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A Ketyl Radical Probe Experiment. The Reactions of *o*-Halobenzophenones with Various Wittig Reagents[#]

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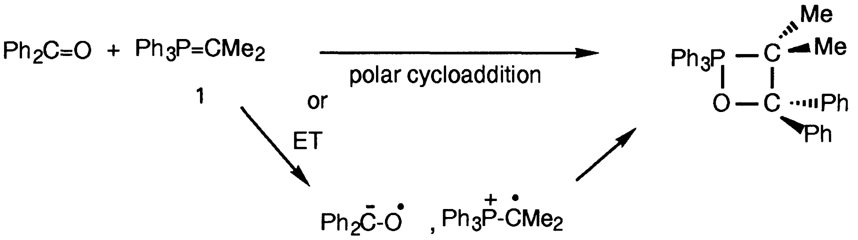
The ketyl radical probe experiments of *o*-, *m*-, or *p*-bromobenzophenone and iodobenzophenone with nonstabilized, semistabilized, and stabilized ylides in THF and [$^2H_8$]THF suggested the presence of radical anion species of sufficient lifetime in the reaction with a nonstabilized ylide.

The Wittig reaction of nonstabilized ylides with aldehydes or ketones is known to proceed through the oxaphosphetane as an only detectable intermediate.[1-4] The intimate mechanism of the oxaphosphetane-formation step has been a matter of great interest since this step was shown to control the stereochemistry of the product alkene.[5] Recently, we have suggested on the bases of the kinetic isotope effect and substituent effect study that electron transfer (ET) may be involved as a rate-determining step in the oxaphosphetane-formation step between benzaldehyde and a nonstabilized ylide (**1**) in THF.[6,7] The same experimental technique for the reaction of benzophenone with **1** indicated that the reaction proceeds either by a polar cycloaddition or by fast ET followed by a slow rate-determining oxaphosphetane formation (Eq. 1).[4] Here, we report the results of a ketyl radical probe experiment, which indicates the possibility of ET in the reaction of benzophenone with **1**.



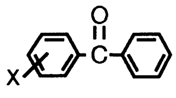
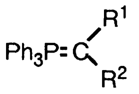
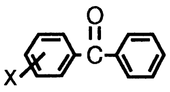
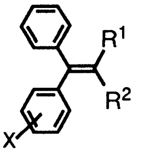
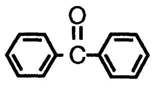
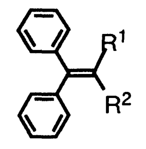
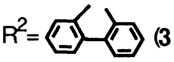
(1)

It was reported two decades ago that electrochemically generated bromobenzophenone radical anion undergoes a dehalogenation reaction.[8a] It can then be expected that when bromo- or iodobenzophenone accepts an electron from any nucleophile the ketyl thus formed would undergo the dehalogenation reaction if the lifetime of the ketyl is long enough, and therefore the detection of a dehalogenated product can be evidence for the nucleophile to have enough ability of transferring an electron to the aromatic ketone.[8] The applicability of the new probe experiment has been tested successfully in the Grignard reaction recently.[9]

As a typical experimental procedure, a THF solution of *o*-bromobenzophenone (1.0 mL, 0.15 mol/L, containing dibenzylether as an internal standard for GC analysis) was added to 2 equiv. of THF solution of **1**

[#] This paper is dedicated to Professor Osamu Shimamura on the occation of his 80th birthday.

Table 1. Recovered Materials in the Reactions of Halobenzophenones with Various Ylides[a]

entry						
1[b]	X = *o*-Br	$R^1=R^2=Me$ (**1**)	76.1±1.4	c)	7.7±0.6	0.8±0.2
2	*m*-Br	**1**	37.8±4.9	56.7±6.2	c)	c)
3	*p*-Br	**1**	22.4±2.3	77.8±0.4	c)	c)
4	*o*-I	**1**	78.7±2.9	c)	14.8±2.4	0.9±0.3
5	*m*-I	**1**	37.4±5.2	54.1±4.2	4.7±0.8	0.4±0.1
6	*p*-I	**1**	45.0±1.5	43.0±0.5	6.5±0.4	0.3±0.1
7	*o*-Br	$R^1=H$, $R^2=Ph$ (**2**)	97.8±0.4	c)	0.8±0.2	c)
8	*m*-Br	**2**	99.1±0.3	c)	c)	c)
9	*p*-Br	**2**	96.5±0.3	c)	c)	c)
10	*o*-I	**2**	96.8±1.4	c)	3.2±0.4	c)
11	*m*-I	**2**	100.0±0.2	c)	c)	c)
12	*p*-I	**2**	102.2±0.2	c)	1.9±0.1	c)
13	*o*-Br	R^1, R^2=  (**3**)	99.3±1.1	c)	c)	c)
14	*o*-I	**3**	100.1±1.9	c)	c)	c)

a) In THF at 0 °C, 2 h. Figures are average GC yields (%) from 2-3 runs. Errors are standard deviations.

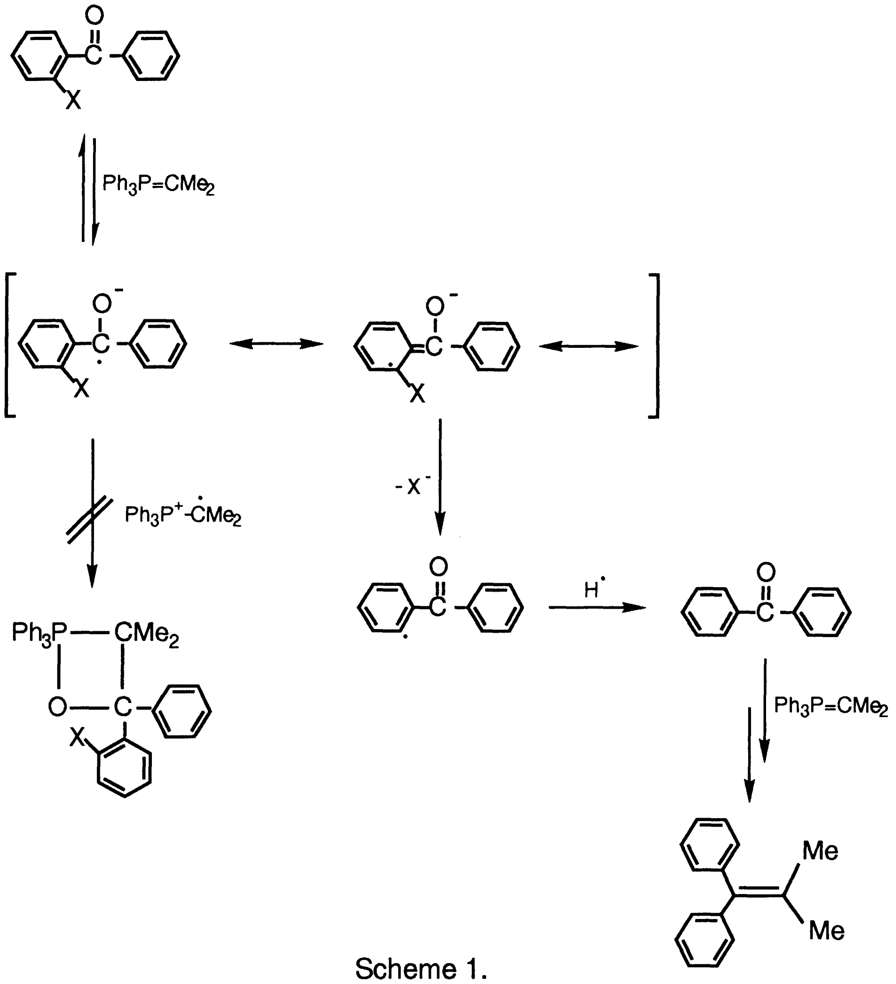
b) *o*-Bromobenzhydrol was also detected in 0.8±0.2% yield. c) Not detected.

(1.0 mL, 0.3 mol/L, prepared from isopropylidenetriphenylphosphonium bromide and sodium hexamethyldisilazide) and allowed to react at 0.0±0.1 °C for 2 h. Fourteen reactions were carried out between various halobenzophenones and three ylides. All products were characterized by NMR and their response factors in GC were calibrated.

The results are listed in Table 1, in which several points are apparent. (1) The treatment of stabilized ylide **3** with *o*-halobenzophenone resulted in complete recovery of the starting materials (entries 13 and 14). (2) The reactions of semistabilized ylide **2** also gave essentially recovered ketone; only *o*-bromo- and *o*-iodobenzophenones and *p*-iodobenzophenone gave trace amount of a dehalogenated product, benzophenone (entries 7, 10, and 12). (3) In contrast, the reactions of nonstabilized ylide **1** with *o*-halobenzophenone gave two dehalogenated products, benzophenone and its Wittig product, in significant yields (entries 1 and 4). The reactions of *m*- and *p*-bromobenzophenones yielded 57-78% of the normal Wittig product, but no dehalogenated product was detected. In the cases of *m*- and *p*-iodobenzophenones, however, dehalogenated products were formed together with the normal Wittig product.

The formation of the dehalogenated products in the reactions of *o*-halobenzophenones with **1** can be rationalized in terms of Scheme 1, where the normal Wittig route is slowed down because of the steric hindrance of *o*-halogen substituents and the dehalogenation route takes place.[6,10,11] The control experiment using [$^2H_8$]THF indicated that the benzophenone radical intermediate abstracts a hydrogen atom from the solvent.[12)] It is noteworthy that for the reactions of **1** with *m*- and *p*-iodobenzophenones both the normal Wittig route and the dehalogenation route occur competitively, while only the normal Wittig products were detected for *m*- and *p*-bromobenzophenones. Since electron-accepting ability is not much different for bromo- and iodo-substituted benzophenones, the difference should primarily arise from the difference in the dehalogenation rate from the ketyl intermediate; this in turn suggests that electron transfer itself occurs even for *m*- and *p*-bromobenzophenones although it is not reflected in the product distribution. The clear difference between ylides **1**-**3** is in line with the relative electron-transfer ability of these ylides estimated previously by the enone isomerization experiment; thus, **1** has much higher electron-transfer ability compared to **2** and **3**.[6)]

The present ketyl radical probe experiment provides the first clear evidence for the occurence of ET from nonstabilized ylide **1** to the aromatic ketones. These results are consistent with the mechanism in that the rate-determining step involves the oxaphosphetane formation from the radical ion pair which is formed via ET from the ylide to the aromatic ketones.



Scheme 1.

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1) For a recent review of the Wittig reaction, see: B. E. Maryanoff and A. B. Reitz, *Chem. Rev.*, **89**, 863 (1989).

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7) Olah proposed an ET mechanism on the basis of the detection of the reduction product (alcohol) in the reaction of hindered ketones with **1**: G. A. Olah and V. V. Krishnamurthy, *J. Am. Chem. Soc.*, **104**, 3987 (1982). See, however Ref. 6.

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9) H. Yamataka, K. Yamaguchi, T. Takatsuka, and T. Hanafusa, *Bull. Chem. Soc. Jpn.*, **65**, 1157 (1992).

10) The time course of the reaction showed that the yield of benzophenone increases rapidly at the early stage of the reaction and then stays constant while 1,1-diphenyl-2-methylpropene and benzhydrol increase gradually. The total material balance becomes less than 100% as the reaction proceeds; this may be due to the formation of a nonvolatile material.

11) An alternative mechanism in which the dehalogenation occurs via ET while the normal Wittig route proceeds via the direct cycloaddition may also explain the results provided the ET step is reversible.

12) The extent of deuterium incorporation in benzophenone obtained by the reaction between *o*-bromobenzophenone and **1** was measured by GC-MS (JMS-DX 300, PEG-HT 1 m) and found quantitative (1D incorporation) within the detection limit.

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