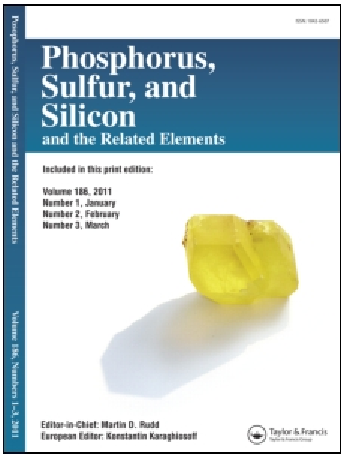

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ROLE OF THROUGH-SPACE 2*p*-3*d* OVERLAP EFFECTS IN LITHIUM-ION CATALYZED WITTIG REACTIONS

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ROLE OF THROUGH-SPACE 2*p*–3*d* OVERLAP EFFECTS IN LITHIUM-ION CATALYZED WITTIG REACTIONS

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The reactions of benzylidene-*bis*-(*o*-methoxyphenyl)methylphosphorane (**17**) with either banzaldehyde or trimethylacetaldehyde in the presence of lithium ion in tetrahydrofuran solution give higher ratios of *cis* : *trans* alkenes than do the corresponding reactions with benzylidenediphenylmethylphosphorane (**16**). However, when the intermediate oxaphosphetanes, **11** and **22** are produced by the action of lithium diphenylphosphide and lithium *bis*-(*o*-methoxyphenyl)phosphide (**5**), respectively, on *trans*-stilbene oxide (**6**), with subsequent addition of methyl iodide, the reactions are stereospecific, and only *cis*-stilbene is produced in each case. The results themselves and also attempted crossover experiments indicate that the oxephosphetanes do not revert to ylide plus aldehyde in the presence of lithium ion.

The above observations, when combined with our knowledge of the preferred geometry of the through space 2*p*–3*d* overlap effect have enabled us to suggest a detailed mechanism for the lithium ion-catalyzed Wittig reaction of benzylidene-*bis*-(*o*-methoxyphenyl)methylphosphorane (**17**) with an aldehyde.

INTRODUCTION

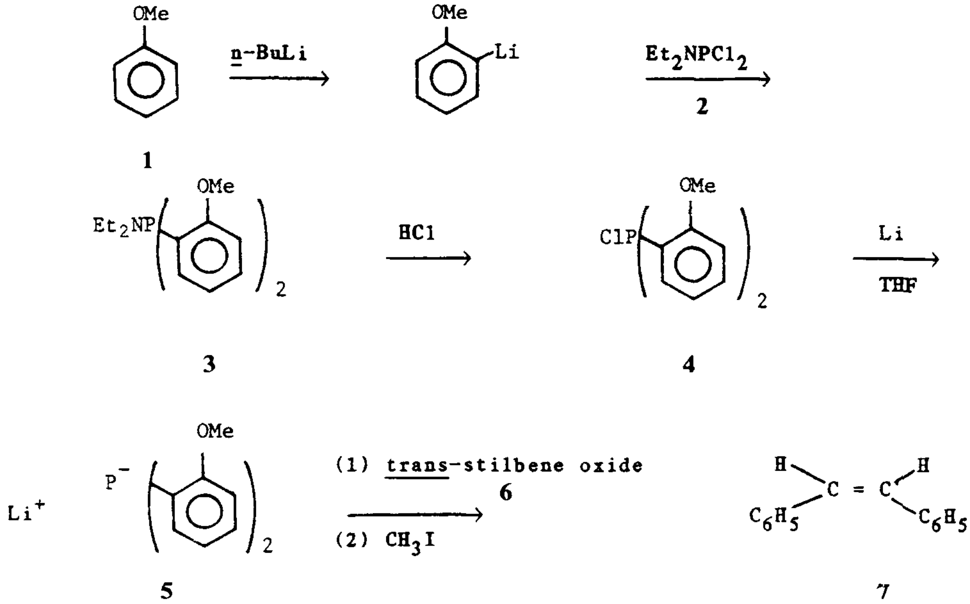
There is general agreement that the Wittig reaction proceeds by not less than two distinct steps; formation of an oxaphosphetane (or a mixture of diasteriomeric oxaphosphetanes), and decomposition of this intermediate to give an alkene (or alkenes) and a phosphine oxide.[1-4] Also, it is well known that Wittig reactions carried out in the presence of lithium ion can give markedly different stereochemical results from those carried out in the presence of sodium or potassium ion, or under salt-free conditions.[5-8] With these facts in mind, we decided to expand our previous investigations of the role of through space 2*p*–3*d* overlap effects in the Wittig reaction.[9,10]

Evidence in support of the through space 2*p*–3*d* overlap effect based on kinetics and spectroscopic studies has been published elsewhere and need not be repeated here.[11-19] Most of these studies have been carried out on compounds having one or more *o*-methoxyphenyl groups bonded to phosphorus, but other neighboring groups have also been investigated. The work of McEwen and Lau[19] is particularly significant with respect to the present studies, because it provides evidence for the preferred geometry of the through space 2*p*–3*d* overlap effect.

RESULTS AND DISCUSSION

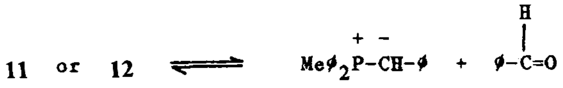
Since Vedejs and Fuchs have demonstrated that the reaction of lithium diphenylphosphide with *trans*-stilbene oxide in tetrahydrofuran at room temperature, with subsequent addition of methyl iodide, affords a high yield of pure *cis*-stilbene,[20] we decided to investigate a possible through space $2p$–$3d$ overlap effect in this type of decomposition of an oxaphosphetane to an alkene plus phosphine oxide. Of course, we repeated the experiment of Vedejs and Fuchs, and we obtained *cis*-stilbene in greater than 99% purity (in 85% yield), in complete agreement with the literature report.

The preparation of lithium *bis*-(*o*-methoxyphenyl)phosphide (**5**) required several steps. Treatment of anisole (**1**) with *n*-butyllithium, with subsequent addition of *N*,*N*-diethylaminodichlorophosphine (**2**), afforded *N*,*N*-diethylamino-*bis*-(*o*-methoxyphenyl)phosphine (**3**) in 50% yield. Passage of dry hydrogen chloride through a refluxing diethyl ether solution of **3** gave a precipitate of diethylammonium chloride (80% yield). The filtrate was concentrated to dryness to give the crude *bis*-(*o*-methoxyphenyl)chlorophosphine (**4**), which was dissolved in tetrahydrofuran and treated with lithium to give a solution of **5**. Reaction of **5** with *trans*-stilbene oxide (**6**) with subsequent addition of methyl iodide and a suitable workup procedure, gave *cis*-stilbene (**7**) in greater than 99% purity and in 61% yield (based on **3**).



We next attempted the reaction of potassium diphenylphosphide (**8**) with *trans*-stilbene oxide (**6**), with subsequent addition of methyl iodide and appropriate workup, but it soon became apparent that this sequence of reactions was a troublesome one. In every reaction attempted, a mixture of *cis*-stilbene (**7**) and *trans*-stilbene (**15**) was obtained, but the *cis* : *trans* ratio varied from 45 : 55 to 2 : 98. Also, the yields of stilbenes varied from 17% to 45%. Clearly, other products were also formed in these reactions, and some conceivable ones, such as β-oxidoylides or the conjugate base of benzyldiphenylphosphine (plus benzaldehyde) could cause formation of *trans*-stilbene as well as *cis*-stilbene. Thus, an alternative method was utilized to generate the oxaphosphetane (**11**, Figure 1) in the presence of potassium ion. *Erythro*(2-hydroxy-1,2-diphenylethyl)methyldiphenylphosphonium iodide was synthesized[29] and treated with potassium hydride in tetrahydrofuran solution at both −78°C and at room temperature. In both experiments, only *cis*-stilbene was isolated (in 80% yield). Thus, no evidence for either the through space $2p$–$3d$ overlap effect or for the Bestmann mechanism (formation of an equilibrating mixture of **13** and **14** with formation of both *cis*-stilbene, **7**, and *trans*-stilbene, **8**) was apparent from these experiments. Although McEwen and Cooney[9] had observed such an effect (enhancement of the ratio of *trans* to *cis* alkene formed) in the reaction of an unstable ylide having a 2,6-dimethoxyphenyl group bonded to phosphorus with aromatic aldehydes, as against the case with a phenyl group bonded to phosphorus in place of the 2,6-dimethoxyphenyl group, there are three major differences between the two systems. The 2,6-dimethoxyphenyl group is more effective than two *o*-methoxyphenyl groups in promoting through space $2p$–$3d$ overlap effects,[11–19] unstable ylides behave differently from semi-stable ylides in Wittig reactions, and an alkyldiarylphosphonio moiety has distinctly different electronic properties from a triarylphosphonio moiety.[21] Consequently, no meaningful comparison can be made between the results observed by McEwen and Cooney[9] and those reported in the present study.

Another important consideration for any Wittig reaction is the possibility of dissociation of the intermediate oxaphosphetane to aldehyde plus ylide. As will be described later, the reaction of the ylide **16** with benzaldehyde in the presence of



$$\mathbf{11}\ \text{or}\ \mathbf{12} \rightleftharpoons \mathrm{Me}\phi_2\overset{+}{\mathrm{P}}\text{–}\overset{-}{\mathrm{C}}\mathrm{H}\text{–}\phi + \phi\text{–}\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}\text{=O}$$

16

lithium ion gives both *cis*- and *trans*-stilbene. Thus, the fact that no *trans*-stilbene is formed in the reaction of either lithium diphenylphosphide or lithium *bis*-(*o*-methoxyphenyl)phosphide (**5**) with *trans*-stilbene oxide (**6**) is compelling evidence that the respective oxaphosphetanes formed in these reactions do not dissociate to ylide plus benzaldehyde. We nevertheless decided to confirm this conclusion by attempting a crossover reaction. The reaction mixture resulting from the addition of one equivalent of *trans*-stilbene oxide (**6**) to a solution of lithium diphenylphosphide in tetrahydrofuran was chilled to −78°C. After addition of a solution of methyl iodide and *m*-chlorobenzaldehyde in tetrahydrofuran, the mixture was allowed to warm to room temperature and then subjected to the standard workup procedure. Only *cis*-stilbene was detected, to the complete exclusion of any *m*-chlorostilbene. The same held true for the reactions carried out in the presence of potassium ion rather than lithium ion. Although several groups have devoted much attention to the question of whether such dissociation influences the regioselectivity of alkene formation in Wittig reactions.[1,3,5,22] it is clear that there is no such effect operative in the reactions described above.

We next turned our attention to Wittig reactions of benzylidenediphenylmethylphosphorane (**16**) and benzylidene-*bis*-(*o*-methoxyphenyl)methylphosphorane (**17**), respectively, with benzaldehyde and trimethylacetaldehyde, respectively. The results

25

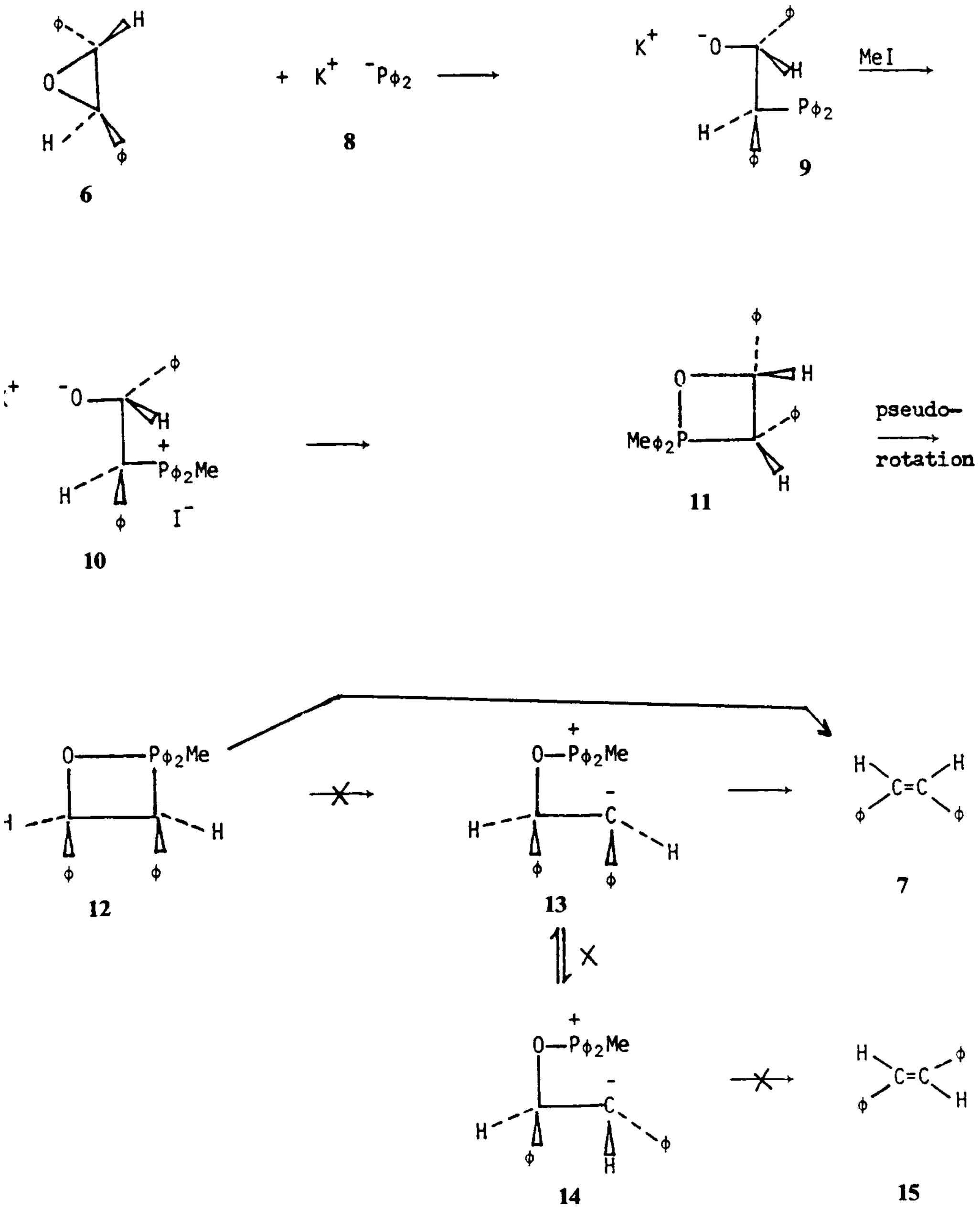


FIGURE 1 Reaction of *trans*-stilbene oxide with potassium diphenylphosphide.

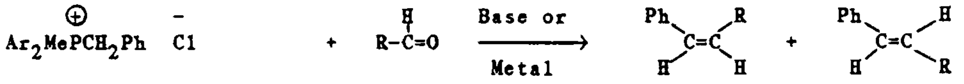
are summarized in Table I, and it is apparent that both the *cis*-alkene and the *trans*-alkene are formed in each reaction. Based on the results of the reactions of the lithium diarylphosphides with *trans*-stilbene oxide, we can conclude that the observed stereoselectivity of alkene formation in the reactions carried out in tetrahydrofuran with lithium ion present must be determined prior to or at the time of oxaphosphetane formation. Specifically, this statement refers to reactions 3, 4, 7, 8, 9, and 11 of Table I. The most striking general observation for these particular reactions is that the presence of the *o*-methoxyphenyl groups in ylide **17** brings about an increase in *cis*-alkene stereoselectivity as against the case of the unsubstituted ylide. Since Allen[23,24] has demonstrated that, with tetrahydrofuran as solvent and with lithium ion present, an increase in steric requirements about phosphorus in semistabilized ylides causes a decrease in *cis*-alkene stereoselectivity in reactions with aldehydes, our results indicate the operation of a specific interaction when *o*-methoxyphenyl groups are bonded to phosphorus. We assume that this specific interaction involves a through space $2p$–$3d$ overlap effect.

The only Wittig reaction mechanism currently extant that places emphasis on the presence of lithium salts in solution is that of Schlosser.[5] In this mechanism, the observed stereoselectivity of alkene formation is postulated to be determined by the ratio of rates for initial betaine formation and the rates of formation of alkenes, presumably *via* oxaphosphetane intermediates. Regardless of its intrinsic merits, this interpretation does not accommodate the results of the Wittig reactions described herein, because it does not take cognizance of through space $2p$–$3d$ overlap effects and also the demonstration of the absence of reversion of oxaphosphetane to ylide plus aldehyde. Also, utilization of any of the current mechanisms for salt free Wittig reactions[1–4] would be inadequate since the effects of lithium ion are known to be profound.

Since the mechanism which we are about to propose utilizes the effects of through space $2p$–$3d$ overlap (as well as effects of lithium salts), it was first deemed

TABLE I

Wittig reactions of **26** and **27** with aldehydes in tetrahydrofuran



26, Ar = *o*-methoxyphenyl
27, Ar = phenyl

Exp.	Phosphonium chloride	Aldehyde	Base or metal	Reaction temperature, °C	Alkenes[a] *cis* : *trans*
1	**27**	PhCHO	K	−78	30 : 70
2	**26**	PhCHO	K	−78	17 : 83
3	**27**	PhCHO	BuLi	−78	65 : 35
4	**26**	PhCHO	BuLi	−78	87 : 13
5	**26**	PhCHO	BuMgCl	−78	42 : 58
6	**26**	PhCHO	NaH	25	49 : 51
7	**26**	PhCHO	BuLi	25	70 : 30
8	**27**	PhCHO	BuLi	25	47 : 53
9	**26**	Me_3CCHO	BuLi	−78	82 : 18
10	**26**	Me_3CCHO	BuLi	25	70 : 30
11	**27**	Me_3CCHO	BuLi	−78	58 : 42

[a] Yields for the reactions in which BuLi was used as base where 50–67%; reproducibility of results, ±3%.

necessary to provide evidence that such overlap effects are operative in the specific phosphonium salt, benzyl-*bis*-(*o*-methoxyphenyl)methylphosphonium chloride (**26**), the precursor of **17**. Proton NMR spectra have been used previously as a probe of the through space 2*p*–3*d* overlap effect.[11–19] If the overlap effect is operative, the methyl and benzylic protons in **26** should exhibit a pronounced upfield chemical shift from the corresponding protons in benzyldiphenylmethylphosphonium chloride (**27**). These anticipated effects are highly visible in the NMR spectra, as revealed in Table II.

Next, a model for the geometry of the through space 2*p*–3*d* overlap effect in the ylide **17** was needed. McEwen and Lau[19] have previously provided a model for the transition state of the S_N2 reaction of a tertiary phosphine having a 2,6-dimethoxyphenyl group bonded to phosphorus with an alkyl halide, and it does not require much perturbation to transform that model into one suitable for the ylide **17**. The ylide is depicted with the phosphorus tetrahedral, but with a small degree of distortion in the direction of formation of an octahedral configuration. In the quasi octahedral configuration, the benzylidene carbanionic carbon, the methyl carbon, the carbon which is bonded to phosphorus in the lower ring and the oxygen of the methoxyl group belonging to the upper ring constitute the incipient equatorial plane, while the oxygen of the methoxyl group belonging to the lower ring and the carbon which is bonded to phosphorus in the upper ring constitute the apical positions. This model indicates a statistical rigidity for the ylide **17**; i.e., most of the ylide molecules have the conformation depicted in **17**. It can also be assumed that the ylide **17** will exhibit a high degree of carbanionic character at the benzylic carbon, because the through space 2*p*–3*d* overlap effects of the *o*-methoxyphenyl groups will bring about a decrease in the double bond character between the benzylic carbon and phosphorus.

It would also seem to be reasonable to assume that lithium ion functions as a Lewis acid catalyst in the reaction of **17** with benzaldehyde. The lithium ion would be expected to bond to the oxygen atom of the benzaldehyde and therefore increase the electrophilic reactivity of the carbonyl carbon atom, as shown in **18**.

Owing to the presence in the reaction mixture of a stronger than usual nucleophilic center in the Wittig reagent, **17**, and a stronger than usual electrophilic center in the benzaldehyde-lithium ion adduct, **18**, this combination of reagents, more than most found in Wittig reactions, would be expected to undergo an initial formation of a new C,C bond. For steric reasons, the major adduct would have the geometry depicted in structure **19** (only one enantiomer shown). Looking down the new C,C

TABLE II

^{1}H NMR absorption data taken in $CDCl_2$ solution

Phosphonium cation	Anion	δ ppm CH_2 d (J_{PH} = 16–17 Hz)	δ ppm CH_3 d (J_{PH} = 13–14 Hz)
benzylmethyldiphenyl	chloride	4.98	2.78
bis-(*o*-anisyl)benzylmethyl	chloride	4.64	2.45
dimethyldiphenyl	iodide	—	2.67
bis-(*o*-anisyl)dimethyl	iodide	—	2.49

bond, we see that the two largest groups on the respective carbon atoms, phenyl and the phosphorus moiety, are anti. The phenyl groups on the respective carbon atoms are gauche with respect to each other, and they are also as far as possible removed from the other groups bonded to phosphorus. This is particularly apparent when models are examined.[25,26]

In order for the oxaphosphetane **22** to be formed, it is necessary for the lithium ion to be transferred from the original aldehyde oxygen to a methoxy group (or elsewhere), with subsequent rotation of an *o*-methoxyphenyl group in order to make an apical position of a new, incipient trigonal bipyramidal oxaphosphetane open to attack by the original aldehyde oxygen atom. Also, rotation about the newly formed C,C bond must occur in order to place the original aldehyde oxygen in a position to close the oxaphosphetane ring. These changes are shown in structures **19**–**21**.

In a departure from other postulated mechanisms of the Wittig reaction,[1-5] we suggest that a lithium ion, functioning as a Lewis acid, might be capable of catalyzing the decomposition of the oxaphosphetane to products. This is shown in the latter part of Figure 2. Coordination of the lithium ion with a lone pair on the oxygen of the Z-oxaphosphetane **22** yields the complex **23**. Pseudorotation gives **24** in which the benzylic moiety which eventually departs occupies an apical position. Owing to the formal positive charge on oxygen, a transition state of the polarity shown in **25** is formed and leads to the products of the decomposition. That a transition state, **25**, is formed rather than a carbocationic intermediate is required by the regiospecificity of the reaction. An unstable carbocation intermediate would be expected to undergo rotation about the carbon–carbon bond in competition with decomposition to give *cis*-stilbene and phosphine oxide. As in the Bestmann[2] mechanism where a carbanionic unstable intermediate is thought to be formed (i.e., when semistable or stable ylides are used in the Wittig reaction), the new carbocation would give rise to *trans*-stilbene plus phosphine oxide. Also, the transition state **25** would not be responsive to the presence of groups bonded to phosphorus which in other situations are able to enter into a through space $2p$–$3d$ interaction. Thus, the reaction of **5** with **6** gives *cis*-stilbene in a regiospecific manner.

This mechanism, with **25** considered to be a transition state rather than an intermediate, is not necessarily inconsistent with the mechanistic suggestions of Vedejs[1] and Schlosser.[4] The sequence **24** → **25** → **7** could be considered to be a lithium ion catalyzed concerted, but not synchronous, process. Also, essentially the same mechanism could occur with potassium ion, rather than lithium ion, present. However, since potassium ion does not function as a Lewis acid, the rate for an analogous pathway with potassium as a spectator cation would be slower than in the lithium ion catalyzed reaction. This, in turn, might account for the lower yields of stilbenes in the reactions with potassium ion present; as mentioned previously for the potassium diphenylphosphide sequence, undesired side reactions could intervene and have an effect on the regioselectivity of alkene formation.

The results of the conversions shown in Figure 2, with the departing carbon in an apical position and cleavage of the oxaphosphetane by a lithium ion-catalyzed process, as described previously, gives *cis*-stilbene as the major alkene. Also, if the phosphorus had been chiral, the sequence of apical attack by the original aldehyde oxygen, pseudorotation, and apical departure of a benzylic carbon would have led to retention of the configuration of the phosphorus atom. This is in accord with existing data on the stereochemistry of the Wittig reaction at phosphorus.[27,28]

26

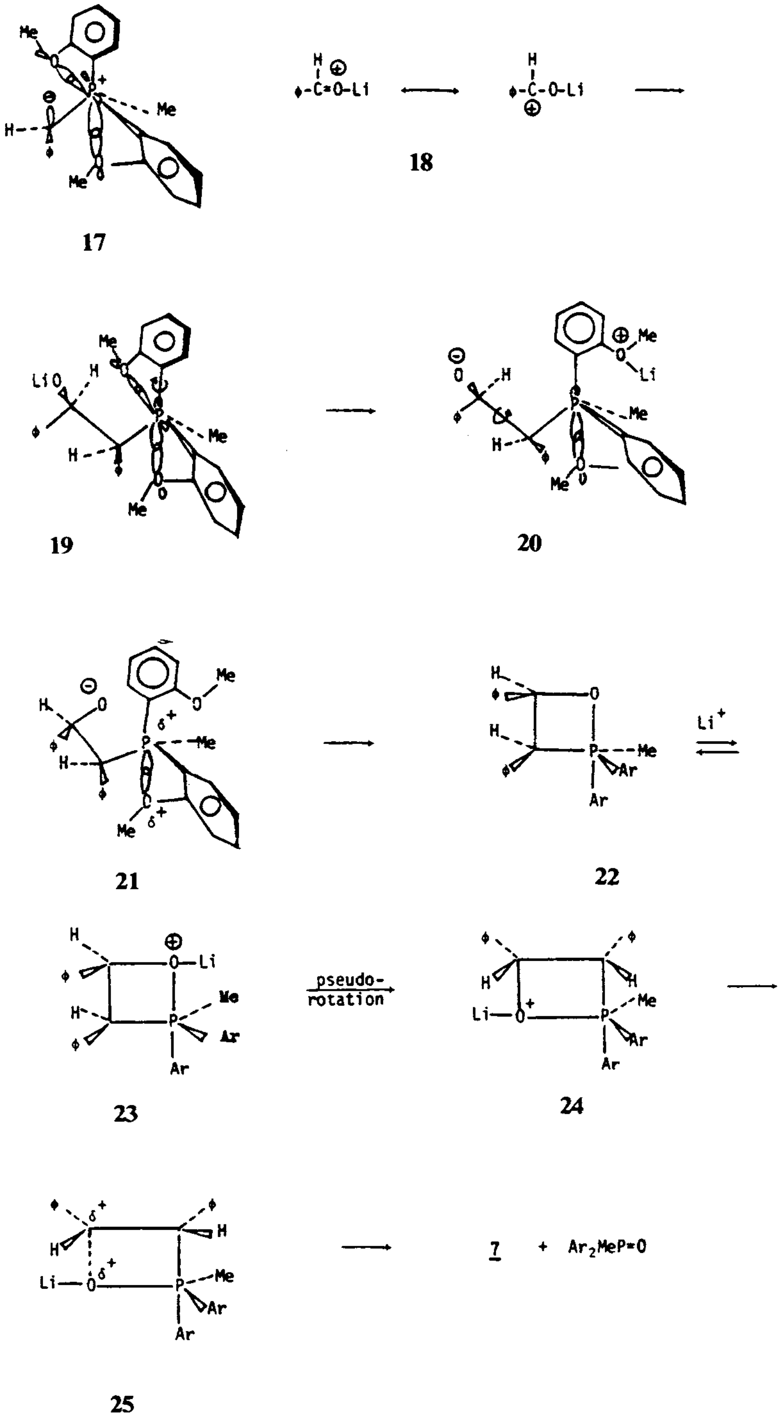


FIGURE 2 Lithium ion catalyzed Wittig reaction of **17** with benzaldehyde.

EXPERIMENTAL

General Procedures. All newly obtained melting points are uncorrected, and were taken in open capillary tubes using a Mel-Temp melting point apparatus. Infrared spectra were recorded on Beckman IR-10 and Perkin-Elmer 727 infrared spectrophotometers. ^{1}H NMR spectra were recorded on a Varian A-60 instrument. Vapor phase chromatography was conducted with a Varian Aerograph Series 2440-10 gas chromatograph. Elemental analyses were performed by the Microanalysis Laboratory of the University of Massachusetts, Amherst.

Thin layer chromatography was conducted on pre-coated silica gel plates (with fluorescent indicator), Eastman Chromagram Sheet no. 13181. Silica gel used for column and flash chromatography was 100–200 mesh, Fisher reagent grade. In those instances where "10%-deactivated" silica gel is specified, the deactivation was achieved by thoroughly mixing fresh (from a new bottle) silica gel with an amount of water equal to one-tenth the mass of the silica gel.

Solvents were dried by standard procedures. Thus, benzene, toluene, and hexane were distilled from calcium hydride. Ethyl ether and tetrahydrofuran were distilled from sodium benzophenone ketyl. Dimethyl formamide was distilled at reduced pressure from anhydrous barium oxide, and was stored over fresh molecular sieves. *N,N*-diethylaminodichlorophosphine (**2**) and dichloromethylphosphine were obtained from Aldrich Chemical Company and were used without purification.

In all experiments that employ air sensitive intermediates, the reaction system was placed under an inert atmosphere prior to the introduction of any reagents or solvents.

Preparation of N,N-Diethylamino-bis-(o-methoxyphenyl)phosphine (**3**). Into a three-neck, 500 mL round bottom flask equipped with a magnetic stirring bar, reflux condenser and pressure equalized addition funnel was added 32 ML (0.14 mole) of anisole, 44 mL (0.14 mole) of *N,N,N′,N′*-tetramethylethylenediamine and 50 mL of hexane, an argon atmosphere being maintained. The reaction vessel was chilled in an ice bath and 130 mL (2.3 *M*, 0.14 mole) of *n*-butyllithium in hexane was slowly added. The reaction mixture was stirred for 19 hours at room temperature. To the resulting thick, pale yellow precipitate was added a solution of 25 mL (0.14 mole) of *N,N*-diethylaminodichlorophosphine (**2**) in 30 mL of hexane. The reaction mixture was stirred for 20 hours at room temperature. The resulting brown solution contained a small amount of brown precipitate which dissolved when the mixture was poured into 100 mL of water. The organic layer was separated from the aqueous layer, and the latter was washed with 100 mL of methylene chloride. The combined organic layer was dried over anhydrous magnesium sulfate, filtered and then concentrated with the aid of a rotary evaporator. When the residue was allowed to stand, 11.5 g (50%) of the aminophosphine **3** was obtained. Recrystallization from hexane gave white, powdery crystals, mp 76–78°C; NMR ($CDCl_3$), $\delta = 0.95$ (t, 6 H, 6 Hz), 2.80–3.30 (m, 4 H), 3.70 (s, 6 H), 6.70–7.50 (m, 8 H). Anal. Calcd. for $C_{18}H_{24}NO_2P$: C = 68.12, H = 7.62, N = 4.41, P = 9.76. Found: C = 67.91, H = 7.86, N = 4.66, P = 9.76.

Preparation of Benzylmethyldiphenylphosphonium Chloride. Into a 250 mL round bottom flask equipped with a reflux condenser and magnetic stirring bar was added 25 mL (0.13 mole) of methyldiphenylphosphine. A solution of 14.30 mL (0.13 mole) of benzyl chloride in 75 mL of benzene was added, and the resulting solution was heated at reflux for 6 hours. The resulting reaction mixture was chilled in an ice-water bath, and the phosphonium salt was collected in quantitative yield by suction filtration as a fine white powder, mp 243–244°C; NMR ($CDCl_3$), δ 2.78 (d, 3 H, 14 Hz), 4.98 (bd, 2 H, 16 Hz), 7.10–8.12 (m, 15 H). Anal. Calcd. for $C_{20}H_{20}PCl$: C = 73.54, H = 6.12, P = 9.48, Cl = 10.86. Found: C = 73.34, H = 6.24, P = 9.24, Cl = 10.75.

Preparation of Methyl-bis-(o-methoxyphenyl)phosphine. Into a 500 mL round bottom flask, equipped with a reflux condenser, a pressure equalized addition funnel and a magnetic stirring bar, was added 155 mL (0.21 mole) of *n*-butyllithium (2.7 M in hexane), an argon atmosphere being maintained. The round bottom flask was chilled in an ice-water bath, and 63 mL (0.42 mole) of freshly distilled tetramethylethylenediamine (TMEDA) was added. A solution of 50 mL (0.42 mole) of anisole in 10 mL of hexane was added dropwise to the rapidly stirred, cooled, *n*-butyllithium/TMEDA/hexane solution. The resulting mixture contained a large amount of yellow precipitate, and was stirred at room temperature for 40 hours. The resulting brown mixture contained a large amount of yellow precipitate. This reaction mixture was chilled in an ice-water bath, and a solution of 25 mL (0.11 mole) dichloromethylphosphine in 25 mL of THF was added dropwise, an argon atmosphere being maintained. A large amount of beige-colored precipitate formed, and the resulting mixture was stirred at room temperature for 5 hours. The resulting reaction mass was poured into 75 mL of saturated ammonium chloride solution, and the beige-colored solid was collected by suction filtration. Recrystallization from 95% ethanol yielded 27.5 g (55%) of the phosphine as white needles, mp 126–127°C (lit. mp 126–127°C)[30]; NMR ($CDCl_3$), δ 1.59 (d, 3 H, 5 Hz), 3.80 (s, 6 H), 6,75–7.40 (m, 8 H).

Preparation of Benzylmethyl-bis-(o-methoxyphenyl)phosphonium Chloride (**26**). Into a 250 mL round bottom flask equipped with a reflux condenser and magnetic stirring bar was added 10.0 g (38 mmoles) of methyl-*bis*-(*o*-methoxyphenyl)phosphine and 100 mL of benzene, an argon atmosphere being maintained. A solution of 4.3 mL (38 mmoles) of benzyl chloride in 10 mL of benzene was added, and the resulting solution was heated at reflux for 3 hours. The resulting reaction mixture was chilled in an ice-water bath, and the fine white powdery precipitate was collected by suction filtration, yielding 9.1 g (62%) of analytically pure phosphonium salt, mp 220–224°C; IR ($CDCl_3$): 1280 cm^{-1} ($P - CH_3$); NMR ($CDCl_3$), δ 2.45 (d, 3 H, 13 Hz), 3.79 (s, 3 H), 4.64 (bd, 2 H, 17 Hz), 6.95–7.85 (m, 8 H). Anal. Calcd. for $C_{22}H_{24}O_2PCl$: C = 68.33, H = 6.21, P = 8.01, Cl = 9.17. Found: C = 68.27, H = 6.22, Cl = 9.13, P = 7.75.

Reaction of Lithium Diphenylphosphide with trans-Stilbene Oxide, with Subsequent Addition of Methyl Iodide. The procedure of Vedejs and Fuchs[20] was followed, and the literature results were reproduced.

Reaction of Lithium Diphenylphosphide with trans-Stilbene Oxide, with Subsequent Addition of Methyl Iodide and 3-Chlorobenzaldehyde. Into an argon charged 100 mL round bottom flask equipped with a magnetic stirring bar and an addition funnel was added a solution of 0.85 mL (4.75×10^{-3} mole) of chlorodiphenylphosphine in 20 mL of THF. To this clear solution was added 0.06 g (9.50×10^{-3} mole) of lithium foil. After the reaction mixture had been stirred for 2.5 hours at room temperature, all of the lithium metal had reacted, and the remaining solution was a homogeneous deep red color. With an argon atmosphere being maintained over the phosphide solution, 0.93 g (4.75×10^{-3} mole) of *trans*-stilbene oxide was added. The resulting yellow solution was stirred at room temperature for 13 hours. The reaction flask was chilled in an ice-water bath, and a solution of 0.60 mL (9.50×10^{-3} mole) of methyl iodide and 0.53 mL (4.75×10^{-3} mole) of 3-chlorobenzaldehyde in 5 mL of tetrahydofuran was added dropwise. The resulting yellow solution containing a tan-colored precipitate was allowed to stir at room temperature for 2 hours. The reaction mixture was poured into a beaker, and the solvent was allowed to evaporate. The remaining crude oil was dissolved in methylene chloride, washed with water, than dried over anhydrous magnesium sulfate, filtered, and the methylene chloride solution concentrated on a rotary evaporator, yielding a golden brown oil. This oil was subjected to wet column chromatography on silica gel (60–200 mesh, 10% deactivated) with pentane as eluant. The first fraction contained pure *cis*-stilbene, identified by GC analysis and its IR spectrum. No *trans*-stilbene or *m*-chlorostilbenes were detected.

The Reaction of bis-(o-Methoxyphenyl)chlorophosphine (**4**) *with Lithium Metal, with Subsequent Addition of trans-Stilbene Oxide and Methyl Iodide.* Into an argon charged 250 mL three neck round bottom flask equipped with a magnetic stirring bar, gas dispersion tube and reflux condenser was added 1.0 g (3.4 mmole) of *N,N*-diethylamino-*bis*-(*o*-methoxyphenyl)phosphine (**3**) and 75 mL of diethyl ether. This solution was heated to reflux and dry HCl gas was passed through until no more precipitate formed (approximately 10 minutes). (Sometimes this precipitate would redissolve). This reaction mixture was heated at reflux for 10 hours. The precipitated diethylammonium chloride (mp 215–223°C)[31] was removed by filtration *in vacuo*. The ether mother liquor was concentrated *in vacuo* to yield the crude *bis*-(*o*-methoxyphenyl)chlorophosphine (**4**) as a white solid. The crude chlorophosphine was dissolved in 25 mL of THF and transferred with a cannula into an argon charged 100 mL three neck round bottom flask equipped with a magnetic stirring bar and pressure equalized addition funnel. To the clear THF solution was added an excess of lithium foil, and this mixture was then vigorously stirred until the deep red phosphide color was obtained. The excess lithium metal was removed, and 0.61 g (3.4 mmole) of *trans*-stilbene oxide (**6**) was added. The characteristic deep red color of the phosphide discharged to a honey brown color over 4.5 hours. A solution of 0.40 mL (6 mmoles) of methyl iodide in 5 mL of THF was added dropwise. A tan-colored precipitate immediately formed, and this mixture was stirred at room temperature for one hour. The reaction mixture was poured into 50 mL of water, and the resulting THF/H_2O solution was extracted with (2×75 mL) portions of methylene chloride. The combined organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated to dryness with the aid of a rotary evaporator. The resulting oil was subjected to wet column chromatography on silica gel (60–200 mesh, 10% deactivated) with pentane as eluant. The first fraction was the stilbene fraction. Gas chromatographic analysis indicated only one peak (*cis*-stilbene) in a yield of 0.11 g (61%) (*trans*-2-octene int. std.). The peak increased upon injection of a sample that had been spiked with authentic *cis*-stilbene. The IR spectrum of the reaction product proved to be identical to the IR spectrum of authentic *cis*-stilbene.

Reaction of Potassium Diphenylphosphide (**8**) *with trans-Stilbene Oxide* (**6**), *with Subsequent Addition of Methyl Iodide.* Into an argon charged 100 mL two neck round bottom flask equipped with a magnetic stirring bar and a pressure equalized addition funnel was added 20 mL of THF and 0.33 g (8.46 mmoles) of potassium metal. A solution of 0.76 mL (4.23 mmoles) of chlorodiphenylphosphine in 5 mL of THF was added dropwise. This clear reaction mixture was heated at reflux for 2.5 hours. The resulting turbid orange-red solution was allowed to cool to room temperature and then 0.82 g (4.23 mmoles) of *trans*-stilbene oxide (**6**) was added while an argon atmosphere was maintained over the reaction solution. The resulting turbid pale yellow solution was stirred for 3.75 hours, and then a solution of 0.54 mL (8.46 mmoles) of methyl iodide in 10 mL of THF was added dropwise. After having been stirred for 13 hours at room temperature, the reaction mixture contained a large amount of tan-colored precipitate. The THF was removed by use of a rotary evaporator, and the yellow brown oily solid residue was dissolved in 50 mL of methylene chloride and washed with 50 mL of water. The organic layer was then dried over anhydrous magnesium sulfate, filtered, and the methylene chloride removed with the aid of a rotary evaporator. The resulting yellow–brown oil was subjected to wet column chromatography on silica gel (60–200 mesh, 10% deactivated) with pentane as eluant. The first fraction would typically contain a mixture of *cis*- and *trans*-stilbene, in varying ratios. The olefin ratio was determined by gas chromatographic analysis (see previous experimental), with the IR spectrum of the mixture of stilbenes being identical with the IR spectrum of an authentic mixture of stilbenes of the appropriate ratio.

Preparation of Erythro-(2-Hydroxy-1,2-diphenylethyl)methyldiphenylphosphonium Iodide. The procedure of Jones and Trippett[29] was used, and the product had mp 222–224°, as reported.

Reaction of Erythro-(2-Hydroxy-1,2-diphenylethyl)methyldiphenylphosphonium Iodide with Potassium Hydride. A suspension of 1.12 g (2.13×10^{-3} mole) of the phosphonium iodide in 30 mL of THF was chilled to −78°C while an argon atmosphere was maintained throughout this and subsequent operations. To this mixture was added 0.50 g of potassium hydride (Aldrich 35% by weight dispersion in oil, 2 equivalents). Hydrogen was evolved. After having been stirred at −78°C for 20 min, the reaction mixture was allowed to warm to room temperature during a one hour period. Some solid products which had formed were allowed to settle, and an aliquot of the supernatant solution was removed for GC and GC/MS analyses. An 80% yield of at least 99% pure *cis*-stilbene was realized by GC analysis. The GC/MS analysis indicated the presence of only *cis*-stilbene and methyldiphenylphosphine oxide. The same results were obtained when the entire sequence of reactions was carried out at room temperature. When *m*-chlorobenzaldehyde was added to the mixture after completion of the reaction of potassium hydride with the phosphonium iodide at −78°C, and then the remainder of the reaction and workup conducted as above, only *cis*-stilbene and methyldiphenylphosphine oxide were found; no *m*-chlorostilbene was present in the reaction mixture. The same results were obtained when all of the procedures were carried out at room temperature. The correlation of peak area with structure in each experiment was based on mass spectral examination of the component responsible for each peak and by spiking the mixture with authentic stilbene samples.

Capillary GC conditions: Column—50 m × 0.20 mm, 0V-1 (Hewlett-Packard) Fused Silica Capillary; Split ratio—60 : 1; Injector temperature—230°C; Temperature program—200°C (4 m hold) −4°C/m–240°C (16 m hold); Solvent—Spectral grade chloroform; Sample size—0.50 μ; Column head pressure—25 PSI He; Column flow—0.75 mL/sec; Make-up gas provided to give total flow of 40 mL/sec at FID detector; FID = H_2 = 20 PSI; Breathing air = 50 PSI. The GC analysis was performed on a Perkin-Elmer Model 3920B Gas Chromatograph Instrument.

Typical Wittig Reaction Between Appropriate Phosphonium Salts and Benzaldehyde in the Presence of Lithium Chloride. To a suspension of 0.33 g (1 mmole) of the phosphonium chloride in 15 mL of anhydrous THF was added dropwise a solution of 0.40 mL (1 mmole) of *n*-butyllithium (2.7 M/hexane) in 5 mL of THF. The resulting homogeneous orange-red solution was allowed to stir at room temperature for 0.5 hours, an argon atmosphere being maintained. The ylide solution was chilled to −78°C in a dry ice/acetone bath, and a solution of 0.10 mL (1 mmole) of benzaldehyde in 5 mL of THF was added dropwise. The orange-red color discharged upon addition of the benzaldehyde solution, and, after the reaction mixture had warmed to room temperature over a 10 hour period, a fine tan precipitate was present. This reaction mixture was poured into 50 mL H_2O and extracted with (2 × 75 mL) portions of methylene chloride. The combined organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated to dryness with a rotary evaporator. The resulting golden brown oil was extracted with a large volume of hot pentane. The pentane solution of the stilbenes was passed through a short silica gel plug and was then concentrated to dryness by simple distillation. The stilbene *cis* : *trans* ratios and yield were determined by gas chromatographic analysis. (See Table I for yield and *cis* : *trans* ratio). Each GC peak increased in area upon spiking with authentic stilbene samples. The IR spectrum of the stilbene mixture proved to be identical to the IR spectrum of an authentic sample of *cis* : *trans* stilbenes.

Reactions with trimethylacetaldehyde were carried out in the same manner; analyses of product ratios were based on NMR integrations.

Wittig Reaction Between Appropriate Phosphonium Salt and Benzaldehyde in the Presence of Potassium Chloride. To a suspension of 0.33 g (1 mmole) of phosphonium chloride in 15 mL of anhydrous THF was added a chunk of potassium metal. After 1.5 hours of stirring at room temperature, the excess potassium was removed, and the resulting homogeneous, deep red solution was chilled to −78°C. A solution of 0.1 mL (1 mmole) of benzaldehyde in 5 mL of THF was added dropwise. The deep red color slowly discharged to a turbid light yellow as the aldehyde solution was added at −78°C. The dry ice/acetone bath was removed, and the reaction mixture was allowed to warm to room temperature over 13 hours. The resulting reaction mixture contained a large amount of white precipitate which dissolved upon pouring the reaction mixture into 50 mL of water. The THF/water solution was extracted with (3 × 50 mL) portions of methylene chloride. The organic layer was dried over anhydrous magnesium sulfate, filtered and then evaporated by use of a rotary evaporator to yield a golden brown oil. This oil was repeatedly washed with hot pentane, with the pentane solution then being passed through a short silica gel plug. The combined pentane washings (approximately 1000 mL) was concentrated by simple distillation. The last 50 mL of pentane was removed by heating the distillation flask over a steam bath to yield the stilbenes as a clear oil. Gas chromatographic analysis indicated that the product consisted of stilbenes (11–33% yields, *trans*-2-octene internal standard), in the ratios given in Table I. Each peak increased in area upon spiking with authentic stilbene samples. The IR spectrum of the stilbene mixture proved to be identical to the IR spectrum of an authentic sample of mixed stilbenes.

Typical Wittig Reaction Between Phosphonium Salt and Benzaldehyde at −78°C in the Presence of Lithium Chloride with Subsequent Addition of 3-Chlorobenzaldehyde. This reaction was carried out as described previously, with the exception that 3.1 mmole of 3-chlorobenzaldehyde was added to the reaction mixture at −78°C after the color had been discharged by the reaction of the ylide with benzaldehyde. The remainder of the reaction and workup were the same as before.

Gas chromatographic analysis (see previous experimental for details) revealed the presence of only *cis* and *trans*-stilbene. See Table I for the specific ratios.

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