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Ligand Coupling of 2-Pyridyl Sulfoxides Having an sp^2 Stereocenter at the α-Position: A Novel Preparation of α-Stilbazoles

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ABSTRACT

Ligand coupling of (E)- and (Z)-styryl 2-pyridyl sulfoxides with methylmagnesium bromide gave (E)- and (Z)-2-styrylpyridine, respectively in a stereospecific manner. A number of (E)-2-styrylpyridine derivatives were prepared by the coupling reaction. Methyl styryl sulfoxide and 2,2'-bipyridyl were obtained as by-products. The mechanism of the reaction is discussed based on quantitative analysis of the products.

INTRODUCTION

The concept of ligand coupling within hypervalent species has recently been presented [1]. This new mechanistic concept was originally proposed for the reaction to form the incipient hypervalent sulfur species, σ-sulfurane, which eventually collapses to afford the ligand coupling product. This concept has been found to be applicable to numerous hypervalent species in which the central atom is other than sulfur, such as phosphorus, iodine, copper, antimony, bismuth, etc. [1, 2].

Ligand coupling is considered to take place between an equatorial and an axial ligand. In the hypervalent species, axial coordinates are usually occupied by electronegative ligands using p-orbitals, whereas equatorial coordinates are of sp^2-hybridized orbitals and generally taken up by π-ligands or electron-donating ligands. If there is any cohesive interaction between the coupling two ligands, they would be extruded from the central valence-shell-expanded atom concertedly, affording a ligand coupling product in which the configuration of both ligands bearing the sp^3 or sp^2 carbon skeleton would hold the original configuration completely. In all the cases we looked at, this stereochemistry has been firmly held. Since the central atom in a hypervalent species, such as the σ-sulfurane, is valence-shell expanded, it would undergo concurrent ligand exchange and pseudo or turnstile rotation, but always tends to revert to the stable octet. All these reactions occurring at a hypervalent atom require rather small energies. A slight variation of stereoelectronic environment around the central valence-shell-expanded sulfur atom is considered to change the mode of the reaction [1, 3] (Schemes 1 and 2).

The reaction of an optically active sulfoxide bearing an sp^3-type chiral center at the α-position with an alkyl Grignard reagent gave a ligand coupling product with retention of the configuration of the chiral center [4]. Thus, optically pure 2-(1-phenylethyl)pyridine was obtained quantitatively by treating optically pure 1-phenylethyl 2-pyridyl sulfoxide with methylmagnesium bromide, with complete retention of the configuration. Optically pure 4-(1-phenylethyl)phenylsulfonylbenzene, obtained in a good yield by the treatment of optically pure 1-phenylethyl 4-benzenesulfonylphenyl sulfoxide with ethylmagnesium bromide, is

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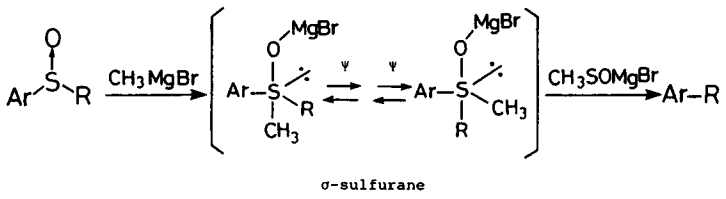


SCHEME 1

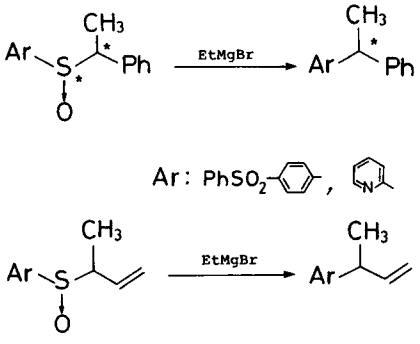
another good example. Yet another example with an sp^3 carbon center has also been observed in the coupling reaction of 4-benzenesulfonylphenyl α-methylallyl sulfoxide with methylmagnesium bromide to give only 4-benzenesulfonyl-α-methylallylbenzene with retention of configuration [5]. All these results imply that the reaction proceeds concertedly [1, 3, 4, 6]. We have also examined coupling reactions of sulfoxides having an sp^2 type of carbon at the α-position, and the preliminary result has revealed that the reaction takes place stereospecifically with retention of the configuration [5].

This article reports detailed accounts of the ligand coupling reaction that allows us also to prepare a number of stereochemically pure 2-styrylpyridine (α-stilbazole) derivatives.

RESULTS AND DISCUSSION

(E)- and (Z)-styryl 2-pyridyl sulfides were prepared by the ordinary method by treating a mixture of (E)- and (Z)-β-bromostyrene with 2-pyridinethiol in basic media. Oxidation of a mixture of the sulfides with the magnesium salt of monoperoxyphthalic acid gave an approximately 15 : 1 mixture of (E)- and (Z)-styryl 2-pyridyl sulfoxides (**1E** and **1Z**), the ratio of which turned out to be 1 : 1 under photochemical conditions (300 nm). These isomers were readily separated by column chromatography on silica gel and identified by nuclear magnetic resonance (NMR) spectroscopy in which the coupling constants of the olefinic protons were observed to be 10.3 Hz for the Z-isomer and 15.4 Hz for the E-isomer. The Z-isomer (**1Z**) was treated with methylmagnesium bromide at room temperature, followed by the standard workup, to give only (Z)-2-styrylpyridine (**2Z**) in 34% yield. None of the E-isomer (**2E**) was detected in the reaction mixture by TLC as well as reverse-phase high-performance liquid chromatography (HPLC) analyses. The E-isomer (**1E**) also afforded stereospecifically (E)-2-styrylpyridine (**2E**) in 33% yield [7]. The stereochemical results indicate that the ligand coupling proceeds concertedly without any isomerization. In both cases of the coupling reactions, 2,2′-bipyridyl (**3**) and methyl styryl sulfoxide (**4**) were also formed (Scheme 3).

In the literature, stilbazoles have been reported to have considerable herbicidal and antifungal activities [8] and are prepared, e.g., by the reaction of 2-picoline and an aromatic aldehyde in refluxing acetic anhydride [9], the Wittig-Horner type of reaction of a benzylphosphonate or the corresponding ylide with 2-pyridinecarboxaldehyde [8, 10], or simply by heating 2-picoline with an arylidene aniline [11]. Although the present ligand coupling of the sulfoxide offers a method to obtain stereochemically pure (E)-2-styrylpyridine, it is necessary to use (E)-styryl 2-pyridyl sulfoxide (**7**). Thus, methyl 2-pyridyl sulfoxide (**5**) was lithiated with *n*-butyllithium, followed by reaction with benzaldehyde to afford the β-hydroxysulfoxide as a diastereomeric mixture. The mixture was subjected to acetylation or mesylation with acetic anhydride or



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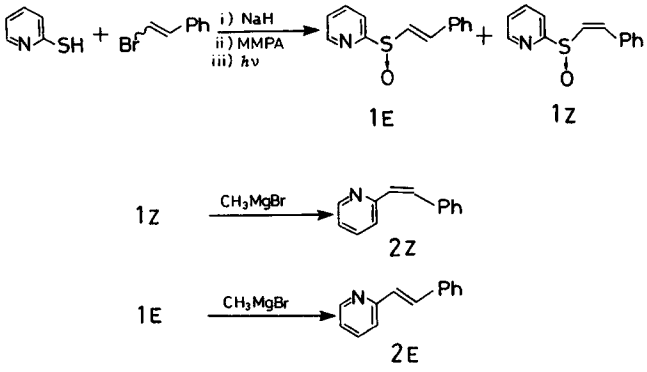

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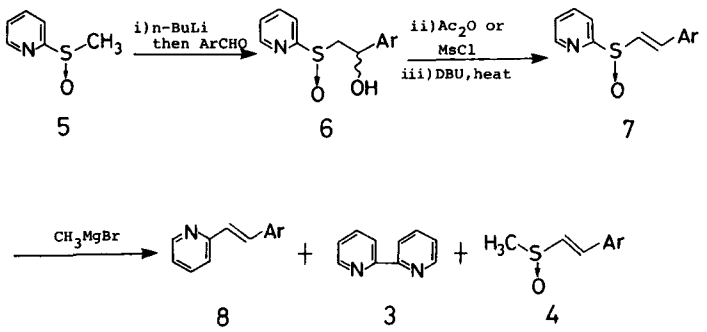


SCHEME 4

methanesulfonyl chloride in methylene chloride. The crude product was heated in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in refluxing benzene to afford the desired **1E** in 77% yield in three steps (Scheme 4). A number of (E)-styryl 2-pyridyl sulfoxide derivatives **(7a–7i)** has been obtained by the following three steps from **5** and the corresponding aromatic aldehydes in a sequence similar to that described in Scheme 4. The yields are listed in Table 1 and results of the coupling of **7** are shown in Table 2.

Although the reaction of the sulfoxides with methylmagnesium bromide afforded the desired ligand coupling product (E)-2-styrylpyridine derivatives **(8)**, the best yield of the coupling was observed in the reaction of 2-pyridyl 2-azastyryl sulfoxide **(7a)**. In the case of 4-dimethylaminostyryl 2-pyridyl sulfoxide **(7i)** none of the desired coupling compound was obtained. The yield of the coupling product seems to depend on the substituents of the aromatic ring. No significant difference of the yield was observed by change in the position of a substituent, e.g., para, meta, or ortho position on the benzene ring (see runs 2–4, for chloride and also runs 6–8 for methyl group). Electron donating substituents on the ring appear to lower the yield from the reaction listed in run 9 due probably to the destabilization of σ-sulfurane formed incipiently, enhancing the facile ligand exchange. The yield of **3** was observed to increase when that of the coupling product decreased. It is noteworthy that the total conversion of the starting material remained always more than 80% in most cases. This may mean that a methyl styryl sulfoxide **(4)**, which is a simple ligand exchange product, is always formed from about a half-equivalent of **3**, since the formation of **3** requires another equivalent of the starting sulfoxide, **7**. For example, in the reaction of 4-chlorostyryl 2-pyridyl sulfoxide (run 2), the yield of **3** was 38% which corresponds to two equivalents of the 4-chlorostyryl methyl sulfoxide formed, namely, 19% (Chart 1). These observations are significant in explaining the mechanisms of the reactions, which are shown in Chart 1. An initial apical attack of methylmagnesium bromide at the sulfur atom of 2-pyridyl styryl sulfoxide forms the σ-sulfurane intermediate **A**, which equilibrates between the two conformers **A** and **B** via pseudo or turnstile rotation. When carbon-carbon bond formation takes place between the apical styryl group and the equatorial 2-pyridyl group, 2-styrylpyridine and methylsulfenoxymagnesium bromide result. Alternatively, disproportionation from σ-sulfurane **A** or **B** would give the same equimolar amounts of methyl styryl sulfoxide (ligand exchange product) and 2-pyridylmagnesium bromide, which reacts

TABLE 1 Preparation of 2-Pyridyl Styryl Sulfoxide from **5**

Run	ArCHO *Ar*	*Product*	Yield (%) *(Three steps)*
1	2-Pyridyl	**7a**	49
2	4-Chlorophenyl	**7b**	63
3	3-Chlorophenyl	**7c**	83
4	2-Chlorophenyl	**7d**	50
5	Phenyl	**1E**	77
6	3-Tolyl	**7e**	55
7	4-Tolyl	**7f**	63
8	2-Tolyl	**7g**	78
9	4-Anisyl	**7h**	60
10	4-Dimethylaminophenyl	**7i**	57

TABLE 2 Reaction of 2-Pyridyl Styryl Sulfoxide with Methylmagnesium Bromide

Run	*Starting Sulfoxide*	*2-Styryl-pyridine*	*Products* (%)	***3*** (%)	***4*** (%)
1	**7a**	**8a**	53	30	14
2	**7b**	**8b**	41	38	19
3	**7c**	**8c**	40	51	21
4	**7d**	**8d**	35	51	22
5	**1E**	**2E**	33	58	22
6	**7e**	**8e**	31	62	34
7	**7f**	**8f**	29	66	27
8	**7g**	**8g**	28	66	27
9	**7h**	**8h**	18	62	34
10	**7i**	**8i**	0	100	50

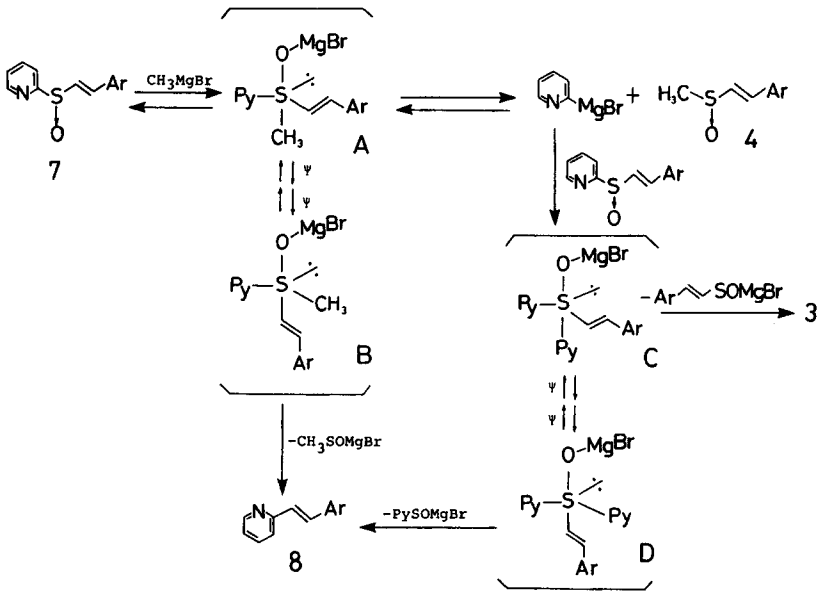
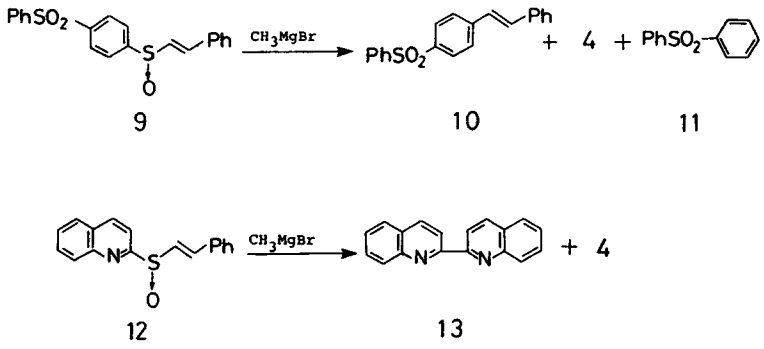


CHART 1

further with the starting sulfoxide to afford another σ-sulfurane intermediate **C**. This intermediate **C** couples successively, giving **3** and 2-styrylsulfenoxymagnesium bromide. The reactions to form the coupling product and/or **3** or **4** appear to compete. Conformer **A** is favored to give 2-pyridylmagnesium bromide and methyl styryl sulfoxide, while conformer **B** would afford the coupling product. The substituent on the aromatic ring may affect the equilibration between the conformers **A** and **B**. The electron donating group on the ring would stabilize the styryl group located at the equatorial position of the conformer **A**, which undergoes ligand exchange smoothly. Another explanation may be the following: a pseudo and/or turnstile rotation of the conformer **B** would compete with simple ligand exchange which gives 2-pyridylmagnesium bromide and methyl styryl sulfoxide, both derived from initially formed σ-sulfurane **A**. The electron-donating group would help the ligand exchange resulting in the formation of 2-pyridylmagnesium bromide in the conformer **A** prior to either pseudo or turnstile rotation.

In other examples of the coupling reaction, 4-benzenesulfonylphenyl (E)-styryl sulfoxide **(9)** gave the coupling product **10** in 65% yield along with 25% of **4**. The ligand exchange product, diphenylsulfone **(11)**, was obtained in 25% yield instead of dimerized product such as 4,4'-dibenzenesulfonylbiphenyl. It was obviously formed after hydrolysis of 4-benzenesulfonylphenylmagnesium bromide with water. The reaction of 2-quinolyl (E)-styryl sulfoxide **(12)** gave 2,2'-biquinolyl **(13)** and **4** in 78% and 37% yields, respectively (Scheme 5).

No similar reactions were observed with vinyl or acetylenic types of sulfoxides. Treatment of methyl 2-pyridyl sulfoxide with vinylmagnesium bromide or vinyl 2-pyridyl sulfoxide with methylmagnesium bromide gave none of the desired 2-vinylpyridine but rather complex mixtures. In



SCHEME 5

the reaction of methyl 2-pyridyl sulfoxide with phenylethynylmagnesium bromide, the starting materials were recovered quantitatively.

CONCLUSION

These stereochemical experiments of (E)- and (Z)-styryl sulfoxides reveal that the ligand coupling reaction occurs with retention of the configuration of a coupling ligand of an sp^2 type of carbon center as well as that of an sp^3 type. These observations may serve as additional evidence for the concerted nature of the ligand coupling. The present results also support the hitherto postulated mechanism involving the σ-sulfurane intermediate proposed earlier by us [1, 3, 4–6].

EXPERIMENTAL

Melting points were determined on a Yanako micromelting point apparatus and were uncorrected. Infrared (IR) spectra were taken on a JASCO IRA-1 spectrometer. Mass spectra (MS) were obtained by use of a JEOL-JMS 303HF spectrometer at 70 eV using direct inlet system. Only significant peaks are described here for IR and MS. ^1H and ^{13}C NMR were measured on a JEOL GXS spectrometer (400 MHz for ^1H and 100 MHz for ^{13}C) and tetramethylsilane was used as an internal standard. Silica gel (Merck 7347, 70–230 mesh) was used for column chromatography. All reactions were carried out under an Ar atmosphere. Tetrahydrofuran (THF) and benzene used as solvents for reactions were dried over sodium benzophenone ketyl, and methylene chloride was dried over phosphorus pentoxide. These solvents were freshly distilled just before use.

Preparation of (E)- and (Z)-styryl 2-pyridyl sulfoxides (**1E** and **1Z**): Sodium hydride (720 mg, 60% in mineral oil) was washed with hexane and suspended in anhydrous hexamethylphosphoramide (hexamethylphosphoric triamide) (HMPA) (10 mL). To this suspension, 2-mercaptopyridine (2 g, 18 mmol) in HMPA (10 mL) was dropped in at 5°C during 10 min. A freshly distilled *cis* and *trans* mixture of 2-bromostyrene (2.21 g, 12 mmol) was added and the mixture was heated at 100°C overnight. After having been cooled, a 4 : 1 mixture of ether and hexane (300 mL) and water (5 mL) were added, and the organic layer was washed with water (5 mL ×5) and brine (5 mL). The extract was dried over $MgSO_4$ and concentrated. To the crude sulfide in methanol (75 mL), the magnesium salt of monoperoxyphthalic acid (1 eq) was carefully added to the mixture at 0°C during 15 min. When the reaction had been completed (monitoring by thin-layer chromatography [TLC]), aq. sodium thiosulfate (5%, 10 mL) was added and the mixture was concentrated to 15 mL under reduced pressure. It was diluted with chloroform (300 mL), and the organic layer was washed with water (10 mL ×2) and brine (5 mL), and dried over $MgSO_4$. The extract was evaporated and purified roughly by column chromatography on silica gel, eluted with ethyl acetate to give a mixture of **1E** and **1Z**, mostly **1E**, which was irradiated under a 300-nm photolamp in degassed benzene (300 mL) at room temperature for 15 min. After removal of the solvent, approximately a 1 : 1 mixture of **1E** and **1Z** were separated on a silica gel column by chromatography and eluted with 35% ethyl acetate in hexane.

1E: 514 mg, 19%, mp 74–75°C (benzene-hexane), ^1H NMR (400 MHz, $CDCl_3$) δ 7.07 (1 H, d, J = 15.4 Hz), 7.36 (1 H, d, J = 15.4 Hz), 7.37 (1 H, td, J = 7.3, 1.1 Hz), 7.33–7.40 (3H, m), 7.44–7.47 (2H, m), 7.94 (1 H, td, J = 7.7, 1.8 Hz), 7.99 (1 H, d, J = 8.0 Hz), 8.64 (1 H, d, J = 4.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.90, 124.57, 127.70, 128.80, 129.63, 131.44, 133.78, 136.10, 138.32, 149.66, 164.67; IR (KBr) 1055 (SO): MS (rel intensity) m/z 229 (M^+, base), 212 (97), 201 (50), 180 (98), 168 (56). Anal. Calcd for $C_{13}H_{11}NOS$: C, 68.10; H, 4.84; N, 6.11. Found: C, 68.22; H, 4.87; N, 6.13.

1Z: 490 mg, 18%, mp 63–64°C (benzene-hexane), ^1H NMR (400 MHz, $CDCl_3$) δ 6.38 (1 H, d, J = 10.3 Hz), 7.29 (1H, J = 10.3 Hz), 7.39 (1 H, ddd, J = 7.7, 4.8, 1.1 Hz), 7.42–7.48 (3 H, m), 7.78 (1 H, d, J = 5.1, 1.5 Hz), 7.79 (1H, d, J = 7.3 Hz), 7.96 (1 H, td, J = 7.3, 1.8 Hz), 8.11 (1 H, dd, J = 8.1, 0.7 Hz), 8.66 (1 H, dm, J = 4.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.87, 124.60, 128.30, 129.50, 130.03, 133.74, 135.38, 138.05, 140.42, 149.76, 165.27; IR (KBr) 1035 (SO); MS (rel. intensity) m/z 229 (M^+, base), 212 (75), 201 (65), 180 (96), 168 (75); Anal. Calcd for $C_{13}H_{11}NOS$: C, 68.10; H, 4.84; N, 6.11. Found: C, 68.32; H, 4.95; N, 6.11.

Preparation of 2-pyridyl styryl sulfoxide (**7**): Methyl 2-pyridyl sulfoxide (**5**) (705 mg, 5 mmol) was lithiated with lithium diisopropylamide prepared freshly by treating *n*-butyllithium (3 mL, 1.5 M in hexane solution) with diisopropylamine (4.5 mmol) in THF (10 mL) at −78°C for 15 min. The lithiosulfoxide was treated with the aromatic aldehyde (4.5 mmol) in THF (3 mL) at −78°C and stirred for 15 min at the same temperature. A mixture of saturated aqueous ammonium chloride solution (5 mL) and ethyl acetate (70 mL) was added to the mixture, and the organic layer was washed with water (5 mL) and brine (5 mL), dried over $MgSO_4$, and concentrated. The crude material was acetylated with acetic anhydride (8 mmol) or mesylated with methanesulfonyl chloride (7 mmol) in methylene chloride (25 mL) in the presence of triethylamine (10 mmol) and 4-dimethylaminopyridine (1 mmol) in an ice bath for 8 to 12 h. The reaction was quenched with water (3 mL), and the organic layer was washed with brine (3 mL), dried over $MgSO_4$ and evaporated to give an oily material which was pure enough to be used directly for the next reaction. A mixture of the oil and DBU (10 mmol) was refluxed in carbon tetrachloride (15

mL) for 3 to 7 h. After having been cooled, the mixture was diluted with methylene chloride (100 mL) and washed with water (5 mL) and brine (5 mL). The organic layer was dried over $MgSO_4$ and evaporated. The crude product was purified by column chromatography on silica gel, then eluted with 5% methanol in ethyl acetate. The yields of **7** are shown in Table 1 and the physical and spectroscopic data are the following;

7a: mp 122–123°C (benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (1 H, ddd, J = 7.7, 4.8, 1.1 Hz), 7.35 (1 H, d, J = 14.7 Hz), 7.35–7.39 (2 H, m), 7.69 (1 H, d, J = 14.7 Hz), 7.69 (1 H, td, J = 7.7, 1.8 Hz), 7.92 (1 H, td, J = 7.7, 1.8 Hz), 7.97 (1 H, dt, J = 6.6, 1.1 Hz), 8.58 (1 H, dd, J = 4.8, 1.1 Hz), 8.64 (1H, dm, J = 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.93, 123.72, 124.16, 124.64, 133.89, 136.62, 136.90, 138.34, 149.85, 149.96, 152.28, 164.13; IR ($CHCl_3$) 1025 (SO); MS (rel. intensity) m/z 230 (M^+, 12), 213 (9), 182 (base), 136 (46); Anal. Calcd for $C_{12}H_{10}N_2OS$: C, 62.59; H, 4.38; N, 12.17. Found: C, 62.49; H, 4.27; N, 11.97.

7b: mp 114–115°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (1 H, d, J = 15.4 Hz), 7.30 (1 H, d, J = 15.4 Hz), 7.32 (2 H, d, J = 8.6 Hz), 7.39 (2 H, d, J = 8.6 Hz), 7.39 (1 H, m), 7.94 (1H, td, J = 8.1, 1.5 Hz), 7.98 (1 H, dm, J = 7.3 Hz), 8.64 (1 H, dm, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.96, 124.67, 128.92, 129.08, 132.11, 132.32, 134.56, 135.50, 138.42, 149.77, 164.46; IR ($CHCl_3$) 1020 (SO); MS (rel. intensity) m/z 265,263 (M^+, 41, 98), 246 (96), 235 (49), 214 (base); Anal. Calcd for $C_{13}H_{10}ClNOS$: C, 59.20; H, 3.82; N, 5.31. Found: C, 59.21; H, 3.80; N, 5.14.

7c: mp 91–92°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (1 H, d, J = 15.6 Hz), 7.26–7.34 (3 H, m), 7.28 (1 H, d, J = 15.6 Hz), 7.39 (1 H, ddd, J= 7.0, 4.8, 1.8 Hz), 7.43 (1 H, s), 7.94 (1 H, td, J = 7.7, 1.1 Hz), 7.98 (1 H, dm, J = 7.7 Hz), 8.64 (1 H, dm, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.85, 124.52, 126.81, 127.76, 129.92, 130.32, 131.76, 131.81, 134.02, 134.48, 138.24, 149.60, 164.27; IR($CHCl_3$) 1030 (SO); MS (rel. intensity) m/z 265,263 (M^+, 48, base), 246 (88), 235 (82), 216 (55), 214 (54), 202 (95); Anal. Calcd for $C_{13}H_{10}ClNOS$: C, 59.20; H, 3.82; N, 5.31. Found: C, 59.07; H, 3.75; N, 5.25.

7d: mp 107–108°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (1 H, d, J = 15.4 Hz), 7.20–7.28 (2 H, m), 7.36–7.41 (2 H, m), 7.50 (1 H, dd, J = 7.3, 2.2 Hz), 7.76 (1 H, d, J = 15.4 Hz), 7.95 (1 H, td, J = 7.7, 1.8 Hz), 8.01 (1 H, d, J = 8.1 Hz), 8.64 (1 H, dm, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.02, 124.62, 126.92, 127.86, 130.10, 130.45, 131.98, 132.08, 134.24, 134.55, 138.39, 149.73, 164.44; IR ($CHCl_3$) 1040 (SO); MS (rel. intensity) m/z 265,263 (M^+, 41, base), 246 (48), 228 (83), 180 (70), 168 (43); Anal. Calcd for $C_{13}H_{10}ClNOS$: C, 59.20; H, 3.82; N, 5.31. Found: C, 59.20; H, 3.76; N, 5.24.

7e: mp 70–71°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (3 H, s), 7.03 (1 H, d, J = 15.6 Hz), 7.14 (1 H, m), 7.23–7.28 (3 H, m), 7.33 (1 H, d, J = 15.6 Hz), 7.37 (1 H, ddd, J = 7.3, 4.8, 1.6 Hz), 7.93 (1 H, td, J = 7.7, 1.5 Hz), 7.99 (1 H, d, J = 8.2 Hz), 8.63 (1 H, dm, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.25, 118.92, 124.55, 124.96, 128.29, 128.70, 130.48, 131.19, 133.73, 136.39, 138.30, 138.48, 149.71, 164.78; IR ($CHCl_3$) 1035 (SO); MS (rel. intensity) m/z 243 (M^+, base), 226 (87), 214 (44), 194 (63), 182 (64); Anal. Calcd for $C_{14}H_{13}NOS$: C, 69.11; H, 5.38; N, 5.76. Found: C, 69.03; H, 5.46; N, 5.62.

7f: mp 94–95°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (3 H, s), 6.99 (1 H, d, J = 15.4 Hz), 7.16 (2 H, d, J = 8.1 Hz), 7.33 (2 H, d, J = 8.1 Hz), 7.34 (1 H, d, J = 15.4 Hz), 7.36–7.39 (1 H, m), 7.94 (1 H, td, J = 8.1, 1.5 Hz), 7.99 (1 H, d, J = 7.3 Hz), 8.63 (1 H, d, J = 4.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.35, 118.93, 124.55, 127.69, 129.51, 130.19, 131.02, 136.53, 138.29, 140.00, 149.71, 164.76; IR ($CHCl_3$) 1020 (SO); MS (rel. intensity) m/z 243 (M^+, base), 226 (99), 214 (46), 195 (33), 182 (47); Anal. Calcd for $C_{14}H_{13}NOS$: C, 69.11; H, 5.38; N, 5.76. Found: C, 69.06; H 5.37; N 5.60.

7g: mp 79–80°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (3 H, s), 6.98 (1 H, d, J = 15.4 Hz), 7.13–7.25 (3 H, m), 7.37 (1 H, ddd, J = 7.3, 4.8, 1.3 Hz), 7.42 (1 H, d, J = 7.7 Hz), 7.62 (1 H, d, J = 15.4 Hz), 7.94 (1 H, td, J = 7.7, 1.5 Hz), 8.00 (1 H, dm, J = 7.7 Hz), 8.63 (1 H, dm, J = 4.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.79, 118.96, 124.57, 126.23, 126.57, 129.50, 130.75, 132.64, 132.81, 134.10, 137.00, 138.34, 149.74, 164.85; IR ($CHCl_3$) 1060 (SO); MS (rel. intensity) m/z 243 (M^+, base), 226 (79), 214 (24), 194 (47), 180 (95); Anal. Calcd for $C_{14}H_{13}NOS$: C, 69.11; H, 5.38; N, 5.76. Found: C, 69.01; H, 5.36; N, 5.74.

7h: mp 103–104°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (3 H, s), 6.87 (1 H, d, J = 7.8 Hz), 6.88 (1 H, d, J = 15.2 Hz), 7.32 (1 H, d, J = 15.2 Hz), 7.37 (1 H, ddd, J = 7.3, 4.7, 1.1 Hz), 7.40 (2 H, d, J = 7.8 Hz), 7.93 (1 H, td, J = 7.7, 1.8 Hz), 8.00 (1 H, dd, J = 8.1, 0.7 Hz), 8.63 (1 H, dm, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.33, 114.20, 118.96, 124.55, 126.51, 128.68, 129.34, 136.69, 138.29, 149.73, 160.85, 164.89; IR ($CHCl_3$) 1015 (SO); MS (rel. intensity) m/z 259 (M^+, 68), 242 (68), 210 (89), 149 (base), 121 (53); Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40. Found: C, 64.78; H, 4.92; N, 5.32.

7i: mp 127–128°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (6 H, s), 6.63 (2H, d, J = 8.8 Hz), 6.74 (1 H, d, J = 15.0 Hz), 7.31 (1 H, d, J = 15.0 Hz), 7.34 (2 H, s, J = 8.8 Hz), 7.33–7.37 (1 H, m), 7.93 (1 H, td, J = 7.7, 1.8 Hz), 8.30 (1 H, dm, J = 7.7 Hz), 8.62 (1 H, dm, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.14, 111.74, 119.06, 121.56, 124.44, 125.54, 129.37, 138.15, 138.97, 149.13, 151.41, 165.32; IR ($CHCl_3$) 1010 (SO); MS (rel. intensity)

m/z 272 (M^+, 55), 256 (12), 224 (43), 223 (50), 194 (73), 162 (base), 145 (88); Anal. Calcd for $C_{15}H_{16}N_2OS$: C, 66.15; H, 5.92; N, 10.29. Found: C, 65.95; H, 5.80; N, 10.18.

Preparation of 4-benzenesulfonylphenyl (E)-styryl sulfoxide (**9**) and 2-quinolyl (E)-styryl sulfoxide (**12**): The reaction was carried out in the same manner described for the preparation of compounds **7a–7i**, except the uses of *p*-benzenesulfonylphenyl methyl sulfoxide for the preparation of **9** and methyl 2-quinolyl sulfoxide for that of **12** instead of methyl 2-pyridyl sulfoxide. Physical and spectroscopic data are the following:

9: mp 145–146°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (1 H, d, J = 15.8 Hz), 7.35–7.40 (4 H, m), 7.40 (1 H, d, J = 15.8 Hz), 7.41–7.45 (2 H, m), 7.53 (1 H, tm, J = 8.0 Hz), 7.59 (1 H, dm, J = 7.3 Hz), 7.80 (2 H, dt, J = 8.8, 1.5 Hz), 7.96 (2 H, dm, J = 7.0 Hz), 8.09 (2 H, dt, J = 8.8, 1.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.33, 127.84, 127.91, 128.30, 128.55, 129.00, 129.47, 130.39, 131.82, 133.16, 133.64, 138.24, 140.75, 144.17; IR ($CHCl_3$) 1020 (SO); MS (rel. intensity) m/z 368 (M^+, 28), 319 (42), 235 (25), 214 (42), 192 (34), 136 (base); Anal. Calcd for $C_{20}H_{16}O_3S_2$: C, 74.97; H, 5.03. Found: C, 73.25; H, 5.03.

12: mp 143–144°C (benzene-hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (1 H, d, J = 15.4 Hz), 7.31–7.60 (3 H, m), 7.42 (1 H, d, J = 15.4 Hz), 7.43–7.47 (2 H, m), 7.64 (1 H, ddd, J = 8.1, 7.0, 1.1 Hz), 7.81 (1 H, ddd, J = 8.4, 7.0 1.5 Hz), 7.90 (1 H, dd, J = 8.4, 1.5 Hz), 8.07 (1 H, d, J = 8.8 Hz), 8.14 (1 H, d, J = 7.7 Hz), 8.41 (1 H, d, J = 8.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 114.88, 127.73, 127.89, 128.08, 128.77, 128.81, 129.25, 129.60, 130.77, 131.47, 133.82, 135.48, 138.88, 147.54, 164.53; IR ($CHCl_3$) 1030 (SO); MS (rel. intensity) m/z 279 (M^+, base), 262 (28), 250 (24), 230 (27), 218 (24), 128 (63); Anal. Calcd for $C_{17}H_{13}NOS$: C, 73.09; H, 4.69; N, 5.01. Found: C, 72.86; H, 4.59; N, 4.95.

General procedure for the coupling reaction of styryl sulfoxide with methylmagnesium bromide: To a stirred solution of sulfoxide (1 mmol) in THF (5 mL) was added methylmagnesium bromide (1.1 mL, 1 M solution in THF) at room temperature during 5 min. The reaction was monitored by TLC until the starting material was completely consumed, which usually required 5–15 min. The mixture was quenched with an aqueous saturated ammonium chloride solution (4 mL) and extracted with chloroform (50 mL). The organic layer was washed with water (4 mL), dried over $MgSO_4$, and evaporated. The crude product was purified by column chromatography on silica gel, elution being effected with a mixture of hexane and ethyl acetate. The yields are given in Table 1. The physical and spectroscopic data are the following:

2Z [12]: oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.69 (1 H, d, J = 12.5 Hz), 6.83 (1 H, d, J = 12.5 Hz), 7.09 (1 H, dd, J = 5.1, 4.7 Hz), 7.16 (1 H, d, J = 8.1 Hz), 7.22–7.28 (5 H, m), 7.44 (1 H, td, J = 7.7, 1.8 Hz), 8.58 (1 H, dm, J = 4.8 Hz).

2E [12]: mp 89–90°C (EtOH-H_2O), lit. 91.5–93°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (1 H, d, J = 16.1 Hz), 7.17 (1 H, ddd, J = 7.7, 2.9, 1.1 Hz), 7.20–7.31 (3 H, m), 7.41 (1 H, dd, J = 7.7, 1.5 H), 7.48 (1 H, d, J = 8.1 Hz), 7.69 (1 H, td, J = 7.7, 1.8 Hz), 7.74 (1 H, dd, J = 7.7, 1.8 Hz), 7.99 (1 H, d, J = 16.1 Hz), 8.63 (1 H, dm, J = 5.1 Hz).

8a: oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (2H, ddd, J = 7.3, 4.8, 1.1 Hz), 7.44 (2 H, d, J = 7.7 Hz), 7.68 (2H, td, J = 7.7, 1.5 Hz), 7.70 (2 H, s), 8.63 (2 H, dm, J = 4.8 Hz); IR (film) 990, 1480, 1600, 2980; Dihydrochloric salt, mp 98–102°C.

8b [13]: mp 82–83°C (EtOH-H_2O), lit. 82.5–83°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (1 H, d, J = 16.1 Hz), 7.16 (1 H, ddd, J = 7.3, 4.8, 1.1 Hz), 7.34 (2 H, d, J = 8.4 Hz), 7.32–7.80 (1 H, m), 7.50 (2 H, d, J = 8.4 Hz), 7.59 (1 H, d, J = 16.1 Hz), 7.66 (1 H, td, J = 7.7, 1.8 Hz), 8.61 (1 H, dm, J = 4.8 Hz).

8c: oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (1 H, d, J = 16.1 Hz), 7.17 (1 H, ddd, J = 7.7, 4.8, 1.1 Hz), 7.26 (1 H, tt, J = 8.1, 1.8 Hz), 7.30 (1 H, t, J = 7.7 Hz), 7.37 (1 H, d, J = 7.7 Hz), 7.43 (1 H, td, J = 7.3, 1.5 Hz), 7.56 (1 H, s), 7.57 (1 H, d, J = 16.1 Hz), 7.67 (1 H, td, J = 7.7, 1.8 Hz), 8.01 (1 H, dm, J = 4.8 Hz), IR (film) 925, 990, 1485, 1580, 1600, 2990; MS (rel. intensity) m/z 217,215 (M^+, 41, base), 180 (11), 152 (5), 104 (5), HMRS Anal. Calcd for $C_{13}H_{10}ClN$: 215.050. Found: 215.048.

8d [14]: mp 75–76°C (EtOH-H_2O), lit. 76–77°; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (1 H, ddd, J = 7.3, 4.8, 1.1 Hz), 7.18 (1 H, d, J = 16.1 Hz), 7.35–7.42 (3 H, m), 7.57–7.61 (2 H, m), 7.63 (1 H, d, J = 16.1 Hz), 7.67 (1 H, td, J = 7.7, 1.8 Hz), 8.61 (1 H, dm, J = 4.8 Hz).

8e: oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (3 H, s), 7.11 (1 H, d, J = 15.7 Hz), 7.11 (1 H, m), 7.17 (1 H, t, J = 7.3 Hz), 7.35 (1 H, d, J = 8.1 Hz), 7.37 (1 H, d, J = 9.5 Hz), 7.59 (1 H, d, J = 15.7 Hz), 7.61 (1 H, td, J = 7.7, 1.8 Hz), 8.58 (1 H, dm, J = 4.0 Hz); IR (film) 905, 975, 1435, 1470, 1590, 3045; MS (rel. intensity) m/z 195 (M^+, base), 194 (70), 180 (20), 152 (12), 115 (19); HMRS Anal. Calcd for $C_{14}H_{13}N$: 195.105. Found: 195.103.

8f [13]: mp 84–85°C (EtOH-H_2O), lit. 83–84·C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (3 H, s), 7.13 (1 H, ddd, J = 7.5, 4.8, 1.1 Hz), 7.13 (1 H, d, J = 16.1 Hz), 7.18 (2 H, d, J =8.1 Hz), 7.37 (1 H, d, J = 8.1 Hz), 7.49 (2 H, d, J = 8.1 Hz), 7.61 (1 H, d, J = 16.1 Hz), 7.65 (1 H, td, J = 7.7, 1.8 Hz), 8.60 (1 H, dm, J = 4.7 Hz).

8g [14]: oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (3 H, s), 7.07 (1 H, d, J = 16.1 Hz), 7.15 (1 H, ddd, J = 7.7, 4.8, 1.1 Hz), 7.18–7.25 (3 H, m), 7.39 (1 H, d, J = 8.1 Hz), 7.65 (1 H, d, J = 5.1 Hz), 7.66 (1 H, td, J= 7.7, 1.8 Hz), 7.88 (1 H, d, J = 16.1 Hz), 8.61 (1 H, dm, J = 4.8 Hz).

8h [10]: mp 68–69°C (EtOH-H_2O), lit. 69°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (3 H, s), 6.92 (2 H, d,

J = 8.6 Hz), 7.05 (1 H, d, J = 16.1 Hz), 7.12 (1 H, ddd, J = 7.5, 5.8, 1.0 Hz), 7.36 (1 H, dm, J = 7.9 Hz), 7.53 (2 H, d, J = 8.6 Hz), 7.59 (1 H, d, J = 16.1 Hz), 7.64 (1 H, td, J = 7.5, 1.8 Hz), 8.59 (1 H, dm, J = 4.8 Hz).

10: mp 117–119°C (benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (1 H, d, J = 16.3 Hz), 7.20 (1 H, d, J = 16.3 Hz), 7.28–7.33 (1 H, m), 7.37 (2 H, tm, J = 7.0 Hz), 7.48–7.59 (4 H, m), 7.61 (2 H, d, J = 8.4 Hz), 7.91 (2 H, d, J = 8.4 Hz), 7.92–7.98 (3 H, m); IR ($CHCl_3$) 905, 1105, 1115, 1305, 1590, 1720, 2940; MS (rel. intensity) m/z 320 (M^+, base), 195 (17), 179 (34), 178 (56), 165 (17); Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03. Found: C, 73.25; H, 4.97.

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