Regioselective Cyclopropanation of (Dimethylvinylidene)carbene into the α,β-Unsaturated Double Bond of Allylic Alcohols in the Presence of Other Olefinic Groups

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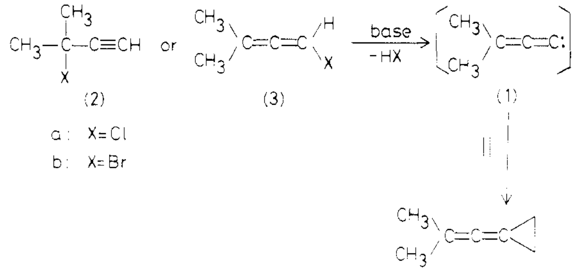
Regioselective cycloaddition of (dimethylvinylidene)carbene (1) into an α,β-unsaturated double in the presence of other olefinic groups to give the corresponding 2-(hydroxymethyl)vinylidenecyclopropanes **8a–e** is described. The reaction is presumably controlled by the allylic hydroxy group, which forms a hydrogen-bonded complex with vinylidenecarbene, or the alkoxide–carbene pair with the carbene C-3 orbital followed by selective addition to the closest α,β-unsaturated double bond.

(Dimethylvinylidene)carbene (**1**), which was generated easily by the elimination of hydrogen halide from propargyl halides **2** or haloallenes **3** has been used extensively in the stereospecific cyclopropanation of olefins to give the corresponding cyclopropanes (Scheme I).[1-5] Raphael and co-workers have completed the synthesis of *trans*-chrysanthemic acid (**6**) by the addition of this unsaturated carbene into α,β-dimethylallyl alcohol (**4**) to give cyclopropane **5** as a key step[6] (Scheme II). However, no extensive studies have been carried out concerning the regioselectivity of vinylidenecarbene addition to the α,β-unsaturated double bond of allylic alcohol in the presence of other carbon-carbon double bonds.

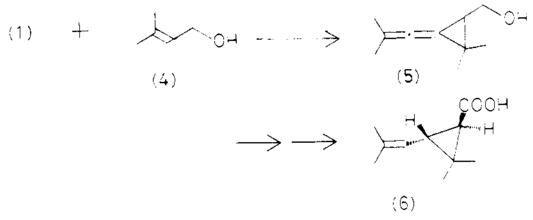
We now report the first example of the regioselective cyclopropanation of vinylidenecarbene to the α,β-unsaturated double bonds of allylic alcohols. Treatment of propargyl chloride (**2a**) with an aqueous solution of potassium hydroxide, a catalytic amount of dibenzo-18-crown-6, and benzene in the presence of dienyl or trienyl allylic alcohols gave cyclopropanes that are the adducts of (dimethylvinylidene)carbene and the α,β-unsaturated double bonds of allylic alcohols (Table I). No evidence for the formation of the cyclopropanes derived from other double bond(s) could be found.[7] The formation of 2-(hydroxymethyl)vinylidenecyclopropanes can be seen easily from ^1H NMR spectra of the methylene hydroxy group that shifted upfield upon cyclopropanation.

Clearly, the reaction is influenced by the hydroxy group of the allylic alcohol. This reaction accomplishes a similar result but proceeds via a different pathway as in the Simmons-Smith reaction although in both cases the hydroxy group plays an important role in the selective addition. In the Simmons-Smith reaction the coordination of (iodomethyl)zinc iodide with a hydroxy group imposed the regio-[8] and stereospecific[9,10] addition of methylene to the α,β-unsaturated double bond of allylic alcohol. However, the formation of 2-(hydroxymethyl)vinylidenecyclopropanes can be explained in terms of a hydrogen-bonded complex between zwitterion carbene and hydroxy group or the anion carbene pair from alkoxide ion and the carbene C-3 orbital proposed by Craig.[11] The free vinylidenecarbene must be anchored by an allylic hydroxy group or alkoxide first, followed by the regioselective addition to the closest α,β-unsaturated double bond during the reaction (Figures 1 and 2).

Scheme I



Scheme II



In conclusion, this methodology provides a rapid, highly regioselective route to 2-(hydroxymethyl)vinylidenecyclopropanes. Due to the versatile chemical properties of vinylidenecyclopropanes,[5,6,12-16] this reaction can be expected to find application in organic synthesis in the future.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 1330 spectrophotometer and ^1H NMR spectra were obtained (with Me_4Si

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[7] The formation of minor amounts of other cyclopropanes is difficult to detect by spectroscopic analysis of the crude product since their signals could be overlapped by those of the starting allylic alcohols and 2-(hydroxymethyl)vinylidenecyclopropanes. However, careful chromatographic analyses (TLC, column chromatography) show that other cyclopropanes do not existed in the crude product.

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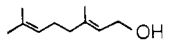
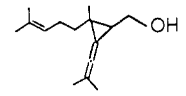
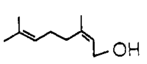
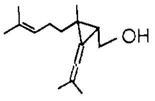
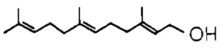
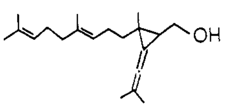
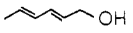
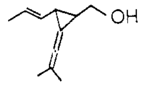
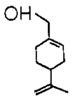
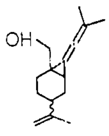
0022-3263/90/1955-5232$02.50/0

Table I

starting material	product	yield, %
 (7a)	 (8a)	43
 (7b)	 (8b)	48
 (7c)	 (8c)	55
 (7d)	 (8d)	27
 (7e)	 (8e)	34

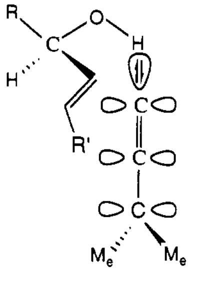


Figure 1. Hydrogen-bonded complex between zwitterion carbene and OH.

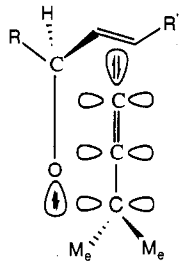


Figure 2. Anion carbene pair from alkoxide ion and carbene C-3 orbital.

as internal standard, δ 0) with a Varian EM-390 spectrometer or a Varian VXR-300/51 FT-NMR. ^{13}C NMR spectra were determined on a Varian VXR-300/51 FT-NMR. Low-resolution mass spectra were obtained on a Finnigan MAT TSQ-46C GC/MS instrument. High-resolution mass spectra were obtained on a JMS-HX 110 mass spectrometer.

General Procedure for the Vinylidene Cyclopropanation. 3-Chloro-3-methyl-1-butyne (**2a**) (20 mmol) was added to a mixture of benzene (25 mL), 50% KOH(aq) (25 mL), and dibenzo-18-crown-6 (0.32 g), in the presence of allylic alcohols **7a–e** (40 mmol). The mixture was stirred strongly over a period of 5 days at room temperature under nitrogen. The mixture was diluted with water (50 mL) and extracted with ether (3 × 30 mL). The combined extracted was dried (Na_2SO_4) and evaporated to afford crude product, which was chromatographed on silica gel (ethyl acetate–hexane, 1:10) to give the corresponding 2-(hydroxymethyl)vinylidenecyclopropanes **8a–e**.

***trans*-2-Methyl-2-(4-methyl-3-pentenyl)-3-(hydroxymethyl)-1-(dimethylvinylidene)cyclopropane (8a)**: colorless oil (43%); IR (CCl_4) 3627 (free OH), 3457 (br, OH), 2011 cm^{-1} (C=C=C); ^{1}H NMR ($CDCl_3$) δ 1.24 (3 H, s, cyclopropyl CH_3), 1.52 (2 H, m, CH_2), 1.61 (3 H, s, olefinic CH_3), 1.68 (3 H, s, olefinic CH_3), 1.71 (6 H, s, allenyl CH_3), 1.86 (1 H, t, J = 7.8 Hz, cyclopropyl CH), 2.09 (2 H, q, J = 7.8 Hz, allylic CH_2), 3.66 (1 H, dd, J = 6.0, 7.8 Hz, OCH), 3.81 (1 H, dd, J = 6.0, 7.8 Hz, OCH), 5.13 (1 H, t, J = 7.8 Hz, vinylic CH); ^{13}C NMR ($CDCl_3$) δ 16.6 (olefinic CH_3), 17.5 (cyclopropyl CH_3), 21.3 (allenyl CH_3), 21.7 (allenyl CH_3), 25.3 (oleinic CH_3), 25.6 (CH_2), 28.2 (C), 32.6 (CH), 39.7 (allylic CH_2), 62.1 (CH_2O), 88.2 (allenyl C-1), 97.9 (allenyl C-3), 124.1 (olefinic CH), 131.5 (olefinic C), 185.8 (=C=); MS, m/e (rel intens) 220 (24), 203 (100), 189 (65); exact mass 220.1835 (calcd for $C_{15}H_{24}O$ 220.1835).

***cis*-2-Methyl-2-(4-methyl-3-pentenyl)-3-(hydroxymethyl)-1-(dimethylvinylidene)cyclopropane (8b)**: colorless oil (48%); IR (CCl_4) 3627 (free OH), 3513 (br, OH), 2008 cm^{-1} (C=C=C); ^{1}H NMR ($CDCl_3$) δ 1.27 (3 H, s, cyclopropyl CH_3), 1.56 (2 H, m, CH_2), 1.61 (3 H, s, olefinic CH_3), 1.68 (3 H, s, olefinic, CH_3), 1.74 (3 H, s, allenyl CH_3), 1.75 (3 H, s, allenyl CH_3), 1.85 (1 H, t, J = 7.5 Hz, cyclopropyl CH), 2.11 (2 H, q, J = 7.5 Hz, allylic CH_2), 3.73 (2 H, m, OCH_2), 5.14 (1 H, t, J = 7.5 Hz, vinylic CH); ^{13}C NMR ($CDCl_3$) δ 17.5 (olefinic CH_3), 21.2 (allenyl CH_3), 21.7 (allenyl CH_3), 23.3 (olefinic CH_3), 25.6 (CH_2), 28.4 (cyclopropyl CH_3), 28.5 (C), 33.3 (allylic CH_2), 34.0 (CH), 61.9 (OCH_2), 88.5 (allenyl C-1), 97.7 (allenyl C-3), 124.2 (olefinic CH), 131.6 (olefinic C), 185.6 (=C=); MS, m/e (rel intens) 220 (3), 189 (100). Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.55; H, 10.93.

***trans*-2-Methyl-2-(4,8-dimethylnona-3,7-dienyl)-3-(hydroxymethyl)-1-(dimethylvinylidene)cyclopropane (8c)**: colorless oil (55%); IR (CCl_4) 3628 (free OH), 3495 (br, OH), 2008 cm^{-1} (C=C=C); ^{1}H NMR ($CDCl_3$) δ 1.25 (3 H, s, cyclopropyl CH_3), 1.52 (2 H, m, CH_2), 1.60 (6 H, s, 2 olefinic CH_3), 1.67 (3 H, s, olefinic CH_3), 1.74 (3 H, s, allenyl CH_3), 1.75 (3 H, s, allenyl CH_3), 1.86 (1 H, t, J = 8.7 Hz, cyclopropyl CH), 1.92–2.51 (6 H, m, 3 allylic CH_2), 3.65 (1 H, dd, J = 8.7, 11.7 Hz, OCH), 3.81 (1 H, dd, J = 8.7, 11.7 Hz, OCH), 5.09 (1 H, t, J = 7.2 Hz, olefinic CH), 5.14 (1 H, t, J = 7.2 Hz, olefinic CH); ^{13}C NMR ($CDCl_3$) δ 15.8 (olefinic CH_3), 16.3 (olefinic CH_3), 17.6 (cyclopropyl CH_3), 21.3 (allenyl CH_3), 21.6 (allenyl CH_3), 25.3 (CH_2), 25.6 (olefinic CH_3), 26.7 (CH_2), 28.4 (C), 32.7 (CH), 39.7 (CH_2), 39.8 (CH_2), 62.0 (CH_2O), 88.4 (allenyl C-1), 97.8 (allenyl C-3), 124.0 (olefinic CH), 124.2 (olefinic CH), 131.2 (olefinic C), 135.1 (olefinic C), 185.7 (=C=); MS, m/e (rel intens) 288 (M^+, 22), 271 (100), 257 (56). Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.09; H, 11.15.

***trans*-2-((*E*)-Prop-1-enyl)-3-(hydroxymethyl)-1-(dimethylvinylidene)cyclopropane (8d)**: pale oil (27%); IR (CCl_4) 3619 (free OH), 3462 (br, OH), 2014 cm^{-1} (C=C=C); ^{1}H NMR ($CDCl_3$) δ 1.67 (3 H, d, J = 5.7 Hz, olefinic CH_3), 1.77 (3 H, s, allenyl CH_3), 1.79 (3 H, s, allenyl CH_3), 1.85–2.33 (2 H, m, cyclopropyl CH), 3.65 (2 H, d, J = 6.9 Hz, CH_2O), 5.16–5.83 (2 H, m, olefinic CH); ^{13}C NMR ($CDCl_3$) δ 17.9 (olefinic CH_3), 21.3 (allenyl CH_3), 21.5 (allenyl CH_3), 27.6 (cyclopropyl CH), 29.7 (cyclopropyl CH), 64.9 (CH_2O), 82.8 (allenyl C-1), 99.3 (allenyl C-3), 125.5 (olefinic CH), 130.4 (olefinic CH), 187.5 (=C=); MS, m/e (rel intens) 164 (M^+, 9), 147 (100), 133 (63); exact mass 164.1198 (calcd for $C_{11}H_{16}O$ 164.1210).

7-(Dimethylvinylidene)-1-(hydroxymethyl)-4-isopropenylbicyclo[4.1.0]heptane (8e): colorless oil (34%); IR (CCl_4) 3640 (free OH), 3500 (br, OH), 2009 cm^{-1} (C=C=C); ^{1}H NMR ($CDCl_3$) δ 1.68 (3 H, s, olefinic CH_3), 1.76 (6 H, s, 2 allenyl CH_3), 1.10–2.30 (8 H, m, 3 CH_2 and 2 CH), 3.53 (2 H, d, J = 7.0 Hz, CH_2O), 4.65 (2 H, br s, olefinic CH); MS, m/e (rel intens) 218 (M^+, 75), 201 (100), 187 (54); exact mass 218.1672 (calcd for $C_{15}H_{22}O$ (218.1660).

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