Mechanism and kinetics of Horner–Wadsworth–Emmons reaction in liquid–liquid phase-transfer catalytic system

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ABSTRACT

Liquid–liquid phase-transfer catalytic (LL-PTC) system suitable for symmetric distyryl compounds could not be used to synthesize asymmetric derivates. Relatively low value, the time-dependence of the interfacial tension with only phosphonate in the organic phase and high background reaction rate demonstrated that "weakly acidic" phosphonate was adsorbed on the interfacial layer and deprotonated by excess "naked" OH^- without the help of the catalyst. Phase-transfer catalyst participated in the transfer process of the carbanion and accelerated the bond-forming reaction. However, the distributing region for the carbanion ion-pair in this PTC system was dependent on the usage of the catalyst and the mechanism would change from the interfacial mechanism to the extraction mechanism. Accordingly, the mechanism including adsorption, deprotonation, ion-exchange reaction, distribution and bond-forming reaction was proposed, and the kinetic model was performed. The activation energy and the dependence of catalytic activity on lipophilicity and accessibility parameter also supported the proposed mechanism. The rate-determining step was not the bond-forming reaction for each mechanism and the apparent reaction rate was relevant to the generation rate of the carbanion and the ion-exchange reaction rate.

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1. Introduction

Horner–Wadsworth–Emmons (HWE) reaction, which is one of the most popular and powerful methods for the generation of C=C bond, for years has remained probably the best-known example involved organophosphorus reactants [1,2]. Even though the principal advantage consists in easy work-up procedure (the formed phosphates can easily be removed by water), HWE reaction is known to proceed at a slow reaction rate, high energy consumption and difficult solvent recycle [3]. Hence, the green synthetic method have been one topic of researches on HWE reaction [4].

Reported green synthetic methods included reaction system with ionic liquid or water [5–7] as solvent, phase-transfer catalytic (PTC) system [8], no solvent system [9], reaction system with the help of microwave [10–12] or ultrasonic wave [13,14], and base-free system [15]. However, above systems mainly involved "moderately acidic" and "acidic" phosphonate, which pK_a value was lower than 23, such as β-keto phosphonate, 1-butyl-2,3-

dimethylimidazolium hexafluoroph osphate and ethyl (diethyl phosphono) acetate. The green synthetic method for HWE reaction of "weakly acidic" phosphonate had been rarely reported, which was attributed to the relatively weak alkaline agent in these green systems. Namely, in these systems, because the deprotonation of "weakly acidic" phosphonate ($pK_a > 23$) hardly occurred or had a low rate, the yield of product was relatively low. It had been found that PTC system also could provide a relatively strong alkaline agent, which could quickly deprotonate the "weakly acidic" substrate and initiate the bond-forming reaction [16], for example liquid–liquid PTC (LL-PTC) system for isomerization of allylbenzene [17] and dehydrobromination of (2-bromoethyl) benzene [18]. However, HWE reaction of "weakly acidic" phosphonate under PTC conditions had rarely been reported [19,20]. In the reported research on HWE reaction of "weakly acidic" phosphonate under LL-PTC conditions, the yield was 78–82% and only benzylphosphonate was involved.

HWE reaction of "weakly acidic" phosphonate and bisphosphonate was the important way for synthesizing fine chemicals – Stilbene and Distyryl derivates [21,22]. In our previous research, HWE reaction of "moderately and weakly acidic" phosphonate had been carried out in both LL-PTC and solid–liquid PTC (SL-PTC) system with tetrabutylammonium bromide (TBAB) and toluene [23,24]. For symmetric products, high yield (about 90%) and geo-
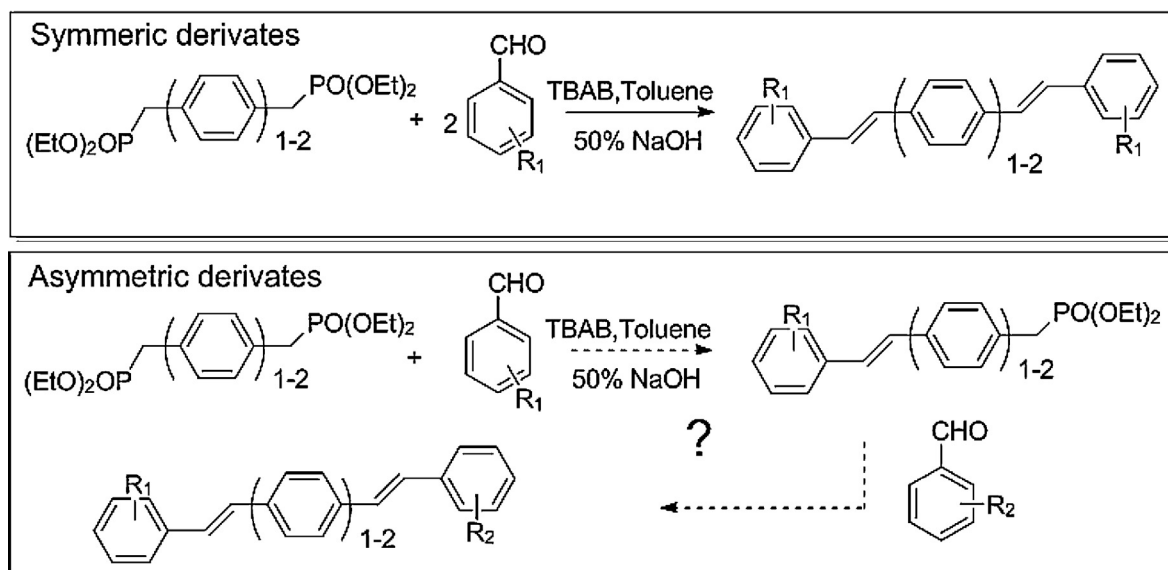
Scheme 1. Synthetic routes of asymmetric product for HWE reaction in LL-PTC system.

metric selectivity were found in each PTC systems. Meanwhile, in SL-PTC system, carbanion was deprotonated by solid NaOH in the interfacial region and HWE reaction followed the interfacial mechanism. According to pK_a value of the substrate and the region where the bond-forming reaction occurred, the mechanism of hydroxide-initiated LL-PTC reaction could be classified into the extraction mechanism and the interfacial mechanism [25–27]. Because OH$^-$ in NaOH aqueous solution had insufficient high alkalinity to initiate the deprotonation reaction [28], for the "weakly acidic" substrate, PTC$^+$OH$^-$ always was treated as the alkaline agent and the extraction mechanism was valid. Because solubility of PTC$^+$OH$^-$ in the organic phase was limited [29], bisphosphonate molecule could also partly been deprotonated, as well as asymmetric derivates might be synthesized in LL-PTC system with high yield (Scheme 1).

In this study, possibility of synthesizing asymmetric distyryl compounds and the mechanism of HWE reaction of "weakly acidic" phosphonate in LL-PTC system were explored. Accordingly, the region where the carbanion was generated, the role of phase-transfer catalyst, the kinetics model and kinetics experiment were investigated. HWE reaction which involves parallel reactions can provide an ideal case to study kinetic model and mechanism for LL-PTC reaction of the "weakly acidic" substrate.

2. Experimental

2.1. Chemical and instruments

Tetraethyl(1,4-phenylenebis(methylene))bis(phosphonate) (BPP) and tetraethyl([1,1'-biphenyl]-4,4'-diylbis(methylene))bis(phosphonate) (DPP) were prepared according to reported procedures [30,31]. Benzaldehyde, toluene, ethanol and TBAB were purchased from Sinopharm Chemical Reagent Corporation Ltd., China and chromatographic grade acetonitrile was purchased from Adamas Reagent Corporation Ltd., China. All chemicals were used directly as received without further purification.

NMR spectra were recorded on a 400 MHz spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C). NMR chemical shifts were reported relative to TMS (0 ppm) for ^{1}H spectra and to CDCl$_3$ (77.23 ppm) for ^{13}C spectra. Analytical high-performance liquid chromatography (HPLC) was performed using a Zorbax Eclipse XDB-C18 column (150 mm × 0.46 mm, 0.5 μm) on an Agilent 1200

system attached with a UV variable wavelength detector. The composition of the sample were estimated with an external standard method. HPLC was operated with a mobile phase consisting of 50:50 (v/v) water/acetonitrile and a flow rate of 1.0 mL/min. Detection wavelength was set at 260 nm and the column temperature was 30 °C.

2.2. Preparation and characterization

2.2.1. Synthesis of asymmetric 1,4-distyrylbenzene derivates

Twenty-gram of 50% (w/w) NaOH aqueous solution was placed in a 100 mL four-necked flask and stirred at 1400 rpm. A solution of phosphonate (5 mmol), tetrabutylammonium bromide (TBAB, 0.25 mmol) in toluene (30 mL) was added at 45 °C. Simultaneously, 5 mmol of benzaldehyde in 7.5 mL of toluene was dropped into the flask over 3 h. Subsequently, 5 mmol of 2-chlorobenzaldehyde in 7.5 mL of toluene was dropwise added. After completion of the reaction as indicated by TLC, the resulting mixture was cooled to the room temperature and transferred into a separatory funnel. The organic phase was separated and filtered, and the precipitate was rinsed twice using 2 mL of 3% HCl solution and 5 mL of ethanol, respectively. The filtrate was washed twice with 10 mL of 3% (v/v) HCl solution and dried over MgSO$_4$. Toluene was removed under reduced pressure, and the residue was purified by column chromatography using petroleum ether as eluent to give a pale yellow solid.

1,4-di((E)-styryl) benzene (1a) FT-IR (KBr, cm^{-1}): 3023 (CH, st); 1643, 1574, 1509, 1489, 1446 (C=C, st); 966 (CH=CH *trans*), 815 (para-substitution), 746 and 690 (monosubstitution); ^{1}H NMR (400 MHz, CDCl$_3$, ppm) δ 7.54 (d, J = 8.3 Hz, 4H, ArH), 7.53 (s, 4H, ArH), 7.38 (t, J = 7.3 Hz, 4H, ArH), 7.29 (m, 2H, ArH), 7.14 (m, 4H, CH=CH); ^{13}C NMR (101 MHz, CDCl$_3$) δ 137.34, 136.72, 128.71, 128.61, 128.28, 127.65, 126.85, 126.52.

1,4-bis((E)-4-dimethylaminostyryl) benzene (1b) FT-IR (KBr, cm^{-1}): 3013(CH, st); 2893, 2799 (CH3, st); 1601, 1519, 1476, 1437 (C=C, st); 1355 1222 (C-N, st); 1183; 1161; 957 (CH=CH *trans*); 821 (para-substitution); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 7.46 (s, 4H, ArH), 7.44 (d, J = 8.7 Hz, 4H, ArH), 7.07 (d, J = 16.2 Hz, 2H, CH=CH), 6.93 (d, J = 16.2 Hz, 2H, CH=CH), 6.74 (d, J = 8.8 Hz, 4H, ArH), 3.01 (s, 12H, CH3);

1,4-bis((E)-2-chlorostyryl) benzene (1c) FT-IR (KBr, cm^{-1}): 3044, 2997 (CH, st); 1567, 1511, 1466, 1434 (C=C, st); 1036;