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REGIOSELECTIVE INSERTION OF VINYLIDENE CARBENE INTO α C-H BOND OF ALKOXIDES

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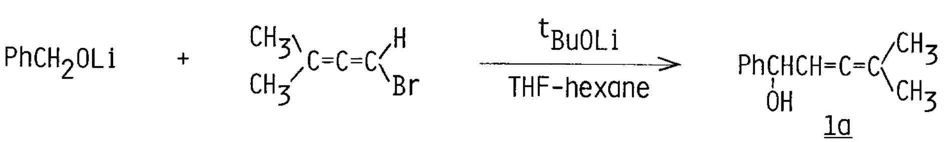
Abstract: Dimethylvinylidene carbene inserted regioselectively into α C-H bond of various alkoxides gave allenylcarbinols in 17-68% yields.

There seems to be ambiguity in the literature concerning the reactivity of vinylidene carbenes (1,2-dienylidenes)[1] to alkoxides and alcohols. Craig and coworkers reported the formation of allenylcarbinols ($R^1CH(OH)CH{=}C{=}CHR^2$) in low yields when they treated 1-bromo-1,2-dienes ($R^2CH{=}C{=}CHBr$) with equimolar amount of sodium alkoxides (R^1CH_2ONa) in aprotic solvent.[2] They clarified that the products were derived from the insertion of vinylidene carbenes into the α C-H bond, they presumed, of alcohols. It is, however, still uncertain under their reaction conditions whether the reactant is the alcohol or the alkoxide. Additionally, it has also been reported that vinylidene carbenes generated in alcoholic solvent gave propargylic ether ($R^1CH_2OC(R^2)(R^3)C{\equiv}CH$) as the main product without the formation of the C-H insertion product.[3] With regard to this argument, we have recently disclosed a novel oxyanionic substituent effect[4] that greatly facilitates the insertion of dichloro-, chlorophenyl-, and (phenylthio)carbene into α C-H bond of alkoxides.[5] In the present communication, we wish to report our results which clearly show the difference between the reactivity of vinylidene carbene to alkoxides and that to alcohols.



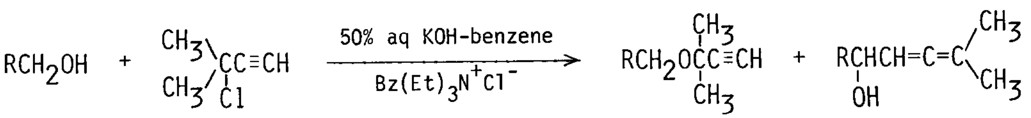
$$PhCH_2OLi + (CH_3)_2C{=}C{=}C(H)Br \xrightarrow[\text{THF-hexane}]{^tBuOLi} \underset{\underline{1a}}{PhCH(OH)CH{=}C{=}C(CH_3)_2} \quad (1)$$

$$PhCH_2OLi + (CH_3)_2C(Cl)C{\equiv}CH \xrightarrow[\text{THF-hexane}]{^nBuLi} \underline{1a} \quad (2)$$

To a solution of lithium benzyloxide (2.5 equiv) and t-BuOLi (2.5 equiv) in THF-hexane was added 1-bromo-3-methyl-1,2-butadiene under nitrogen at room temperature. Total reaction mixture was heated under reflux for 2 h. After aqueous work-up, followed by column chromatography, the allenylcarbinol **1a** was isolated in 65% yield (eq 1) (method A). Alternatively, allenylcarbinols were also obtained employing 3-chloro-3-methyl-1-butyne as a precursor of the carbene (method B). Thus, for example, to a solution of 3-chloro-3-methyl-1-butyne and benzyl alcohol (1 equiv) in THF was added n-BuLi (hexane solution) at -78°C and the mixture was allowed to warm to room temperature taking 1 h. In this reaction **1a** was obtained in 68% yield, based on the alcohol consumed (39% conversion)(eq 2).

Not only benzylic alkoxides, whose C-H bonds are activated additionally by a phenyl substitution,[6] but also various kinds of simple primary and secondary alkoxides underwent regioselective C-H insertion to give the corresponding allenylcarbinols. These results are summarized in Table I. In the reaction of allyl alkoxide, the addition to olefin proceeded competitively (entry 10).

In each reaction, we could not detect the formation of either propargylic or allenic ether. It should be noted that under the present reaction conditions alkoxides, but not alcohols, are the exclusive reactant. In order to clarify the difference in reactivity between alkoxides and alcohols, we examined the reaction of alcohols with vinylidene carbene generated under phase transfer conditions (eq 3).[7,8] The reaction with n-octyl alcohol gave the corresponding propargylic ether **2** (40% yield) together with a trace amount of the C-H insertion product **1c** (<1%). In the reaction of benzyl alcohol, which is expected to be more reactive toward C-H insertion, the propargylic ether and **1a** were obtained in 17% and 16% yield, respectively. These results not only show the difference in reactivity between alkoxides and alcohols, but also suggest the enhancement of the reactivity of α C-H bond of alkoxide by the oxyanionic substitution.[9]

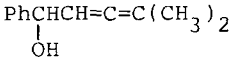
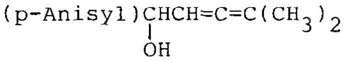
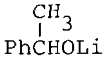
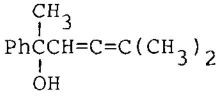
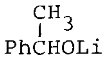
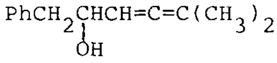
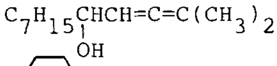
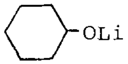
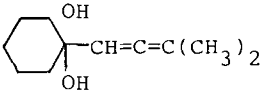
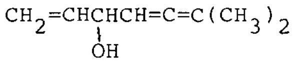
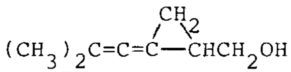


$$RCH_2OH + (CH_3)_2C(Cl)C{\equiv}CH \xrightarrow[Bz(Et)_3N^+Cl^-]{50\%\ aq\ KOH\text{-}benzene} RCH_2OC(CH_3)_2C{\equiv}CH + RCH(OH)CH{=}C{=}C(CH_3)_2 \qquad (3)$$

2 **1**

The present reaction provides a new method for preparing allenylcarbinols, and has the following advantages over the synthesis using the reaction of allenic organometallics and carbonyl compounds.[10] Allenylcarbinols can be obtained without the formation of propargylic transposition by-products. Moreover, optically pure tertiary alcohols can be prepared starting from the readily available optically pure secondary alcohols. As shown in entry 5, when (-)-α-phenethyl alkoxide was allowed to react with the vinylidene carbene, insertion proceeded without racemization to give optically pure alcohol **1c**.[11]

Table I Reaction of Dimethylvinylidene Carbene with Alkoxide[a)]

entry	Alkoxides	Method[b)]	Products[c)]	Yields[d)]
1	$PhCH_2OLi$	A	**1a**;  $PhCH(OH)CH{=}C{=}C(CH_3)_2$	65%
2	$PhCH_2OLi$	B	**1a**	68%
3	(p-Anisyl)CH_2OLi	A	**1b**;  (p-Anisyl)$CH(OH)CH{=}C{=}C(CH_3)_2$	50%
4	 $PhCH(CH_3)OLi$	A	**1c**;  $PhC(CH_3)(OH)CH{=}C{=}C(CH_3)_2$	35%
5[e)]	(-)  $PhCH(CH_3)OLi$ [f)]	B	**1c**	52%
6	$PhCH_2CH_2OLi$	A	**1d**;  $PhCH_2CH(OH)CH{=}C{=}C(CH_3)_2$	50%
7	$PhCH_2CH_2OLi$	B	**1d**	51%
8	$C_8H_{17}OLi$	A	**1e**;  $C_7H_{15}CH(OH)CH{=}C{=}C(CH_3)_2$	35%
9		A	**1f**; 	39%
10	$CH_2{=}CHCH_2OLi$	A	**1g**;  $CH_2{=}CHCH(OH)CH{=}C{=}C(CH_3)_2$	17%
				14%

(a) Unless otherwise noted, reactions were performed employing 2.5 equiv and 1.0 equiv of alkoxides in methods A and B, respectively. (b) For the details of methods A and B, see text. (c) All products showed satisfactory spectral data (IR, ^1H NMR, and mass). (d) Yields refer to the isolated yields after purification by column chromatography. In method B, yields were based on the alcohol consumed. Conversions for entries 2, 5, and 7 were 39, 66, and 31%, respectively. (e) Two equiv of 3-chloro-3-methyl-1-butyne was employed. (f) (-)-α-Phenethyl alcohol was used.

References and Notes

(1) Review: (a) Hartzler, H. D. "Carbenes"; Moss, R. A.; Jones, M., Jr., Eds.; Wiley: New York, 1975; Vol II, Chapter 2. (b) Stang, P. J. *Chem. Rev.* **1978**, *78*, 383.

(2) (a) Beard, C. D.; Craig, J. C.; Solomon, M. D. *J. Am. Chem. Soc.* **1974**, *96*, 7944. (b) Beard, C. D.; Craig, J. C. *Ibid.* **1974**, *96*, 7950.

(3) (a) Hennion, G. F.; Maloney, D. E. *J. Am. Chem. Soc.* **1951**, *73*, 4735. (b) Hennion, G. F.; Boisselle, A. P. *J. Org. Chem.* **1961**, *26*, 2677.

(4) (a) Evans, D. A.; Baillargeon, D. C. *Tetrahedron Lett.* **1978**, 3315, 3319 and references cited therein. (b) Steigerwald, M. L.; Goddard, W. A. III; Evans, D. A. *J. Am. Chem. Soc.* **1979**, *101*, 1994.

(5) (a) Harada, T.; Oku, A. *J. Am. Chem. Soc.* **1981**, *103*, 5965. (b) Harada, T.; Akiba, E.; Oku, A. *J. Am. Chem. Soc.* **1983**, *105*, 2771.

(6) Kirmse, W, "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971; Chapter 7 and references cited therein.

(7) The reaction procedure was as follows: To a vigorously stirred mixture of 50% aqueous KOH (5 mL), benzene (0.4 mL), benzyltriethylammonium chloride (15 mg), and the alcohol (3 mmol) was added 3-chloro-3-methyl-1-butyne (1 mmol) at room temperature, and the total mixture was stirred for 4 h. After aqueous work-up, the products were analyzed by VPC and isolated by column chromatography.

(8) (a) Sasaki, T.; Eguchi, S.; Ogawa, T. *J. Org. Chem.* **1974**, *39*, 1927. (b) Patrick, T. B. *Tetrahedron Lett.* **1974**, 1407.

(9) This is also supported by the following report that benzyl methyl ether did not react with vinylidene carbenes: Patrick, T. B.; Schitzenhofer, D. L. *Tetrahedron Lett.* **1975**, 3259.

(10) Moreau, J. -L. "The Chemistry of Ketenes, Allenes, and Related Compounds"; Patai, S., Eds.; Wiley: New York, 1980; Chapter 10.

(11) Enantiomeric purity of the product was checked using a chiral shift reagent, tris-[*d*,*d*-dicampholylmethanato]europium (III). $[\alpha]^{30}_{D}$ -25° (c 0.77, CCl_4).

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