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ASYMMETRIC SYNTHESIS OF PERMETHRIC ACID. STEREOCHEMISTRY OF CHIRAL COPPER CARBENOID REACTION

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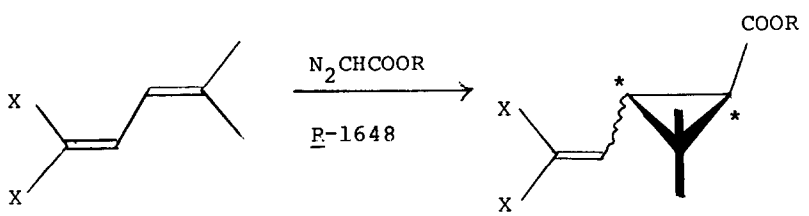
Summary The most effective optical isomer (1R-cis) of permethric acid (2, R = H), a potent intermediate in the production of synthetic pyrethroid, was enantioselectively prepared.

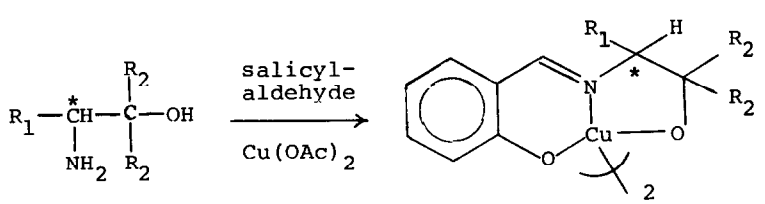
Certain kinds of cyclopropanecarboxylic acids are useful as acid components of synthetic pyrethroids.[1] Optically active form of such a compound produces the more selective insecticide, which is more active to the insects and less toxic to the mammals. Among these carboxylic acids are 1R-trans-chrysanthemic acid (1, R = H) and 1R-cis-permethric acid, namely 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid (2, R = H).

Chiral copper complex catalysed decomposition of diazoalkanes affords optically active products.[2] We applied this chiral carbenoid reaction to the synthesis of alkyl chrysanthemate 1 (Eq. 1, X = methyl). An extensive search has been carried out both for the catalyst[3] and for the diazo compound[4] to achieve an e.e. of 90% and the cis/trans ratio of 10/90. The catalyst of the choice was R-1648 (6, R_1 = methyl, R_2 = 2-octyloxy-5-t-butylphenyl), a copper chelate derived from optically active amino alcohol 5, and the diazo ester employed was l-menthyl diazoacetate.



(Eq. 1)

3 (X = Me), 4 (X = Cl) 1 (X = Me), 2 (X = Cl)



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Based on these observations, it was anticipated that the replacement of 2,5-dimethyl-2,4-hexadiene (3) with 1,1-dichloro-4-methyl-1,3-pentadiene (4) in Eq. 1 would accomplish the asymmetric synthesis of permethric acid 2. Several experiments have been carried out along this line but without success.

l-Menthyl diazoacetate was decomposed in the olefin 4 in the presence of S-1648, the same catalyst of the opposite configuration, to give the ester 2 (R = l-menthyl, bp. 130°/0.3 mm) in 52% yield. GC analysis established the isomeric composition: 1R-cis, 12.3%; 1S-cis, 23.6%; 1R-trans, 15.3% and 1S-trans, 48.8%. The e.e. was calculated to be 31% for the cis isomer and 51% for the trans isomer. The same reaction in the use of R-1648 gave the 1R-trans ester 2 (R = l-menthyl) as the main product (48.4%).

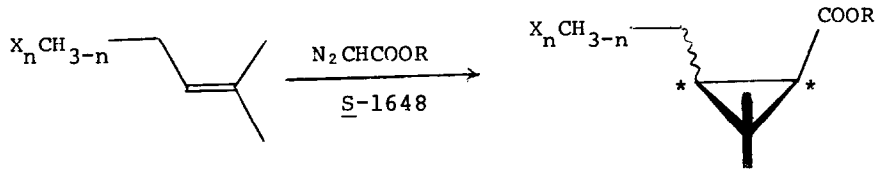
Kuraray explored[5] another kind of olefin, 2-methyl-5,5,5-trichloro-2-pentene (7a, X = Cl, n = 3), as an acceptor of the carbene moiety (Eq. 2). The cyclopropanated product 8a (X = Cl, n = 3) is smoothly converted into permethric acid 2 (R = H) upon treatment with an excess of alkali. Fortunately the employment of the new olefin 7a in our system proved to provide a stereoselective route[6] to the most desired acid 1R-cis 2.

Purified ethyl diazoacetate (bp. 42°/4.5 mm) was added to a solution of the catalyst S-1648 (0.01 equiv.) in olefin 7a (10 equiv.) at 30° in the course of 4.75 hr. A mixture of the adduct 8a (R = ethyl, bp. 80°/0.2 mm) and potassium hydroxide (3 equiv.) in 85% ethanol was heated under reflux for 5 hr to give the acid 2 (R = H) in 92% yield from 8a. Its isomeric composition was established[7] by GC as the corresponding ester 2 (R = d-2-octyl): 1R-cis, 80.6%; 1S-cis, 3.9%; 1R-trans, 8.6% and 1S-trans, 6.9%. The e.e. was calculated to be 91% for the cis isomer and 11% for the trans isomer.

Similarly l-menthyl diazoacetate was decomposed in the presence of the catalyst S-1648 to give the adduct 8a (R = l-menthyl, bp. 120-140°/0.2 mm), which was directly analysed by GC. The isomeric composition was 1R-cis, 81.5%; 1S-cis, 3.1%; 1R-trans, 9.2% and 1S-trans, 6.9%. The e.e. was 93% for the cis isomer and 19% for the trans isomer.

Dramatic change in the product distribution is brought about by the use of monoene 7a in place of diene 3 or 4. First, the thermodynamically less favourable isomer (cis-8a) predominates over the more favoured one (trans-8a). Second, the preferred enantiomer has the opposite absolute configuration at the C-1 carbon atom. Thus, the catalyst S-1648 predominantly gives 1S-trans ester (1 or 2) in Eq. 1 and 1R-cis ester (8a) in Eq. 2.

The crucial role of halogen atoms at the homoallylic position of 7a is evident from the results shown in Table 1. In the reaction of Eq. 2 all the olefins 7b,c,d (X = Cl or Br, n = 1 or 2) gave the products 8b,c,d having the same stereochemistry as 8a.[8]



(Eq. 2)

7 8

Table 1. Asymmetric syntheses of haloethyl-cyclopropanecarboxylic acids

Compound	X	n	R	% Yield	cis/trans	% e.e cis	% e.e trans
a	Cl	3	Ethyl	59	85/15	91	11
			l-Menthyl	54	85/15	93	19
b	Cl	2	Ethyl	71	88/12	85	31
			l-Menthyl	57	86/14	90	24
c	Cl	1	Ethyl	73	84/16	90	51
			l-Menthyl	59	83/17	--*	23
d	Br	1	Ethyl	47	79/21	--*	--*
			l-Menthyl	56	83/17	95	23

Olefin 7b (bp. 58°/20 mm) was prepared by the reduction of 7a with $(n\text{-Bu})_3SnH$. Olefin 7c (bp. 85°/120 mm) and 7d (bp. 48°/20 mm) was obtained by HX treatment of 2-cyclopropyl-2-propanol.

Stereochemical correlation of the product 8b,c,d with 8a was carried out through stepwise reduction with $(n\text{-Bu})_3SnH$.

The products were analysed by GC as d-2-octyl esters or l-menthyl esters.

*) Complete resolution was not achieved.

Appendix Some of the other cyclopropanecarboxylic acids prepared in our laboratory are listed in Table 2. l-Menthyl diazoacetate was decomposed in each one of the olefins in the presence of the catalyst R- or S-1648. The product, l-menthyl cyclopropanecarboxylate, was directly analysed by GC. The results are summarized in the Table.

Table 2. Asymmetric syntheses of substituted cyclopropanecarboxylic acids

Olefin	Catalyst Config.	cis/trans	% e.e. cis	% e.e. trans	Product Config.
Styrene	R	14/86	(+)54	(+)69	1S,2S
	S	18/82	(-)78	(-)81	
1-Octene	R	17/83	46	(+)76*	1S,2S
	S	22/78	64	(-)84*	
trans-4-Octene	R	--	--	(+)82	2S,3S
	S	--	--	(-)84	
trans-Anethole	R	9/91	44	(+)81	
	S	12/88	60	(-)89	
1,1-Diphenylethylene	R	--	--	(+)75*	1S
	S	--	--	(-)64*	
α -Methylstyrene	R	40/60	86	68	
	S	36/64	68	58	

*) Determined by GC as d-2-octyl ester.

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