PERKIN 1 COMMUNICATION

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

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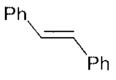
Bromination reactions of (*E*)-stilbene and (*E*)-chalcone in a water suspension medium proceeded efficiently and stereoselectively, and the reaction products were collected easily by filtration.

The addition reaction of bromine to olefin is still difficult to control in most cases. For example, the reaction of (*E*)-stilbene **1** with bromine in CH_2Cl_2 gives a 84:16 mixture of *meso*-**2** and *rac*-**3**.[1] 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.[1] 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.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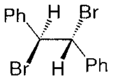
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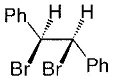
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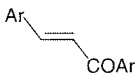
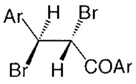
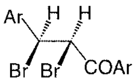
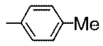

4a: Ar=Ph

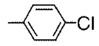

erythro-**5**

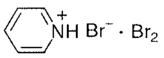

threo-**6**

b: Ar=



c: Ar=

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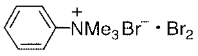

8

$(n\text{-}Bu)_4\overset{+}{N}\,Br^- \cdot Br_2$

9

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 **4a** 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).

Table 1 Bromination reactions of (*E*)-stilbene **1** in solution, gas/solid, solid/solid and water suspension media

Conditions	Time/h	Yield (%)	*meso*-**2**:*rac*-**3**[a]
CH_2Cl_2	12	98	84:16[b]
Gas/solid	64	20	62:38[b]
Solid/solid	168	71	100:0
Water suspension	15	88	100:0

[a] The ratio was determined by ^{13}C NMR, see ref. 1. [b] Data from ref. 1.

Table 2 Bromination reactions of (*E*)-chalcone **4a** with **7** in solution, solid/solid and water suspension media

Conditions	Time/h	Yield (%)	*erythro*-**5a**:*threo*-**6a**[a]
CH_2Cl_2	0.5	90	86:14
Solid/solid	4	89	100:0
Water suspension	1.5	90	100:0

[a] The ratio was determined by ^1H NMR, see ref. 5.

Table 3 Bromination reaction of (*E*)-chalcone **4a** in the solid state

Reagents	Time/h	Yield (%)	*erythro*-**5a**:*threo*-**6a**[a]
7	4	89	100:0
8	4	91	100:0
9	168	83	100:0

[a] The ratio was determined by ^1H NMR, see ref. 5.

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).

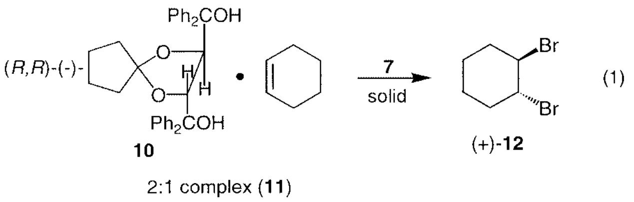
It has been reported that gas/solid bromination of a single crystal of 4,4′-dimethylchalcone **4b**, which crystallizes in a chiral space group ($P2_12_12_1$), yields optically active *erythro*-**5b** in 6% ee.[2] The enantioselectivity of the asymmetric bromination of **4b** was found to improve when 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,[3] 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

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

Chalcones	Time/h	Yield (%)	*erythro*-**5** : *threo*-**6**[a]
4a	1.5	90	100 : 0
4b	4	90	100 : 0
4c	2	87	100 : 0

[a] The ratio was determined by ^{1}H NMR.



(1)

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[5] was obtained in 56% yield by distillation of the reaction mixture.

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); δ_H (300 MHz; CDCl$_3$; Me$_4$Si) 7.6–7.2 (10H, m), 5.48 (2H, s); δ_C (75 MHz; CDCl$_3$; Me$_4$Si) 140.02, 129.02, 128.77, 127.91, 56.08.

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}; δ_H (300 MHz; CDCl$_3$; Me$_4$Si) 7.4–8.1 (10H, m), 5.83 (1H, d, *J* 11.4), 5.65 (1H, d, *J* 11.4).

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4 R. E. Lutz, D. F. Hinkley and R. H. Jordan, *J. Am. Chem. Soc.*, 1951, **73**, 4647.
5 The optical purity was determined by GC (Chirasil-dex CB, Chrompak, The Netherlands).

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