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ELECTRON TRANSFER IN THE REACTION OF BENZALDEHYDE WITH A NONSTABILIZED YLIDE

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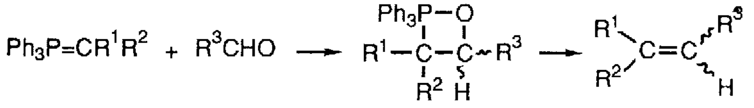
Summary: The Wittig reaction of benzaldehyde with isopropylidenetriphenylphosphorane was suggested to proceed via a single electron transfer mechanism on the basis of ^{14}C kinetic isotope effect and substituent effect experiments.

The mechanism of the Wittig reaction has been a matter of interest for many years.[2] It is now recognized that the mechanistic details are strongly dependent on the structure of the reactants and the reaction conditions and that oxaphosphetane **2** is the only detectable intermediate in the reaction of nonstabilized ylides (eq 1).[3-5] The oxaphosphetane-formation step in eq 1 is of particular importance since the preferential cis-olefin formation usually observed for nonstabilized ylides has been attributed to the stereochemistry of the initially formed oxaphosphetane. Here we wish to report that **2a** (R^1=R^2=Me, R^3=Ph) forms via a single electron transfer (SET) mechanism in the reaction of benzaldehyde with nonstabilized ylide **1a** (R^1=R^2=Me).



1

2

(1)

It has been shown that the formation of **2** from benzaldehyde and nonstabilized ylides is fast even at -78 °C while the rate of decomposition of the intermediate to olefin is slow at -25 °C.[4] This suggests the possibility that kinetic isotope effect (KIE) and substituent effects for the initial oxaphosphetane-formation step can be measured under suitably selected conditions. Thus, we determined the carbonyl carbon KIE and the substituent effects for the reaction of benzaldehyde and **1a** to give **2a** by the competition experiments in THF under Li salt-free conditions at 0 °C.[6,7] The material balance of the reaction was found excellent (101±1%) by ^1H NMR.

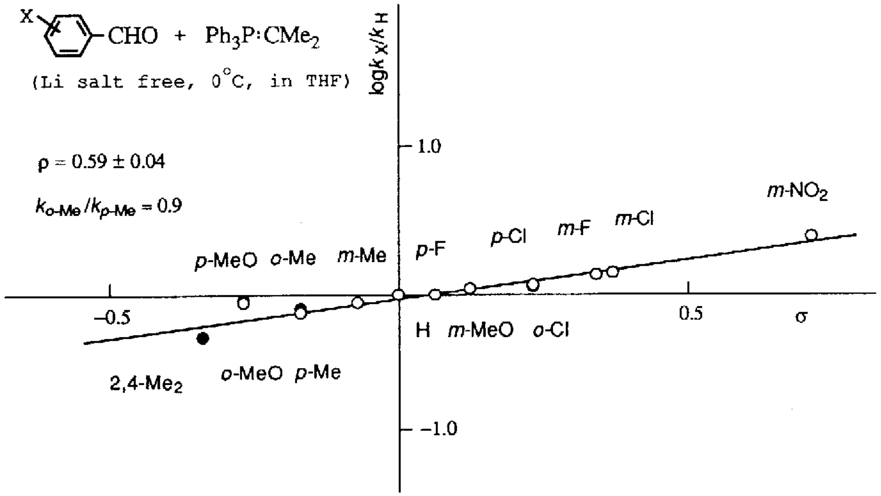


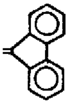
Figure 1. Substituent effects in the oxaphosphetane formation between benzaldehyde and **1a**.

General procedures to determine the KIE and the substituent effects were the same as reported previously.[8]

The observed ^{14}C KIE for benzaldehyde-7-^{14}C was near unity ($^{12}k/^{14}k$ = 1.003±0.002); this indicates the absence of bonding change at the carbonyl carbon on going from the reactant to the rate-determining transition state of the oxaphosphetane-formation step. The Hammett plot[9] (Figure 1) showed a small ρ value and no steric rate retardation due to ortho substituents. These results are similar to those for the reactions of MeLi[8b] and allyl-MgBr[11] which were concluded previously to proceed via a rate-determining SET mechanism, and suggest that the Wittig reaction also goes through the SET mechanism.[12]

In order to examine the electron-donor ability of ylides, enone isomerization experiments were carried out. To a THF solution of a ylide (0.1 M, M = mol dm^{-3}, 0.1 mmol) was added a solution of cis-2,2,6,6-tetramethylhept-4-en-3-one (0.1 M, 0.05 mmol) containing diphenylether (internal standard). After usual workup, the extent of cis-trans isomerization was determined by GLC (OV1, 2 m). The results (Table 1) clearly indicate that considerable enone isomerization occurred for nonstabilized ylide **1a**. The high degree of isomerization for **1a** suggests the high electron-donor ability of the nonstabilized ylide.[13] In contrast, little or no isomerization was observed for semistabilized and stabilized ylides (**1b** and **1c**). Since the reduction potential of benzaldehyde is less

Table 1. Cis-Trans Isomerization during the Reaction of cis Enone with various Ylides in THF at 0 °C[a]

ylide		reaction time min	%cis enone	%trans enone
$Ph_3P{=}CMe_2$	(1a)	15	86.1	13.9
		60	33.2	66.8
$Ph_3P{=}CHPh$	(**1b**)	15	98.2	1.8
		60	96.7	3.3
$Ph_3P{=}$ 	(**1c**)	15	97.1	2.9
		60	98.4	1.6
Blank			98.5	1.5

[a] The Wittig product was not detected. %Enone was normalized: 100% = %cis enone + %trans enone.

negative (E_{red} = -1.84 V vs. SCE) than that of cis-enone (-2.28 V) these results are compatible with the SET mechanism of the Wittig reaction of benzaldehyde with **1a.**[16]

It has been shown that the Wittig reaction of nonstabilized ylides with an aldehyde tends to give thermodynamically less stable cis olefin (when R^1=H in eq 1) while stabilized ylides yield trans olefin.[2] The origin of the preferential cis-olefin formation for nonstabilized ylides has been a matter of great interest and several rationalizations have been presented.[2,3,14,15,17] Since recent studies have indicated that the stereochemistry of **2** is retained during the decomposition to olefin,[4c,18] the origin of the preferential formation of cis-2 for nonstabilized ylides is a critical mechanistic problem in the Wittig reaction. The present KIE and substituent effect results are important in that they suggest that the oxaphosphetane-formation step is not a direct cycloaddition as usually assumed but a reaction between the radical cation of the ylide and the radical anion of the aldehyde. It is obvious that further investigation is desired to clarify the mechanistic problem.

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References and Notes

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6. To a mixture of benzaldehydes (^{12}C and ^{14}C-labeled compounds or two differently ring-substituted compounds) dissolved in dry THF (0.1 M) was added a deficient amount of ylide **1a** (prepared with sodium hexamethyldisilazide as a base and isopropyltriphenylphosphonium bromide 0.1 M THF soln) at 0 °C. The solution was allowed to react for 10 s, quenched by dil HCl, and worked up as usual. The relative amount of the remaining aldehydes was determined by a liquid scintillation counter (KIE) or GLC (substituent effect).
7. The possibility of retro-oxaphosphetane formation was checked by the following isotope tracer experiments. To a THF solution of PhCHO (0.6 mmol) was added 1a (1.2 mmol) and the mixture was allowed to react for 1 min. Then Ph^{14}CHO (1.2 mmol) was added and after 10 s the reaction mixture was worked up in a usual manner. Benzaldehyde was recovered and its radioactivity was compared with that of the benzaldehyde added. The same procedure was repeated by starting with Ph^{14}CHO and then adding PhCHO. Both experiments gave the same results in that the scrambling of isotope occurs only slightly, indicating that the observed KIE and substituent effects are essentially of kinetic nature.
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9. (a) Filled circles represent the data of the derivatives with ortho substituents. The points of the MeO derivatives often deviate from the correlation line for the reactions carried out in the nonpolar solvent,[5,8b,10] and therefore the ρ value was calculated from the other points. (b) Schlosser et al. reported $\rho = 1.1$ for a related reaction: M. Schlosser, A. Piskala, C. Tarchini, and H. B. Tuong, Chimia, 29, 341 (1978).
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12. (a) There may be another possibility in which complex formation between benzaldehyde and the ylide is rate determining. Although this possibility cannot completely be eliminated, we feel it less probable because the substituent effect is expected to give a negative ρ value if the complex formation is rate determining, which is incompatible with the observed small positive ρ value. (b) Rationalization of near-unity ^{14}C KIEs and small positive ρ values for ET processes was given in the literature: Ref. 8b; H. Yamataka, T. Matsuyama, and T. Hanafusa, J. Am. Chem. Soc., J. Am. Chem. Soc., 111, 4912 (1989); H. Yamataka, Y. Kawafuji, K. Nagareda, N. Miyano, and T. Hanafusa, J. Org. Chem. in press.
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