Synthesis of β- and γ-Carbolines and Their *N*-Oxides from 2(or 3)-Ethynylindole-3(or 2)-carbaldehydes

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Isoquinoline-type carbolines *i.e.* β-, and γ-carbolines and their *N*-oxides were synthesized from 2(or 3)-ethynylindole-3(or 2)-carbaldehydes, which were synthesized by electrophilic substitution with dichloromethyl methyl ether in the presence of titanium tetrachloride, or by lithiation with *tert*-butyllithium, followed by formylation with methyl formate.

Key words ethynylindolecarbaldehyde; carboline; cyclization; *N*-oxide; palladium-catalyzed reaction; *ortho*-lithiation

β-Carboline (9*H*-pyrido[3,4-*b*]indole) and γ-carboline (5*H*-pyrido[4,3-*b*]indole) which contain isoquinolinic nitrogen in the ring offer a rich source of biologically important molecules.[1] In particular, β-carbolines have been found in natural products that may have various types of pharmaceutical activity. As a result, there are many studies on the synthesis of β-carbolines, however synthetic studies for γ-carboline derivatives having a wide scope and generality are relatively few. Furthermore, few examples for the synthesis of carboline *N*-oxides are known.[2]

Most preparative methods for β- and γ-carbolines involve electrophilic cyclization reactions of 2- or 3-monosubstituted indole derivatives and are applications of well known isoquinoline syntheses such as the Pictet-Spengler reaction,[3a] the Bischler-Napieralski reaction,[3b] and the Pomerantz-Fritshch reaction.[3c] On the other hand, there are few synthetic methods for β- and γ-carbolines involving cyclization reactions between two functional groups on adjacent positions of indole derivatives,[4] even though cyclization reactions are useful methods for the construction of condensed aromatic rings.[5]

We have already reported the simple and general synthesis of isoquinoline 2-oxides from 2-ethynylbenzaldehydes which were prepared by the palladium-catalyzed reaction of 2-halobenzaldehydes with terminal acetylenes.[6] Recently, the general synthesis of naphthyridines and their *N*-oxides by the same method has also been reported.[7]

In order to examine the generality of this cyclization reaction, we now report the synthesis of β- and γ-carbolines and their *N*-oxides containing the isoquinolinic nitrogen from 2-ethynylindolecarbaldehydes.

Synthesis of *o*-Ethynylindolecarbaldehydes (3, 6) 3-Ethynyl-1-(phenylsulfonyl)indoles (**2a**—**c**) were synthesized by palladium-catalyzed cross-coupling reactions of 3-iodo-1-(phenylsulfonyl)indole[8] (**1**). 3-Ethynyl-1-(phenylsulfonyl)indole-2-carbaldehydes (**3a**—**c**) were synthesized *via* lithiation of **2a**—**c** followed by electrophilic substitution with ethyl formate, as shown in Chart 2.

2-Ethynyl-1-(phenylsulfonyl)indoles (**5a**—**c**) were synthesized by palladium-catalyzed cross-coupling reactions of 2-iodo-1-(phenylsulfonyl)indole[9] (**4**), which was prepared *via* lithiation of 1-(phenylsulfonyl)indole[8] and electrophilic substitution with iodine. Although formylation of **5a**—**c** with the Vilsmeier reagent (*N*,*N*-dimethyl formamide (DMF)–phosphoryl chloride) did not proceed, 2-ethynyl-1-(phenylsulfonyl)indole-3-carbaldehydes (**6a**, **c**) were synthesized by formylation with dichloromethyl methyl ether in the presence of titanium tetrachloride in dichloromethane. However, 2-

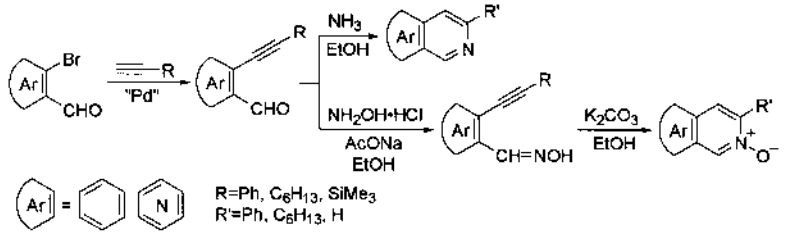

Chart 1

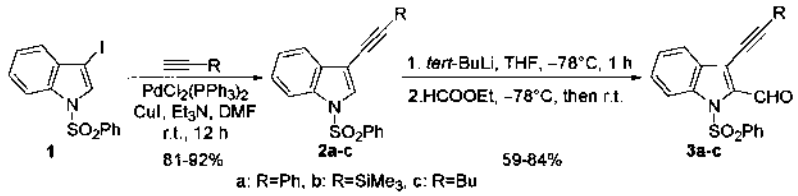

Chart 2

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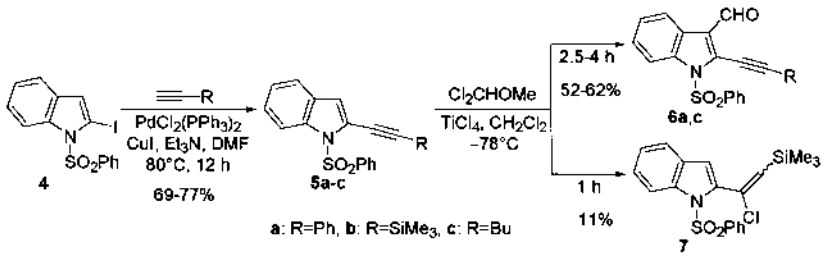

Chart 3

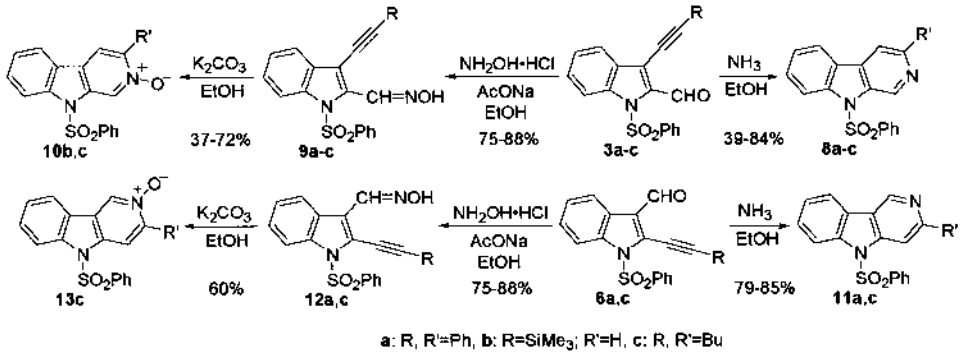

Chart 4

(trimethylsilylethynyl)indole-3-carbaldehyde (**6b**) was not obtained under these conditions, and instead 2-[1-chloro-2-(trimethylsilyl)ethen-1-yl]-1-(phenylsulfonyl)indole (**7**) was obtained.

Synthesis of Pyridoindoles (Carbolines) (8, 11) and Their *N*-Oxides (10, 13) 2(or 3)-Ethynylindole-3(or 2)-carbaldehydes (**3a**—**c**, **6a**, **c**) were allowed to react with ammonia in ethanol in a sealed tube at 120 °C for 4 h to give the corresponding pyridoindoles (carbolines) (**8a**—**c**, **11a**, **c**). Next, **3a**—**c** and **6a**, **c** were converted to the corresponding oximes (**9a**—**c**, **12a**, **c**) by a conventional procedure, which were cyclized under the basic conditions to give the corresponding pyridoindole (carboline) *N*-oxides (**10b**, **c**, **13c**), except for 3-(phenylethynyl)-1-(phenylsulfonyl)-indole-2-carbaldehyde oxime (**9a**) and 2-(phenylethynyl)-1-(phenylsulfonyl)indole-3-carbaldehyde oxime (**12a**), which gave multi products under the reaction conditions.

Since the desulfonylation of *N*-sulfonyl nitrogen heteroaromatics such as indoles, carbolines, *etc*. with tetrabutylammonium fluoride[10] has been achieved by us, the results described in this paper supply a practical method for the construction of carbolines containing isoquinolinic nitrogen.

Experimental

General Comments Tetrahydrofuran (THF) and Et_2O were distilled from sodium/benzophenone ketyl before use. *tert*-BuLi was titrated using 2,5-dimethoxybenzyl alcohol before use. All melting points and boiling points are uncorrected. IR spectra were taken on a JASCO IR-810 spectrophotometer. ^{1}H-NMR spectra were recorded on Varian Gemini 2000 (300 MHz) and Hitachi R-300 (300 MHz) spectrometers. Chemical shifts are expressed in δ (ppm) values with tetramethylsilane (TMS) as the internal reference, and coupling constants are expressed in hertz (Hz). The following abbreviations are used: s=singlet, d=doublet, t=triplet, m=multiplet, dd=doublet of doublet, br=broad, and brs=broad singlet. Mass spectra (MS) and high resolution mass spectra (HR-MS) were recorded on JMS-DX303 and JMS-AX500 instruments.

General Procedure for the Synthesis of Ethynyl-1-(phenylsulfonyl)indoles (2, 5) A mixture of an iodo-1-(phenylsulfonyl)indole (**1**, **4**) (2 mmol), an alkyne (2.5—4 mmol), $Pd(PPh_3)_2Cl_2$ (60 mg), CuI (30 mg), Et_3N (300 mg), and DMF (10 ml) was stirred at room temperature for 3-iodo derivative (**1**)[8] or at 80 °C for 2-iodo derivative (**4**)[9] for 12 h. The mixture was diluted with H_2O and extracted with Et_2O. The residue obtained from the Et_2O extract was purified by silica gel column chromatography using AcOEt–hexane (1 : 10) as an eluent to give the product which was purified by distillation or recrystallization.

3-(Phenylethynyl)-1-(phenylsulfonyl)indole (**2a**): Colorless needles from hexane, mp 82—84 °C, lit.[11] mp 81—82 °C. Yield 81%. IR (KBr) cm^{-1}: 2220, 1280, 1190. ^{1}H-NMR ($CDCl_3$) δ: 7.31—7.38 (5H, m), 7.43—7.48 (2H, m), 7.53—7.56 (3H, m), 7.70 (1H, d, J=7.6 Hz), 7.81 (1H, s), 7.89 (1H, d, J=7.8 Hz), 7.90—7.93 (2H, m). MS *m/z*: 357 (M^+). HR-MS *m/z*: 357.0831 (Calcd for $C_{22}H_{15}NO_2S$: 357.0824).

1-(Phenylsulfonyl)-3-(trimethylsilylethynyl)indole (**2b**): Colorless granules from hexane, mp 112—113 °C. Yield 92%. IR (KBr) cm^{-1}: 2180, 1380, 1195. ^{1}H-NMR ($CDCl_3$) δ: 0.28 (9H, s), 7.29—7.36 (2H, m), 7.42—7.47 (2H, m), 7.53 (1H, d, J=7.5 Hz), 7.62 (1H, d, J=6.9 Hz), 7.75 (1H, s), 7.87—7.90 (2H, m), 7.97 (1H, d, J=7.5 Hz). MS *m/z*: 353 (M^+). HR-MS *m/z*: 353.0918 (Calcd for $C_{19}H_{19}NO_2SSi$: 353.0906). *Anal.* Calcd for $C_{19}H_{19}NOSSi \cdot 1/5H_2O$: C, 63.90; H, 5.48; N, 3.92; S, 8.98. Found: C, 64.12; H, 5.45; N, 3.87; S, 8.91.

3-(Hexyn-1-yl)-1-(phenylsulfonyl)indole (**2c**): Colorless needles from hexane, mp 82—83 °C. Yield 81%. IR ($CHCl_3$) cm^{-1}: 2250, 1380, 1180. ^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, t, J=7.0 Hz), 1.53 (4H, m), 2.44 (2H, t, J=7.0 Hz), 7.65 (1H, s), 7.14—8.02 (9H, m). MS *m/z*: 337 (M^+). HR-MS *m/z*: 337.1158 (Calcd for $C_{20}H_{19}NO_2S$: 337.1135). *Anal.* Calcd for $C_{20}H_{19}NO_2S \cdot 1/4H_2O$: C, 70.25; H, 5.75; N, 4.10; S, 9.38. Found C, 70.24; H, 5.79; N, 4.11; S, 9.56.

2-(Phenylethynyl)-1-(phenylsulfonyl)indole (**5a**): Colorless needles from hexane, mp 98—100 °C. Yield 77%. IR (KBr) cm^{-1}: 2210, 1450, 1190. ^{1}H-NMR ($CDCl_3$) δ: 6.94 (1H, s), 7.24—7.53 (9H, m), 7.62—7.66 (2H, m), 7.99—7.96 (2H, m), 8.26 (1H, d, J=8.0 Hz). MS *m/z*: 357 (M^+). HR-MS *m/z*: 357.0853 (Calcd for $C_{22}H_{15}NO_2S$: 357.0823). *Anal.* Calcd for $C_{22}H_{15}NO_2S \cdot 2/5H_2O$: C, 72.47; H, 4.37; N, 3.84; S, 8.79. Found C, 72.17; H, 4.33; N, 3.81; S, 9.08.

1-(Phenylsulfonyl)-2-(trimethylsilylethynyl)indole (**5b**): Yellow oil, bp 130 °C (3 mmHg). Yield 69%. IR (liquid) cm^{-1}: 2150, 1395, 1190. ^{1}H-NMR ($CDCl_3$) δ: 0.32 (9H, s), 6.89 (1H, s), 7.24—7.27 (1H, m), 7.35—7.55 (5H, m), 7.96—7.98 (2H, m), 8.24 (1H, d, J=8.4 Hz). MS *m/z*: 353 (M^+). HR-MS *m/z*: 353.0894 (Calcd for $C_{19}H_{19}NO_2SSi$: 353.0905).

2-(Hexyn-1-yl)-1-(phenylsulfonyl)indole (**5c**): Brown oil, bp 115 °C (4 mmHg). Yield 70%. IR (liquid) cm^{-1}: 2245, 1455, 1195. ^{1}H-NMR ($CDCl_3$)

δ: 0.98 (3H, t, J=7.2 Hz), 1.49—1.67 (4H, m), 2.54 (2H, t, J=6.9 Hz), 6.77 (1H, s), 7.23—7.54 (6H, m), 7.94 (1H, d, J=7.6 Hz), 8.21 (1H, d, J=7.6 Hz). MS *m/z*: 337 (M^+). HR-MS *m/z*: 337.1169 (Calcd for $C_{20}H_{19}NO_2S$: 337.1135).

General Procedure for the Synthesis of 3-Ethynyl-1-(phenylsulfonyl)-indole-2-carbaldehyde (3) To a hexane solution of *tert*-BuLi (2.2 mmol) was slowly added an 3-ethynyl-1-(phenylsulfonyl)indole (**2**) (2 mmol) in THF (10 ml) at −78 °C for 1 h under an argon atmosphere, and the mixture was stirred for 1 h at this temperature. After addition of ethyl formate (4 mmol) at −78 °C, the mixture was stirred for 45 min at the same temperature, allowed to warm to room temperature during 15 min, and then quenched with saturated aqueous NH_4Cl solution and extracted with Et_2O. The Et_2O extract was washed with saturated aqueous NaCl solution and dried over $MgSO_4$. The evaporated residue was purified by silica gel column chromatography using AcOEt–hexane (1 : 10) as an eluent to give the product which was purified by recrystallization.

3-(Phenylethynyl)-1-(phenylsulfonyl)indole-2-carbaldehyde (**3a**): Brown granules from hexane, mp 156—157 °C. Yield 84%. IR (KBr) cm^{-1}: 2220, 1670, 1370, 1180. ^{1}H-NMR ($CDCl_3$) δ: 7.36—7.46 (6H, m), 7.53—7.64 (4H, m), 7.65—7.87 (3H, m), 8.23 (1H, d, J=8.4 Hz), 10.53 (1H, s). MS *m/z*: 385 (M^+). HR-MS *m/z*: 385.0758 (Calcd for $C_{23}H_{15}NO_3S$: 385.0772). *Anal.* Calcd for $C_{23}H_{15}NO_3S \cdot 4/3H_2O$: C, 67.47; H, 4.35; N, 3.42; S, 7.83. Found: C, 67.85; H, 3.92; N, 3.42; S, 7.73.

1-(Phenylsulfonyl)-3-(trimethylsilylethynyl)indole-2-carbaldehyde (**3b**): Colorless needles from hexane, mp 129—131 °C. Yield 70%. IR (KBr): 2155, 1683, 1372, 1177 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.32 (9H, s), 7.38—7.46 (3H, m), 7.54—7.57 (2H, m), 7.74 (1H, d, J=8.0 Hz), 7.87 (2H, m), 8.24 (1H, d, J=8.0 Hz), 10.41 (1H, s). MS *m/z*: 318 (M^+). HR-MS *m/z*: 381.0829 (Calcd for $C_{20}H_{19}NO_3SSi$: 381.0855). *Anal.* Calcd for $C_{20}H_{19}NO_3SSi \cdot 1/3H_2O$: C, 61.99; H, 5.12; N, 3.61,S; 8.27. Found: C, 61.54; H, 5.01; N, 3.49; S, 8.22.

3-(Hexyn-1-yl)-1-(phenylsulfonyl)indole-2-carbaldehyde (**3c**): Colorless prisms from hexane, mp 86—87 °C. Yield 59%. IR ($CHCl_3$) cm^{-1}: 2230, 1680, 1365, 1190. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, t, J=7.2 Hz), 1.51—1.66 (4H, m), 2.56 (2H, t, J=6.9 Hz), 7.36—7.45 (3H, m), 7.53—7.56 (2H, m), 7.72 (1H, d, J=7.8 Hz), 7.84 (1H, d, J=8.4 Hz), 7.85 (1H, d, J=7.8 Hz), 8.25 (1H, d, J=8.4 Hz), 10.42 (1H, s). MS *m/z*: 365(M^+). HR-MS *m/z*: 365.1077 (Calcd for $C_{21}H_{19}NO_3S$: 365.1085). *Anal.* Calcd for $C_{21}H_{19}NO_3S \cdot 2/3H_2O$: C, 66.82; H, 5.43; N, 3.71; S, 8.49. Found: C, 66.42; H, 5.22; N, 3.71; S, 8.22.

General Procedure for the Synthesis of 2-Ethynyl-1-(phenylsulfonyl)-indole-3-carbaldehyde (6) To a solution of $TiCl_4$ (759 mg, 4 mmol) and dichloromethyl methyl ether (460 mg, 4 mmol), in CH_2Cl_2 (10 ml), 2-ethynyl-1-(phenylsulfonyl)indole (2 mmol) in CH_2Cl_2 (5 ml) was added slowly at −78 °C. After stirring for 2 h, the mixture was diluted with H_2O, made alkaline with saturated aqueous Na_2CO_3, and extracted with $CHCl_3$. The residue obtained from the Et_2O extract was purified by silica gel column chromatography using AcOEt–hexane (1 : 10) as an eluent to give the product which was purified by recrystallization.

2-(Phenylethynyl)-1-(phenylsulfonyl)indole-3-carbaldehyde (**6a**): Colorless needles from hexane–$CHCl_3$, mp 171—173 °C. Yield 50%. IR (KBr) cm^{-1}: 2190, 1685, 1380, 1180. ^{1}H-NMR ($CDCl_3$) δ: 7.38—7.51 (7H, m), 7.58—7.63 (1H, m), 7.69—7.72 (2H, m), 8.03—8.06 (2H, m), 8.26—8.30 (2H, m), 10.36 (1H, s). MS *m/z*: 385 (M^+). HR-MS *m/z*: 385.0740 (Calcd for $C_{23}H_{15}NO_3S$: 385.0773). *Anal.* Calcd for $C_{23}H_{15}NO_3S \cdot 3/4H_2O$: C, 69.25; H, 4.17; N, 3.51; S, 8.04. Found: C, 69.06; H, 4.10; N, 3.46; S, 8.29.

2-(Hexyn-1-yl)-1-(phenylsulfonyl)indole-3-carbaldehyde (**6c**): Colorless granules from hexane, mp 88—90 °C. Yield 62%. IR ($CHCl_3$) cm^{-1}: 2230, 1670, 1380, 1190. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (3H, t, J=6.6 Hz), 1.51—1.59 (2H, m), 1.70—1.75 (2H, m), 2.65 (2H, t, J=6.9 Hz), 7.34—7.52 (4H, m), 7.60—7.65 (1H, m), 7.99—8.02 (2H, m), 8.24 (2H, t, J=6.3 Hz), 10.21 (1H, s). IR ($CHCl_3$) cm^{-1}: 2230, 1670, 1380, 1190. MS *m/z*: 365 (M^+). HR-MS *m/z*: 365.1098 (Calcd for $C_{21}H_{19}NO_3S$: 365.1085). *Anal.* Calcd for $C_{21}H_{19}NO_3S \cdot 1/3H_2O$: C, 67.90; H, 5.34; N, 3.77; S, 8.63. Found: C, 67.70; H, 5.24; N, 3.66, S; 8.74.

2-[1-Chloro-2-(trimethylsilyl)ethen-1-yl]-1-(phenylsulfonyl)indole (**7**): Colorless needles from hexane, mp 120—121 °C. Yield 11%. IR (KBr) cm^{-1}: 1370, 1188. ^{1}H-NMR ($CDCl_3$) δ: −0.04 (9H, s), 6.44 (1H, s), 6.64 (1H, s), 7.26—7.54 (6H, m), 8.01—8.07 (3H, m). MS *m/z*: 389 (M^+). HR-MS *m/z*: 389.0667 (Calcd for $C_{19}H_{20}ClNO_2SSi$: 389.0673). *Anal.* Calcd for $C_{19}H_{20}ClNO_2SSi \cdot 1/3H_2O$: C, 57.63; H, 5.26; N, 3.54; S, 8.10. Found: C, 57.80; H, 5.00; N, 3.51; S, 7.99.

General Procedure for the Synthesis of Ethynyl-1-(phenylsulfonyl)indolecarbaldehyde Oxime (9, 12) A mixture of an ethynyl-1-(phenylsulfonyl)indolecarbaldehyde (**3**, **6**) (1 mmol), $NH_2OH \cdot HCl$ (104 mg, 1.5 mmol), and AcONa (123 mg, 1.5 mmol) in EtOH (5 ml) was stirred at room temperature for 12 h. After removal of the solvent *in vacuo*, H_2O was added to the residue, and the mixture was extracted with $CHCl_3$. The $CHCl_3$ extract was washed with saturated aqueous NaCl solution and dried over $MgSO_4$. The residue was purified by silica gel column chromatography using $CHCl_3$–EtOH (100 : 1) as an eluent to give the product which was purified by distillation or recrystallization.

3-(Phenylethynyl)-1-(phenylsulfonyl)indole-2-carbaldehyde Oxime (**9a**): Colorless needles from AcOEt–hexane, mp 165—167 °C. Yield 88%. IR ($CHCl_3$) cm^{-1}: 3575, 3450—3150, 2220, 1450, 1370, 1180. ^{1}H-NMR ($CDCl_3$) δ: 7.33—7.58 (10H, m), 7.70—7.77 (3H, m), 8.20 (1H, d, J=8.1 Hz), 8.36 (1H, s), 8.83 (1H, s). MS *m/z*: 400 (M^+). HR-MS *m/z*: 400.0861 (Calcd for $C_{23}H_{16}N_2O_3S$: 400.0881). *Anal.* Calcd for $C_{23}H_{16}N_2O_3S$: C, 68.99; H, 4.03; N, 7.00; S, 8.01. Found: C, 68.89; H, 4.01; N, 7.04; S, 7.79.

1-(Phenylsulfonyl)-3-(trimethylsilylethynyl)indole-2-carbaldehyde Oxime (**9b**): Colorless prisms from hexane, mp 195—199 °C. Yield 79%. IR (KBr) cm^{-1}: 3284, 2159, 1447, 1148. ^{1}H-NMR ($CDCl_3$) δ: 0.281 (9H, s), 7.30—7.45 (4H, m), 7.50—7.55 (1H, m), 7.73—7.76 (2H, m), 7.75 (1H, d, J=7.5 Hz), 8.18 (1H, d, J=8.2 Hz), 8.29 (1H, br), 8.78 (1H, s). MS *m/z*: 396 (M^+). *Anal.* Calcd for $C_{20}H_{20}N_2O_3SSi$: C, 60.58; H, 5.08; N, 7.06; S; 8.09. Found: C, 60.53; H, 5.06; N, 6.87; S, 7.90.

3-(Hexyn-1-yl)-1-(phenylsulfonyl)indole-2-carbaldehyde Oxime (**9c**): Colorless needles from hexane–$CHCl_3$, mp 140—142 °C. Yield 75%. IR ($CHCl_3$) cm^{-1}: 3575, 3450—3150, 2240, 1450, 1380, 1180. ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, t, J=7.0 Hz), 1.48—1.58 (2H, m), 1.61—1.70 (2H, m), 2.56 (2H, t, J=7.0 Hz), 7.29—7.43 (4H, m), 7.47—7.52 (1 H, m), 7.59—7.61 (1H, d, J=8.0 Hz), 7.71—7.73 (2H, m), 8.17 (1H, d, J=8.0 Hz), 8.83 (1H, s), 9.77 (1H, s). MS *m/z*: 380 (M^+). HR-MS *m/z*: 380.1195 (Calcd for $C_{21}H_{20}N_2O_3S$: 380.1195). *Anal.* Calcd for $C_{21}H_{20}N_2O_3S \cdot 1/2H_2O$: C, 64.76; H, 5.43; N, 7.19; S, 8.23. Found: C, 64.68; H, 5.35; N, 7.03; S, 8.36.

2-(Phenylethynyl)-1-(phenylsulfonyl)indole-3-carbaldehyde Oxime (**12a**): Colorless needles from hexane, mp 155—157 °C. Yield 88%. IR ($CHCl_3$) cm^{-1}: 3575, 3450—3150, 2210, 1380, 1185. ^{1}H-NMR ($CDCl_3$) δ: 7.31—7.36 (1H, m), 7.39—7.48 (7H, m), 7.52—7.58 (1H, m), 7.66—7.69 (2H, m), 7.97—8.00 (2H, m), 8.11 (1H, d, J=8.0 Hz), 8.28 (1H, d, J=9.0 Hz), 8.51 (1H, s). MS *m/z*: 400 (M^+). HR-MS *m/z*: 400.0834 (Calcd for $C_{23}H_{16}N_2O_3S$: 400.0881). *Anal.* Calcd for $C_{23}H_{16}N_2O_3S$: C, 68.99; H, 4.03; N, 7.00; S, 8.01. Found: C, 68.76; H, 4.05; N, 6.99; S, 8.05.

2-(Hexyn-1-yl)-1-(phenylsulfonyl)indole-3-carbaldehyde Oxime (**12c**): Colorless needles from hexane, mp 129—131 °C. Yield 75%. IR ($CHCl_3$) cm^{-1}: 3575, 3450—3100, 2220, 1380, 1190. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (3H, t, J=7.0 Hz), 1.53—1.58 (2H, m), 1.68—1.70 (2H, m), 2.61 (2H, t, J=7.0 Hz), 7.28—7.33 (2H, m), 7.38—7.47 (3H, m), 7.54—7.56 (1H, m), 7.93—7.96 (2H, m), 8.07 (1H, d, J=8.0 Hz), 8.23 (1H, d, J=8.0 Hz), 8.38 (1H, s). MS *m/z*: 380 (M^+). HR-MS *m/z*: 380.1221 (Calcd for $C_{21}H_{20}N_2O_3S$: 380.1193). *Anal.* Calcd for $C_{21}H_{20}N_2O_3S$: C, 66.30; H, 5.30; N, 7.30; S. 8.43. Found: C, 66.16; H, 5.55; N, 7.10; S, 8.37.

General Procedure for the Synthesis of Pyridoindoles (Carbolines) (8, 11) A solution of an ethynylindolecarbaldehyde (**3**, **6**) (1 mmol) in EtOH (5 ml) which was saturated with NH_3 was heated at 120 °C for 4 h in a sealed tube. After removal of the EtOH, H_2O was added to the residue, and the mixture was extracted with $CHCl_3$. The $CHCl_3$ extracted was washed with saturated aqueous NaCl solution and dried over $MgSO_4$. The residue was purified by silica gel column chromatography using $CHCl_3$–EtOH (100 : 1) as an eluent.

3-Phenyl-9-(phenylsulfonyl)-9*H*-pyrido[3,4-*b*]indole (**8a**): Colorless needles from hexane, mp 167—170 °C. Yield 61%. IR ($CHCl_3$) cm^{-1}: 1375, 1180. ^{1}H-NMR ($CDCl_3$) δ: 7.34—7.51 (7H, m), 7.64—7.69 (1H, t, J=5.6 Hz), 7.88—7.91 (2H, m), 8.03—8.10 (3H, m), 8.22 (1H, s), 8.39 (1H, d, J=8.4 Hz), 9.69 (1H, s). MS *m/z*: 384 (M^+). HR-MS *m/z*: 384.0918 (Calcd for $C_{23}H_{16}N_2O_2S$: 384.0932). *Anal.* Calcd for $C_{23}H_{16}N_2O_2S \cdot 1/2H_2O$: C, 70.21; H, 4.35; N, 7.12; S, 8.15. Found: C, 70.32; H, 4.25; N, 7.04; S, 8.39.

9-(Phenylsulfonyl)-9*H*-pyrido[3,4-*b*]indole (**8b**): Colorless needles from hexane, mp 195—196 °C. Yield 37%. IR (KBr) cm^{-1}: 1370, 1171. ^{1}H-NMR ($CDCl_3$) δ: 7.36—7.50 (4H, m), 7.66 (1H, t, J=1.2 Hz), 7.81—7.89 (3H, m), 7.99 (1H, d, J=7.5 Hz), 8.38 (1H, d, J=8.7 Hz), 8.61 (1H, d, J=5.1 Hz), 9.65 (1H, s). MS *m/z*: 308 (M^+). HR-MS *m/z*: 308.0582 (Calcd for $C_{17}H_{12}N_2O_2S$: 308.0619). *Anal.* Calcd for $C_{17}H_{12}N_2O_2S \cdot 1/3H_2O$: C, 64.95; H, 4.06; N, 8.91; S, 10.20. Found: C, 65.08; H, 3.88; N, 8.91; S, 10.38.

3-Butyl-9-(phenylsulfonyl)-9*H*-pyrido[3,4-*b*]indole (**8c**): Colorless needles from hexane, mp 143—144 °C. Yield 84%. IR ($CHCl_3$) cm^{-1}: 1380, 1180. ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, t, J=7.0 Hz), 1.38—1.46 (2H, m),

1.73—1.83 (2H, m), 2.93 (2H, t, J=8.0 Hz), 7.31—7.50 (4H, m), 7.59—7.64 (2H, m), 7.85 (2H, d, J=7.0 Hz), 7.94 (1H, d, J=7.0 Hz), 8.35 (1H, d, J=8.0 Hz), 9.52 (1H, s). MS *m/z*: 364 (M^+). HR-MS *m/z*: 364.1222 (Calcd: for $C_{21}H_{20}N_2O_2S$: 364.1244). *Anal.* Calcd for $C_{21}H_{20}NO_2S$: C, 69.21; H, 5.53; N, 7.69; S, 8.80. Found: C, 69.22; H, 5.59; N, 7.79; S, 8.54.

3-Phenyl-5-(phenylsulfonyl)-5*H*-pyrido[4,3-*b*]indole (**11a**): Colorless needles from hexane, mp 111—113 °C. Yield 61%. IR ($CHCl_3$) cm^{-1}: 1375, 1175. ^{1}H-NMR ($CDCl_3$) δ: 7.36—7.57 (8H, m), 7.88—7.91 (2H, m), 8.02 (1H, d, J=8.1 Hz), 8.13—8.16 (2H, m), 8.32 (1H, d, J=8.7 Hz), 8.66 (1H, s), 9.26 (1H, s). MS *m/z*: 384 (M^+). HR-MS *m/z*: 384.0948 (Calcd for $C_{23}H_{16}N_2O_2S$: 384.0932). *Anal.* Calcd for $C_{23}H_{16}N_2O_2S \cdot 1/3H_2O$: C, 70.75; H, 4.30; N, 7.17; S, 8.21. Found: C, 70.92; H, 4.31; N, 7.07; S, 8.12.

3-Butyl-5-(phenylsulfonyl)-5*H*-pyrido[4,3-*b*]indole (**11c**): Colorless needles from Et_2O–hexane, mp 97—98 °C. Yield 85%. IR ($CHCl_3$) cm^{-1}: 1375, 1180. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (3H, t, J=7.0 Hz), 1.42—1.44 (2H, m), 1.78—1.83 (2H, m), 2.99 (2H, t, J=7.0 Hz), 7.35—7.42 (3H, m), 7.42—7.54 (2H, m), 7.84—7.87 (2H, m), 7.95—7.97 (1H, m), 8.05 (1H, m), 8.16 (1H, d, J=8.0 Hz), 9.10 (1H, s). MS *m/z*: 364 (M^+). HR-MS *m/z*: 364.1223 (Calcd for $C_{21}H_{20}N_2O_2S$: 364.1244). *Anal.* Calcd for $C_{21}H_{20}NO_2S$: C, 69.21; H, 5.53; N, 7.69; S, 8.80. Found: C, 68.94; H, 5.53; N, 7.53; S, 8.99.

General Procedure for the Synthesis of Pyridoindole (Carboline) *N*-Oxides (10, 13) A mixture of an ethynyl-1-(phenylsulfonyl)indolecarbaldehyde oxime (**9**, **12**) (1 mmol) and K_2CO_3 (307 mg, 1.5 mmol) in EtOH (10 ml) was stirred at room temperature for 12 h. After removal of the EtOH *in vacuo*, H_2O was added to the residue, and the mixture was extracted with $CHCl_3$. The $CHCl_3$ extract was washed with saturated aqueous NaCl solution and dried over $MgSO_4$. The residue was purified by recrystallization.

9-(Phenylsulfonyl)-9*H*-pyrido[3,4-*b*]indole 2-Oxide (**10b**): Colorless needles from hexane, mp 192—197 °C. Yield 37%. IR (KBr) cm^{-1}: 3050—3025, 1390, 1180. ^{1}H-NMR ($CDCl_3$) δ: 7.40—7.45 (3H, m), 7.56—7.60 (2H, m), 7.72 (1H, d, J=6.6 Hz), 7.86—7.91 (3H, m), 8.24 (1H, d, J=6.6 Hz), 8.30 (1H, d, J=8.4 Hz), 9.33 (1H, s). MS *m/z*: 324 (M^+). HR-MS *m/z*: 324.0587 (Calcd for $C_{17}H_{12}N_2O_3S$: 324.0569). *Anal.* Calcd for $C_{17}H_{12}N_2O_3S \cdot 1/2H_2O$: C, 61.25; H, 3.93; N, 8.40; S, 9.62. Found: C, 61.29; H, 4.03; N, 8.47; S, 9.50.

3-Butyl-5-(phenylsulfonyl)-9*H*-pyrido[3,4-*b*]indole 2-Oxide (**10c**): Colorless needles from hexane, mp 202—204 °C. Yield 72%. IR ($CHCl_3$) cm^{-1}: 1495, 1450, 1380, 1280, 1190. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (3H, t, J=7.5 Hz), 1.46—1.61 (2H, m), 1.78 (2H, m), 3.03 (2H, t, J=7.5 Hz), 7.45—7.38 (3H, m), 7.61—7.52 (2H, m), 7.66 (1H, s), 7.85—7.92 (3H, m), 8.29 (1H, d, J=7.5 Hz), 9.37 (1H, s). MS *m/z*: 380 (M^+). HR-MS *m/z*: 380.1188 (Calcd for $C_{21}H_{20}N_2O_3S$: 380.1195). *Anal.* Calcd for $C_{21}H_{20}N_2O_3S \cdot 4/5H_2O$: C, 63.88; H, 5.51; N, 7.09. Found: C, 63.83; H, 5.42; N, 6.94.

3-Butyl-5-(phenylsulfonyl)-5*H*-pyrido[4,3-*b*]indole 2-oxide (**13c**): Colorless needles from hexane, mp 158—160 °C. Yield 60%. IR ($CHCl_3$) cm^{-1}: 1400, 1380, 1170. ^{1}H-NMR ($CDCl_3$) δ: 1.04 (3H, t, J=7.0 Hz), 1.50—1.53 (2H, m), 1.84 (2H, m), 3.10 (2H, t, J=8.0 Hz), 7.38—7.45 (3H, m), 7.53—7.61 (2H, m), 7.79—7.83 (3H, m), 8.14 (1H, s), 8.27 (1H, d, J=8.0 Hz), 8.84 (1H, d, J=8.0 Hz), 8.84 (1H, s). MS *m/z*: 380 (M^+). HR-MS *m/z*: 380.1176 (Calcd for: $C_{21}H_{20}N_2O_3S$: 380.1193).

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