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Author(s)
TANAKA, Koichi, SHIRAISHI, Ryusuke, TODA, Fumio

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A new method for stereoselective bromination of stilbene and chalcone in a water suspension medium

Koichi Tanaka,* Ryusuke Shiraishi* and Fumio Toda**

*Department of Applied Chemistry, Faculty of Engineering, Ehime University, Matsuyama, Ehime 790-8577, Japan
**Department of Chemistry, Faculty of Science, Okayama University of Science, 1-1 Ridai-cho, Okayama 700-0005, Japan

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Bromination reactions of (E)-stilbene and (E)-chalcone in a water suspension medium proceeded efficiently and stereoselectively, and the reaction products were collected easily by filtration.

The reaction of (E)-stilbene 1 with bromine in CH$_2$Cl$_2$ gives a 84:16 mixture of meso-2 and rac-3. Treatment of crystalline 1 with bromine vapor gives 2 and 3 in a 62:38 mixture in only 20% yield, although the reaction proceeds without passing through any liquid phases. We have now found that the bromination reaction of 1 and chalcone 4 could be controlled perfectly when carried out in the solid state by mixing both powdered 1 or 4 and solid brominating reagent 7. More interestingly, the bromination reactions proceeded more efficiently and selectively when carried out in a water suspension medium and the products were collected easily by filtration. This method has a big advantage as no organic solvent is necessary during the reaction and separation of the product. This provides a new simple, efficient and stereoselective bromination procedure.

After keeping a mixture of powdered 1 and powdered 7 at room temperature for 168 h in the solid state, water was added to the reaction mixture and then the product was isolated by filtration to give only meso-2 in 71% yield (Table 1). Bromination reaction of chalcone 4 with 7 in the solid state was also found to proceed efficiently and stereoselectively. For example, when a mixture of powdered 4 and powdered 7 was kept in the solid state for 4 h at room temperature, erythro-5a was obtained exclusively in 89% yield (Table 2). As well as 7, phenyltrimethylammonium tribromide 8 was also effective for stereoselective bromination of 4a, but the sterically bulky reagent 9 takes a long time for the reaction to go to completion (Table 3).

Very interestingly, bromination of the crystalline powder of 1 with 7 in a water suspension medium proceeded much more efficiently and conveniently. For example, a suspension of both powdered 1 and 7 in a small amount of water was stirred at room temperature for 15 h. The reaction mixture was filtered and air-dried to give meso-2 in 88% yield (Table 1). Bromination of chalcones 4a-c was also found to proceed very efficiently and selectively in a water suspension medium. For example, a suspension of powdered chalcone 4a and 7 in a small amount of water was stirred at room temperature for 1.5 h to give erythro-5a in 90% yield. Similar treatment of 4b and 4c with 7 in a water suspension gave erythro-5b and 5c in 90 and 87% yield, respectively (Table 4).

It has been reported that gas/solid bromination of a single crystal of 4,4'-dimethylchalcone 4b, which crystallizes in a chiral space group (P2$_1$/c), yields optically active erythro-5b in 6% ee.$^5$ The enantiomeric purity of the asymmetric bromination of 4b was found to improve when the reaction was carried out in a water suspension medium. For example, when the powdered chiral crystal of 4b, which shows a (−)-Cotton effect in the solid-state CD spectrum,$^7$ was stirred in a small amount of water containing 7 for 3 h, optically active adduct (−)-5b in 13% ee was obtained in 73% yield.

Enantioselective bromination of cyclohexene in the inclusion crystal of 11 with optically active host compound 10 was also reported.$^3$
accomplished [reaction (1)]. When a solution of a mixture of (−)-10 and cyclohexene in ether was kept at room temperature for 12 h, a 2:1 inclusion complex 11 was obtained as colorless prisms (mp 134–137°C) in 72% yield. When a powdered mixture of 11 and 7 was kept at room temperature in the solid state for 3 days, (−)-trans-1,2-dibromocyclohexane 12 in 12% ee was obtained in 56% yield.

In conclusion, the bromination reaction of (E)-stilbene 1 and (E)-chalcones 4 in a water suspension medium provides a simple, efficient, stereoselective and environmentally benign method which is superior to previously reported methods.

Experimental

Typical procedure for the bromination reaction of (E)-stilbene in a water suspension medium

Crystals of 1 were finely powdered by grinding with a pestle and mortar for a few minutes. A suspension of the crystalline powder of 1 (0.5 g, 2.8 mmol), 7 (1.33 g, 4.2 mmol) and water (5 ml) was stirred at room temperature for 15 h. The reaction mixture was filtered, washed with water and air-dried to give meso-2 as a colorless powder (0.84 g, 88% yield). The crude crystals thus obtained were recrystallized from toluene to give pure meso-2 as colorless needles. Data for meso-2: mp 243–245°C (lit., 1 244–245°C; δH (300 MHz; CDCl3; Me4Si) 7.6–7.2 (10H, m), 5.48 (2H, s); δC (75 MHz; CDCl3; Me4Si) 140.02, 129.02, 128.77, 127.91, 56.08.

Table 4 Bromination reactions of (E)-chalcone 4a–c with 7 in a water suspension medium

<table>
<thead>
<tr>
<th>Chalcones</th>
<th>Time/h</th>
<th>Yield (%)</th>
<th>erythro-5:threo-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>1.5</td>
<td>90</td>
<td>100:0</td>
</tr>
<tr>
<td>4b</td>
<td>4</td>
<td>90</td>
<td>100:0</td>
</tr>
<tr>
<td>4c</td>
<td>2</td>
<td>87</td>
<td>100:0</td>
</tr>
</tbody>
</table>

* The ratio was determined by 1H NMR.

Typical procedure for the bromination reaction of (E)-chalcone in a water suspension medium

Crystals of 4a were finely powdered by grinding with a pestle and mortar for a few minutes. A suspension of crystalline powder of 4a (1.97 g, 9.5 mmol), 7 (3.63 g, 11.4 mmol) and water (20 ml) was stirred at room temperature for 1.5 h. The reaction mixture was filtered, washed with water and air-dried to give erythro-5a as a colorless powder (3.12 g, 90% yield). The crude crystals thus obtained were recrystallized from toluene to give pure erythro-5a as colorless needles. Data for erythro-5a: mp 161–162°C (lit., 4 160°C; ν(C=O) 1678 cm⁻¹; δH (300 MHz; CDCl3; Me4Si) 7.4–8.1 (10H, m), 5.83 (1H, d, J 11.4), 5.65 (1H, d, J 11.4).

References

5 The optical purity was determined by GC (Chirsasil-dex CB, Chrompak, The Netherlands).