  Bull. Chem. Soc. Jpn., 59, 221—227 (1986)

A Convenient Synthesis of Ethyl 3-(2,2-Dihaloethenyl)-2,2-dimethylcyclopropanecarboxylates and Its Modifications for cis-Isomer Enrichment[1)]

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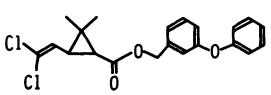
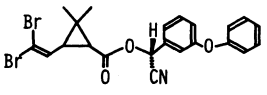
(Received July 19, 1985)

A synthesis of the title compounds **5** involves the reaction between 3-methyl-2-buten-1-ol and triethyl orthoacetate to produce ethyl 3,3-dimethyl-4-pentenoate, which is followed by the addition of various carbon tetrahalides to the double bond. The reaction of resulting adducts with a base affords **5** in high yields. Stereoselective preparation of the cis-isomer was achieved by the following two methods: First one involves selective transformation of ethyl 4-bromo-6,6,6-trichloro-3,3-dimethylhexanoate to ethyl 6,6,6-trichloro-3,3-dimethyl-4-hexenoate (**8a**) with piperidine followed by the selective conversion of **8a** to *cis*-2,2-dichloroethenyl compound (*cis*-**5a**). Second one is based on the stereoselective cyclization of ethyl 4,6,6,6-tetrachloro-3,3-dimethylhexanoate (*t*-BuONa/solvent/HMPA) to ethyl *cis*-2,2-dimethyl-3-(2,2,2-trichloroethyl)cyclopropanecarboxylate which is transformed into *cis*-**5a** without cis-trans isomerization.

The esters of 3-(2,2-dihaloethenyl)-2,2-dimethylcyclopropanecarboxylic acid belong to the most important class of agricultural insecticides at present.[2)] Particularly, 3-phenoxybenzyl ester of the dichloroethenyl analog (permethrin, **1a**) exibits higher activity than natural pyrethroids, moderate stability under natural conditions, and in additon, low mammalian toxicity.[3,4)] Furthermore, one optical isomer of α-cyano-3-phenoxybenzyl ester of the *cis*-dibromoethenyl analog (decamethrin, **1b**) has been known as the most powerful insecticide so far reported.[5)]



permethrin (**1a**)
(*cis*-, *trans*- and racemic mixture)

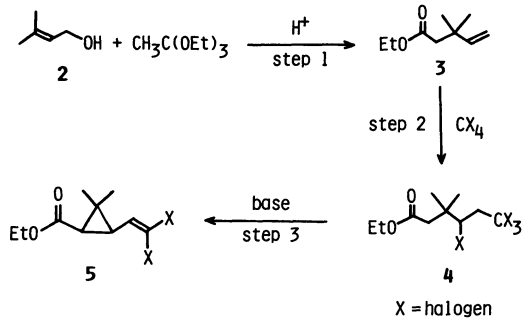


decamethrin (**1b**)

The known methods to prepare the acid moiety of these potent artificial pyrethroids include the followings:[6)] (1) The construction of substituted ethenyl groups by the Wittig reaction of 3-formyl-2,2-dimethylcyclopropanecarboxylate with phosphonium ylides.[7)] (2) Reaction of diazoacetates with appropriate dienes.[8)] (3) Rearrangement of substituted α-halocyclobutanones.[9)] (4) Other methods to construct ethenylcyclopropanes, for example, cyclization of 4-haloalkanoates,[10)] the Michael addition of allylic sulfones to 3-methyl-2-butenoates,[11)] addition of allenic carbenes,[12)] and addition of phosphonium ylides to 4-oxobutenoates.[13)] These methods were, however, difficult to apply to industrial production of the target compounds by following reasons: The starting materials are not readily available, the reagents required are expensive and/or the operation is tedious. Furthermore, these methods usually afforded a mixture of cis- and trans-isomers (cis/trans= 50/50—10/90).

This paper details a new and industrially acceptable method for the synthesis of ethyl 3-(2,2-dihaloethenyl)-2,2-dimethylcyclopropanecarboxylates and its modification for the stereochemically controlled preparation of the corresponding *cis*-dichloroethenyl compound.[14,15)]

The method developed herein is based on the reaction between 3-methyl-2-buten-1-ol (**2**) and triethyl orthoacetate to produce ethyl 3,3-dimethyl-4-pentenoate (step 1), and the subsequent addition of a carbon tetrahalide to the double bond (step 2). The dehydrohalogenation and cyclization of the resulting halide with a base (step 3) afford the desired cyclopropanecarboxylate **5**, as shown in the following scheme.



Scheme 1.

Preparation of Ethyl 3,3-Dimethyl-4-pentenoate 3 (Step 1). The pentenoate **3** was obtained by heating a mixture of 3-methyl-2-buten-1-ol (**2**) and triethyl orthoacetate (TEOA) in the presence of acidic catalyst under the removal of ethanol formed as the reaction proceeded.[16,17)]

The effect of various acidic catalysts on the yield of **3** was studied. Table 1 shows clearly that phosphoric acid is the best catalyst from the viewpoint of the yield and the reaction rate. When phenol was used as the catalyst, 3-methyl-2-butenyl phenyl ehter was obtained as a by-product. The formation of another by-product, i.e., 3-methyl-2-butenyl 3,3,-dimethyl-4-pentenoate (**6**), was observed in all cases in the range

Table 1. Effect of Acidic Catalysts on Preparation of **3**[a]

Catalyst[b]	Reaction time / h	Yield of **3** / %
Phenol	25	76
H_3PO_4	6	81
Oxalic acid	27	65
$(CH_3)_2CHCO_2H$	23	70
$Hg(OAc)_2$	23	69
Hydroquinone	23	51

a) Molar ratio of **2**:TEOA=1:2. b) The amount of the catalyst was 5.0 mol% based on **2** except for case of H_3PO_4 (1.0 mol%).

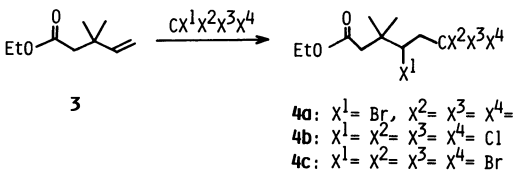
of 5—20% yields. The amount of **6** depended on the molar ratio of **2**/TEOA. The increase of the ratio of TEOA to **2** clearly suppressed the formation of **6** to improve the yield of **3** remarkably up to 89%.

Ethyl bis(3-methyl-2-butenyl) orthoacetate or tris(3-methyl-2-butenyl) orthoacetate would be the precursor of **6**. The possibility of transesterification of **3** giving **6** was excluded by the fact that heating **3** with **2** in the presence of an acidic catalyst did not afford **6**.

Thus, in order to attain the maximum yield of **3**, an excess of TEOA (preferably more than three equivalents to **2**) should be used in the presence of phosphoric acid. Most of the excess orthoacetate can be recovered by fractional distillation.

Addition of Carbon Tetrahalide to 3 (Step 2). The addition was first investigated either in the presence of a radical initiator or under irradiation.[18]

Heating a solution of **3** and AIBN in bromotrichloromethane at 104 °C for 10 h successfully induced the desired addition reaction to afford ethyl 4-bromo-6,6,6-trichloro-3,3-dimethylhexanoate (**4a**) in 89% yield. Similarly, ethyl 4,6,6,6-tetrachloro-3,3-dimethylhexanoate (**4b**) was obtained in 86% yield by refluxing a solution of **3** in carbon tetrachloride in



3

4a: X^1= Br, X^2= X^3= X^4= Cl
4b: X^1= X^2= X^3= X^4= Cl
4c: X^1= X^2= X^3= X^4= Br

the presence of BPO. Addition of carbon tetrabromide to **3** was effected by heating them with AIBN or under irradiation of visible light to afford ethyl 4,6,6,6-tetrabromo-3,3-dimethylhexanoate (**4c**) in 60% yield.

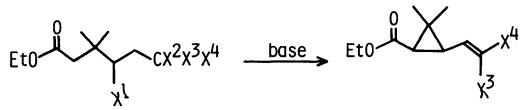
Furthermore, other radical initiators, such as transition metal-amine complexes,[19,20] were found to be good alternatives in carbon tetrachloride case. For example, heating a mixture of DMF and $FeCl_3 \cdot 6H_2O$–$BuNH_2$ complex in carbon tetrachloride at 100 °C for 15 h afforded the desired adduct **4b** in 90% yield. Other than above complex, $FeCl_2$–$BuNH_2$, CuCl–$BuNH_2$, and $Cu(CN)_2$–$BuNH_2$ were found to be also effective. In carbon tetrabromide case, the use of these metal complexes resulted low yields of **4c**.

Preparation of Ethyl 3-(2,2-Dihaloethenyl)-2,2-dimethylcyclopropanecarboxylate (5) (Step 3). This simultaneous cyclization and dehydrohalogenation were successfully achieved by treating the adduct **4** with an appropriate base as shown in Table 2. A wide variety of bases could be utilized for the preparation of dichloroethenyl compound **5a**. In the case of the tetrabromo adduct **4c**, the use of too strong bases such as *t*-BuOK and a high reaction temperature should be avoided because of decomposition of the resulting cyclopropanecarboxylate **5c**. The cis/trans ratio of **5** changed with the reaction conditions used. In general, the use of EtONa or EtOK as a base favored the formation of trans-isomer of **5**.

There was observed the formation of ethyl 2-haloethynyl-3,3-dimethylcyclopropanecarboxylate (**7**) (2—15% yields). The amount of formation of **7** increased when the reaction was carried out at high

Table 2. Preparation of **5** from Adduct **4**

Adduct	Base	Solvent	Temp / °C	Time / h	Product	Cis/trans	Yield / %
4a	*t*-BuOK	THF	60	4	**5a**	45/55	70
4b	*t*-BuOK	THF	22	3			
			60	3.5	**5a**	50/50	73
4b	*t*-BuONa	THF	5	3	**5a**	50/50	92
4b	EtONa	EtOH	22	1			
			80	1.5	**5a**	34/66	94
4b	EtOK	EtOH	22	2			
			80	1.5	**5a**	26/74	96
4b	$NaNH_2$	THF–EtOH	22	5.5	**5a**	50/50	94
4b	EtONa	Heptane	98	22	**5a**	24/76	68
4c	EtONa	EtOH	22	18	**5b**	20/80	79



4a: X^1= Br, X^2= X^3= X^4= Cl
4b: X^1= X^2= X^3= X^4= Cl
4c: X^1= X^2= X^3= X^4= Br

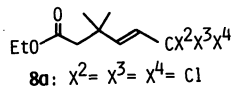
5a: X^3= X^4= Cl
5b: X^3= X^4= Br

temperature or in protic solvents. In general, the reaction with the tetrabromo adduct **4c** gave more amount of the acetylenic compound, i.e., **7b** (10—15%) as compared with the case of the chloro analog (2—10%).

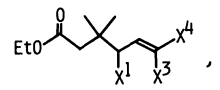
With respect to the reaction mechanism, we observed the formation of three intermediates **8a, 9b,** and **10a** at the beginning of the reaction of **4b** with a base. In the reaction of **4c**, detectable intermediates were only **9c** and **10b**. The ratio of the intermediates formed changed with the reaction conditions. In general, the use of *t*-alkoxide as a base favored the formation of **10**, while the reaction with ethoxide resulted in the predominant formation of **8** and **9**.

As the reaction proceeded, these intermediates formed were gradually converted to **5**. Among the intermediates, the intermediate **9** was found to be the most reactive. The rate of disappearance of **8a** was considerably lower in protic solvents than that in aprotic solvents, while the intermediate **10** was converted into **5** at a moderate rate in both solvents.

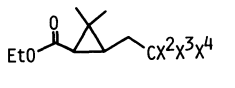
7a: X^4= Cl
7b: X^4= Br



8a: X^2= X^3= X^4= Cl
8b: X^2= X^3= X^4= Br



9a: X^1= Br, X^3= X^4= Cl
9b: X^1= X^3= X^4= Cl
9c: X^1= X^3= X^4= Br



10a: X^2= X^3= X^4= Cl
10b: X^2= X^3= X^4= Br

Stereoselective Preparation of *cis*-5a. The title stereocontrolled preparation becomes interesting target because cis-isomer of above new artificial pyrethroids usually exhibit enhanced insecticidal activity than trans-isomers.[21] To this end, we intended to modify the above process. At the beginning of the reaction at step *3*, three intermediates **7, 8,** and **9** were produced and were gradually converted into **5**. In order to examine the stereochemical aspect of this reaction, we planned to isolate **8a** and **9b** by the treatment of **4a** or **4b** with amines.

Fortunately, selective dehydrohalogenation was achieved. For example, the compound **8a** was prepared by treating **4a** with piperidine in benzene or DMF in 75—85% yields, whereas treatment of **4b** with pyrrolidine in toluene or DMF afforded **9b** in 87—90% yields.[22]

Cyclization of **8a** or **9b** to **5a** was carried out using a variety of bases and solvents. Typical results are summarized in Table 3. Under all conditions examined (run 1—5), the compound **9b** was transformed mainly into *trans*-**5a**. In contrast, the cis/trans ratio of **5a** derived from **8a** changed significantly depending on the reaction conditions. The treatment of **8a** with EtONa in refluxing benzene (run 6) gave **5a** with an isomer ratio of ca. 50/50, while the use of $NaNH_2$ increased the cis content to some extent (run 7). This result suggests that absence of alcohol may favor the formation of *cis*-**5a**.[23] Therefore, the ethanol formed was removed from the reaction mixture as quickly as possible by distillation to afford cis-rich **5a** (run 9). The presence of THF accelerated the cyclization, favoring formation of the cis-isomer (cf. run 7 and 8). As a result, the cyclopropane **5a** of 90% cis content was attained (run 10).

Alternative approach involving stereoselective preparation of *cis*-**10a** from **4b** was also studied. Treatment of **4b** with *t*-BuONa or *t*-BuOK gave **10a** selectively. The cis/trans ratio of the product

Table 3. Cyclization of Intermediates **8a** and **9b** to **5a**

Run	Starting material	Base	Solvent	Temp °C	Yield %	cis/trans
1	**9b**	EtONa	EtOH	25	92	22/78
2	**9b**	EtONa	Benzene	80	≃100	13/87
3	**9b**	*t*-BuONa	Hexane	60	94	17/83
4	**9b**	*t*-BuOK	Toluene	25	78	13/87
5	**9b**	$NaNH_2$	THF	25	98	29/71
6	**8a**	EtONa	Benzene	80	94	54/46
7	**8a**	$NaNH_2$	Benzene	80	88	66/34
8	**8a**	$NaNH_2$	THF	60	98	71/29
9	**8a**	EtONa	Benzene	(80)[a]	92	79/21
10	**8a**	EtONa	Hexane/THF	(60)[a]	94	90/10

a) Ethanol formed during the reaction was removed as an azeotropic mixture.

Table 4. Stereoselective Cyclization of **4b** to **10a**

Run	Base	Solvent	Temp °C	Yield %	cis trans
1	*t*-BuONa	Benzene/ *t*-BuOH	80	74	30/70
2	*t*-BuONa	*t*-BuOH/ HMPA	4—8	86	73/27
3	*t*-BuONa	THF/HMPA	−26	81	79/21
4	*t*-BuONa	Hexane/ HMPA	−60	88	88/12

changed dramatically depending on the solvent and reaction temperature employed. The cyclization in a mixture of benzene and *t*-butyl alcohol at the reflux temperature afforded *trans*-**10a** as the main product (cis/trans=30/70).[24] In contrast, cis-rich **10a** was obtained by carrying out the reaction in hexane in the presence of HMPA at low temperature. Table 4 shows some typical results. The observed stereoselective cyclization of **4b** to **10a** may be attributed to a solvent effect in favor of kinetic control, as no isomerization between *cis*-**10a** and *trans*-**10a** was observed under these conditions. It is worthy to note that the preferential cyclization of γ-halo ester to *cis*-cyclopropanecarboxylate is unprecedented, though the predominant formation of trans-isomer was well-known in the preparation of chrysanthemic acid.[10]

The cyclopropane **10a** (cis/trans=30/70) was transformed into **5a** (cis/trans=28/72) by treating with a base such as EtONa or DBU. Furthermore, the treatment of **10a** (cis/trans=75/25) with NaOH afforded the corresponding carboxylic acid of **5a** (cis/trans=75/25). The original stereochemical integrity was thus retained during these transformations.[25]

In contrast to **4a** and **4b**, tetrabromo adduct **4c** gave **9c** as sole product upon the treatment with DABCO or DBU. Cyclization of **9c** with bases afforded *trans*-**5b** mainly in high yields. When **4c** was treated with a *t*-butoxide ion in a common solvent, such as THF or benzene, *trans*-**10b** was produced again. The highest cis content (50%) of **5b** was obtained upon the successive treatment of **4c** with $NaNH_2$ and DBU in a mixture of *t*-butyl alcohol and hexane, hereby **10b** being the responsible intermediate (glpc).

Experimental

General. All the melting points and boiling points are uncorrected. IR spectra were recorded on a Hitachi EPI-G3 grating spectrophotometer. NMR spectra were measured with Varian HA-100 spectrometer and Hitach-Perkin-Elmer R-20B using TMS as an internal standard. Mass spectra were recorded on Hitachi RMU-6E mass spectrometer (70eV). Analytical determinations by glpc were performed on a Hitachi 163 gas chromatograph (5 mm o.d.×1 m, 2% EGA on Uniport B or diasolid ZS).

General Procedure for the Examination of the Reaction Conditions of Step 1. A catalyst (5.0 mol% except for the case of H_3PO_4 (1.0 mol%)) was added to a mixture of 3-methyl-2-buten-1-ol (**2**)[27] (4.3 g, 50 mmol) and cited amount of TEOA in Tables 1 and 2 at room temperature. The mixture was heated to 140—150 °C under removal of ethanol. The yield of ethyl 3,3-dimethyl-4-pentenoate (**3**) was determined by glpc, decahydronaphthalene being used as an internal standard.

Large Scale Preparation of the Pentenoate 3. A mixture of 43 g (0.50 mol) of **2**, 0.24 kg (1.5 mol) of TEOA and 3.4 ml (50 mmol) of phosphoric acid was heated at 140 °C with stirring for 14 h under removal of ethanol. After excess TEOA was removed, the residue was distilled to give 66 g (85%) of **3**, bp 74—78 °C/55 mmHg† (lit,[17] 35—45 °C (bath)/0.1 mmHg). ^1H NMR (CCl_4) δ=5.86 (dd, 1H), 5.1—4.7 (m, 2H), 4.06 (q, 2H), 2.19 (s, 2H) 1.22 (t, 3H), 1.12 (s, 6H). The elemental analysis gave a satisfactory result.

Ethyl 4-Bromo-6,6,6-trichloro-3,3-dimethylhexanoate (4a). Fifty milligrams of AIBN was added to a solution of 1.6 g (10 mmol) of **3** in 5.0 ml of bromotrichloromethane. The mixture was heated at 104 °C for 10 h. After the unreacted bromotrichloromethane was removed, the residue was distilled to give 3.2 g (89%) of **4a**, bp 102—105 °C/0.1 mmHg. IR (neat): 1730, 1225, 1200, 1155, 1035, 960, 805, 710, 655 cm^{-1}. ^1H NMR (CCl_4) δ=4.49 (dd, 1H), 4.08 (q, 2H), 3.4—3.15 (m, 2H), 2.60 (d, 1H), 2.23 (d, 1H), 1.23 (t, 3H), 1.23 (s, 3H), 1.13 (s, 3H). MS *m/z*: 353 (M^+), 41 (base). Found: C, 33.83; H, 4.35%. Calcd for $C_{10}H_{16}BrCl_3O_2$: C, 33.88; H, 4.55%.

Ethyl 4,6,6,6-Tetrachloro-3,3-dimethylhexanoate (4b). A mixture of 6.2 g (40 mmol) of **3**, 50 ml of carbon tetrachloride and 50 mg of BPO was heated at 80 °C for 20 h under argon atmosphere. After having been cooled to room temperature, the reaction mixture was washed with aq $NaHCO_3$ and water. The mixture was dried ($MgSO_4$) and distilled to give 11 g (86%) of **4b**, bp 107—108 °C/0.15 mmHg. IR (neat): 1730, 1180, 1130, 1090, 975, 800, 685 cm^{-1}. ^1H NMR (CCl_4) δ=4.37 (dd, 1H), 4.07 (q, 2H), 3.40—2.85 (m, 2H), 2.56 (d, 1H), 2.22 (d, 1H), 1.27 (t, 3H), 1.22 (s, 3H), 1.13 (s, 3H). MS *m/z*: 308 (M^+), 46 (base). Found: C, 38.91; H, 5.07; Cl, 45.84%. Calcd for $C_{10}H_{16}Cl_4O_2$: C, 38.74; H, 5.20; Cl, 45.74%.

Addition of Carbon Tetrabromide to 3. a) Using AIBN as a Radical Initiator: Fifty milligrams of AIBN was added to a mixture of 1.6 g (10 mmol) of **3** and 3.3 g (10 mmol) of carbon tetrabromide. The mixture was heated at 120 °C for 5 h under argon atmosphere. The crude product was purified by chromatography (silica-gel column) to give 3.0 g (60%) of ethyl 4,6,6,6-tetrabromo-3,3-dimethylhexanoate (**4c**). IR (neat): 1735, 1220, 1150, 1032, 610 cm^{-1}. ^1H NMR (CCl_4) δ=4.35 (q, 1H), 4.07 (q, 2H), 3.55 (m, 2H), 2.61 (d, 1H), 2.27 (d, 1H), 1.32 (s, 3H), 1.28 (t, 3H), 1.21 (s, 3H). MS *m/z*: 324 (M^+), 88 (base). Found: C,

† 1 mmHg≈133.3 Pa.

24.87; H, 3.25; Br, 65.60%. Calcd for $C_{10}H_{16}Br_4O_2$: C, 24.62; H, 3.31; Br, 65.51%.

b) Addition under Irradiation: A mixture of **3** (0.78 g) and carbon tetrabromide (3.3 g) continuously purged with argon, was irradiated with a 100 W sunlight lamp for 10 h at room temperature. The resulting darkbrown oil was purified by chromatography (silica-gel column) to give **4c** (1.5 g).

Ethyl 3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate (5a). The THF solution of **4a** [0.71 g (2.0 mmol)] (5 ml) was added dropwise to 0.45 g of *t*-BuOK in 15 ml of THF and the mixture was heated under reflux for 2 h. After an additional 0.11 g of *t*-BuOK was added, the mixture was heated under reflux for 1 h. The mixture was poured into aq NH_4Cl and extracted with ether. The ether extract was dried ($MgSO_4$) and concentrated in vacuo. Distillation gave 0.35 g (74%) of **5a**, bp 80—83 °C/0.8 mmHg (lit,[8] 119—120 °C/15 mmHg). IR (neat): 1730, 1182 cm^{-1}. ^1H NMR (CCl_4) δ=6.22 (d, *cis*-H) 5.56 (d, *trans*-H) (total 1H, cis/trans=45/55), 4.05 (bq, 2H), 2.35—1.4 (m, 2H), 1.4—1.05 (m, 9H). MS *m/z*: 236 (M^+), 91 (base). Found: C, 50.44; H, 5.83; Cl, 29.63%. Calcd for $C_{10}H_{14}Cl_2O_2$: C, 50.65; H, 5.95; Cl, 29.90%. The cis- and trans-isomers could be separated by chromatography (silica-gel column). The ^1H NMR spectra of them are identical with those reported.[28] The fore-cut (45 mg) at the above distillation was composed with **5a** and ethyl *trans*-2-(2-chloroethynyl)-3,3-dimethylcyclopropanecarboxylate (**7a**). The acetylenic ester **7a** was alternatively prepared from **5a** by the treatment with NaH in THF-HMPA at room temperature for 14—26 h. *trans*-**7a** (from *trans*-**5a**): Bp 66 °C/1 mmHg. Yield 75%. IR (neat): 2220, 1735, 1280, 1170, 1050 cm^{-1}. ^1H NMR (CCl_4) δ=4.04 (q, 2H), 1.81 (d, 1H), 1.58 (d, 1H), 1.28 (s, 3H), 1.24 (t, 3H), 1.20 (s, 3H). MS *m/z*: 200 (M^+), 127 (base). Found: C, 59.95; H, 6.48; Cl, 17.42. Calcd for $C_{10}H_{13}ClO_2$: C, 59.86; H, 6.53; Cl, 17.67. *cis*-**7a** (from *cis*-**5a**): Yield 28%. ^1H NMR (CCl_4) δ=4.04 (q, 2H), 1.58 (s, 2H), 1.30 (s, 3H), 1.23 (t, 3H), 1.16 (s, 3H). MS *m/z*: 200 (M^+), 127 (base).

The formation of the intermediates **8a** and **10a** was observed at the beginning of the reaction by glpc analysis.

Cyclopropanecarboxylate 5a from the Carbon Tetrachloride adduct 4b. Typical Procedure 1 (*t*-BuONa/THF): A suspension of 4.2 g (22 mmol) of *t*-BuONa in 80 ml of dry THF was cooled to 5 °C. A solution of 3.1 g (10 mol) of the adduct **4b** in 20 ml of dry THF was added dropwise to the above susepnsion and the mixture was stirred at ca. 5 °C for 3 h. The mixture was neutralized with dry HCl in ether and filtered. The filtrate was diluted with ether, washed with water and dried ($MgSO_4$). Distillation gave 2.2 g (92%) of a mixture of *cis*- and *trans*-**5a**, bp 73—78 °C/0.6 mmHg. The cis/trans ratio was 50/50 based on NMR analysis.

Typical Procedure 2 (EtONa/EtOH): To an ethanolic EtONa (prepared from Na metal (1.0 g, 44 mmol) and dry ethanol (80 ml)) was added dropwise, while cooling with ice, 20 ml of an ethanolic solution containing 6.2 g (20 mmol) of **4b**. The mixture was stirred for 1 h at room temperature, then heated under reflux for 1.5 h. The mixture was worked up and distillation of the crude product gave 4.5 g (94%) of **5b**, bp 72—74 °C/0.4 mmHg. The cis/trans ratio was 34/66 based on the glpc analysis (2% EGA, 120 °C).

Ethyl 3-(2,2-Dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate (5b). An ethanolic solution (5 ml) of EtONa (0.62 g) was added dropwise to 1.5 g (3 mmol) of **4c** in 16 ml of dry ethanol under ice cooling. The mixture was warmed to room temperature and stirred for 6 h. An additional 2.5 ml of ethanolic EtONa (about 0.3 g) was added, and the mixture was stirred for another 12 h. The mixture was worked up and distillation gave 0.77 g (79%) of **5b**, bp 98—101 °C/0.4 mmHg (lit,[29] 95—97 °C/0.4 mmHg). IR (neat): 1725, 1223, 1175 cm^{-1}. ^1H NMR (CCl_4): δ=6.72 (bd, *cis*-H), 6.10 (d, *trans*-H) (total 1H, cis/trans=2/8), 4.10 (q, 2H), 2.3—1.5 (m, 2H), 1.5—1.1 (m, 9H). MS *m/z*: 253, 41 (base). Found: C, 37.07; H, 4.40; Br, 49.27%. Calcd for $C_{10}H_{14}Br_2O_2$: C, 36.84; H, 4.33; Br, 49.02%. The fore-cut (74 mg) was mainly composed with *trans*-**7b**. Yield 10%. IR (neat): 2220, 1735 cm^{-1}. ^1H NMR (CCl_4): δ=4.05 (q, 2H), 2.0—1.4 (m, 2H), 1.5—1.0 (m, 9H). MS *m/z*: 245 (M^+), 41 (base).

Ethyl 4,6,6-Trichloro-3,3-dimethyl-5-hexenoate (9b). A solution of pyrrolidine (0.71 mg) in toluene was added to a toluene solution of **4b** (1.6 g). The mixture was stirred at 100—110 °C for 4 h and worked up. Distillation gave 1.2 g (87%) of **9b**, bp 87—90 °C/0.12 mmHg. IR (neat): 1735, 1613, 1220, 1035, 880 cm^{-1}. ^1H NMR (CCl_4) δ=5.96 (d, 1H), 4.85 (d, 1H), 4.06 (q, 2H), 2.41 (d, 1H), 2.23 (d, 1H), 1.23 (t, 3H), 1.11 (s, 6H). Found: C, 44.18; H, 5.39; Cl, 38.65%. Calcd for $C_{10}H_{15}Cl_3O_2$: C, 43.90; H, 5.53; Cl, 38.87%.

Ethyl 6,6,6-Trichloro-3,3-dimethyl-4-hexenoate (8a). Piperidine (5.1 g, 60 mmol) was added dropwise to a solution of ethyl 4-bromo-6,6,6-trichloro-3,3-dimethylhexanoate (**4a**) (11 g, 30 mmol) in benzene (45 ml) at room temperature. The mixture was refluxed for 5 h, diluted with ether, and washed (water, 1 M HCl(1 M=1 mol dm^{-3}), aq $NaHCO_3$, water) and dried ($MgSO_4$). Distillation afforded 7.0 g (85%) of **3a**, bp 82—83 °C/0.5 mmHg. IR (neat): 1730, 1615, 1225, 1175, 1030 cm^{-1}. ^1H NMR (CCl_4) δ=6.26 (d, 1H, *J*=15 Hz), 5.96 (d, 1H, *J*=15 Hz), 4.01 (q, 2H), 2.26 (s, 2H), 1.21 (t, 3H), 1.19 (s, 6H). Found: C, 44.12; H, 5.35; Cl, 38.11%. Calcd for $C_{10}H_{15}Cl_3O_2$: C, 43.90; H, 5.53; Cl, 38.87%.

Rearrangement of 8a to 9b. A solution of **8a** (1.1 g, 4 mmol) in xylene was heated at 130 °C for 5 h under argon atmosphere. The solution was concentrated in vacuo and the residue was distilled to give 0.93 g of a colorless oil which was composed of **9b** (90%) and a by-product (10%). The by-product separated by chromatography (silica-gel column) was identified to be 4-(2,2-dichloroethenyl)-2,2-dimethyl-4-butenolide. Mp 26.5—28.0 °C (lit,[30] 27.0—28.0 °C). IR (neat): 1790, 1625, 1235, 1160, 1000, 920 cm^{-1}. ^1H NMR (CCl_4) δ=5.50 (d, 1H), 4.78 (d, 1H), 2.33 (d, 1H), 2.25 (d, 1H), 1.21 (s, 3H), 1.05 (s, 3H).

Ethyl 3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate (5a) from 8a and 9b (Typical Procedures). From Ethyl 4,6,6-Trichloro-3,3-dimethyl-5-hexenoate (9b). A solution of 0.55 g (2.0 mmol) of **9b** in dry ethanol (2.0 ml) was added dropwise to a solution of Na methal (57 mg, 2.5 mmol) in dry ethanol (10 ml). The mixture was stirred at room temperature for 5 h, cooled with ice and then neutralized by adding dry HCl in ether. The mixture was concentrated to one-tenth its original volume and diluted with ether. The mixture was poured into ice water,

and the ethereal layer was washed (aq $NaHCO_3$, brine) and dried ($MgSO_4$). Distillation gave 0.44 g (92%) of **5a**, bp 75—76 °C/0.25 mmHg. cis/trans=22/78 (glpc, 2% EGA).

From Ethyl 6,6,6-Trichloro-3,3-dimethyl-4-hexenoate (8a). **a) $NaNH_2$/THF**: A solution of the compound **8a** (0.41 g, 1.5 mmol) in dry THF (1.5 ml) was added dropwise to a suspension of $NaNH_2$ (78 mg, 2 mmol) in 20 ml of dry THF. The mixture was heated under reflux with stirring for 5 h poured into ice-water. The aqueous mixture was extracted with ether, washed (aq $NaHCO_3$, brine) and dried ($MgSO_4$). Distillation afforded 0.35 g (98%) of **5a**, bp 72—74 °C/0.2 mmHg. cis/trans=71/29 (glpc).

b) EtONa/Hexane-THF: Dry THF (6 ml) was added to a hexane suspension (20 ml) of EtONa (15 mmol). Then, a solution of **8a** (2.7 g, 9.9 mmol) in hexane (4 ml) was added dropwise to the suspension at the boiling temperature. Ethanol formed was azeotropically removed during the reaction. After 8 h the reaction mixture was worked up as described above. Distillation gave 2.2 g (94%) of **5a**, bp 77—80 °C/0.3 mmHg. cis/trans=90/10 (glpc).

Ethyl 2,2-Dimethyl-3-(2,2,2-Trichloroethyl)cyclopropanecarboxylate (10a). **a) *t*-BuONa/PhH**: To a mixture of *t*-BuOH (60 ml) and dry benzene (30 ml) was added portionwise Na metal (0.28 g, 12 mmol). The resulting mixture was heated under reflux until Na metal disappeared. A benzene solution (5 ml) of **4b** (3.1 g, 10 mmol) was added dropwise and the mixture was stirred for 2 h. Then, the reaction mixture was acidified by introducing dry HCl, diluted with water and extracted with ether. The ethereal layer was washed (aq $NaHCO_3$, brine) and dried ($MgSO_4$). Distillation afforded 2.0 g (74%) of **10a**, bp 78—80 °C/0.1 mmHg. cis/trans=30/70 (glpc). IR (neat): 1730, 1180, 1135, 765 cm^{-1}. ^1H NMR spectrum of trans-isomer (CCl_4) δ=4.08 (q, 2H), 2.85—2.65 (m, 2H), 1.72 (bq, 1H), 1.36 (d, 1H), 1.24 (t, 3H), 1.24 (s, 3H), 1.20 (s, 3H). ^1H NMR spectrum of cis-isomer (CCl_4) δ=4.06 (q, 2H), 3.2—2.95 (m, 2H), 1.7—1.5 (m, 2H), 1.26 (t, 3H), 1.24 (s, 6H). Found: C, 43.80; H, 5.41; Cl, 38.87%. Calcd for $C_{10}H_{15}Cl_3O_2$: C, 43.90; H, 5.53; Cl, 38.87%.

b) *t*-BuONa/Hexane-HMPA: Powdered *t*-BuONa (7.2 g, 75 mmol) was added portionwise to a solution of **4b** (16 g, 52 mmol) and HMPA (10 ml) in dry hexane (50 ml) at −60 °C over a period of 50 min. The mixture was stirred for additional 7 h under cooling and for 12 h at room temperature. Then the mixture was worked up. Distillation gave 12 g (88%) of **10a**, bp 80—83 °C/0.5 mmHg. cis/trans=88/12 (glpc).

Attempted Isomerization between *cis*- and *trans*-10a. **a) *t*-BuONa/Hexane-HMPA**: Powdered *t*-BuOK (30 mg) was added to a solution of *trans*-**10a** (0.54 g) and HMPA (0.40 ml) in hexane (2.0 ml) at −60 °C. The mixture was stirred for 5 h at the temperature and then for 15 h at room temperature. Glpc analysis showed no trans-cis isomerization of **10a** at each temperature.

b) LDA/THF: A solution of LDA in THF (0.40 ml, 0.20 mmol) was added to a solution of *cis*-**10a** (0.54 g) in dry THF (2.0 ml) at −10 °C. The mixture was stirred for 6 h at the temperature and then for 12 h at room temperature. Glpc analysis indicated no cis-trans isomerization.

Ethyl 3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate (5a) from 10a. A solution of **10a** (cis/trans=30/70) (2.7 g, 9.9 mmol) in dry ethanol (20 ml) was added dropwise to an ethanolic NaOEt (prepared from Na metal (0.25 g, 11 mmol) and dry ethanol (80 ml)). The mixture was heated under reflux for 5 h. The reaction mixture was worked up as described above. Distillation afforded 1.9 g (80%) of **5a**, bp 75—76 °C/0.25 mmHg. cis/trans=28/72 (glpc).

3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic Acid from 4a. A solution of **4a** (cis/trans=75/25) (9.6 g, 35 mmol) in ethanol (5 ml) was added dropwise to a solution of NaOH (6.0 g, 0.15 mmol) in water (30 ml) and ethanol (5 ml). The mixture was heated at 100 °C for 5 h under vigorous stirring. The reaction mixture was washed with ether. The aqueous layer was acidified with concd HCl and extracted with ether–AcOEt (2:1). The latter organic layer was washed with brine and dried ($MgSO_4$). Distillation gave 6.3 g (86%) of the desired acid as a viscous oil, bp 105 °C/0.3 mmHg. cis/trans=75/25 (glpc after esterification with CH_2N_2).

Ethyl 4,6,6-Tribromo-3,3-dimethyl-5-hexenoate (9c). An ethanolic solution of EtONa (prepared from Na metal (94 mg, 4.1 mmol) and dry ethanol (5 ml)) was added dropwise to an ice-cooled solution of ethyl 4,6,6,6-tetrabromo-3,3-dimethylhexanoate (**4c**) (2.0 g, 4.1 mmol) in dry ethanol (10 ml). After 2 h the reaction mixture was worked up as described above. Distillation afforded 0.85 g (51%) of **9c**, bp 130—133 °C/0.3 mmHg. IR (neat): 1730, 1600, 1225, 1150, 1030 cm^{-1}. ^1H NMR (CCl_4) δ=6.64 (d, 1H), 4.95 (d, 1H), 4.12 (q, 2H), 2.38 (bd, 2H), 1.4—1.1 (m, 9H). Found: C, 29.78; H, 3.65; Br, 58.67%. Calcd for $C_{10}H_{15}Br_3O_2$: C, 29.51; H, 3.71; Br, 58.91%.

Ethyl 3-(2,2-Dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate (5b). **a) EtONa/EtOH**: A solution of **4c** (0.41 g, 1.0 mmol) in dry ethanol (1.5 ml) was added dropwise to an ethanolic EtONa (prepared from Na metal (30 mg, 1.3 mmol) and dry ethanol (5 ml)) at room temperature. After 3 h the reaction mixture was worked up and distillation gave 0.27 g (83%) of **5b**, bp 95—98 °C/0.3 mmHg. cis/trans=20/80 (NMR).

b) *t*-BuONa and DBU/*t*-BuOH-Hexane: To an ice-cooled solution of **4c** (9.8 g, 20 mmol) in *t*-BuOH (40 ml) and hexane (20 ml), $NaNH_2$ (1.2 g, 31 mmol) was added portionwise. The mixture was stirred for 1 h at 4—5 °C and for 1 h at room temperature. Then, DBU (3.1 g, 21 mmol) was added to the mixture at 4—5 °C. The mixture was stirred at room temperature for 45 min then heated under reflux for 5 h. After acidified with 1 M HCl, the mixture was evaporated in vacuo. The residue was extracted with ether and the ethereal solution was washed (aq $NaHCO_3$, brine) and dried ($MgSO_4$). Distillation gave 5.7 g (87%) of **5b**, bp 88 °C/0.1 mmHg. cis/trans=50/50 (NMR).

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