Generation of Alkylidenecarbenes by the Alkenation of Carbonyl Compounds with Lithiotrimethylsilyldiazomethane

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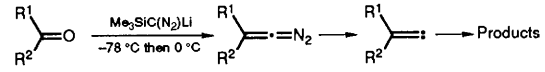
The reaction of carbonyl compounds and lithiotrimethylsilyldiazomethane, which generate alkylidenecarbenes, gives a terminal acetylene from an aldehyde and cyclopentene derivatives from ketones.

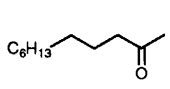
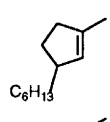
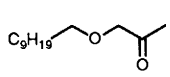
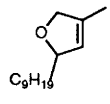
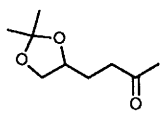
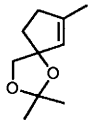
Intramolecular C–H insertion of alkylidenecarbene is a useful reaction to synthesize cyclopentene derivatives.[1] Dimethyl diazomethylphosphonate (DAMP) has been conveniently used for the generation of the carbene by the Wittig–Horner type alkenation of the carbonyl group followed by decomposition of the resulting diazo alkene.[2] We have been using the reagent in our general synthetic strategy to create a new chiral quaternary centre from a chiral tertiary centre;[3] however, DAMP was found to have some shortcomings. The reaction must be carried out at low temperature (−78 °C) over a long period (5–10 h) using an excess (2–3 fold) of reagent and an excess (2–3 fold) of potassium *tert*-butoxide, because of the instability and low nucleophilicity of the corresponding anion of DAMP. In addition, preparation of DAMP on a large scale is troublesome[4] and the safety of the reagent is not well known. Therefore, we attempted to use a safe and easily available reagent trimethylsilyldiazomethane[5] instead of DAMP, applying the analogy of the Wittig–Horner reaction and the Peterson reaction.†

We found that similar results to those with DAMP were obtained by mixing only 1.5 equiv. of lithiotrimethylsilyldiazomethane **1** and carbonyl compounds at −78 °C and warming the mixture to 0 °C. As shown in Table 1, terminal acetylene was obtained from the aldehyde and cyclopentene derivatives from ketones. For comparison, yields of the products when DAMP was used as a reagent under the standard conditions are also shown in parentheses.

No detectable amount of epoxy silane or hydroxy diazo silane was produced under our conditions, although it has been reported that the reaction of **1** and carbonyl compounds gives epoxy silanes after decomposition of the hydroxy diazo silanes.[6]

Table 1 Production of terminal acetylene and cyclopentene derivatives



Isolated yield (%)[a]	Substrate	Product
61 (56)	$C_9H_{19}CHO$	$C_9H_{19}CH{\equiv}CH$
49 (45)		
72 (66)		
72 (68)		

[a] Numbers in parentheses are yields when dimethyl diazomethylphosphonate was used as the reagent in the presence of Bu^{t}OK.

† *Typical procedure*: butyllithium (1.6 mol dm^{-3} in hexane, 0.8 ml, 1.3 mmol) was added to a solution of trimethylsilyldiazomethane (1.0 mol dm^{-3} in diethyl ether, 1.5 ml, 1.5 mmol) in tetrahydrofuran (THF, 2 ml) at −78 °C. After stirring for 30 min, a carbonyl compound (1 mmol) in a small amount of THF was added to the mixture, which was stirred at −78 °C for 1 h and then at 0 °C for 1 h. Saturated aqueous ammonium chloride was added, and the entire mixture was extracted with hexane. The organic layer was dried (Na_2SO_4) and evaporated. The pure product was isolated by column chromatography on silica gel.

It is also known that the reaction of **1** and benzophenone gives the rearranged alkyne in good yield[7] under similar conditions to ours. Although the authors assume there are two different mechanisms, the reaction may include free carbene as an intermediate, since the generation of free alkylidenecarbenes is obvious in our results.

Received, 3rd February 1992; Com. 2/00590E

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