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Synthesis of stilbene, 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl via Horner–Wadsworth–Emmons reaction in phase-transfer catalysis system

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ABSTRACT

Stilbenes, 1,4-distyrylbenzenes and 4,4′-distyrylbiphenyls were synthesized via Horner–Wadsworth–Emmons (HWE) reaction in liquid–liquid (LL) and solid–liquid (SL) phase transfer catalysis (PTC) systems. The effect of the side reaction, reactants and the third phase on the activity of HWE reaction were investigated. For aldehydes bearing electron-donating substitute, the yields were more than 90% and the products were all (*E*)-isomers in both PTC systems. The SL-PTC system was milder than LL-PTC system for HWE reaction due to the different mechanisms. The side reaction of aldehyde was similar to Cannizzaro reaction, whereas the molar ratio of benzoic acid to benzyl alcohol as the products was not 1:1. The limited third phase was discovered to exist in LL-PTC system. In SL-PTC system, the third phase could increase substantially the reaction rate. Moreover, the aqueous phase in LL-PTC system could be reused four times without sacrifice of the yield and reaction rate.

1. Introduction

Stilbene, 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl bear remarkable optical, photochemical and photophysical properties [1]. They have widespread applications in many fields ranging from fine chemistry and materials science to biomedicine. They can be used as fluorescent whitening agents in textile, paper manufacturing and household detergents [2], two-photon absorbing materials [3–6] and blue electroluminescent materials [7–11] in the optoelectronic device, drugs and antitumor agents in pharmacology [12,13], molecular probes and labels in bioassay [14] and etc. With the discovery of new applications, such as molecular conformational switches [15], integral part of phenylene vinylene-based oligomers and polymers [16], energy transporter in one-dimensional channels [17,18] and bridge spanning redox-active moieties [19,20], they have drawn great interests of more and more researchers.

Many synthetic methods for stilbenes, 1,4-distyrylbenzenes and 4,4′-distyrylbiphenyls have been developed. The condensation reactions of arylmethyl compound are the most common methods, such as Grignard reaction, Knoevenagel reaction, Wittig reaction and Horner–Wadsworth–Emmons (HWE) reaction. Particularly, HWE reaction is the main pathway employed in industry. Some other condensation routes for new stabilized carbanion have also been reported [21]. Nonetheless, the low atom economy, the high (*Z*)-factor and the high cost of solvents are the main disadvantages of the condensation reaction. Hence, the new synthetic method of stilbenes, 1,4-distyrylbenzenes and 4,4′-distyrylbiphenyls has been a hot area of research. The dimerization reactions had been used been used for many years, such as Meerwein arylation [22], Stille coupling reaction [23] and Heck reaction [24]. As one of basic organic synthetic methods, Heck reactions has been extensively investigated in the synthesis of stilbene, 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl [25–30]. However, the high cost of catalyst, ligand and dipolar aprotic solvent limits their application in industry. As an alternative to these methods, we proposed here an easy and convenient phase transfer catalysis (PTC) routes via HWE reaction (Scheme 1).

PTC is one of the most widely used synthetic techniques and has had more than 700 industrial applications [31,32]. The major advantages of PTC include its simplicity, use of inexpensive reagents

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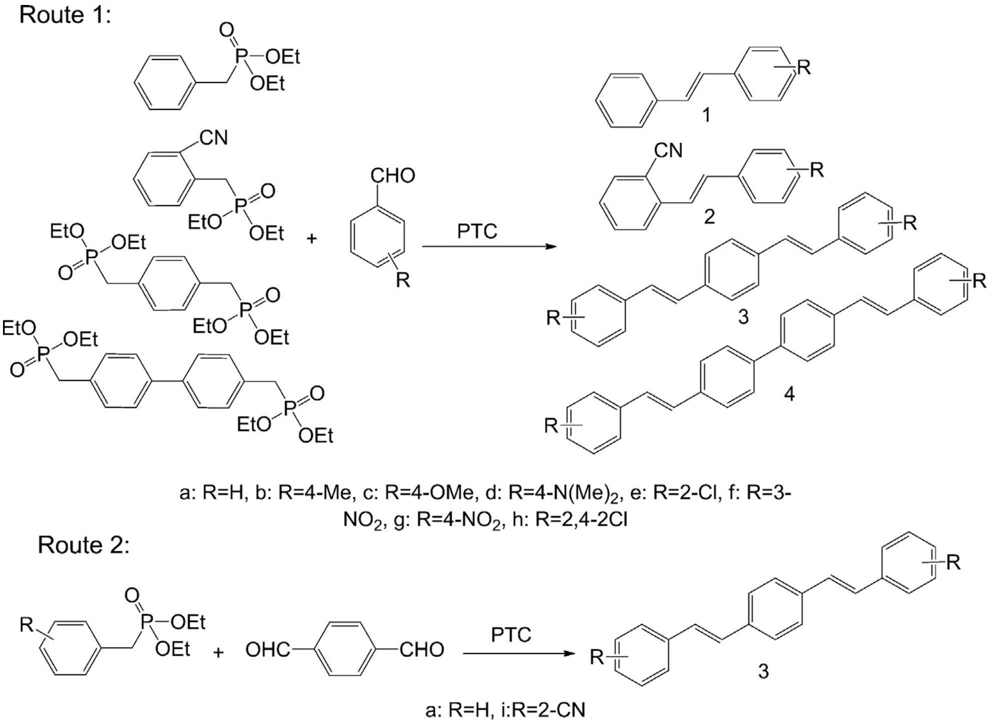


Scheme 1. The synthetic routes of stilbene, 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl in PTC system.

under mild conditions, high reaction rate and high selectivity to the desired product [33]. HWE reaction under PTC conditions was firstly reported in 1974 [34]. The synthesis of α,β-unsaturated compounds via HWE reaction in solid–liquid PTC (SL-PTC) system was then researched [35,36]. At present, HWE reaction in PTC system have been used in the synthesis of polymer [37] and dipolar organometallic complexes [38,39]. Nevertheless, those reactions suffer from one or more problems, such as long reaction time, low yield and expensive solvent. Moreover, there are few studies on the mechanism of HWE reaction under PTC conditions and the parameters influenced the activity of HWE reaction in PTC system have rarely been investigated.

In this work, HWE reactions for monophosphonate or bisphosphonate with aldehyde were preceded in liquid–liquid PTC (LL-PTC) and SL-PTC system (Scheme 1). The yield and geometric selectivity for HWE reaction in these two PTC systems were compared. The effects of the side reaction, reactants and the third phase on the activity of HWE reaction in both PTC systems were studied. Furthermore, the reusability of the aqueous phase in LL-PTC system was discussed. These results will provide a potential application for HWE reaction in industry and show new insights into the mechanisms of PTC reaction.

2. Experimental

2.1. Chemical and instruments

Diethyl benzylphosphonate (DEBP), diethyl 2-cyanobenzylphosphonate (DCBP), tetraethyl (1,4-phenylenebis(methylene)) bis(phosphonate) (TEPP) and tetraethyl ([1,1′-biphenyl]-4,4′-diylbis(methylene))bis(phosphonate) (TEBP) were prepared according to the literature [40–42]. Other chemicals were purchased from Sinopharm Chemical Reagent Co. Ltd. and used directly as received without further purification. Dry toluene was obtained by distillation under nitrogen in the presence of sodium and benzophenone.

^{1}H and ^{13}C NMR spectra were recorded at 298 K on a Bruker ARX 400 spectrometer (at 400.13 and 100.62 MHz). $CDCl_3$ was used as solvent and chemical shifts were internally referenced to Me_4Si (0 ppm). IR spectra were obtained on a Thermo Electron Corporation Nicolet 380 FT-IR spectrophotometer. Elemental analysis (EA) was performed on an Elementar Vario (III) to determine the carbon, hydrogen and nitrogen contents of the product. High performance liquid chromatography (HPLC) analysis was performed on the Agilent 1200 system equipped with a Zorbax Eclipse XDB-C18 column (150 mm × 0.46 mm, 0.5 μm) and a UV variable wavelength detector (VWD).

2.2. Method

2.2.1. General synthesis of stilbene in LL-PTC system

20 g of 50% (m/m) NaOH aqueous solution was placed in a 100 mL four-necked flask and stirred at 1400 rpm. A solution of DEBP (10 mmol), TBAB (0.5 mmol) in toluene (30 mL) was added at 35 °C. Simultaneously, 10 mmol of aldehyde in 15 mL of toluene was dropped into the flask over an appropriate period. After completion of the reaction as indicated by TLC, the resulting mixture was cooled to room temperature and transferred into a separatory funnel. The aqueous phase was separated and the organic phase was washed twice with 10 mL of 3% (v/v) HCl solution and water, respectively. Subsequently, the organic phase was dried over $MgSO_4$. The toluene was removed under reduced pressure and the residue was recrystallized from n-hexane.

2.2.2. General synthesis of 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl in LL-PTC system

The procedure was similar to that for the synthesis of stilbenes in LL-PTC system. The resulting mixture was transferred to a separatory funnel. After the phases had been separated, the organic phase was filtered. The precipitate was rinsed twice using 3% HCL solution and ethanol, respectively.

2.2.3. *General synthesis of stilbenes in SL-PTC system*

A mixture of the DEBP (10 mmol), TBAB (0.5 mmol), solid NaOH (40 mmol) and dry toluene (30 mL) was stirred at 1400 rpm. Aldehyde (10 mmol) in 15 mL of toluene was added dropwise at 35 °C. The resulting mixture was stirred for the appropriate time. After completion of the reaction as indicated by TLC, 10 mL of H_2O was added to dissolve the excess of solid NaOH. The resulting mixture was cooled to room temperature and transferred to a separatory funnel. The aqueous layer was separated and the treatment of the organic phase was similar to that in the synthesis of stilbenes in LL-PTC system.

2.2.4. *General synthesis of 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl in SL-PTC system*

The procedure was similar to that for the synthesis of stilbenes in SL-PTC system. After completion of the reaction as indicated by TLC, 10 mL of H_2O was added. The aqueous layer was separated. The organic layer was filtered and the precipitate was washed twice with 3% HCL solution and ethanol, respectively.

2.2.5. *The side reaction of aldehyde in PTC system*

A solution of TBAB (0.5 mmol), aldehyde (10 mmol) in toluene (30 mL) was placed in a 100 mL flask and stirred at 1400 rpm. 20 g of 50% (m/m) NaOH aqueous solution or 40 mmol of solid NaOH was added at 35 °C. After the completion of the reaction as indicated by TLC, the aqueous phase was separated and washed twice with 5 mL of toluene. The pH value of the aqueous phase was adjusted to 2 with HCl solution. The resulting precipitate was filtered and rinsed twice with 3% HCl solution. The organic layer was washed with three 5 mL-portions of 3% HCl solution. The organic phase was dried over $MgSO_4$ and evaporated to dryness. The crude products were purified by recrystallization from ethanol.

2.2.6. *The effect of reactants on the rate of HWE reaction in PTC system*

A solution of phosphonate, aldehyde and TBAB (0.5 mmol) in toluene (30 mL) was placed in a 100 mL four-necked flask equipped with a mechanical stir, a thermometer and a sample port, and stirred at 1400 rpm. 20 g of 50% (m/m) NaOH aqueous solution or 40 mmol of solid NaOH was added at 35 °C. The sample (about 50 μL) was withdrawn from the reaction mixture at a regular time interval and put into test tube. Subsequently, 0.2 mL of 10% (v/v) hydrochloric acid was added to quench the reaction. Finally, the solution was diluted to 10 mL with 50% (v/v) aqueous acetonitrile. The contents of the stilbene, aldehyde and toluene were estimated by HPLC with an external standard method. The HPLC was operated with a mobile phase consisting of 50:50 (v/v) water/acetonitrile and a flow rate of 1.0 mL/min. The detection wavelength was set at 260 nm and the column temperature was 30 °C.

2.2.7. *The effect of the third phase(ω phase) on HWE reaction in SL-PTC system*

A mixture of solid NaOH (40 mmol), dry toluene (15 mL) and water was stirred at 1400 rpm. A solution of benzaldehyde (10 mmol), DEBP (10 mmol) and TBAB (0.5 mmol) in toluene (15 mL) was added at 35 °C. The sample (about 50 μL) was withdrawn from the reaction mixture at a regular time interval. The treatment and analysis of sample were similar to that described in Section 2.2.6.

2.2.8. *The reuse of the aqueous phase in LL-PTC system*

20 g of 50% (m/m) NaOH aqueous solution was placed in a 100 mL flask and stirred at 1400 rpm. A solution of DEBP (10 mol), benzaldehyde (10 mol), TBAB (0.5 mmol) in toluene (30 mL) was added at 35 °C. After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature and transferred to a separatory funnel. The aqueous phase was separated and the treatment of the organic phase was similar to that described in Section 2.2.1. The weight of the aqueous phase was adjusted to 20 g by adding 50% (m/m) NaOH aqueous solution. Subsequently, the resulting solution was reused by adding the fresh organic phase.

3. Result and discussion

3.1. *Synthesis of stilbene, 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl in PTC system*

A series of stilbenes, 1,4-distyrylbenzenes and 4,4′-distyrylbiphenyls were prepared according to the synthetic route 1 and 2 shown in Scheme 1. The yield and geometric selectivity for each reaction were listed in Table 1. The structure of the product was fully characterized by IR, ^{1}H NMR and ^{13}C NMR spectrometry and element analysis. The datum were given in the Supplementary Information.

It can be observed from Table 1 that the activity of HWE reaction is varied with PTC system. The yield of stilbenes with electron donating group did not change significantly with PTC system, whereas the yield of stilbenes containing electron-withdrawing group in SL-PTC system was higher than that in LL-PTC system. All the yields of 1,4-distyrylbenzenes and 4,4′-distyrylbiphenyls in SL-PTC system were lower than those in LL-PTC system. These may be attributed to the different mechanisms of HWE reaction in these two PTC systems. In LL-PTC system, HWE reaction undergoes the extraction mechanism. Hydroxide ion (OH^-) which is extracted by PTCs into the organic phase can deprotonate phosphonate quickly. Subsequently, the reaction of the carbanion and aldehyde proceed in the organic phase. However, the interfacial mechanism is preferred in SL-PTC system. The phosphonate molecules aggregate in the interfacial region and the available OH^- on the surface of solid NaOH can deprotonate the phosphonate. Subsequently, the PTCs cation in the interfacial region couples with the carbanion. Finally, the carbanion is transferred into the organic phase and reacts with the aldehyde. The basicity of OH^- in the interfacial region is weaker than that extracted into the organic phase [43]. Consequently, the rate of the deprotonation reaction in LL-PTC system is higher than that in SL-PTC system, and the reactants are prone to undergo side reactions in LL-PTC system, especially for aldehyde containing electron-withdrawing group. Hence, SL-PTC system is milder than LL-PTC system for HWE reaction. In HWE reaction for TEBP or TEPP, the products would easily deposit on the surface of solid NaOH due to their poor dissolution in toluene. Less free OH^- is available and in turn the carbanion could not be generated efficiently. Consequently, the extensive side reaction occurs and the yield is decreased in SL-PTC system.

The products were predominantly the (*E*)-isomers in both PTC systems, especially for aldehyde with electron-donating substitute or nitro group. In HWE reaction, the four-center transition state (TS) has two conformation - *cis* TS and *trans* TS. The *cis* TS is later (more oxaphosphetane-like) and hence less flexible. The *cis* TS is constrained to be closer to planar which leads to unfavorable 1,2 interactions. Although the *trans* TS is semi-puckered, it is less hindered and favored (Scheme 2) [44]. Therefore, *E* selectivity in HWE reactions was found. For HWE reaction of 2-halobenzaldehyde or 2,4-dihalobenzaldehyde with DEBP, the proportion of (*Z*)-stilbene increased due to the cooperative ortho halo effect [45]. However, there was no (*Z*)-isomer product in HWE reaction for DCBP, TEPP or DPP. The steric hindrance of the cyano group and the conjugation of the π bond can overcome the cooperative ortho halo effect.

Table 1
The yield and *E/Z* ratio of stilbene, 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl in HWE reaction under PTC conditions.

Compound number	LL-PTC		SL-PTC		Compound number	LL-PTC		SL-PTC	
	Yield	*E/Z*[b]	Yield	*E/Z*[b]		Yield	*E/Z*[b]	Yield[a]	*E/Z*[b]
1a	0.95	>99/1	0.96	>99/1	**3a**	0.93	>99/1	0.88	>99/1
1b	0.96	>99/1	0.97	>99/1	**3b**	0.94	>99/1	0.84	>99/1
1c	0.95	>99/1	0.93	>99/1	**3c**	0.95	>99/1	0.85	>99/1
1d	0.89	>99/1	0.90	>99/1	**3d**	0.92	>99/1	0.80	>99/1
1e	0.71	83/17	0.85	83/17	**3e**	0.57	>99/1	0.55	>99/1
1f	0.45	>99/1	0.65	>99/1	**3f**	0.33	>99/1	0.24	>99/1
1g	0.37	>99/1	0.55	>99/1	**3g**	0.28	>99/1	0.20	>99/1
1h	0.56	78/22	0.70	78/22	**3h**	0.43	>99/1	0.36	>99/1
1a[c]	0.20[f]	>99/1	0.23	>99/1	**3a**[c]	0.14	>99/1	0.20	>99/1
2a	0.96	>99/1	0.96	>99/1	**4a**	0.93	>99/1	0.86	>99/1
2b	0.94	>99/1	0.93	>99/1	**4b**	0.94	>99/1	0.84	>99/1
2c	0.95	>99/1	0.94	>99/1	**4c**	0.94	–	0.83	–
2d	0.91	>99/1	0.92	>99/1	**4d**	0.92	>99/1	0.81	>99/1
2e	0.84	>99/1	0.86	>99/1	**4e**	0.66	>99/1	0.58	>99/1
2f	0.61	>99/1	0.65	>99/1	**4f**	0.34	>99/1	0.30	>99/1
2g	0.58	>99/1	0.61	>99/1	**4g**	0.30	>99/1	0.25	>99/1
2h	0.70	>99/1	0.78	>99/1	**4h**	0.46	>99/1	0.36	>99/1
2a[c]	0.30[d]	>99/1	0.35	>99/1	**4a**[c]	0.15	>99/1	0.20	>99/1
3a[e]	0.65	>99/1	0.58	>99/1	**3i**[e]	0.78	>99/1	0.64	>99/1

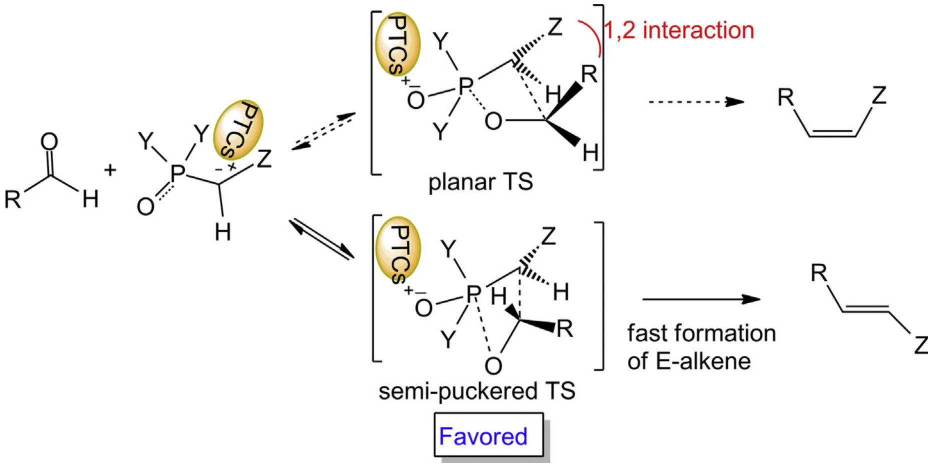
[a] LL-PTC condition: Aldehyde (10 mmol), Phosphonate (10 mmol) or Disphosphonate (5 mmol), TBAB (0.5 mmol), 50% (m/m) NaOH (20 g) and Toluene (30 mL); SL-PTC condition: Aldehyde (10 mmol), Phosphonate (10 mmol) or Disphosphonate (5 mmol), TBAB (0.5 mmol), Solid NaOH (40 mmol) and Toluene (30 mL).
[b] The *Z*/*E* ratio of 1a-2h was detected by HPLC; The *Z*/*E* ratio of 3a-4h was detected by ^{1}H NMR.
[c] The experiments were carried out without phase-transfer catalyst.
[d] The yield was detected by HPLC.
[e] 3a and 3i were synthesized with the route 2.

Although HWE reaction could occur in both PTC systems without PTCs, the yield of the product was relatively low. This may be attributed to the heterogeneous reaction [46]. Few carbanions are generated in the interface of two liquid phases or the surface of solid NaOH, and they could not be transferred into the organic phase or the interfacial region. Hence, the reaction of carbanion with aldehyde is heterogeneous. The probability of effective collision between the carbanion and aldehyde is much less than that in homogeneous phase. Therefore, the yields of 1a, 2a, 3a and 4a were much lower than that in PTC system with PTCs.

Interestingly, the effect of aldehyde or phosphonate on the yield and geometric selectivity in LL-PTC system was similar to that in SL-PTC system. The yield of the product containing electron-donating group was more than 90% and much higher than that of the product with electron-withdrawing group. Meanwhile, the yield of the stilbene was higher than that of 1,4-distyrylbenzene or 4,4′-distyrylbiphenyl. These phenomena could be ascribed to the following two factors: 1) the accompanying side reaction occurs more easily for the aldehyde containing electron-withdrawing substitute; 2) the insoluble product dispersing in the organic phase would increase the thickness of interfacial layer, thus decreasing the transfer rate of the active intermediate and enhancing the side reactions. The benzoic acid was detected in the aqueous phase when 3-nitrobenzaldehyde or 4-nitrobenzaldehyde was used in the both PTC systems.

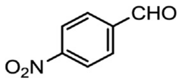
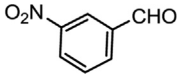
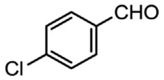
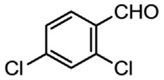
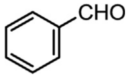
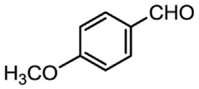
3.2. *The side reaction of aldehyde*

The experiments on the side reaction of aldehyde in PTC system were carried out in absence of phosphonate. It was demonstrated in Table 2 that the side reaction of aldehyde was similar to Cannizzaro reaction, whereas the molar ratio of carboxylic acid to benzyl alcohol was not 1:1. The benzyl alcohol was only detected by HPLC and could not be isolated in the reaction for benzaldehyde or



Scheme 2. The transition state structure model and rationale of selectivity in HWE reaction for DEBP under PTC conditions.

Table 2
The reaction time and consists of product in the side reaction of aldehyde.

Entry	Aldehyde	LL-PTC		SL-PTC	
		Time(min)	Acid/Alcohol (mol/mol)	Time (min)	Acid/ Alcohol (mol/mol)
1		10	55/45	35	65/35
2		3	50/50	25	55/45
3		50	82/18	90	92/8
4		30	78/22	65	88/12
5		120	>99/1	160	>99/1
6		240	>99/1	320	>99/1

* LL-PTC condition: Aldehyde (10 mmol), TBAB (0.5 mmol), 50% (m/m) NaOH (20 g) and Toluene (30 mL); SL-PTC condition: Aldehyde (10 mmol), TBAB (0.5 mmol), NaOH (40 mmol) and Toluene (30 mL).

4-methoxylbenzaldehyde. However, the molar ratio was close to 1:1 in the reaction for 3-nitrobezaldehyde or 4-nitrobezaldehyde. In both PTC systems, the molar ratio of benzyl alcohol to carboxylic acid and the reaction rate increased with the electron withdrawing ability of the substitute in benzaldehyde. Moreover, the molar ratio in LL-PTC system was higher than that in SL-PTC system for the aldehyde containing the electron-withdrawing substitute.

Cannizzaro reaction is a base-induced disproportionation of an aldehyde. The nucleophilic addition of hydroxide anion to the carbonyl carbon of the aldehyde is the first reaction step. The resulting alkoxide is deprotonated to form a dianion, known as the Cannizzaro intermediate, in a strong basic environment. Then the intermediate reacts with another aldehyde to give the products - carboxylic acid and benzyl alcohol [47]. However, in the PTC system, the region where the Cannizzaro intermediate is generated is varied with the reactivity of aldehydes, resulting in that the following reactions and the consists of final products are different.

For aldehyde bearing electron-donating substitute, the Cannizzaro intermediate is generated in the organic phase. The electron-donating substitute can decrease the electrophilicity of the carbon in the aldehyde group. The OH^- which can react with the aldehyde group must have a relatively high nucleophilicity. Due to the hydrogen-bond interaction with water molecule, the OH^- in the interfacial region of PTC system is not enough nucleophilic to react with the aldehyde group and the Cannizzaro intermediate cannot be generated. Conversely, the OH^- which is extracted into the organic phase by PTCs is "naked" and has a stronger nucleophilicity and basicity than those in the interfacial region [47–49]. Therefore, the alkoxide and Cannizzaro intermediate are generated in the organic phase and couple with the cation of PTCs. However, due to the limited amount of the naked OH^- in the organic phase, the intermediate is unstable and quickly decompose to the carboxylic acid [50].

For aldehydes containing electron-withdrawing substitute, the Cannizzaro intermediate can be generated in both the organic phase and the interfacial region. In the organic phase, the "naked" OH^- can react quickly with aldehyde. The electron-withdrawing substitute in the benzene ring can increase the electrophilicity of the carbon in the aldehyde group. Because the activity of the nucleophilic addition reaction for the carbonyl carbon increases, the OH^- in the interfacial region can react with aldehyde group. Due to the relatively high area of the interfacial region and the excess amount of OH^-, the alkoxide in the interfacial region is deprotonated quickly. The generated Cannizzaro intermediate is stable in the interfacial region. Subsequently, the reaction of the Cannizzaro intermediate with another aldehyde occurs to give the products – carboxylic acid and benzyl alcohol. However, the reaction rate in the interfacial region increases with the electron withdrawing ability of the substitute in benzaldehyde. Especially, the Cannizzaro reaction in the interfacial region is main reaction for 3-nitrobenzaldehyde and 4-nitrobenzaldehyde in both PTC system. Therefore, the molar ratio of product is close to 1:1.

Because the area of the interfacial region in LL-PTC system is relatively high, the reaction rate of the Cannizzaro intermediate in the interfacial region under LL-PTC conditions are higher than those under SL-PTC conditions. Consequently, the rate of side reaction for aldehyde and the content of benzyl alcohol in products are relatively high in LL-PTC system. Moreover, due to the high lattice energy of the crystalline structure for solid NaOH, the rate of generating available OH^- in SL-PTC system is lower than that in LL-PTC system. Both HWE reaction and the side reaction have a high rate in LL-PTC system.

3.3. The effect of aldehyde on the activity of HWE reaction in PTC system

The effect of aldehyde on the activity of HWE reaction was studied taking DEBP and PTCs in excess. Interestingly, which reaction, HWE reaction or side reaction, dominates in PTC system is decided by the substitute in benzaldehyde. In the reaction of 3-nitrobenzaldehyde or 4-nitrobenzaldehyde under LL-PTC conditions, the stilbene could be detected, whereas more than 60% of aldehyde underwent the side reaction (Fig. 1). Conversely, no

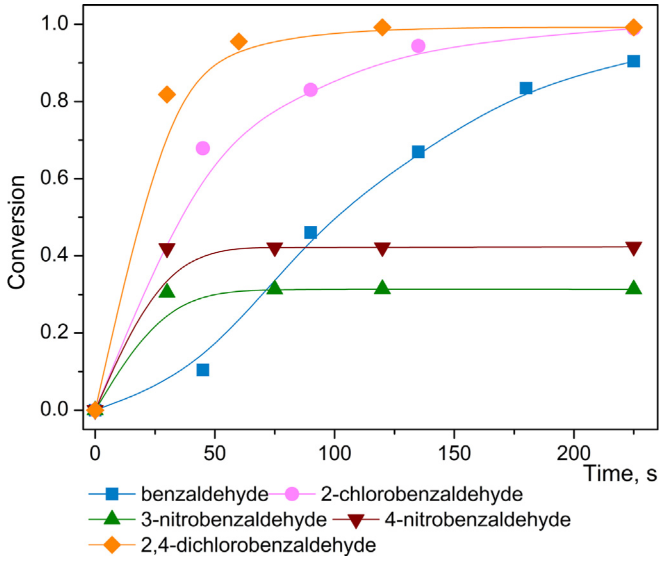


Fig. 1. The effect of various aldehydes bearing electron-withdrawing substitute on the rate of HWE reaction in LL-PTC system: 10 mmol of DEBP, 2.5 mmol of benzaldehyde, 0.5 mmol of TBAB, 20 g of 50% (m/m) NaOH, 30 mL of toluene, 1400 rpm, 35 °C.

byproducts were detected for the other aldehydes, even for benzaldehyde in SL-PTC system (Fig. 2). These results demonstrate that the generating rate of Cannizzaro intermediate is higher than that of the carbanion and the side reaction dominates for 3-nitrobenzaldehyde or 4-nitrobenzaldehyde in LL-PTC system. For the other aldehydes, the rate of HWE reaction is much higher than that of the side reaction and the side reaction occurs hardly. Therefore, the inhibiting role of the competing side reaction turns out to be less significant when aldehyde with electrophilic substitute is used in both PTC systems. In the following experiment, benzaldehyde and phosphonate could be added simultaneously into the flask.

The reaction rate in LL-PTC system increased in the sequence: 4-(dimethylamino)benzaldehyde < 4-methoxybenzaldehyde < 4-methylbenzaldehyde < benzaldehyde< 2-choloraldehyde < 2,4-dichlorobenzaldehyde, which was the opposite to the order of the electron donating ability of the substitutes in benzene ring. In view of nucleophilic nature of HWE reaction, aldehydes containing electron-withdrawing substituents have a higher reactivity than that containing electron-donating substitute owing to the increase of the positive charge of the carbon in the aldehyde group.

3.4. *The effect of phosphonate on the activity of HWE reaction in PTC system*

To explore the effect of phosphonate on the activity of HWE reaction in PTC system, the process of HWE reaction was investigated (Fig. 3). Although the yield of 1a had little change with PTC system, the reaction rate in SL-PTC system was much lower than that in LL-PTC system. It is also attributed to different mechanisms in these two systems. The carbanion generated easily in LL-PTC system due to high reactivity of the available OH^- ("naked OH^-"). The reaction rate in LL-PTC system decreased in the following order: DCBP > TEPP > TEBP > DEBP which was the same as the order of pK_a value for phosphonates. The lower the pK_a value of phosphonates is, the more easily the deprotonation reaction occurs. Meanwhile, the electron-withdrawing substitute and π-conjugation can increase the stability of the oxaphosphetane intermediate. Therefore, HWE reaction for DCBP, TEPP or TEBP has a higher activity than that for DEBP in both PTC systems.

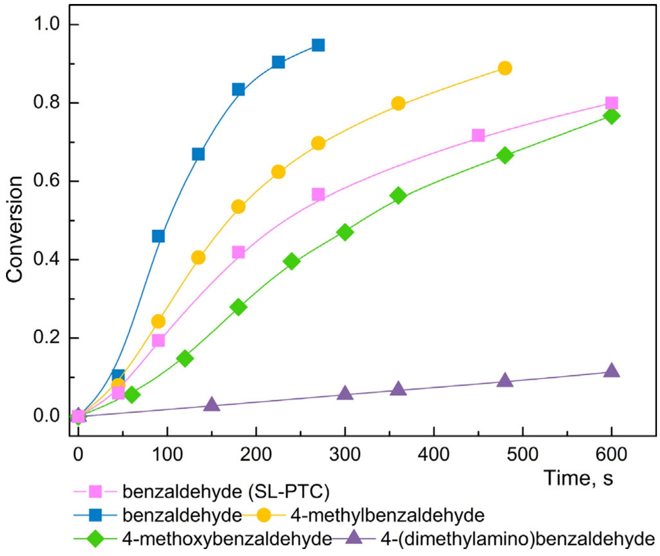


Fig. 2. The effect of aldehydes bearing electron-donating substitute on the rate of HWE reaction in PTC system: 10 mmol of DEBP, 2.5 mmol of benzaldehyde, 0.5 mmol of TBAB, 20 g of 50% (m/m) NaOH or 40 mmol of solid NaOH, 30 mL of toluene, 1400 rpm, 35 °C.

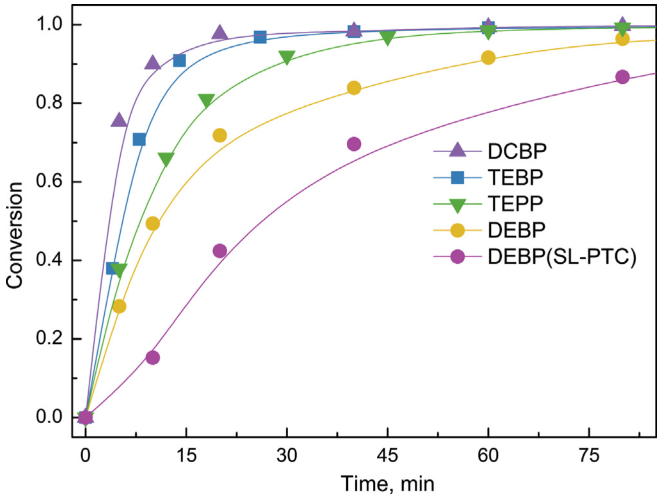


Fig. 3. The effect of phosphonate on the process of HWE reaction in PTC system: 10 mmol of phosphonate or 5 mmol of disphosphonate, 10 mmol of benzaldehyde, 0.5 mmol of TBAB, 20 g of 50% (m/m) NaOH or 40 mmol of solid NaOH, 30 mL of toluene, 1400 rpm, 35 °C.

3.5. *The third phase in LL-PTC system*

The conversion of the traditional LL-PTC into liquid–liquid–liquid PTC (TL-PTC) offers several advantages, such as catalyst recovery, waste reduction, better selectivity and improving cost-effectiveness. Above all, the third phase (the middle catalyst-rich phase) can enhance the reaction rate by several orders of magnitude [51]. In the synthesis of 1a and 2a, there was one phase exciting between the organic phase and the aqueous phase (Fig. 4a and b), and the volume of the third phase was less than 1 mL. However, in the synthesis 3a and 4a, the third phase was not found. The 3a or 4a is dispersed in the organic phase owning to their poor dissolubility. Thus, the viscosity of the organic phase is increased and the third phase could not be separated. The aggregation of the PTCs in the third phase may be one of the reasons for the high activity of HWE reaction in LL-PTC system. The constituents of the third phase and their effect on the volume of third phase will be discussed in a separated work.

3.6. *The third phase in SL-PTC system*

As water is added, SL-PTC system can be changed to solid–liquid (ω)-liquid (org) PTC system. It is known that the ω phase also enhances the reaction rate in SL-PTC, and there is an optimum quantity beyond which the rate falls dramatically [52]. Thus the experiments were done by carefully adding trace quantities of water in 30 mL of the organic phase. It has been shown in Fig. 5 that the small amounts of water increases substantially the reaction rates compared to those under anhydrous conditions, whereas the reaction rate decreases with the addition of excess water. The polar H_2O molecule can overcome the lattice energy of the crystalline structure for the solid NaOH. Hence, with the increasing in the amount of available NaOH, much more carbanions are generated in the interfacial region. When an excessive amount of water has been added, there is sufficient water for saturation of the hydration shell of OH^-. Therefore, the basicity of OH^- decreases considerably and the carbanion cannot be generated efficiently. Meanwhile, a little water can distribute into the organic phase and the degree of

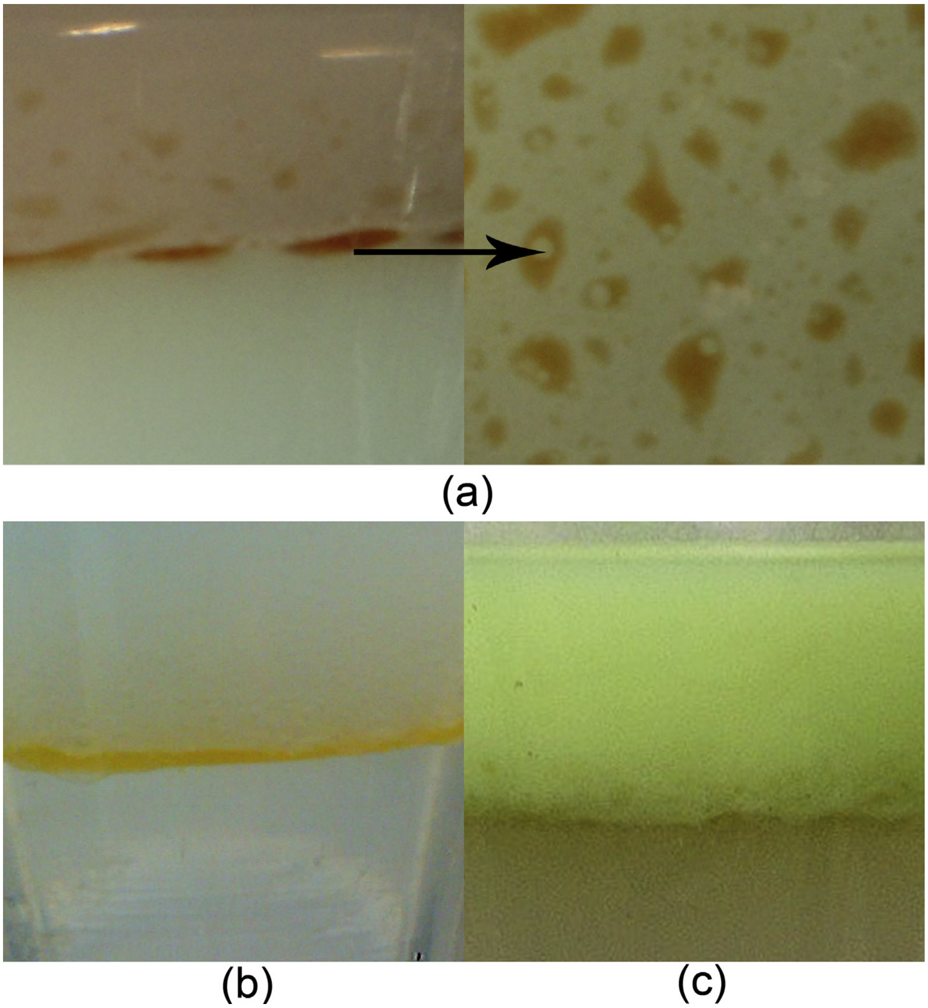
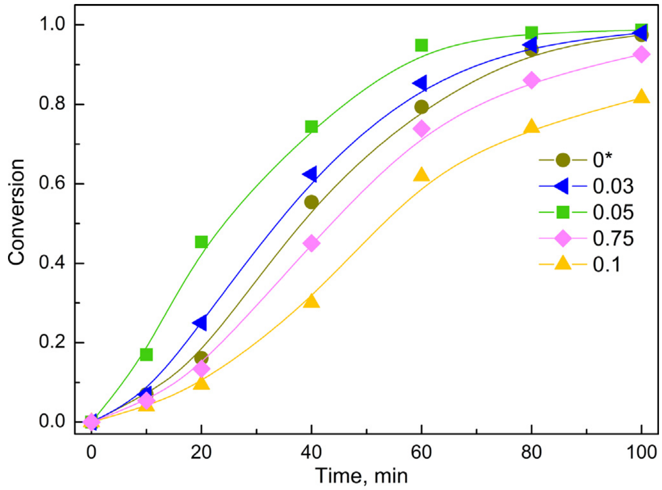


Fig. 4. The image of the third phase in LL-PTC system (a) the reaction of DCBP with benzaldehyde; (b) the reaction of DCEP with benzaldehyde; (c) the reaction of TEBP with benzaldehyde: 10 mmol of benzaldehyde, 10 mmol of phosphonate or 5 mmol of disphosphonate, 0.5 mmol of TBAB, 20 g of 50% (m/m) NaOH and 30 mL of toluene.



* the weight of the added water in SL-PTC system

Fig. 5. The effect of water on the process of HWE reaction in SL-PTC system: 10 mmol of DEBP, 10 mmol of benzaldehyde, 0.5 mmol of TBAB, 40 mmol NaOH, 30 mL of toluene, 1400 rpm, 35 °C.

hydration of the ion-pair increases, resulting in the decrease of its reactivity. Thus, the dehydration treatment for the organic solvent is not required in SL-PTC system, which can decrease the cost of organic solvent.

3.7. Reusability of the liquid phase in LL-PTC system

In LL-PTC system, the aqueous phase was reused by adding the fresh organic phase and PTCs. It can been observed that the rate of HWE reaction in LL-PTC system decreases slightly and the yield of the product is unchanged with the reuse times of the aqueous phase (Fig.6). The yield and reaction rate when the aqueous phase was reused five times were still higher than that where the aqueous phase contained 40% NaOH. The result shows that the decreasing concentration of NaOH and the increasing concentration of salt in the reused aqueous phase decrease only slightly the generating rate of available OH^- and the transferring rate of active intermediate. The aqueous phase can be reused four times without sacrifice of the yield and the reaction rate. Unexpectedly, due to the high viscosity of the aqueous phase, the separation of two phases needed a long time and the weight of the aqueous phase was less than 20 g. Accordingly, the following research will be targeted at the exploration of new PTC system in which the aqueous phase can be separated and reused easily.

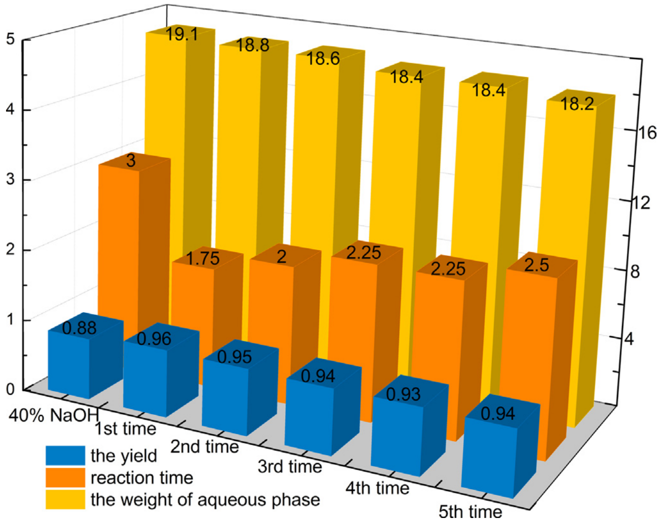


Fig. 6. The dependence of the yield, the reaction time and the weight of aqueous phase on the reuse time: 10 mmol of DEBP, 10 mmol of benzaldehyde, 0.5 mmol of TBAB, 30 mL of toluene, 1400 rpm, 35 °C.

4. Conclusions

The synthesis of stilbene, 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl via HWE reaction were developed in LL-PTC and SL-PTC systems. These synthetic routes showed a high yield and geometric selectivity. For the aldehyde with electron-donating substitute, the yield of the product in both PTC systems was more than 90%. The (*E*)-isomer was the predominate product in both PTC systems, especially in the synthesis of 1,4-distyrylbenzenes or 4,4′-distyrylbiphenyls.

The activity of HWE reaction in PTC system was dependent on the reaction mechanism and the side reaction of aldehyde. The HWE reaction in LL-PTC system and SL-PTC system proceed through the extractive mechanism and interfacial mechanism, respectively. The available OH^- was generated in the organic phase under LL-PTC conditions, whereas in the interfacial region under SL-PTC conditions. The basicity of the available OH^- in organic phase was stronger than that in interfacial region. Consequently, the rate of HWE reaction and the side reaction of aldehyde were relatively high in LL-PTC system. For aldehyde containing electron-withdrawing substitute, the yield of the product in LL-PTC system was lower than that in SL-PTC system. Meanwhile, the products with 1,4-distyrylbenzene and 4,4′-distyrylbiphenyl structure would hinder the generation of the available OH^- due to their poor dissolvability in the organic phase. The side reaction of aldehyde in PTC system was similar to Cannizzaro reaction. However, the amounts of acid and alcohol formed were different. For benzaldehyde with electron-donating substitute, the Cannizzaro intermediate was generated only in the organic phase and decomposed immediately to the benzoic acid. For benzaldehyde with electron-withdrawing substitute, the Cannizzaro intermediate could be generated not only in the organic phase but also in the interfacial region. In the interfacial region, Cannizzaro intermediate could react with another aldehyde molecule. The inhibiting role of the competing side reaction for aldehyde with electron-withdrawing was more significant than that for benzaldehyde with electron-donating substitute in both PTC system.

The electrophilicity of the substitute in benzaldehyde and the pK_a of phosphonate had subtle influences on the rate of HWE reaction in PTC system. Meanwhile, the limited volume of the third phase existed in this LL-PTC system. The ω phase which was generated by the addition of a trace amount of water in SL-PTC system could increase the reaction rate. In addition, the aqueous phase can be recycled four times without sacrifice of the yield in HWE reaction under LL-PTC condition, thereby leading to high cost-effectiveness and waste reduction.

It is anticipated that this simple, controllable and economical method will provide a potential application of HWE reaction in chemical industry.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.dyepig.2013.05.017.

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