Manganese(III)-Mediated Direct Introduction of 3-Oxobutanamides into Methoxynaphthalenes

Zhi-qi Cong, Hiroshi Nishino*

Department of Chemistry, Graduate School of Science and Technology, Kumamoto University, Kurokami 2-39-1, Kumamoto 860-8555, Japan
Fax +81(96)3423374; E-mail: nishino@sci.kumamoto-u.ac.jp
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Abstract: The oxidation of methoxynaphthalenes with manganese(III) acetate in the presence of N-aryl-3-oxobutanamides gave the directly 3-oxobutanamide-substituted methoxynaphthalenes in moderate to good yields along with small amounts of naphtho[2,1-b]furans and benzo[e]indolinones. The optimized reaction conditions and the mechanism for the formation of the products are discussed.

Key words: oxidations, manganese, radicals, aromatic substitutions, cyclizations

The redox radical process is an important tool for the formation of the carbon–carbon bond in organic synthesis. Manganese(III) acetate is well known as a mild one-electron oxidant and widely used to construct the carbon–carbon bond using oxidatively formed carbon radicals. Accordingly, the intramolecular oxidative free-radical cyclization or annulation and intermolecular addition using manganese(III) acetate have been extensively investigated. In recent years, our research group has developed various manganese(III) based oxidative reactions, and we and other groups have found that the reaction of aromatic substrates with active methylene species, such as malonic acids, malonates, malonamide, α-cyanoacetamide, malononitrile, β-keto esters, and β-diketones gave various interesting functionalized products. For example, the reaction of methoxynaphthalenes with ethyl 3-oxobutanoate afforded substituted products in moderate yields together with a small amount of naphtho[2,1-b]furans (Scheme 1). Dimethyl malonate also gave similar results. Since the naphthohuron skeleton is found in a wide range of natural and unnatural compounds, which exhibit important biological and pharmacological activities, it is worthwhile to explore the possible manganese(III) acetate mediated oxidation of methoxy-substituted naphthalenes with N-aryl-3-oxobutanamides, which are expected to develop an efficient method for the formation of functionalized naphtho[2,1-b]furans or benzo[e]indolinones. Therefore, we initially examined the reaction using N-phenyl-3-oxobutanoamide, which gave a complex product distribution and a poor yield of the expected cyclization products. However, by changing the reaction conditions, the directly 3-oxobutanamide-substituted naphthalenes were unexpectedly formed in fairly good yields. In general, 2-substituted 1,3-dicarbonyl compounds are versatile intermediates in organic synthesis. In addition, the manganese(III) acetate based oxidation showed an efficient method for the alkylation of 1,3-dicarbonyl compounds. In view of the potential synthetic utility of this approach and as a continuation of our interest in the development of efficient synthetic methodologies using manganese(III) acetate, we scrutinized the direct introduction of 3-oxobutanamides into methoxynaphthalenes.

Scheme 1

Based on our previously related research experience, 2,7-dimethoxynaphthalene (1a) was selected as an aromatic substrate for the reaction aimed at optimizing the reaction conditions since the obtained products could be readily separated and characterized. The reaction of 1a with N-phenyl-3-oxobutanamide (2a) in the presence of manganese(III) acetate was examined in boiling acetic acid since manganese(III) acetate is only soluble in hot carboxylic acid (Scheme 2). A mixture of 1a and 2a in a molar ratio of 1:2 was heated in glacial acetic acid, and manganese(III) acetate (6 equiv) was added just before refluxing (Method A). The reaction was complete within 1 minute similar to the previously reported result, and the 3-oxobutanamide-substituted naphthalene 3aa, naphtho[2,1-b]furan 4aa, and benzoindolinone 5aa were obtained in 18, 23 and 7% yield, respectively (Table 1, entry 1). To overcome the lower conversion of the starting material 1a, an excess amount of manganese(III) acetate was used (Table 1, entries 2, 3). As a result, 1a was completely consumed when 12 equivalents of the oxidant were added. However, the total yield of the products was only slightly improved (a 9% increase in yield). It seemed that the use of a large amount of the oxidant resulted in the self-oxida-
This result encouraged us to apply the process using other products. When the reaction was carried out at 70 °C, a maximum yield of 63% was achieved (Table 1, entry 4). When the reaction was carried out at 70 °C, a maximum yield of 63% was achieved (Table 1, entry 4).

In order to improve the conversion of 1a, we adopted the high-dilution conditions of 2a in a molar ratio of 1:0.3 in glacial acetic acid just before refluxing, and then another portion of 2a (1.0 equiv) dissolved in AcOH was dropwise added through a dropping funnel. The oxidized substrate was consumed in 2 minutes and the substituted product 3aa was preferentially produced in 63% yield along with 4aa and 5aa in 14% and 8% yields, respectively (Table 1, entry 4). When the reaction was carried out at 70 °C, a maximum yield of 63% (79%) was achieved (Table 1, entry 5).

This result encouraged us to apply the process using other N-aryl-3-oxobutanamides 2b–i because of the good selectivity of 2a in the formation of the directly substituted product 3aa. The reaction of 1a with N-(2-chlorophenyl)- (2b), N-(4-chlorophenyl)- (2c), N-(2-methoxyphenyl)- (2d), N-(4-methoxyphenyl)- (2e), N-(2-nitrophenyl)- (2f), N-(2-methylphenyl)- (2g), N-(4-methylphenyl)- (2h), and N-(4-fluorophenyl)-3-oxobutanamide (2i) gave the corresponding substitution products 3ab–3ai in good yields together with a small amount of the addition products 4ab–4ai and 5ab–5ai, respectively (Table 1, entries 6–13). Use of 2,6-dimethoxy- (1b), 2-methoxy- (1c), 1,7-dimethoxy- (1d), and 1-methoxynaphthalene (1e) instead of 1a also afforded similar products (Table 1, entries 14–17).

The mechanism for the formation of three products 3, 4, and 5 could be explained as follows. Analogous to the previously reported oxidative radical reaction pathway,4,11 the manganese(III)-3-oxobutanamide enolate complex 2¢ is formed by the ligand-exchange reaction of manganese(III) acetate with the naphthofuran 2 and then oxidized by an excess amount of manganese(III) to yield the intermediate cation C. It was expected that the aromatization process accompanied by deprotonation should be fast, giving the substitution product D. Since product D still has an active methine proton, product D should be oxidized by an excess amount of manganese(III) acetate to give 3 (Scheme 3, path a).4,11 On the other hand, the intermediate cation C could be intramolecularly attacked by the acetyl oxygen or amide nitrogen. The O-cyclization followed by elimination of methanol would give the naphthofuran F, which would then be converted into acetoxymethylnaphthofuran 4 via the benzyl-type oxidation (path b).4,11 On the other hand, when the amide nitrogen would attack intramolecularly at the positive charge in cation C, a benzoinolino H would be produced, and the hydroxybenzoinolino 5 would be eventually obtained by further oxidation (path c).
Table 1 Reaction of Methoxynaphthalenes 1a–e with 3-Oxobutanamides 2a–i in the Presence of Mn(OAc)₃·2H₂O

<table>
<thead>
<tr>
<th>Entry</th>
<th>1</th>
<th>2</th>
<th>Molar ratioᵇ</th>
<th>Temp (°C)</th>
<th>Time (min)</th>
<th>Recovery (%)</th>
<th>Product(s) (Yield, %)ᶜ</th>
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<tr>
<td>1ᵈ</td>
<td>1a</td>
<td>2a</td>
<td>1:2:6</td>
<td>reflux</td>
<td>1</td>
<td>30</td>
<td>3aa (18) 4aa (23) 5aa (7)</td>
</tr>
<tr>
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<td>1a</td>
<td>2a</td>
<td>1:2:8</td>
<td>reflux</td>
<td>1</td>
<td>14</td>
<td>3aa (17) 4aa (25) 5aa (12)</td>
</tr>
<tr>
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<td>1a</td>
<td>2a</td>
<td>1:3:12</td>
<td>reflux</td>
<td>1</td>
<td>–</td>
<td>3aa (22) 4aa (19) 5aa (16)</td>
</tr>
<tr>
<td>4ᵉ</td>
<td>1a</td>
<td>2a</td>
<td>1:1:3:6</td>
<td>reflux</td>
<td>2</td>
<td>4</td>
<td>3aa (63) 4aa (14) 5aa (8)</td>
</tr>
<tr>
<td>5ᵉ</td>
<td>1a</td>
<td>2a</td>
<td>1:1:2:6</td>
<td>70</td>
<td>2</td>
<td>7</td>
<td>3aa (79) 4aa (5) 5aa (5)</td>
</tr>
<tr>
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<td>1a</td>
<td>2b</td>
<td>1:1:2:6</td>
<td>70</td>
<td>2</td>
<td>9</td>
<td>3ab (76) 4ab (1) 5ab (11)</td>
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<tr>
<td>7ᵉ</td>
<td>1a</td>
<td>2c</td>
<td>1:1:2:6</td>
<td>70</td>
<td>2</td>
<td>10</td>
<td>3ac (70) 4ac (4) 5ac (9)</td>
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<td>2d</td>
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<td>2</td>
<td>9</td>
<td>3ad (59) 4ad (trace) 5ad (15)</td>
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<td>2e</td>
<td>1:1:2:6</td>
<td>70</td>
<td>2</td>
<td>37</td>
<td>3ae (30) 4ae (3) 5ae (trace)</td>
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<tr>
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<td>1a</td>
<td>2f</td>
<td>1:1:2:6</td>
<td>70</td>
<td>2</td>
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<tr>
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<td>2g</td>
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<td>2</td>
<td>12</td>
<td>3ag (53) 4ag (19) 5ag (trace)</td>
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<td>2h</td>
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<td>2</td>
<td>10</td>
<td>3ah (51) 4ah (8) 5ah (9)</td>
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<td>2i</td>
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<td>2</td>
<td>14</td>
<td>3ai (60) 4ai (13) 5ai (15)</td>
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<td>2a</td>
<td>1:1:2:6</td>
<td>70</td>
<td>3</td>
<td>24</td>
<td>3ba (35) 4ba (9) 5ba (4)</td>
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<tr>
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<td>1c</td>
<td>2a</td>
<td>1:1:2:6</td>
<td>70</td>
<td>2</td>
<td>14</td>
<td>3ca (35) 4ca (15) 5ca (12)</td>
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<tr>
<td>16ᵉ</td>
<td>1d</td>
<td>2a</td>
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<td>70</td>
<td>2</td>
<td>21</td>
<td>3da (28) 4da (9) –</td>
</tr>
<tr>
<td>17ᵉ</td>
<td>1e</td>
<td>2a</td>
<td>1:1:2:6</td>
<td>70</td>
<td>2</td>
<td>13</td>
<td>3ea (67) – –</td>
</tr>
</tbody>
</table>

ᵃ The reaction was carried out in glacial AcOH.
ᵇ 1:2 Mn(OAc)₃·2H₂O.
ᶜ Isolated yield based on the amount of the added methoxynaphthalene 1.
ᵈ The reaction was conducted using Method A described in the experimental section.
ᵉ The reaction was carried out using Method B mentioned in the experimental section.
ᶠ An intractable mixture of 4ab and 5ab was obtained and the yield was estimated on the basis of the integration of the NH and OH peaks in the 1H NMR spectrum.

In conclusion, we have developed an efficient way to directly prepare the 3-oxobutanamide-substituted naphthalenes 3 by the oxidation of methoxynaphthalenes 1 with manganese(III) acetate by controlling the proportion of the 3-oxobutanamides 2 in the reaction mixture at 70 °C. The reaction is very simple and the reaction times are very short. Although it was difficult to improve the yield of 3, this is an interesting procedure to prepare heterocyclic compounds using the functionalized naphthalenes 3. Further studies on the synthesis of functionalized heterocyclic compounds using 3 are now in progress.

The NMR spectra were recorded using a JNM AL300 FT NMR spectrometer at 300 MHz for ¹H and at 75 MHz for ¹³C with tetramethylsilane as the internal standard. The chemical shifts are given in δ values (ppm) and the coupling constants in Hz. The IR spectra of the neat samples were measured using the KBr disc or CHCl₃ solution by a Shimadzu 8400 FT IR spectrometer and expressed in cm⁻¹. The EI MS spectra were recorded by a Shimadzu QP-5050A gas chromatograph-mass spectrometer at an ionizing voltage of 70 eV. The elemental analyses were performed at the Instrumental Analysis Center of Kumamoto University, Kumamoto, Japan. Mn(OAc)₃·4H₂O was purchased from Wako Pure Chemical Ind., Ltd. Mn(OAc)₃·2H₂O was prepared according to the method described in the literature.¹² Methoxynaphthalenes 1a–e were prepared by the methylation of the corresponding naphthols using dimethyl sulfate in anhyd acetone in the presence of anhyd K₂CO₃.

Oxidation of Methoxynaphthalenes 1 with Manganese(III) Acetate in the Presence of N-Aryl-3-oxobutanamides 2; Comounds 3aa, 4aa, and 5aa; Typical Procedure (Table 1, Entry 1)

Method A: To a heated solution of 2,7-dimethoxynaphthalene (1a; 188 mg, 1 mmol) and N-phenyl-3-oxobutanamide (2a; 354 mg, 2 mmol) in glacial AcOH (25 mL) was added Mn(OAc)₃·2H₂O (1.608 g, 6 mmol) was added just before refluxing. The reaction was complete within 1 min when the dark-brown color of the solution turned clear red. The mixture was then cooled to r.t., and the solvent was removed in vacuo. The residue was triturated with aq NaHCO₃ (20 mL), dried (MgSO₄), and concentrated to dryness. The products were separated by silica gel TLC (Wako B-10) by eluting with CHCl₃ (3 × 20 mL). The combined organic extracts were washed with sat. aq NaHCO₃ (2 × 20 mL) and H₂O (2 × 20 mL), dried (MgSO₄), and concentrated to dryness. The products were separated by silica gel TLC (Wako B-10) by eluting with CHCl₃, and 3aa (76 mg, 18%; Rₘ = 0.22), 4aa (89 mg, 23%; Rₘ = 0.43), and 5aa (24 mg, 7%; Rₘ = 0.33) were obtained together with recovered 1a (56 mg, 30%; Rₘ = 0.73). The products were further purified by recrystallization.
from appropriate solvents. Entries 2 and 3 in Table 1 were carried out with this method.

**Method B (Table 1, Entry 4):** A mixture of 2,7-dimethoxynaphthalene (1a; 188 mg, 1 mmol), N-phenyl-3-oxobutanamide (2a; 35.4 mg, 0.2 mmol), and glacial AcOH (18 mL) was placed in a three-necked flask equipped with a condenser and a dropping funnel. To the heated solution was added Mn(OAc) \(_2\)·2H\(_2\)O (1.608 g, 6 mmol) just before refluxing, and then another portion of 2a (177 mg, 1 mmol) dissolved in glacial AcOH (7 mL) was dropwise added within 2 min. The mixture was cooled to r.t., and the solvent was removed in vacuo. The residue was worked up by the same procedure as described for Method A to give the products 3aa (333 mg, 79%), 4aa (21 mg, 5%), and 5aa (17 mg, 5%) along with recovered 1a (13 mg, 7%). Entries 5–17 in Table 1 were carried out by this method at 70 °C.

**Scheme 3**

2-Acetoxy-2-(2,7-dimethoxy-1-naphthyl)-N-phenyl-3-oxobutanamide (3aa)
Colorless needles (from MeOH); mp 161.5–162 °C.
IR (KBr): 3427, 3389, 1768, 1730, 1701 cm\(^{-1}\).
\(^1\)H NMR (CDCl\(_3\)): \(\delta = 8.43 (1 \text{ H, s, NH}), 7.78 (1 \text{ H, d, } J = 9.0 \text{ Hz, H-5}), 7.66–7.63 (2 \text{ H, m, H-4, H-8}), 7.47 (2 \text{ H, d, } J = 8.1 \text{ Hz, H-2', H-6'}), 7.26 (2 \text{ H, td, } J = 7.8, 1.8 \text{ Hz, H-3', H-5'}), 7.08–6.99 (3 \text{ H, m, H-3, H-6, H-4'}), 3.87 (3 \text{ H, s, OCH}_3), 3.79 (3 \text{ H, s, OCH}_3), 2.35 (3 \text{ H, s, COCH}_3), 2.25 (3 \text{ H, s, COCH}_3).
\(^13\)C NMR (CDCl\(_3\)): \(\delta = 199.2, 168.3, 164.5, 158.1, 155.8, 137.4, 134.3, 132.2, 130.1, 128.9, 125.8, 124.5, 119.8, 116.7, 115.8, 110.9, 104.1, 89.6, 56.2, 55.0, 26.3, 21.1.
MS: \(m/z = 421 \text{ (M\(^{+}\), 12%).}
Anal. Calcd for C\(_{24}\)H\(_{23}\)NO\(_6\): C, 68.40; H, 5.50; N, 3.32. Found: C, 68.20; H, 5.46; N, 3.25.
2-Acetoxy-N-(2',chlorophenyl)-2-(2,7-dimethoxy-1-naphthyl)-3-oxobutanamide (3ab)

Colorless needles (from MeOH); mp 166–166.5 °C.

IR (KBr): 3373, 3346, 1759, 1730, 1707 cm⁻¹.

1H NMR (CDCl₃): δ = 8.99 (1 H, s, NH), 8.35 (1 H, dd, J = 1.5, 8.1 Hz, H-6), 7.82 (1 H, d, J = 8.7 Hz, H-5), 6.76 (1 H, d, J = 9.3 Hz, H-6), 7.61 (1 H, s, H-8), 7.54 (1 H, dd, J = 1.5, 8.1 Hz, H-3'), 7.23 (1 H, t, J = 8.1 Hz, H-5), 7.11 (1 H, d, J = 9.0 Hz, H-6), 7.05–6.99 (2 H, m, H-3'), 3.92 (3 H, s, OCH₃), 3.81 (3 H, s, OCH₃), 2.37 (3 H, s, COCH₃), 2.30 (3 H, s, COCH₃).

13C NMR (CDCl₃): δ = 198.0, 168.1, 164.8, 158.4, 155.5, 134.3, 134.0, 132.4, 132.3, 130.3, 129.7, 127.7, 125.7, 124.8, 122.8, 116.9, 115.7, 110.8, 103.8, 56.2, 55.1, 26.4, 21.1.


2-Acetoxy-2-(2,7-dimethoxy-1-naphthyl)-N-(2'-nitrophenyl)-3-oxobutanamide (3af)

Yellow microcrystals (from MeOH); mp 205.5–206.5 °C.

IR (KBr): 3345, 1759, 1730, 1705 cm⁻¹.

1H NMR (CDCl₃): δ = 11.25 (1 H, s, NH), 8.76 (1 H, dd, J = 1.2, 8.4 Hz, H-3'), 8.18 (1 H, dd, J = 1.5, 8.4 Hz, H-6'), 7.83 (1 H, d, J = 9.0 Hz, H-5), 7.68 (1 H, d, J = 9.0 Hz, H-4'), 7.60 (1 H, td, J = 8.4, 1.5 Hz, H-5'), 7.54 (1 H, s, H-8), 7.15 (1 H, dd, J = 8.4, 1.5 Hz, H-4'), 7.13 (1 H, d, J = 8.7 Hz, H-3), 7.01 (1 H, dd, J = 2.4, 9.0 Hz, H-6), 3.95 (3 H, s, OCH₃), 3.80 (3 H, s, OCH₃), 2.42 (3 H, s, COCH₃), 2.37 (3 H, s, COCH₃).

13C NMR (CDCl₃): δ = 197.1, 168.4, 166.0, 158.5, 155.6, 136.5, 135.9, 134.2, 133.9, 132.5, 130.4, 125.8, 126.3, 123.6, 112.1, 116.7, 114.9, 110.8, 103.7, 90.1, 56.1, 55.0, 26.5, 21.1.

Anal. Calcd for C₂₃H₂₁NO₇: C, 66.10; H, 4.75; N, 6.01. Found: C, 66.15; H, 4.69; N, 6.00.

2-Acetoxy-2-(2,7-dimethoxy-1-naphthyl)-N-(2'-methylphenyl)-3-oxobutanamide (3ag)

Colorless needles (from MeOH); mp 160–161 °C.

IR (KBr): 3358, 3161, 1759, 1725, 1695 cm⁻¹.

1H NMR (CDCl₃): δ = 8.84 (1 H, s, NH), 7.92 (1 H, d, J = 7.5 Hz, H-5), 7.81 (2 H, m, J = 8.7 Hz, H-8, H-4), 7.67 (1 H, d, J = 9.0 Hz, H-6'), 7.17–6.98 (5 H, m, m, 3.91 (3 H, s, OCH₃), 3.85 (3 H, s, OCH₃), 2.35 (3 H, s, COCH₃), 2.30 (3 H, s, COCH₃), 2.14 (3 H, s, CH₃).

13C NMR (CDCl₃): δ = 199.7, 168.8, 164.2, 158.3, 155.0, 135.7, 134.2, 132.2, 130.3, 131.0, 127.8, 126.7, 125.8, 124.7, 121.6, 116.9, 111.6, 110.5, 104.6, 89.3, 56.0, 55.2, 26.2, 21.1, 17.3.

Anal. Calcd for C₂₅H₂₅NO₇: C, 68.95; H, 5.79; N, 3.22. Found: C, 69.03; H, 5.59; N, 3.31.

2-Acetoxy-2-(2,7-dimethoxy-1-naphthyl)-N-(4'-methylphenyl)-3-oxobutanamide (3ah)

Colorless needles (from MeOH); mp 169–170 °C.

IR (KBr): 3396, 1771, 1715, 1695 cm⁻¹.

1H NMR (CDCl₃): δ = 8.32 (1 H, s, NH), 7.80 (1 H, d, J = 9.3 Hz, H-5), 7.66 (1 H, d, J = 9.0 Hz, H-4), 7.60 (1 H, d, J = 2.4 Hz, H-8), 7.36 (2 H, d, J = 8.4 Hz, H-2', H-6'), 7.09 (2 H, d, J = 8.7 Hz, H-3', H-5'), 7.08 (1 H, d, J = 9.0 Hz, H-3), 7.01 (1 H, dd, J = 2.4, 9.0 Hz, H-6), 3.90 (3 H, s, OCH₃), 3.78 (3 H, s, OCH₃), 2.36 (3 H, s, COCH₃), 2.28 (3 H, s, COCH₃), 2.26 (3 H, s, CH₃).

13C NMR (CDCl₃): δ = 199.3, 168.2, 164.3, 158.3, 155.8, 134.7, 134.3, 134.1, 132.2, 130.2, 129.5, 125.8, 119.9, 116.8, 116.3, 111.0, 104.1, 90.0, 56.4, 55.1, 26.5, 21.3, 20.8.

Anal. Calcd for C₂₅H₂₅NO₇: C, 68.95; H, 5.79; N, 3.22. Found: C, 69.03; H, 5.65; N, 3.22.

2-Acetoxy-N-(4'-fluorophenyl)-2-(2,7-dimethoxy-1-naphthyl)-3-oxobutanamide (3ai)

Colorless microcrystals (from MeOH); mp 127–129 °C.

IR (KBr): 3381, 3309, 1757, 1718, 1684 cm⁻¹.

1H NMR (CDCl₃): δ = 8.44 (1 H, s, NH), 7.80 (1 H, d, J = 8.7 Hz, H-5), 7.68 (1 H, s, H-8), 7.67 (1 H, d, J = 9.0 Hz, H-4), 7.44 (1 H, d, J = 8.7 Hz, H-2' or H-6'), 7.43 (1 H, d, J = 8.7 Hz, H-6' or H-2'), 7.08 (1 H, d, J = 9.3 Hz, H-3), 7.02 (1 H, dd, J = 2.4, 9.0 Hz, H-6), 6.97 (1 H, d, J = 8.7 Hz, H-3' or H-5'), 6.94 (1 H, d, J = 8.7 Hz, H-5' or H-3'), 3.89 (3 H, s, OCH₃), 3.82 (3 H, s, OCH₃), 2.34 (3 H, s, COCH₃), 2.26 (3 H, s, COCH₃).

2-Acetoxy-2-(2,6-dimethoxy-1-naphthyl)-N-phenyl-3-oxobutanamide (3ba)
Colorless microcrystals (from MeOH); mp 180–181 °C.

IR (KBr): 3413, 1718 cm⁻¹.

1H NMR (CDCl₃): δ = 8.50 (1 H, s, NH), 8.19 (1 H, d, J = 8.4 Hz, H-8), 7.76 (1 H, d, J = 9.0 Hz, H-4), 7.47 (2 H, d, J = 8.4 Hz, H-2, H-6), 7.47 (2 H, t, J = 8.1 Hz, H-3', H-5'), 7.20 (1 H, d, J = 9.0 Hz, H-3), 7.47 (1 H, dd, J = 2.7, 9.6 Hz, H-7), 7.04–7.09 (2 H, m, H-5, H-4'), 3.83 (6 H, s, OCH₃), 2.34 (3 H, s, COCH₃), 2.22 (3 H, s, COCH₃).

13C NMR (CDCl₃): δ = 131.7, 131.2, 128.8, 127.6, 124.5, 119.9, 119.4, 117.6, 114.3, 89.4, 56.5, 55.1, 26.3, 21.1.

Anal. Calc'd for C₂₃H₂₁NO₅: C, 70.58; H, 4.87; N, 3.60. Found: C, 70.79; H, 4.87; N, 3.60.

2-Acetoxy-2-(2-methoxy-1-naphthyl)-N-phenyl-3-oxobutanamide (3ca)
Colorless microcrystals (from MeOH); mp 163–164.5 °C.

IR (KBr): 3341, 1757, 1719, 1699 cm⁻¹.

1H NMR (CDCl₃): δ = 8.64 (1 H, s, NH), 8.19 (1 H, d, J = 8.4 Hz, H-8), 7.90 (1 H, d, J = 8.7 Hz, H-5), 7.79 (1 H, d, J = 8.1 Hz, H-4), 7.51–7.08 (8 H aromat., m), 3.91 (3 H, s, OCH₃), 2.35 (3 H, s, COCH₃), 2.25 (3 H, s, COCH₃).

13C NMR (CDCl₃): δ = 198.6, 168.2, 164.7, 155.2, 137.3, 132.7, 132.5, 130.4, 129.0, 128.9, 127.1, 124.9, 127.4, 124.0, 120.0, 117.4, 113.8, 89.8, 56.9, 26.4, 21.3.

Anal. Calc'd for C₂₃H₂₁NO₅: C, 70.58; H, 4.87; N, 3.60. Found: C, 70.66; H, 5.37; N, 3.68.

2-Acetoxy-2-(4,6-dimethoxy-1-naphthyl)-N-phenyl-3-oxobutanamide (3da)
Colorless microcrystals (from MeOH); mp 177–177.5 °C.

IR (KBr): 3341, 1751, 1716, 1683 cm⁻¹.

1H NMR (CDCl₃): δ = 8.79 (1 H, brs, NH), 8.52 (1 H, d, J = 9.6 Hz, H-8), 7.61 (1 H, d, J = 2.7 Hz, H-5), 7.42 (2 H, d, J = 7.5 Hz, H-2', H-6'), 7.30–7.23 (4 H, m, H-7, H-2', H-3', H-5'), 7.05 (1 H, t, J = 7.2 Hz, H-4'), 6.73 (1 H, d, J = 8.1 Hz, H-3), 3.99 (3 H, s, OCH₃), 3.92 (3 H, s, OCH₂), 3.26 (3 H, s, COCH₃).

13C NMR (CDCl₃): δ = 203.5, 170.6, 164.4, 157.3, 155.9, 137.2, 128.8, 128.2, 127.5, 127.2, 124.5, 126.1, 121.2, 120.0, 119.5, 102.9, 101.1, 89.8, 55.5, 55.2, 26.9, 20.9.

Anal. Calc'd for C₂₃H₂₁NO₅: C, 70.80; H, 5.50; N, 3.32. Found: C, 70.68; H, 5.47; N, 3.26.

2-Acetoxy-2-(4-methoxy-1-naphthyl)-N-phenyl-3-oxobutanamide (3ea)
Colorless microcrystals (from MeOH); mp 177–177 °C.

IR (KBr): 3307, 1746, 1719, 1698 cm⁻¹.

1H NMR (CDCl₃): δ = 8.77 (1 H, s, NH), 8.55 (1 H, d, J = 8.4 Hz, H-5), 8.33 (1 H, dd, J = 1.2, 7.8 Hz, H-8), 7.58 (1 H, t, J = 8.4 Hz, H-7), 7.52 (1 H, t, J = 8.1 Hz, H-6), 7.41–7.48 (3 H, m, H-2, H-2', H-6'), 7.25 (1 H, t, J = 7.8 Hz, H-3', H-5'), 7.05 (1 H, t, J = 8.1 Hz, H-4'), 6.76 (1 H, d, J = 8.4 Hz, H-3), 4.00 (3 H, s, OCH₃), 2.37 (3 H, s, COCH₃).

13C NMR (CDCl₃): δ = 198.8, 168.3, 164.6, 156.0, 153.4, 137.4, 131.1, 131.2, 128.8, 127.6, 124.5, 119.9, 119.4, 117.6, 114.3, 89.4, 56.5, 55.1, 26.3, 21.1.

Anal. Calc'd for C₂₃H₂₁NO₅: C, 70.58; H, 4.51; N, 3.32. Found: C, 70.51; H, 4.39; N, 3.34.

2-Acetoxy-2-(4-methoxy-1-naphthyl)-N-phenyl-3-oxobutanamide (3fa)
Colorless microcrystals (from MeOH); mp 177–177 °C.

IR (KBr): 3309, 3018, 1732, 1670 cm⁻¹.

1H NMR (CDCl₃): δ = 9.90 (1 H, s, NH), 8.07 (1 H, d, J = 2.7 Hz, H-9), 7.88 (2 H, d, J = 7.8 Hz, H-2', H-6'), 7.78 (1 H, d, J = 9.0 Hz, H-6), 7.70 (1 H, d, J = 8.7 Hz, H-4 or H-5), 7.43 (1 H, d, J = 8.7 Hz, H-5 or H-4), 7.40 (2 H, t, J = 8.1 Hz, H-3', H-5'), 7.18 (1 H, td, J = 7.5, 1.2 Hz, H-4'), 7.12 (1 H, dd, J = 2.7, 8.7 Hz, H-7), 5.37 (2 H, s, CH₂), 3.87 (3 H, s, OCH₃), 2.14 (3 H, s, COCH₃).
7.75 (1H, d, J = 9.0 Hz, H-4 or H-5), 7.49 (1H, d, J = 9.0 Hz, H-5 or H-4), 7.34–7.20 (3H, m, H-4', H-5', H-6'), 7.14 (1H, dd, J = 8.7, 2.1 Hz, H-7), 5.47 (2H, s, CH$_2$), 3.85 (3H, s, OCH$_3$), 2.39 (3H, s, COCH$_3$), 2.16 (3H, s, CH$_3$).

$^1$H NMR (CDCl$_3$); δ = 9.10 (1H, s, NH), 8.15 (1H, d, J = 8.7 Hz, H-9), 7.87–7.89 (3H, m, H$_{arom}$), 7.79 (1H, d, J = 8.4 Hz, H-7), 7.39–7.60 (5H, m, H$_{arom}$), 7.16–7.23 (1H, m, H-4'), 5.37 (2H, s, CH$_2$), 2.18 (3H, s, COCH$_3$).

$^1$C NMR (CDCl$_3$); δ = 182.8, 172.6, 164.7, 152.8, 138.2, 129.1, 128.0, 127.7, 127.0, 125.7, 125.1, 124.8, 124.6, 119.8, 111.7, 55.7, 20.9.

Anal. Calcld for C$_{23}$H$_{19}$NO$_5$: C, 70.94; H, 4.92; N, 3.60. Found: C, 73.39; H, 4.67; N, 3.88.

2-Acetoxymethyl-9-methoxy-1-(phenylcarbamoyl)naphtho[2,1-b]furan (4da)

Colorless needles (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 197–199 °C.

IR (KBr): 3283, 1736, 1695 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 148–150 °C.

IR (KBr): 3283, 1736, 1695 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 148–150 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3273, 3190, 1750, 1651 cm$^{-1}$.

Colorless microcrystals (from EtOH); mp 177–177.5 °C.
1-Acetyl-1-hydroxy-8-methoxy-3-(2'-nitrophenyl)-1H-benzo[e]indol-2(3H)-one (5af)

Colorless microcrystals (from EtOH); mp 177–177.5 °C.

IR (KBr): 3414, 3325, 1724, 1680 cm⁻¹.
13C NMR (CDCl₃): δ 196.5, 173.8, 163.3, 161.6, 148.2, 140.2, 131.4, 130.1, 126.7, 124.7, 124.3, 121.1, 119.9, 118.0, 110.7, 110.4, 109.2, 90.3, 55.9, 55.6, 22.0.

Anal. Calcd for C₂₂H₁₉NO₄: C, 73.12; H, 5.30; N, 3.88. Found: C, 73.29; H, 5.06; N, 3.67.

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References


(9) The total yield of the products 3aa, 4aa, and 5aa was 48% (entry 1), 54% (entry 2), and 57% yield (entry 3), respectively.