Effect of the Phosphonate Group on the Reactivity of Carbenes. Neighbouring Phosphonate Group Participation

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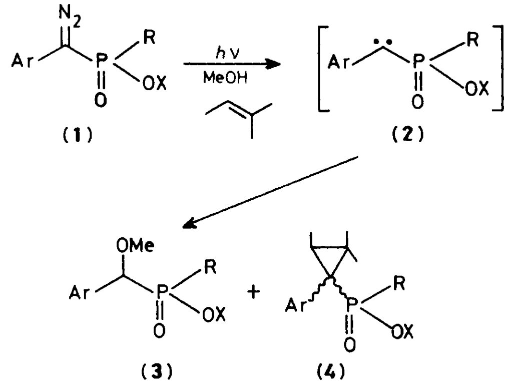
The electrophilicity of phosphonylcarbenes is dramatically reduced as one changes the neighbouring group from the phosphonate ester to the acid anion, and phosphonate carbenes are experimentally classified as typical nucleophiles; the results are nicely explained in terms of neighbouring phosphonate group participation in which the vacant p orbital strongly interacts with the phosphonate oxygen anion resulting in suppression of the availability of the vacant p orbital.

Particular attention has been paid recently to α-diazophosphonic acid salts as potential photolabile[1] mimics of phosphate derivatives, and several α-diazophosphonic acids have been synthesized and characterized.[2–5] However, little is known about the effect of the phosphonate anion on the reactivity of photolytically generated carbenes from the α-diazophosphonate salts. We estimated the reactivities of these carbenes systematically and found that the electrophilicity of phosphonylcarbenes is dramatically reduced as the carbene substituents are changed from the phosphonyl ester to its anion.



X = Me or Na

a; Ar = Ph, R = OMe
b. Ar = 4-ClC$_6$H$_4$, R = OMe
c; Ar = R = Ph

These results are nicely explained in terms of neighbouring group participation by the phosphonate anion.

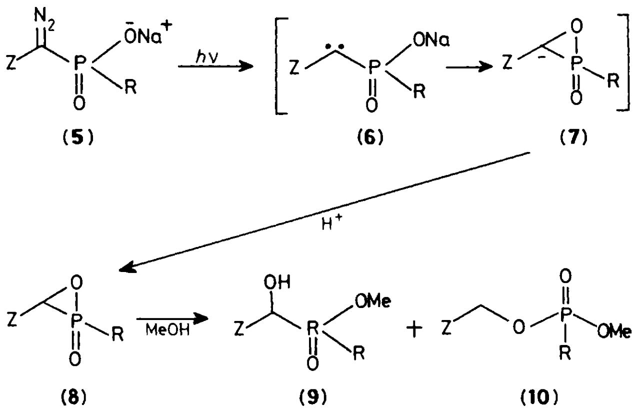
Irradiation of dimethyl α-diazobenzylphosphonate (**1a**; X = Me) in a 1 : 3.8 binary mixture of methanol and 2-methylbut-2-ene afforded α-methoxyphosphonate (**3**) and cyclopropanes (**4**) (mixture of *syn*- and *anti*-isomers) in 17.8 and 81.1% yield, respectively. When the monosodium salt of α-diazobenzylphosphonate[2] (**1a**; X = Na) was irradiated under the same conditions, followed by neutralization and esterification by CH_2N_2, however, the formation of the cyclopropanes (**4**) was greatly reduced and the α-methoxyphosphonate (**3**) became the major product. It is probable that these products are derived from the photolytically generated carbene (**2**), which either underwent insertion into the OH bond of methanol or added to the double bond of the alkene since either the diester or the sodium salt of the diazophosphonate was completely recovered in the dark under otherwise identical conditions.

O–H insertion–addition selectivities ($k_{OH}/k_{addn.}$) were calculated by the equation of Doering and Henderson using the mole fraction of products and substrates and are listed in Table 1. It is evident from the data in Table 1 that the neighbouring phosphonate group exerts a dramatic effect on the relative reactivities of the carbene (**2**). Thus, the carbene derived from (**1a**; X = Na) is 20 times more reactive towards methanol relative to the alkene than the carbene derived from (**1a**; X = Me). A similar dramatic increase in the O–H insertion product in going from the ester to the sodium salt is observed in the photolysis of the diazo derivatives of *p*-chlorobenzylphosphonate (**1b**) and benzylphosphinate (**1c**).

Table 1. Photolysis[a] of diazophosphonate in methanol–2-methylbut-2-ene. Effect of neighbouring phosphonate groups on insertion-addition selectivities.

Diazo compd.	X	% Yield[b] (3)	% Yield[b] (4)	$k_{OH}/k_{addn.}$
(**1a**)	Me	17.8	81.1	0.84
	Na	72.5	16.4	16.80
(**1b**)	Me	17.4	80.3	0.82
	Na	62.8	27.6	8.65
(**1c**)	Me	38.3	57.4	2.54
	Na	73.9	13.5	20.8

[a] Irradiations were carried out on 10 mM degassed solution of (**1**) in a 1 : 3.8 binary mixture of methanol and 2-methylbut-2-ene at 0 °C.
[b] Determined by g.c.



R = OMe or ONa

a; Z = Et$_2$NSO$_2$
b; Z = $Pr^{i}_{2}O_3P$
c; Z = Me$_2$NCO

The difference in the reactivity caused by the phosphonate group is obviously too great to be attributable to differences in inductive, conjugative, or steric effects, but can be better explained in terms of neighbouring group participation. Thus, it is reasonable to assume that the neighbouring phosphonate anion can interact with the vacant p orbital of singlet carbene. Such interaction should greatly reduce the electrophilicity of the carbene towards external reagents by suppressing the availability of its vacant p orbital. The phosphonylcarbene (**2**) in this study should be classified as an electrophile and therefore reacts by accepting electrons from the external substrates, *e.g.*, methanol and alkenes, to the empty p orbital. Once the phosphonate is introduced, the vacant p orbital interacts effectively with the internal phosphonate oxygen anion and therefore is no longer available to the external reagents. In other words, the carbene tends to behave as a nucleophile *via* the carbenic lone pair rather than as an electrophile. Simple alkenes such as but-2-ene are efficient trapping agents for many electrophilic carbenes, but not always reactive towards nucleophilic carbene. On the other hand, methanol is shown to be equally reactive to both electrophilic and nucleophilic carbenes, since the former carbene can attack the lone pair electron of oxygen while the latter undergoes protonation. Thus, the phosphonate carbene (**2**; X = Na) showed enhanced reactivity towards alcohol relative to the alkenes.

It is important to compare our result with that of Bartlett who reported[5] that similar phosphonate carbenes (**6**) generated from the mono- or di-sodium salts of the phosphonates (**5a**), (**5b**), and (**5c**) in methanol do not undergo O–H insertion into the alcohol but give rise to α-hydroxyphosphonate (**9**) and/or phosphate (**10**); they explained their results in terms of the oxaphosphirane anion (**7**) intermediate resulting from intramolecular trapping of the carbenes by phosphonate anion and subsequent protonation and reaction with methanol. The

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[†] When the diazo compounds (**1a,b**) and acrylonitrile were allowed to stand for 2 h at 50 °C, <5% only of the expected cyclopropanes (**12**) was formed. So irradiation was carried out at −10 °C for 0.5 h.

intervention of oxaphosphirane intermediates proposed by Bartlett unambiguously supports the above idea that the phosphonate anion can interact effectively with the carbenic centre. However, we cannot detect the products analogous to (**9**) and (**10**) in our reaction mixtures. The reason for this difference between the carbenes (**2**) and (**6**) probably lies partly in the difference in carbene substituents. Thus, the oxaphosphirane anion intermediate will be greatly stabilized by adjacent strongly electron-withdrawing substituents, *e.g.*, the carbonyl group in the case of carbenes (**6**), and therefore these carbenes will show more anionic than carbenic character. Phenylphosphonylcarbenes (**2**), on the other hand, are stabilized by the interaction of their vacant p orbital with the aromatic π orbital and therefore are less susceptible to accept a negative charge developing at the benzyl carbon atom in the transition state for the formation of oxaphosphirane intermediates. Thus, these carbenes will behave more like a carbene than an anion. Evidence to support the above explanation is obtained by the finding that phenylphosphonylcarbenes (**2**; X = Na) react with alkenes to give cyclopropanes, whereas aminocarbonylphosphonylcarbene (**6c**) affords no trace of cyclopropane when generated in the butenes.[7]

Electrophilic and nucleophilic character are not absolute terms. Any carbene can show both electrophilic and nucleophilic characteristics depending on the nature of reagents with which the carbene reacts.[8] Carbenic philicity has been relatively well characterized[9] on the basis of reactivity towards electron-rich and electron-poor alkenes. Thus, it is of immediate interest to know how the philicity will be affected by the neighbouring phosphonate participation on the basis of cyclopropanation. Thus, the diazophosphonates (**1a**) were irradiated in a binary mixture of hex-1-ene and acrylonitrile under conditions in which the thermal 1,3-dipolar cycloaddition of the diazo compound especially to the electron-poor alkene leading to cyclopropane *via* pyrazoline was negligible,[10] and the selectivities were determined from the product and substrate ratio. The results in Table 2 clearly indicate that the philicity was dramatically changed from slightly electrophilic to highly nucleophilic in going from ester carbene to anion carbene. Thus, the phosphonate anion carbene shows little reactivity towards normal simple alkenes, as has been observed for most typical nucleophilic carbenes, *e.g.*, dimethoxycarbene,[11] diamino- and amino(alkylthio)-carbenes.[12]

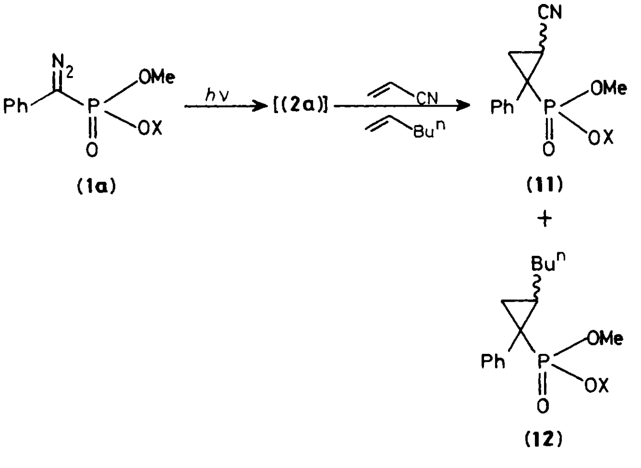

Table 2. Photolysis[a] of diazophosphonate in alkenes. Effect of neighbouring phosphonate groups on selectivities in cyclopropanation

Diazo compd.	X	% Yield[b] (**11**)	(**12**)	k(ac.)/k(hex.)[c]
(**1a**)	Me	38.1	60.5	3.34
	Na	64.2	<1	>340

[a] Irradiations were carried out on a 10 mM solution of (**1**) in a 5.3 : 1 binary mixture of hex-1-ene and acrylonitrile at −10 °C. [b] Determined by g.c. [c] k(acrylonitrile)/k(hex-1-ene).

We have recently found[13] that the neighbouring carboxylate group exerts a similar dramatic effect on the philicity of carbenes and explained this in terms of the neighbouring group participation by carboxylate group as advanced above. While neighbouring group participation by such a typical participating group in carbenium ion chemistry has been extensively and systematically studied,[14] there has been almost no study on its companion 6-electron species, the carbene.[15] Thus, the present findings clearly provide an additional example of typical neighbouring group participation in carbene chemistry and would suggest the generality of this kind of effect which has been well documented in carbenium ion chemistry.

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References

1 See for review, V. Chowdhry and F. H. Westheimer, *Annu. Rev. Biochem.*, 1979, **48**, 293; A. M. Tometsko and F. M. Richards, *Ann. N.Y. Acad. Sci.*, 1980, **346**; H. Bayley and J. R. Knowles, *Methods Enzymol.*, 1977, **46**, 69; J. R. Knowles, *Acc. Chem. Res.*, 1972, **5**, 155.
2 J. A. Goldstein, C. McKenna, and F. H. Westheimer, *J. Am. Chem. Soc.*, 1976, **98**, 7327.
3 P. A. Bartlett and K. P. Long, *J. Am. Chem. Soc.*, 1977, **99**, 1267.
4 P. A. Bartlett, N. I. Carruthers, B. M. Winter, and K. P. Long, *J. Org. Chem.*, 1982, **47**, 1284.
5 P. A. Bartlett and N. I. Carruthers, *J. Chem. Soc., Chem. Commun.*, 1982, 536.
6 W. Kirmse, K. Loosen, and H.-D. Sluma, *J. Am. Chem. Soc.*, 1981, **103**, 5935.
7 H. Tomioka and K. Hirai, unpublished observation.
8 C. Mayor and C. Wentrup, *J. Am. Chem. Soc.*, 1975, **97**, 7467.
9 See for review, R. A. Moss, *Acc. Chem. Res.*, 1980, **13**, 58; 1989, **22**, 15.
10 R. W. Hoffman and M. Reiffen, *Chem. Ber.*, 1976, **109**, 2565.
11 R. W. Hoffman, B. Hagenbruch, and D. M. Smith, *Chem. Ber.*, 1977, **110**, 23.
12 H. Tomioka, K. Tabayashi, and Y. Izawa, *Chem. Lett.*, 1985, 1103.
13 See for example, J. B. Lambert, H. W. Maek, A. G. Holcomb, and E. S. Magyar, *Acc. Chem. Res.*, 1979, **12**, 317.
14 See for review, K. G. Taylor, *Tetrahedron*, 1982, **38**, 2751.