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DICHLOROCARBENE CYCLOPROPANATION OF ALLYLIC ALCOHOLS

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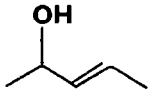
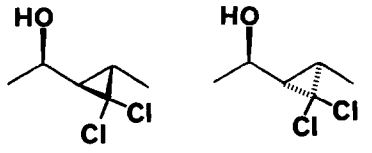
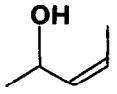
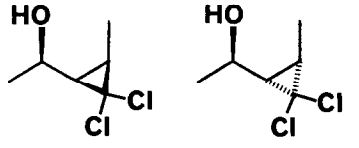
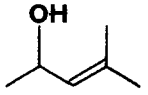
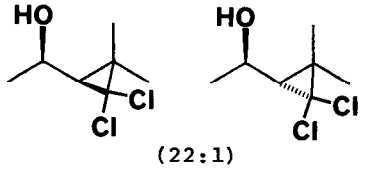
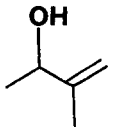
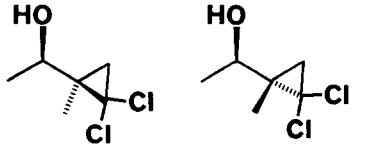
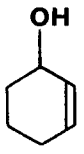
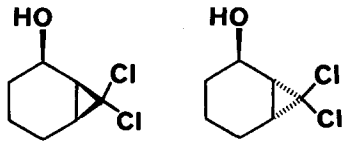
Abstract: Dichlorocarbene reacts with secondary allylic alcohols to form largely a single diastereomeric cyclopropane regardless of the olefin substitution pattern at the position beta to the carbinol carbon.

The observation of oxygen directed epoxidation[1a], hydroboration[1b], osmylation[1c] and hydrogenation[1d] resulting in the formation of a single diastereomer in acyclic systems prompted us to study the cyclopropanation of allylic alcohols with dichlorocarbene[2]. Although oxygen-directed Simmons-Smith cyclopropanation has been used extensively with cyclic alkenes[3], the success of this method in acyclic alkenes depends on the olefin substitution pattern[4].

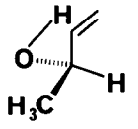
We have found that dichlorocarbene reacts stereoselectively with acyclic secondary allylic alcohols regardless of the olefin substitution pattern at the position beta to the carbinol carbon (Table I). The stereochemical outcome of the cyclopropanation is determined by reductive dechlorination (Li/NH_3) followed by comparison with material obtained from Simmons-Smith cyclopropanation[3,4] of the corresponding allylic alcohol. Authentic samples of the minor diastereomer are prepared by a Mitsunobu reaction[5] ($PhCO_2H/EtO_2CN{=}NCO_2Et/Ph_3P$/benzene), followed by hydrolysis of the inverted benzoate.

TABLE I[8]

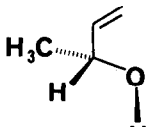
STARTING MATERIAL	REACTION TIME	PRODUCTS	YIELD
	4 hrs.	 (8:1)[9]	68%
	4 hrs.	 (51:1)	75%
	2 hrs.	 (22:1)	77%
	4 hrs.	 (1:1)	53%
	40 hrs.	 (10:1)	54%

Typical procedure: To a solution (1 mmole) of the allylic alcohol in chloroform (2 mL) at 0^{o} C is added benzyltriethylammonium chloride (5 mg). Aqueous 50% sodium hydroxide (1 mL) is added dropwise and the reaction mixture is stirred gently at 0^{o}C until disappearance of starting material as judged by TLC. The reaction is added to water (4 mL) and extracted with diethyl ether (3 x 3 mL). The organic layer is dried ($MgSO_4$) and concentrated in vacuo. The reaction mixture is analyzed by gas chromatography, then purified by flash chromatography.

The formation of the major product is consistent with cyclopropanation from the face containing the hydroxy group of a conformer related to the most stable rotamer (I)[6] of the allylic alcohol. Cyclopropanation of



I



II

Observed relative energy[6a]	0.0 kcal/mole	0.52 kcal/mole
Calculated relative energy[6b]	0.0 kcal/mole	0.60 kcal/mole

cyclohex-1-en-3-ol demonstrates that dichlorocarbene reacts with the olefin from the face of the molecule bearing the alcohol[7]. Since the reaction of the diphenyl t-butyl silyl ether of trans-pent-3-en-2-ol with dichlorocarbene is almost stereorandom (87% yield of a 1.3:1 product distribution), the source of stereoselection in the alcohol may be hydrogen bonding with the active reagent. As expected, a decrease in stereoselectivity is observed in the reaction of 2-methyl but-1-en-3-ol with dichlorocarbene due to an unfavorable $A^{(1,2)}$ strain in the conformer corresponding to rotamer I. The stereochemical outcome of the reaction of but-1-en-3-ol with dichlorocarbene could not be determined, since dichlorocarbene does not react readily with unsubstituted allylic alcohols.

The products of these reactions are of substantial synthetic value since, inter alia, oxymercuration of the reduced forms of these cyclopropane carbinols results in stereoselective formation of 2-methyl-1,3-diols[10].

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2. For an isolated example of a stereoselective reaction of dihalocarbene with an acyclic allylic alcohol see: Kleveland, K.; Skattebol, L.; Sydnes, L.K.; Acta. Chem. Scand. B **31**, 463 (1977).

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7. For reaction of Seyferth's reagent with cyclic allylic alcohols see: Seyferth, D.; Mai, V.A.; J. Am. Chem. Soc. **92**, 7412 (1970).

8. Product distributions are determined by capillary gas chromatography (50 m OV-101 column) and are corrected for molar response factors. All products are characterized by ^{1}H-NMR (270 MHz), ^{13}C-NMR, IR and MS (CI).

9. Stereochemical assignment is made from the ^{13}C-NMR spectrum of the oxymercurated product of the reduced cyclopropane.

10. An application of this method to the synthesis of a natural product is currently in progress in our laboratories.

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