Role of the Through-Space 2p-3d Overlap Effect in the Wittig Reaction

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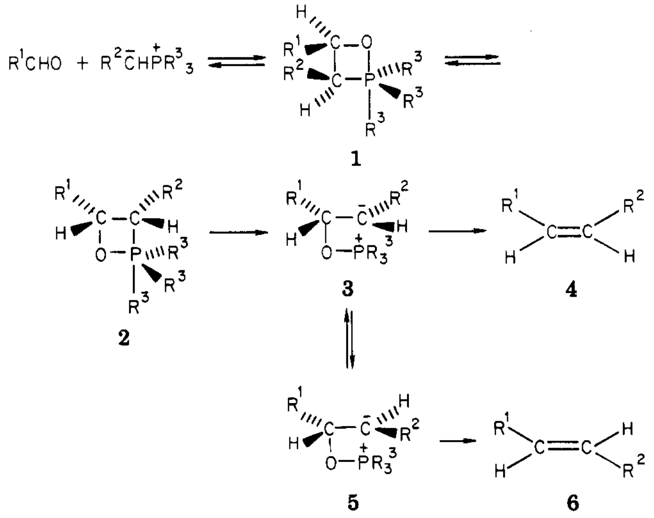
Received July 26, 1982

Reactions of the ylide derived from triphenyl(3-phthalimidopropyl)phosphonium bromide with aromatic aldehydes have been reported to give exclusively the *Z* alkenes. On the basis of the Bestmann mechanism for the Wittig reaction, and also because of the fact that a 2,6-dimethoxyphenyl group enters into a strong through-space 2p–3d overlap interaction with an adjacent phosphonio group, we postulated that the reactions of the ylide derived from (2,6-dimethoxyphenyl)diphenyl(3-phthalimidopropyl)phosphonium bromide with aromatic aldehydes would give substantial ratios of *E*:*Z* alkenes. This proved to be the case.

Ylides derived from alkyltriphenylphosphonium halides are classified "unstable" and undergo the Wittig reaction with most aldehydes and ketones. Where applicable, the alkenes produced generally contain a preponderance of the thermodynamically less stable *Z* isomer over the *E* isomer. Bohlman et al.[1] and Bergelson et al.[2] were the first workers to recognize the preparative value of this *Z* selectivity. A complete explanation for the *Z* stereoselectivity in reactions of unstable ylides remains unknown, although attempts to rationalize the results have been made.[3-5]

One technique for increasing the ratio of *E*:*Z* alkene produced by a Wittig reaction involving an unstable ylide is to use an ylide having alkyl groups bonded to phosphorus.[6,7] Some understanding of this effect can be gained by consideration of the Bestmann mechanism[5,8,9] of the Wittig reaction.

According to this mechanism, cycloaddition of a phosphorus ylide to an aldehyde initially occurs to form an oxaphosphetane (**1**), in which the substituents R^1 and R^2 are cis. A pseudorotation about the pentacoordinate phosphorus occurs (which is probably not rate determining[10]) to form **2**, in which the departing carbanionic center occupies an apical position in the phosphorus trigonal bipyramid. Carbon–phosphorus bond rupture then occurs to form the zwitterion **3**. If R^2 is unable to stabilize an adjacent carbanion, and if R^3 is phenyl, a rapid elimination of triphenylphosphine oxide occurs, and a large proportion of *Z* olefin (**4**) is produced. If, however, R^2 is a carbanion stabilizing group, or if R^3 is an electron-donating group (e.g., alkyl, cycloalkyl), the lifetime of intermediate **3** is extended (i.e., phosphine oxide elimination is slowed). Rotation about the carbon–carbon bond now becomes possible, with the result that the more thermodynamically stable zwitterion **5** is produced. Elimination of phosphine oxide from **5** then leads to the more stable *E* olefin (**6**) as product.



Although the Bestmann mechanism is able to accommodate the usually observed stereochemical preferences in the Wittig reactions of unstable Wittig reagents, serious questions remain unanswered. Thus, a principal drawback is the inability of the mechanism to account for the very high stereoselectivity required in the initial cycloaddition to form **1**.[11] Also, the mechanism does not address the issue of the existence of an initial oxaphosphetane–betaine equilibrium, nor does it account for the results of certain crossover experiments.[12,13] In addition, the effects of solvent polarity[14] and addition of lithium salts[15] are difficult to rationalize by the Bestmann mechanism (or any other mechanism[3,4,15,16]). Thus, while the Bestmann mechanism offers considerable insight into the mechanism of the Wittig reaction, it is not the last word on the subject. Nevertheless, the Bestmann mechanism has influenced us to consider the through-space 2p–3d overlap effect as applied to the Wittig reaction.

Kinetics data for the S_N2 reactions of various triarylphosphines with benzyl chloride, benzyl bromide, and *n*-butyl chloride, and of aryldiethylphosphines with ethyl iodide, have been presented in previous publications.[17-20]

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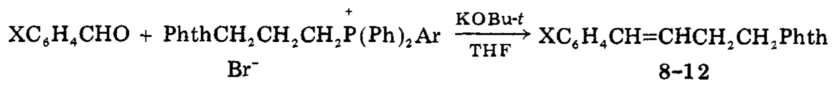
Table I. Yields and Stereochemical Results for the Reactions



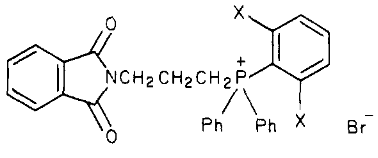
$$XC_6H_4CHO + PhthCH_2CH_2CH_2\overset{+}{P}(Ph)_2Ar \; Br^- \xrightarrow[THF]{KOBu\text{-}t} XC_6H_4CH{=}CHCH_2CH_2Phth \quad \mathbf{8\text{-}12}$$

X	Ar	alkene	yield, %	*Z* isomer, %	*E* isomer, %	lit. results[24]
H	Ph	8	60	97.3	2.7	59% yield, 100% *Z*
H	2,6-$C_6H_3(OMe)_2$	8	37	60.6	39.4	
p-Cl	Ph	9	58	91.2	8.8	57% yield, 100% *Z*
p-Cl	2,6-$C_6H_3(OMe)_2$	9	28	85.3	14.7	
p-MeO	Ph	10	59	94.2	5.8	56% yield, 100% *Z*
p-MeO	2,6-$C_6H_3(OMe)_2$	10	30	71.1	28.9	
p-Me	Ph	11	54	100.0	0.0	56% yield, 100% *Z*
p-Me	2,6-$C_6H_3(OMe)_2$	11	31	41.3	58.7	
m-NO_2	Ph	12	55	100.0	0.0	57% yield, 100% *Z*
m-NO_2	2,6-$C_6H_3(OMe)_2$	12	49	40.9	59.1	

Four particularly important effects were observed. (1) The presence of an *o*-methoxy substituent on an aryl group of the phosphine causes a significant increase in the rate of the reaction. (2) The ratio of the rates of reaction of a given triarylphosphine with benzyl chloride and with *n*-butyl chloride is about 20, probably the smallest ratio ever reported for S_N2 reactions of these alkyl chlorides. (3) Rate and activation parameter profiles for the reactions of the isomeric anisyldialkylphosphines and anisyldialkylamines, respectively, with alkyl halides are distinctly different. (4) Diphenyl(2,6-dimethoxyphenyl)phosphine undergoes the quaternization reaction with alkyl halides faster than any other phosphine we have used, including tri-*o*-anisylphosphine and bis(*o*-methoxyphenyl)phenylphosphine. A rationalization of these observations has been presented that is based partly on the concept of through-space overlap of a pair of 2p electrons of the oxygen atom of a 2-methoxyphenyl group with an empty 3d orbital of phosphorus in an early transition state. Most recently, we have provided evidence that suggests that the preferred geometry of the through-space 2p–3d overlap effect involves an incipient $3d_{z^2}$ orbital of the phosphorus.[21]

It has also been suggested[17-20] that, if the through-space 2p–3d overlap effect exists in the transition state of an S_N2 reaction, it will also be apparent in the phosphonium cation that is the product of the reaction. Three lines of support for this concept have been offered. (1) An X-ray diffraction study[22] of benzyl(2-methoxyphenyl)diphenylphosphonium bromide has revealed that the P–O distance is substantially shorter than the sum of the van der Waals radii of phosphorus and oxygen. Furthermore, the bond angles indicate that the *o*-methoxy group is actually leaning toward the phosphorus in order to facilitate a P–O bonding interaction, and energy minimization calculations, in which the total steric energy is made up primarily of bond-stretching energies and van der Waals nonbonded interactions, also indicate that a weak P–O bonding interaction exists. (2) For reasons cited in the previous papers,[17-20] the chemical shift of the protons of the methylene group directly bonded to phosphorus in the phosphonium salt represents the best probe of the overlap effect in the NMR spectrum of each compound. An upfield shift of the methylene hydrogens is expected when the electron density at phosphorus is increased owing to the overlap effect, and this is observed. (3) The rates of alkaline cleavage of a series of benzyltriarylphosphonium chlorides in 50% v/v aqueous dioxane at 10.1 °C have been determined.[23] The salts containing *o*-methoxy groups have been found to undergo reaction much more slowly than those containing *p*-methoxy groups. For example, benzylbis(*o*-methoxypheny)phenylphosphonium chloride reacts but 2.6 × 10^{-3} times as fast as benzylbis(*p*-methoxyphenyl)phenylphosphonium chloride. Benzyl(2,6-dimethoxyphenyl)diphenylphosphonium chloride reacts about 10 times slower than the bis(*o*-methoxyphenyl) compound. These are the results anticipated, based on the operation of the through-space 2p–3d overlap effect in the ortho-substituted compounds.

In the light of these findings, it was considered possible that a through-space 2p–3d overlap effect might influence the stereochemical outcome of Wittig reactions. The expected effect would be enhancement of the amount of *E* alkene produced. A well-defined reaction system was sought, one in which essentially only *Z* product was known to be formed by a Wittig reaction of an unstable triphenylphosphorus ylide. Such a system was provided by the recent work of Braun and co-workers,[24] who examined the reactions of the ylide derived from triphenyl(3-phthalimidopropyl)phosphonium bromide (7, X = H) with variously substituted benzaldehydes. The reactions were conducted under nitrogen at temperatures of from 0 to 65 °C, in THF as solvent, and with potassium *tert*-butoxide as the ylide-producing base. Braun et al. reported the exclusive production of the *Z* alkenes, in yields of nearly 60%.[24]



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We decided to examine what effect the use of a 2,6-dimethoxyphenyl group (in the place of one of the three phenyl groups) in the ylide would have upon the stereoselectivity of the reactions studied by Braun et al. In order to do this, (2,6-dimethoxyphenyl)diphenyl(3-phthalimidopropyl)phosphonium bromide, (7, X = OMe), had to be synthesized. This was accomplished by reaction of (2,6-dimethoxyphenyl)diphenylphosphine[20] with *N*-(3-bromopropyl)phthalimide in refluxing toluene.[25]

In the interest of providing results that were directly comparable with those previously reported, reaction con-

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[21] McEwen, W. E.; Lau, K. W. *Abstr. Pap.—Am. Chem. Soc.* **1982**, 183rd, ORG 114.

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[24] Olsen, D. K.; Torian, B. E.; Morgan, C. D.; Braun, L. L. *J. Org. Chem.* **1980**, *45*, 4049. These workers mentioned in a footnote that small amounts of the *E* isomer might have been present in each reaction mixture.

[25] The phosphonium bromide 7 (X = OMe) was found to be very hygroscopic and had to be stored in a desiccator under dry nitrogen.

Table II. Properties of Alkenes Obtained from Wittig Reactions

reagents	alkene[a]	mp, °C	IR ($\mathrm{CHCl_3}$), $\mathrm{cm^{-1}}$	NMR, δ (J, Hz)[b]
PhCHO + 7 (X = H)	8	61–62	1770, 1710	2.62 (q, 2 H), 3.72 (t, 2 H), 5.60 (2 overlapping t, 1 H), 6.45 (d, 1 H, J = 12.5)
PhCHO + 7 (X = MeO)	8	56–60	1770, 1710	enhancement of absorption of E isomer[c]
p-$\mathrm{ClC_6H_4CHO}$ + 7 (X = H)	9	97.5–101	1775, 1715	2.69 (q, 2 H), 3.79 (t, 2 H), 5.70 (2 overlapping t, 1 H), 6.45 (d, 1 H)
p-$\mathrm{ClC_6H_4CHO}$ + 7 (X = OMe)	9	76–93	1775, 1715	enhancement of absorption of E isomer[c]
p-$\mathrm{MeOC_6H_4CHO}$ + 7 (X = H)	10	102–106	1775, 1710	2.73 (q, 2 H), 3.76 (s, 3 H), 3.81 (t, 2 H), 5.57 2 overlapping t, 1 H), 6.43 (d, 1 H)
p-$\mathrm{MeOC_6H_4CHO}$ + 7 (X = OMe)	10	70–102	1775, 1710	enhancement of absorption of E isomer[c]
p-$\mathrm{MeC_6H_4CHO}$ + 7 (X = H)	11	118–119[d]	1770, 1705	2.30 (s, 3 H), 2.72 (q, 2 H), 3.81 (t, 2 H), 5.63 (2 overlapping t, 1 H), 6.49 (d, 1 H)
p-$\mathrm{MeC_6H_4CHO}$ + 7 (X = OMe)	11	92–118	1770, 1705	enhancement of absorption of E isomer[c]
m-$\mathrm{NO_2C_6H_4CHO}$ + 7 (X = H)	12	100–106	1775, 1710	2.73 (q, 2 H), 3.83 (t, 1 H), 5.87 (2 overlapping t, 1 H), 6.58 (d, 1 H)
m-$\mathrm{NO_2C_6H_4CHO}$ + 7 (X = OMe)	12	92.5–112	1775, 1710	enhancement of absorption of E isomer[c]

[a] See Table I. [b] Absorption of aromatic H's not given. [c] Copies of spectra available on request. Also cf. ref 24. [d] After crystallization from ethanol.

ditions employed for the Wittig reactions were identical with those of Braun et al. A higher yield of product might have been obtained, however, had the aldehydes been added slowly to a slight excess of preformed ylide.[4] We also decided to repeat the work of Braun and co-workers. All of the pertinent data are given in Table I. Although we found small amounts of the E isomer in three of the five examples reported by Braun et al.,[24] we nevertheless confirmed the findings of these workers that the Z isomer was predominant in all of the reactions of the ylide derived from triphenyl(3-phthalimidopropyl)phosphonium bromide with the various substituted benzaldehydes.

Reaction of the ylide derived from (2,6-dimethoxyphenyl)diphenyl(3-phthalimidopropyl)phosphonium bromide (7, X = OMe), with the substituted benzaldehydes was carried out under the same conditions. The results are provided in Table I. A reasonable rationale is that through-space 2p–3d overlap has increased the stability of intermediates of types 3 and 5 of the Bestmann mechanism and has allowed for at least partial equilibration between them, thus giving rise to an enhanced yield of the E alkene. The increase in the relative proportion of E olefins was observed uniformly for reactions of all aldehydes examined. It is interesting that the greatest enhancement effects were found for reaction with p-tolualdehyde (with an electron-donating substituent present) and m-nitrobenzaldehyde (with an electron-withdrawing substituent present). For these compounds, the E olefin actually became the principal product. From these results, it would appear that the stereochemical outcome of the Wittig reaction with a "through-space" stabilized ylide is remarkably insensitive to the electronic nature of the substituted benzaldehyde. The reason why this is so is unclear at present. It is known that carbonyl compounds having electron-withdrawing substituents generally react at more rapid rates in Wittig reactions than do carbonyl compounds having electron-donating substituents and tend to give more Z product,[3,26] so that the behavior of m-nitrobenzaldehyde would appear to be somewhat anomalous. However, so too the behavior of p-chlorobenzaldehyde must also be regarded as anomalous (by these criteria), since it gave the highest observed production of E olefin under conventional Wittig reaction conditions.[27]

Evidence that the change in Z:E ratios upon the use of 7 (X = OMe) is not attributable to a steric effect has been provided by Allen.[28–30] He has found that the cis:trans ratio of the alkenes formed in Wittig reactions of ylides derived from benzyltriarylphosphonium salts (generated in ethanolic sodium ethoxide) with benzaldehyde, acetaldehyde, or trimethylacetaldehyde increases as steric crowding at phosphorus increases. This proves to be true regardless of whether electron-donating (e.g., o-Me) or electron-withdrawing (e.g., o-Cl) substituents are present in the aryl groups of the ylide. (However, a small decrease in the cis:trans ratio of alkenes is observed when one of the aryl groups in the ylide is an o-methoxyphenyl group; Allen, in anticipation of and in agreement with our efforts, attributes this result to the operation of a through-space

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(26) Gosney, I.; Rowley, A. G. "Organophosphorus Reagents in Organic Synthesis"; J. I. G. Cadogan, Ed.; Academic Press: New York, 1979, pp 17–153.

(27) A possible concern as to whether the results are meaningful owing to the relatively low yields of alkenes can be overcome by use of simple arithmetic. If the worst possible case is envisioned, namely, that the adduct diastereomer that would otherwise have given the Z alkene decomposed to side products infinitely faster than the other adduct diastereomer, and if we then add the "missing" Z alkene to that actually found, we get the following results: Even in this worst possible case, the

X	Ar	Z alkene, %	E alkene, %
H	Ph	98	2
H	2,6-$\mathrm{C_6H_3(OMe)_2}$	85	15
p-Cl	Ph	95	5
p-Cl	2,6-$\mathrm{C_6H_3(OMe)_2}$	96	4
p-MeO	Ph	97	3
p-MeO	2,6-$\mathrm{C_6H_3(OMe)_2}$	91	9
p-Me	Ph	100	0
p-Me	2,6-$\mathrm{C_6H_3(OMe)_2}$	82	18
m-$\mathrm{NO_2}$	Ph	100	0
m-$\mathrm{NO_2}$	2,6-$\mathrm{C_6H_3(OMe)_2}$	71	29

anticipated through-space electron-donation effect is observed in all cases except for the reaction with p-chlorobenzaldehyde, and in that case there is no change within experimental error. On the other hand, if the best possible case is envisioned, namely, that the adduct diastereomer that would otherwise have given the E alkene decomposed to side products infinitely faster than the other adduct diastereomer, and if we add the "missing" E alkene to that actually found, we get results in which the case for the through-space electron-donation effect becomes overwhelming. Since both of these scenarios are equally improbable, we might as well confine our attention to the actual experimental results given in Table I. It should also be emphasized that, on the basis of the Bestmann mechanism and of the through-space 2p–3d overlap effect, lower yields of alkenes would be *expected* for the reactions of the ylide derived from 7 (X = OMe) as against the reactions of the ylide derived from 7 (X = H).

(28) Allen, D. W. *J. Chem. Res., Synop.* **1980**, 384.

(29) Allen, D. W. *Z. Naturforsch. B* **1980**, *35*, 981.

(30) Allen, D. W. *Z. Naturforsch. B* **1980**, *35*, 1455.

2p–3d overlap effect.) It is therefore a reasonable expectation that any purely steric effect upon the stereoselectivity of Wittig reactions of 7 (X = OMe) would have been manifested in a direction opposite to the effect actually brought about by through-space electron donation. Also, the fact that there is relatively little change in the fluctuation of cis:trans ratios of alkenes produced by the reaction of the various ylides of type $Ar_3P^+–^-CHPh$ with benzaldehyde, in which intermediate oxaphosphetanes can readily revert to reagents, and with acetaldehyde, in which the intermediate oxaphosphetanes do not readily revert to reagents, suggests that such early equilibration is not of major importance in determining the ratios of isomeric alkenes that are formed.

As shown in Table I, the yields of alkenes derived from the reactions of 7 (X = OMe) are less than those derived from the reactions of the unsubstituted compound, 7 (X = H). The interpretation of this result is uncomplicated. It is known that, upon replacing phenyl groups bonded to phosphorus in the ylide with electron-donating alkyl groups, the last step of the Wittig reaction (i.e., loss of phosphine oxide from the Wittig intermediate) becomes more difficult.[3,26] Schlosser's explanation of this observation is essentially as follows. Assuming a betaine-like structure for the precursor to the alkene, replacement of the "stationary" phenyl groups (on phosphorus) by electron-donating alkyl groups should result in a stabilization of the Wittig intermediate. However, the transition state leading to products requires less electron donation toward phosphorus so that the amount of stabilization afforded the transition state (upon changing to alkyl groups on phosphorus) will be less than that for the betaine. Therefore, the energy barrier that must be overcome in order to produce products increases, and the reaction rate is slowed.

A similar argument may be used to rationalize the observations made in this study, viz., that yields of product were uniformly lower when the "through-space" stabilized ylide was employed.

In conclusion, the results obtained in this study have served to demonstrate that through-space donation of electron density toward phosphorus influences the stereochemical outcome of the Wittig reaction, with a greater proportion of *E* olefin being produced.

Experimental Section

General Procedures. All newly obtained melting points are uncorrected and were taken in open capillary tubes with use of a Mel-Temp melting point apparatus. Infrared spectra were recorded on Beckman IR-10 and Perkin-Elmer 727 infrared spectrophotometers. Ultraviolet spectra were recorded on a Perkin-Elmer 202 ultraviolet–visible spectrophotometer. ^1H 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 carried out on precoated 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. Dimethylformamide was distilled at reduced pressure from anhydrous barium oxide and was stored over fresh molecular sieves.

Triphenyl(3-phthalimidopropyl)phosphonium Bromide (7, X = H). This compound, mp 240–242 °C, was prepared by a literature procedure.[24]

(2,6-Dimethoxyphenyl)diphenylphosphine. This compound, mp 114–115 °C, was prepared as described previously.[20]

(2,6-Dimethoxyphenyl)diphenyl(3-phthalimidopropyl)phosphonium Bromide (7, X = OMe). To a solution of 4.40 g (0.0164 mol) of *N*-(3-bromopropyl)phthalimide[31] in 40 mL of anhydrous toluene contained in a 125-mL, round-bottom flask was added 5.28 g (0.0164 mol) of 2,6-dimethoxyphenyl)diphenylphosphine. The reaction mixture was magnetically stirred and refluxed for 48 h. After the mixture was allowed to cool to room temperature in a dry-nitrogen-filled bag, the toluene layer was removed by decantation, and the glassy, yellow-orange solid residue was scraped out of the flask. The product was ground with a mortar and pestle, washed thoroughly with anhydrous ether, and dried to yield 9.07 g (94%) of (2,6-dimethoxyphenyl)diphenyl(3-phthalimidopropyl)phosphonium bromide, mp 108 °C dec, which was stored in a desiccator: IR ($CHCl_3$) 1775, and 1710 (C=O), 1430 (PPh) cm^{-1}; NMR ($CDCl_3$) δ 2.37 (m, 2 H), 3.1–4.1 (br m, 4 H), 3.65 (s, 3 H), 3.74 (s, 3 H), 7.25 (m, 3 H), 7.5–8.0 (m, 14 H).

Reaction of 7 (X = H) with Benzaldehyde. The procedure for the Wittig reaction was similar to that employed by Braun et al.[24] However, the workup was somewhat different. As the prototype of all of the reactions, a full description of the entire procedure is given here.

A dry 100-mL, three-neck, round-bottom flask was fitted with a gas inlet, a solid addition port, and a condenser fitted with a bubbler. Dry nitrogen gas was passed through the apparatus for 15 min. Into the flask was placed a suspension of 2.65 g (0.0050 mol) of triphenyl(3-phthalimidopropyl)phosphonium bromide in 40 mL of dry THF, and then 0.53 g (0.0050 mol) of freshly distilled, dry benzaldehyde was added. The reaction mixture was maintained under a positive pressure of dry nitrogen and was stirred, while being cooled in an ice–water bath, for 20 min. Next, 0.62 g (0.0055 mol, 1.1 equiv) of potassium *tert*-butoxide was added in a single portion. Within 1 min, the reaction mixture became a deep yellow-orange color, and it was stirred for an additional 20 min in the ice–water bath. The bath was then removed, and the reaction mixture was allowed to warm to room temperature during 1 h (the color was a deep orange). The reaction mixture was heated to reflux and was refluxed for 21 h. The reaction mixture (which was now a faint-green color and contained a fine precipitate of potassium bromide) was gravity filtered while it was still warm, the reaction flask and precipitate being rinsed with additional dry THF. The solvent was removed from the filtrate by rotary evaporation to yield 2.36 g of a green oil. The oil was subjected to wet-column chromatography, using 10% deactivated 100–200-mesh silica gel, packed and eluted with reagent grade benzene:spectral grade ethyl acetate (95:5). The first fraction isolated from the column consisted of a mixture of (*E*)- and (*Z*)-*N*-(4-phenyl-3-butenyl)phthalimides: needles, mp 61–62 °C; IR ($CHCl_3$) 1770, 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 2.62 (q, 2 H), 3.72 (t, 2 H), 5.60 (2 over lapping t, 1 H), 6.45 (d, 1 H, J = 12.5 Hz), 7.12 (s, 4 H), 7.5–7.8 (m, 4 H); UV ($CHCl_3$) λ_{max} 245 nm (ϵ 14 000), 255 (ϵ 10 700).

Gas chromatographic analysis of the *N*-(4-phenyl-3-butenyl)phthalimide mixture was conducted in order to determine the relative proportion of *Z* and *E* isomers. Conditions used are as follows: column, 3% OV-17 on Supelcoport, 6 ft × $^1/_8$ in.; temperature, 250 °C (isothermal); solvent, spectral grade chloroform; sample concentration approximately 0.2 g/10 mL solution; sample size, 1 μL; carrier gas, nitrogen (40 psi); flow rate, 25 mL/min. The isomer distribution was determined to be 97% *Z* (retention time, 10.7 min), 3% *E* (retention time, 12.7 min). Corrected for differing response ratio of *Z* and *E* isomers, the isomer distribution was 97.3% *Z* and 2.7% *E*. Coinjection of the mixture of isomeric *N*-(4-phenyl-3-butenyl)phthalimides with pure (*Z*)-*N*-(4-phenyl-3-butenyl)phthalimide resulted in growth of the larger peak over the smaller. Similarly, a "mixed" GC analysis of the reaction material with pure *E* isomer resulted in a growth of the peak having a retention time of 12.7 min relative to the 10.7-min peak.

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Table III. Preparation of (*E*)-*N*-(4-aryl-3-butenyl)phthalimides, 8-12

product	Ar	method[a]	mp, °C	*Z*:*E*[b]
8	Ph	A	146.5-147.5	
9	*p*-ClPh	B	130.5-132	11:89
10	*p*-MeOPh	B	136.5-138	30:70
11	*p*-MePh	B	123.5-124	4:96
12	*m*-NO$_2$Ph	C	138-140	15:85

[a] Method A: via the cinnamaldehyde.[24] Method B: via iodine-catalyzed isomerization in pentane. Method C: via iodine-catalyzed isomerization in benzene. [b] Isomer ratio in equilibrated product (by gas chromatography), before purification by recrystallization (for methods B and C).

Other Wittig Reactions. The results of the other Wittig reactions of 7 (X = H) or 7 (X = OMe) with benzaldehyde and with substituted benzaldehydes are presented in Table II.

Calculation of Absolute Yields of Alkenes from GC Peak Areas. In order to convert peak areas to absolute yields, it was necessary to prepare pure cis and trans isomers of each product, so that solutions of standard concentration could be analyzed. In all instances, pure cis isomer was prepared by recrystallizing a portion of the reaction product from ethanol (until only one peak appeared in a gas chromatogram). Pure *E* isomer was produced by two methods: (a) through reaction of an appropriate *trans*-4-aryl-3-butenylamine hydrochloride with phthalic anhydride[24] or (b) iodine-catalyzed isomerization of the cis isomer to the more thermodynamically stable trans form.

Isomerization of the *cis*-*N*-(4-aryl-3-butenyl)phthalimides to the trans isomers proved to be the most convenient means whereby the latter compounds could be obtained. Thus, it was found that, for **9**-**11**, irradiation (with a 200-W visible lamp) of a pentane solution of the cis isomer, in the presence of a catalytic amount of iodine, afforded an equilibrium mixture of cis and trans product, in which the trans isomer was the principal component. Recrystallization of the solid product from ethanol then afforded pure trans product (recrystallization was continued until the sample displayed only one peak by gas chromatography). Compound **12** was only sparingly soluble in pentane; therefore, the isomerization of this compound was accomplished in benzene. The results are shown in Table III.

With pure samples of the cis and trans isomer of each product available, gas chromatographic standards were accurately prepared so that peak areas could be interpreted as absolute yields. The relative response ratio was calculated from a minimum of six data points by linear regression line analysis (each correlation coefficient having a value of $r = 1.00$). The isomer distribution data presented in Tables I and II have been corrected in this manner.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research.

Registry No. 7 (X = H), 7743-29-5; 7 (X = OMe), 84812-12-4; (*E*)-8, 74592-04-4; (*Z*)-8, 74591-93-8; (*E*)-**9**, 74592-05-5; (*Z*)-**9**, 74591-94-9; (*E*)-**10**, 84812-13-5; (*Z*)-**10**, 74591-96-1; (*E*)-**11**, 84812-14-6; (*Z*)-**11**, 74591-95-0; (*E*)-**12**, 84812-15-7; (*Z*)-**12**, 74591-98-3; PhCHO, 100-52-7; *p*-ClC$_6$H$_4$CHO, 104-88-1; *p*-MeOC$_6$H$_4$CHO, 123-11-5; *p*-MeC$_6$H$_4$CHO, 104-87-0; *m*-NO$_2$C$_6$H$_4$CHO, 99-61-6; *N*-(3-bromopropyl)phthalimide, 5460-29-7; (2,6-dimethoxyphenyl)diphenylphosphine, 66417-43-4.

Reduction of Unsymmetrical Benzils Using Sodium Dithionite

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Received March 30, 1982

Contrary to a previous report, reduction of unsymmetrical benzils by sodium dithionite (sodium hydrosulfite) in general yields a mixture of isomeric benzoins. Whereas the reduction of aldehydes and ketones by dithionite apparently takes place by a nucleophilic addition mechanism, the reduction of benzils proceeds by an electron-transfer mechanism. The inital product of the reduction is the (*Z*)-α,α'-stilbenediol which is produced stereospecifically. The ultimate benzoin products, then, result from the two different modes of ketolization of the stilbenediol intermediate.

Sodium dithionite (sodium hydrosulfite) has long been recognized as a powerful reducing agent for a variety of functional groups.[1] Synthetic and mechanistic studies of the reduction of simple carbonyl compounds by this reagent have been a much more recent development and have received considerable attention in the past few years.[2]

Table I. Benzoin Product Yields from Dithionite Reduction of Unsymmetrically Substituted Benzils

		% yield	
benzil	X	2	3
1a	Cl	60	40
1b	CH$_3$	40	60
1c	OCH$_3$	37	63
1d	OH	27	73

In contrast to the reduction of aldehydes and ketones, reduction of benzil to benzoin with sodium dithionite has been known for some time.[3] Extension of the reaction to unsymmetrical benzils (**1**) was reported by van Es and Backeberg[4] to proceed with quantitative and exclusive reduction at the most electron-deficient carbonyl group. Thus, only benzoin **2** was obtained when X was electron withdrawing and only benzoin **3** when X was electron releasing (eq 1).

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