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STEREOSPECIFIC SYNTHESIS OF CIS-DIHALOVINYLCYCLOPROPANECARBOXYLIC ACID

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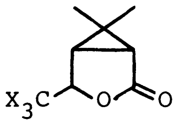
Intramolecular cycloaddition of the carbenoid derived from diazoacetate 4 gave the bicyclic lactone 1. Conversion of the lactone 1 to stereochemically pure cis-dihalovinylcyclopropanecarboxylic acids 7 was achieved by reduction with zinc and acetic acid.

Certain esters of dihalovinylcyclopropanecarboxylic acid are now among the most important chemicals for controlling agricultural pests.1) There are two methods which have been used commercially for preparation of the acid. The one is the addition of diazoacetate to 1,1-dichloro-4-methyl-1,3-pentadiene,2) and the other is the dehydrohalogenation of 3,3-dimethyl-4,6,6,6-tetrachlorohexanoate.3) Under normal conditions, these methods usually afford approximately a 1:1 mixture of cis- and trans-isomers, and the mixture is used for commercial product as it is. Recently, however, much attention has been focused on the cis-isomer, because it gives the most powerful insecticides.4) Several approaches to the cis-isomer have been published in literature.5) All of these utilize cis-3-formyl-2,2-dimethylcyclopropanecarboxylate or its equivalent as a key intermediate and thus require a Wittig condensation for generation of the dihalovinyl function. In order to avoid Wittig conditions and to achieve the total synthesis from readily available materials, we have conceived a route using a bicyclic lactone 1 containing trihalomethyl group on the γ-position of the lactone ring. Theoretically, construction of the three-membered ring in this bicyclic system could be achieved in various ways. In this communication we wish to report a successful approach to the lactone 1 through a carbenoid intermediate.6)



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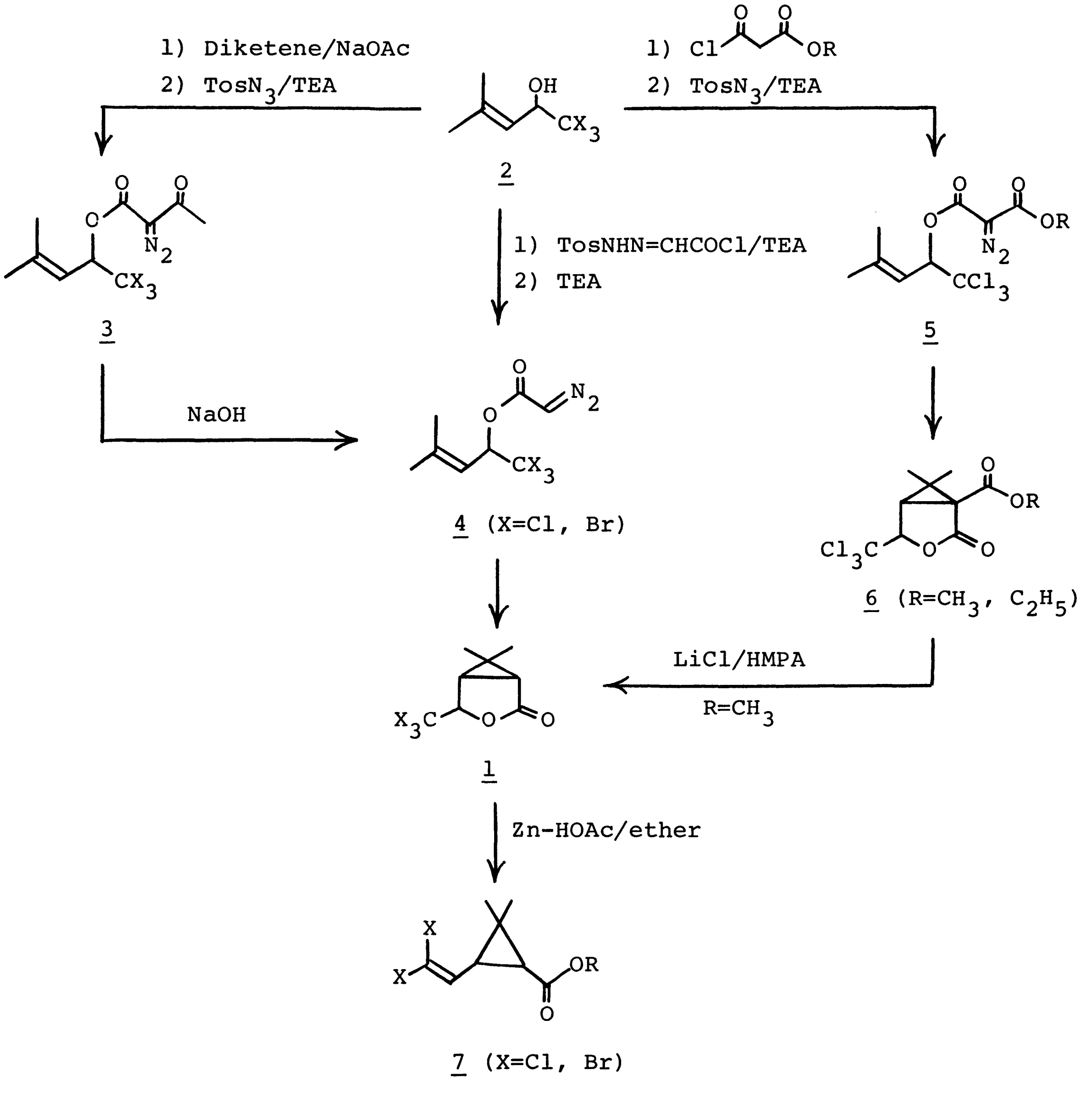
The necessary starting material is 1,1,1-trihalo-4-methyl-3-penten-2-ol 2, which was prepared from isobutene and trichloro- or tribromoacetaldehyde according to the literature procedure.7) As precursors to the carbenoid two diazo compounds, i.e., diazoacetate 4 and diazomalonate 5, were examined. The reaction of the alcohol 2 with diketene in the presence of sodium acetate gave the corresponding acetoacetate in almost quantitative yield. This intermediate was converted to the diazoacetoacetate 3 by reaction with tosylazide in the presence of triethylamine.8) After several trials, it was found that selective removal of the acetyl group in 3 could be accomplished by treatment with sodium hydroxide in aqueous acetonitrile at room temperature. Under these conditions no significant hydrolysis of the ester function was observed. The over-all yields of 4 from the alcohol 2 were 75% for X=Cl and 71% for X=Br. As an alternative route to the diazoacetate 4, we also examined the condensation of 2 with the tosylhydrazone of glyoxylic acid chloride, followed by treatment with base, according to the procedure developed by House.9) By this process the diazoacetate 4(X=Cl) was obtained in 48% over-all yield.

Catalytic decomposition of the diazoacetate 4 was examined under various conditions, and typical results are summarized in Table 1. When the carbenoid was generated by the use of copper or copper(II) oxide as a catalyst, the desired product 1 was obtained in very low yield. However, when the reaction was performed in the presence of a soluble catalyst, such as bis(2,4-pentanedionato)-copper(II), and the diazo compound was slowly added to the refluxing solution containing the catalyst, the trichloromethyl bicyclic lactone 1 could be obtained in 68% yield. Under similar conditions, the tribromo derivative was obtained in 35% yield.



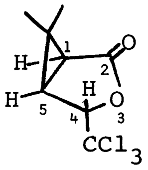
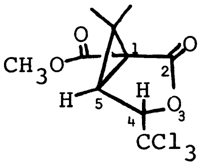
The nmr spectral data of the products obtained are shown in Table 2. The proton assignable to C_4-H was observed as a singlet, and C_1-H and C_5-H as two doublets. This means that the product is composed of single stereoisomer. Inspection of a Dreiding model of the bicyclic lactone having configuration shown in the Table indicates that the dihedral angle between C_4-H and C_5-H is very close to 90°. Furthermore, when we tried to construct the other isomer, with the *gem*-methyl and trichloromethyl on the same side of the γ-lactone ring, trichloromethyl and inside methyl were found too close to each other. Thus we have concluded that the intramolecular cycloaddition of the carbenoid proceeds only in one direction, owing to steric hindrance, and only one bicyclic lactone with the *anti* configuration is obtained.

The sencond precursor to the carbenoid was prepared as follows. Condensation of the alcohol 2 with malonic ester chloride in the presence of pyridine, followed by a diazo transfer reaction with tosylazide and triethylamine, afforded the diazomalonate 5 in 59%(Me) and 73%(Et) over-all yields. Treatment of the diazomalonate 5 in the presence of copper or bis(2,4-pentanedionato)copper(II) afforded the desired alkoxycarbonyl bicyclic lactone 6 in fair yield. Again, C_4-H on the lactone ring was observed as a singlet in the nmr spectrum. The alkoxycarbonyl in 6 must be removed at this stage. Otherwise, if the lactone ring were cleaved, there would be no way to differentiate the cis and trans carboxyl groups. Although the dealkoxycarbonylation was examined under various conditions, the reaction always accompanied partial cleavage of the cyclopropane ring. For example, when the ester lactone 6(R=Me) was treated in HMPA at 100° in the presence of lithium chloride, the bicyclic lactone 1 was obtained in 37% yield. The product was, of course, exactly identical with the one derived from 4.

Table 1. Decompositions of Diazoacetate 4 and Diazomalonate 5

Product	Bp (Mp)	Cat./Solv.	Yield (%)
1 (X=Cl)	91∿3°/0.23 mm	$Cu(AcAc)_2$/Dioxane	68
		$Cu(AcAc)_2$/Toluene	50
		$Cu(AcAc)_2$/n-Octane	8
		Cu/Toluene	2
		CuO/Toluene	12
1 (X=Br)	(101∿3°)	$Cu(AcAc)_2$/Toluene	35
6 (R=Me)	121∿3°/0.3 mm	Cu/n-Octane	45
	(118∿120°)	$Cu(AcAc)_2$/Toluene	55
6 (R=Et)	123∿5°/0.3 mm	Cu/n-Octane	54

Table 2. Nmr Spectra of Bicyclic Lactones 1 and 6

		δ ppm ($CDCl_3$)
	1	4.60 (s, 1H) ($J_{4H-5H} \fallingdotseq 0$) 2.37 (d, 1H) } ($J_{5H-1H}=6Hz$) 2.15 (d, 1H) 1.28 (s, 6H)
	6	4.57 (s, 1H) 3.81 (s, 3H) 2.80 (s, 1H) 1.37 (s, 6H)

Finally, the trihalomethyl bicyclic lactone 1 was converted to cis-dihalovinylcyclopropanecarboxylic acid 7 in almost quantitative yield by treatment with zinc powder and acetic acid in ether. The nmr spectra of the products and GC analyses after treatment of the products with diazomethane clearly indicated the complete absence of trans-isomer in the products.

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