REACTION OF INDOLE-2,3-DICARBOXYLIC ANHYDRIDE WITH GRIGNARD REAGENTS: SYNTHESIS OF 2-ACYLINDOLES

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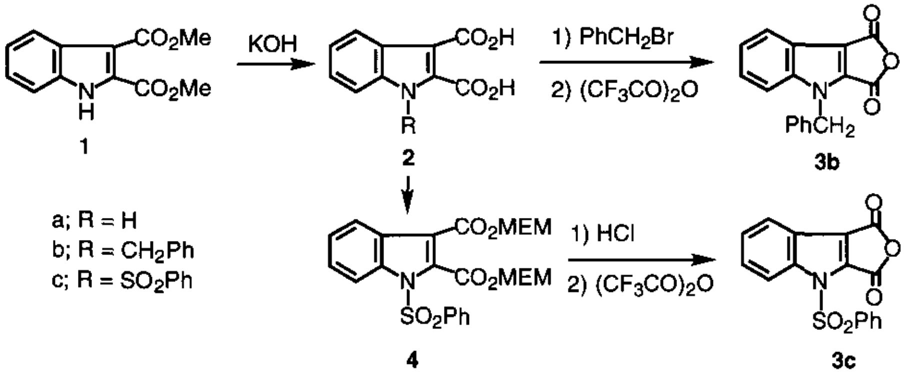
Abstract - Reaction of indole-2,3-dicarboxylic anhydride with methylmagnesium bromide and phenylmagnesium bromide gave 2-acetyl- and 2-benzoyl-indole-3-carboxylic acids, but with *tert*-butylmagnesium chloride, 3-pivaloylindole-2-carboxylic acids were obtained as the main products. Treatment of 2-acylindole-3-carboxylic acids with copper chromite in quinoline or potassium hydroxide gave the corresponding 2-acylindoles.

We have reported that the reduction of 1-benzylindole-2,3-dicarboxylic anhydride (**3b**) with sodium borohydride gave a 2-hydroxymethylindole-3-carboxylic acid, which was converted to murrayaquinone-A *via* a Diels-Alder reaction of 4*H*-furo[3,4-*b*]indole with methyl acrylate.[1] Reduction of the 2-carbonyl group of **3b** is much easier than that of the 3-carbonyl group, because a nitrogen in the indole is more enolizable with the 3-carbonyl group than the 2-carbonyl group.[2] Reaction of substituted phthalic anhydrides with Grignard reagents was controlled by electronic and steric factors.[3] However, in reaction of pyridinedicarboxylic anhydride with Grignard reagents[4] and 1-benzenesulfonyl-2-lithioindole,[5] a nitrogen in the pyridine decides the reactivity of the anhydride toward nucleophiles. In this paper we report the reactivity of 1-benzyl- (**3b**) and 1-benzenesulfonylindole-2,3-dicarboxylic anhydrides (**3c**) with Grignard reagents and the synthesis of 2-acylindoles.

The anhydrides (**3b,c**) were prepared from dimethyl indole-2,3-dicarboxylate (**1**)[6] as follows. Hydrolysis

Scheme 1

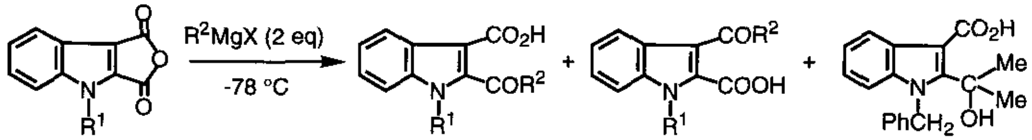


of **1** with potassium hydroxide gave an indole-2,3-dicarboxylic acid (**2a**)(R=H)(60%). The acid (**2a**) was reacted with benzyl bromide in the presence of sodium hydride in *N,N*-dimethylformamide to afford the corresponding 1-benzylindole-2,3-dicarboxylic acid (**2b**)(R=CH_2Ph)(87%), which was treated with trifluoroacetic anhydride in refluxing dichloromethane to yield anhydride (**3b**)(78%). Synthesis of 1-benzenesulfonylindole-2,3-dicarboxylic anhydride (**3c**) was performed by conversion of **2a** to the corresponding 2-methoxyethoxymethyl(MEM) ester, followed by benzenesulfonylation[7] and treatment of **4** with 10% hydrochloric acid, then trifluoroacetic anhydride.

Reaction of 1-benzylindole-2,3-dicarboxylic anhydride (**3b**) with phenylmagnesium bromide in tetrahydofuran at -78°C gave 2-benzoyl-1-benzylindole-3-carboxylic acid (**5a**) in 84% yield. In a similar manner, treatment of **3b** with methylmagnesium bromide afforded a mixture of 2-acetyl-1-benzylindole-3-carboxylic acid (**5c**) and 1-benzyl-2-(1-hydroxy-1-methylethyl)indole-3-carboxylic acid (**7**) in 45% and 30% yields, respectively. When 1-benzenesulfonylindole-2,3-dicarboxylic anhydride (**3c**) reacted with phenylmagnesium bromide and methylmagnesium bromide, 1-benzenesulfonyl-2-benzoyl- (**5b**) and 2-acetylindole-3-carboxylic acid (**5d**) were isolated in 52% and 69% yield, respectively.

However, treatment of **3b** with *tert*-butylmagnesium chloride yielded a mixture of 1-benzyl-2-pivaloylindole-3-carboxylic acid (**5e**) and 3-pivaloylindole-2-carboxylic acid (**6e**) in 43% and 34% yields, respectively. In a similar manner, reaction of **3c** with *tert*-butylmagnesium chloride yielded a mixture of 1-benzenesulfonyl-2-pivaloylindole-3-carboxylic acid (**5f**) and 3-pivaloylindole-2-carboxylic acid (**6f**) in 2% and 24% yields, respectively.

Scheme 2



3b,c
b; R = CH_2Ph
c; R = SO_2Ph

5 **6** **7**

a; R^1 = CH_2Ph, R^2 = Ph
c; R^1 = CH_2Ph, R^2 = Me
e; R^1 = CH_2Ph, R^2 = *t*-Bu

b; R^1 = SO_2Ph, R^2 = Ph
d; R^1 = SO_2Ph, R^2 = Me
f; R^1 = SO_2Ph, R^2 = *t*-Bu

Table 1

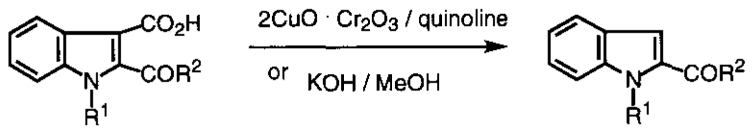
			Yield(%)		
R^1	R^2MgX	Time	5	6	7
CH_2Ph	PhMgBr	1 h	84	-	-
SO_2Ph	PhMgBr	1 h	52	-	-
CH_2Ph	MeMgBr 1)	1 h	45	-	30
SO_2Ph	MeMgBr	3 h	69	-	-
CH_2Ph	*tert*-BuMgCl	1 h	43	34	-
SO_2Ph	*tert*-BuMgCl 1)	24 h	2	24	-

1) 5 eq

Treatment of **5a** with copper chromite in refluxing quinoline gave 2-benzoyl-1-benzylindole (**8a**) in 80% yield and an alkaline hydrolysis of **5b** with potassium hydroxide in hot methanol afforded 2-benzoylindole

(**8**)(R^1 = H, R^2 = Ph) in 70% yield. In a similar manner, the conversion of **5a** to **8a**, **5c-e** were changed to 2-acetyl-1-benzylindole (**8c**), 2-acetyl-1-benzenesulfonylindole (**8d**), and 1-benzyl-2-pivaloylindole (**8e**) in 80%, 69%, and 88% yields, respectively.

Scheme 3



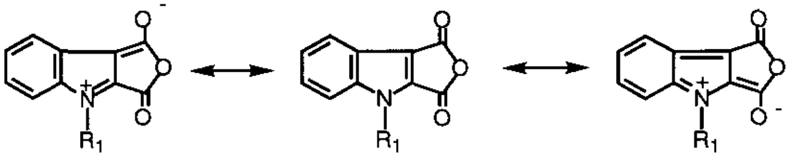
5a-e **8a-e**

Table 2

5	R^1	R^2	Method	Yield(%)
a	CH_2Ph	Ph	A	80
b	SO_2Ph	Ph	B	70
c	CH_2Ph	Me	A	80
d	SO_2Ph	Me	A	69
e	CH_2Ph	*tert*-Bu	A	88

method A: copper chromite / quinoline
method B: KOH / MeOH

The structure of two isomeric products (**5e,f**) and (**6e,f**) was readily assigned by comparison of the C-4 protons of 2-pivaloylindole-3-carboxylic acids (**5e**; δ 8.24, **5f**; δ 8.06-8.13) with those of 3-pivaloylindole[8] (δ 8.45) and 3-pivaloylindole-2-carboxylic acids (**6e**; δ 7.01-7.57, **6f**; δ 7.20-7.50) with 3-pivaloylindole-2-carboxylic acid[8] (δ 6.90–7.62). A carbonyl group at the 2-position in indole-2,3-dicarboxylic anhydride (**3**) is more reactive toward a nucleophile than a carbonyl group at the 3-position because a benzenoid structure (**9**) is more stable than a quinoid structure (**10**). Therefore, reaction of **3b** with phenylmagnesium bromide and methylmagnesium bromide gave 2-acyl-1-benzylindole-3-carboxylic acids (**5**) but with the bulkier *tert*-butylmagnesium chloride the reaction afforded a mixture of 1-benzyl-2-pivaloylindole-3-carboxylic acid (**5e**) and 1-benzyl-3-pivaloylindole-2-carboxylic acid (**6e**) because of the steric hindrance of the benzyl group. We expected that the 1-benzenesulfonyl group, an electron-withdrawing group, in indole-2,3-dicarboxylic anhydride (**3c**) activates the carbonyl group at the 3-position rather than at the 2-position, but the results of the reactivity of **3c** toward Grignard reagents were similar to the reactivity of **3b.**



9b,c **3b,c** **10b,c**

b; $R^1 = CH_2Ph$, **c**; $R^1 = SO_2Ph$

EXPERIMENTAL

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. The

^{1}H-NMR spectra were determined on a JEOL JNM-GSX 270 spectrometer using tetramethylsilane as an internal standard. The IR spectra were recorded with a JASCO FT/IR-7000 spectrophotometer. The high MS were recorded on a JOEL JMS-HX100 spectrometer. Column chromatography was performed on E. Merck silica gel 60 (70-230 mesh or 230-400 mesh). Tetrahydrofuran (THF) was distilled from sodium and benzophenone prior to use. Phenylmagnesium bromide (1.0 M solution in THF) and methylmagnesium bromide (1.4 M solution in toluene and THF) were purchased from Aldrich. *tert*-Butylmagnesium chloride (1 M solution in THF) was purchased from Kanto Chemical.

Indole-2,3-dicarboxylic Acid (2a)

A solution of dimethyl indole-2,3-dicarboxylate (**1**)[6] (9.32 g, 40 mmol) in methanol (40 mL) and 4N potassium hydroxide solution (40 mL, 160 mmol) was heated at 70 ℃ for 2 h under stirring. The reaction mixture was diluted with water, and washed with Et_2O. The aqueous solution was acidified with 10% hydrochloric acid to give the indole-2,3-dicarboxylic acid (**2a**) (4.88 g, 60%), mp 258-260°C (MeOH-H_2O) as a pale yellow solid. IR (nujol) 3220, 1700 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 7.28 (1H, dt, J = 8, 1 Hz, H-5 or H-6), 7.37 (1H, dt, J = 8, 1 Hz, H-6 or H-5), 7.59 (1H, dd, J = 8, 1 Hz, H-7), 8.16 (1H, br d, J = 8 Hz, H-4), 12.66 (1H, br s, NH). *Anal.* Calcd For $C_{10}H_7NO_4$: C, 58.39; H, 3.43; N, 6.81. Found: C, 58.40; H, 3.64; N, 6.76.

1-Benzylindole-2,3-dicarboxylic Anhydride (3b)

Benzyl bromide (18 mL, 0.15 mol) was added dropwise to a suspension of sodium hydride (10.00 g, 0.25 mole, 60% dispersion in mineral oil) and indole-2,3-dicarboxylic acid (**2a**)(10.25 g, 0.05 mol) in *N,N*-dimethylformamide (100 mL) at 0 °C. After the mixture stirred for 1 h at rt, the mixture was poured into water and washed with Et_2O. The aqueous layer was acidified (pH=1) with concentrated hydrochloric acid to give a precipitate, which was collected by filtration to afford 1-benzylindole-2,3-dicarboxylic acid (**2b**)(12.82 g, 87%), mp 203-204°C (lit.,[9] mp 198 °C)(MeOH-H_2O) as a pale yellow solid. IR (nujol) 1693 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 6.13 (2H, s, CH_2Ph), 7.04-7.44 (8H, m, aromatic protons), 8.45-8.50 (1H, m, H-4). *Anal.* Calcd for $C_{17}H_{13}NO_4$: C, 69.15; H, 4.44; N, 4.74. Found: C, 69.19; H, 4.58; N, 4.72.

A suspension of 1-benzylindole-2,3-dicarboxylic acid (**2b**)(8.85 g, 30 mmol) and trifluoroacetic anhydride (8.5 mL, 60 mmol) in CH_2Cl_2 (60 mL) was refluxed for 2 h. The reaction mixture was evaporated off to afford a solid, which was washed with *n*-hexane-CH_2Cl_2 (3 : 1) to give 1-benzylindole-2,3-dicarboxylic anhydride (**3b**) (6.52g, 78%), mp 150-152°C (AcOEt) as a pale yellow solid. IR (nujol) 1836, 1772 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 5.85 (2H, s, CH_2Ph), 7.08-7.51 (8H, m, aromatic protons), 8.23-8.29 (1H, m, H-4). *Anal.* Calcd for $C_{17}H_{11}NO_3$: C, 73.65; H, 4.00; N, 5.05. Found: C, 73.65; H, 4.19; N, 5.08.

Bis(2-methoxyethoxymethyl) 1-Benzenesulfonylindole-2,3-dicarboxylate (4)

To a mixture of indole-2,3-dicarboxylic acid (**2a**)(5.33 g, 26 mmol) and *N,N*-diisopropylethylamine (9.2 mL, 53 mmol) in CH_2Cl_2 (100 mL) was added 2-methoxyethoxymethyl chloride (6.0 mL, 52 mmol) at 0 °C under argon and the mixture was stirred for 1 h. Water was added to the reaction mixture, which was extracted with CH_2Cl_2. The organic extracts were washed with water, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (*n*-hexane : AcOEt = 10 : 1) to give bis(2-methoxyethoxymethyl) indole-2,3-dicarboxylate (8.16g, 82%). IR (neat) 3298, 1712 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 3.38 (3H, s, OCH_3), 3.39 (3H, s, OCH_3), 3.50-3.95 (4H, m, OCH_2CH_2O), 5.58 (2H, s, CO_2CH_2O), 5.62 (2H, s, CO_2CH_2O), 7.20-7.45 (3H, m, aromatic protons), 8.09 (1H, dd, *J* = 8, 1 Hz, H-4), 9.78 (1H, br s, NH); HRMS *m/z* (M^+) calcd for $C_{18}H_{23}NO_8$: 381.1424. Found: 381.1432.

Benzenesulfonyl chloride (2.8 mL, 22 mmol) was added to a suspension of bis(2-methoxyethoxymethyl) indole-2,3-dicarboxylate (8.16 g, 21 mmol) and tetra-*n*-butylammonium bisulfate (728 mg, 2.1 mmol) in 50% potassium hydroxide solution (21 mL) and methylene chloride (63 mL) at -20°C and the reaction mixture was stirred for 2 h. The reaction mixture was poured into water, extracted with CH_2Cl_2, and washed with water. The extracts were dried over Na_2SO_4, and evaporated off to give a residue, which was chromatographed (*n*-hexane : AcOEt =10 : 1) to afford bis(2-methoxyethoxymethyl) 1-benzenesulfonylindole-2,3-dicarboxylate (**4**) (8.98 g, 80%) as a brown oil. IR (neat) 1724 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 3.38 (3H, s, OCH_3), 3.42 (3H, s, OCH_3), 3.54-4.06 (8H, m, OCH_2CH_2O), 5.58 (2H, s, CO_2CH_2O), 5.74 (2H, s, CO_2CH_2O), 7.33-7.65 (5H, m, aromatic protons), 7.99-8.20 (4H, m, aromatic protons); HRMS *m/z* (M^+) calcd for $C_{24}H_{27}NO_{10}S$: 521.1356. Found: 521.1387.

1-Benzenesulfonylindole-2,3-dicarboxylic Anhydride (3c)

A mixture of bis(2-methoxyethoxymethyl) 1-benzenesulfonylindole-2,3-dicarboxylate (**4**)(8.98 g, 17 mmol) and 10% hydrochloric acid (9 mL) in THF (86 mL) was refluxed for 2 h. The mixture was poured into water and extracted with CH_2Cl_2. The organic extracts were washed with water, dried over with Na_2SO_4, and concentrated to give 1-benzenesulfonylindole-2,3-dicarboxylic acid (5.95 g, 100%), mp 222-223°C (decomp)(from MeOH-H_2O). IR (nujol) 1729, 1682 cm^{-1}; ^1H-NMR (DMSO-d_6) δ: 7.33-7.77 (5H, m, aromatic protons), 7.96-8.14 (4H, m, aromatic protons). *Anal.* Calcd for $C_{16}H_{11}NO_6S$: C, 55.65; H, 3.21; N, 4.06. Found: C, 55.50; H, 3.35; N, 3.94.

A suspension of 1-benzenesulfonylindole-2,3-dicarboxylic acid (5.95g, 17 mmol) and trifluoroacetic anhydride (4.9 mL, 35 mmol) in CH_2Cl_2 (34 mL) was refluxed for 2 h. After the mixture was cooled, a separated precipitate was collected by filtration to yield 1-benzenesulfonylindole-2,3-dicarboxylic anhydride (**3c**)(4.36 g, 77%), mp 228-229°C (AcOEt). IR (nujol) 1840, 1778 cm^{-1}; ^1H-NMR (DMSO-d_6) δ: 7.34-7.78 (5H, m, aromatic protons), 7.96-8.14 (4H, m, aromatic protons). *Anal.* Calcd for $C_{16}H_9NO_5S$: C, 58.71; H, 2.77; N, 4.28. Found: C, 58.52; H, 3.06; N, 4.52.

Reaction of Indole-2,3-dicarboxylic Anhydride (3b,c) with Grignard Reagents (General Procedure)

To a solution of indole-2,3-dicarboxylic anhydride (**3**)(0.2 mmol) in THF (2-4 mL) at -78 °C under argon was added Grignard reagents (0.4 mmol). The reaction mixture was acidified with 10% hydrochloric acid and the mixture was extracted with CH_2Cl_2. The combined extracts were washed with water and dried over Na_2SO_4. The solvent was evaporated off to afford a residue, which was purified by column chromatography (CH_2Cl_2 : MeOH = 10 : 1).

2-Benzoyl-1-benzylindole-3-carboxylic Acid (5a); mp 258-260°C (from EtOH). IR (nujol) 1669 cm^{-1}; ^1H-nmr (DMSO-d_6) δ: 5.35 (2H, s, C*H*$_2$Ph), 7.00-7.74 (9H, m, aromatic protons), 8.09-8.15 (1H, m, H-4). *Anal.* Calcd for $C_{23}H_{17}NO_3$: C, 77.73; H, 4.82; N, 3.94. Found: C, 77.68; H, 5.00; N, 3.89.

1-Benzenesulfonyl-2-benzoylindole-3-carboxylic Acid (5b); mp 238-240°C (from EtOH). IR (nujol) 1679 cm^{-1}; ^1H-NMR (DMSO-d_6) δ: 7.38-8.18 (14H, m, aromatic protons). HRMS *m/z* (M^+) calcd for $C_{22}H_{15}NO_5S$: 405.0671. Found: 405.0695. **5b** was identified as methyl 1-benzenesulfonyl-2-benzoylindole-3-carboxylate by treatment of diazomethane; mp 174-175.5°C (from AcOEt-*n*-hexane). IR (nujol) 1716, 1669 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 3.67 (3H, s, CH_3), 7.36-7.66 (8H, m, aromatic protons), 7.90-8.20 (6H, m, aromatic protons). *Anal.* Calcd for $C_{23}H_{17}NO_5S$: C, 65.86; H, 4.08; N, 3.34. Found: C, 65.66; H, 4.27; N, 3.37.

2-Acetyl-1-benzylindole-3-carboxylic Acid (5c); mp 198.5-200°C (from EtOH). IR (nujol) 1707, 1658 cm^{-1}; ^1H-NMR (DMSO-d_6) δ: 2.44 (3H, s, CH_3), 5.42 (2H, s, C*H*$_2$Ph), 7.02-7.58 (8H, m, aromatic protons), 8.03-8.11 (1H, m, H-4). *Anal.* Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.51; H, 5.30; N, 4.76.

1-Benzyl-2-(1-hydroxy-1-methylethyl)indole-3-carboxylic Acid (7); mp 166-167°C (from EtOH). IR (nujol) 1633 cm^{-1}; ^1H-NMR (DMSO-d_6) δ: 1.68 (6H, s, 2 x CH_3), 5.93 (2H, s, C*H*$_2$Ph), 6.92-7.30 (8H, m, aromatic protons), 7.88-7.93 (1H, m, H-4). *Anal.* Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.44; H, 6.21; N, 4.49.

2-Acetyl-1-benzenesulfonylindole-3-carboxylic Acid (5d); mp 249-251°C (from EtOH). IR (nujol) 1714, 1679 cm^{-1}; ^1H-NMR (DMSO-d_6)) δ: 2.73 (3H, s, CH_3), 7.36-7.80 (5H, m, aromatic protons), 7.93-8.09 (4H, m, aromatic protons). *Anal.* Calcd for $C_{17}H_{13}NO_5S$: C, 59.47; H, 3.82; N, 4.08. Found: C, 58.97; H, 4.03; N, 3.76.

1-Benzyl-2-pivaloylindole-3-carboxylic Acid (5e); mp 228-230°C (from EtOH). IR (nujol) 1696, 1661 cm^{-1}; ^1H-NMR (DMSO-d_6)) δ: 1.28 (9H, s, $C(CH_3)_3$), 5.27 (2H, s, C*H*$_2$Ph), 7.07-7.35 (8H, m, aromatic protons), 8.24 (1H, br d, *J* = 8 Hz, H-4). *Anal.* Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 75.05; H, 6.38; N, 4.27.

1-Benzyl-3-pivaloylindole-2-carboxylic Acid (6e); mp 219-220°C (from EtOH). IR (nujol) 1683 cm^{-1}; ^1H-NMR (DMSO-d_6) δ: 1.21 (9H, s, $C(CH_3)_3$), 5.86 (2H, s, C*H*$_2$Ph), 7.01-7.55 (9H, m, aromatic protons). *Anal.* Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 74.82; H, 6.42; N, 4.09.

1-Benzenesulfonyl-2-pivaloylindole-3-carboxylic Acid (5f): mp 92-97°C (from *n*-hexane). IR ($CHCl_3$) 1707 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 1.39 (9H, s, $C(CH_3)_3$), 7.30-7.57 (5H, m, aromatic protons), 7.91-7.98 (2H, m, H-2'), 8.06 (1H, dd, J = 8, 1 Hz, H-4 or H-7), 8.13 (1H, br d, J = 7 Hz, H-7 or H-4). HRMS *m/z* (M^+) calcd for $C_{20}H_{19}NO_5S$: 385.0984. Found: 385.0984.

1-Benzenesulfonyl-3-pivaloylindole-2-carboxylic Acid (6f): mp 142-145°C (from AcOEt-*n*-hexane). IR ($CHCl_3$) 1690 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 1.16 (9H, s, $C(CH_3)_3$), 7.20-7.50 (6H, m, arom), 7.92 (2H, br d, J = 8 Hz, H-2'), 8.06 (1H, br d, J = 8 Hz, H-7). HRMS *m/z* (M^+) calcd for $C_{20}H_{19}NO_5S$: 385.0984. Found: 385.0974. **6f** was identified as methyl 1-benzenesulfonyl-3-pivaloylindole-2-carboxylate by treatment of diazomethane; mp 75-76°C (AcOEt-*n*-hexane). IR (nujol) 1717, 1670 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 1.25 (9H, s, $C(CH_3)_3$), 3.90 (3H, s, CH_3), 7.26-7.63 (6H, m, aromatic protons), 7.99-8.04 (2H, m, H-2'), 8.11 (1H, dt, J = 8, 1 Hz, H-7). *Anal.* Calcd for $C_{21}H_{21}NO_5S$: C, 63.14; H, 5.30; N, 3.51. Found: C, 63.05; H, 5.24; N, 3.86.

Conversion of 2-Acylindole-3-carboxylic Acid (5) to 2-Acylindole (8)

1) Copper Chromite in Quinoline

2-Benzoyl-1-benzylindole (8a)

A mixture of 2-benzoyl-1-benzylindole-3-carboxylic acid (**5a**)(36 mg, 0.1 mmol) and copper chromite (4 mg) in quinoline (1 mL) was heated to reflux for 20 min. Water was added to the mixture and the aqueous mixture was extracted with CH_2Cl_2. The extracts were washed with water, then with 5% hydrochloric acid and water. The solution was dried over Na_2SO_4 and evaporated off to give a residue, which was purified by column chromatography (*n*-hexane : AcOEt = 10 : 1) to yield 2-benzoyl-1-benzylindole (**8a**)(25 mg, 80%), mp 108-109°C (from AcOEt-*n*-hexane). IR (nujol) 1644 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 5.87 (2H, s, CH_2Ph), 7.06-7.92 (14H, m, aromatic protons). *Anal.* Calcd for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 84.97; H, 5.68; N, 4.55.

2-Acetyl-1-benzylindole (8c)

Using a procedure similar to that described for the preparation of **8a**, **8c** (80%) was obtained from **5a**, mp 129.5-131°C (lit.,[10] mp 130-131.5°C)(MeOH). IR (nujol) 1665 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 2.61 (3H, s, CH_3), 5.86 (2H, s, CH_2Ph), 7.20-7.40 (9H, m, aromatic protons), 7.73 (1H, dt, J = 8, 1 Hz, H-4 or H-7).

2-Acetyl-1-benzenesulfonylindole (8d)

Using a procedure similar to that described for the preparation of **8a**, **8d** (69%) was obtained from **5d**, mp 89-90°C (lit.,[11] mp 89-90°C)(MeOH). IR (nujol) 1690 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 2.65 (3H, s, CH_3), 7.14 (1H, d, J = 1 Hz, H-3), 7.27-7.60 (6H, m, aromatic protons), 7.92-7.99 (2H, m, H-2'), 8.17 (1H, br d, J = 8 Hz, H-4 or H-7).

1-Benzyl-2-pivaloylindole (8e)

Using a procedure similar to that described for the preparation of **8a**, **8e** (88%) was obtained from **5e**, mp 77-78°C (from *n*-hexane). IR (nujol) 1657 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 1.32 (9H, s, $C(CH_3)_3$), 5.69 (2H, s, CH_2Ph), 6.93-7.00 (2H, m, aromtic protons), 7.12-7.39 (7H, m, aromtic protons), 7.74 (1H, dt,

J = 8, 1 Hz, H-4). *Anal.* Calcd for $C_{20}H_{21}NO$: C, 82.43; H, 7.26; N, 4.81. Found: C, 82.27; H, 7.27; N, 4.63.

2) Potassium Hydroxide in Methanol

2-Benzoylindole (8b)

A solution of 1-benzenesulfonyl-2-benzoylindole-3-carboxylic acid (**5b**)(61 mg) in 4N potassium hydroxide solution (0.15 mL) and methanol (1.5 mL) was heated to reflux for 5 h and water was added to the mixture. The aqueous solution was extracted with CH_2Cl_2 and the extracts were washed with water, dried over Na_2SO_4, and evaporated off to give a residue. The residue was purified by column chromatography (*n*-hexane : AcOEt = 20 : 1) to a solid, which was recrystallized from *n*-hexane-$CHCl_3$ to afford 2-benzoylindole (**10b**)(23 mg, 70%), mp 149-150°C (lit.,[12] mp 151-152°C)(from $CHCl_3$-*n*-hexane). IR ($CHCl_3$) 3425, 1625 cm^{-1}; ^1H-nmr ($CDCl_3$) δ: 7.12-7.75 (8H, m, aromtic protons), 7.96-8.02 (2H, m, aromtic protons), 9.28 (1H, br s, NH).

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Received, 21st March, 1997