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 BF₃•Et₂O 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 (BF₃•Et₂O).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 Csp²-Csp² 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.

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 BF₃•Et₂O at room temperature for 2 hr gave 6ab and 7ab in 38 and 24% yields, respectively.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Phenol</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>6</th>
<th>7</th>
<th>5</th>
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<tr>
<td>1a</td>
<td>2b</td>
<td>dioxane</td>
<td>rt</td>
<td>0.5</td>
<td>33 (6ab)</td>
<td>19 (7ab)</td>
<td>1 (5a)</td>
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<tr>
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<td>rt</td>
<td>2</td>
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<td>24 (7ab)</td>
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<td>rt</td>
<td>6</td>
<td>4 (6ab)</td>
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<tr>
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<td>Et₂O</td>
<td>rt</td>
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<td>44 (6ab)</td>
<td>-</td>
<td>-</td>
<td></td>
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<tr>
<td>1a</td>
<td>2c</td>
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<td>55 (6ac)</td>
<td>-</td>
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<tr>
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<td>-</td>
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<td>2</td>
<td>71 (6bb)</td>
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<tr>
<td>1b</td>
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<td>rt</td>
<td>5</td>
<td>-</td>
<td>59 (7bc)</td>
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<td>1b</td>
<td>2c</td>
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<td>1.5</td>
<td>22 (6bc)</td>
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</table>

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).

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 (6%) and 1a (6%).

Figure 1. Time Course of Reaction of 1a with 2c in Et₂O in the Presence of BF₃·Et₂O

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>4 (anti)</th>
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</thead>
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<tr>
<td>1a</td>
<td>dioxane</td>
<td>rt</td>
<td>24</td>
<td>-</td>
<td>27 (3aa) 53 (4aa)</td>
</tr>
<tr>
<td>1a</td>
<td>Et₂O</td>
<td>0</td>
<td>3</td>
<td>59 (8aa)</td>
<td>-</td>
</tr>
<tr>
<td>1b</td>
<td>dioxane</td>
<td>rt</td>
<td>24</td>
<td>-</td>
<td>29 (3ba) 45 (4ba)</td>
</tr>
<tr>
<td>1b</td>
<td>Et₂O</td>
<td>0</td>
<td>3</td>
<td>15 (8ba)</td>
<td>16 (3ba) 28 (4ba)</td>
</tr>
<tr>
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<td>dioxane</td>
<td>rt</td>
<td>24</td>
<td>-</td>
<td>18 (3ca) 58 (4ca)</td>
</tr>
<tr>
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<td>Et₂O</td>
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<td>3</td>
<td>8 (8ca)</td>
<td>11 (3ca) 28 (4ca)</td>
</tr>
<tr>
<td>1d</td>
<td>dioxane</td>
<td>rt</td>
<td>24</td>
<td>-</td>
<td>38 (3da) 43 (4da)</td>
</tr>
<tr>
<td>1d</td>
<td>Et₂O</td>
<td>0</td>
<td>3</td>
<td>13 (8da)</td>
<td>12 (3da) 19 (4da)</td>
</tr>
<tr>
<td>1e</td>
<td>Et₂O</td>
<td>0</td>
<td>3</td>
<td>65 (8ea)</td>
<td>-</td>
</tr>
</tbody>
</table>

Scheme 3
In the case of 2-naphthol (2a), we have not yet isolated \([3,3\text{-dimethyl-2-(naphthalen-2-yloxy)}\text{-indolin-1-yl}]\)[4-nitrophenyl)methanone (8aa). Therefore the reaction was reexamined under reaction conditions similar to those used for monocyclic phenols described above.

When the reaction was carried out in an ice bath using diethyl ether as solvent, we found that the 2-naphthyl ether compound (8aa) was produced in 59% yield. Similarly, 2-nitrobenzoyl derivative (1e) gave only the 2-naphthyl ether (8ea) in good yield. On the other hand, the 4-chlorobenzoyl (1b), benzoyl (1c) and 3-methylbenzoyl (1d) derivatives of 1 gave mixtures of the ether derivative and a pair of atropisomers (Scheme 3).

The structure of 8aa was confirmed by single crystal X-ray analysis. The computer-generated molecular structure is depicted in Figure 2.

The ether 8aa was treated with BF₃·Et₂O to give a mixture of syn and anti atropisomers (3aa, 4aa) besides 5a and 1a (Scheme 4). The observed syn:anti product ratio (ca. 1:2) is identical with that observed in the BF₃·Et₂O-catalyzed coupling reaction of the 2-hydroxyindoline derivative (1a) with 2-naphthol (2a) at rt.

However, the syn/anti product ratio is quite different from that observed in its equilibrium reaction products. Heating 4aa (anti) in 1,4-dioxane at 60 °C for 72 h caused transformation into an equilibrium mixture of the atropisomers \([3aa \text{ (syn) / 4aa \text{ (anti)}} = 1.2]\). This indicates that the BF₃·Et₂O-catalyzed rearrangement reaction products from the 2-naphthyl ether are kinetically controlled ones.

![Scheme 4](image-url)
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 $^1$H-NMR spectrum of the coupling products (9a and 10a) showed a regularly observed characteristic spectral feature attributable to a pair of the atropisomers, in which a downfield shift of C2-H proton signal was recognized in the syn isomer due to C-H•••O< type weak interaction [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.

![Diagram of reaction scheme 5](image)

**Scheme 5**

In the Lewis-acid catalyzed rearrangement of phenolic ethers, evidence has been found for inter- and intramolecular processes. 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).

![Diagram of reaction scheme 6](image)

**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, ε=2.2) comparable to that of benzene. The recombination behavior of the ion pair may be explained by the primary FMO (frontier molecular orbital) interaction between the largest LUMO coefficient (C2) of indoline cation and the largest HOMO coefficient (C1) of the naphthol (Scheme 7).

In conclusion, the formation reaction of the diastereomeric atropisomers in the BF$_3$·Et$_2$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 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 benzoil chloride to 3,3-dimethyl-3H-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)** BF$_3$·Et$_2$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 Et$_2$O (200 mL) and treated with water. The organic layer was separated, washed with aqueous NaHCO$_3$ solution and dried over anhydrous MgSO$_4$. The Et$_2$O 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 BF$_3$·Et$_2$O for given hour to give 6, 7 and 5a.

**[3,3-Dimethyl-2-(4-tolyl)indolin-1-yl][4-nitrophenyl]methanone (6ab)** Yellow plates from EtOH; mp 176-179 °C; $^1$H-NMR (300 MHz, CDCl$_3$) δ: 1.38 (3H, s, C$_3$-Me), 1.43 (3H, s, C$_3$-Me), 2.26 (3H, s, C$_A$-Me), 5.66 (1H, s, C$_2$-H), 6.52 (2H, br s, C$_A$-2, C$_A$-6-H), 6.92 (2H, d, J= 8.3 Hz, C$_A$-3, C$_A$-5-H), 7.19-7.29 (3H, m, C4, C5, C6-H), 7.41 (2H, d, J= 8.6 Hz, C$_{COA}$,2, C$_{COA}$,6-H), 8.02 (3H, br d, J= 8.6 Hz, C$_{COA}$,3, C$_{COA}$,5-H, C7-H); MS m/z: 402 (M$^+$); Anal. Calcd for C$_{22}$H$_{22}$N$_2$O$_4$: 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 (NO$_2$).

**[2-(2-Hydroxy-5-methylphenyl)-3,3-dimethyl-indolin-1-yl][4-nitrophenyl]methanone (7ab)** Pale yellow powder from EtOH; mp 273-279 °C; $^1$H-NMR (300 MHz, DMSO-d$_6$) δ: 0.92 (3H, s, C$_3$-Me), 1.41 (3H, s, C$_3$-Me), 2.05 (3H, s, C$_A$-5-Me), 5.26 (1H, s, C$_2$-H), 6.43 (1H, s, C$_A$-6-H), 6.48 (1H, br d, J= 7.9 Hz, C$_A$-4-H), 6.81 (1H, d, J= 7.9 Hz, C$_A$-3-H), 7.18-7.37 (5H, m, aromatic C-H), 8.11 (2H, br s, C$_{COA}$,3, C$_{COA}$,5-H), 8.26 (1H, br s, C7-H), 9.00 (1H, br s, C$_A$-2-OH); MS m/z: 402 (M$^+$); Anal. Calcd for C$_{24}$H$_{22}$N$_2$O$_4$: 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 (NO$_2$).

**[2-(4-Methoxyphenoxy)-3,3-dimethylindolin-1-yl][4-nitrophenyl]methanone (6ac)** Yellow plates from EtOH; mp 129-131 °C; $^1$H-NMR (300 MHz, CDCl$_3$) δ: 1.39 (3H, s, C$_3$-Me), 1.47 (3H, s, C$_3$-Me), 3.75 (3H, s, C$_A$-4-OMe), 5.62 (1H, br s, C$_2$-H), 6.58 (2H, br s, C$_A$-2, C$_A$-6-H), 6.66 (2H, d, J= 8.9 Hz, C$_A$-3, C$_A$-5-H), 7.20-7.26 (3H, m, C4, C5, C6-H), 7.34 (2H, d, J= 8.3 Hz, C$_{COA}$,2, C$_{COA}$,6-H), 8.05 (3H, br d, J= 8.3 Hz, C$_A$-3, C$_A$-5-H, C7-H); MS m/z: 418 (M$^+$); Anal. Calcd for C$_{24}$H$_{22}$N$_2$O$_4$: 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 (NO$_2$).

**[2-(2-Hydroxy-5-methoxyphenyl)-3,3-dimethylindolin-1-yl][4-nitrophenyl]methanone (7ac)** Yellow needles from EtOH; mp 253-254 °C; $^1$H-NMR (300MHz, DMSO-d$_6$) δ: 0.93 (3H, s, C$_3$-Me), 1.41 (3H, s, C$_3$-Me), 3.51 (3H, s, C$_A$-5-OMe), 5.23 (1H, s, C2-H), 6.14 (1H, d, J= 2.9 Hz, C$_A$-6-H), 6.55 (1H, br d, J= 8.6 Hz, C$_A$-3-H), 6.64 (1H, dd, J= 2.9, 8.6 Hz, C$_A$-4-H), 7.18-7.29 (3H, m, C4, C5, C6-H), 7.38 (2H, br s, C$_{COA}$,2, C$_{COA}$,6-H), 8.13 (2H, br s, C$_{COA}$,3, C$_{COA}$,5-H), 8.24 (1H, br s, C7-H), 8.81 (1H, br s,
C_{6}H_{2}-OH); MS m/z: 418 (M'); Anal. Calcd for C_{24}H_{32}N_{2}O_{4}: 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 (NO_{2}).

(4-Chlorophenyl)[3,3-dimethyl-2-(4-tolyloxy)indolin-1-yl]methanone (6bb) Colorless prisms from EtOH; mp 154-156 °C; ¹H-NMR (300 MHz, CDCl₃) δ: 1.35 (3H, s, C₃-Me), 1.42 (3H, s, C₃-Me), 2.28 (3H, s, C_{Ar}-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_{COA}-3, C_{COA}-5-H), 7.12-7.25 (3H, m, C₄, C₅, C₆-H), 7.17 (2H, d, J= 8.4 Hz, C_{COA}-3, C_{COA}-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 C_{23}H_{22}ClNO_{2}: 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-d₆) δ: 0.93 (3H, s, C₃-Me), 1.40 (3H, s, C₃-Me), 2.03 (3H, s, C_{Ar}-Me), 5.55 (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_{3a}-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 C_{23}H_{22}ClNO_{2}: 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 (300 MHz, 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, C_{2a}-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 C_{23}H_{22}ClNO_{3}: 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-d₆) 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, C_{2a}-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}-2-0H); MS m/z: 407 (M'); Anal. Calcd for C_{23}H_{22}ClNO_{3}: 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-ylxylo)indolin-1-yl](4-nitrophenyl)methanone (8aa)** Yellow plates from EtOH; mp 154-156 °C; ¹H-NMR (300 MHz, CDCl₃) δ (ppm): 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 C₇₇H₇₂N₂O₄: C, 73.69; H, 4.96; N, 6.39. Found: C, 74.04; H, 5.00; N, 6.41; IR (KBr) cm⁻¹: 1660 (NC=O), 1480, 1346 (NO₂). Calcd. for C₇₇H₇₄N₂O₄: 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).

**[3,3-Dimethyl-2-(naphthalen-2-ylxylo)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 C₂₇H₂₂CINO₂: C, 82.42; H, 5.89; N, 3.56. Found: C, 82.63; H, 5.91; N, 3.17; IR (KBr) cm⁻¹: 3160-2850 (aromatic C-H), 1656 (C=O), 1594 (C=C), 1002 (O-).

**[3,3-Dimethyl-2-(naphthalen-2-ylxylo)indolin-1-yl](3-toly)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, C₆-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 C₂₈H₂₄N₂O₂: 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), 1650 (C=O), 1596 (C=C), 990 (O-).

**[3,3-Dimethyl-2-(naphthalen-2-ylxylo)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 C₂₇H₂₄N₂O₄: 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 (C=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 BF₃·Et₂O (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 BF₃·Et₂O (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; ¹H-NMR (270MHz, CDCl₃) δ: 0.98 (3H, s, C3-Me), 1.60 (3H, s, C3-Me), 3.60 (3H, s, C₄naph2-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 C₂₃H₂₅N₂O₅: 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 (NO₂).

**[2-(2-Methoxynaphthalen-1-yl)-3,3-dimethylindolin-1-yl][4-nitrophenyl]methanone (10a) (anti)** Yellow prisms from EtOH; mp 175-176 °C; ¹H-NMR (270 MHz, CDCl₃) δ: 1.01 (3H, s, C3-Me), 1.63 (3H, s, C3-Me), 3.48 (3H, s, C₄naph2-OMe), 5.73 (1H, s, C2-H), 6.89 (1H, d, J= 8.3 Hz, C₅naph3-H), 7.13-7.36 (7H, m, aromatic C-H), 7.23 (1H, dd, J= 8.3 Hz, C₅naph4-H), 7.55 (2H, d, J= 8.6 Hz, C₅Ar2, C₅Ar6-H), 7.73 (2H, d, J= 8.6 Hz, C₅Ar3, C₅Ar5-H), 8.51 (1H, d, J= 7.9 Hz, C7-H); MS m/z: 452 (M⁺); Anal. Calcd for C₂₃H₂₅N₂O₅: 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 (NO₂).

**(2,3-Dimethyl-1H-indol-1-yl)(4-nitrophenyl)methane (5a)** Yellow oil; ¹H-NMR (400 MHz, CDCl₃) 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, C₅Ar2, C₅Ar6-H), 8.31 (2H, d, J= 8.8 Hz, C₅Ar3, C₅Ar5-H); MS m/z: 294 (M⁺); IR (film) cm⁻¹: 1684 (NC=O), 1602 (C=C), 1522, 1342 (NO₂).

**(4-Chlorophenyl)[2-(2-methoxynaphthalen-1-yl)-3,3-dimethylindolin-1-yl]methanone (9b) (syn)** Colorless prisms from EtOH; mp 181-182 °C; ¹H-NMR (270 MHz, CDCl₃) δ: 0.97 (3H, s, C3-Me), 1.58 (3H, s, C3-Me), 3.66 (3H, s, C₄naph2-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 C₂₃H₂₅ClNO₂: 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; ¹H-NMR (270 MHz, CDCl₃) δ: 0.98 (3H, s, C3-Me), 1.61 (3H, s, C3-Me), 3.44 (3H, s, C₄naph2-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 C₂₃H₂₅ClNO₂: 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]phenylmethanone (9c) (syn)** Colorless prisms from EtOH; mp 145-147 °C; ¹H-NMR (300 MHz, DMSO-d₆) δ: 0.97 (3H, s, C3-Me), 1.59 (3H, s,
C3-Me), 3.58 (3H, s, C\textsubscript{nap}-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\textsuperscript{+}); \textit{Anal.} Calcd. for C\textsubscript{28}H\textsubscript{25}NO\textsubscript{2}: C, 82.53; H, 6.18; N, 3.44. Found: C, 82.33; H, 6.13; N, 3.43; IR (KBr) cm\textsuperscript{-1}: 1638 (\textit{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; \textit{\textsuperscript{1}H-NMR} (300 MHz, DMSO-\textit{d}\textsubscript{6}) \delta: 0.95 (3H, s, C3-Me), 1.62 (3H, s, C3-Me), 3.46 (3H, s, C\textsubscript{nap}-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\textsuperscript{+}); \textit{Anal.} Calcd. for C\textsubscript{28}H\textsubscript{25}NO\textsubscript{2}: C, 82.53; H, 6.18; N, 3.44. Found: C, 82.33; H, 6.13; N, 3.43. IR (KBr) cm\textsuperscript{-1}: 1638 (\textit{NC}=O), 1594 (C=C).

\textbf{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-K\textalpha\ 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-92\textsuperscript{7}), 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 Structure\textsuperscript{7} crystallographic software package.

Crystal Data of 8aa: Crystal Data; C\textsubscript{27}H\textsubscript{22}N\textsubscript{2}O\textsubscript{4}, M=438.47, monoclinic, Space group \textit{P2}\textsubscript{1}/\textit{a}, a=12.281 (2), b=20.134 (5), c=9.854 (1) Å, β=111.39 (1), V=2268 (7) Å\textsuperscript{3}, Dc=1.284 g cm\textsuperscript{-3}, Z=4, R=0.057, Rw=0.094. The X-Ray crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC ref. No. 702823).

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\textbf{REFERENCES (AND NOTES)}


