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AN IMPROVED PREPARATION OF CYCLOPROPYL PHOSPHONATES AND THEIR APPLICATION IN ARYLIDENE CYCLOPROPANE FORMATION

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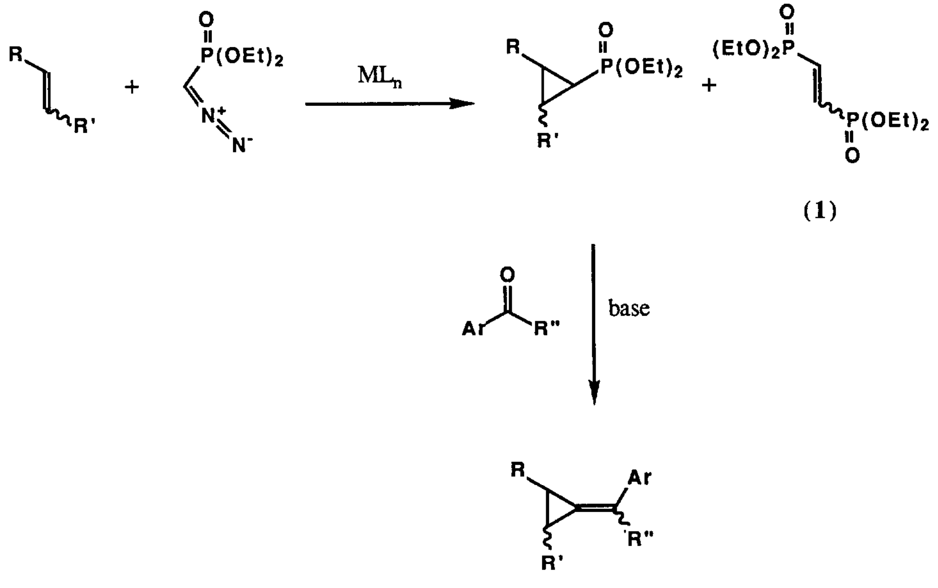
Abstract: Cuprous trifluoromethanesulphonate is a highly efficient catalyst for cyclopropanation of olefins using diethyl diazomethyl phosphonate (DAMP). The resultant cyclopropyl phosphonates undergo Wadsworth-Emmons olefination with aromatic carbonyl compounds.

In order to explore the chemical reactivity of the synthetically versatile alkylidene cyclopropane unit, efficient preparative methods are required; considerable recent activity has been directed towards improved synthetic procedures and incorporation of varied ancillary functionality.[1] In connection with a study of the intramolecular variant of the palladium(0) catalysed [3+2] cycloaddition reactions of alkylidene cyclopropanes to unsaturated acceptors,[2] we required a flexible route to a wide range of variously substituted arylidene cyclopropanes. Since the direct addition of an aryl substituted vinylidene carbene is precluded by competing Wolff rearrangement,[3] we chose to examine the application of the Wadsworth-Emmons reaction *via* intermediate cyclopropyl phosphonates (Scheme 1).



(1)

R" = Ph, H

Scheme 1

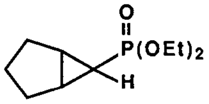
Although a three step process involving Michaelis-Arbuzov reaction of a *gem*-dibromocyclopropane with triethyl phosphite followed by debromination has been proposed as a route to cyclopropyl phosphonates,[4] we elected to reexamine the original one pot procedure of Seyferth[5] whereby the carbene derived by metallic copper induced decomposition of diazomethyl phosphonates is added to an olefin. Yields in this latter process are relatively low, even in the presence of a vast excess of the olefin, because of competing "carbene dimerisation" to give the 1,2-bis(dialkylphosphono)ethene (1).

We reasoned that use of a homogeneous transition metal salt as catalyst in place of copper metal could lead to more efficient generation of an active carbenoid species, and hence, by the appropriate mode of addition, minimize formation of the unwanted phosphonate dimer. Although use of rhodium acetate or rhodium pivalate initiated smooth decomposition of diethyl diazomethyl phosphonate (DAMP) at room temperature, rapid deactivation of these catalysts was observed and repeated additions of fresh catalyst were necessary to drive phosphonate decomposition to completion. It was found that cuprous trifluoromethanesulphonate proved to be a particularly effective catalyst for this reaction, standard conditions requiring slow addition of the diazomethyl phosphonate *via* a syringe pump to a well stirred dichloromethane solution of the olefin and cuprous triflate (≈2.5-5 mole% relative to DAMP) maintained between 4 and 8°C. In contrast to the original procedure, use of a two to three fold excess of olefin is sufficient to minimize competing self-reaction of DAMP, and synthetically valuable olefin is easily recovered. The efficiency of the process may well be a reflection of the ability of cuprous triflate[6] not only to coordinate with olefins, but also to form the copper carbenoid and hence to bring the two reacting species into close proximity on the metal itself. The utility of the sequence is illustrated by a variety of functionalised olefinic substrates (Table 1), the tolerance of acetal groups without competing cleavage being noteworthy.[7]

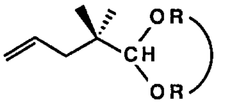
Table 1

Olefin	Cyclopropyl Phosphonate	Yield[(a)](%)
Cyclopentene	(2)	62
Dihydropyran	(3)	71
(4)	(5)	53(76)
(6)	(7)	73
(8)	(9)	64(98)
(10)	(11)	79

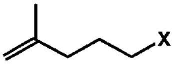
(a) based on DAMP. Yields in parentheses refer to those based on recovered olefins.



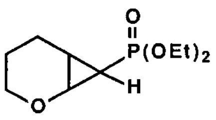
(2)



(4) R = Me
(6) R--R = CH_2-CH_2



(8) X = $OSiMePh_2$
(10) X = Cl



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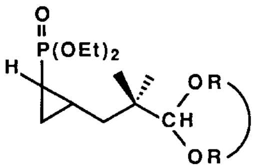
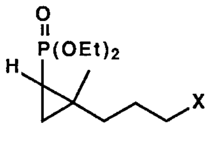
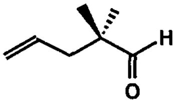


(5) R = Me
(7) R--R = CH_2-CH_2



(9) X = $OSiMePh_2$
(11) X = Cl

It was also of interest to determine that the above procedure is incompatible with aldehydic functionality. Thus, reaction of the olefinic aldehyde (12) gave, in addition to the desired cyclopropyl phosphonate (18%), a 1:1 mixture of two diastereoisomers (16%) whose spectroscopic properties are in accord with their formulation as dioxolanes (13) derived by an unusual reaction of two molecules of aldehyde with one of the diazomethyl phosphonate. A plausible mechanism involving the action of copper(I) as a Lewis acid template,[8] as in (14), may be operative.



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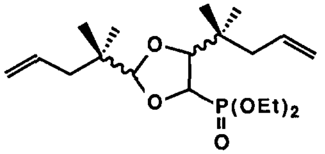

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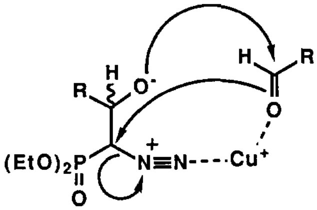


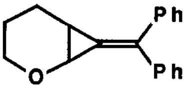
(14)

The second stage of the desired sequence (Scheme 1) requires a particularly demanding test of the Wadsworth-Emmons olefination in formation of the strained tri- or tetrasubstituted double bond of the arylidene cyclopropane system. Some representative examples of the reaction are collected in Table 2.

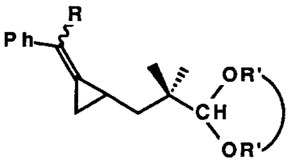
Table 2

Cyclopropyl Phosphonate	Arylidene Cyclopropane	Yield(%)
(3)	(15)	63
(5)	(18)	52(a)
(7)	(16)	81
(7)	(17)	75
(9)	(19)	40(a)

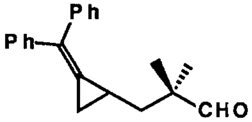
(a) The appropriate deprotection step is included in the work up.



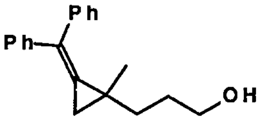
(15)



(16) R = H R'--R' = CH_2-CH_2
(17) R = Ph R'--R' = CH_2-CH_2



(18)



(19)

As is often the case with such reactions, the optimum experimental procedure is substrate dependent. Thus, whereas reaction of phosphonates (3) and (7) with benzophenone and benzaldehyde respectively using n-butyllithium as base furnished olefins (15) and (16) directly, formation of olefins (17) and (18) was best achieved through isolation of the corresponding β-hydroxyphosphonate and subsequent exchange of the lithium counterion for sodium. In this respect, we note that use of sodium hydride in dimethylformamide at 90°C gives improved yields of olefins relative to those reported in similar systems by Hirao[4] using sodium hydride and 18-crown-6 in tetrahydrofuran. Contrastingly, isolation of the β-hydroxyphosphonate from (9) with benzophenone proved impractical and better results were obtained by direct addition of sodium *tert*-butoxide to the initially formed lithium alkoxide. A further observation of interest relating to formation of the first carbon-carbon bond is that the appearance of the typical deep blue colour of benzophenone ketyl is strongly suggestive of an electron transfer component.

In summary, the use of cuprous triflate as a catalyst in the addition of diethyl diazomethyl phosphonate to olefins provides a highly efficient method for formation of cyclopropyl phosphonates, which in turn undergo Wadsworth-Emmons olefination with aromatic carbonyl compounds.

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