Study of the Wittig reaction of benzyltriphenylphosphonium salt and benzaldehyde via ylide-mediated phase-transfer catalysis Substituent and solvent effects

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Abstract

The Wittig reaction of benzyltriphenylphosphonium salt and benzaldehyde in two-phase organic solvent/water (NaOH) medium was investigated, focusing on the effects of substituent and organic solvent. The substituents chosen for study include CH_3, F, Cl, Br, CH_3O, NO_2, and CF_3. The organic solvents include polar solvents ($CHCl_3$ and CH_2Cl_2) and nonpolar solvents (n-C_6H_{14}, C_6H_6, and CCl_4). It was found that the rate of agitation was insignificant and the reaction of benzylidenetriphenylphosphorane and benzaldehyde in the organic phase is the decisive step for determining the Z/E ratio of the product stilbene. In general, the polar solvents exhibit more favorable Z-selectivity. The Z/E ratio of the product stilbene may change substantially by interchanging the substituents on the benzyl group of phosphorus atom and on the phenyl group of aryl aldehyde. In contrast to the *meta*- and *para*-substituted benzaldehydes and the *ortho*-substituted benzylidene ylides, the *ortho*-substituted benzaldehydes bearing heteroatom substituent exhibit a pronounced enhancement for the Z-selectivity with the order of effectiveness of substituents being $CF_3 > (Cl, Br) > CH_3O > F > NO_2$. The concerted asynchronous cycloaddition mechanism involving a four-centered transition state is suggested to be operating in these systems. © 1999 Elsevier Science B.V. All rights reserved.
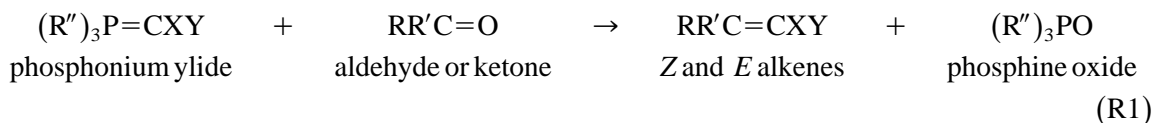
Keywords: Wittig reaction; Benzylidine ylides; Nonpolar solvents

1. Introduction

The Wittig reaction is one of the most important and versatile reactions in organic chemistry for synthesizing alkenes with unambiguous positioning of the double bond. Since its discovery in the early 1950s [1,2], the Wittig reaction has been studied very extensively from both theoretical and synthetic aspects [3–12] and highly recognized for its simplicity, efficiency, and generality. The

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prototype Wittig reaction involves the reaction of a phosphonium ylide with an aldehyde or a ketone as depicted in reaction (R1).

$$(R'')_3P=CXY \quad + \quad RR'C=O \quad \rightarrow \quad RR'C=CXY \quad + \quad (R'')_3PO$$

phosphonium ylide   aldehyde or ketone Z and E alkenes   phosphine oxide

(R1)

The stereoselectivity is highly dependent on the substituents bonded to the ylidic carbon and to the phosphorus atom, and on the exact reaction conditions. According to their general reactivity, three categories of phosphonium ylides, namely nonstabilized, semistabilized, and stabilized ylides, have been classified. The Wittig reaction has been shown to yield preferentially E alkenes for stabilized ylides having strongly conjugating substituents (e.g., COOMe or CN); mixtures of the Z and E alkenes for semistabilized ylides bearing mildly conjugating substituents (e.g., phenyl, vinyl or allyl); and mainly contrathermodynamic Z alkenes for nonstabilized ylides lack such conjugating functionalities (e.g., alkyl). Most of the studies of the Wittig reactions were carried out homogeneously in organic solvents (e.g., THF, C_6H_6, CCl_4, $CHCl_3$, DMF, and MeOH). Solutions of phosphonium ylides were generated by the reactions of phosphonium salts and bases [e.g., sodium hexamethyldisilazide (NaHMDS), LiHMDS, PhLi, BuLi or $NaNH_2$]. In contrast, less work has been reported for the heterogeneous Wittig reactions carried out in liquid–liquid [13–16] and solid–liquid [17–21] phases. In the liquid–liquid phase transfer Wittig reaction, the deprotonation of phosphonium ions in the aqueous phase or at the interphase generates ylides that diffuse into the organic phase for reacting with aldehyde or ketone. This two-phase Wittig reaction has been classified as one of the 'phase transfer catalysis of ylide-mediated reactions', [22] even though the phosphonium salt is consumed in the reaction and in general this reaction does not need the help of a phase transfer catalyst. However, it is useful to extend the concept of phase transfer catalysis to include Wittig reactions, since in this way very similar reactions (like Wittig–Horner and Hornor–Emmons reactions) can be considered together [23,24]. In this paper, we studied the two-phase Wittig reactions of various benzyltriphenylphosphonium (BTPP) salts and benzaldehydes in various organic solvent/water (NaOH) media, focusing on the effects of substituent and organic solvent. The reaction system was chosen because of the convenience for two-phase reactions and the versatility of varying the organic solvents and the substituents on both ylide and aldehyde for studying their effects on the Z/E ratio of the product stilbene.

2. Experimental

2.1. Materials

Chlorobenzyl chlorides, bromobenzyl bromides, methylbenzyl bromides, chlorobenzyl bromides, bromobenzaldehydes, tolualdehydes, and 2-trifluoromethylbenzaldehyde (Aldrich); 2-fluorobenzyl chloride, 2,5-dimethybenzyl chloride; 3,5-dimethylbenzyl bromide, 2-phthalic dicarboxaldehyde, and 2-benzyloxybenzaldehyde (Lancaster); 2,6-dichlorobenzaldehyde; benzaldehyde, 2,4-dimethoxybenzaldehyde, 2,3,4- and 3,4,5-trimethoxybenzaldehydes, and triphenylphosphine (Merck); chlorobenzaldehydes (2- and 4- (Ferak); 3- (Aldrich)); dimethylaldehydes (2,4- (Acros); 2,5- (Aldrich); 3,4- and 3,5- (Lancaster)); benzyl bromide (Riedel-de Haën); and 2-nitrobenzaldehyde (Janssen) were used. Other chemicals were of the highest reagent grade commercially available. Deionized water was obtained from reverse osmosis (Millipore Milli-RO 20).

2.2. Procedures

2.2.1. Synthesis of benzyltriphenylphosphonium salts

In general, BTPP salts were prepared by the reaction of equimolar amounts (0.04 mol) of triphenylphosphine and benzyl halides under magnetic stirring in 6 ml CH_2Cl_2 in a 125-ml Erlenmeyer flask fitted with a grounded stopper. After the reaction was complete ($\sim$ 3 h), the white precipitate of product was obtained by filtration, washed with CH_2Cl_2 and *n*-hexane. The pure BTPP salt was obtained by recrystallizing its crude product in CH_2Cl_2.

2.2.2. Synthesis of stilbenes

The general procedures for synthesizing symmetric and unsymmetric stilbenes were as follows. The reactor was a 200-ml three-necked flask fitted with a flate-bladed stirring paddle driven by a laboratory stirrer (RW 20 IKA-WERK). The reaction was started by mixing 25 ml of CH_2Cl_2 solution containing the desired BTPP salt (about 4 g) and benzaldehyde (about 0.9 ml) with 100 ml of 0.1 N aqueous NaOH solution in the flask under agitation and at room temperature. During the reaction, the fading of the color of ylide (ranging from yellow to violet) was observed. Allowed a sufficient time for the reaction to complete (within 30 min), then the mixture of products [*Z*- and *E*-stilbenes and triphenylphosphine oxide (Ph_3PO)] was obtained by concentrating the CH_2Cl_2 layer using a rotatory evaporator. Stilbenes were separated from Ph_3PO by dissolving the mixture of products in aqueous EtOH solution and extracted several times with petroleum ether. *Z*- and *E*-stilbenes were separated by the method of progressive thin layer chromatography using PLC plates (silica gel 60 F254, 20 × 20 × 0.2 cm, Merck) and cyclohexane or cyclohexane/acetone (e.g., 9/1 by volume) as the mobil phase. The development of TLC was carried out successively. When the mobil phase developed to a certain distance (e.g., 5 cm), the plate was taken out from the developing chamber, evaporated to dryness, and visualized by the irradiation of UV light (Raytech Ultraviolet Equipment, 250–400 nm). The process was repeated until the separation of *Z*- and *E*-isomers was obtained. Then, the region containing the desired *Z*- or *E*-isomer was scraped out and extracted by acetone. The *Z*- and *E*-stilbenes obtained were identified by ^{1}H NMR and GC/MS.

2.2.3. Kinetic experiment

The same reactor and equipment mentioned above were used for the kinetic experiment. The kinetic run was started by adding 25 ml of aqueous solution (containing a known amount of NaOH) to 25 ml of organic phase solution (containing known amounts of BTPP salt, aldehyde, and internal standard) in the flask. Both solutions were thermostated at the desired temperature for at least 30 min. The reactor was submerged into a thermostated water bath in which the temperature was controlled with $\pm 0.2°C$. At a chosen time, 0.2 ml of the organic layer was withdrawn and put into the extraction sample bottle which contained 0.6 ml of *n*-C_6H_{14} and 0.3 ml of H_2O (0.6 N HCl). The extraction bottle was shaked vigorously for 30 s, and then allowed to stand for a few minutes to allow the two phases to separate. The organic phase was then analyzed by ^{1}H NMR (Bruker WP 200 FT-NMR and AMX 400 FT-NMR) and GC (Shimadzu GC-9A). The correlation between the NMR and GC measurements can be expressed by $((A_s/p)/(A_{is}/q))_{NMR} = C_s/C_{is} = f \times (A_s/A_{is})_{GC}$, where $A =$ peak area, $C =$ concentration, s = unknown sample, is = internal standard, p and $q =$ number of equivalent hydrogen atoms corresponding to the measured ^{1}H NMR peak, and $f =$ response factor. Since the rate of reaction was generally very rapid, the kinetic study of the reaction was not feasible,

therefore only the final concentrations of the *Z*- and *E*-stilbenes were analyzed. The amounts of *Z*-and *E*-stilbenes were analyzed by ^{1}H NMR and/or GC using the internal standard method. The internal standards used were triphenylmethane (TM) for NMR analysis and TM, naphthalene (NP), and biphenyl (BP) for GC analysis.

3. Results and discussion

The liquid–liquid two-phase Wittig reaction of BTPP ion ($Ph_3PCH_2C_6H_4X^+$) and benzaldehyde (YC_6H_4CHO) can be simplified as depicted in Scheme 1. The abbreviations of some of the stilbene derivatives are illustrated in Scheme 2, in which the first substituent in the abbreviated formula of stilbene = the substituent originating from the benzyl group of BTPP ion (e.g., Cl in 2,3'-ClMeSB); the second substituent in the abbreviated formula of stilbene = the substituent originating from benzaldehyde (e.g., Me in 2,3'-ClMeSB); the unprimed number before the abbreviated formula of stilbene = the position of the substituent at the benzyl group of the original BTPP ion (e.g., 2 in 2,3'-ClMeSB); and the primed number before the abbreviated formula of stilbene = the position of the substituent at the phenyl group of the original benzaldehyde (e.g., 3' in 2,3'-ClMeSB).
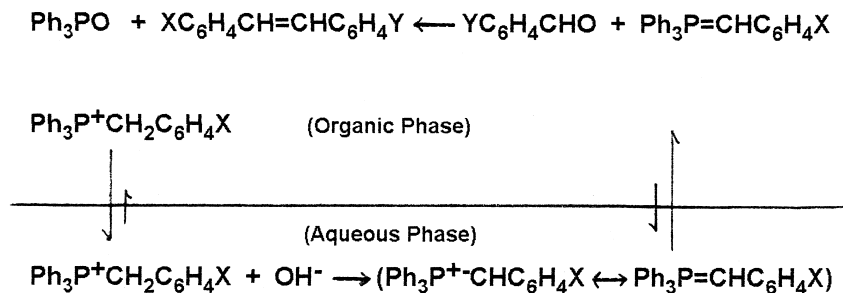
The effects of organic solvent, agitation, temperature, substituent, concentrations of $Ph_3PCH_2C_6H_4X^+$ ion, YC_6H_4CHO, and NaOH on the yield and stereoselectivity (*Z/E* ratio) of stilbene were investigated. The substituents (X and Y) chosen for study included F, Cl, Br, Me, MeO, $PhCH_2O$ (BnO), and NO_2 groups. The organic solvents include polar solvents ($CHCl_3$ and CH_2Cl_2) and nonpolar solvents (n-C_6H_{14}, C_6H_6, and CCl_4).

3.1. Synthesis of chlorostilbenes and dichlorostilbenes
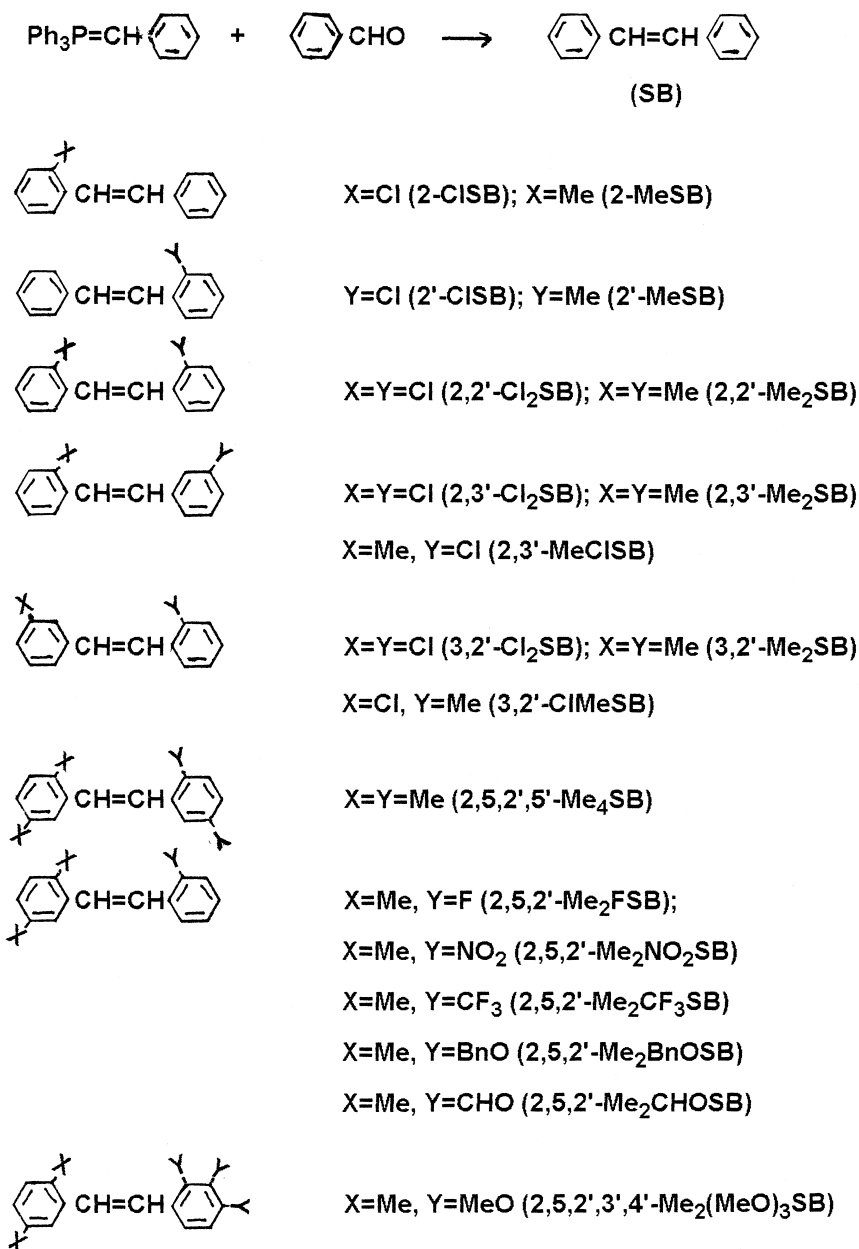
Chlorostilbenes and symmetric and unsymmetric dichlorostilbenes were synthesized by the Wittig reactions of various combinations of $Ph_3PCH_2C_6H_4X^+$ ion and YC_6H_4CHO (X or Y = H or Cl). The results are summarized as follows.

3.1.1. Chlorostilbenes (CISB)

For $[Ph_3PCH_2C_6H_4Cl^+Cl^-]_o = 0.060$ M, $[NaOH]_o = (0.1, 0.2, 0.3,$ and $0.5)$ M, $[C_6H_5CHO]_o = (0.059, 0.12, 0.59,$ and $1.2)$ M, $T = (5, 10, 15,$ and $20)$ °C, agitation rate (r) = (260, 460, 660, and

$$Ph_3PO \ + \ XC_6H_4CH{=}CHC_6H_4Y \ \longleftarrow \ YC_6H_4CHO \ + \ Ph_3P{=}CHC_6H_4X$$

$$Ph_3P^+CH_2C_6H_4X \qquad \text{(Organic Phase)}$$

―――――――――――――――――――――――――――――――――――

(Aqueous Phase)

$$Ph_3P^+CH_2C_6H_4X \ + \ OH^- \longrightarrow (Ph_3P^{+\cdot}CHC_6H_4X \longleftrightarrow Ph_3P{=}CHC_6H_4X)$$

Scheme 1.

Scheme 2.

940) rpm, and in CH_2Cl_2, the total yield of ClSB and the corresponding Z/E ratios are ($55 \pm 4\%$; 0.91 ± 0.03), ($82 \pm 5\%$; 1.5 ± 0.2), and ($95 \pm 3\%$; 2.7 ± 0.3) for 2-, 3-, and 4-ClSB, respectively.

3.1.2. Dichlorostilbenes (Cl_2SB)

For $[Ph_3PCH_2C_6H_4Cl^+Cl^-]_o = 0.060$ M, $[NaOH]_o = (0.1, 0.2, 0.3,$ and $0.5)$ M, $[ClC_6H_4CHO]_o = (0.059, 0.12, 0.59,$ and $1.2)$ M, $T = (5, 10, 15,$ and $20)$ °C, $r = (260, 460, 660,$ and $940)$ rpm, and in

CH_2Cl_2, the total yields of Cl_2SB and the corresponding Z/E ratios are $(86 \pm 4\%; 1.8 \pm 0.1)$, and $(93 \pm 4\%; 2.0 \pm 0.2)$ for 2,2'- and 4,4'-Cl_2SB, respectively.

3.1.3. Effects of substituent and solvent

The effects of Cl-substituent and solvent (CH_2Cl_2 and $CHCl_3$) on the yields and the Z/E ratios of ClSB and Cl_2SB are shown in Table 1. The main features deduced from the results in Table 1 are as follows.

(1) The yields and the Z/E ratios of 2-, 3-, and 4-ClSB and 2,2'- and 4,4'-Cl_2SB do not depend significantly on the concentrations of YC_6H_4CHO (0.059–0.12 M) and NaOH (0.10–0.50 M), and agitation rate (260–940 rpm). The Z/E ratio increases slightly as the temperature decreases. The yield and the Z/E ratio of 2-ClSB are considerably lower than those of 3- and 4-ClSB.

(2) Under similar reaction conditions, the order of decreasing Z/E ratio is (2-> 4-, and 3-$ClC_6H_4CHO > C_6H_5CHO$ for a given 2- or 3-$ClC_6H_4CH_2PPh_3^+$ ion (entries (1, 4, 7, and 8), and (2, 5, 7', and 9)) and (2-ClC_6H_4CHO, C_6H_5CHO) > (4-, and 3-ClC_6H_4CHO) for 4-$ClC_6H_4CH_2PPh_3^+$ ion (entries 3, 6, 8', and 9').

(3) Under similar reaction conditions, the order of decreasing Z/E ratio is (4-> 3-> 2-$ClC_6H_4CH_2PPh_3^+$ ion) for C_6H_5CHO (entries 1, 2, and 3); (3- and 4- > 2-$ClC_6H_4CH_2PPh_3^+$ ion) for 2-ClC_6H_4CHO (entries 4, 7', and 8'); (3- ~ 2- ~ 4-$ClC_6H_4CH_2PPh_3^+$ ion for 3-ClC_6H_4CHO (entries 5, 7, and 9'); (4-> 2- and 3-$ClC_6H_4CH_2PPh_3^+$ ion for 4-ClC_6H_4CHO (entries 6, 8, and 9). It is worth notifying that 2-ClC_6H_4CHO exhibits unusual stereoselectivity for the Z-isomer, especially in $CHCl_3$ (entries 4, 7', and 8').

(4) The Z/E ratio of a given unsymmetric stilbene ($XC_6H_4CH=CHC_6H_4Y$) may change substantially by interchanging the substituents on the benzyl group of the phosphonium ion and on aryl aldehyde, i.e., by the ($XC_6H_4CH_2PPh_3^+ + YC_6H_4CHO$) reaction and the ($YC_6H_4CH_2PPh_3^+ + XC_6H_4CHO$) reaction, especially for the 2-chloro substituent (entries 1 vs. 1'; 7 vs. 7'; 8 vs. 8'). In

Table 1
Effect of substituents on the yields and the Z/E ratios of chloro- and dichlorostilbenes produced by the two-phase Wittig reactions of related benzaldehydes and BTPP ions

Entry	Stilbene	Z/E ratio (yield %)				Entry	Stilbene	Z/E ratio (yield %)			
		CH_2Cl_2	a	$CHCl_3$	a			CH_2Cl_2	a	$CHCl_3$	a
1	2-ClSB	0.92 (55)	0.84 (57)	0.92 (52)	1.1 (54)	1'	2'-ClSB	2.1 (50)	–	–	–
2	3-ClSB	1.5 (82)	1.3 (82)	1.5 (79)	1.5 (79)	3	4-ClSB	2.7 (98)	2.5 (87)	2.9 (97)	2.9 (89)
4	2,2'-Cl_2SB	1.8 (86)	1.5 (79)	3.5 (80)	2.7 (89)	5	3,3'-Cl_2SB	1.7 (92)	1.7 (92)	1.9 (94)	1.9 (94)
6	4,4'-Cl_2SB	2.1 (93)	1.9 (95)	2.3 (93)	2.3 (93)						
7	2,3'-Cl_2SB	1.4 (90)	1.4 (85)	1.7 (87)	1.9 (83)	7'	3,2'-Cl_2SB	3.3 (81)	3.5 (91)	5.5 (81)	6.1 (82)
8	2,4'-Cl_2SB	1.2 (90)	1.5 (90)	1.5 (83)	1.6 (80)	8'	4,2'-Cl_2SB	2.7 (95)	2.9 (95)	5.3 (96)	4.5 (98)
9	3,4'-Cl_2SB	1.2 (92)	1.1 (90)	1.2 (94)	1.2 (89)	9'	4,3'-Cl_2SB	1.3 (90)	1.3 (91)	1.5 (92)	1.4 (92)

$[NaOH]_o = 0.30$ M, 660 rpm, 20°C.
Entries (1–9, 2'–9'): $[ClC_6H_4CH_2PPh_3^+ Cl^-]_o = 0.060$ M.
Entry (1–3): $[C_6H_5CHO]_o = 0.059$ M.
Entries (4–9, 7'–9'): $[ClC_6H_4CHO]_o = 0.059$ M.
Entry 1': $[C_6H_5CH_2PPh_3^+ Cl^-]_o = 0.060$ M, $[2-ClC_6H_4CHO]_o = 0.059$ M.
2-ClSB = 2'-ClSB, 2,3'-Cl_2SB = 3,2'-Cl_2SB, 2,4'-Cl_2SB = 4,2'-Cl_2SB, and 3,4'-Cl_2SB = 4,3'-Cl_2SB, however, they were produced by interchanging the substituents on the benzyl group of the phosphonium ion and on benzaldehydes; e.g., 2,3'-Cl_2SB was produced by the Wittig reaction of 2-$ClC_6H_4CH_2PPh_3^+$ ion and 3-ClC_6H_4CHO whereas 3,2'-Cl_2SB by 3-$ClC_6H_4CH_2PPh_3^+$ ion and 2-ClC_6H_4CHO.
a: $[LiBr]_o = 0.015$ M in H_2O.

contrast, the yield of $XC_6H_4CH=CHC_6H_4Y$ does not vary significantly by interchanging the substituents on phosphonium ion and aryl aldehyde.

(5) In general, $CHCl_3$ and CH_2Cl_2 show similar solvent effect on the yields of ClSB and Cl_2SB. In contrast, the Z/E ratio in $CHCl_3$ is substantially larger than in CH_2Cl_2 for 2,2′-, 3,2′- or 4,2′-Cl_2SB.

(6) The presence of 0.015 M LiBr in the aqueous phase generally does not change significantly the yields and the Z/E ratio of ClSB and Cl_2SB.

3.2. Synthesis of stilbenes containing mono-methyl-substituted phenyl group

Methylstilbenes (MeSB), symmetric and unsymmetric dimethylstilbenes (Me_2SB), chloromethyl-stilbenes (ClMeSB), and bromomethylstilbenes (BrMeSB) were synthesized by the Wittig reactions of various combinations of $Ph_3PCH_2C_6H_4X^+$ ion and YC_6H_4CHO (X or Y = H, Me, Cl or Br). The results are summarized as follows.

3.2.1. Methylstilbenes (MeSB)

For $[Ph_3PCH_2C_6H_4CH_3^+Br^-]_o = (0.009, 0.027, 0.060,$ and $0.072)$ M, $[C_6H_5CHO]_o = (0.059, 0.12, 0.59,$ and $1.2)$ M, $[NaOH]_o = (0.10, 0.20, 0.30,$ and $0.50)$ M, $r = (260, 520, 700,$ and $950)$ rpm, and in CH_2Cl_2, the Z/E ratios of MeSB are (1.2 ± 0.1), (1.6 ± 0.1), and (1.8 ± 0.1) for 2-, 3-, and 4-MeSB, respectively.

3.2.2. Dimethylstilbenes (Me₂SB)

For $[Ph_3PCH_2C_6H_4CH_3^+Br^-]_o = (0.007, 0.027, 0.068,$ and $0.072)$ M, $[CH_3C_6H_4CHO]_o = (0.035, 0.068, 0.14,$ and $0.69)$ M, $[NaOH]_o = (0.10, 0.20, 0.30,$ and $0.50)$ M, 20, $r = (260, 520, 700,$ and $950)$ rpm, and in CH_2Cl_2, the Z/E ratios are (1.5 ± 0.1), (1.5 ± 0.1), and (1.8 ± 0.1) for 2,2′-, 3,3′-, and 4,4′-Me_2SB, respectively.

3.2.3. Effects of substituent and solvent

The effects of substituent and solvent on the Z/E ratios of stilbenes are shown in Table 2. The main features deduced from these results are as follows.

(1) For most of the MeSB, Me_2SB, MeClSB, and MeBrSB, the Z/E ratio is between 1 and 2 and does not depend significantly on the stirring rate, temperature, and concentrations of phosphonium ion, aryl aldehyde, and NaOH.

(2) In general, the 3- and 4-Me-, Cl-, and Br-substituents exhibit similar effects on the Z/E ratios. In contrast, the 2-Cl-, and Br-substituent may exhibit considerably different Z-selectivity, especially in 2,2′-MeClSB (entry 19) and 2,2′-MeBrSB (entry 28).

(3) The Z/E ratio may change substantially by interchanging the substituents on the benzyl group of the phosphonium ion and on aryl aldehyde, especially for 2-substituted stilbenes (entries 10, 16, 17, 19, 22, 25, 28, and 31; 10′, 16′, 17′, 19′, 22′, 28′, 28′, and 31′).

(4) The effects of Cl- and Br-substituents are similar and both show more favorable effect on the Z-selectivity than the Me-substituent.

(5) In general, $CHCl_3$ shows more favorable effect on the Z-selectivity than CH_2Cl_2.

3.3. Synthesis of stilbenes containing dimethyl-substituted phenyl group

Stilbenes containing dimethyl-substituted phenyl group were synthesized by the Wittig reactions of various combinations of $Ph_3PCH_2C_6H_3Me_2^+$ or $Ph_3PCH_2C_6H_4X^+$ ion and $Me_2C_6H_3CHO$ or

Table 2
Effect of substituents on the Z/E ratios of methyl-, dimethyl-, chloromethyl-, and bromomethyl-stilbenes produced by the two-phase Wittig reactions of related benzaldehydes and BTPP ions

Entry	Stilbene	Z/E ratio		Entry	Stilbene	Z/E ratio	
		CH_2Cl_2	$CHCl_3$			CH_2Cl_2	$CHCl_3$
10	2-MeSB	1.2	1.3	10′	2′-MeSB	0.90	1.3
11	3-MeSB	1.5	1.6	11′	3′-MeSB	1.7	1.9
12	4-MeSB	1.8	1.9	12′	4′-MeSB	1.7	1.9
13	2,2′-Me$_2$SB	1.5	2.2	14	3,3′-Me$_2$SB	1.5	1.6
15	4,4′-Me$_2$SB	1.8	2.0				
16	2,3′-Me$_2$SB	1.1	1.3	16′	3,2′-Me$_2$SB	0.78	1.1
17	2,4′-Me$_2$SB	1.3	1.2	17′	4,2′-Me$_2$SB	0.84	1.2
18	3,4′-Me$_2$SB	1.3	1.3	18′	4,3′-Me$_2$SB	1.5	1.5
19	2,2′-MeClSB	4.1	5.9	19′	2,2′-ClMeSB	1.6	2.5
20	3,2′-MeClSB	1.1	1.2	20′	2,3′-ClMeSB	1.4	1.9
21	4,2′-MeClSB	1.1	1.2	21′	2,4′-ClMeSB	1.2	1.7
22	2,3′-MeClSB	2.4	3.8	22′	3,2′-ClMeSB	1.1	1.5
23	3,3′-MeClSB	1.3	1.3	23′	3,3′-ClMeSB	1.6	1.9
24	4,3′-MeClSB	1.3	1.3	24′	3,4′-ClMeSB	1.4	1.6
25	2,4′-MeClSB	1.8	2.6	26	3,4′-MeClSB	1.3	1.3
27	4,4′-MeClSB	1.6	2.6				
28	2,2′-MeBrSB	4.5	6.8	28′	2,2′-BrMeSB	1.8	3.0
29	3,2′-MeBrSB	1.1	1.2	29′	2,2′-BrMeSB	1.4	2.0
30	4,2′-MeBrSB	1.1	1.2	30′	2,4′-BrMeSB	1.4	1.9
31	2,3′-MeBrSB	2.1	3.5	31′	3,2′-BrMeSB	1.1	1.5
32	3,3′-MeBrSB	1.4	1.5	32′	3,3′-BrMeSB	1.8	2.1
33	4,3′-MeBrSB	1.3	1.3	33′	3,4′-BrMeSB	1.5	1.7
34	2,4′-MeBrSB	1.7	2.7	34′	4,2′-BrMeSB	1.2	1.9
35	3,4′-MeBrSB	1.3	1.3	35′	4,3′-BrMeSB	2.0	2.5
36	4,4′-MeBrSB	1.7	2.6	36′	4,4′-BrMeSB	2.1	2.5

$[NaOH]_o = 0.30$ M, 20°C, 700 rpm.
Entries (10–12): $[MeC_6H_4CH_2PPh_3^+ Br^-]_o = 0.060$ M, $[C_6H_5CHO]_o = 0.12$ M.
Entries (10′–12′): $[C_6H_5CH_2PPh_3^+ Br^-]_o = 0.060$ M, $[MeC_6H_4CHO]_o = 0.069$ M.
Entries (13–15): $[MeC_6H_4CH_2PPh_3^+ Br^-]_o = 0.060$ M, $[MeC_6H_4CHO]_o = 0.069$ M.
Entries (16–18, 16′–18′): $[MeC_6H_4CH_2PPh_3^+ Br^-]_o = 0.060$ M, $[MeC_6H_4CHO]_o = 0.069$ M.
Entries (19–27): $[MeC_6H_4CH_2PPh_3^+ Br^-]_o = 0.060$ M, $[ClC_6H_4CHO]_o = 0.071$ M.
Entries (19′–24′): $[ClC_6H_4CH_2PPh_3^+ Br^-]_o = 0.060$ M, $[MeC_6H_4CHO]_o = 0.071$ M.
Entries (28–36): $[MeC_6H_4CH_2PPh_3^+ Br^-]_o = 0.060$ M, $[BrC_6H_4CHO]_o = 0.071$ M.
Entries (28′–36′): $[BrC_6H_4CH_2PPh_3^+ Br^-]_o = 0.060$ M, $[MeC_6H_4CHO]_o = 0.071$ M.

YC_6H_4CHO (X or Y = H, Me, F, Cl, Br, CF$_3$, NO$_2$, MeO, BnO or CHO). The investigation focused on the effects of *ortho* substitutents on the yield and the Z/E ratio of the product stilbene. The results are summarized as follows.

3.3.1. Dimethylstilbenes (Me$_2$SB) and tetramethylstilbenes (Me$_4$SB)

For $[Ph_3PCH_2C_6H_3Me_2^+Cl^-]_o = 0.060$ M, $[NaOH]_o = (0.10, 0.20, 0.30,$ and $0.50)$ M, $T = (5, 10, 20,$ and $30)$ °C, $r = (270, 430, 670,$ and $940)$ rpm, and in CH_2Cl_2, the total yields and the corresponding Z/E ratios of stilbenes are $(93 \pm 2\%; 0.91 \pm 0.02)$, $(96 \pm 2\%; 1.2 \pm 0.2)$, $(95 \pm 2\%; 1.2 \pm 0.1)$, and $(91 \pm 1\%; 1.1 \pm 0.1)$ for 2,5-Me$_2$SB (with $[C_6H_5CHO]_o = (0.79, 0.99, 2.0,$ and $3.0)$ M), 3,5-Me$_2$SB (with $[C_6H_5CHO]_o = (0.059, 0.079, 0.25,$ and $1.5)$ M), 2,5,2′,5′-Me$_4$SB (with $[2,5-Me_2C_6H_3CHO]_o = (0.35, 0.50, 0.71,$ and $1.8)$ M), and 3,5,3′,5′-Me$_4$SB (with $[3,5-Me_2C_6H_3CHO]_o = (0.17, 0.25, 0.31,$ and $0.62)$ M), respectively.

In contrast, under similar conditions for the reactions of $Ph_3PCH_2C_6H_5^+Cl^-$ with 2,5-$Me_2C_6H_3CHO$ and 3,5-$Me_2C_6H_3CHO$, the total yields and the corresponding Z/E ratios of stilbenes are $(91 \pm 3\%; 1.2 \pm 0.1)$ and $(97 \pm 2\%; 1.4 \pm 0.1)$ for 2,5-Me_2SB and 3,5-Me_2SB, respectively.

3.3.2. Fluoro-, chloro-, and bromo-dimethylstilbenes (FMe$_2$SB, ClMe$_2$SB, and BrMe$_2$SB)

For the reactions of 2,5-$Me_2C_6H_3CH_2PPh_3^+Cl^-$ with 2-FC_6H_4CHO, 2-ClC_6H_4CHO, 3-ClC_6H_4CHO, 4-ClC_6H_4CHO, and 2-BrC_6H_4CHO under conditions similar to those of Section 3.3.1, the total yields and the corresponding Z/E ratios of stilbenes are $(91 \pm 3\%; 2.3 \pm 0.1)$, $(95 \pm 3\%; 3.7 \pm 0.2)$, $(97 \pm 1\%; 0.70 \pm 0.01)$, $(97 \pm 1\%; 0.74 \pm 0.01)$, and $(96 \pm 2\%; 4.0 \pm 0.1)$ for 2,5,2′-Me_2FSB, 2,5,2′-Me_2ClSB, 2,5,3′-Me_2ClSB, 2,5,4′-Me_2ClSB, and 2,5,2′-Me_2BrSB, respectively.

In contrast, for the reactions of $Ph_3PCH_2C_6H_4X^+Cl^-$ with 2,5-$Me_2C_6H_3CHO$, 2,5-$Me_2C_6H_3CHO$, 2,5-$Me_2C_6H_3CHO$, and 2,5-$Me_2C_6H_3CHO$, the total yields and the corresponding Z/E ratios of stilbenes are $(80 \pm 2\%; 1.6 \pm 0.1)$, $(81 \pm 3\%; 1.8 \pm 0.1)$, $(79 \pm 2\%; 1.3 \pm 0.1)$, and $(89 \pm 2\%; 2.0 \pm 0.1)$ for 2,2′,5′-FMe_2SB, 2,2′,5′-$ClMe_2SB$, 3,2′,5′-$ClMe_2SB$, and 2,2′,5′-$BrMe_2SB$, respectively.

3.3.3. Trifluoromethyl-, nitro-, trimethoxy-, benzyloxy-, and dichlorodimethylstilbenes (CF$_3$Me$_2$SB, NO$_2$Me$_2$SB, (MeO)$_3$Me$_2$SB, BnOMe$_2$SB, and Cl$_2$Me$_2$SB)

For the reactions of 2,5-$Me_2C_6H_3CH_2PPh_3^+Cl^-$ with 2-$CF_3C_6H_4CHO$, 2-$NO_2C_6H_4CHO$, 2,3,4-$(MeO)_3C_6H_2CHO$, 2-$BnOC_6H_4CHO$, and 2,6-$Cl_2C_6H_3CHO$ under conditions similar to those of Section 3.3.1, the total yields and the corresponding Z/E ratios of stilbenes are $(97 \pm 1\%; 5.6 \pm 0.1)$, $(91 \pm 5\%; 1.1 \pm 0.1)$, $(86 \pm 2\%; 3.6 \pm 0.1)$, $(87 \pm 2\%; 1.3 \pm 0.1)$, and $(97 \pm 2\%; 0.07 \pm 0.01)$ for 2,5,2′-Me_2CF_3SB, 2,5,2′-Me_2NO_2SB, 2,5,2′,3′,4′-$Me_2(MeO)_3SB$, 2,5,2′-Me_2BnOSB, and 2,5,2′,6′-Me_2Cl_2SB, respectively.

3.3.4. Effects of substituent and solvent

The effects of substituents (Me, F, Cl, Br, CF$_3$, NO$_2$, MeO, BnO, and CHO) and solvents (CCl$_4$, CHCl$_3$, CH$_2$Cl$_2$, C$_6$H$_6$, and n-C$_6$H$_{14}$) on the yields and the corresponding Z/E ratios of stilbenes are shown in Table 3. The main features deduced from these results are as follows.

(1) The yields and the Z/E ratios of these dimethylstilbenes do not depend significantly on the concentrations of aryl aldehydes (0.050–0.20 M) and NaOH (0.10–0.40 M), temperature (5–30°C), and agitation rate (270–940 rpm).

(2) For the 2,5-$Me_2C_6H_3CH_2PPh_3^+$-ArCHO reaction system, the polar aprotic solvents generally exhibit higher yield and more favorable Z-selectivity of stilbene than the nonpolar solvents for *meta*- and *para*-substitutents of benzaldehydes (entries 37–53). In contrast, the substituent (F-, Cl-, Br-, CH$_3$O-, NO$_2$-, or CF$_3$-) at the *ortho* position of benzaldehyde exhibits a pronounced enhancement for the Z-selectivity, especially in nonpolar solvents (entries 43, 44, 45, 48, 49, and 53). The order of effectiveness of substituents on the Z-selectivity is CF$_3$ > (Cl, Br) > CH$_3$O > F > NO$_2$.

(3) For the $Ph_3PCH_2C_6H_5^+$-ArCHO reaction system, the order of decreasing Z/E ratio is 2,3,4-$(MeO)_3C_6H_2CHO$ > 2,4-$(MeO)_2C_6H_3CHO$ > ((2,5-, 3,5-, 2,4-, and 3,4-)$Me_2C_6H_3CHO$, 3,4,5-$(MeO)_3C_6H_2CHO$) in (CHCl$_3$, CH$_2$Cl$_2$, CCl$_4$, C$_6$H$_6$, and n-C$_6$H$_{14}$) (entries 37′, 38′, 39′, 40′, 54′, 55′, and 56′). The polar solvents (CHCl$_3$, and CH$_2$Cl$_2$) exhibit higher yield and more Z-selectivity of stilbene than the nonpolar solvents (CCl$_4$, C$_6$H$_6$, and n-C$_6$H$_{14}$). Noticeably, the yield of 2,2′,5′-NO_2Me_2SB is nearly zero in CCl$_4$, C$_6$H$_6$ or n-C$_6$H$_{14}$ (entry 48′).

Table 3

Effect of substituents on the Z/E ratios of dimethyl- and tetramethyl-stilbenes and methoxystilbenes produced by the two-phase Wittig reactions of related benzaldehydes and BTPP ions

Entry	Stilbene	Z/E ratio (yield %)					Entry	Stilbene	Z/E ratio (yield %)				
		CCl_4	$CHCl_3$	CH_2Cl_2	C_6H_6	C_6H_{12}			CCl_4	$CHCl_3$	CH_2Cl_2	C_6H_6	C_6H_{12}
37	2.5-Me$_2$SB	0.44 (93)	1.1 (94)	0.93 (93)	0.63 (91)	0.76 (84)	37′	2′,5′-Me$_2$SB	0.53 (91)	2.1 (94)	1.2 (93)	0.89 (97)	0.55 (67)
38	3.5-Me$_2$SB	0.35 (78)	1.3 (99)	1.1 (96)	0.60 (92)	0.32 (43)	38′	3′,5′-Me$_2$SB	0.33 (88)	1.5 (99)	1.4 (98)	0.62 (98)	0.33 (44)
39′	2′,4′-Me$_2$SB	0.35 (75)	1.2 (96)	0.76 (86)	0.54 (76)	0.30 (19)	40′	3′,4′-Me$_2$SB	0.41 (51)	1.7 (82)	1.5 (64)	0.70 (62)	0.41 (25)
41	2,5,2′,5′-Me$_4$SB	0.52 (95)	1.9 (98)	1.2 (95)	0.84 (95)	0.63 (85)	42	3,5,3′,5′-Me$_4$SB	0.30 (84)	1.2 (99)	1.1 (92)	0.54 (65)	0.34 (45)
43	2,5,2′-Me$_2$FSB	3.5 (80)	3.0 (91)	2.3 (92)	3.4 (87)	3.2 (57)	43′	2,2′,5′-FMe$_2$SB	0.83 (31)	2.8 (91)	1.6 (84)	1.0 (41)	0.50 (18)
44	2,5,2′-Me$_2$ClSB	7.4 (95)	5.8 (98)	3.6 (96)	6.8 (85)	5.1 (95)	44′	2,2′,5′-ClMe$_2$SB	1.2 (37)	4.0 (82)	1.8 (80)	1.5 (49)	1.2 (24)
45	2,5,2′-Me$_2$BrSB	6.7 (92)	5.8 (99)	4.0 (98)	6.0 (92)	5.4 (84)	45′	2,2′,5′-BrMe$_2$SB	1.1 (24)	4.0 (83)	2.0 (91)	1.2 (36)	0.82 (35)
46	2,5,3′-Me$_2$ClSB	0.28 (98)	0.74 (99)	0.71 (99)	0.43 (99)	0.32 (81)	46′	3,2′,5′-ClMe$_2$SB	0.58 (35)	2.3 (89)	1.3 (79)	0.71 (42)	0.47 (35)
47	2,5,4′-Me$_2$ClSB	0.24 (99)	0.79 (98)	0.75 (99)	0.41 (99)	0.24 (99)							
48	2,5,2′-Me$_2$NO$_2$SB	2.8 (90)	2.0 (99)	1.1 (99)	2.0 (94)	1.9 (66)	48′	2,2′,5′-NO$_2$Me$_2$SB	–(~0)	3.5 (72)	1.4 (64)	–(~0)	–(~0)
49	2,5,2′-Me$_2$CF$_3$SB	9.7 (91)	9.5 (99)	5.7 (99)	9.6 (93)	9.8 (69)	50	2,5′,2′-Me$_2$-BnOSB	1.5 (66)	1.9 (93)	1.3 (88)	1.4 (64)	1.1 (64)
51	2,5,2′,6′-Me$_2$Cl$_2$ SB	0.04 (97)	0.10 (99)	0.08 (99)	0.04 (99)	0.04 (98)	52	2,5,2′-Me$_2$CHOSB	0.66 (53)	1.5 (96)	1.7 (93)	0.80 (42)	0.95 (10)
53	2,5,2′,3′,4′-Me$_2$ (MeO)$_3$SB	4.5 (79)	5.9 (94)	3.6 (88)	5.2 (79)	3.0 (77)	54′	2′,3′,4′-(MeO)$_3$SB	3.8 (44)	5.8 (89)	3.5 (82)	4.6 (55)	3.0 (60)
55′	3′,4′,5′-(MeO)$_3$SB	0.30 (81)	1.0 (80)	1.0 (83)	0.50 (68)	0.50 (43)	56′	2′,4′-(MeO)$_2$SB	2.4 (44)	2.8 (83)	2.0 (68)	3.0 (58)	1.3 (15)

[NaOH]$_o$ = 0.30 M, 20°C, 940 rpm.

Entries (37, 38, 41, 42): [XC$_6$H$_3$CH$_2$PPh$_3^+$ Cl$^-$]$_o$ = 0.060 M (X = 2,5-Me$_2$ (entries 37, 41), 3,5-Me$_2$ (entries 38, 42)), [C$_6$H$_5$CHO]$_o$ = 0.99 M (entry 37), and 0.080 M (entry 38), [2,5-Me$_2$C$_6$H$_3$CHO]$_o$ = 0.50 M (entry 41), [3,5-Me$_2$C$_6$H$_3$CHO]$_o$ = 0.16 M (entry 42).

Entries (37′–40′): [C$_6$H$_5$CH$_2$PPh$_3^+$ Cl$^-$]$_o$ = 0.060 M, [2,5-Me$_2$C$_6$H$_3$CHO]$_o$ = 0.50 M (entry 37′), [3,5-Me$_2$C$_6$H$_3$CHO]$_o$ = 0.43 M (entry 38′), [2,4-Me$_2$C$_6$H$_3$CHO]$_o$ = 0.15 M (entry 39′), [3,4-Me$_2$C$_6$H$_3$CHO]$_o$ = 0.16 M.

Entries (43–47): [Me$_2$CH$_2$PPh$_3^+$ Cl$^-$]$_o$ = 0.060 M, [2-FC$_6$H$_4$CHO]$_o$ = 0.060 M (entry 43), [2-ClC$_6$H$_4$CHO]$_o$ = 0.088 M (entry 44), [2-BrC$_6$H$_4$CHO]$_o$ = 0.060 M (entry 45), [3-ClC$_6$H$_4$CHO]$_o$ = 0.093 M (entry 46), [4-ClC$_6$H$_4$CHO]$_o$ = 0.12 M (entry 47).

Entries (43′-46′): [XC$_6$H$_4$CH$_2$PPh$_3^+$ Cl$^-$]$_o$ = 0.060 M (X = 2-F (entry 43′), 2-Cl (entry 44′), 2-Br (entry 45′), 3-Cl (entry 46′)), [2,5-Me$_2$C$_6$H$_3$CHO]$_o$ = 0.16 M (entry 43′), 0.071 M (entry 44′), 0.13 M (entry 45′), 0.21 M (entry 46′).

Entries (48–53): [2,5-Me$_2$C$_6$H$_3$CH$_2$PPh$_3^+$ Cl$^-$]$_o$ = 0.060 M, 2-CF$_3$C$_6$H$_4$CHO]$_o$ = 0.060 M (entry 49), [2-(PhCH$_2$O)C$_6$H$_4$CHO]$_o$ = 0.080 M (entry 50), [2,6-Cl$_2$C$_6$H$_3$CHO]$_o$ = 0.060 M (entry 51), [2-CHOC$_6$H$_4$CHO]$_o$ = 0.090 M (entry 52), [2,3,4-(MeO)$_3$C$_6$H$_2$CHO]$_o$ = 0.25 M (entry 53).

Entry 48′: 2-NO$_2$C$_6$H$_4$CH$_2$PPh$_3^+$ Cl$^-$]$_o$ = 0.060 M, [2,5-Me$_2$C$_6$H$_3$CHO]$_o$ = 0.84 M.

(4) The yields and the Z/E ratios may change considerably by interchanging the substituent on the benzyl group of the phosphonium ion and on the aryl aldehyde, especially in CCl_4 (entries 43 vs. 43', 44 vs. 44', 45 vs. 45', 46 vs. 46', and 48 vs. 48').

(5) The bis-Wittig reaction (i.e., a double intermolecular Wittig reaction) was observed in the $2,5\text{-}Me_2C_6H_3CH_2PPh_3^+\text{-}2\text{-}CHOC_6H_4CHO$ reaction system, especially in CCl_4 (entry 52) [25].

3.4. Discussion

The mechanism of the homogeneous Wittig reaction was generally expressed in terms of two main steps: (1) nucleophilic addition of the phosphorus ylide to the carbonyl compound to give intermediate (betaines (reaction (M1)) and oxaphosphetanes (reaction (M2)); (2) irreversible decomposition of the intermediates to give alkenes and phosphine oxide (reactions (M3) and (M4)) [2,24]. The Wittig reaction of benzylidenetriphenylphosphorane ($Ph_3P=CHPh'$) with benzaldehyde ($Ph''CHO$) is depicted in Scheme 3.

In 1973, Vedejs and Snoble [26] and Vedejs et al. [27] reported for the first time the observation of oxaphosphetanes by ^{31}P NMR spectroscopy and in 1981 established 1,2-oxaphosphetanes as principal intermediates in a variety of Wittig reactions involving nonstabilized phosphorus ylides and alkenes or ketones. In 1996, Borisova et al. [10] reported the first experimental evidence of the formation of betaines. McEwen and Ward [28] studied the metal ion effects on the Wittig reactions and observed that in most cases where lithium ion was present, the product mixture was enriched with the Z alkene, while when sodium or potassium ions were present, the E alkene predominated. Vedejs et al. [27] and Vedejs and Marth [29] have developed a model involving a concerted asynchronous cycloaddition of the ylide to an aldehyde to form the oxaphosphetane, involving a four-centered transition state with early C-C bond formation, in which the ylidic carbon attacks the carbonyl group with the C=O axis skewed relatively to the C=P axis. This one-step, nonsynchronous cycloaddition mechanism has been widely accepted. A theoretical model study of the Wittig reaction by Mari et al. [30] has provided evidence to support the asynchronous cycloaddition mechanism (borderline two-step mechanism) with early C–C bond formation in the transition state. Oxaphosphetanes are thermally unstable and in
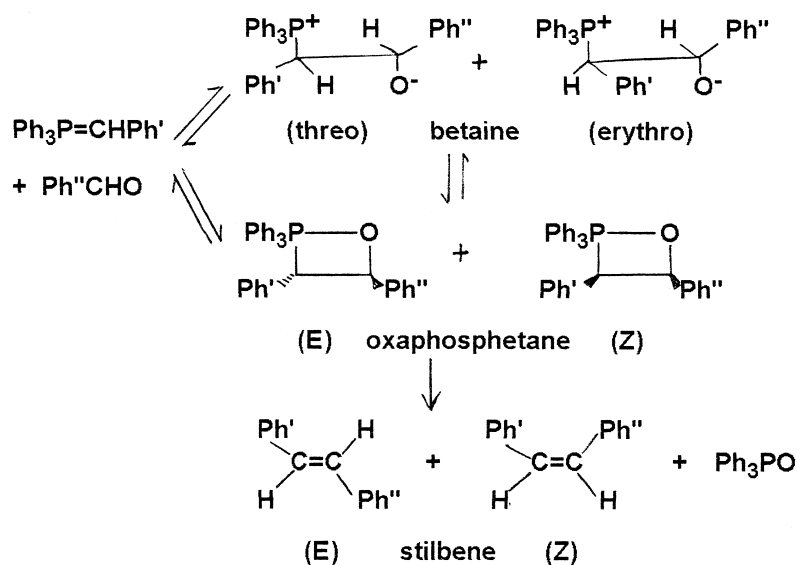
Scheme 3.

principle can disintegrate to alkene and phosphine oxide or to ylide and aldehyde (retro-Wittig reaction), depending on their structures and reaction conditions. As emphasized by Bestmann [31], the first oxaphosphetane produced should have an axial (apical) P–O bond and must undergo pseudorotation [32] to one conformation possessing an axial P–C bond to fragment into products. This rationale related to the general rule of 'apical entry / apical departure' for nucleophilic substitution reactions at trigonal bypyramidal phosphorus [33]. As reported by Vedejs and Marth [34], the rates of pseudorotation of unconstrained oxaphosphetanes were much faster than rates of decomposition and the barriers to pseudorotation should not control the rate of the Wittig decomposition step. The transition state for the decomposition of oxaphosphetane to alkene was viewed as an asynchronous cycloreversion with advanced P–C bond breaking. As pointed out by Vedejs and Marth [29], the variation in the stereochemistry of Wittig reaction is attributed mainly to kinetic control in nearly all cases and there is no single dominant transition state geometry. Two limiting geometries are the puckered *cis*-selective geometry and the planar *trans*-selective geometry. The delicate interplay of 1,2 and 1,3 steric interactions between substituents on the four-centered array is responsible for the selectivity of *cis* or *trans* diastereomer. In the puckered *cis*-selective geometry, the 1,2 interactions of the ylide α substituent with the aldehyde group and with the adjacent phosphorus substituent are smaller than in the corresponding transform. The puckered transition states are increasingly important as the 1,3 interactions associated with bulk α to the carbonyl group become dominant. In the planar *trans*-selective four-centered transition state, *trans* selectivity results from dominant product-like 1,2 interactions, since 1,3 interactions are relieved due to the increase in basal bond angles in trigonal bipyramidal phosphorus compared to the distorted square-pyramidal geometry. In general, nonstabilized or moderated (semistabilized) ylides react via early reactant-like transition states having phosphorus in a distorted square-pyramidal geometry. In contrast, stabilized ylides react via late product-like transition states having phosphorus in a trigonal-bipyramidal geometry. Vedejs et al. [35] deduced an important generalization for all Wittig reactions: 'the kinetic *cis / trans* preference for disubstituted oxaphosphetane formation is at least as high as the olefin Z/E ratio'.

Factors which have been shown to affect the olefin Z/E ratios include temperature, solvent, types of ylide and aldehyde, and additives (especially Li^+ and I^- ions). In this work, we studied the two-phase Wittig reactions of BTPP salts and benzaldehydes, focusing mainly on the effects of organic solvent and substituent on the yield and the Z/E ratio of the product stilbene. Since it was generally observed that the effect of stirring rate was insignificant, therefore the generation of phosphorus ylide either in the aqueous phase or at the interface did not play a key role in these Wittig reactions. This result implies that the reaction of benzylidenetriphenylphosphorane and benzaldehyde in the organic phase is the decisive step, which follows the second-order kinetics [36]. It was reported that lithium salt had a pronounced impact on the stereoselectivity of initial oxaphosphetane formation, leading in general to an increase in the proportion of the *E*-alkene [37,38]. We found that the presence of lithium salt in the aqueous phase had no significant effect on the Z/E alkene ratio. This result is similar to that observed in the protic solvent like EtOH [37]. As mentioned above, stabilized ylides bearing π-acceptor groups at the α carbon generally exhibit dominant *E*-alkene selectivity, while nonstabilized ylides, bearing alkyl group, render predominantly *Z* alkene. In contrast, semistabilized ylides like benzyl ylides usually yield mixtures of *Z* and *E* isomers. In particular, the reactions of benzylidenetriphenylphosphoranes with aryl aldehydes under salt free conditions are practically nonselective, giving nearly 1:1 mixtures of the product stilbenes. It is known that carbonyl compounds having electron-withdrawing substituent generally react at more rapid rates in Wittig reactions than do carbonyl compounds having electron-donating substituent, and tend to give more proportion of *Z* alkene. Johnson and Kyllingstad [39] studied the Wittig reaction of $R_3P=CHC_6H_4X$ and

YC_6H_4CHO (R = Ph, 4-ClC_6H_4, or n-C_4H_9; X = Y = 4-OMe or 4-NO_2) in benzene. They found that the formation of *E*-alkene could be strongly favored by use of phosphonium ylides carrying electron-donating phosphorus substituents (e.g., R = n-C_4H_9) and that for the same phosphonium group, the most effective way of obtaining better yield of *Z* alkene was to employ the more nucleophilic substituent (e.g., 4-OMe). Allen and Ward [40] showed that increasing steric crowding at phosphorus in Wittig reactions of semistabilized phosphonium ylides in EtOH led to an increase in *Z/E* alkene ratio. It was emphasized that *ortho* substitute ion on phosphorus-aryl group of semistabilized ylides (Ar_3P=CHPh) would induce difference in *Z/E* alkene ratio [40–42]. Yamataka et al. [42] studied the relative reactivity and stereoselectivity in the Wittig reactions of substituted benzaldehyde (YC_6H_4CHO, Y = 2-, 3-, and 4-Me; 2-, 3-, and 4-Cl; 3-F, or 3-CF_3) and benzylidenetriphenylphosphoranes (Ph_3P=CHC_6H_4X, X = 2- and 4-) Me; 2- and 4-Me, or 2- and 4-Cl) in THF. They found that the *Z/E* ratio of the product stilbene (about 40/60 (Li-salt free) and 60/40 (Li-salt present) was essentially unchanged by the change in concentration, the molar ratio and the mode of mixing ylide and aldehyde, and it varied only slightly with most substituents X and Y except the *ortho* substituent. They also found that 2-ClC_6H_4CHO and 2-$MeOC_6H_4CHO$ reacted much faster than the corresponding 4-substituted counterparts and increased substantially the *Z/E* ratio under Li-salt free conditions. This observation was different from the related reactions of nonstabilized ylides with YC_6H_4CHO, which did not show such aberrant rate and *Z*-selectivity for 2-ClC_6H_4CHO and 2-$MeOC_6H_4CHO$. In general, our results support the above arguments. The *ortho*-substituted benzaldehydes with substituent bearing heteroatom afford substantially enhanced *Z*-selectivity compared to their *meta*- and *para*-substituted counterparts, especially for 2-$CF_3C_6H_4CHO$ in either polar aprotic or nonpolar solvent. This anomal *ortho* effect is generally rationalized by invoking the through space $2p$–$3d$ overlap effect [43] to form a σ complex by a weak interaction between the carbonyl oxygen and the electron deficient phosphorus atom of the ylide during the formation of oxaphosphetane intermediate [42,44]. To avoid steric repulsion, the aldehyde phenyl group should point away from the ylide and the C–P–O–C dihedral angle could be varied relatively freely. Assumed other things being equal, the σ complex would be expected to render a nearly 1:1 mixture of *Z*- and *E*-oxaphosphetane, leading to nearly 1:1 mixture of *Z*- and *E*-stilbene. However, for *ortho*-substituted benzaldehyde bearing substituent like F, Cl, Br, MeO, NO_2, or CF_3, the *cis*-selectivity of the oxaphosphetane could become more favorable due to the chelating stabilization, since the phosphorus atom (adopting a hypervalent octahedral structure) would coordinate to two-electron-donating atoms, the carbonyl oxygen atom and the heteroatom of the *ortho* substituent [42]. Such *ortho* chelating stabilization is likely to enhance the *Z*-selectivity of the product stilbene, compared to the corresponding *meta*- and *para*-substituted counterparts. In contrast, such enhanced *Z*-selectivity was not observed for the *ortho*-substituted benzylidene ylides (entries 1, 7, and 8 (Table 1); 19′, 20′, 21′, 28′, 29′, and 30′ (Table 2); and 48′ (Table 3)), which is similar to the observation of Yamataka et al. [42]. Finally, it is worth mentioning the study by Bellucci et al. [21] of Wittig reactions of $Ph_3PCH_2C_6H_4R^+X^-$ or $Ph_2ClPCH_2C_6H_4R^+X^-$ and $R'C_6H_4CHO$ (X = Cl, Br, or l; R or R' = H, 4-Me, 4-OMe, or 4-CF_3) in solid (KOH)–liquid (CH_2Cl_2) two-phase system catalyzed by 18-crown-6. They demonstrated that all BTPP iodides reacted with benzaldehydes (with either electron-donating or withdrawing substituent) to yield the practically pure *Z* stilbenes, while benzylchlorodiphenylphosphonium bromides reacted with benzaldehydes to produce pure *E* stilbenes, regardless of the nature of *para* substituent on the benzyl group or on the benzaldehyde phenyl group. Here, the solvation effect of crown ether, which may affects the formation and the reactivity of ylide, plays an important role in making the transition state earlier for reactions of BTPP halides and in shifting the transition state to a nearly planar late one for reactions of benzylchlorodiphenylphosphonium bromides.

4. Conclusion

In the Wittig reactions of BTPP salts and benzaldehydes in two-phase organic solvent/water (NaOH) media, it was observed that the rate of agitation was insignificant and the reaction of benzylidenetriphenylphosphorane and benzaldehyde in the organic phase is the decisive step responsible for the stereoselectivity. In general, the polar solvents ($CHCl_3$ and CH_2Cl_2) exhibit more favorable Z-selectivity of the product stilbene than do the nonpolar solvents (n-C_6H_{14}, C_6H_6, and CCl_4). The *ortho*-substituted benzaldehydes bearing heteroatom substituent exhibit a pronounced enhancement for the Z-selectivity with the order of effectiveness of substituents being $CF_3 > $ (Cl, Br) $>$ MeO $>$ F $>$ NO_2.

Acknowledgements

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