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SYNTHESIS OF 2- AND 3-BENZOYLINDOLES BY FRIEDEL-CRAFTS REACTION OF INDOLE-2,3-DICARBOXYLIC ANHYDRIDES WITH ANISOLES

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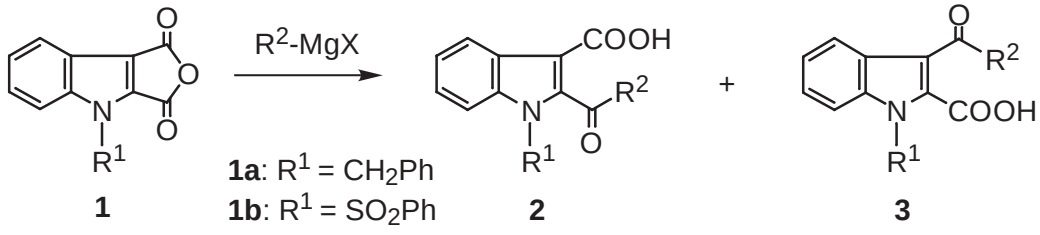
Abstract - Reaction of 1-benzylindole-2,3-dicarboxylic anhydride with anisole in the presence of titanium(IV) chloride gave 2-(4-methoxybenzoyl)indole-3-carboxylic acid as the sole product. However, 1-benzenesulfonylindole-2,3-dicarboxylic anhydride with anisole afforded 3-(4-methoxybenzoyl)indole-2-carboxylic acid. These carboxylic acids could be converted to the corresponding benzoylindoles.

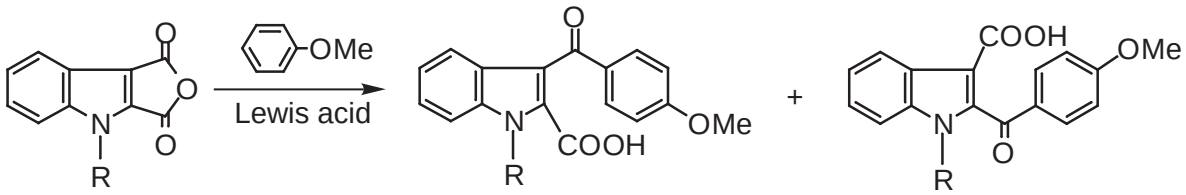
We have shown that the 2-carbonyl group of indole-2,3-dicarboxylic anhydride (**1**) is more reactive than the 3-carbonyl group of that toward Grignard reagents.[1] Reaction of **1** with MeMgBr and PhMgBr gave 2-acylindole-3-carboxylic acids (**2**, R^2 = Me, Ph) as a sole product and 3-acylindole-2-carboxylic acids (**3**, R^2 = Me, Ph) were not isolated, but with *tert*-butylmagnesium chloride afforded a mixture of 2-acylindole-3-carboxylic acid (**2**, R^2 = *t*-Bu) and 3-acylindole-2-carboxylic acid (**3**, R^2 = *t*-Bu) due to the steric hindrance. Similar results were obtained from the reaction of **1** with Wittig reagents.[2,3] We also reported that 1-benzylindole-2,3-dicarboxylic anhydride (**1a**) was a useful synthon in the synthesis of murrayaquinone-A[4] and ellipticine.[5,6] In these reactions, it is quite difficult to obtain **3** as a major product. However, if the reaction of the anhydride (**1**) with a nucleophile is done in the presence of a Lewis acid, the reactivity of the 3-carbonyl group of **1** toward a nucleophile was activated by coordination of an indole nitrogen with the Lewis acid. Herein, we show Friedel-Crafts reaction of **1** with anisoles in the presence of Lewis acid and its application to the synthesis of 2- and 3-benzoylindoles.

Scheme 1



Reaction of 1-benzylindole-2,3-dicarboxylic anhydride (**1a**)[1] with anisole in the presence of aluminum chloride (5 equivalents) gave 1-benzyl-3-(4-methoxybenzoyl)indole-2-carboxylic acid (**4a**) in 79% yield, but 1-benzyl-2-(4-methoxybenzoyl)indole-3-carboxylic acid (**5a**), the isomer of **4a**, was not isolated. (Entry 1) Next, we treated the anhydride (**1a**) with anisole in the presence of titanium(IV) chloride (5 equivalents) as a Lewis acid to provide **4a** in 99% yield. (Entry 2) In the presence of 1 equivalent of titanium(IV) chloride, the yield of **4a** is low (78%) and **1a** was isolated in 19% yield as the corresponding indole-2,3-dicarboxylic acid. (Entry 3) Finally, we obtained **4a** in 93% yield by treatment of **1a** with 1 equivalent of anisole in the presence of 2 equivalents of titanium(IV) chloride. (Entry 4) Boron trifluoride etherate is not effective in this reaction. On the contrary, treatment of 1-benzenesulfonylindole-2,3-dicarboxylic anhydride (**1b**) with anisole in the presence of titanium(IV) chloride afforded 1-benzenesulfonyl-2-(4-methoxybenzoyl)indole-3-carboxylic acid (**5b**) in 81% yield. (Entry 5) In this case, 1-benzenesulfonyl-3-(4-methoxybenzoyl)indole-2-carboxylic acid (**4b**), the isomer of **5b**, was not found. (Scheme 1) These results are shown in Table 1.

Scheme 2



1 **4** **5**

a: R = CH_2Ph
b: R = SO_2Ph

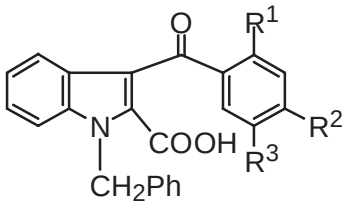
Table 1

Entry	R	Lewis acid (eq)	Anisole (eq)	Yield(%) **4**	**5**
1	CH_2Ph	$AlCl_3$ (5)	5	79	-
2	CH_2Ph	$TiCl_4$ (5)	5	99	-
3	CH_2Ph	$TiCl_4$ (1)	5	78 (19)	-
4	CH_2Ph	$TiCl_4$ (2)	1	93	-
5	SO_2Ph	$TiCl_4$ (2)	1	-	81

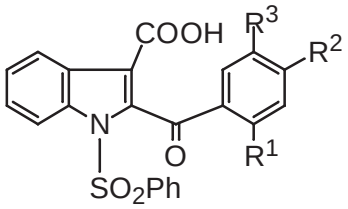
( ): Starting material was recovered as 1-benzylindole-2,3-dicarboxylic acid.

In a similar manner, 1-benzyl-3-(4-methoxybenzoyl)indole-2-carboxylic acids (**4b-e**) and 1-benzenesulfonyl-2-(4-methoxybenzoyl)indole-3-carboxylic acids (**5b-f**) were obtained from the anhydride (**1**). In this reaction, an inseparable mixture of 2-bromo-4-methoxybenzoyl derivatives (**4d**, **5d**) and 4-bromo-2-methoxybenzoyl derivatives (**4e**, **5e**) was isolated from the reaction of the anhydride

(**1a**,**b**) with 3-bromoanisole. However, several efforts were made to obtain the carboxylic acid (**4f**) from **1a** with 4-bromoanisole, but the results were less than satisfactory. These results are shown in Table 2.



4



5

a: R^1, R^3 = H, R^2 = OMe, **b**: R^1, R^2 = OMe, R^3 = H,
c: R^1, R^3 = OMe, R^2 = H, **d**: R^1 = Br, R^2 = OMe, R^3 = H,
e: R^1 = OMe, R^2 = Br, R^3 = H, **f**: R^1 = OMe, R^2 = H, R^3 = Br

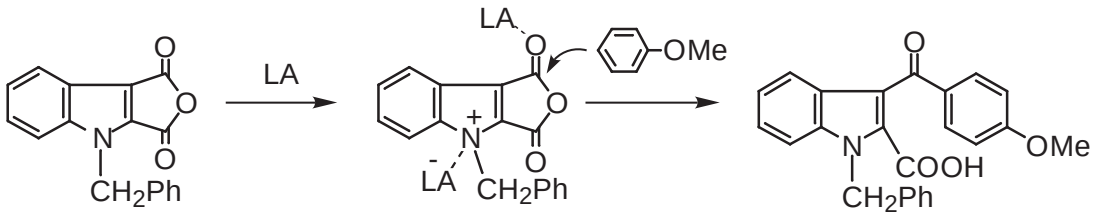
Table 2

Anhydride	R^1	R^2	R^3	Product	Yield(%)
1a	H	OMe	H	**4a**	87
1a	OMe	OMe	H	**4b**	87
1a	OMe	H	OMe	**4c**	72
1a	Br	OMe	H	**4d**	66[a)]
	OMe	Br	H	**4e**	
1b	H	OMe	H	**5a**	98
1b	OMe	OMe	H	**5b**	77
1b	OMe	H	OMe	**5c**	85
1b	Br	OMe	H	**5d**	74
	OMe	Br	H	**5e**	
1b	OMe	H	Br	**5f**	44

a) 5-Equivalents of 3-bromoanisole were used.

A plausible mechanism of the formation of 1-benzyl-3-(4-methoxybenzoyl)indole-2-carboxylic acid (**4a**) is as follows: an indole nitrogen of 1-benzylindole-2,3-dicarboxylic anhydride (**1a**) could react with Lewis acid to produce the intermediate (**6**), which activates the 3-carbonyl group of **1a** by coordination of Lewis acid with an indole nitrogen and a 3-carbonyl oxygen, then anisole could attack the 3-carbonyl group of **1a** to provide **4a**. However, an indole nitrogen of 1-benzenesulfonylindole-2,3-dicarboxylic anhydride (**1b**), which was deactivated by the benzenesulfonyl group, might not coordinate with the Lewis acid. (Scheme 3)

Scheme 3

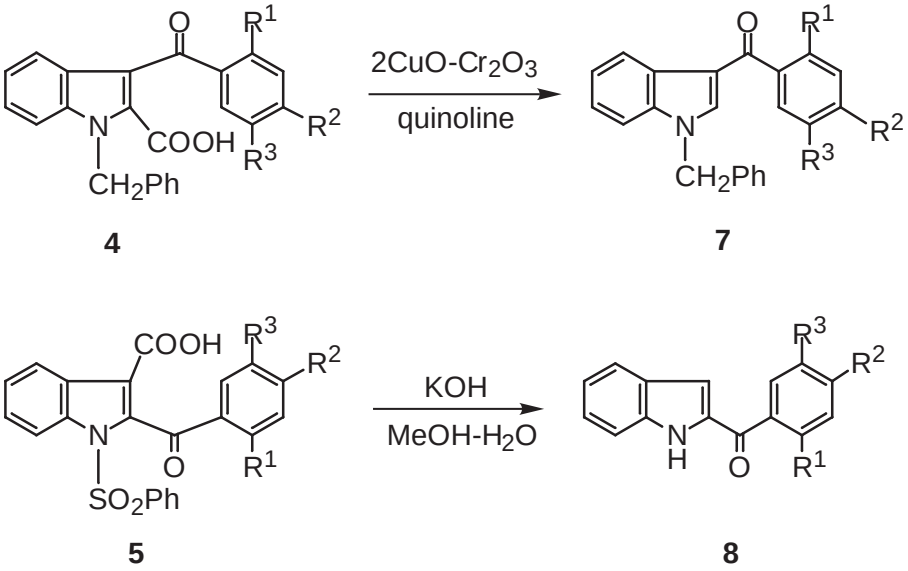


1 **6** **4a**

LA = Lewis acid

Decarboxylation of the 2-carboxylic acids (**4**) was performed in hot quinoline in the presence of copper-chromite ($2CuO \cdot Cr_2O_3$)[1] to afford 1-benzyl-3-(4-methoxybenzoyl)indoles (**7**) in 84-97% yields. In this reaction, a mixture of the carboxylic acids (**4d**) and (**4e**) gave 1-benzyl-3-(2-bromo-4-methoxybenzoyl)indole (**7d**) and 1-benzyl-3-(4-bromo-2-methoxybenzoyl)indole (**7e**) in 39% and 30% yields. Treatment of the 3-carboxylic acids (**5**) under alkaline hydrolysis condition[1] provided 2-(4-methoxybenzoyl)indoles (**8**) in 84-91% yields, respectively. In this conversion condition, 2-(2-bromo-4-methoxybenzoyl)indole (**8d**) and 2-(4-bromo-2-methoxybenzoyl)indole (**8e**) were obtained from a mixture of the carboxylic acids (**5d**) and (**5e**) in 42% and 49% yields. (Scheme 4) These results are shown in Table 3.

Scheme 4



4 **7**

5 **8**

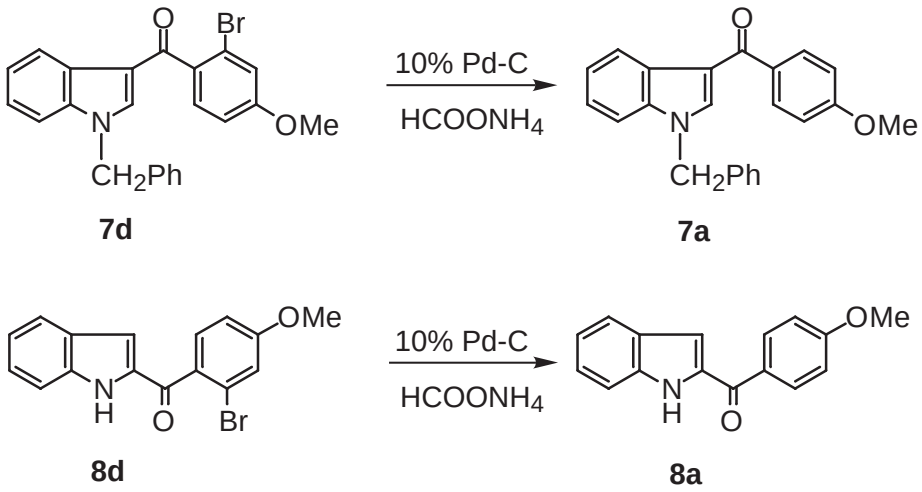
a: R^1, R^3 = H, R^2 = OMe, **b**: R^1, R^2 = OMe, R^3 = H,
c: R^1, R^3 = OMe, R^2 = H, **d**: R^1 = Br, R^2 = OMe, R^3 = H,
e: R^1 = OMe, R^2 = Br, R^3 = H, **f**: R^1 = OMe, R^2 = H, R^3 = Br

Table 3

Carboxylic acid	R^1	R^2	R^3	Product	Yield(%)
4a	H	OMe	H	**7a**	87
4b	OMe	OMe	H	**7b**	97
4c	OMe	H	OMe	**7c**	84
4d,**4e**	Br	OMe	H	**7d**	39
	OMe	Br	H	**7e**	30
5a	H	OMe	H	**8a**	84
5b	OMe	OMe	H	**8b**	89
5c	OMe	H	OMe	**8c**	94
5d,**5e**	Br	OMe	H	**8d**	42
	OMe	Br	H	**8e**	49
5f	OMe	H	Br	**8f**	88

The identification of two isomeric products, 2-bromo-4-methoxybenzoyl derivatives (**7d** and **8d**) and 4-bromo-2-methoxybenzoyl derivatives (**7e** and **8e**), was readily performed by the reduction of **7d** and **8d**. Reduction of 1-benzyl-3-(2-bromo-4-methoxybenzoyl)indole (**7d**) with 10% Pd-C and ammonium formate in hot methanol gave 1-benzyl-3-(4-methoxybenzoyl)indole (**7a**) in 76% yield. In a similar manner, 2-(4-methoxybenzoyl)indole (**8a**) was obtained from **8d** in 77% yield. (Scheme 5)

Scheme 5



7d **7a**

8d **8a**

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). Dichloromethane was distilled from calcium hydride prior to use.

Reaction of Indole-2,3-dicarboxylic Anhydride (1) with Anisoles (General Procedure)

To a solution of indole-2,3-dicarboxylic anhydride (**1a**)[1] (1 mmol) and anisole (1 mmol) in dichloromethane (5 mL) was added titanium(IV) chloride (2 mL of a 1 M dichloromethane solution, 2 mmol) and the mixture was stirred for a few hours at rt. Water was added to the reaction mixture and the mixture was extracted with $CHCl_3$: MeOH (10 : 1). The combined extracts were washed with water and dried over Na_2SO_4, then concentrated under reduced pressure to give a solid. The solid was mixed well with *n*-hexane and collected by filtration or purified by column chromatography ($CHCl_3$: MeOH) to afford (methoxybenzoyl)indolecarboxylic acid.

1-Benzyl-3-(4-methoxybenzoyl)indole-2-carboxylic Acid (4a)

4a; mp 200-201°C (*n*-hexane-AcOEt). IR (Nujol) ν: 1678, 1603 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 3.84 (3H, s, OCH_3), 5.85 (2H, s, CH_2), 7.00-7.77 (13H, m, aromatic protons). *Anal.* Calcd for $C_{24}H_{19}NO_4$: C, 74.79; H, 4.97; N, 3.64. Found: C, 74.81; H, 5.01; N, 3.58.

1-Benzyl-3-(2,4-dimethoxybenzoyl)indole-2-carboxylic Acid (4b)

4b; mp 163-164°C (AcOEt). IR (Nujol) ν: 1716, 1605 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.59 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 6.09 (2H, s, C*H*$_2$Ph), 6.53 (1H, d, *J* = 2 Hz, H-3'), 6.60 (1H, dd, *J* = 9, 2 Hz, H-5'), 6.87-7.33 (8H, m, aromatic protons), 7.45 (1H, br d, *J* = 9 Hz, H-4), 7.50 (1H, d, *J* = 9 Hz, H-6'). *Anal.* Calcd for $C_{25}H_{21}NO_5$: C, 72.28; H, 5.10; N, 3.37. Found: C, 72.25; H, 5.11; N, 3.30.

1-Benzyl-3-(2,5-dimethoxybenzoyl)indole-2-carboxylic Acid (4c)

4c; mp 118-119°C (*n*-hexane-AcOEt). IR (Nujol) ν: 1707 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.57 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 6.13 (2H, s, C*H*$_2$Ph), 6.68 (1H, br d, *J* = 9 Hz, H-3'), 6.97-7.34 (10H, m, aromatic protons), 7.48 (1H, br d, *J* = 9 Hz, H-4). *Anal.* Calcd for $C_{25}H_{21}NO_5$: C, 72.28; H, 5.10; N, 3.37. Found: C, 72.29; H, 5.10; N, 3.41.

1-Benzenesulfonyl-2-(4-methoxybenzoyl)indole-3-carboxylic Acid (5a)

5a; mp 262-264°C (MeOH). IR (Nujol) ν: 1674 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 3.87 (3H, s, OCH_3), 7.02-8.20 (13H, m, aromatic protons). *Anal.* Calcd for $C_{23}H_{17}NO_6S$: C, 63.44; H, 3.94; N, 3.22. Found: C, 63.44; H, 3.99; N, 3.13.

1-Benzenesulfonyl-2-(2,4-dimethoxybenzoyl)indole-3-carboxylic Acid (5b)

5b; mp 272-273°C (acetone). IR (Nujol) ν: 1671, 1644 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 3.50 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 6.60 (1H, d, *J* = 2 Hz, H-3'), 6.71 (1H, dd, *J* = 9, 2 Hz, H-5'), 7.34-8.10 (10H, m, aromatic protons). *Anal.* Calcd for $C_{24}H_{19}NO_7S$: C, 61.93; H, 4.11; N, 3.01. Found: C, 61.83; H, 4.10; N, 3.10.

1-Benzenesulfonyl-2-(2,5-dimethoxybenzoyl)indole-3-carboxylic Acid (5c)

5c; mp 258-260°C (MeOH). IR (Nujol) ν: 1677, 1662 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 3.42 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 7.09 (1H, d, *J* = 9 Hz, H-3'), 7.25 (1H, dd, *J* = 9, 3 Hz, H-4'), 7.37-7.45 (2H, m, aromatic protons), 7.46 (1H, d, *J* = 3 Hz, H-6'), 7.63-8.08 (7H, m, aromatic protons). *Anal.* Calcd for $C_{24}H_{19}NO_7S$: C, 61.93; H, 4.11; N, 3.01. Found: C, 61.90; H, 4.10; N, 3.10.

1-Benzenesulfonyl-2-(5-bromo-2-methoxybenzoyl)indole-3-carboxylic Acid (5f)

5f; mp 272-274°C (MeOH). IR (Nujol) ν: 1680, 1664 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 3.51 (3H, s, OCH_3), 7.15 (1H, d, *J* = 9 Hz, H-3'), 7.35-8.08 (11H, m, aromatic protons). *Anal.* Calcd for $C_{23}H_{16}BrNO_6S$: C, 53.71; H, 3.14; N, 2.72. Found: C, 53.71; H, 3.15; N, 2.75.

Preparation of 3-Methoxybenzoyl-1-benzylindoles (7) from 1-Benzyl-3-methoxybenzoylindole-2-carboxylic Acids (4) by Copper Chromite in Quinoline (General Procedure)

A mixture of 1-benzyl-3-methoxybenzoylindole-2-carboxylic acid (**4**)(0.1 mmol) and copper chromite (4 mg) in quinoline (1 mL) was heated at 150°C for 2-3 h. Water was added to the mixture and the mixture was extracted with dichloromethane. The extracts were washed with water, then with 5% hydrochloric acid and water. The solution was dried over sodium sulfate and evaporated off to give a residue, which was purified by column chromatography (*n*-hexane : AcOEt = 10 : 1) to yield 1-benzyl-3-methoxybenzoylindole (**7**).

1-Benzyl-3-(4-methoxybenzoyl)indole (7a)

7a; mp 173-174°C (acetone). IR (Nujol) ν: 1612 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.87 (3H, s, OCH_3), 5.37 (2H, s, C*H*$_2$Ph), 6.94-7.00 (2H, m, H-3' and H-5'), 7.12-7.36 (8H, m, aromatic protons), 7.63(1H, s, H-2), 7.82-7.87 (2H, m, H-2' and H-6'), 8.36-8.41 (1H, m, H-4). *Anal.* Calcd for $C_{23}H_{19}NO_2$: C, 80.92; H, 5.61; N, 4.10. Found: C, 80.85; H, 5.75; N, 4.15.

1-Benzyl-3-(2,4-dimethoxybenzoyl)indole (7b)

7b; mp 124-125°C (MeOH). IR (Nujol) ν: 1609 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.73 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 5.31 (2H, s, C*H*$_2$Ph), 6.50-6.55 (2H, m, H-3' and H-5'), 7.09-7.43 (9H, m, aromatic protons), 7.50 (1H, s, H-2), 8.34-8.40 (1H, m, H-4). *Anal.* Calcd for $C_{24}H_{21}NO_3$: C, 77.61; H, 5.70; N, 3.77. Found: C, 77.58; H, 5.68; N, 3.81.

1-Benzyl-3-(2,5-dimethoxybenzoyl)indole (7c)

7c; mp 122-123°C (MeOH). IR (Nujol) ν: 1618 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.70 (3H, s, OCH_3), 3.76 (3H, s, OCH_3), 5.30 (2H, s, C*H*$_2$Ph), 6.89-7.33 (11H, m, aromatic protons), 7.50 (1H, s, H-2), 8.37-8.41 (1H, m, H-4). *Anal.* Calcd for $C_{24}H_{21}NO_3$: C, 77.61; H, 5.70; N, 3.77. Found: C, 77.62; H, 5.71; N, 3.81.

1-Benzyl-3-(2-bromo-4-methoxybenzoyl)indole (7d)

7d; mp144-145°C (MeOH). IR (Nujol) ν: 1621 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.85 (3H, s, OCH_3), 5.32 (2H, s, C*H*$_2$Ph), 6.90 (1H, dd, *J* = 9, 2 Hz, H-5'), 7.10-7.14 (2H, m, aromatic protons), 7.18 (1H, d, *J* = 2 Hz, H-3'), 7.26-7.35 (6H, m, aromatic protons), 7.39 (1H, d, *J* = 9 Hz, H-6'), 7.43 (1H, s, H-2), 8.32-8.36 (1H, m, H-4). HRMS *m/z* (M^+) calcd for $C_{23}H_{18}NO_2Br$: 419.0521. Found: 419.0546.

1-Benzyl-3-(4-bromo-2-methoxybenzoyl)indole (7e)

7d; mp178-179°C (MeOH). IR (Nujol) ν: 1612 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.75 (3H, s, OCH_3), 5.31 (2H, s, C*H*$_2$Ph), 7.10-7.34 (12H, m, aromatic protons), 8.34-8.38 (1H, m, H-4). HRMS *m/z* (M^+) calcd for $C_{23}H_{18}BrNO_2Br$: 419.0521. Found: 419.0546.

Preparation of 2-Methoxybenzoylindoles (8) from 1-Benzenesulfonyl-2-methoxybenzoylindole-3-carboxylic Acid (5) by Potassium Hydroxide in MeOH (General Procedure)

A solution of 1-benzenesulfonyl-2-methoxybenzoylindole-3-carboxylic acid (**5**)(0.2 mmol) in 4*N* potassium hydroxide solution (0.2 mL) and MeOH (2 mL) was heated to reflux 6-8 h and water was added to the mixture. The aqueous solution was extracted with dichloromethane and the extracts were washed with water, dried over sodium sulfate, and evaporated off to give a residue. The residue was purified by column chromatography (*n*-hexane : AcOEt = 20 : 1) to afford 2-benzoylindoles (**8**).

2-(4-Methoxybenzoyl)indole (8a)

8a; mp 191-192°C (lit.,[7] mp 190-191°C)($CHCl_3$-*n*-hexane). IR (Nujol) ν: 3492, 1622 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.92 (3H, s, OCH_3), 6.98-7.76 (7H, m, aromatic protons), 8.00-8.08 (2H, m, aromatic protons), 9.32 (1H, br s, NH)

2-(2,4-Dimethoxybenzoyl)indole (8b)

8b; mp139-140°C (*n*-hexane-AcOEt). IR (Nujol) ν: 3308, 1614 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.83 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 6.56 (1H, dd, *J* = 9, 2 Hz, H-5'), 6.57 (1H, d, *J* = 2 Hz, H-3'), 6.94 (1H, dd, *J* = 2, 1 Hz, H-3), 7.10-7.67 (5H, m, aromatic protons), 9.32 (1H, br s, NH). *Anal.* Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.38; N, 4.98. Found: C, 72.59; H, 5.38; N, 4.98.

2-(2,5-Dimethoxybenzoyl)indole (8c)

8c; mp101-102°C (*n*-hexane-AcOEt). IR (Nujol) ν: 3320, 1608 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.78 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 6.95-7.16 (5H, m, aromatic protons), 7.33-7.68 (3H, m, aromatic protons), 9.22 (1H, br s, NH). *Anal.* Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.38; N, 4.98. Found: C, 72.59; H, 5.38; N, 4.98.

2-(2-Bromo-4-methoxybenzoyl)indole (8d)

8d; mp191-192°C (*n*-hexane-AcOEt). IR (Nujol) ν: 3305, 1620 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.89 (3H, s, OCH_3), 6.90 (1H, dd, *J* = 2, 1 Hz, H-3), 6.94 (1H, dd, *J* = 8.5, 2.5 Hz, H-5'), 7.12-7.41 (2H, m, aromatic protons), 7.24 (1H, d, *J* = 2.5 Hz, H-3'), 7.47 (1H, br d, *J* = 8 Hz, H-7 or H-4), 7.54 (1H, d, *J* = 8.5 Hz, H-6'), 7.66 (1H, br d, *J* = 8 Hz, H-4 or H-7), 9.27 (1H, br s, NH). HRMS *m/z* (M^+) calcd for $C_{16}H_{12}NO_2Br$: 329.0052. Found: 329.0019.

2-(4-Bromo-2-methoxybenzoyl)indole (8e)

8e; mp143-144°C (*n*-hexane-AcOEt). IR (Nujol) ν: 3310, 1631 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.83 (3H, s, OCH_3), 6.90 (1H, dd, *J* = 2, 1 Hz, H-3), 7.11-7.67 (7H, m, aromatic protons), 9.23 (1H, br s, NH). HRMS *m/z* (M^+) calcd for $C_{16}H_{12}NO_2Br$: 329.0052. Found: 329.0019.

2-(5-Bromo-2-methoxybenzoyl)indole (8f)

8f; mp151-153°C (*n*-hexane-AcOEt). IR (Nujol) ν: 3276, 1630 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.81 (3H, s, OCH_3), 6.90–7.69 (8H, m, aromatic protons), 9.24 (1H, br s, NH). *Anal.* Calcd for $C_{16}H_{12}NO_2Br$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.18; H, 3.66; N, 4.22.

Preparation of 1-Benzyl-3-(4-methoxybenzoyl)indole (7a) by Reduction of 1-Benzyl-3-(2-bromo-4-methoxybenzoyl)indole (7d)

A mixture of 1-benzyl-3-(2-bromo-4-methoxybenzoyl)indole (**7d**)(21 mg, 0.05 mmol), ammonium formate (19 mg, 0.3 mmol), and 10% Pd-C (4 mg) in MeOH (1 mL) was refluxed for 1 h. The mixture was filtered through Celite and the filtrate was concentrated. The residue was purified by column chromatography ($CHCl_3$) to yield 1-benzyl-3-(4-methoxybenzoyl)indole (**7a**)(13 mg, 76%).

Preparation of 2-(4-Methoxybenzoyl)indole (8a) by Reduction of 2-(2-Bromo-4-methoxybenzoyl)indole (8d)

Using a procedure similar to that described for reduction of **7d**, **8a** (77%) was obtained from **8d**.

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