 7.28-7.32 (3H, m), 7.51 (1H, ddd, *J* = 1.5, 7.3, 7.6 Hz), 7.65 (1H, d, *J* = 8.6 Hz), 7.94 (1H, d, *J* = 1.5 Hz), 7.99 (1H, d, *J* = 8.3 Hz), 8.08 (1H, d, *J* = 8.6 Hz); $^{13}$C-NMR (100 MHz, $CDCl_3$) , 105.8, 112.1, 120.3, 125.7, 126.3, 127.1, 127.2, 127.4, 127.7, 128.4, 128.5, 128.6, 128.9, 129.5, 131.0, 131.5, 133.0, 134.1, 138.8, 140.1, 140.6, 168.1. HRMS (ESI) calcd for $C_{27}H_{17}NOBrS$: 482.0214 ($M+H^+$). Found: 482.0219.

**6-Bromo-9-(2-phenyl-1-naphthyl)-3-ethylnaphtho[2,3-*d*]thiazol-2(3*H*)-one (13)**

To a solution of **12** (1.00 g, 2.07 mmol) in THF (10 mL), *n*-BuLi (1.55M in hexane, 1.3 mL, 2.07 mmol) and iodoethane (199 μL, 2.49 mmol) were added dropwise. After stirring the mixture at 60°C for 24 h, the reaction was quenched with aqueous 1M HCl and extracted with EtOAc. The organic extract was washed with water, saturated aqueous $NaHCO_3$, and saturated aqueous brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* and the resulting residue was purified by column

chromatography on silica gel (*n*-hexane/EtOAc = 95/5 then 82/18) to give **13** (0.99 g, 94%) as colorless crystals: mp >300°C (EtOAc/*n*-hexane); IR (KBr) 761, 828, 850, 1051, 1226, 1246, 1295, 1428, 1446, 1458, 1510, 1620, 1678 $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$) δ 1.39 (3H, d, *J* = 7.3 Hz), 3.92-4.01 (1H, m), 4.05-4.13 (1H, m), 7.00-7.15 (6H, m), 7.20 (1H, d, *J* = 9.0 Hz), 7.25-7.32 (3H, m), 7.51 (1H, dd, *J* = 7.1, 7.8 Hz), 7.65 (1H, d, *J* = 8.3 Hz), 7.99 (1H, d, *J* = 8.1 Hz), 8.03 (1H, d, *J* = 2.0 Hz), 8.09 (1H, d, *J* = 8.5 Hz); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 12.6, 37.9, 104.9, 120.2, 125.7, 126.3, 126.5, 127.0, 127.3, 127.6, 128.2, 128.3, 128.5, 128.6, 128.9, 129.5, 129.6, 131.2, 131.4, 132.9, 133.0, 136.2, 140.1, 140.6, 169.9 . HRMS (ESI) calcd for $C_{29}H_{21}NOBrS$: 510.0527($M+H^+$). Found: 510.0526.

**3-Ethyl-9-(2-phenyl-1-naphthyl)naphtho[2,3-*d*]thiazol-2(3*H*)-one (14)**

To a solution of **13** ( 51mg, 0.1 mmol) in DMF (1 mL) under argon atmosphere were added 5% Pd-C (11 mg, 0.005 mmol) and $HCO_2NH_4$ (125 mg, 1.97 mmol). After stirring at 100°C for 16 h, the mixture was filtered through a pad of celite to remove the Pd catalyst. The filtrate was diluted with EtOAc/*n*-hexane (4:1), washed with water and brine, dried over $Na_2SO_4$, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5:1) to give **14** (34 mg, 78%) as colorless solids: mp 247-250°C (EtOAc/*n*-hexane); IR (KBr) 3048, 2961, 1685, 1616, 1494, 1429, 1378, 1304, 1227, 1144, 822, 767, 715 $cm^{-1}$ ; $^1$H-NMR (400 MHz, $CDCl_3$) δ 1.39 (3H, t, *J* = 7.2 Hz), 3.94-4.15 (2H, m), 7.00-7.04 (3H, m), 7.12 (3H, dd, *J* = 1.6, 7.2 Hz), 7.22-7.30 (2H, m), 7.34-7.36 (2H, m) 7.44 (1H, ddd, *J* = 1.2, 8.4, 14 Hz), 7.49 (3H, ddd, *J* = 0.8, 7.2, 14 Hz), 7.55 (1H, d, *J* = 8.4 Hz), 7.85 (1H, d, *J* = 8.4 Hz), 7.97 (1H, d, *J* = 8.4 Hz), 8.07 (1H, d, *J* = 8.4 Hz); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 12.7, 37.8, 106.0, 125.0, 125.6, 125.9, 126.0, 126.1, 126.8, 126.9, 127.5, 127.6, 128.2, 128.5, 128.7, 129.3, 130.5, 131.1, 131.7, 131.9, 132.9, 135.3, 140.0, 140.8, 169.5. LRMS (EI) m/z 431 ($M^+$). HRMS (FAB, NBA) calcd for $C_{29}H_{22}NOS$: 432.1344 ($M+H^+$). Found: 432.1449.

**3-Ethyl-9-(2-phenyl-1-naphthyl)naphtho[2,3-*d*]thiazol-3-ium chloride (15)**

A carefully degassed suspension of **14** (1.33g, 3.08 mmol) in aqueous 5M NaOH (20 mL), ethylene glycol (20 mL), and diglyme (20 mL) was heated at 150°C for 4 h under nitrogen atmosphere. The reaction mixture was cooled to 23°C and diluted with EtOAc. The organic extract was washed with saturated aqueous $NH_4Cl$ and water, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to give the crude aminothionaphthol (1.22 g). The crude aminothionaphthol was suspended in triethyl orthoformate (7 mL) under nitrogen atmosphere and HCl (2.1 M in EtOAc, 5 mL) was added at 23°C. After stirring the mixture for 4 h, the mixture was diluted with *n*-hexane (6mL) and stirred for 1 h. The resulting precipitates were collected by filtration to give **15** (1.11g, 80%) as pale brown solids. The pure sample was obtained by reprecipitation from $CH_2Cl_2$/ether as slightly yellow crystals: mp >178°C (decomp) ($CH_2Cl_2$/ether); IR (KBr) 3403, 3055, 2918, 1655, 1562, 1525, 1493, 1443, 1343, 893, 823, 768,

704 $cm^{-1}$; $^1$H-NMR (400 MHz, $CD_3OD$) δ 1.72 (3H, t, *J* = 7.1 Hz), 4.94 (2H, q, *J* = 7.3 Hz), 6.84-7.03 (4H, m) 7.02 (2H, m), 7.25 (1H, ddd, *J* = 1.2, 7.2, 14.0 Hz), 7.51 (1H, ddd, *J* = 0.9, 7.1, 15.0 Hz), 7.60-7.64 (2H, m), 7.71-7.76 (2H, m), 8.06 (1H, d, *J* = 8.1 Hz), 8.23 (1H, d, *J* = 8.4 Hz), 8.33 (1H, d, *J* = 8.4 Hz), 8.97 (1H, s), 10.4 (1H, s). HRMS (FAB, NBA) calcd for $C_{29}H_{22}NS$: 416.1473 ($M^+$-Cl). Found: 416.1490.

**3-Ethyl-9-(2-phenyl-1-naphthyl)-6-(1-pyrrolidinyl)naphtho[2,3-*d*]thiazol-2(3*H*)-one (16)**

A suspension of **13** (411 mg, 0.805 mmol), $Pd(OAc)_2$ (9.0 mg, 0.040 mmol), BINAP (75.2 mg, 0.121 mmol), sodium *t*-butoxide (108 mg, 1.13 mmol) and pyrrolidine (134 μL, 1.61 mmol) in toluene (8 mL) was heated at 75°C for 3 h with stirring under nitrogen atmosphere. After cooling the mixture to 23°C, the mixture was quenched with aqueous 1 M HCl and extracted with toluene. The organic extract was washed with water, saturated aqueous $NaHCO_3$, and saturated aqueous brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 1/0 then 9/1) to give **16** (366 mg, 91%) as pale yellow crystals: mp 283°C (decomp) (EtOAc/*n*-hexane); IR (KBr) 701, 760, 806, 838, 849, 1140, 1225, 1294, 1421, 1446, 1458, 1510, 1620, 1676 $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$) δ 1.37 (3H, t, *J* = 7.1 Hz), 2.02-2.06 (4H, m), 3.36-3.42 (4H, m), 3.88-3.97 (1H, m), 4.02-4.12 (1H, m), 6.75 (1H, d, *J* = 8.8 Hz), 7.02-7.06 (3H, m), 7.15-7.20 (5H, m), 7.24-7.30 (2H, m), 7.47 (1H, ddd, *J* = 1.5, 6.8, 8.2 Hz), 7.64 (1H, d, *J* = 8.5 Hz), 7.95 (1H, d, *J* = 8.1 Hz), 8.04 (1H, d, *J* = 8.3 Hz); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 12.8, 25.6, 37.7, 47.7, 104.07, 104.14, 114.6, 120.1, 123.7, 125.9, 126.2, 127.5, 128.0, 128.5, 128.7, 128.9, 130.8, 131.9, 132.4, 133.9, 135.7, 139.6, 140.9, 145.6, 170.0. HRMS (FAB, NBA) calcd for $C_{33}H_{28}N_2OS$: 500.1922 ($M+H^+$). Found: 500.1934.

**3-Ethyl-9-(2-phenyl-1-naphthyl)-6-(1-pyrrolidinyl)naphtho[2,3-*d*]thiazol-3-ium chloride (17)**

A carefully degassed suspension of **16** (806 mg, 1.61 mmol) in aqueous 2M KOH (8.1 mL), ethylene glycol (8.1 mL) and diglyme (8.1 mL) was heated at 160°C for 2 h under nitrogen atmosphere. The reaction mixture was cooled to 23°C and diluted with EtOAc. The whole was washed with saturated aqueous $NH_4Cl$ and water, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to give the crude aminothionaphthol (1.04 g). The crude aminothionaphthol was suspended in triethyl orthoformate (16 mL) under nitrogen atmosphere and HCl (4M in EtOAc, 4 mL) was added at 23°C. After stirring for 18 h, the resulting precipitates were collected by filtration to give **17** (693 mg, 81%) as pale yellow crystals. The pure sample was obtained by reprecipitation from $CH_2Cl_2$/ether as slightly yellow crystals: mp 284°C (decomp) ($CH_2Cl_2$/ether); IR (KBr) 701, 762, 831, 1032, 1248, 1382, 1451, 1506, 1541, 1615 $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$) δ 1.77 (3H, t, *J* = 7.1 Hz), 2.10-2.14 (4H, m), 3.46-3.50 (4H, m), 4.99 (1H, dt, *J* = 7.1, 14.2 Hz), 5.28 (1H, dt, *J* = 7.3, 14.4 Hz), 6.93-7.07 (7H, m), 7.14

(1H, dd, *J* = 2.4, 9.2 Hz), 7.29 (1H, ddd, *J* = 1.2, 6.8, 11.5 Hz), 7.52-7.56 (2H, m), 7.72 (1H, d, *J* = 8.3 Hz), 8.03-8.05 (2H, m), 8.18 (1H, d, *J* = 8.8 Hz), 12.35 (1H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 14.8, 25.5, 47.7, 48.2, 103.1, 110.1, 120.0, 125.4, 126.6, 126.8, 127.3, 127.49, 127.53, 128.0, 128.4, 128.50, 128.54, 130.1, 130.5, 131.7, 132.9, 135.4, 137.2, 140.0, 167.0. HRMS (FAB, NBA) calcd for $C_{33}H_{29}N_2S$: 485.2051 ($M^+$-Cl). Found: 485.2084.

**6-Bromo-3-ethyl-9-(2-phenyl-1-naphthyl)naphtho[2,3-*d*]thiazol-3-ium chloride (18)**

A carefully degassed suspension of **13** (388 mg, 0.761 mmol) in aqueous 2M NaOH (6.1 mL), ethylene glycol (6.1 mL) and diglyme (6.1 mL) was heated at 150°C for 2 h under nitrogen atmosphere. The reaction mixture was cooled to 23°C and diluted with EtOAc. The organic extract was washed with saturated aqueous $NH_4Cl$ and water, dried over $MgSO_4$, and filtered. The filtrate was concentrated *in vacuo* to give the crude aminothionaphthol (412.4 mg). The crude aminothinaphthol was suspended in triethyl orthoformate (2.3 mL) under nitrogen atmosphere and HCl (4M in EtOAc, 0.76 mL) was added at 23°C. After stirring for 18 h, the resulting precipitates were collected by filtration to give **18** (382 mg, 95%) as pale yellow crystals. The pure sample was obtained by reprecipitation from $CH_2Cl_2$/ether as slightly yellow crystals: mp 150°C (decomp) ($CH_2Cl_2$/ether); IR (KBr) 703, 764, 820, 893, 919, 1065, 1308, 1335, 1425, 1494, 1482, 1574, 1610 $cm^{-1}$; $^1$H-NMR (400 MHz, $CDCl_3$) δ 1.81 (3H, t, *J* = 7.3 Hz), 5.15 (1H, m), 5.36 (1H, m), 6.83 (1H, d, *J* = 8.5 Hz), 6.95-7.06 (5H, m), 7.30 (1H, ddd, *J* = 1.2, 6.8, 8.3 Hz), 7.56 (1H, ddd, *J* = 1.0, 6.8, 8.1 Hz), 7.61 (1H, s), 7.67 (1H, dd, *J* = 2.0, 9.3 Hz), 7.74 (1H, d, *J* = 8.5 Hz), 8.06 (1H, d, *J* = 8.1 Hz), 8.22 (1H, d, *J* = 8.5 Hz), 8.44 (1H, d, *J* = 1.7 Hz), 8.45 (1H, s), 12.73 (1H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 14.9, 49.0, 13.5, 123.2, 124.8, 126.7, 127.6, 127.7, 127.8, 128.0, 128.2, 128.4, 128.6, 128.8, 130.0, 130.9, 131.0, 131.3, 132.6, 132.8, 133.4, 135.8, 137.0, 139.6, 140.4, 170.0. HRMS (FAB, NBA) calcd for $C_{29}H_{21}NBrS$: 494.0578 ($M^+$-Cl). Found: 494.0534.

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