Neighbouring Phosphonate Group Participation in Carbene Chemistry

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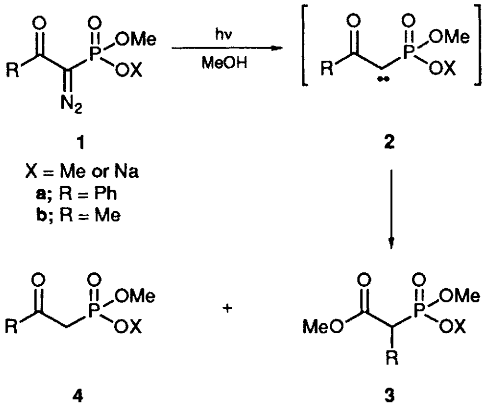
Systematic studies of the effect of the neighbouring phosphonate group on the reactivities of carbene showed that the neighbouring phosphonate group exerts prominent effects on both the product distribution and the reaction products; the results are interpreted as indicating the extent of participation, which seems to be sensitive to the carbenic substituents.

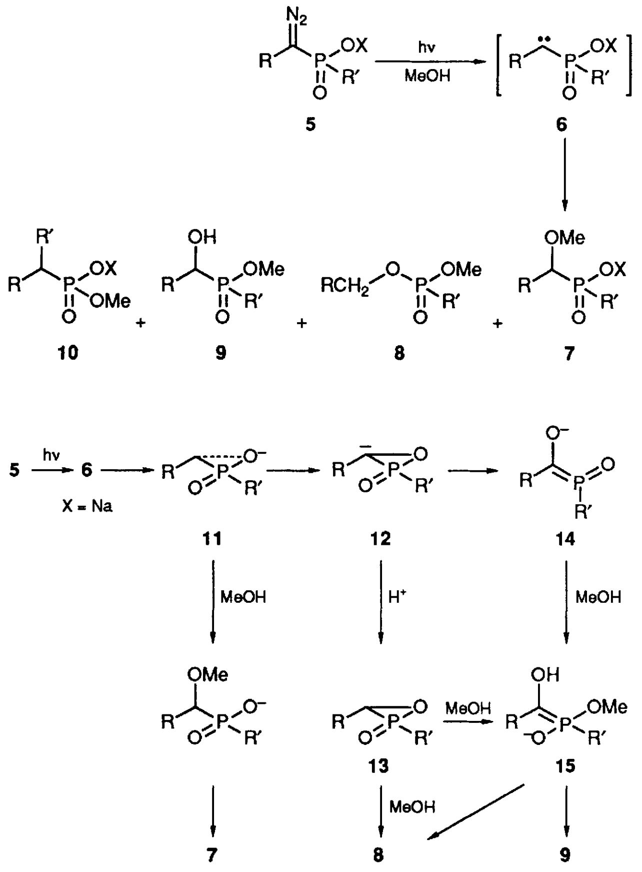
In the nucleophilic displacement reaction, the reactions proceed particularly rapidly and/or with retained stereochemistry when the nucleophile and the leaving groups are in the same molecule.[1] In marked contrast, the effect of the neighbouring group on the reactivity of carbene has been much less dramatic than that in carbenium ion chemistry.[2] This is apparently because carbene is much less electrophilic than carbenium ion. Another reason may be that the internal nucleophiles that have been used in carbene reactions are heavily weighted with neutral heteroatom substituents, *e.g.* ether, carbonyl and halogens.[2] Recently, however, we have found that neighbouring anionic groups such as carboxylate and phosphonate anions, known to act as one of the most effective participants in the nucleophilic displacement reaction, also exert a dramatic effect on the reactivities of carbene.[3,4]

The results are explained by assuming that the vacant p orbital of the singlet carbene interacts effectively with the neighbouring oxygen anion thus suppressing its electrophilicity. In order to obtain a deeper insight into the nature of the interaction, we studied the effect of carbenic substituents on the mode of participation by neighbouring phosphonate anion and found that the extent of participation was highly sensitive to the carbenic substituents.

Irradiation of dimethyl α-diazophenacylphosphonate **1a** (X = Me) in methanol afforded α-methoxycarbonylbenzylphosphonate **3a** and phenacylphosphonate **4a** in a ratio of *ca.* 1:1. However, when the monosodium salt of α-diazophenacylphosphonate **1a** (X = Na) was irradiated under the same conditions, followed by neutralization and esterification by CH_2N_2 the formation of the phenacylphosphonate **4** was almost completely eliminated and the benzylphosphonate **3** became the sole isolable product. A similar but less dramatic effect of ester residue was also observed in the photolysis of the diazo derivatives of acetonylphosphonate **1b**.

It is probable that these products are derived from the photolytically generated carbene **2**, which either undergoes the Wolff rearrangement (WR) leading to **3** or abstracts two hydrogens from the solvent giving rise to **4**. Accepting[5] that the WR takes place in the singlet state of keto carbene while the double hydrogen abstraction is a characteristic reaction of the corresponding triplet, the results suggest that the neighbouring phosphonate anion group completely suppresses the reaction from the triplet state of carbene. This can be interpreted as indicating that the singlet state is stabilized by the neighbouring phosphonate group as a result of the





Scheme 1

Table 1 Photolysis[a] of α-ketodiazophosphonate **1** in methanol

Diazo compound	X	% Yield[b]	
		3	**4**
1a	Me	41.2	32.6
	Na	46.1	0
1b	Me	87.5	12.3
	Na	79.5	0

[a] Irradiations (>300 nm) were carried out on 10 mM degassed solution of **1** in methanol at 0 °C. [b] Determined by GLC.

Table 2 Photolysis[a] of diazophosphinates **5** in methanol

				% Yield[b]			
5	R	R′	X	**7**	**8**	**9**	**10**
a	Ph	OMe	Me	>99	0	0	0
			Na	>99	0	0	0
b	H	Ph	Me	48.7	0	0	35.1
			Na	5.4	52.9	0	1.8
c	MeO_2C	OMe	Me	>99	0	0	0
			Na	0	0	>99	0

[a,b] See footnotes in Table 1.

intramolecular interaction with the vacant p orbital, thus, preventing the intersystem crossing to the triplet state.

Evidence to support the idea that the neighbouring phosphonate anion can strongly interact with the carbenic centre was obtained when the effect of phosphonate groups on the reaction patterns of the carbene was studied by systematically changing the carbenic substituents. Thus, generation of phenylphosphonylcarbene **6a** by irradiation of the corresponding diazomethane **5a** in methanol afforded O–H insertion product **7a** into the alcohol irrespective of substituents X. Similar generation of ester carbene **5b** (X = Me) also afforded O–H insertion product **7b** along with **10b**, the latter being formed as a result of phenyl migration followed by addition of the solvent.[6] Irradiation of the sodium salt of **5b** (X = Na) gave, however, phosphonate **8b** at the complete expense of **7b** and **10b**. However, generation of methoxycarbonylcarbene **6c** (X = Me) in methanol afforded O–H insertion product **7c** as a major product, while similar generation of the corresponding phosphonate anion carbene **6c** (X = Na) again resulted in the almost complete elimination of **7c** but gave rise to the formation of α-hydroxyphosphonate **9c** in this case.

The results clearly showed that the neighbouring phosphonate groups exerted enormous effects not only on both the product distribution and the reaction products; the mode of participation seemed to be sensitive to the carbenic substituents. The formation of apparently migrated products, *i.e.* **8** as well as **9** strongly suggest that the phosphonate anion becomes bonded fully or partially to the carbenic centre during the progress of the reaction. Bartlett *et al.* have also isolated[7] analogous migration products, *e.g.* **8** and **9** in the photolysis of sodium [diazo(dimethylamino)sulphonylmethyl]phosphonate **5** ($R = Et_2NSO_2$, X = Na) and explained in terms of the intermediacy formation of oxaphosphirane **13** as a result of the intramolecular trapping of the carbene centre by phosphonate anion followed by protonation. Subsequent nucleophilic attack of methanol on phosphorus is followed either by P–C bond fission leading to **8** or by P–O bond breaking affording **9**. Although a similar mechanism can be applied to explain the present results, the sensitivity of bond fission selectivity on carbenic substituents cannot be explained in terms of the common oxaphosphirane intermediate **12**. For example, it has been shown[8] that the opening of the ring in azaphosphirane as a result of nucleophilic attack at phosphorus occurs with P–N bond breaking but P–C bond fission increases as electron-withdrawing groups are introduced on the α-carbon. On the contrary, completely reversed trends were observed in the present reactions. Moreover, exclusive formation of the O–H insertion product **7** from carbene **6a** can be interpreted as indicating that the nucleophilic attack should occur on benzylcarbon of the oxaphosphirane intermediate in this case. The results are then better explained by assuming that the extent of the interaction between the carbenic centre and oxygen anion is sensitively changed as carbenic substituents change from Ph **6a** to H **6b** to MeO_2C **6c**. Thus, **6a** is stabilized by the interaction of its vacant p orbital with the aromatic π orbital and, therefore, less susceptible to accept a negative charge developing at benzyl carbon atom in the transition state for the formation of oxaphosphirane intermediates. It is reasonable then to regard **6a** as a typical phosphonate-participating carbene (*e.g.* **11**) that can react with methanol *via* protonation to give **7a**. However, the parent phosphinylcarbene **6b** should be strongly electrophilic and will be quenched by the neighbouring phosphonate oxygen anion leading to the oxaphosphirane anion **12**, which is then immediately protonated by the solvent to give the oxaphosphirane intermediate **13**. Nucleophilic attack of the solvent on phosphorus followed by P–C bond breaking would give the observed product **8b**. Absence of the P–O bond fission product, *i.e.* **9b** in the reaction mixture is not clear at present. It is well-known, however, that α-hydroxyphosphonates rearrange to phosphates when treated with a catalytic amount of base. It may be that **9b** is simply unstable under these conditions and undergoes rearrangement to give **8b**. Carbene **6c** is also expected to be highly electrophilic and will be trapped by intramolecular phosphonate oxygen anion leading to oxaphosphirane anion. The anion must be stabilized by the adjacent CO as well as P=O and should undergo Wolff-type rearrangement of the oxygen anion giving rise to the Wolff intermediate, *i.e.* metaphosphinate **14**, which undergoes addition of the alcohol to produce **9c**. It is well documented[10] that methyleneoxophosphorane bonds are efficiently trapped by the alcohol.

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