

Synthesis of stilbenes promoted by the mixture of zinc and iron powder

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Stilbenes have been synthesised by a one-pot reaction of aldehydes with benzyl bromide. The reaction was promoted by both triphenylphosphine and the mixture of zinc and iron together in sealed tube. The yields ranged from moderate to excellent.

Keywords: one-pot reaction, stilbenes, zinc and iron mixture, aldehyde, sealed tube

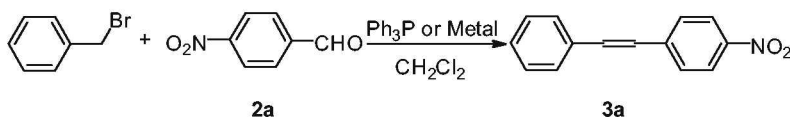
Stilbenes have been isolated from various plants and they have wide range of biological activity and potential therapeutic value.^{1–8} A number of methods^{9–13} have been reported for the preparation of olefins including the well known Wittig reaction. However, these methods have limitations.^{14–17} Recently more efficient methods for the preparation of carbon–carbon double bonds have been developed.¹⁸ Using metallic reagent, such as Pd,^{19–20} Cd,²¹ Zn,^{22–25} Zn–Cu couple.²⁶ These involve only one step, and the experimental procedure was significantly simplified. Many substituted olefins have now been obtained using this method including α , β -unsaturated esters,^{19–23} amides^{20,24} and nitriles.²⁵ However, all of these olefins contain strong electron-withdrawing substituents. No olefins with weak electron-withdrawing group substituents such as stilbenes have been synthesised. We here report a one-pot synthesis of stilbenes.

Benzyl bromide and 4-nitrobenzaldehyde **2a** were used as starting materials to optimise the reaction conditions. We investigated the effects of different metallic reagents, solvents and temperatures on reaction (Scheme 1). All the metallic reagents we chose were cheap. The results were summarised in Table 1.

As Table 1 shows, stilbenes could not be obtained by the classical Reformatsky type condensation without the addition of Ph₃P (Table 1, entries 1–3). Fortunately, the reaction took place when triphenylphosphine was added into the mixture. It should be noted that the yield was significantly improved when the reaction was carried out in a sealed tube, in contrast to the yield in a Schlenk tube (Table 1, entries 8). Thus, all the optimised reactions were carried out in sealed tube.

Table 1 also indicates that metallic reagent plays an important role in this reaction. The reaction did not proceed without metallic reagent. The mixture of Zn and Fe improved the yield better than Zn and Fe, alone (Table 1, entries 4–7). Examination of solvent effect revealed that CH₂Cl₂ was the best choice (Table 1, entries 8–11). On the basis of the results, a gradual increase in yield was observed when the temperature was increased from 60 to 80 °C (Table 1, entries 12–14).

Having determined the optimal reaction conditions, we were interested in exploring the scope of this one-pot reaction. Various stilbenes have been synthesised in moderate yields, and all the products were identified by MS, IR and ¹H NMR. The results are summarised in Table 2 (Scheme 2).



Scheme 1

Table 1 Optimisation of the synthesis of stilbenes

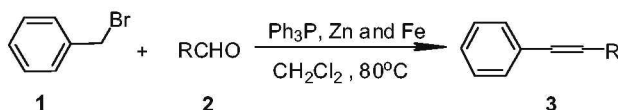
Entry	Temperature/°C	Solvent	Additive	Metallic reagent	Time/h	Yield/% ^a
1	60	CH ₂ Cl ₂	–	Zn	10	–
2	60	CH ₂ Cl ₂	–	Fe	10	–
3	60	CH ₂ Cl ₂	–	Zn–Cu	10	–
4	60	CH ₂ Cl ₂	Ph ₃ P	–	10	–
5	60	CH ₂ Cl ₂	Ph ₃ P	Zn	10	36 ^b
6	60	CH ₂ Cl ₂	Ph ₃ P	Fe	10	33 ^b
7	60	CH ₂ Cl ₂	Ph ₃ P	Zn and Fe	10	41 ^b
8	60	CH ₂ Cl ₂	Ph ₃ P	Zn and Fe	15	45 ^b 62 ^c
9	120	–	Ph ₃ P	Zn and Fe	15	36 ^c
10	120	DMF	Ph ₃ P	Zn and Fe	15	44 ^c
11	80	CH ₃ CN	Ph ₃ P	Zn and Fe	15	54 ^c
12	70	CH ₂ Cl ₂	Ph ₃ P	Zn and Fe	15	75 ^c
13	80	CH ₂ Cl ₂	Ph ₃ P	Zn and Fe	15	90 ^c
14	100	CH ₂ Cl ₂	Ph ₃ P	Zn and Fe	15	79 ^c

^aIsolated yield.

^bThe reaction was proceed in Schlenk tube.

^cThe reaction was proceed in sealed tube.

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Scheme 2

Table 2 Synthesis of stilbenes

Entry	Product	R	Yield/% ^a	Z/E ^b
1	3a	4-NO ₂ C ₆ H ₄	90	20:80
2	3b	4-ClC ₆ H ₄	80	30:70
3	3c	C ₆ H ₅	69	30:70
4	3d	2-NO ₂ C ₆ H ₄	88	13:87
5	3e	2-CH ₃ OC ₆ H ₄	68	35:65
6	3f	4-CH ₃ C ₆ H ₄	71	20:80
7	3g	4-BrC ₆ H ₄	85	30:70
8	3h	C ₆ H ₅ CH=CH	65	35:65
9	3i	C ₃ H ₇	—	—

^aIsolated yield, product characterised by ¹H NMR, IR and MS.^bRatio determined by ¹H NMR (300 MHz, CDCl₃) analysis.

As Table 2 shows, the corresponding products were not obtained when an aliphatic aldehyde was treated with the other reactants under the same condition except for the formation of **3h**.

The ratios of Z/E isomers were determined by the ¹H NMR spectra. It was reported that the signals of vinyl proton of (Z)-stilbenes were at lower field than those of the corresponding (E)-compounds. For example, ¹H NMR spectrum shows that the chemical shift of vinyl proton of (E)-1-nitro-4-styrylbenzene was 7.27 ppm,²⁷ while the corresponding chemical shift of (Z)-1-nitro-4-styrylbenzene compound was 6.65 ppm. The result was in accordance with our result.

In conclusion, stilbenes were obtained through the one-pot reaction of benzyl bromide with an aldehyde promoted by triphenylphosphine and a mixture of Zn and Fe in a sealed tube. No expensive metallic reagents were needed for this reaction. Thus, an economical and simple method for the synthesis of stilbenes was provided.

Experimental

Melting points were recorded on Digital Melting Point Apparatus WRS-1B and uncorrected. TLC was performed using precoated silica gel 60 GF₂₅₄ (0.25 mm) and column chromatography was performed using silica gel (300–400 mesh). ¹H NMR spectra were recorded on a FT-Bruker AT-300 instrument using CDCl₃ as solvent with tetramethylsilane (TMS) as the internal standard. J-values are given in Hz. IR spectra were measured on a Bruker Vector55 instrument. MS were measured on a HP5989B instrument.

General procedure for preparation of stilbenes

Triphenylphosphine (1.2 mmol), benzyl bromide (1.2 mmol), the aldehyde (1.0 mmol) and the mixture of Zn and Fe (1.2 mmol) were added into a sealed tube. The mixture was stirred and heated at 80°C for 15 h. The product was purified by chromatography on silica gel with ethyl acetate and petroleum ether (60–90°C). The physical and spectroscopic data of all compounds are as follows. Zinc (dust) which was commercial available (24 g) was stirred with 2% HCl (60 mL) for 1 min. Then the acid was removed by filtration, and washed in a 100 mL beaker with a 60 mL portion of 2% HCl, three 20 mL portions of distilled water, two 20 mL portions of 95% EtOH, and finally with 60 mL of absolute Et₂O. (The wash solutions were removed each time by filtration.) The material was then dried thoroughly. Iron was disposed as mentioned above.

1-Nitro-4-styrylbenzene (3a): M.p. 153–155°C (Lit.²⁷ m.p. 156–157°C); ¹H NMR (300 MHz, CDCl₃): δ 8.21 (d, *J* = 8.7 Hz, 2H), 7.63 (d, *J* = 8.7 Hz, 2H), 7.55 (*J* = 7.4 Hz, 2H), 7.42–7.31 (m, 3H), 7.27 (E) + 6.65 (Z) [d, *J* = 16.3 Hz (E), 12.0 Hz (Z), 1H], 7.14 (E) + 6.55 (Z) [d, *J* = 16.3 Hz (E), 12.0 Hz (Z), 1H]. EI-MS (*m/z*): 225 (M⁺, 65), 207 (20), 195 (30), 152 (25), 76 (15). IR (cm⁻¹): 1643, 1587, 1508, 837, 764, 689.

1-Chloro-4-styrylbenzene (3b):²⁸ ¹H NMR (300 MHz, CDCl₃): δ 7.51 (d, *J* = 7.1 Hz, 2H), 7.06–7.45 (m, 7H), 7.23 (E) + 6.64 (Z) [d, *J* = 16.3 Hz (E), 12.0 Hz (Z), 1H], 7.11 (E) + 6.53 (Z) [d, *J* = 16.3 Hz (E), 12.0 Hz (Z), 1H]. EI-MS (*m/z*): 214 (M⁺, 80), 152 (10), 89 (25), 76 (20), 44 (20). IR (cm⁻¹): 1644, 1551, 1491, 861, 786, 694.

1,2-Diphenylethene (3c): M.p. 122–124°C (Lit.²⁹ m.p. 120–122°C); ¹H NMR (300 MHz, CDCl₃): δ 7.52 (d, *J* = 7.4 Hz, 4H), 7.36 (t, *J* = 7.2 Hz, 4H), 7.28 (t, *J* = 7.2 Hz, 2H), 7.11 (E) + 6.60 (Z) (s, 2H). EI-MS (*m/z*): 258 (M⁺, 180), 180 (M⁺, 75), 152 (10), 108 (20), 44 (10). IR (cm⁻¹): 1644, 1570, 1551, 850, 744, 689.

1-Nitro-2-styrylbenzene (3d):³⁰ ¹H NMR (300 MHz, CDCl₃): δ 7.97 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 7.7 Hz, 2H), 7.64–7.26 (m, 7H), 7.51 (E) + 6.92 (Z) [d, *J* = 16.0 Hz (E), 12.0 Hz (Z), 1H], 7.38 (E) + 6.76 (Z) [d, *J* = 16.0 Hz (E), 12.0 Hz (Z), 1H]. EI-MS (*m/z*): 225 (M⁺, 5), 208 (20), 165 (35), 77 (15), 51 (7). IR (cm⁻¹): 1606, 1567, 1523, 856, 777, 699.

1-Methoxy-2-styrylbenzene (3e):³¹ ¹H NMR (300 MHz, CDCl₃): δ 7.82 (d, *J* = 8.7 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 2H), 7.35–7.28 (m, 6H), 7.22 (E) + 6.83 (Z) [d, *J* = 16.3 Hz (E), 12.0 Hz (Z), 1H], 7.07 (E) + 6.71 (Z) [d, *J* = 16.3 Hz (E), 12.0 Hz (Z), 1H], 3.86 (s, 3H). EI-MS (*m/z*): 210 (M⁺, 100), 179 (15), 165 (50), 152 (25), 91 (15). IR (cm⁻¹): 1689, 1589, 1490, 968, 751, 693.

1-Methyl-4-styrylbenzene (3f):²⁸ ¹H NMR (300 MHz, CDCl₃): δ 7.49 (d, *J* = 7.5 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.15 (d, *J* = 7.9 Hz, 2H), 7.09 (E) + 6.56 (Z) [d, *J* = 16.4 Hz (E), 12.0 Hz (Z), 1H], 7.04 (E) + 6.45 (Z) [d, *J* = 16.4 Hz (E), 12.0 Hz (Z), 1H], 2.35 (s, 3H). EI-MS (*m/z*): 194 (M⁺, 100), 179 (95), 165 (8), 152 (7), 115 (10). IR (cm⁻¹): 2920, 1644, 1576, 1507, 968, 804, 693.

1-Bromo-4-styrylbenzene (3g):³² ¹H NMR (300 MHz, CDCl₃): δ 7.51 (m, 4H), 7.38 (m, 5H), 7.21 (E) + 6.63 (Z) [d, *J* = 16.4 Hz (E), 12.0 Hz (Z), 1H], 7.09 (E) + 6.51 (Z) [d, *J* = 16.4 Hz (E), 12.0 Hz (Z), 1H]. EI-MS (*m/z*): 258 (M⁺, 55), 178 (100), 152 (13), 89 (25), 76 (18). IR (cm⁻¹): 1689, 1644, 1562, 965, 809, 677.

1,4-Diphenylbuta-1,3-diene (3h):³³ ¹H NMR (300 MHz, CDCl₃): δ 7.80 (t, 4H), 7.64 (t, 4H), 7.39 (t, 2H), 7.12 (d, *J* = 16.4 Hz, 2H), 6.81 (d, *J* = 16.4 Hz, 2H). EI-MS (*m/z*): 51.10 (13.3), 57.10 (26.42), 104.15 (10.40), 119.20 (56.68), 144.10 (39.06), 206.10 (M⁺, 100). IR (cm⁻¹): 1722, 1600, 1493, 987, 749.

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