One-Pot Oxidative Allylation of Morita–Baylis–Hillman Adducts with Allyltrimethylsilane Promoted by Dess–Martin Periodinane/Boron Trifluoride–Diethyl Ether Complex

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Abstract: Morita–Baylis–Hillman adducts undergo smooth one-pot oxidative conjugate addition with allyltrimethylsilane in the presence of Dess–Martin periodinane/boron trifluoride–diethyl ether complex under mild reaction conditions to afford various homoallylated \( \beta \)-keto ester derivatives in good yields with high 1,4-selectivity.

Key words: Morita–Baylis–Hillman adducts, hypervalent iodine reagents, allylations, conjugate additions, \( \beta \)-keto esters

The ready availability and versatility of Morita–Baylis–Hillman adducts and their acetates makes them valuable synthetic intermediates for the synthesis of a variety of heterocycles, such as quinolines, pyrimidinones, isoxazolines, pyrazolines, indolizines, azetidinone, diazacyclophanes, and chromanones, as well as biologically active natural products, including \( \alpha \)-alkylidene-\( \beta \)-lactams, \( \alpha \)-methylene-\( \gamma \)-butyrolactones, and mikanec acids, and frontalin, trimethoprim, sarkomycin, ilmofosine, nuciferol, and many others.1,2 Consequently, various nucleophiles, such as metal hydrides, halides, azides, cyanides, alcohols, amines, arenes, and active methylene compounds, have been used to prepare a wide range of synthetic intermediates.3–5 However, the allylation of Morita–Baylis–Hillman adducts with allyltrimethylsilane via an oxidative Michael reaction has not yet been reported. The stereoselective addition of allylmetal reagents to carbon electrophiles is one of the most important carbon–carbon bond-forming reactions in organic synthesis.6 Lewis acid catalyzed carbon–carbon bond-forming reactions in particular are of great significance because of their high reactivity, selectivity, and mild reaction conditions.7 Hypervalent iodine reagents have also occupied an important place in natural and synthetic organic chemistry because of their potential applications in the construction of carbon–carbon and carbon–heteroatom bonds.8 One of the most significant advances was the discovery of the Dess–Martin periodinane (DMP) reagent which offered a mild oxidation procedure for alcohols to be converted into their corresponding carbonyl compounds.9 The reagent’s widespread use over the past decade attests to its benign nature and its ability to succeed under mild oxidation conditions. As an oxidizing agent, DMP overcomes many of the disadvantages associated with the oxidative methods developed so far.10

In this paper, we report an efficient and selective one-pot oxidative Michael reaction of Morita–Baylis–Hillman adducts with allyltrimethylsilane using DMP/boron trifluoride–diethyl ether complex (BF3·OEt2) as a novel reagent system. We first examined the oxidative allylation of methyl 2-[hydroxy(phenyl)methyl]acrylate (1a) with allyltrimethylsilane (2) in the presence of equimolar amounts of DMP and BF3·OEt2 in dichloromethane. The reaction went to completion at room temperature and the product, methyl 2-benzoylehex-5-enoate (3a), was obtained in 85% yield (Scheme 1).

Next, we examined the reactivity of various Morita–Baylis–Hillman adducts in this reaction. Interestingly, several substrates reacted readily with allyltrimethylsilane (2) to produce a variety of homoallylated \( \beta \)-keto esters (Table 1). This method worked well with substrates derived from either aliphatic or aromatic aldehydes. In all cases, the reactions were clean and afforded the Michael adducts in good yields and without the formation of undesired intramolecular Nazarov cyclization products. Furthermore, this method is highly selective for the preparation of mono-homoallylated \( \beta \)-keto esters, whereas base-promoted alkylations of \( \beta \)-keto esters produce a mixture of the mono- and dialkylated products. The reac-
tion conditions were compatible with various functional-

ties, such as halides, aryl methyl ethers, esters, alkenes,

d and nitriles (Table 1). All of the products were character-

dized by $^1$H NMR and infrared spectroscopy, and mass

spectrometry. We also examined the use of various other

hypervalent iodine reagents in the reaction, including

iodosylbenzene (PhIO), (diacetoxyiodo)benzene

[PhI(OAc)$_2$], and 2-iodoxybenzoic acid (IBX), but DMP

was found to give the best conversion. Other oxidants,

such as Oxone and potassium bromate, failed to produce

the desired product, and the use of either DMP or

BF$_3$·OEt$_2$ alone did not give the expected product. Dichlo-
rromethane gave the best results as the solvent. The scope

of the DMP/BF$_3$·OEt$_2$ promoted oxidative allylation was

investigated with respect to various Morita–Baylis–

Hillman adducts and the results are presented in Table 1.

Table 1  One-Pot Oxidative Allylation of Morita–Baylis–Hillman Adducts Using the DMP/BF$_3$·OEt$_2$ System

<table>
<thead>
<tr>
<th>Entry</th>
<th>Morita–Baylis–Hillman Adduct</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OH CO$_2$Me</td>
<td>3a</td>
<td>12</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>F OH CO$_2$Me</td>
<td>3b</td>
<td>10</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>Cl OH CO$_2$Me</td>
<td>3c</td>
<td>11</td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td>MeO OH CO$_2$Me</td>
<td>3d</td>
<td>10</td>
<td>78</td>
</tr>
<tr>
<td>5</td>
<td>Br OH CO$_2$Et</td>
<td>3e</td>
<td>12</td>
<td>80</td>
</tr>
<tr>
<td>6</td>
<td>OPh OH CO$_2$Me</td>
<td>3f</td>
<td>12</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>Me OH CO$_2$Me</td>
<td>3g</td>
<td>14</td>
<td>84</td>
</tr>
<tr>
<td>8</td>
<td>MeO OH CO$_2$Me</td>
<td>3h</td>
<td>13</td>
<td>87</td>
</tr>
<tr>
<td>9</td>
<td>OH CO$_2$Me</td>
<td>3i</td>
<td>14</td>
<td>65</td>
</tr>
<tr>
<td>10</td>
<td>OH CO$_2$Me</td>
<td>3j</td>
<td>15</td>
<td>75</td>
</tr>
</tbody>
</table>
In conclusion, we have described a selective and efficient method for the conjugate addition of allyltrimethylsilane to in-situ-generated enones of Morita–Baylis–Hillman adducts using the DMP/BF₃·OEt₂ reagent system. The method has several advantages, such as operational simplicity, mild reaction conditions, clean reaction profiles, a simple workup procedure, and the use of inexpensive and readily available reagents, which make it a useful and attractive process for the preparation of homoallylated β-keto esters.

Melting points were recorded on Buchi R-535 apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer FT-IR 240-c spectrophotometer using KBr optics. ¹H NMR spectra were recorded on a Varian-unity 300 spectrometer in CDCl₃ using TMS as an internal standard. ¹³C NMR spectra were recorded on a Bruker Avance 300 spectrometer in CDCl₃. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV. HRMS were recorded on a Micromass Quatro LC triple quadrupole mass spectrometer for ESI analysis.

Homoallylated β-Keto Ester Derivatives 3; General Procedure
To a stirred solution of Morita–Baylis–Hillman adduct 1 (1 mmol) in anhyd CH₂Cl₂ (10 mL) was added Dess–Martin periodinane (1.1 mmol), and the mixture was stirred at r.t. until complete oxidation had taken place. Then, allyltrimethylsilane (2) (1.5 mmol) and BF₃·OEt₂ (1.2 mmol) were added in sequence, and the mixture was stirred at r.t. until the starting material had completely disappeared (see Table 1 for individual reaction times). The mixture was then quenched with sat. aq NaHCO₃ (10 mL) and extracted with CH₂Cl₂ (2 × 10 mL). The combined organic layers were washed with sat. aq NaHCO₃ (10 mL) and then dried (Na₂SO₄). Removal of the solvent, followed by chromatography (silica gel, EtOAc–hexane, 1:9) afforded the pure allyl derivative 3.

3a
Colorless oil.
IR (near): 3065, 2945, 2863, 1742, 1658, 1545, 1410, 1162, 1019, 845 cm⁻¹.

3b
Colorless liquid.
IR (near): 2958, 2848, 1760, 1644, 1565, 1445, 1142, 1007, 758 cm⁻¹.

3c
Light-brown liquid.
IR (near): 2956, 2854, 1744, 1654, 1542, 1436, 1138, 1020, 965 cm⁻¹.

3d
Colorless liquid.
IR (near): 2963, 2852, 1752, 1647, 1538, 1424, 1159, 1019, 856 cm⁻¹.

3e
Colorless oil.
IR (near): 3065, 2945, 2863, 1742, 1658, 1545, 1410, 1162, 1019, 845 cm⁻¹.

Table 1 One-Pot Oxidative Allylation of Morita–Baylis–Hillman Adducts Using the DMP/BF₃·OEt₂ System (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Morita–Baylis–Hillman Adduct</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td><img src="CO%E2%82%82Me" alt="OH" /></td>
<td>3k</td>
<td>12</td>
<td>85</td>
</tr>
<tr>
<td>12</td>
<td><img src="CN" alt="OH" /></td>
<td>3l</td>
<td>12</td>
<td>80</td>
</tr>
<tr>
<td>13</td>
<td><img src="CO%E2%82%82Me" alt="OH" /></td>
<td>3m</td>
<td>17</td>
<td>75</td>
</tr>
<tr>
<td>14</td>
<td><img src="CO%E2%82%82Me" alt="O₂N" /></td>
<td>3n</td>
<td>12</td>
<td>78</td>
</tr>
</tbody>
</table>

* Yield refers to the pure product after chromatography.
IR (neat): 3072, 2925, 2853, 1737, 1690, 1565, 1418, 1287, 1191, 1023, 915, 758 cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ = 1.19 (t, J = 6.8 Hz, 3 H), 2.01–2.16 (m, 4 H), 4.07–4.30 (m, 3 H), 4.97–5.05 (m, 2 H), 5.69–5.83 (m, 1 H), 7.34 (t, J = 8.3 Hz, 1 H), 7.68 (d, J = 8.3 Hz, 1 H), 7.87 (d, J = 8.3 Hz, 1 H), 8.02 (s, 1 H).

1H NMR (CDCl₃, 200 MHz): δ = 1.73–2.00 (m, 4 H), 3.49 (s, 3 H), 3.63 (s, 3 H), 3.67 (s, 3 H), 4.10 (t, J = 6.6 Hz, 1 H), 4.75–4.89 (m, 2 H), 5.49–5.71 (m, 1 H), 6.69 (d, J = 9.1 Hz, 1 H), 6.84 (dd, J = 2.4, 8.3 Hz, 1 H), 7.13 (d, J = 2.4 Hz, 1 H).

1H NMR (CDCl₃, 200 MHz): δ = 0.89 (t, J = 6.8 Hz, 3 H), 1.20–1.44 (m, 6 H), 1.47–1.63 (m, 2 H), 1.86–2.04 (m, 2 H), 2.34–2.58 (m, 2 H), 3.40 (t, J = 6.8 Hz, 1 H), 3.71 (s, 3 H), 4.95–5.05 (m, 2 H), 5.64–5.80 (m, 1 H).

ESI-MS: ml/z = 227 (M + 1).

HRMS: ml/z caleld for C₁₆H₂₀O₅Na: 249.1466; found: 249.1478.

3k

Colorless liquid.

IR (neat): 1754, 1657, 1579, 1457, 1244, 1137, 1022, 957, 751 cm⁻¹.

1H NMR (CDCl₃, 200 MHz): δ = 1.15–1.40 (m, 4 H), 1.56–2.10 (m, 10 H), 2.35–2.57 (m, 1 H), 3.55 (t, J = 6.6 Hz, 1 H), 3.70 (s, 3 H), 4.94–5.06 (m, 2 H), 5.60–5.86 (m, 1 H).

ESI-MS: ml/z = 261 (M + Na).

3l

Colorless liquid.

IR (neat): 2948, 2853, 2238, 1737, 1647, 1557, 1427, 1203, 1009, 839, 748 cm⁻¹.

1H NMR (CDCl₃, 200 MHz): δ = 2.05–2.18 (m, 4 H), 4.43–4.50 (t, J = 6.7 Hz, 1 H), 5.22–5.30 (m, 2 H), 5.90–6.06 (m, 1 H), 7.50–7.56 (m, 3 H), 7.82 (d, J = 8.3 Hz, 2 H).

ESI-MS: ml/z = 196 (M).


