Convenient Synthesis of 4-Alkyl, Alkenyl, and Alkynyl Substituted *N*-(Phenylsulfonyl)indoles

Hiroyuki ISHIBASHI,* Susumu AKAMATSU, Hiroko IRIYAMA, and Masazumi IKEDA

Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto 607, Japan.
Received March 14, 1994; accepted May 16, 1994

The indolone 1 reacted with organomagnesium or lithium reagents to give the carbinols 6 and 10, which, upon treatment under appropriate acidic conditions or neutral thermal conditions, gave the 1-phenylsulfonylindoles 8 and 11 bearing various kinds of alkyl, alkenyl, and alkynyl substituents at the 4-position. The indolone 1 was also converted to the 4-cyanoindole 14 *via* the cyanohydrin *O*-trimethylsilyl ether 13.

Keywords 4-alkylindole; 4-alkenylindole; 4-alkynylindole; Grignard reagent; organolithium compound; cupric chloride

The synthesis of indoles bearing a carbon-substituent at the 4-position is of particular interest in organic synthesis, because of the utility of this class of compounds as precursors for many therapeutically useful materials related to the ergot alkaloids, such as lysergic acid.[1] Previous reports from our laboratory[2] have shown that the acid-catalyzed reactions of the 7-arylthio-4,5,6,7-tetrahydroindol-4-one **1** with alcohols or thiols provide ready access to 4-alkoxy and 4-alkylthioindoles **3**. Formation of **3** from **1** can be rationalized in terms of a ready aromatization of the intermediate vinyl ether **2** with elimination of *p*-chlorobenzenethiol. Our interest has now been focused on the synthesis of 4-alkylindoles by using **1** as a common intermediate, as an extension of the method. The attack of carbon nucleophiles such as Grignard reagents on the carbonyl carbon atom of **1** would provide the carbinols **6**, and subsequent dehydration under appropriate conditions might give the 4-alkylindoles **8** through the intermediacy of 6,7-dihydroindoles **7**. In the present paper, we wish to describe an application of this methodology to the synthesis of indoles bearing various carbon-substituents at the 4-position.

Grignard coupling of **1** with methylmagnesium bromide (**4a**) took place smoothly at room temperature to give the carbinol **6a** in nearly quantitative yield. The ^{1}H-NMR spectrum of **6a** exhibited signals due to the methyl protons at C_4 and the proton at C_7 as a singlet (δ 1.33) and triplet (δ 4.80, $J=2$ Hz), respectively. This indicates that compound **6a** is a single stereoisomer, though the relative stereochemistry between C_4 and C_7 is unknown. The carbinol **6a** was then treated with TsOH in refluxing benzene to give the 4-methylindole **8a** in 87% yield, with elimination of *p*-chlorobenzenethiol.

Similarly, compound **6b** gave the 4-ethylindole **8b** in 70% yield. The carbinol **6c** derived from **1** and 2-(1,3-dioxolan-2-yl)ethylmagnesium bromide (**4c**), however, gave a complex mixture of products when heated with TsOH. It was assumed that the acetal function of the desired **8c** or of the starting material **6c** might be partially changed to the corresponding thioacetal by reaction with *p*-chlorobenzenethiol generated during the course of formation of **8c** from **6c**. In fact, a similar reaction in the presence of cupric chloride ($CuCl_2$) as a thiol scavenger gave **8c** in 74% yield. The vinyl derivative **6d** also gave a complex mixture of products when treated with TsOH, probably due to the lability of the resulting vinylindole **8d** under the acidic conditions employed. We found, however, that **8d** was obtained in good yield (69%) just by heating **6d** in refluxing toluene. This may be a result of ready formation of the intermediate conjugated diene **7d** (R = CH = CH_2).

Reactions of the indolone **1** with organolithium reagents **5e—g** gave the carbinols **6e—g**, respectively. The aromatization of 6e was performed by treatment with TsOH in refluxing benzene to give the 4-(phenylsulfonylmethyl)-indole **8e** in 91% yield. The carbinol **6f** derived from the lithio derivative of formaldehyde dimethyl mercaptal *S*-oxide (FAMSO) was converted to the aldehyde **8h** by treatment with $CuCl_2$ in aqueous acetone. Heating **6g** in 10% H_2SO_4 in methanol gave the indol-4-ylacetic ester **8i** in 88% yield.

Reactions of **1** with alkynyllithiums **9a—e** also pro-

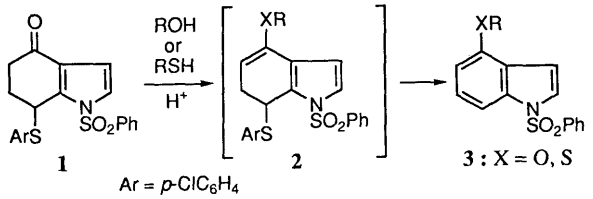


Chart 1

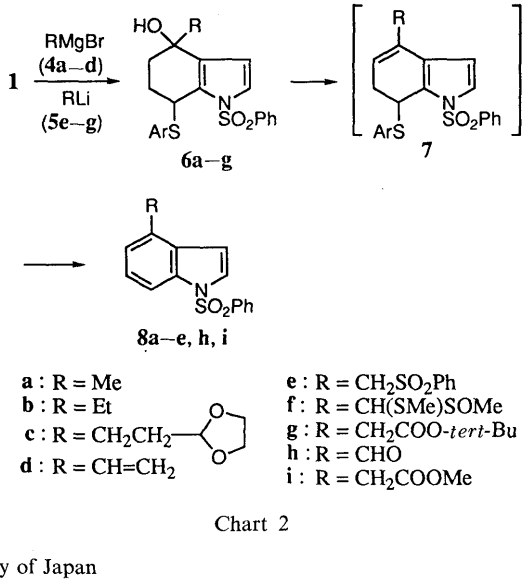
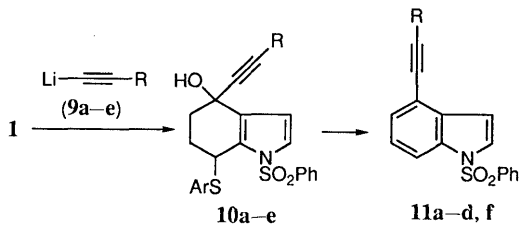


Chart 2



a : R = Ph
b : R = C_6H_{13}
c : R = $SiMe_3$
d : R = CH_2OCO-*tert*-Bu
e : R = COO-*tert*-Bu
f : R = COOEt

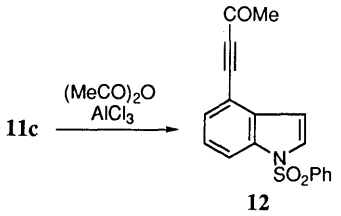


Chart 3

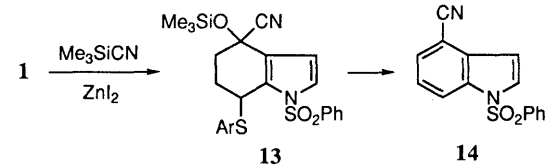


Chart 4

ceeded smoothly to give the carbinols **10a**—**e**, respectively. Compounds **10a**—**c** were found to aromatize readily just by heating in refluxing toluene to give the corresponding 4-alkynylindoles **11a**, **11b**, and **11c** in 65, 59, and 88% yields, respectively.

Compounds **10d** and **10e**, however, were stable under the above thermal conditions, so we treated **10d** with TsOH in refluxing benzene in the presence of $CuCl_2$ to give the desired 4-alkynylindole **11d** in 57% yield. A similar treatment of **10e** in refluxing ethanol gave the ethyl ester **11f** in 63% yield. On the other hand, treatment of the silylethynyl derivative **11c** with acetic anhydride in the presence of $AlCl_3$[3] gave the acetyl derivative **12** in 89% yield.

Finally, we also examined transformation of **1** to the 4-cyanoindole **14**. Thus, treatment of **1** with trimethylsilylnitrile in the presence of a catalytic amount of ZnI_2 gave quantitatively the cyanohydrin *O*-trimethylsilyl ether **13**, which was then heated with $POCl_3$ in pyridine[4] at 60 °C to give **14** in 63% yield.

In summary, we have found that the indolone **1** serves as a useful intermediate for the synthesis of indoles bearing various kinds of alkyl, alkenyl, and alkynyl substituents at the 4-position. Of the compounds herein obtained, 4-alkynylindoles such as **11** and **12** are a class of compounds whose synthesis and reactions have received little attention.[5] We are examining the potential usefulness of compounds **11** and **12** for the elaboration of the ergot alkaloids and related compounds. The *N*-sulfonyl protecting group of indoles can easily be removed by alkaline hydrolysis[6] or by reduction with Mg–MeOH.[7]

Experimental[8]

4-Methyl-1-phenylsulfonyl-1*H*-indole (8a) Methylmagnesium bromide (**4a**) in tetrahydrofuran (THF) (1.92 ml, 1.92 mmol) was added to a solution of **1** (200 mg, 0.48 mmol) in THF (5 ml), and the mixture was stirred at room temperature for 4 h. A saturated NH_4Cl solution (20 ml) was added to the reaction mixture, and the whole was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, and the solvent was evaporated off to give quantitatively the carbinol **6a** [^{1}H-NMR ($CDCl_3$) δ: 1.33 (3H, s), 4.80 (1H, t, J=2 Hz), 6.33 (1H, d, J=3.5 Hz)]. Compound **6a** was then dissolved in benzene (10 ml), and the mixture was heated under reflux for 1 h in the presence of $TsOH \cdot H_2O$ (91 mg, 0.48 mmol). The reaction mixture was washed with a saturated $NaHCO_3$ solution and dried over $MgSO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel (hexane–AcOEt, 20 : 1) to give **8a** (113 mg, 87%), mp 92—92.5 °C (from MeOH). IR (CCl_4) 1600, 1375 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.40 (3H, s), 6.62 (1H, d, J=3.5 Hz), 6.8—7.45 (5H, m), 7.52 (1H, d, J=3.5 Hz), 7.7—8.0 (3H, m). *Anal.* Calcd for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16. Found: C, 66.19; H, 4.85; N, 5.10.

4-Ethyl-1-phenylsulfonyl-1*H*-indole (8b) According to a procedure similar to that described above for **6a**, the indolone **1** (200 mg, 0.48 mmol) was allowed to react with ethylmagnesium bromide (0.96 mmol), and the resulting crude carbinol **6b** was heated in benzene in the presence of TsOH for 1 h. After work-up as described above for **8a**, the crude material was chromatographed on silica gel (hexane–AcOEt, 20 : 1) to give **8b** (96 mg, 70%), mp 72—73.5 °C (from hexane–AcOEt). ^{1}H-NMR ($CDCl_3$) δ: 1.26 (3H, t, J=7 Hz), 2.83 (2H, q, J=7 Hz), 6.70 (1 H, d, J=4 Hz), 6.9—7.5 (5H, m), 7.56 (1H, d, J=4 Hz), 7.7—8.0 (3H, m). *Anal.* Calcd for $C_{16}H_{15}NO_2S$: C, 67.35; H, 5.30; N, 4.91. Found: C, 67.02; H, 5.24; N, 5.24.

4-[2-(1,3-Dioxolan-2-yl)ethyl]-1-phenylsulfonyl-1*H*-indole (8c) 2-(2-Bromoethyl)-1,3-dioxolane (1.3 g, 7.2 mmol) was added dropwise to a stirred suspension of magnesium turnings (108 mg, 4.5 mmol) in dry THF (5 ml), and the mixture was stirred at room temperature for 30 min to give a solution of 2-(1,3-dioxolan-2-yl)ethylmagnesium bromide (**4c**). This solution was then added to a solution of **1** (450 mg, 1.08 mmol) in THF (20 ml) at −20 °C, and the mixture was stirred at the same temperature for 1 h. After work-up as described above for **6a**, the crude material was chromatographed on silica gel (hexane–AcOEt, 2 : 1) to give **6c** (539 mg, 96%). Compound **6c** (483 mg, 0.93 mmol) was then dissolved in benzene (7 ml), and the mixture was heated under reflux for 5 min in the presence of a catalytic amount of $TsOH \cdot H_2O$ and $CuCl_2 \cdot 2H_2O$ (159 mg, 0.93 mmol). After work-up as described above for **8a**, the crude material was chromatographed on silica gel (hexane–AcOEt, 5 : 1) to give **8c**[9] (246 mg, 74%) as an oil. ^{1}H-NMR ($CDCl_3$) δ: 1.8—2.2 (2H, m), 2.75—3.1 (2H, m), 3.6—4.1 (4H, m), 4.90 (1H, t, J=5 Hz), 6.82 (1H, d, J=4 Hz), 7.0—7.55 (5H, m), 7.63 (1H, d, J=4 Hz), 7.8—8.05 (3H, m).

4-Ethenyl-1-phenylsulfonyl-1*H*-indole (8d) According to a procedure similar to that described above for **6a**, the indolone **1** (127 mg, 0.3 mmol) was allowed to react with vinylmagnesium bromide (**4d**) (1.2 mmol) at room temperature for 1 h. After work-up as described above for **6a**, the crude carbinol **6d** was dissolved in toluene (5 ml), and the mixture was heated under reflux for 1.5 h. The solvent was evaporated off and the residue was chromatographed on silica gel (hexane–AcOEt, 10 : 1) to give **8d** (59 mg, 69%) as an oil. ^{1}H-NMR ($CDCl_3$) δ: 5.37 (1H, dd, J=10.5, 1.5 Hz), 5.77 (1H, dd, J=17, 1.5 Hz), 5.86 (1H, d, J=4 Hz), 7.03 (1H, dd, J=17, 10.5 Hz), 7.3—7.6 (5H, m), 7.65 (1H, d, J=4 Hz), 7.8—8.1 (3H, m). *Anal.* Calcd for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62; N, 4.93. Found: C, 67.40, H, 4.85; N, 4.60.

1-Phenylsulfonyl-4-phenylsulfonylmethyl-1*H*-indole (8e) BuLi (15% hexane solution) (0.68 ml, 1.07 mmol) was added to a solution of methyl phenyl sulfone (168 mg, 1.07 mmol) in dry THF (5 ml) at −78 °C, and the mixture was stirred at the same temperature for 5 min. A solution of **1** (150 mg, 0.35 mmol) in THF (1 ml) was added to the above solution containing phenylsulfonylmethyllithium (**5e**), and the mixture was stirred at −78 °C for 15 min. After work-up as described above for **6a**, the crude material was chromatographed on silica gel (hexane–AcOEt, 8 : 1) to give quantitatively **6e** [^{1}H-NMR ($CDCl_3$) δ: 3.42 (2H, s), 4.18 (1H, s), 4.87 (1H, br s), 6.36 (1H, d, J=3.5 Hz)]. Compound **6e** was then dissolved in benzene (3 ml), and the mixture was heated under reflux for 1 h in the presence of $TsOH \cdot H_2O$ (66 mg, 0.35 mmol). After work-up as described above for **8a**, the crude material was chromatographed on silica gel (hexane–AcOEt, 3 : 1) to give **8e** (133 mg, 91%), mp 142—143 °C (from hexane–AcOEt) (lit.[9] mp

146—147 °C). ^{1}H-NMR ($CDCl_3$) δ: 4.52 (2H, s), 6.46 (1H, d, J=4 Hz), 6.9—7.7 (11H, m), 7.7—8.2 (3H, m).

1-Phenylsulfonyl-1*H*-indole-4-carbaldehyde (8h) BuLi (15% hexane solution) (1.15 ml, 1.8 mmol) was added to a solution of FAMSO (228 mg, 1.8 mmol) in dry THF (5 ml) at −20 °C, and the mixture was stirred at the same temperature for 30 min. A solution of **1** (150 mg, 0.36 mmol) in dry THF (1 ml) was added to the above solution containing the lithio derivative **5f** at −78 °C, and the mixture was stirred at the same temperature for 25 min. After work-up as described above for **8a**, the crude material containing **6f** was dissolved in acetone (9 ml), a solution of $CuCl_2 \cdot 2H_2O$ (612 mg, 3.6 mmol) in water (1 ml) was added, and the mixture was heated under reflux for 30 min. Acetone was removed by evaporation, water (10 ml) was added to the residue, and the whole was extracted with AcOEt. The organic phase was dried over $MgSO_4$, the solvent was evaporated off, and the residue was chromatographed on silica gel (hexane–AcOEt, 4 : 1) to give **8h** (86 mg, 84%), mp 99.5—100 °C (from hexane–AcOEt) (lit.[9] mp 101.5—102 °C). IR (CCl_4): 1695 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.2—8.0 (9H, m), 8.20 (1H, d, J=8 Hz), 10.07 (1H, s).

Methyl 1-Phenylsulfonyl-1*H*-indole-4-acetate (8i) A solution of *tert*-butyl acetate (209 mg, 1.8 mmol) in THF (1 ml) was added to a solution of lithium diisopropylamide (LDA) (1.8 mmol) in THF (7 ml) at −78 °C, and the mixture was stirred at the same temperature for 5 min. A solution of **1** (150 mg, 0.36 mmol) in THF (1 ml) was added to the above solution containing the lithioacetate **5g**, and the mixture was stirred at −78 °C for 1 h. After work-up as described above for **6a**, the crude material containing **6g** [^{1}H-NMR ($CDCl_3$) δ: 1.44 (9H, s), 2.54 (2H, s), 4.66 (1H, s), 4.83 (1H, br s), 6.33 (1H, d, J=3.5 Hz)] was dissolved in a mixture of MeOH (4.5 ml) and concentrated H_2SO_4 (0.5 ml), and the mixture was heated under reflux for 7 h. Water (15 ml) was added to the reaction mixture and the whole was extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$, the solvent was evaporated off, and the residue was chromatographed on silica gel (hexane–AcOEt, 7 : 1) to give **8i** (104 mg, 88%), mp 62—63 °C (from hexane–AcOEt) (lit.[9] mp 65—66 °C). IR (CCl_4): 1740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.62 (3H, s), 3.77 (2H, s), 6.70 (1H, d, J=4 Hz), 7.0—7.5 (5H, m), 7.56 (1H, d, J=4 Hz), 7.7—8.0 (3H, m).

4-Phenylethynyl-1-phenylsulfonyl-1*H*-indole (11a) BuLi (15% hexane solution) (0.46 ml, 0.72 mmol) was added to a solution of phenylacetylene (74 mg, 0.72 mmol) in dry THF (10 ml) at −78 °C, and the mixture was stirred at the same temperature for 30 min. A solution of **1** (150 mg, 0.36 mmol) in THF (5 ml) was added to the above solution containing the lithium acetylide **9a**, and the mixture was stirred at room temperature for 12 h. After work-up as described above for **6a**, the crude material containing the carbinol **10a** was dissolved in toluene (10 ml), and the mixture was heated under reflux for 3 h. The solvent was evaporated off, and the residue was chromatographed on silica gel (hexane–AcOEt, 20 : 1) to give **11a** (83 mg, 65%) as an oil. IR (CCl_4): 1600, 1375 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.85 (1H, d, J=4 Hz), 7.0—7.7 (11H, m), 7.7—8.1 (3H, m). *Anal.* Calcd for $C_{22}H_{15}NO_2S$: C, 73.93; H, 4.23; N, 3.92. Found: C, 73.80; H, 4.32; N, 3.51.

4-(1-Octynyl)-1-phenylsulfonyl-1*H*-indole (11b) According to a procedure similar to that described above for **10a**, the indolone **1** (150 mg, 0.36 mmol) was allowed to react with 1-lithio-1-octyne (**9b**) (1.43 mmol), and the resulting crude carbinol **10b** was heated in toluene (10 ml) under reflux for 6 h. The solvent was evaporated off and the residue was chromatographed on silica gel (hexane–AcOEt, 30 : 1) to give **11b** (76 mg, 58%) as an oil. IR (CCl_4): 2220, 1585, 1375 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.6—2.0 (11H, m), 2.43 (2H, t, J=6 Hz), 6.74 (1H, d, J=4 Hz), 6.9—7.45 (5H, m), 7.51 (1H, d, J=4 Hz), 7.6—8.1 (3H, m). *Anal.* Calcd for $C_{22}H_{23}NO_2S$: C, 72.30; H, 6.34; N, 3.83. Found: C, 72.68; H, 6.24; N, 3.52.

1-Phenylsulfonyl-4-trimethylsilylethynyl-1*H*-indole (11c) According to a procedure similar to that described above for **10a**, the indolone **1** (300 mg, 0.72 mmol) was allowed to react with lithium (trimethylsilyl)-acetylide (**9c**) (1.43 mmol), and the resulting crude carbinol **10c** was heated in toluene (10 ml) under reflux for 7 h. The solvent was evaporated off and the residue was chromatographed on silica gel (hexane–AcOEt, 30 : 1) to give **11c** (241 mg, 88%) as an oil. IR (CCl_4): 2140, 1585, 1375 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.32 (9H, s), 6.81 (1H, d, J=4 Hz), 7.0—7.5 (5H, m), 7.58 (1H, d, J=4 Hz), 7.7—8.1 (3H, m). *Anal.* Calcd for $C_{19}H_{19}NO_2SSi$: C, 64.56; H, 5.42; N, 3.96. Found: C, 64.17; H, 5.20; N, 3.66.

1-Phenylsulfonyl-4-(3-pivaloyloxy-1-propynyl)-1*H*-indole (11d) A solution of 3-pivaloyloxy-1-propyne (201 mg, 1.43 mmol) in THF (1 ml) was added to a solution of LDA (1.43 mmol) in THF (10 ml) at −78 °C, and the mixture was stirred at the same temperature for 30 min. A solution of **1** (150 mg, 0.36 mmol) in THF (5 ml) was added to the above solution containing the lithium acetylide **9d**, and the mixture was stirred at −78 °C for 9 h. After work-up as described above for **6a**, the crude material was chromatographed on silica gel (hexane–AcOEt, 5 : 1) to give the carbinol **10d** (122 mg, 61%). Compound **10d** (116 mg, 0.21 mmol) was then dissolved in benzene (10 ml) containing $TsOH \cdot H_2O$ (4 mg, 0.01 mmol) and $CuCl_2 \cdot 2H_2O$ (35 mg, 0.21 mmol), and the mixture was heated under reflux for 1 h. Water (10 ml) was added to the reaction mixture, and the organic layer was separated, then dried over $MgSO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel (hexane–AcOEt, 15 : 1) to give **11d** (48 mg, 57%) as an oil. IR (CCl_4): 2230, 1730 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (9H, s), 4.88 (2H, s), 6.74 (1H, d, J=4 Hz), 7.1—7.5 (5H, m), 7.55 (1H, d, J=4 Hz), 7.65—8.0 (3H, m). *Anal.* Calcd for $C_{22}H_{21}NO_4S$: C, 66.82; H, 5.35; N, 3.54. Found: C, 66.91; H, 5.66; N, 3.48.

Ethyl 3-(1-Phenylsulfonyl-1*H*-indol-4-yl)propiolate (11f) According to a procedure similar to that described above for **9d**, *tert*-butyl propiolate (362 mg, 2.87 mmol) was lithiated with LDA (2.87 mmol). A solution of **1** (300 mg, 0.72 mmol) in THF (1 ml) was added to the above solution containing the lithium acetylide **9e** at −78 °C, and the mixture was stirred at the same temperature for 30 min. After work-up as described above for **10d**, the crude material was chromatographed on silica gel (hexane–AcOEt, 5 : 1) to give quantitatively the hydroxy ester **10e** [^{1}H-NMR ($CDCl_3$) δ: 1.43 (9H, s), 3.50 (1H, s), 4.82 (1H, br s), 6.36 (1H, d, J =3.5 Hz)]. Thus obtained **10e** (190 mg, 0.35 mmol) was dissolved in EtOH (5 ml) containing $TsOH \cdot H_2O$ (66 mg, 0.35 mmol) and $CuCl_2 \cdot 2H_2O$ (59 mg, 0.35 mmol), and the mixture was heated under reflux for 6 h. The solvent was evaporated off, water (10 ml) was added to the residue, and the whole was extracted with CH_2Cl_2. The organic phase was washed with a saturated $NaHCO_3$ solution and dried over $MgSO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel (hexane–AcOEt, 10 : 1) to give **11f** (77 mg, 63%) as an oil. IR (CCl_4): 2210, 1705 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.33 (3H, d, J=7 Hz), 4.30 (2H, q, J=7 Hz), 6.90 (1H, d, J=4 Hz), 7.1—7.6 (5H, m), 7.67 (1H, d, J=4 Hz), 7.8—8.25 (3H, m). *Anal.* Calcd for $C_{19}H_{15}NO_4S$: C, 64.58; H, 4.28; N, 3.96. Found: C, 64.23; H, 3.99; N, 3.60.

4-(1-Phenylsulfonyl-1*H*-indol-4-yl)-3-butyn-2-one (12) Acetic anhydride (246 mg, 2.4 mmol) was added to a stirred suspension of $AlCl_3$ (643 mg, 4.8 mmol) in CH_2Cl_2 (10 ml), and the mixture was stirred at room temperature for 30 min, during which time it became homogeneous. A solution of silylalkyne **11c** (284 mg, 0.8 mmol) in CH_2Cl_2 (1 ml) was added to the above solution at −40 °C, and the mixture was stirred at the same temperature for 15 min. Water (10 ml) was added to the reaction mixture and the organic layer was separated. The aqueous layer was further extracted with CH_2Cl_2, and the combined organic phases were washed successively with a saturated $NaHCO_3$ solution and brine, then dried over $MgSO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel (hexane–AcOEt, 7 : 1) to give **12** (277 mg, 89%), mp 105—106 °C (from hexane–AcOEt). IR (CCl_4): 2180, 1670 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.47 (3H, s), 6.83 (1H, d, J=3.5 Hz), 7.0—7.6 (5H, m), 7.67 (1H, d, J=3.5 Hz), 7.7—8.2 (3H, m). *Anal.* Calcd for $C_{18}H_{13}NO_3S$: C, 66.59; H, 4.05; N, 4.33. Found: C, 66.77; H, 4.25; N, 4.03.

1-Phenylsulfonyl-1*H*-indole-4-carbonitrile (14) Trimethylsilylnitrile (167 mg, 1.7 mmol) was added to a mixture of **1** (200 mg, 0.47 mmol) and ZnI_2 (5 mg, 0.016 mmol) in dry CH_2Cl_2 (10 ml) at 0 °C, and the mixture was stirred at room temperature overnight. Water (10 ml) was added to the reaction mixture, and the organic layer was separated, then dried over $MgSO_4$. The solvent was evaporated off to give quantitatively the cyanohydrin *O*-trimethylsilyl ether **13** [^{1}H-NMR ($CDCl_3$) δ: 0.30 (9H, s), 4.83 (1H, br s), 6.40 (1H, d, J=3.5 Hz)]. $POCl_3$ (0.09 ml, 1 mmol) was added to a solution of **13** (175 mg, 0.34 mmol) in pyridine (1 ml), and the mixture was heated at 60 °C for 5 h and then at 80 °C for 1 h. A 10% HCl solution (10 ml) was added to the reaction mixture at 0 °C, and the whole was extracted with diethyl ether. The organic phase was washed with brine, and dried over $MgSO_4$. The solvent was evaporated off and the residue was chromatographed on silica gel (hexane–AcOEt, 4 : 1) to give **14** (61 mg, 63%), mp 175—176 °C (from hexane–AcOEt). IR ($CHCl_3$): 2220 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.90 (1H, d, J=4 Hz), 7.3—8.1 (8H, m), 8.30 (1H, d, J=8 Hz). *Anal.* Calcd for $C_{15}H_{10}N_2O_2S$:

C, 63.82; H, 3.57; N, 9.92. Found: C, 63.70; H, 3.61; N, 9.84.

Acknowledgment This work was supported by a Grant-in-Aid for Scientific Research (No. 05671774) from the Ministry of Education, Science and Culture, Japan.

References and Notes

1) For reviews of the synthesis of 4-alkylindoles and their elaboration to the ergot alkaloids, see D. C. Horwell, *Tetrahedron*, **35**, 3123 (1980); A.P. Kozikowski, *Heterocycles*, **16**, 267 (1981); M. Somei, *Yuki Gosei Kagaku Kyokai Shi*, **40**, 387 (1982); M. Natsume, *Yakugaku Zasshi*, **108**, 109 (1988).
2) *a*) H. Ishibashi, T. Tabata, K. Hanaoka, H. Iriyama, S. Akamatsu, M. Ikeda, *Tetrahedron Lett.*, **34**, 489 (1993); *b*) H. Ishibashi, S. Akamatsu, H. Iriyama, K. Hanaoka, T. Tabata, M. Ikeda, *Chem. Pharm. Bull.*, **42**, 271 (1994).
3) L. Birkofer, A. Ritter, H. Uhlenbrauck, *Chem. Ber.*, **96**, 3280 (1963).
4) M. Oda, A. Yamamuro, T. Watabe, *Chem. Lett.*, **1979**, 1427.
5) For a synthesis of 4-ethynylindole, see A.P. Kozikowski, M. Okita, M. Kobayashi, H. G. Floss, *J. Org. Chem.*, **53**, 863 (1988).
6) A. P. Kozikowski, Y.-Y. Chen, *J. Org. Chem.*, **46**, 5248 (1981); M. G. Saulnierand, G. W. Gribble, *ibid.*, **47**, 2810 (1982). See also ref. 2*b*).
7) K. Okabe, M. Natsume, *Tetrahedron*, **36**, 7615 (1991).
8) Methylmagnesium bromide (**4a**), ethylmagnesium bromide (**4b**), and vinylmagnesium bromide (**4d**) were purchased from Kanto Chemical Co., Inc. as 1 M solutions in THF. ^{1}H-NMR spectra were measured on a JEOL JNM-PMX 60 (60 MHz) spectrometer using tetramethylsilane as an internal standard. For other general experimental details, see ref. 2*b*).
9) M. Fuji, H. Muratake, M. Natsume, *Chem. Pharm. Bull.*, **40**, 2338 (1992).