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ROLE OF 2-NAPHTHYL ETHER INTERMEDIATE IN FORMATION OF ISOLABLE ATROPISOMERS DERIVED FROM THE COUPLING REACTION OF (2-HYDROXY-3,3-DIMETHYLINDOLIN-1-YL)-(SUBSTITUTED PHENYL)METHANONES WITH 2-NAPHTHOL

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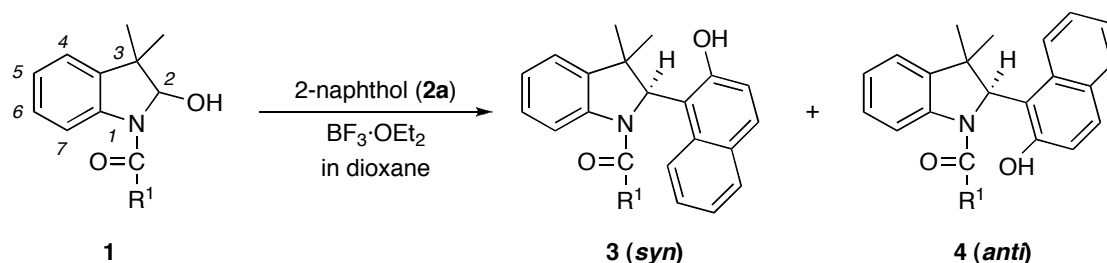
Abstract – The formation pathway of the atropisomers derived from the reaction of (2-hydroxy-3,3-dimethylindolin-1-yl)(4-substituted phenyl)methanones with 2-naphthol in the presence of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ was discussed on the basis of the isolation of the 2-naphthyl ether intermediate whose structure was determined by single crystal X-ray analysis. The results indicate that the coupling reaction proceeds through stepwise mechanism, *i.e.*, the ether intermediate formation followed by Fries-type rearrangement.

INTRODUCTION

In the previous papers,¹ we reported a simple method for synthesis of 2-aryl substituted indoline derivatives based on condensation of (2-hydroxy-3,3-dimethylindolin-1-yl)(substituted phenyl)methanones (so-called, 1-acyl-2-hydroxy-3,3-dimethylindolin, **1**) with various electron-rich aromatic compounds (*e.g.*, 2-naphthol, **2a**) in the presence of boron trifluoride diethyl ether ($\text{BF}_3 \cdot \text{Et}_2\text{O}$).^{1c} The reaction proceeds under mild reaction conditions and provides an important method for synthesis of isolable diastereomeric atropisomers (**3** and **4**) arising from restricted rotation around a $\text{Csp}^3\text{-Csp}^2$ bond (Scheme 1)². We have isolated 16 pairs of atropisomers and clarified important structural features and characterized weak interactions intervened in the restricted rotation.

During the course of the study of the coupling reaction of (2-hydroxy-3,3-dimethylindolin-1-yl)(4-nitrophenyl)methanone (**1a**) with 4-methylphenol (**2b**), we isolated the corresponding ether

derivative (**6ab**) besides the 2-aryl derivative (**7ab**) and the elimination product (**5a**) via the Wagner-Meerwein type rearrangement.

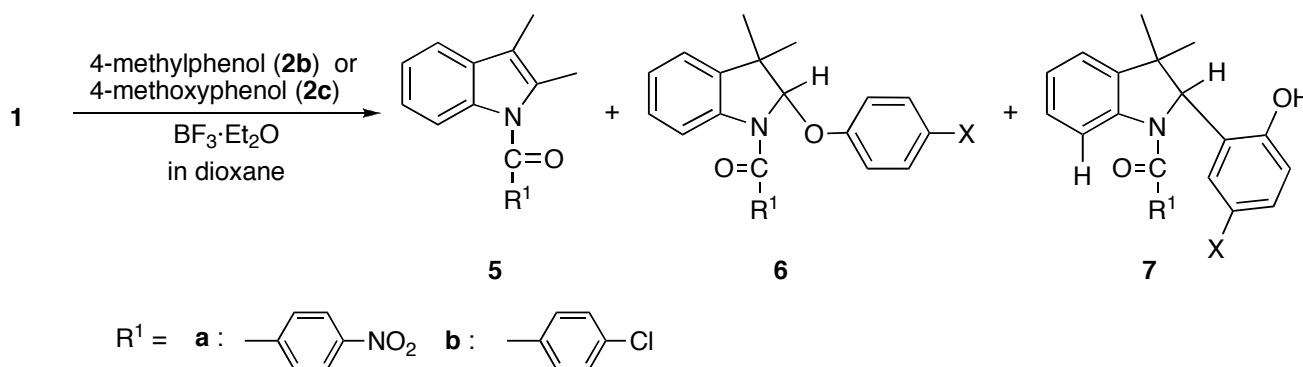


Scheme 1

This paper describes a possible formation pathway of the atropisomers in connection with the isolation of the intermediary phenyl ethers.

RESULTS AND DISCUSSION

The reaction of **1a** (4-nitrophenyl derivative) with 4-methylphenol (**2b**) in the presence of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ at room temperature for 2 hr gave **6ab** and **7ab** in 38 and 24% yields, respectively.



Substrate	Phenol	Solvent	Temp (°C)	Time (h)	6	Yield (%) 7	5
1a	2b	dioxane	rt	0.5	33 (6ab)	19 (7ab)	1 (5a)
1a	2b	dioxane	rt	2	38 (6ab)	24 (7ab)	3 (5a)
1a	2b	dioxane	rt	6	4 (6ab)	66 (7ab)	4 (5a)
1a	2b	Et ₂ O	rt	3	44 (6ab)	-	-
1a	2c	Et ₂ O	rt	3	55 (6ac)	-	-
1b	2b	dioxane	rt	72	-	19 (7bb)	13 (5b)
1b	2b	Et ₂ O	0	2	71 (6bb)	-	-
1b	2c	Et ₂ O	rt	5	-	59 (7bc)	-
1b	2c	Et ₂ O	0	1.5	22 (6bc)	-	-

Scheme 2

The yields of the reaction products under various reaction conditions are summarized in Scheme 2. As can be seen in Scheme 2, the formation of the phenyl ether derivative (**6**) is preferred for short reaction times in ethereal solvents at room temperature and when the reaction was performed under milder reaction conditions, the product ratio (**7/6**) decreased with an increase of the 2-phenyl ether derivative (**6**).

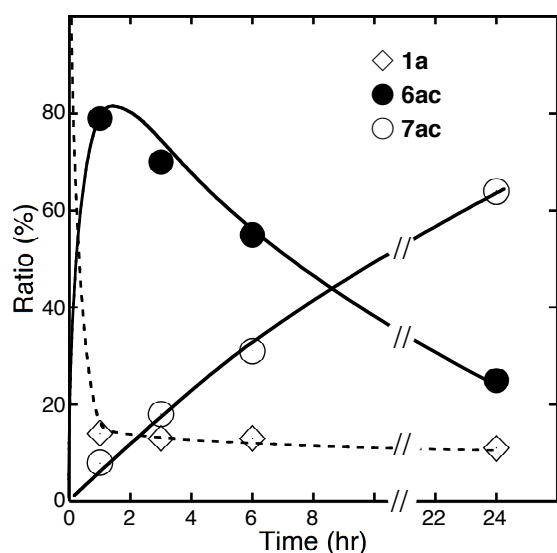
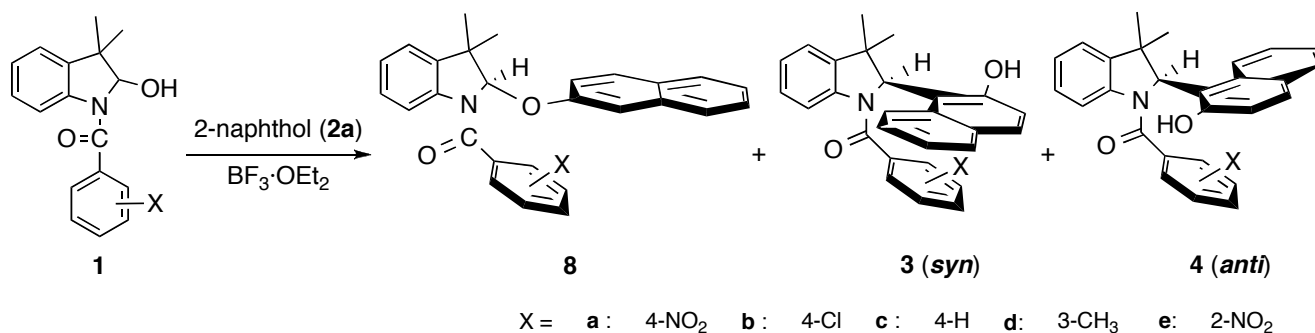


Figure 1. Time Course of Reaction of **1a** with **2c** (6%) and **1a** (6%) in Et₂O in the Presence of BF₃·Et₂O

In order to confirm the isomerization of **6** to **7**, the time-course study in Et₂O was performed. As depicted in Figure 1, at the early stage of the reaction, the 2-phenyl ether (**6ac**) formed rapidly and immediately reached a maximum point, and decreased with increase of the 2-aryl derivative (**7ac**), indicating that the phenol ether derivative is an intermediary product, at least, in the reaction condition used. This assumption is supported by the fact that **6ab** was treated with BF₃·Et₂O in dioxane at room temperature to give the corresponding 2-aryl derivative **7ab** (20%) besides **5a**

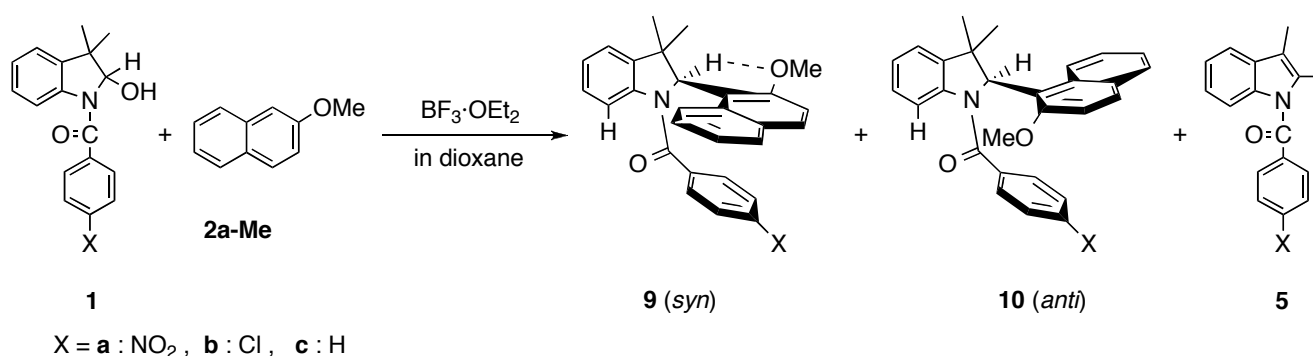


Substrate	Solvent	Temp (°C)	Time (h)	8	Yield (%) 3 (syn)	4 (anti)
1a	dioxane	rt	24	-	27 (3aa)	53 (4aa)
1a	Et ₂ O	0	3	59 (8aa)	-	-
1b	dioxane	rt	24	-	29 (3ba)	45 (4ba)
1b	Et ₂ O	0	3	15 (8ba)	16 (3ba)	28 (4ba)
1c	dioxane	rt	24	-	18 (3ca)	58 (4ca)
1c	Et ₂ O	0	3	8 (8ca)	11 (3ca)	28 (4ca)
1d	dioxane	rt	24	-	38 (3da)	43 (4da)
1d	Et ₂ O	0	3	13 (8da)	12 (3da)	19 (4da)
1e	Et ₂ O	0	3	65 (8ea)	-	-

Scheme 3

Next, we explored the possibility of direct Friedel-Craft type reaction using 2-methoxynaphthol (**2a-Me**) under the reaction conditions used in the previous study (Scheme 5). Inspection of the $^1\text{H-NMR}$ spectrum of the coupling products (**9a** and **10a**) showed a regularly observed characteristic spectral feature attributable to a pair of the atropisomers,^{1b} in which a downfield shift of $>\text{C2-H}$ proton signal was recognized in the *syn* isomer due to $\text{C-H}\cdots\text{O}<$ type weak interaction⁴ [δ 6.13 (*syn*), δ 5.73 (*anti*)].

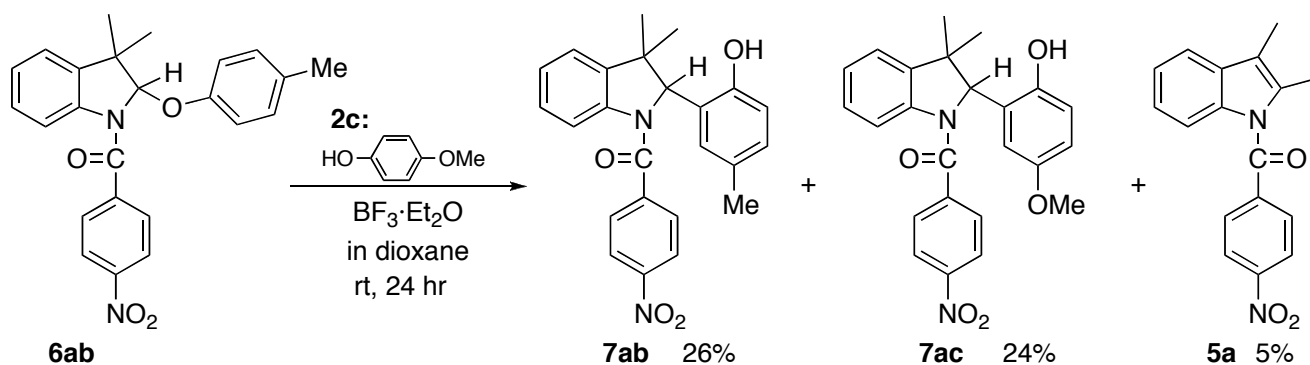
The reaction with **2a-Me** was found to proceed significantly slower than the reaction with **2a**, showing an increase of the elimination product (**5**) via the Wagner-Meerwein type rearrangement. This fact indicates that the product via direct Friedel-Craft reaction is present in only small amounts at least under the reaction condition used.



Substrate	Temp (°C)	Time (h)	Yield (%)		
			9 (syn)	10 (anti)	5
1a	rt	48	12 (9a)	25 (10a)	32 (5a)
1b	rt	70	15 (9b)	65 (10b)	19 (5b)
1c	rt	48	9 (9c)	38 (10c)	21 (5c)

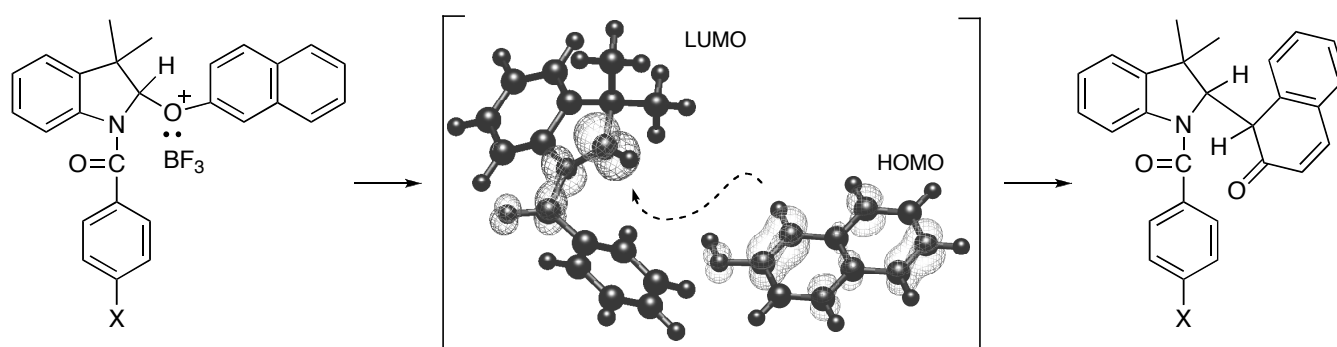
Scheme 5

In the Lewis-acid catalyzed rearrangement of phenolic ethers, evidence has been found for inter- and intramolecular processes.⁵ The intermolecular nature of the reaction was confirmed by the exchange reaction of **6ab** with external-additive 4-methoxyphenol (**2c**). The reaction gave the non-exchanged product (**7ab**) and the exchange product (**7ac**) in 26% and 24% yields, respectively (Scheme 6).



Scheme 6

The result of the exchange reaction suggests that the rearrangement reaction is considered to proceed partly through an intramolecular pathway because the non-exchanged reaction product (formally speaking) persists in the reaction product although there exists a large excess of phenols during the whole reaction period. The non-exchanged reaction product was presumably derived from the internal return of the external ion-pair intermediate (a loosely-dissociated ion-pair intermediate) rather than free ions in view of the low dielectric constant of the solvent (1,4-dioxane, $\epsilon=2.2$) comparable to that of benzene. The recombination behavior of the ion pair may be explained by the primary FMO (frontier molecular orbital) interaction⁶ between the largest LUMO coefficient (C2) of indoline cation and the largest HOMO coefficient (C1) of the naphthol (Scheme 7).



Scheme 7

In conclusion, the formation reaction of the diastereomeric atropisomers in the $\text{BF}_3 \cdot \text{Et}_2\text{O}$ -catalyzed coupling reaction of **1** with **2** proceeds through the 2-naphthyl ether intermediate followed by Fries-type rearrangement.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were measured on a HITACHI 270-30 IR spectrophotometer. NMR spectra were taken with JNM-EX 270, JNM-AL 300, JNM-GX 400 and JNM-A 500 NMR spectrometers in CDCl_3 or $\text{DMSO}-d_6$ solution, using tetramethylsilane (TMS) as an internal standard. Chemical shifts are expressed as δ (ppm) and coupling constants (J) are described as Hz. EI MS and high resolution MS (HR-MS) spectra were measured on a JEOL GC-Mate spectrometer.

Materials (2-Hydroxy-3,3-dimethylindolin-1-yl)(substituted phenyl)methanones (**1a-e**) were prepared by addition of substituted benzoyl chloride to 3,3-dimethyl-3*H*-indole followed by treatment of the corresponding 2-chloro derivatives with water.^{1c} Phenols were commercially available compounds.

Reaction of 1 with phenolic compounds 2 (General procedure) $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (10.0 mmol) was added to

a solution of (2-hydroxy-3,3-dimethylindolin-1-yl)(substituted phenyl)methanones (**1**) (2.0 mmol) and phenols (**2**) (4.0 mmol) in dry dioxane (10 mL) and the mixture was heated at given temperature under an Ar atmosphere until the reaction had completed by TLC. After cooling, the reaction mixture was diluted with Et₂O (200 mL) and treated with water. The organic layer was separated, washed with aqueous NaHCO₃ solution and dried over anhydrous MgSO₄. The Et₂O was evaporated off. The residue was chromatographed on silica gel eluting with benzene/EtOAc (100:1). The products separated were crystallized from appropriate solvent.

Reaction of 1a with monocyclic phenols (2b-c) According to the general procedure, the reaction of **1a** (2.0 mmol) with monocyclic phenols in dry dioxane (at rt) or ether (at 0 °C or rt) was carried out in the presence of BF₃·Et₂O for given hour to give **6**, **7** and **5a**.

[3,3-Dimethyl-2-(4-tolyloxy)indolin-1-yl](4-nitrophenyl)methanone (6ab) Yellow plates from EtOH; mp 176-179 °C; ¹H-NMR (300 MHz, CDCl₃) δ: 1.38 (3H, s, C3-Me), 1.43 (3H, s, C3-Me), 2.26 (3H, s, C_{Ar}4-Me), 5.66 (1H, s, C2-H), 6.52 (2H, br s, C_{Ar}2, C_{Ar}6-H), 6.92 (2H, d, *J* = 8.3 Hz, C_{Ar}3, C_{Ar}5-H), 7.19-7.29 (3H, m, C4, C5, C6-H), 7.41 (2H, d, *J* = 8.6 Hz, C_{COAr}2, C_{COAr}6-H), 8.02 (3H, br d, *J* = 8.6 Hz, C_{COAr}3, C_{COAr}5-H, C7-H); MS *m/z*: 402 (M⁺); *Anal.* Calcd for C₂₄H₂₂N₂O₄: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.14; H, 5.49; N, 6.73; IR (KBr) cm⁻¹: 1666 (NC=O), 1601 (C=C), 1478, 1344 (NO₂).

[2-(2-Hydroxy-5-methylphenyl)-3,3-dimethyl-indolin-1-yl](4-nitrophenyl)methanone (7ab) Pale yellow powder from EtOH; mp 273-279 °C; ¹H-NMR (300 MHz, DMSO-*d*₆) δ: 0.92 (3H, s, C3-Me), 1.41 (3H, s, C3-Me), 2.05 (3H, s, C_{Ar}5-Me), 5.26 (1H, s, C2-H), 6.43 (1H, s, C_{Ar}6-H), 6.48 (1H, br d, *J* = 7.9 Hz, C_{Ar}4-H), 6.81 (1H, d, *J* = 7.9 Hz, C_{Ar}3-H), 7.18-7.37 (5H, m, aromatic C-H), 8.11 (2H, br s, C_{COAr}3, C_{COAr}5-H), 8.26 (1H, br s, C7-H), 9.00 (1H, br s, C_{Ar}2-OH); MS *m/z*: 402 (M⁺); *Anal.* Calcd for C₂₄H₂₂N₂O₄: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.81; H, 5.47; N, 7.16; IR (KBr) cm⁻¹: 3420 (OH), 1630 (NC=O), 1601 (C=C), 1524, 1348 (NO₂).

[2-(4-Methoxyphenoxy)-3,3-dimethylindolin-1-yl](4-nitrophenyl)methanone (6ac) Yellow plates from EtOH; mp 129-131 °C; ¹H-NMR (300 MHz, CDCl₃) δ: 1.39 (3H, s, C3-Me), 1.47 (3H, s, C3-Me), 3.75 (3H, s, C_{Ar}4-OMe), 5.62 (1H, br s, C2-H), 6.58 (2H, br s, C_{Ar}2, C_{Ar}6-H), 6.66 (2H, d, *J* = 8.9 Hz, C_{Ar}3, C_{Ar}5-H), 7.20-7.26 (3H, m, C4, C5, C6-H), 7.34 (2H, d, *J* = 8.3 Hz, C_{COAr}2, C_{COAr}6-H), 8.05 (3H, br d, *J* = 8.3 Hz, C_{Ar}3, C_{Ar}5-H, C7-H); MS *m/z*: 418 (M⁺); *Anal.* Calcd for C₂₄H₂₂N₂O₅: C, 68.89; H, 5.30; N, 6.69. Found: C, 68.82; H, 5.27; N, 6.57; IR (KBr) cm⁻¹: 1648 (NC=O), 1596 (C=C), 1518, 1344 (NO₂).

[2-(2-Hydroxy-5-methoxyphenyl)-3,3-dimethylindolin-1-yl](4-nitrophenyl)methanone (7ac) Yellow needles from EtOH; mp 253-254 °C; ¹H-NMR (300MHz, DMSO-*d*₆) δ: 0.93 (3H, s, C3-Me), 1.41 (3H, s, C3-Me), 3.51 (3H, s, C_{Ar}5-OMe), 5.23 (1H, s, C2-H), 6.14 (1H, d, *J* = 2.9 Hz, C_{Ar}6-H), 6.55 (1H, br d, *J* = 8.6 Hz, C_{Ar}3-H), 6.64 (1H, dd, *J* = 2.9, 8.6 Hz, C_{Ar}4-H), 7.18-7.29 (3H, m, C4, C5, C6-H), 7.38 (2H, br s, C_{COAr}2, C_{COAr}6-H), 8.13 (2H, br s, C_{COAr}3, C_{COAr}5-H), 8.24 (1H, br s, C7-H), 8.81 (1H, br s,

C_{Ar}2-OH); MS m/z: 418 (M⁺); *Anal.* Calcd for C₂₄H₂₂N₂O₅: C, 68.89; H, 5.30; N, 6.69. Found: C, 68.72; H, 5.24; N, 6.84; IR (KBr) cm⁻¹: 3448 (OH), 1634 (NC=O), 1592 (C=C), 1508, 1346 (NO₂).

(4-Chlorophenyl)[3,3-dimethyl-2-(4-tolyloxy)indolin-1-yl]methanone (6bb) Colorless prisms from EtOH; mp 154-156 °C; ¹H-NMR (300MHz, CDCl₃) δ: 1.35 (3H, s, C3-Me), 1.42 (3H, s, C3-Me), 2.28 (3H, s, C_{Ar}4-Me), 5.77 (1H, s, C2-H), 6.57 (2H, d, *J*= 7.7 Hz, C_{Ar}2, C_{Ar}6-H), 6.96 (2H, d, *J*= 8.4 Hz, C_{COAr}3, C_{COAr}5-H), 7.12-7.25 (3H, m, C4, C5, C6-H), 7.17 (2H, d, *J*= 8.4 Hz, C_{COAr}3, C_{COAr}5-H), 7.24 (2H, d, *J*= 7.7 Hz, C_{Ar}2, C_{Ar}6-H), 7.80 (1H, br s, C7-H); MS m/z: 391 (M⁺); *Anal.* Calcd for C₂₄H₂₂ClNO₂: C, 73.56; H, 5.66; N, 3.57. Found: C, 73.85; H, 5.70; N, 3.47; IR (KBr) cm⁻¹: 1666 (NC=O), 1594 (C=C).

(4-Chlorophenyl)[2-(2-hydroxy-5-methylphenyl)-3,3-dimethylindolin-1-yl]methanone (7bb)

Colorless powder from EtOH; mp 228-230 °C; ¹H-NMR (300 MHz, DMSO-*d*₆) δ: 0.93 (3H, s, C3-Me), 1.40 (3H, s, C3-Me), 2.03 (3H, s, C_{Ar}5-Me), 5.35 (1H, s, C2-H), 6.42 (1H, s, C_{Ar}6-H), 6.59 (1H, br s, C_{Ar}4-H), 6.81 (1H, d, *J*= 7.9 Hz, C_{Ar}3-H), 7.16-7.36 (7H, m, aromatic C-H), 8.22 (1H, br s, C7-H), 9.18 (1H, br s, C_{Ar}2-OH); MS m/z: 391 (M⁺); *Anal.* Calcd for C₂₄H₂₂ClNO₂: C, 73.56; H, 5.66; N, 3.57. Found: C, 73.41; H, 5.45; N, 3.57; IR (KBr) cm⁻¹: 3500-3200 (OH), 1622 (NC=O), 1588 (C=C).

(4-Chlorophenyl)[2-(4-methoxyphenoxy)-3,3-dimethylindolin-1-yl]methanone (6bc) Colorless prisms from EtOH; mp 154-156 °C; ¹H-NMR (300MHz, CDCl₃) δ: 1.37 (3H, s, C3-Me), 1.46 (3H, s, C3-Me), 3.77 (3H, s, C_{Ar}4-OMe), 5.73 (1H, s, C2-H), 6.62 (2H, br s C_{Ar}2, C_{Ar}6-H), 6.70 (2H, br s C_{Ar}3, C_{Ar}5-H), 7.07-7.52 (7H, m, aromatic C-H), 7.83 (1H, br s C7-H). MS m/z: 407 (M⁺); *Anal.* Calcd for C₂₄H₂₂ClNO₃: C, 70.67; H, 5.44; N, 3.43. Found: C, 70.80; H, 5.41; N, 3.41; IR (KBr) cm⁻¹: 1658 (NC=O), 1592 (C=C).

(4-Chlorophenyl)[2-(2-hydroxy-5-methoxyphenyl)-3,3-dimethylindolin-1-yl]-methanone (7bc)

Colorless powder from EtOH; mp 248-249°C; ¹H-NMR (300 MHz, DMSO-*d*₆) δ: 0.93 (3H, s, C3-Me), 1.38 (3H, s, C3-Me), 3.48 (3H, s, C_{Ar}5-OMe), 5.32 (1H, s, C2-H), 6.13 (1H, s, C_{Ar}6-H), 6.61 (2H, s, C_{Ar}3, C_{Ar}4-H), 7.10-7.39 (7H, m, aromatic C-H), 8.18 (1H, br s, C7-H), 9.00 (1H, br s, C_{Ar}2-OH); MS m/z: 407 (M⁺); *Anal.* Calcd for C₂₄H₂₂ClNO₃: C, 70.67; H, 5.44; N, 3.43. Found: C, 70.35; H, 5.44; N, 3.43; IR (KBr) cm⁻¹: 3500-3300 (OH), 1628 (NC=O), 1590 (C=C).

Catalytic Rearrangement of 6ab to 7ab A solution of **6ab** (1.0 mmol) in dry dioxane (5 mL) containing BF₃·Et₂O (5.0 mmol) was stirred at room temperature for 24 hr. The same work-up as described in the general procedure gave **7ab**, **5a** and **1a**.

Phenol-exchange reaction of 6ab A solution of **6ab** (0.5 mmol) and **2c** (0.5 mmol) in dry dioxane (5 mL) containing BF₃·Et₂O (2.5 mmol) was stirred at rt for 24 h. The same work-up as described in the general procedure gave **7ab**, **7ac** and **5a**.

Time Course of reaction of 1a with 2c BF₃·Et₂O (10.0 mmol) was added to a solution of **1a** (2.0 mmol) and *p*-methoxyphenols (**2c**) (4.0 mmol) in dry Et₂O (10 mL) and the mixture was stirred at 0 °C under an Ar atmosphere. At appropriate intervals of time, a small amount of the reaction mixture was

withdrawn by a syringe, quenched with water, and extracted with Et₂O. After evaporation of the solvent under reduced pressure, the residue was analyzed by ¹H-NMR. The relative ratio of the reaction product (**6ac**, **7ac**) and **1a** were evaluated by the spectral integration of the methyl group.

Reaction of 1a-e with 2a (Formation of the naphthyl ether 8aa-ea) A solution of **1a** (1.0 mmol) and **2a** (1.0 mmol) in dry dioxane (5 mL) containing BF₃·Et₂O (5.0 mmol) was stirred at 0 °C. The same work-up as described in the general procedure gave **8aa**. Similarly, the reactions of **1b-e** with **2a** gave the corresponding products, respectively.

[3,3-Dimethyl-2-(naphthalen-2-yloxy)indolin-1-yl](4-nitrophenyl)methanone (8aa) Yellow plates from EtOH; mp 154-156 °C; ¹H-NMR (300 MHz, CDCl₃) δ: 1.45 (3H, s, C3-Me), 1.48 (3H, s, C3-Me), 5.92 (1H, br s, C2-H), 6.91-7.85 (15H, m, aromatic C-H); MS m/z: 438 (M⁺), 295 (M⁺-143); *Anal.* Calcd. for C₂₇H₂₂N₂O₄: C, 73.96; H, 5.06; N, 6.39. Found: C, 74.04; H, 5.00; N, 6.41; IR (KBr) cm⁻¹: 1660 (NC=O), 1480, 1346 (NO₂), 998 (-O-).

(4-Chlorophenyl)[3,3-dimethyl-2-(naphthalen-2-yloxy)-indolin-1-yl]methanone (8ba) Colorless prisms from EtOH, mp 159-161 °C; ¹H-NMR (300 MHz, CDCl₃) δ (ppm): 1.41 (3H, s, C3-Me), 1.46 (3H, s, C3-Me), 6.01 (1H, s, C2-H), 6.90-7.77 (15H, m, aromatic C-H); MS m/z : 427 (M⁺), 284 (M⁺-143); *Anal.* Calcd. for C₂₇H₂₂ClNO₂: C, 75.78; H, 5.18; N, 3.27. Found: C, 75.72; H, 4.96; N, 3.17; IR (KBr) cm⁻¹: 3160-2850 (aromatic C-H), 1662 (NC=O), 1594 (C=C), 1002 (-O-).

[3,3-Dimethyl-2-(naphthalen-2-yloxy)indolin-1-yl]-(phenyl)methanone (8ca) Colorless prisms from EtOH, mp 107-108 °C; ¹H-NMR (300 MHz, CDCl₃) δ (ppm): 1.41 (3H, s, C3-Me), 1.44 (3H, s, C3-Me), 6.04 (1H, s, C2-H), 6.84-7.74 (15H, m, aromatic C-H), 7.75 (1H, brs, C7-H); MS m/z: 393 (M⁺), 250 (M⁺-143); *Anal.* Calcd. for C₂₇H₂₃NO₂: C, 82.42; H, 5.89; N, 3.56. Found: C, 82.63; H, 5.91; N, 3.61; IR (KBr) cm⁻¹: 3050-2800 (aromatic C-H), 1656 (NC=O), 1596 (C=C), 992 (-O-).

[3,3-Dimethyl-2-(naphthalen-2-yloxy)indolin-1-yl](3-tolyl)methanone (8da) Colorless powder from EtOH, mp 109-111 °C; ¹H-NMR (300 MHz, CDCl₃) δ (ppm): 1.41 (3H, s, C3-Me), 1.44 (3H, s, C3-Me), 1.86 (3H, s, C_{Ar}-3-Me), 6.00 (1H, s, C2-H), 6.84-7.75 (14H, m, aromatic C-H), 7.93 (1H, brs, C7-H); MS m/z: 407 (M⁺), 264 (M⁺-143); *Anal.* Calcd. for C₂₈H₂₅NO₂: C, 82.53; H, 6.18; N, 3.44. Found: C, 82.28; H, 6.10; N, 3.26; IR (KBr) cm⁻¹: 3052-2868 (aromatic C-H), 1660 (NC=O), 1596 (C=C), 990 (-O-).

[3,3-Dimethyl-2-(naphthalen-2-yloxy)indolin-1-yl](2-nitrophenyl)methanone (8ea) Yellow plates from EtOH, mp 158-160 °C; ¹H-NMR (300 MHz, CDCl₃) δ (ppm): 1.36 (3H, s, C3-Me), 1.44 (3H, s, C3-Me), 5.64 (1H, brs, C2-H), 6.45-8.30 (14H, m, aromatic C-H), 8.00 (1H, brs, C7-H); MS m/z: 438 (M⁺), 295 (M⁺-143). *Anal.* Calcd. for C₂₇H₂₂N₂O₄: C, 73.96; H, 5.06; N, 6.39. Found: C, 73.69; H, 4.96; N, 6.49. IR (KBr) cm⁻¹: 3100-2950 (aromatic C-H), 1664 (NC=O), 1598 (C=C), 1484, 1350 (NO₂), 1006 (-O-).

Catalytic Rearrangement of 8aa to 3aa and 4aa A solution of **8aa** (0.7 mmol) in dry dioxane (5 mL)

containing $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (5.0 mmol) was stirred at rt or 60 °C for 24 h. The same work-up as described in the general procedure gave **3aa**, **4aa**, **5a** and **1a**.

Reaction of 1a-c with 2-methoxynaphthalene 2a-Me A solution of **1a-c** (1.0 mmol) and **2a-Me** (1.0 mmol) in dry dioxane (5 mL) containing $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (5.0 mmol) was stirred at rt. The same work-up as described in the general procedure gave **5a-c**, **9a-c** and **10a-c**.

[2-(2-Methoxynaphthalen-1-yl)-3,3-dimethylindolin-1-yl](4-nitrophenyl)methanone (9a) (syn) Pale yellow prisms from EtOH; mp 210-211 °C; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ : 0.98 (3H, s, C3-Me), 1.60 (3H, s, C3-Me), 3.60 (3H, s, C_{naph} 2-OMe), 6.13 (1H, s, C2-H), 6.72-7.79 (13H, m, aromatic C-H), 8.51 (1H, d, J = 7.9 Hz, C7-H); MS m/z : 452 (M^+). *Anal.* Calcd for $\text{C}_{28}\text{H}_{24}\text{N}_2\text{O}_4$: C, 74.32; H, 5.35; N, 6.19. Found: C, 74.39; H, 5.11; N, 6.25; IR (KBr) cm^{-1} : 1644 (NC=O), 1594 (C=C), 1514, 1346 (NO_2).

[2-(2-Methoxynaphthalen-1-yl)-3,3-dimethylindolin-1-yl](4-nitrophenyl)methanone (10a) (anti) Yellow prisms from EtOH; mp 175-176 °C; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ : 1.01 (3H, s, C3-Me), 1.63 (3H, s, C3-Me), 3.48 (3H, s, C_{naph} 2-OMe), 5.73 (1H, s, C2-H), 6.89 (1H, d, J = 8.3 Hz, C_{naph} 3-H), 7.13-7.36 (7H, m, aromatic C-H), 7.23 (1H, d, J = 8.3 Hz, C_{naph} 4-H), 7.55 (2H, d, J = 8.6 Hz, C_{Ar} 2, C_{Ar} 6-H), 7.73 (2H, d, J = 8.6 Hz, C_{Ar} 3, C_{Ar} 5-H), 8.51 (1H, d, J = 7.9 Hz, C7-H); MS m/z : 452 (M^+); *Anal.* Calcd for $\text{C}_{28}\text{H}_{24}\text{N}_2\text{O}_4$: C, 74.32; H, 5.35; N, 6.19. Found: C, 74.04; H, 5.20; N, 6.20; IR (KBr) cm^{-1} : 1642 (NC=O), 1596 (C=C), 1520, 1346 (NO_2).

(2,3-Dimethyl-1H-indol-1-yl)(4-nitrophenyl)methanone (5a) Yellow oil; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ : 2.22 (3H, s, C3-Me), 2.30 (3H, s, C2-Me), 6.96 (1H, d, J = 8.4 Hz, C4-H), 7.04 (1H, dd, J = 8.1, 8.4 Hz, C5-H), 7.19 (1H, dd, J = 7.7, 8.1 Hz, C6-H), 7.43 (1H, d, J = 7.7 Hz, C7-H), 7.83 (2H, d, J = 8.8 Hz, C_{Ar} 2, C_{Ar} 6-H), 8.31 (2H, d, J = 8.8 Hz, C_{Ar} 3, C_{Ar} 5-H); MS m/z : 294 (M^+); IR (film) cm^{-1} : 1684 (NC=O), 1602 (C=C), 1522, 1342 (NO_2).

(4-Chlorophenyl)[2-(2-methoxynaphthalen-1-yl)-3,3-dimethylindolin-1-yl]methanone (9b) (syn) Colorless prisms from EtOH; mp 181-182 °C; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ : 0.97 (3H, s, C3-Me), 1.58 (3H, s, C3-Me), 3.66 (3H, s, C_{naph} 2-OMe), 6.16 (1H, s, C2-H), 6.58-7.71 (13H, m, aromatic C-H), 8.47 (1H, br s, C7-H); MS m/z : 441 (M^+); *Anal.* Calcd for $\text{C}_{28}\text{H}_{24}\text{ClNO}_2$: C, 76.08; H, 5.48; N, 3.17. Found: C, 75.67; H, 5.41; N, 3.44; IR (KBr) cm^{-1} : 1642 (NC=O), 1596 (C=C).

(4-Chlorophenyl)[2-(2-methoxynaphthalen-1-yl)-3,3-dimethylindolin-1-yl]methanone (10b) (anti) Colorless needles from EtOH; mp 169-170 °C; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ : 0.98 (3H, s, C3-Me), 1.61 (3H, s, C3-Me), 3.44 (3H, s, C_{naph} 2-OMe), 5.82 (1H, s, C2-H), 6.70-7.73 (13H, m, aromatic C-H), 8.37 (1H, br s, C7-H); MS m/z : 441 (M^+); *Anal.* Calcd for $\text{C}_{28}\text{H}_{24}\text{ClNO}_2$: C, 76.08; H, 5.48; N, 3.17. Found: C, 76.04; H, 5.45; N, 3.19; IR (KBr) cm^{-1} : 1620 (NC=O), 1592 (C=C).

[2-(2-Methoxynaphthalen-1-yl)-3,3-dimethylindolin-1-yl](phenyl)methanone (9c) (syn) Colorless prisms from EtOH; mp 145-147 °C; $^1\text{H-NMR}$ (300 MHz, $\text{DMSO}-d_6$) δ : 0.97 (3H, s, C3-Me), 1.59 (3H, s,

C3-Me), 3.58 (3H, s, C_{naph}-2-OMe), 6.23 (1H, br s, C2-H), 6.65-7.70 (14H, m, aromatic C-H), 8.52 (1H, br s, C7-H); MS m/z: 407 (M⁺); *Anal.* Calcd. for C₂₈H₂₅NO₂: C, 82.53 ; H, 6.18 ; N, 3.44. Found: C, 82.33; H, 6.13; N, 3.43; IR (KBr) cm⁻¹: 1638 (NC=O), 1594 (C=C).

[2-(2-Methoxynaphthalen-1-yl)-3,3-dimethylindolin-1-yl](phenyl)methanone (10c) (*anti*) Colorless prisms from EtOH; mp 185-187 °C; ¹H-NMR (300 MHz, DMSO-*d*₆) δ: 0.95 (3H, s, C3-Me), 1.62 (3H, s, C3-Me), 3.46 (3H, s, C_{naph}-2-OMe), 5.90 (1H, br s, C2-H), 6.65-7.70 (14H, m, aromatic C-H), 8.41 (1H, br s, C7-H); MS m/z: 407 (M⁺); *Anal.* Calcd. for C₂₈H₂₅NO₂: C, 82.53 ; H, 6.18 ; N, 3.44. Found: C, 82.33 ; H, 6.13 ; N, 3.43. IR (KBr) cm⁻¹: 638 (NC=O), 1594 (C=C).

Single Crystal X-Ray Analysis of 8aa A colorless prismatic crystal having approximate dimensions of 0.10 x 0.20 x 0.10 mm of **8aa** was mounted on a glass fiber. All measurements were made on a Rigaku AFC7R four-circle autodiffractometer with graphite monochromated Mo-Kα radiation. The data were collected at a temperature of 20 ± 1 °C to a maximum 2θ value of 55.0°. The structure was solved by direct method (SIR-92⁷), and hydrogen atoms were placed at the calculation. A full-matrix least-squares technique was using with anisotropic thermal parameters for non-hydrogen atoms and riding model for hydrogen atoms. All calculations were performed using the Crystal Structure⁷ crystallographic software package.

Crystal Data of **8aa**: Crystal Data; C₂₇H₂₂N₂O₄, M=438.47, monoclinic, Space group *P2₁/a*, a=12.281 (2), b=20.134 (5), c=9.854 (1) Å, β=111.39 (1), V=2268 (7) Å³, D_c=1.284 g cm⁻³, Z=4, R=0.057, R_w=0.094. The X-Ray crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC ref. No. 702823).

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