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A Facile Synthesis of Annulated 2,2′-Bipyridine Ligands with Alkylsulfanyl and Alkylsulfonyl Substituents in the 6 and 6' Positions [1]

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3,3′-Bis(isopropylsulfanyl)-5,5′-bi-1,2,4-triazine **2** is easily transformed into annulated 2,2′-bipyridines **4** and **6** with fused cycloalkene rings *via* [4+2]cycloaddition/retro cycloaddition reaction with cyclic enamines **3a–d**. Oxidation of **4** and **6** with potassium permanganate under phase transfer catalysis conditions provided a series of the corresponding sulfonyl derivatives **7** and **8.**

Key words: bi-1,2,4-triazine, cyclic enamines, [4+2]cycloaddition, annulated 2,2′-bipyridines with attached cycloalkene rings

2,2′-Bipyridine is one of the most versatile ligands in coordination and supramolecular chemistry, because it easily forms well-defined chelate complexes with many metals [2]. Particularly interesting and useful are its annulated derivatives with benzo fusion incorporated into larger macropolycyclic structures, since they form stable luminescent complexes with a variety of lanthanide cations [3]. The transition metal complexes of chiral cycloalkenobipyridines have also been investigated. They have recently been employed as catalysts in a number of asymmetric reactions such as asymmetric cyclopropanation of alkenes [4], asymmetric alkylation of aldehydes [5], asymmetric hydrogenation and hydrosilylation [6] and asymmetric palladium catalysed allylic alkylation [7]. Although there are several methods to synthesize annulated bipyridines with benzo fusion [8] only a limited number of reports have appeared regarding their analogues with attached cycloalkene ring. The preparation of these ligands often rely on the transition-metal mediated heteroaryl cross-coupling reactions of specially prepared pyridines [9] or on the Kröhnke-type synthesis from α,β-unsaturated ketones [10]. More recent approaches employ cobalt(I) catalysed [2+2+2] cycloadditions between 5-hexenenitrile and 1,3-diynes [11] or the double intramolecular Diels-Alder reactions of α,β-unsaturated hydrazones with 1,3-dialkynes [12]. Alternatively, the construction of the fused pyridine ring can be achieved *via* intermolecular or intramolecular Diels-Alder reactions of 1,2,4-triazines with inverse electron-demand [13]. We have applied this methodology to the direct synthesis of symmetrical and unsymmetrical annulated 2,2′-bipyridines *via* reaction of 5,5′-bi-1,2,4-triazines with cyclic enamines **3a–d** [14,15]. The method employs

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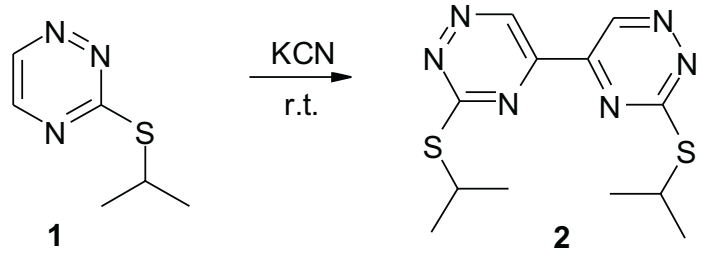
readily available reagents and an operationally simple experimental procedure. We have now extended these studies to provide a synthesis of novel cycloalkeno[c]fused 2,2′-bipyridines **4, 6–8** bearing isopropylsulfanyl and isopropylsulfonyl substituents in the 6 and 6' positions. Since both substituents are good leaving groups and can be easily replaced by nucleophiles [16], their preparation would considerably broaden the scope of the overall 2,2′-bipyridine synthesis.

RESULTS AND DISCUSSION

The required 3,3′-bis(isopropylsulfanyl)-5,5′-bi-1,2,4-triazine (**2**) have been prepared in good yield by a direct dimerization of 3-(isopropylsulfanyl)-1,2,4-triazine (**1**) with potassium cyanide using literature procedure [17] (Scheme 1).

Scheme 1

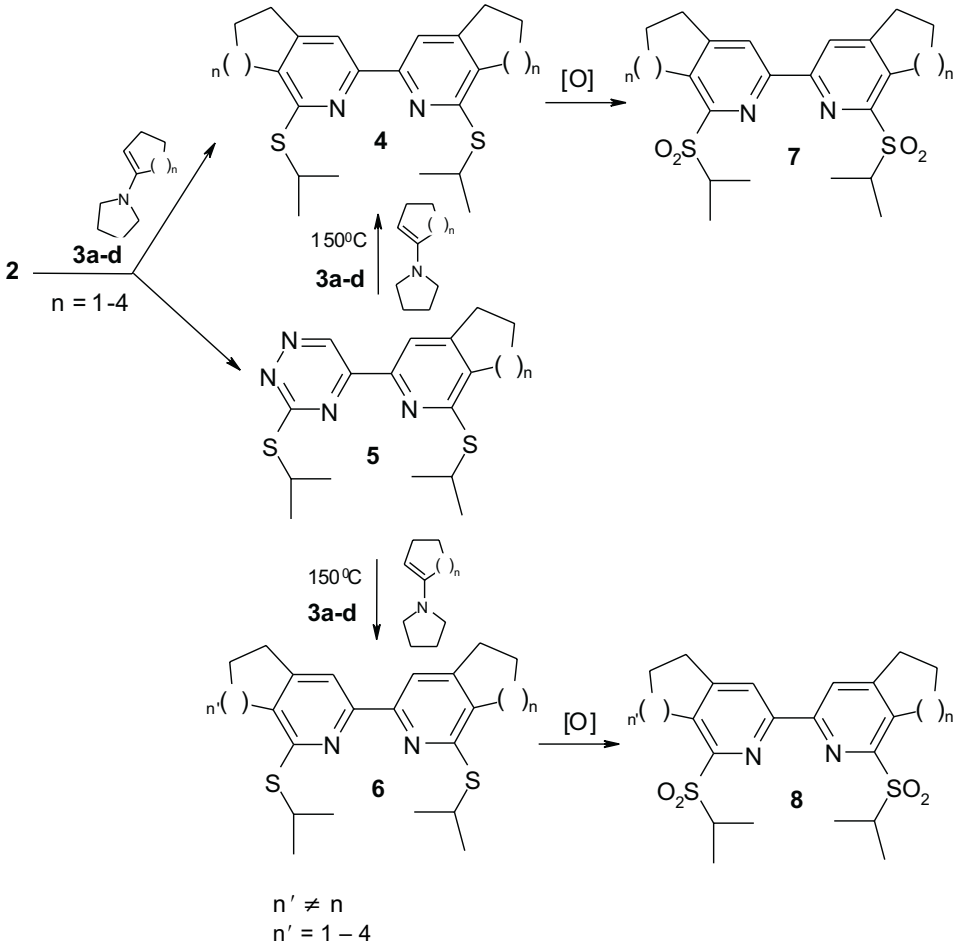


Heating **2** with four-fold amount of 1-pyrrolidino-1-cyclopentene (**3a**, n = 1) without a solvent at 150°C for 16 h gives 1,1′-bis(isopropylsulfanyl)-6,7,6′,7′-tetrahydro- 5H,5H′-3,3′-bi-cyclopenta[c]pyridine (**4a**) (Scheme 2). Compound **4a** precipitated from the reaction mixture. Recrystallization of **4a** from toluene gave pure product. Also 1-pyrrolidino-1-cyclohexene (**3b**), 1-pyrrolidino-1-cycloheptene (**3c**), and 1-pyr- rolidino-1-cyclooctene (**3d**) reacted efficiently with **2** at this temperature giving directly symmetrical cycloalkeno[c]fused 2,2′-bipyridines **4b–d** in good yield. Structures of new compounds were clearly supported by ^{1}H NMR and elemental analysis. Their ^{1}H NMR spectra showed chemical shifts characteristic for isolated protons of the pyridine ring at 7.77–8.02 ppm in addition to signals for the aliphatic protons ranging from 1.48 to 2.99 ppm (see Experimental). When the reactions of **2** with an excess of **3a–d** are carried out in dioxane at room temperature, 5-(heteroaryl)-1,2,4-triazines **5a,c–d** are formed exclusively. The formation of 6-membered ring in the reaction of **2** with **3b** under these conditions is less favorable and needs a higher temperature for completion. This regioselective annulation of compound **2** could be attributed to the decrease of the reactivity of the second triazine ring in compounds **5a-d** under such reaction conditions. However, treatment of **5a** with an excess of five membered enamine without solvent at 150°C for 10 h afforded the desired compound **4a** in 62% yield. These reaction conditions when applied to the remaining enamines **3b–d** led to the same results (Scheme 2).

Monoannulated derivatives **5a-d** consisting of the two different heterocyclic units, *i.e*. annulated pyridine and 1,2,4-triazine, appeared to be valuable intermediates for the synthesis of the unsymmetrical, annulated 2,2′-bipiridines **6a–f**. The reaction of **5a** with six-, seven- and eight-membered enamines **3b–d** without solvent at 150°C for 17 h gave unsymmetrical derivatives **6a–c**. Similarly, heating **5b** with **3c** or **3d** gives **6d–e**, and the reaction of **5c** with eight membered enamine **3d** yields unsymmetrical 2,2′-bipyridine **6f** respectively. Optimal reaction conditions required the use of four equivalents of the corresponding enamine. The progress of reaction was followed on the TLC after aliquot work up.

Oxidation of symmetrical 2,2′-bipyridines **4a–c** with potassium permanganate under the phase transfer catalysis conditions provided a series of alkylsulfonyl derivatives **7a–c** in good yield. Also unsymmetrical derivatives **6a–c** oxidized easily under these conditions afforded the corresponding sulfones **8a–c**.

Scheme 2



In summary, we have developed an efficient route to annulated 2,2′-bipyridines bearing alkylsulfanyl and alkylsulfonyl groups in the 6 and 6'positions. The presence of such leaving groups in both fused pyridine rings makes these compounds attractive as building blocks for the synthesis of macrocycles.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were measured with a Magna IR-760 spectrophotometer. The ^{1}H NMR spectra were recorded in deuteriochloroform on a Varian-Gemini 200 MHz spectrometer. Mass spectra were measured with an AMD 604 (AMD Intectra GmbH, Germany) spectrometer [electron impact and liquid secondary ion mass spectrometry (LSIMS) methods]. Elemental analyses were recorded on Perkin-Elmer 2400 – CHN analyzer. Column chromatography was performed on silica gel (230-400 mesh, 60 Merck). All solvents used were dried and distilled according to standard procedures [18]. Merck $60F_{254}$ plates were used for analytical (TLC) chromatography

Synthesis of 3,3′-bis(isopropylsulfanyl)-5,5′-bi-1,2,4-triazine (2). A solution of 3-isopropylsulfanyl-1,2,4-triazine (**1**) (8 g, 50 mmol) in water (100 mL) was stirred until complete dissolution. The excess of potassium cyanide (30 g) was added as a solid in 5 portions. An immediate precipitate (intensely colored) was formed. This solution was then stirred with of ethyl ether (100 mL) for 15 min and the organic layer was separated. Water layer was extracted with chloroform (10×100 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo* to give **2** as a yellow solid. The product was purified by flash chromatography using chloroform as eluent to furnish 7.95 g (98%) of **2**. M.p. 174–175°C. ^{1}H NMR ($CDCl_3$): δ = 1.54 (d, 6 H, J = 6.8 Hz), 4.18 (sep, 1 H, J = 6.8 Hz), 9.86 (s, 1 H). Anal. Calcd for $C_{12}H_{16}N_6S_2$: C, 46.75; H, 5.20; N, 27.27. Found: C, 46.74; H, 5.23; N, 27.40.

Synthesis of 1,1′-bis(isopropylsulfanyl)-6,6′,7,7′-tetrahydro-5H,5H′-3,3′-bi-cyclopenta[c]pyridine (4a). The solution of **2** (0.5 g, 1.54 mmol) and **3a** (5 mL) was heated at 150°C for 16 h. After cooling the acetone (3 mL) was added and the precipitated solid was filtered off. The crude product was crystallized from toluene to give 0.39 g (63%) as a white solid **4a.** M.p. 274–275°C. ^{1}H NMR ($CDCl_3$): δ = 1.50 (d, 6 H, J = 6.8 Hz), 2.14 (qui, 2 H, J = 7.4 Hz), 2.81 (t, 2H, J = 7.4 Hz), 2.99 (t, 2 H, J = 7.4 Hz), 4.30 (sep, 1 H, J = 6.8 Hz), 8.02 (s, 1 H). Anal. Calcd for $C_{22}H_{28}N_2S_2 \cdot 0.3H_2O$: C, 67.80; H, 7.34; N, 7.19. Found: C, 67.88; H, 7.25; N, 7.10.

1,1′-Bis(isopropylsulfanyl)-5,5′,6,6′,7,7′,8,8′-octahydro-3,3′-biisoquinoline (4b). The solution of **2** (0.5 g, 1.54 mmol) and **3b** (5 mL) was heated at 150°C for 14 h. After cooling the acetone (3 mL) was added and the precipitated solid was filtered off. The crude product was crystallized from toluene to give 0.27 g (41%) as a white solid **4b**. M.p. 207–208°C. ^{1}H NMR ($CDCl_3$): δ = 1.49 (d, 6 H, J = 6.8 Hz), 1.70–1.90 (m, 4 H), 2.57 (t, 2 H, J = 5.9 Hz), 2.78 (t, 2 H, J = 7.4 Hz), 4.25 (sep, 1 H, J = 6.8 Hz), 7.77 (s, 1 H). Anal. Calcd for $C_{24}H_{32}N_2S_2$: C, 69.90; H, 7.77; N, 6.80. Found: C, 69.95; H, 7.72; N, 6.81.

1,1′-Bis(isopropylsulfanyl)-6,6′,7,7′,8,8′,9,9′-octahydro-5H,5H′-3,3′-bicyclohepta[c]pyridine (4c). The solution of **2** (0.5 g, 1.54 mmol) and **3c** (5 mL) was heated at 150°C for 3 h. After cooling the acetone (3 mL) was added and the precipitated solid was filtered off. The crude product was crystallized from toluene to give 0.56 g (78%) as a white solid **4c**. M.p. 193–194 °C. ^{1}H NMR ($CDCl_3$): δ = 1.48 (d, 6 H, J = 6.8 Hz), 1.56–1.74 (m, 4 H), 1.76–1.92 (m, 2 H), 2.82 (t, 2 H, J = 5.3 Hz), 2.88 (t, 2 H, J = 5.3 Hz), 4.15 (sep, 1 H, J = 6.8 Hz), 7.82 (s, 1 H). Anal. Calcd for $C_{26}H_{36}N_2S_2$: C, 70.91; H, 8.18; N, 6.36. Found: C, 70.93; H, 8.21; N, 6.22.

1,1′-Bis(isopropylsulfanyl)-5,5′,6,6′,7,7′,8,8′,9,9′,10,10′-dodecahydro-3,3′-bicycloocta[c]pyridine (4d). The solution of **2** (0.5 g, 1.54 mmol) and **3d** (5 mL) was heated at 150°C for 1.5 h. After cooling the acetone (3 mL) was added and the precipitated solid was filtered off. The crude product was crystallized from toluene to give 0.15 g (20%) as a white solid **4d**. M.p. 224–225°C. ^{1}H NMR ($CDCl_3$): δ = 1.45 (d, 6 H, J = 6.8 Hz), 1.54–1.78 (m, 4 H), 1.76–1.92 (m, 4 H), 2.82 (t, 2 H, J = 5.3 Hz), 2.88 (t, 2 H, J = 5.3 Hz), 4.15 (sep, 1 H, J = 6.8 Hz), 7.82 (s, 1 H). Anal. Calcd for $C_{28}H_{40}N_2S_2$: C, 71.79; H, 8.55; N, 5.98. Found: C, 71.80; H, 8.68; N, 5.86.

Synthesis of 1-(isopropylsulfanyl)-3-[3-(isopropysulfanyl)-1,2,4-triazin-5-yl]-6,7-dihydro-5H-cyclopenta[c]pyridine (5a). A mixture of 3,3′-bis(isopropylsulfanyl)-5,5′-bi-1,2,4-triazine (**2**) (0.5 g, 1.54 mmol) and 1-pyrrolidino-1-cyclopentene (**3a**) (0.89 g, 6.2 mmol) in dry dioxane (15 mL) was stirred at room temperature for 1 h. The solvent was evaporated under reduced pressure and the residue was crystallized from ethanol-water to give 0.42 g (74%) as a yellow solid **5a.** M.p. 116–117°C. ^{1}H NMR ($CDCl_3$): δ = 1.50 (d, 6 H, J = 6.8 Hz), 1.53 (d, 6 H, J = 6.8 Hz), 2.17 (qui, 2 H, J = 7.4 Hz), 2.83 (t, 2 H, J = 7.2 Hz), 2.99 (t, 2 H, J = 7.4 Hz), 4.18 (sep, 1 H, J = 6.8 Hz), 4.23 (sep, 1 H, J = 6.8 Hz), 8.08 (s, 1 H), 9.87 (s, 1 H). Anal. Calcd for $C_{17}H_{22}N_4S_2 \cdot 0.1H_2O$: C, 58.65; H, 6.38; N, 16.10. Found: C, 58.37; H, 6.21; N, 15.80.

1-(Isopropylsulfanyl)-3-[3-(isopropylsulfanyl)-1,2,4-triazin-5-yl]-5,6,7,8-tetrahydroisoquinoline (5b). A mixture of 3,3′-bis(isopropylsulfanyl)-5,5′-bi-1,2,4-triazine (**2**) (0.5 g, 1.54 mmol) and 1-pyrrolidino-1-cyclohexene (**3b**) (0.94 g, 6.2 mmol) in dry dioxane (15 mL) was refluxed for 1.5 h. The solvent was evaporated under reduced pressure and the residue was crystallized from ethanol-water to give 0.34 g (58%) as a yellow solid **5b**. M.p. 113–114°C. ^{1}H NMR ($CDCl_3$): δ = 1.50 (d, 6 H, J = 6.8 Hz), 1.53 (d, 6 H, J = 6.8 Hz), 1.96–1.72 (m, 4 H), 2.60 (t, 2H, J = 6.0 Hz), 2.80(t, 2 H, J = 5.8 Hz), 4.19 (sep, 1 H, J = 6.6 Hz), 4.20 (sep, 1 H, J = 6.8 Hz), 7.90 (s, 1 H), 9.86 (s, 1 H). Anal. Calcd for $C_{18}H_{24}N_4S_2 \cdot 0.5H_2O$: C, 58.54; H, 6.78; N, 15.18. Found: C, 58.69; H, 6.77; N, 15.19. HRMS (LSIMS): m/z calcd for $C_{18}H_{25}N_4S_2$(M+H) (M^+), 361.15207; found, 361.15327.

1-(Isopropylsulfanyl)-3-[3-(isopropylsulfanyl)-1,2,4-triazin-5-yl]-6,7,8,9-tetrahydro-5H-cyclohepta[c] pyridine (5c). A mixture of 3,3′-bis(isopropylsulfanyl)-5,5′-bi-1,2,4-triazine (**2**) (0.5 g, 1.54 mmol) and 1-pyrrolidino-1-cycloheptene (**3c**) (1.02 g, 6.2 mmol) in dry dioxane (15 mL) was stirred at room temperature for 0.5 h. The solvent was evaporated under reduced pressure and the residue was crystallized from ethanol-water to give 0.42 g (70%) as a yellow solid **5c**. M.p. 119–120°C. ^{1}H NMR ($CDCl_3$): δ = 1.49 (d, 6 H, J = 7.3 Hz), 1.53 (d, 6 H, J = 6.8 Hz), 1.57–1.75 (m, 4 H), 1.77–1.97 (m, 2 H), 2.86 (t, 2 H, J = 5.3 Hz), 2.91 (t, 2 H, J = 5.2 Hz), 4.13 (sep, 1 H, J = 7.3 Hz), 4.20 (sep, 1 H, J = 6.8 Hz), 7.93 (s, 1 H), 9.85 (s, 1 H). Anal. Calcd for $C_{19}H_{26}N_4S_2$: C, 60.96; H, 6.95; N, 14.97. Found: C, 60.83; H, 6.88; N, 14.90.

1-(Isopropylsulfanyl)-3-[3-(isopropylsulfanyl)-1,2,4-triazin-5-yl]-5,6,7,8,9,10-hexahydrocycloocta[c] pyridine (5d). A mixture of 3,3′-bis(isopropylsulfanyl)-5,5′-bi-1,2,4-triazine (**2**) (0.5 g, 1.54 mmol) and 1-pyrrolidino-1-cyclooctene (**3d**) (1.11 g, 6.2 mmol) in dry dioxane (15 mL) was stirred at room temperature for 22 h. The solvent was evaporated under reduced pressure and the residue was crystallized from ethanol-water to give 0.42 g (30%) as a yellow solid **5d**. M.p. 132–133°C. ^{1}H NMR ($CDCl_3$): δ = 1.49 (d, 6 H, J = 7.3 Hz), 1.52 (d, 6 H, J = 7.2 Hz), 1.38–1.36 (m, 4 H), 1.76–1.78 (m, 4 H), 2.82 (t, 2 H, J = 6.3 Hz), 2.91 (t, 2 H, J = 6.3 Hz), 4.18 (sep, 1 H, J = 7.3 Hz), 4.21 (sep, 1 H, J = 6.8 Hz), 7.93 (s, 1 H), 9.85 (s, 1 H). Anal. Calcd for $C_{20}H_{28}N_4S_2$: C, 62.85; H, 7.22; N,14.43. Found: C, 62.79; H, 6.99; N, 14.20.

Synthesis of 1-(isopropylsulfanyl)-3-[1-(isopropylsulfanyl)-6,7-dihydro-5H-cylopenta[c]pyridin-3-yl]-5,6,7,8-tetrahydroisoquinoline (6a). The mixture of **5a** (0.3 g, 0.87 mmol) and 1-pyrrolidino-1-cyclohexene (**3b**) (3 mL) was heated at 150°C for 22 h. The crude product was purified by chromatography column using hexane/chloroform (5:1) to give 0.33 g (95%) as a white solid **6a**. M.p. 213–214°C. ^{1}H NMR ($CDCl_3$): δ = 1.48 (d, 6 H, J = 6.8 Hz), 1.50 (d, 6 H, J = 6.8 Hz), 1.74–1.56 (m, 4 H), 1.76–1.92 (m, 2 H), 2.82 (t, 2 H, J = 5.3 Hz), 2.53–2.59 (m, 4 H), 2.88 (t, 2 H, J = 5.3 Hz), 4.24 (sep, 1 H, J = 6.8 Hz), 4.28 (sep, 1 H, J = 6.8 Hz), 7.92 (s, 1 H), 7.95 (s, 1 H). Anal. Calcd for $C_{23}H_{30}N_2S_2$: C, 69.35; H, 7.54; N, 7.03. Found: C, 69.53; H, 7.51; N, 6.99.

Synthesis of 1-(isopropylsulfanyl)-3-[(1-isopropylsulfanyl)-6,7-dihydro-5H-cylopenta[c]pyridin-3-yl]-6,7,8,9-tetrahydrocyclohepta[c]pyridine (6b). The mixture of **5a** (0.3 g, 0.87 mmol) and 1-pyrrolidine-1-cycloheptene (**3c**) (5 mL) was refluxed at 150°C for 17 h. The crude product was purified by chromatography column to give 0.32 g (87%) as a white solid **6b**. M.p. 176–177°C. ^{1}H NMR ($CDCl_3$): δ = 1.45 (d, 6 H, J = 6.8 Hz), 1.48 (d, 6 H, J = 6.8 Hz), 1.55–1.65 (m, 4 H), 1.80–1.85 (m, 4 H), 2.56 (t, 2 H, J = 5.3 Hz), 2.78–2.90 (m, 6 H), 4.14 (sep, 1 H, J = 6.8 Hz), 4.23 (sep, 1 H, J = 6.8 Hz), 7.78 (s, 1 H), 7.81 (s, 1 H). Anal. Calcd for $C_{24}H_{32}N_2S_2 \cdot 0.1H_2O$: C, 69.90; H, 7.77; N, 6.80. Found: C, 70.03; H, 7.83; N, 6.78.

Synthesis of 1-(isopropylsulfanyl)-3-[1-(isopropylsulfanyl)-6,7-dihydro-5H-cyclopenta[c] pyridin-3-yl]-5,6,7,8,9,10-hexahydrocycloocta[c]pyridine (6c). The mixture of **5a** (0.3 g, 0.87 mmol) and 1-pyrrolidine-1-cyclooctene (**3d**) was refluxed at 150°C for 3 h. The crude product was purified by chromatography column to give 0.2 g (53%) as a white solid **6c**. M.p. 179–180°C. ^{1}H NMR (CDCl3): δ = 1.45 (d, 6 H, J = 6.8 Hz), 1.48 (d, 6 H, J = 6.8 Hz), 1.56–1.74 (m, 2 H), 1.76–1.92 (m, 4 H), 2.08–2.19

(m, 4 H), 2.75–2.99 (m, 8 H), 4.12 (sep, 1 H, J = 6.8 Hz), 4.21 (sep, 1 H, J = 6.8 Hz), 7.83 (s, 1 H), 7.95 (s, 1 H). Anal. Calcd for $C_{25}H_{34}N_2S_2$: C, 70.42; H, 7.98; N, 6.57. Found: C, 70.37; H, 7.71; N, 6.67.

1-(Isopropylsulfanyl)-3-[1-(isopropylsulfanyl)-5,6,7,8-tetrahydroisoquinolin-3-yl]-6,7,8,9-tetrahydro-5H-cyclohepta[c]pyridine (6d). The mixture of **5b** (0.5 g, 1.38 mmol) and 1-pyrrolidine-1-cycloheptene (**3c**) was refluxed at 150°C for 6 h. The crude product was purified by chromatography column to give 0.55 g (96%) as a white solid **6d**. M.p. 172–173°C. ^{1}H NMR ($CDCl_3$): δ = 1.45 (d, 6 H, J = 6.8 Hz), 1.48 (d, 6 H, J = 6.8 Hz), 1.56–1.74 (m, 2 H), 1.76–1.92 (m, 2 H), 2.08–2.19 (m, 4 H), 2.75–2.99 (m, 8 H), 4.12 (sep, 1 H, J = 6.8 Hz), 4.21 (sep, 1 H, J = 6.8 Hz), 7.83 (s, 1 H), 7.95 (s, 1 H). Anal. Calcd for $C_{25}H_{34}N_2S_2$: C, 70.13; H, 7.99; N, 6.55. Found: C, 69.95; H, 7.78; N, 6.60.

1-(Isopropylsulfanyl)-3-[1-(isopropylsulfanyl)-5,6,7,8-tetrahydroquinolin-3-yl]-5,6,7,8,9,10-hexahydrocycloocta[c]pyridine (6e). The mixture of **5b** (0.5 g, 1.38 mmol) and 1-pyrrolidine-1-cyclooctene (**3d**) was refluxed at 150°C for 11 h. The crude product was purified by chromatography column to give 0.24 g (39%) as a white solid **6e**. M.p. 156–157°C. ^{1}H NMR ($CDCl_3$): δ = 1.20–1.40 (m, 4 H), 1.30 (d, 6 H, J = 6.8 Hz), 1.48 (d, 6 H, J = 6.8 Hz), 1.55–1.65 (m, 4 H), 1.55–1.87 (m, 8 H), 2.80–2.92 (m, 4 H), 4.16 (sep, 1 H, J = 6.8 Hz), 4.21 (sep, 1 H, J = 6.8 Hz), 7.60 (s, 1 H), 7.70 (s,1 H). Anal. Calcd for $C_{26}H_{36}N_2S_2$: C, 70.91; H, 8.18; N, 6.36. Found: C, 70.70; H, 8.21; N, 6.25.

1-(Isopropylsulfanyl)-3-[1-(isopropylsulfanyl)-6,7,8,9-tetrahydro-5H-cyclohepta[c]pyridin-3-yl]-5,6,7,8,9,10-hexahydrocycloocta[c]pyridine (6f). The mixture of **5c** (0.5 g, 1.34 mmol) and 1-pyrrolidine-1-cyclooctene (**3d**) was refluxed at 150°C for 5 h. The crude product was purified by chromatography column to give 0.23 g (38%) as a white solid **6f**. M.p. 184–185°C. ^{1}H NMR ($CDCl_3$): δ = 1.39–1.40 (m, 4 H), 1.47 (d, 12 H, J = 6.8 Hz), 1.55–1.65 (m, 4 H), 1.55–1.87 (m, 10 H), 2.80–2.92 (m, 8 H), 4.16 (sep, 1 H, J = 6.8 Hz), 4.21 (sep, 1 H, J = 6.8 Hz), 7.84 (s, 1 H), 7.85 (s,1 H). Anal. Calcd for $C_{27}H_{36}N_2S_2$: C, 71.36; H, 8.37; N, 6.17. Found: C, 71.21; H, 8.59; N, 6.14.

Oxidation of 7a–c and 8a–c. General procedure. To a stirred solution **4a–c** or **6a–c** (1 mmol) in benzene (100 mL) was added $KMnO_4$ (8.1 mmol) dissolved in water at room temperature. Then was added CH_3COOH (3.4 mL) and catalytic amounts of $B_4N^+Br^-$. The mixture was stirred at room temperature for 2 h. A sat. $Na_2S_2O_5$salution was added to the mixture until the purple color disappeared. The organic layer was separated and the water layer was extracted with benzene. Organic phase were combined and dried over $MgSO_4$, filtered and evaporated. The crude product was crystallized from benzene to give pure product as a white solid.

1,1′-Bis(isopropylsulfonyl)-6,6′,7,7′-tetrahydro-5H,5H′-3,3′-bicyclopenta[c]pyridine (7a). Yield 98%, m.p. 281–282°C. ^{1}H NMR ($CDCl_3$): δ = 1.35 (d, 6 H, J = 6.8 Hz), 3.00 (t, 2 H, J = 7.5 Hz), 3.36 (t, 2 H, J = 7.6 Hz), 3.86 (sep, 1 H, J = 6.8 Hz), 8.36 (s, 1 H). Anal. Calcd for $C_{22}H_{28}N_2S_2O_4 \cdot 2H_2O$: C, 54.54; H, 6.61; N, 5.78. Found: C, 54.55; H, 5.95; N, 5.84. HR MS: (M+H); Calcd. 449.15688. Found: 449.15713.

1,1′-Bis(isopropylsulfonyl)-5,5′,6,6′,7,7′,8,8′-octahydro-3,3′-biisoquinoline (7b). Yield 72%, m.p. 247–248°C. ^{1}H NMR ($CDCl_3$): δ = 1.48 (d, 6 H, J = 6.8 Hz), 1.85–1.95 (m, 4 H), 2.94 (t, 2 H, J = 6.8 Hz), 3.32 (t, 2 H, J = 6.8 Hz), 4.33 (sep, 1 H, J = 6.8 Hz), 8.07 (s, 1 H). Anal. Calcd for $C_{24}H_{32}N_2S_2O_4$: C, 60.50; H, 6.72; N, 5.88. Found: C, 60.35; H, 6.49; N, 5.82. HRMS (LSIMS): m/z calcd for $C_{24}H_{32}O_4N_2S_2Na$(M+H) (M^+), 499.17012; found, 499.17141.

1,1′-Bis(isopropylsulfonyl)-6,6′,7,7′,8,8′,9,9′-octahydro-5H,5H′-3,3′-bicyclohepta[c]pyridine (7c). Yield 98%, m.p. 267–268°C. ^{1}H NMR ($CDCl_3$): δ = 1.50 (d, 6 H, J = 6.8 Hz), 1.70–1.75 (m, 4 H), 1.76–1.78 (m, 2 H), 2.98 (t, 2 H, J = 5.8 Hz), 3.41 (t, 2 H, J = 5.9 Hz), 4.32 (sep, 1 H, J = 6.8 Hz), 8.32 (s, 1 H). Anal. Calcd for $C_{26}H_{36}N_2S_2O_4$: C, 61.90; H, 7.14; N, 5.55. Found: C, 61.68; H, 7.22; N, 5.48.

1-(Isopropylsulfonyl)-3-[1-(isopropylsulfonyl)-6,7-dihydro-5H-cylopenta[c]pyridin-3-yl]-5,6,7,8-tetrahydroisoquinoline (8a). Yield 79%, m.p. 243–244°C. ^{1}H NMR ($CDCl_3$): δ = 1.37 (d, 6 H, J = 6.8 Hz), 1.44 (d, 6 H, J = 6.8 Hz), 1.84–1.87 (m, 4 H), 2.12–2.24 (m, 2 H), 2.94–3.02 (m, 2 H), 3.05–3.09 (m, 2 H), 3.31–3.37 (m, 2 H), 3.41–3.45 (m, 2 H), 3.97 (sep, 1 H, J = 6.8 Hz), 4.35 (sep, 1 H, J = 6.8 Hz), 8.21 (s, 1 H), 8.28 (s, 1 H). Anal. Calcd for $C_{23}H_{30}N_2S_2 \cdot 0.5H_2O$: C, 58.60; H, 6.58; N, 5.94. Found: C, 58.62; H, 6.36; N, 5.90.

1-(Isopropylsulfonyl)-3-[1-(isopropylsulfonyl)-6,7-dihydro-5H-cylopenta[c]pyridin-3-yl]-6,7,8,9-tetrahydro-5H-cyclohepta[c]pyridine (8b). Yield 93%, m.p. 234–235°C. ^{1}H NMR ($CDCl_3$): δ = 1.36 (d, 6 H, J = 6.8 Hz), 1.47 (d, 6 H, J = 6.8 Hz), 1.73–1.87 (m, 4 H), 2.12–2.24 (m, 2 H), 2.94–3.02 (m, 2 H), 3.05–3.09 (m, 2 H), 3.31–3.37 (m, 2 H), 3.41–3.45 (m, 2 H), 3.97 (sep, 1 H, J = 6.8 Hz), 4.35 (sep, 1 H, J =

6.8 Hz), 8.21 (s, 1 H), 8.28 (s, 1 H). Anal. Calcd for $C_{24}H_{32}N_2S_2 \cdot 0.3H_2O$: C, 59.83; H, 6.72; N, 5.82. Found: C, 59.90; H, 6.70; N, 5.82.

1-(Isopropylsulfonyl)-3-[1-(isopropylsulfonyl)-5,6,7,8-tetrahydroquinolin-3-yl]-6,7,8,9-tetrahydro-5H-cyclohepta[c]pyridine (8c). Yield 89%, m.p. 252–253°C. ^{1}H NMR ($CDCl_3$): δ = 1.45 (d, 6 H, J = 6.8 Hz), 1.48 (d, 6 H, J = 6.8 Hz), 1.75–1.84 (m, 4 H), 1.84–1.87 (m, 6 H), 2.95–3.00 (m, 4 H), 3.31–3.38 (m, 4 H), 4.31 (sep, 1 H, J = 6.4 Hz), 4.32 (sep, 1 H, J = 6.8 Hz), 8.06 (s, 1 H), 8.10 (s, 1 H). Anal. Calcd for $C_{25}H_{34}N_2S_2O_4 \cdot 0.5H_2O$: C, 60.12; H, 7.01; N, 5.61. Found: C, 59.86; H, 6.66; N, 5.55.

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