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The Allylic Rearrangement. II.[1] Reactions of 5,5,5-Trichloro-3-penten-2-one with Nucleophiles[2]

Akira TAKEDA, Sadao TSUBOI, Takashi MORIWAKE, and Eiji HIRATA

Department of Synthetic Chemistry, School of Engineering, Okayama University, Tsushima, Okayama

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Reactions of 5,5,5-trichloro-3-penten-2-one (**1**) with a number of nucleophiles have been carried out. It was found that the Grignard reagents (**5**) primarily attacked the carbonyl carbon of **1** yielding the corresponding tertiary alcohols (**7**). The reaction sequence of ethylmagnesium bromide (**5a**) is given as an example. The reaction of **5a** with **1** gave 6,6,6-trichloro-3-methyl-4-hexen-3-ol (**7a**) as the major constituent of the primary product. The hexenol **7a** readily underwent the allylic rearrangement by heating at distilling temperature (88—90°C/6 mmHg) to afford 4,6,6-trichloro-3-methyl-5-hexen-3-ol (**8a**), which was in turn converted into 6,6-dichloro-3-methyl-3,4-epoxy-5-hexene (**9a**) by treatment with sodium methoxide. The stereoselective synthesis of *dl-erythro*-4,6,6-trichloro-3-methyl-5-hexen-3-ol (**8a**-I) was achieved by using 3,5,5-trichloro-4-penten-2-one (**3**) as the starting material in place of **1**. *dl-trans*-6,6-Dichloro-3-methyl-3,4-epoxy-5-hexene (**9a**-I) was derived by the cyclization of **8a-I** with a base. The stereochemistry of **8a** and **9a** was discussed on the basis of NMR data. Nucleophiles such as methanol, hydrogen chloride, anilines, thiophenol, sodium acetate, sodium phenolate, and diethyl sodiomalonate gave the products of the conjugate addition (**15**). Ethyl sodioacetoacetate gave 2-chloro-3-acetonyl-4-ethoxycarbonyl-5-methylfuran (**17**).

As a class of compounds with polyfunctionality 3,3,3-trichloro-1-propenyl ketones have attracted the attention of several authors.[3a] Nevertheless, only a little is known of their chemical properties, and their behavior toward nucleophiles still remains uninvestigated. We have recently reported on the allylic rearrangement of 5,5,5-trichloro-3-penten-2-one (**1**) and phenyl 3,3,3-trichloro-1-propenyl ketone (**2**), and also some reactions of the rearranged products (**3**, and **4**) as an α-chloroketone.[1] To extend our knowledge of its chemical properties we carried out reactions of compound **1** with a number of nucleophiles such as ethylmagnesium bromide (**5a**), methylmagnesium iodide (**5b**), phenylmagnesium bromide (**5c**), diethyl sodiomalonate, ethyl sodioacetoacetate, methanol, and anilines. This paper will describe and discuss the results of these reactions.

$$CCl_3\text{-}CH\text{=}CH\text{-}\underset{\underset{O}{\|}}{C}\text{-}R \rightleftharpoons Cl_2C\text{=}CH\text{-}\underset{Cl}{CH}\text{-}\underset{\underset{O}{\|}}{C}\text{-}R$$

1, $R=CH_3$ **3**, $R=CH_3$

2, $R=C_6H_5$ **4**, $R=C_6H_5$

It was found that the Grignard reagent (**5**) primarily attackted the carbonyl carbon of **1** yielding the corresponding tertiary alcohols (**7**). The reaction sequence of ethylmagnesium bromide (**5a**) is given in Scheme 1 as an example. When **5a** reacted with **1** at a lower temperature (−10—−30°C), *trans*-6,6,6-trichloro-3-methyl-4-hexen-3-ol (**7a**) was formed as

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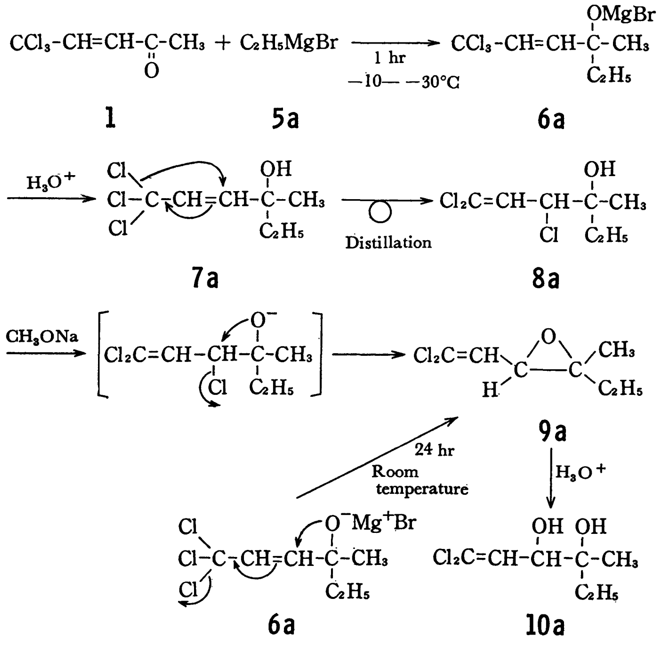
[1] The first paper of this series: A. Takeda and S. Tsuboi, *J. Org. Chem.*, **35**, 2690 (1970).

[2] Presented in part at the 20th Anniversary Local Meeting of Chugoku-Shikoku Branch, the Chemical Society of Japan, October 7, 1970 (Hiroshima).

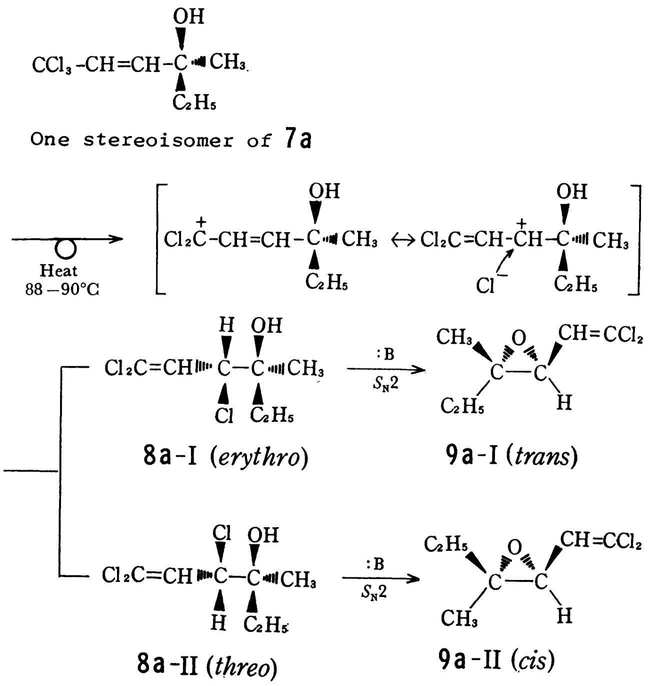
[3] a) H. Gault and G. Mennicken, *C. R. Acad. Sci. Paris*, **229**, 1239 (1949). b) I. Salkind, *J. Russ. Phys. Chem. Soc.*, **30**, 906 (1898).

the sole primary product in a 53% yield together with a trace of 6,6-dichloro-3-methyl-3,4-epoxy-5-hexene (**9a**).[4] It is reasonable to consider that the highly electron-withdrawing group of trichloromethyl retards the transfer of the ethylenic electrons to the carbonyl carbon, thus preserving its reactivity to afford the 1,2-adduct rather than the 1,4-adduct, since the reaction of Grignard reagents with alkylideneacetone tends to result in the predominant formation of the 1,4-adducts.[5] Kohler[6] also reported that the 1,4-adduct, *i. e.* phenyl 3,3,3-trichloro-2-phenylpropyl ketone (**15j**) was the only product in the reaction of the ketone **2** with phenylmagnesium bromide (**5c**), but we confirmed that both the ketone **15j** and the 1,2-adduct, *i.e.* 4,4,4-trichloro-1,1-diphenyl-2-buten-1-ol (**7e**), were formed in a ratio of 3 : 4 in the same reaction.



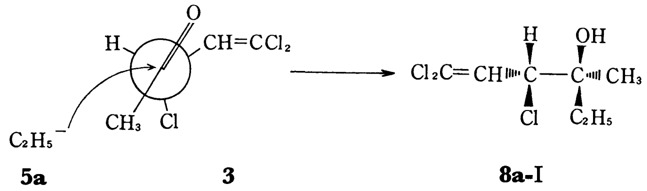
Scheme 1.

The chlorine atom of the hexenol **7a** is so labile on heating that it readily undergoes the allylic rearrangement to afford 4,6,6-trichloro-3-methyl-5-hexen-3-ol (**8a**) at distilling temperature (88—90°C/6 mmHg). The hexenol **8a** exists in two diastereomeric forms, *i.e. dl-erythro* (**8a**-I) and *dl-threo* (**8a**-II), which correspond to the peaks with the retention times[7] of 13.5 min (**8a**-I) and 14.5 min (**8a**-II) on glpc but were indistinguishable by means of either tlc[8] or by IR spectrum. The planar structure of the intermediate carbonium ion enabled the chlorine atom of **7a** to migrate to its allylic position, from both sides of the plane with equal chances, yielding a mixture of nearly equal amounts of the diastereomers, **8a**-I and **8a**-II. The hexenol **8a** was further transformed into the epoxide **9a** in a 33% yield by treatment with a base in dry ether, which also consisted of two diastereomeric epoxides, **9a**-I and **9a**-II. The steric course of these reactions is illustrated in Scheme 2.



Scheme 2.

The stereoselective synthesis of **8a**-I was achieved by using the ketone **3** as the starting material in place of **1**. It is presumed from Cram's rule[9] that the reagent **5a** can attack the carbonyl carbon of the ketone **3** more readily from the opposite side of the 2,2-dichlorovinyl group as shown in Scheme 3. In fact the reaction of **5a** with **3** afforded only the hexenol **8a**-I in a 73% yield, which was then converted into *trans*-6,6-dichloro-3-methyl-3,4-epoxy-5-hexene (**9a**-I) in a 88% yield. The *trans* structure of **9a**-I was supported by NMR data, the signal due to the methyl protons appearing at a higher field (δ, s, 1.24 ppm) in **9a**-I than the



Scheme 3.

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[4] On March 30, 1971, we received a copy of the doctoral dissertation of Mr. François de Champs submitted to the Faculty of Science, the University of Paris, on October 31, 1970, entitled "Etude de la transposition allylique et de quelques proprietes de cetones α,β-ethyleniques γ,γ,γ-trichlorees". Champs obtained similar results. He suggested the possible formation of an epoxide in a small quantity.

[5] E. R. Alexander and G. R. Coraor, *J. Amer. Chem. Soc.*, **73**, 2721 (1951).

[6] E. P. Kohler, *Am. Chem. J.*, **38**, 511 (1907); *Chem. Abstr.*, **2**, 824 (1908).

[7] Column, 10% Apiezon Grease L on Chromosorb W, 3 mm×1 m; column temp., 120°C; carrier gas, N_2 (0.5 kg/cm², 42 m*l*/min); detector, FID.

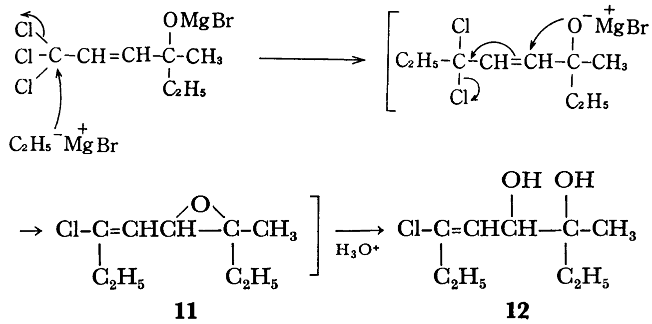
[8] Conditions of preparative tlc: support, silica gel G (E. Merck AG, Darmstadt), 0.8 mm; developer, *n*-hexane-acetone-chloroform (5 : 2 : 1, v/v); eluent, acetone.

[9] D. J. Cram and F. A. Abd Elhafez, *J. Amer. Chem. Soc.*, **74**, 5828 (1952); D. J. Cram and K. R. Kopecky, *ibid.*, **81**, 2748 (1959); J. H. Stocker, P. Sidisunthorn, B. M. Benjamin, and C. J. Collins, *ibid.*, **82**, 3913 (1960).

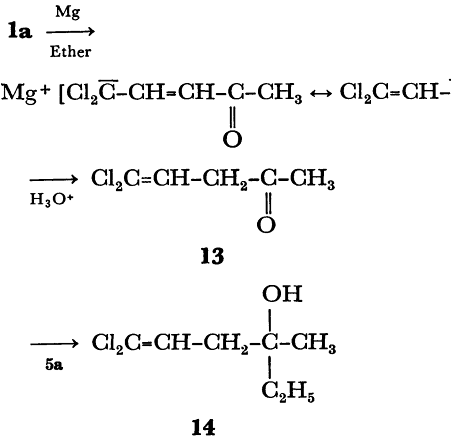
methyl protons of the diastereomeric epoxide **9a**-II (δ, s, 1.30 ppm).[10] A similar differential shielding effect of the 2,2-dichlorovinyl group was also observed in 5,5-dichloro-2-methyl-2,3-epoxy-4-pentene (**9b**), which exhibited the signal due to the *cis* methyl protons at δ 1.28 ppm and the signal due to the *trans* methyl protons at δ 1.34 ppm. The prolonged reaction of **1** with **5a**, being conducted at room temperature, caused the cyclization of the intermediate **6a** to afford the epoxide **9a** in a 25% yield. It is assumed that the cyclization occurred in a concerted manner in which the oxyanion of **6a** attacks the carbon atom allylic to the chlorine of the trichloromethyl group as shown in Scheme 1. The treatment of the epoxide **9a** (**9a**-I/**9a**-II = *ca.* 1 : 1) with a 20% H_2SO_4 gave an epimeric mixture of 6,6-dichloro-3-methyl-5-hexene-3,4-diol (**10a**) in a 52% yield. The same treatment of the *trans* isomer (**9a**-I) gave *dl-erythro*-6,6-dichloro-3-methyl-5-hexene-3,4-diol (**10a**-I).

When the reagent **5a** was used in much excess in the Grignard reaction, 6-chloro-3-methyl-5-octene-3,4-diol (**12**) was obtained in addition to the compounds **8a** and **9a**. Small amounts of the by-products such as 5,5-dichloro-4-penten-2-one (**13**) and 6,6-dichloro-3-methyl-5-hexen-3-ol (**14**) were also isolated. The possible ways in which compounds **12**, **13**, and **14** were produced are shown in Schemes 4 and 5.[11] The pentenone **13** was prepared in a 29% yield in an alternative synthesis from **1** and magnesium.

The yields, properties, spectral data, and analyses of the tertiary alcohols **7**, the rearranged alcohols **8**, and the epoxides **9** obtained in analogous ways are listed in Tables 1, 2, and 3 respectively.

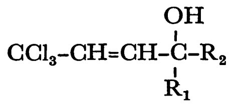


Scheme 4.



Scheme 5.

Nucleophiles such as methanol,[12a] hydrogen chloride, aniline, thiophenol gave the products of conju-

TABLE 1.  **7**

$$\mathrm{CCl_3\text{-}CH{=}CH\text{-}\overset{\overset{\textstyle OH}{|}}{\underset{\underset{\textstyle R_1}{|}}{C}}\text{-}R_2}$$

Compd.	R_1	R_2	Procedure Ketones	 Grignard Reagent	Yield %	Anal (Calcd), % C	 H	IR (cm^{-1}, liquid)	NMR δ ppm
7c	CH_3	C_6H_5	**1**	**5c**	58	52.64 (52.94	4.17 4.45)	3500 (OH) 1625 (C=C)	1.64 (s, 3H, $-CH_3$) 2.56 (s, 1H, -OH) 6.42 (2d, 2H, -CH=CH-) 7.30 (broad s, $-C_6H_5$)[a]
7d	C_6H_5	C_2H_5	**2**	**5a**	45[c]	51.32 (51.55	4.75 4.69)	3550 (OH) 1625 (C=C) 1605 and 1590 (benzene ring)	0.87 (t, 3H, J=7.5 Hz, $-CH_2\underline{CH_3}$) 1.92 (q, 2H, J=7.5 Hz, $-\underline{CH_2}CH_3$) 2.10 (s, 1H, -OH) 6.43 (s, 2H, $-\underline{CH}{=}\underline{CH}-$) 7.31 (broad s, $\underline{5H}$, $-\underline{C_6H_5}$)[a]
7e	C_6H_5	C_6H_5	**2**	**5c**	57[c]	58.90 (58.66	3.93 4.00)	3510 (OH) 1625 (C=C) 1605 and 1586 (benzene ring)	2.50 (s, 1H, -OH) 6.50 and 6.90 (2d, 2H, -CH=CH-) 7.31—8.00 (m, 10, $2\text{-}C_6H_5$)[b]

a) Measured in CCl_4. b) Measured in $CDCl_3$. c) In addition to 1,2-adducts, 1,4-adducts were also obtained (see Experimental).

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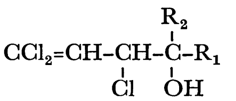
[10] The substituents in heterocyclopropanes tend to cause methyl protons *cis* to them to appear at higher fields than those *trans* to them. *Cf.* L. M. Jackman and S. Sternhell, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, 2nd Edition," Pergamon Press Ltd., London W. 1 (1969), p. 229.

[11] Excess magnesium, which was present unreacted in the Grignard reagent, probably reacted with **1** to give pentenone **13**.

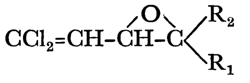
[12] a) Champs (*loc. cit.*) described the formation of compounds **15a** (mp 25.5°C) and **15b** (bp 108—110°C/15 mmHg) as due to conjugate addition to **1** of methanol and hydrogen chloride, respectively. b) Champs detected the formation of 5,5,5-trichloro-4-diethylamino-2-pentanone in a 40% yield on NMR spectra.

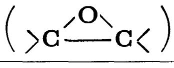
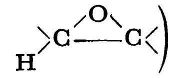
TABLE 2.  8

$CCl_2=CH-CH(Cl)-C(R_2)(OH)-R_1$

Compd.	R_1	R_2	Procedure Ketones	Procedure Grignard Reagent	Yield %	Bp (mmHg) °C	Anal (Calcd), % C	Anal (Calcd), % H	IR (cm^{-1}, liquid)	NMR δ ppm
8b	CH_3	CH_3	**1**	**5b**	43	65—70 (4)	35.65 (35.42	4.51 4.46)	3420 (OH) 1612 (C=C) 755 (C-Cl)	1.25 (s, 3H, *cis*-CH_3) 1.33 (s, 3H, *trans*-CH_3) 4.57 (d, 1H, J=10.1 Hz, >CHCl) 6.11 (d, 1H, J=10.1 Hz, Cl_2C=CH-)$^{a)}$
8c	CH_3	C_6H_5	**1**	**5c**	73	126—128 (3)$^{c)}$	49.82 (49.75	4.30 4.18)	3600—3500 (OH) 1623 (C=C)	1.72 (s, 3H, -CH_3) 2.34 (s, 1H, -OH) 4.93 (d, 1H, J=11 Hz, >CHCl) 6.03 (d, 1H, J=11 Hz, =CH-)$^{b)}$
8d	C_6H_5	C_2H_5	**2**	**5a**	45	128—131 (0.22)$^{d)}$	51.48 (51.55	4.88 4.69)	3600 (OH) 1622 (C=C)	0.69 (t, 3H, J=7.5 Hz, -$CH_2\underline{CH_3}$) 1.96 (q, 2H, J=7.5 Hz, -$\underline{CH_2}CH_3$) 2.12 (s, 1H, -OH) 4.92 (d, 1H, J=9.5 Hz, >CHCl) 5.94 (d, 1H, J=9.5 Hz, Cl_2C=CH-) 7.31 (broad s, 5H, -C_6H_5)$^{a)}$

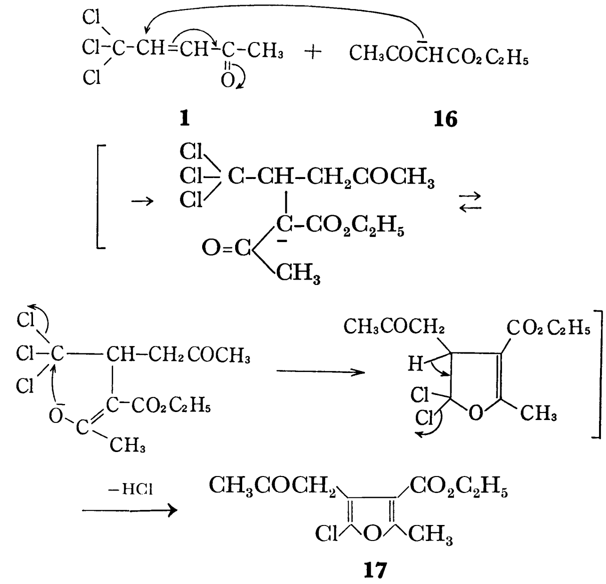
a) Measured in CCl_4. b) Measured in $CDCl_3$. c) NMR spectrum indicates that this fraction consists of **7c** (27%) and **8c** (73%). d) Tlc analysis[17] of this fraction showed two spots at R_f values of 0.80 and 0.67 in the ratio 1 : 1. The 0.80 R_f component was separated by preparative tlc[18] and identified as phenyl 2-trichloromethylbutyl ketone (**15i**) by comparison of its IR spectrum with that of the authentitic sample. The 0.67 R_f component was separated by preparative tlc.[18] NMR spectrum showed it to be a mixture of **7d** and **8d** (3 : 5).

TABLE 3.  9

Compd.	R_1	R_2	Yield %	Bp (mmHg) °C	Anal (Calcd), % C	Anal (Calcd), % H	IR (cm^{-1}, liquid)	NMR (CCl_4) δ ppm
9b	CH_3	CH_3	36	60—61 (13)	43.02 (43.15	4.63 4.83)	3040 1618 (C=C) 670 (C-Cl)	1.28 (s, 3H, -CH_3, *cis* to Cl_2C=CH-) 1.34 (s, 3H, -CH_3, *trans* to Cl_2C=CH-) 3.32 (d, 1H, J=7.2 Hz, >CHCl) 5.70 (d, 1H, J=7.2 Hz, Cl_2C=CH-)
9c	CH_3	C_6H_5	69	110 (3)	58.01 (57.67	4.65 4.40)	3070 1620 (C=C) 1251 	1.61 and 1.63 (2s, 3H, *cis* and *trans* -CH_3) 3.40 (d, 1H, J=7.0 Hz, ) 5.81 (d, 1H, J=7.0 Hz, =CH-) 7.25 (s, 5H, -C_6H_5)

gate addition (**15**). Neither acetic acid nor phenol reacted with **1**, but a 90 wt% aqueous acetic acid caused hydration of **1** to give chloralacetone.[3b)] On the contrary, both acetate and phenolate anions were found to be sufficiently nucleophilic to produce the compounds **15g** and **15h** when their conjugate acids were used as solvents. Diethyl sodiomalonate and **1** in dry ether afforded 5,5,5-trichloro-4-diethoxycarbonylmethyl-2-pentanone (**15f**) in a 70% yield indicating that the conjugate addition of the carbanion of sodiomalonate had occurred. These compounds, with the exception of **15h**, exhibited no IR absorption bands in the region of 1600—1700 cm^{-1}. On treatment of **1** with diethylamine in ether a resinous material was obtained with deposition of a large amount of diethylammonium chloride.[12b)]

The reaction of **1** with ethyl sodioacetoacetate **16** gave exclusively a crystalline solid melting at 62°C in a 18% yield to which the structure 2-chloro-3-acetonyl-4-ethoxycarbonyl-5-methylfuran (**17**) was assigned on the basis of elemental analysis and spectral data. No other distillable products were obtained. Formation of the furan compound can be best interpreted by setting up a mechanism where the ambident anion of **16** attacks β and γ carbons of **1** as shown in Scheme 6, although no intermediate compounds have been isolated as yet.



Scheme 6.

Experimental

The melting points and boiling points are uncorrected. Elemental analyses were carried out by Mr. Eiichiro Amano. Analytical determinations by glpc were performed on a Hitachi K-53 model gas chromatograph (3 mm o.d. × 1 m, 10% Apiezon Grease L on Chromosorb W), and the preparative isolations by glpc were performed on a Yanagimoto GCG-550T model gas chromatograph (3 mm o.d. × 2.25 m, 10% Apiezon Grease L on Chromosorb W). The mass spectra were obtained with a Hitachi RMS-4 model mass spectrometer. We are indebted to Mr. Hiroshi Ooyama, Hokko Chemical Industry Co., Ltd., and Mr. Heizan Kawamoto and Miss Hiromi Ootani for the NMR measurements. The microanalyses and spectral measurements were performed on the samples collected by glpc or tlc.

Ketones **1** and **3** were prepared by the methods reported previously.[1] Tertiary alcohols, **7c**, **7d**, and **7e**, listed in Table 1, were prepared in the same way as in the preparation of **7a**. Rearranged tertiary alcohols **8b**, **8c**, and **8d** were prepared by Procedure B. Epoxides **9b** and **9c** were obtained from **8b** and **8c** in the same ways as **9a**.

trans-6,6,6-Trichloro-3-methyl-4-hexen-3-ol (7a). Ethylmagnesium bromide (**5a**) was prepared from 5.5 g (0.05 mol) of ethyl bromide and 1.4 g (0.055 g atom) of magnesium in 20 m*l* of dry ether. The unreacted magnesium metal was recovered by decantation. To a solution of 7.5 g (0.04 mol) of **1** in 25 m*l* of dry ether was added dropwise the ethereal solution of **5a** with stirring at −30°C. The reaction mixture was stirred for additional 2 hr at −20—−10°C, and then acidified with 10% HCl. The ethereal layer was washed with water and dried over Na_2SO_4. Removal of the solvent gave 6.4 g (74% yield) of the residual oil containing **7a** as the major product. Tlc analysis[13] showed two spots at the R_f values 0.73 and 0.84, in a ratio of 9 : 1. Pure sample of **7a** with the R_f value of 0.73 was obtained by preparative tlc[14]: IR (cm^{-1}, liquid) 3425 (OH), 2980, 1620 (C=C), 735 (C-Cl); NMR (CCl_4) δ 0.91 (t, 3H, J=7.2 Hz, $-CH_2C\underline{H}_3$), 1.30 (s, 3H, $\rangle C(OH)C\underline{H}_3$), 1.58 (q, 2H, J=7.2 Hz, $-C\underline{H}_2CH_3$), 2.02 (s, 1H, -OH), 6.08 and 6.38 (dd, 2H, J=14.5 Hz, *trans* $-C\underline{H}=C\underline{H}-$).

dl-erythro-*4,6,6-Trichloro-5-hexen-3-ol (8a-I).* The Grignard reagent **5a** was prepared from 4.9 g (0.045 mol) of ethyl bromide, 1.1 g (0.045 g atom) of magnesium in 30 m*l* of dry ether. The ethereal solution of **5a** was added dropwise to a solution of **3** (6 g, 0.032 mol) in 24 m*l* of dry ether with stirring at −30°C. The stirring was continued for additional 1 hr at −30——20°C. The reaction mixture was then acidified with 10% HCl. The ethreal layer was washed with water, dried over Na_2SO_4. The removal of the solvent gave 5.3 g (76%) of the crude product. Tlc analysis of this product showed two spots with the R_f values 0.61 and 0.72, in a ratio of the spot areas 20 : 1, corresponding to the R_f values of **8a** (R_f=0.61) and **3** (R_f=0.72).[15a] The analytical sample of **8a-1** was obtained by preparative tlc:[15b] IR (cm^{-1}, liquid) 3475 (OH), 3040, 2980, 1720, 1620 (C=C), 740 (C-Cl); NMR (CCl_4) δ 0.93 (t, 3H, J= 7.2 Hz, $-CH_2C\underline{H}_3$), 1.27 (s, 3H, $\rangle C(OH)-C\underline{H}_3$), 1.61 q, 2H, J=7.2 Hz, $-C\underline{H}_2CH_3$), 2.50 (s, 1H, -OH), 4.57 (d, 1H, J=9.0 Hz, $=CH-C\underline{H}Cl-$), 6.1 (d, 1H, J=9.0 Hz, $Cl_2C=C\underline{H}-$). Glpc analysis[7] of the purified sample indicated that it consisted of two components with the retention times, 13.5 min (**8a-II**, 1 part) and 14.6 min (**8a-I**, 9 parts).

Found: C, 38.58; H, 5.26%. Calcd for $C_7H_{11}Cl_3O$: C, 38.65; H, 5.10%.

The Epimeric Mixture of 4,6,6-Trichloro-5-hexen-3-ol (8a). Procedure A: Distillation of hexenol **7a** (5.4 g, 0.025 mol) afforded the crude product of **8a** (4.4 g, 81%), bp 88—90°C/6 mmHg; IR (cm^{-1}, liquid) 3475 (OH), 3040, 2980, 1720, 1620 (C=C), 920, 740 (C-Cl); NMR (CCl_4) δ 0.95 (t, 3H, J=7.2 Hz, $-CH_2C\underline{H}_3$), 1.14 (s, $\rangle \overset{OH}{C}-C\underline{H}_3$, *threo*) and 1.27 (s, $\rangle \overset{OH}{C}-C\underline{H}_3$, *erythro*) (epimeric mixture, 3H), 1.55 (q, 2H, J=7.2 Hz, $-C\underline{H}_2CH_3$), 1.95 (s, 1H, -OH), 4.59 (d, 1H, J=9.0 Hz, $=CHC\underline{H}Cl-$), 6.1 (d, 1H, J=9.0 Hz, $Cl_2C=CH-$). Glpc analysis[7] of this product showed three peaks. The components, retention times (min), and integrated percentages are as follows: 1, 4.7, 2%; 2, 13.5, 55%; 3, 14.6, 43%. Component 1 was identified as **9a** by comparison of its retention time with the authentic sample described in the next section.

Procedure B: The reaction of **5a** with **1** was carried out in the same way as the preparation of the hexenol **7a** using 15 g (0.08 mol) of **1** as the starting material. Distillation of the crude product gave 13.1 g of a clean oil, bp 78—100°C/4 mmHg. Glpc analysis[7] indicated that this fraction contained three components, which were fractionated by preparative glpc and identified by comparison of the IR spectra with those of the authentic samples; peaks (nos), compounds (nos), retention times (min), and the integrated peak areas are: 1, **9a**, 4.7, 14%; 2, **8a-II**, 13.5, 50%; 3, **8a-I**, 14.6, 36%.

Procedure C: The reaction of **5a** with **1** was conducted in a similar manner to Procedure B at room temperature for 24 hr, using 15 g (0.08 mol) of **1** as the starting material.

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[13] Conditions of tlc: support, silica gel GF_{254} (E. Merk AG, Darmstadt), 0.1 mm; developer, benzene-methanol (9 : 1 v/v); spray reagent, H_2SO_4-$KMnO_4$ (7 : 3 w/w). The spot of **1** on tlc appeared at R_f 0.84.

[14] Conditions of preparative tlc: support, silica gel GF_{254} (E. Merk AG, Darmstadt), 1 mm; developer, benzene-methanol (9 : 1 v/v); eluent, acetone.

[15] a) Conditions of tlc: support, silica gel GF_{254} (E. Merk AG, Darmstadt), 0.3 mm; developer, *n*-hexane-acetone-chloroform (5 : 1 : 1 v/v). b) The same support (1 mm) and the same developer as above were used. Eluent, acetone.

The ethereal extract of the crude product was distilled *in vacuo*. The results of the glpc analysis of each fractions are as follows:

Fractions (bp, °C/mmHg)	Weight (g)	Compounds detected by glpc[7] (retention times, min)			
		9a (4.7)	unknown (12.2)	**8a**-II (13.5)	**8a**-I (14.6)
I (59—69/12)	2.4	81	1	9	9
II (69—84/5)	3.3	45	20	21	14
III (84—90/5)	1.7	3.5	18	48	30
IV (>90/5)	1.0	—	—	—	—

The last fraction turned white crystals in a cooler. One recrystallization from petroleum ether (bp 45—55°C) gave 0.9 g of white crystals, to which the structure 6,6-dichloro-3-methyl-5-hexene-3,4-diol (**10**) was assigned: mp 81°C; IR (cm^{-1}, nujol) 3300 (OH), 1620 (C=C), 910, 800—650 (C–Cl); NMR ($CDCl_3$) δ 0.9 (t, 3H, J=6.8 Hz, $-CH_2C\underline{H}_3$), 1.20 (s, 3H, $\rangle\overset{OH}{C}\text{-}C\underline{H}_3$), 1.43 (broad q, 2H, J=6.8 Hz, $-C\underline{H}_2\text{-}CH_3$), 2.01 (s, 2H, 2OH), 4.16 (d, 1H, J=9 Hz, $\rangle C\underline{H}OH$), 6.02 (d, 1H, J=9 Hz, $Cl_2C\text{=}CH\text{-}$).

Found: C, 42.40; H, 5.99%. Calcd for $C_7H_{12}Cl_2O_2$: C, 42.23; H, 6.08%.

Procedure D: The reaction of **5a** with **1** was carried out in a similar manner to Procedure C except that excess ethylmagnesium bromide (equivalent to 0.16 mol) was used on 18.7 g (0.1 mol) of **1**. The ethereal extract of the crude product was worked up as usual. The fraction distilling at 44—112°C/5 mmHg was collected and analyzed by glpc.[7] Peaks (nos), retention times (min), and the integrated peak areas are: 1, 2.9, 13%; 2, 4.7, 11%; 3, 7.9, 9%; 4, 10.1, 2%; 5, 12, 5%; 6, 13.5, 27%; 7, 14.6, 21%; 8, 16, 10%. Components 1, 2, 6, and 7 were identified as compounds **13**, **9a**, **8a**-II, and **8a**-I, by comparison of the IR spectra and retention times with those of the authentic samples. Components 3 and 8 were collected by preparative glpc and analyzed. The structure 6,6-dichloro-3-methyl-5-hexen-3-ol (**14**) was assigned to component 3 on the basis of the IR spectrum and analysis: IR (cm^{-1}, liquid) 3450 (OH), 2980, 1612 (C=C), 918, 700 (C–Cl).

Found: C, 46.41; H, 6.75%. Calcd for $C_7H_{12}Cl_2O$: C, 45.92; H, 6.61%.

The structure 6-chloro-3-methyl-5-octene-3,4-diol (**12**), was assigned to component 8: IR (cm^{-1}, liquid) 3400 (OH), 2980, 1615 (C=C), 1460, 904 (=C–H).

Found: C, 55.99; H, 8.59%. Calcd for $C_9H_{17}ClO_2$: C, 56.01; H, 8.89%.

*The Epimeric Mixture of 6,6-Dichloro-3-methyl-3,4-epoxy-5-hexene (**9a**).* Sodium methoxide (1.2 g, 0.022 mol) was added in several portions to a solution of 2.2 g (0.01 mol) of **8a** in 20 m*l* of dry ether at 0°C. The mixture was stirred at 0°C for 1 hr and then allowed to cool to room temperature. The mixture was poured into 20 m*l* of water and neutralized with dilute HCl. The ethereal layer was washed with water and dried over Na_2SO_4. After evaporation of the solvent the residual oil was distilled to yield 0.6 g (33%) of **9a**: bp 50—51°C/4 mmHg; IR (cm^{-1}, liquid) 3040 (=C–H and $H\text{–}C\overset{O}{\text{—}}C\langle$), 2960—70, 1617 (C=C), 1250 ($\rangle C\overset{O}{\text{—}}C\langle$), 905, 865, 835, 812, 803, 690—660 (C–Cl); NMR (CCl_4) δ 0.97 (t, J=7.2 Hz, $-CH_2C\underline{H}_3$) and 1.0 (t, J=7.2 Hz, $-CH_2C\underline{H}_3$) (epimeric mixture, 3H), 1.24 (s, $\rangle C\overset{O}{\text{—}}C\text{–}C\underline{H}_3$, *cis* to $Cl_2C\text{=}CH\text{–}$) and 1.30 (s, $\rangle C\overset{O}{\text{—}}C\text{–}C\underline{H}_3$, *trans* to $Cl_2C\text{=}CH\text{–}$) (epimeric mixture, 3H), 1.35—1.90 (m, 2H, $-C\underline{H}_2CH_3$), 3.28 (d, 1H, J=7.5 Hz, $H\text{–}C\overset{O}{\text{—}}C\langle$), 5.69 (d, 1H, J=7.5 Hz, $Cl_2C\text{=}C\underline{H}\text{–}$). Glpc analysis[7] of this product showed two very close peaks (the ratio of peak areas, 1 : 1) at the retention times (min), 4.5 and 4.7.

Found: C, 46.39; H, 5.88%. Calcd for $C_7H_{10}Cl_2O$: C, 46.44; H, 5.57%.

dl-*trans-6,6-Dichloro-3-methyl-3,4-epoxy-5-hexene (**9a-I**).* From 1 g (0.005 mol) of hexenol **8a**-I, treated with sodium methoxide in the same way as in the cyclization of the epimeric mixture (**8a**), 0.6 g (66%) of the glpc[7] pure product (**9a**-I) with the retention time (min) of 4.5 was obtained, oil: bp 62—64°C/6 mmHg; NMR (CCl_4) δ 0.97 (t, 3H, J=7.2 Hz, $-C\underline{H}_2CH_3$), 1.24 (s, 3H, $-C\overset{O}{\text{—}}C\text{–}CH_3$, *cis* to $Cl_2C\text{=}C\underline{H}\text{–}$), 1.35—1.80 (broad q, 2H, J=7.2 Hz, $-C\underline{H}_2CH_3$, *trans* to $Cl_2C\text{=}C\underline{H}\text{–}$), 3.28 (d, 1H, J=7.5 Hz, $\underline{H}\text{–}C\overset{O}{\text{—}}C\text{–}$), 5.69 (d, 1H, J=7.5 Hz, $Cl_2C\text{=}C\underline{H}\text{–}$). The IR spectrum of the purified sample (liquid) was identical with that of the epimeric mixture **9a**.

*The Epimeric Mixture of 6,6-Dichloro-3-methyl-5-hexene-3,4-diol (**10a**).* A mixture of 0.88 g (0.005 mol) of **9a** (**9a**-I/**9a**-II = *ca.* 1 : 1) and 50 m*l* of 20% H_2SO_4 was heated with stirring for 1 hr at 50°C. The ethereal extract of the reaction mixture was washed with water, and dried over Na_2SO_4. Removal of the solvent gave 0.5 g (52%) of white crystals (**10a**): mp 69—75°C (two recrystallizations from *n*-hexane); IR (cm^{-1}, nujol) 3300 (OH), 1620 (C=C), 910, 800—650 (C–Cl); NMR ($CDCl_3$) δ 0.94 (t, 3H, J=6.8 Hz, $-CH_2C\underline{H}_3$), 1.10 (s, 1.2H, $-CH_3$) and 1.20 (s, 1.8H, $-CH_3$) (epimeric mixture, 3H), 1.43 (broad q, 2H, J=6.8 Hz, $-C\underline{H}_2\text{-}CH_3$), 2.32 (s, 2H, 2–OH), 4.26 (d, 1H, J=9 Hz, $\rangle C\underline{H}OH$), 8.02 (d, 1H, J=9 Hz, $Cl_2C\text{=}C\underline{H}\text{–}$).

dl-*erythro-6,6-Dichloro-3-methyl-5-hexene-3,4-diol (**10a-I**).* Hydrolysis of **9a**-I (0.57 g, 0.003 mol) carried out as above, afforded 0.34 g (55%) of white crystals exhibiting only one spot in tlc (R_f=0.17):[16] mp 75—82°C (two recrystallizations from *n*-hexane); IR (cm^{-1}, liquid) 3300 (OH), 1620 (C=C), 910, 800—650 (C–Cl); NMR ($CDCl_3$) δ 0.94 (t, 3H, J=6.8 Hz, $-CH_2C\underline{H}_3$), 1.20 (s, 3H, $-CH_3$), 1.43 (broad q, 2H, $-C\underline{H}_2CH_3$), 2.15 (s, 2H, 2OH), 4.26 (d, 1H, J=9 Hz, $\rangle C\underline{H}\text{–}OH$), 6.02 (d, 1H, J=9 Hz, =CH–).

*5,5-Dichloro-4-penten-2-one (**13**).* A solution of 9.4 g (0.05 mol) of **1** in 30 m*l* of dry ether was added dropwise to 1.2 g (0.05 g atom) of magnesium at room temperature under the atmosphere of nitrogen. After being stirred for 2 hr, the mixture was acidified with 10% HCl. The ethereal layer was washed with water, dried over Na_2SO_4, and the solvent was then evaporated. The residual oil was distilled to give 2.2 g (29%) of **13**, oil: bp 51—55°C/5 mmHg; IR (cm^{-1}, liquid) 3050 (=C–H), 1720 (C=O), 1625 (C=C), 910; NMR (CCl_4) δ 2.20 (s, 3H, $-COCH_3$), 3.24 (d, 2H, J=6.75 Hz, $=CH\text{-}C\underline{H}_2\text{–}$), 6.03 (t, 1H, $=C\underline{H}\text{-}CH_2\text{–}$); mass spectrum (80 eV) *m/e* (relative intensity) 152 (31), 133 (14), 125 (35), 109 (53), 89 (42), 73 (44), 61 (38), 53 (34), 49 (39), 43 (100).

Found: C, 39,13; H, 3.89%. Calcd for $C_5H_6Cl_2O$: C, 39.25; H, 3.95%.

*Reaction of Ketone **2** with Grignard reagents **5a**, and **5c**.* Working up in the same ways as for **7a**, the reaction of ketone **2** (5 g, 0.02 mol) with **5a** (0.02 mol) gave 5.0 g of a

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[16] Conditions of tlc: support, Silica gel GF_{254} (E. Merk AG, Darmstadt), 0.2 mm; developer, *n*-hexane–acetone–chloroform (5 : 2 : 1 v/v); spray reagent, H_2SO_4–$KMnO_4$ (7 : 3 w/w).

light yellow oil. Tlc analysis[17] of this oil showed two spots at the R_f values 0.80 and 0.67, in the ratio 1 : 1. Pure sample of phenyl 2-trichloromethylbutyl ketone (**15i**) with the R_f value of 0.80 was separated by preparative tlc,[18] yield 45%; IR (cm^{-1}, liquid) 1692 (C=O), 1603 and 1586 (benzene ring); NMR (CCl_4) δ 0.98 (t, 3H, J=7.5 Hz, $-CH_2\text{-}C\underline{H}_3$). 2.0 (m, 2H, $-C\underline{H}_2CH_3$), 3.25 (m, 2H, $-C\underline{H}_2COC_6H_5$), 3.58 (m, 1H, $CCl_3CH\langle$), 7.2—8.1 (m, 5H, $-C_6H_5$); mass spectrum (70 eV) (relative intensity) 278 (9, M^+, 3Cl), 206 (19), 120 (80), 105 (100), 77 (74).

Found: C, 51.37; H, 4.69%. Calcd for $C_{12}H_{13}Cl_3O$: C, 51.55; H, 4.69%.

The compound **7d** with the R_f value of 0.67 was similarly separated.

Ketone ***2*** *(5 g, 0.02 mol) and equimolar amount of* ***5c***, worked up in the same ways as for **7a**, gave a mixture of light yellow needles (2.1 g) and a light brown oil (4.9 g). The crystals were separated by filtration and identified as compound **15j**: 125—126°C (from benzene); IR (cm^{-1}, liquid) 1680 (C=O), 1600 (benzene ring); NMR (CCl_4) δ 3.91 (d, 2H, J=6 Hz, $-CH_2CO$), 4.60 (t, 1H, J=6 Hz, $CCl_3CH\langle$), 7.2—8.05 (m, 10H, $2C_6H_5$).

Found: C, 59.00; H, 4.12%. Calcd for $C_{16}H_{13}Cl_3O$: C, 58.66; H, 4.00%.

Tlc analysis[17] of the oily filtrate showed four spots at the R_f values 0.31, 0.52, 0.61, and 0.73, in the ratio 1 : 12 : 2 : 1. The spot of **15j** appeared at R_f 0.61. The component with the R_f value of 0.52 was separated by preparative tlc[18] and identified as **7e**.

5,5,5-Trichloro-4-methoxy-2-pentanone ***(15a)***. A solution of 5 g (0.027 mol) of **1** in 80 m*l* of dry methanol was refluxed for 9 hr. Excess methanol was removed *in vacuo*, and the residue, on distillation, gave 3.5 g (60%) of **15a**: bp 78°C/3 mmHg; IR (cm^{-1}, liquid) 1720 (ketone C=O); NMR (CCl_4) δ 2.19 (s, 3H, $-COCH_3$), 2.76 (dd, 1H, J=7.0 and 17.5 Hz, $-C\underline{H}_2COCH_3$), 3.10 (dd, 1H, J=3.7 and 17.5 Hz, $-C\underline{H}_2COCH_3$), 3.68 (s, 3H, $-OCH_3$), 4.24 (dd, 1H, J= 3.7 and 7.0 Hz, $\rangle CHOCH_3$).

Found: C, 32.83; H, 4.07%. Calcd for $C_6H_9Cl_3O_2$: C, 32.83; H, 4.14%.

4,5,5,5-Tetrachloro-2-pentanone ***(15b)***. To a solution of 5 g (0.027 mol) of **1** in 30 m*l* of dry ether was passed dry hydrogen chloride gas at 0°C for 24 hr. The solvent was removed *in vacuo*, and the residue, on distillation, gave 5.9 g (98%) of **15b**: bp 87°C/3.5 mmHg; IR (cm^{-1}, liquid) 1720 (ketone C=O) and 790—770 (C–Cl); NMR ($CDCl_3$) δ 2.25 (s, 3H, $-CH_3$), 3.14 (dd, 1H, J=17.4 and 7.9 Hz, $-C\underline{H}_2\text{-}CO-$), 3.49 (dd, 1H, J=17.4 and 3.8 Hz, $-C\underline{H}_2CO-$), 4.97 (dd, 1H, J=7.9 and 3.8 Hz, $\rangle C\underline{H}Cl-$).

Found: C, 27.10; H, 2.91%. Calcd for $C_5H_6Cl_4O$: C, 26.82; H, 2.70%.

5,5,5-Trichloro-4-anilino-2-pentanone ***(15c)***. Fifteen grams (0.08 mol) of **1** and 7.4 g (0.08 mol) of aniline were dissolved in 10 m*l* of ether. The mixture was allowed to stand at room temperature for 10 hr, and then at 0°C— −5°C for 24 hr. The resulting solid was recrystallized from ether to afford 21.7 g (98%) of **15c**: mp 45°C; IR (cm^{-1}, nujol) 3320 (NH), 1703 (C=O), 1596 (benzene C=C), 768 and 750 (C–Cl).

Found: C, 47.40; H, 4.35; N, 4.90%. Calcd for $C_{11}H_{12}Cl_3NO$: C, 47.09; H, 4.31; N, 4.99%.

*5,5,5-Trichloro-4-(*p*-chloroanilino)-2-pentanone* ***(15d)***. A mixed solution of 15 g (0.08 mol) of **1** and 10.2 g (0.08 mol) of *p*-chloroaniline in 30 m*l* of ether similarly gave 22.8 g of a crude product, which was recrystallized from benzene to afford 21.6 g (90%) of **15d**: mp 115°C; IR (cm^{-1}, nujol) 3230 (NH), 1702 (C=O), 1590 (benzene C=C), 798 and 767 (C–Cl); NMR ($CDCl_3$) δ 2.2 (s, 3H, $-CH_3$), 2.85 (dd, 1H, J=16 and 8.0 Hz, $-C\underline{H}_2COCH_3$), 3.33 (dd, 1H, J=16 and 3.5 Hz, $-C\underline{H}_2COCH_3$), 4.87 (dd, 1H, $\rangle C\underline{H}CH_2COCH_3$), 6.65—7.22 (m, A_2B_2 with strong doublet centered at 6.93, 4H, aromatic).

Found: C, 41.92; H, 3.49; N, 4.13%. Calcd for $C_{11}H_{12}Cl_4NO$: C, 41.94; H, 3.52; N, 4.45%.

5,5,5-Trichloro-4-phenylmercapto-2-pentanone ***(15e)***. To a stirred solution of 10 g (0.053 mol) of **1** in 30 m*l* of benzene was added a solution of 6 g (0.053 mol) of thiophenol in 30 m*l* of benzene at 50°C. After the mixture was stirred at 50°C for 5 hr, the solvent was removed, and the residual solid was recrystallized from petroleum ether (bp 40—55°C) to afford 15 g (95%) of **15e**: mp 58°C; IR (cm^{-1}, nujol) 1720 (C=O), 1580 (benzene C=C), and 780—730 (C–Cl).

Found: C, 44.37; H, 3.56%. Calcd for $C_{11}H_{11}Cl_3OS$: C, 44.39; H, 3.73%.

5,5,5-Trichloro-4-diethoxycarbonylmethyl-2-pentanone ***(15f)***. To a stirred solution of 8.6 g (0.053 mol) of diethyl malonate in 80 m*l* of dry ether, 3.6 g (0.053 mol) of sodium ethoxide was added in several portions, and a solution of 10 g (0.053 mol) of **1** in 10 m*l* of dry ether was added dropwise at 0—5°C. The reaction mixture was stirred at 0°C for 1 hr, finally at room temperature for 1 hr, and then was made weakly acidic with dilute HCl (pH *ca.* 5). The ethereal extract of the organic layer was washed with water and dried over Na_2SO_4. Removal of the solvent left a yellow liquid which, on distillation, gave 13 g (70%) of **15f**: bp 155—157°C/5 mmHg; IR (cm^{-1}, liquid) 1745 and 1730 (C=O), and 790—760 (C–Cl).

Found: C, 41.74; H, 5.20%. Calcd for $C_{12}H_{17}Cl_3O_5$: C, 41.46; H, 4.93%.

5,5,5-Trichloro-4-acetoxy-2-pentanone ***(15g)***. A mixed solution of 1.5 g (0.018 mol) of sodium acetate and 3.4 g (0.018 mol) of **1** in 20 m*l* of acetic acid was refluxed for 30 min. It was diluted with 100 m*l* of water and then extracted with ether. The ethereal extract was washed with water and dried over Na_2SO_4. After recovery of the starting meterial at 94—96°C/20 mmHg, 0.4 g (9%) of the liquid distilling at a higher temperature was collected. Glpc analysis[7] showed it to contain 79% **15g**: IR (cm^{-1}, liquid) 2950, 1760 (acetoxy C=O), 1718 (ketone C=O), 770 (C–Cl).

Found: C, 33.72; H, 3.51%. Calcd for $C_7H_9Cl_3O_3$: C, 33.97; H, 3.66.

5,5,5-Trichloro-4-phenoxy-2-pentanone ***(15h)***. A mixed solution of 3.1 g (0.027 mol) of sodium phenoxide and 5 g (0.027 mol) of **1** in 45 m*l* of phenol was heated with stirring at 100°C for 4 hr. The reaction mixture was poured into a large amount of water and the organic layer was extracted with chloroform. The extract was washed with water and dried over Na_2SO_4. After recovery of chloroform and the starting materials, the fraction distilling at 123—125°C/3 mmHg was collected (1.4 g). Glpc analysis[19] showed it to contain 80% **15h** which was separated by preparative glpc: IR (cm^{-1}, liquid) 3050, 1723 (C=O), 1625 and 1593 (benzene ring), 770, 760, 700; NMR (CCl_4) δ 2.08 (s, 3H, $-COC\underline{H}_3$), 3.05 (m, 2H, $-C\underline{H}_2COCH_3$), 5.36 (dd, 1H, J=

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[17] Conditions of tlc: support, Silica gel GF_{254} (E. Merk AG, Darmstadt), 0.2 mm; developer, *n*-hexane-acetone (3 : 1 v/v); spray reagent, H_2SO_4–$KMnO_4$ (7 : 3 w/w).

[18] Conditions of tlc: support, Silica gel GF_{254} (E. Merk AG, Darmstadt), 1 mm; developer, *n*-hexane-acetone (3 : 1 v/v); eluent, acetone.

[19] Observed on a 1 m 10% Silicone SE-30 on Diasolid L. Column temp., 180°C; carrier gas, N_2 (0.7 kg/cm^2, 60 m*l*/min); detector, FID.

6 and 4.8 Hz, $\rangle C\underline{H}CH_2$–), 6.85—7.35 (m, 5H, C_6H_5O–); mass spectrum (70 eV) *m/e* (relative intensity) 280 (4, M^+, 3Cl), 163 (15), 105 (70), 94 (98), 87 (35), 65 (37), 51 (51), 43 (100), 39 (47).

Found: C, 47.20; H, 4.15%. Calcd for $C_{11}H_{11}Cl_3O_2$: C, 46.92; H, 3.94%.

2-Chloro-3-acetonyl-4-ethoxycarbonyl-5-methylfuran (**17**). Sodium (2.3 g, 0.1 g atom) was dissolved in 80 m*l* of absolute ethanol with moderate cooling. To the resulting solution was added 13 g (0.1 mol) of ethyl acetoacetate at room temperature with stirring. A solution of 18.7 g (0.1 mol) of **1** in 20 m*l* of absolute ethanol was then added dropwise at 0°C with stirring. After stirring was continued for additional 2 hr at room temperature, 200 m*l* of water was added with cooling. After being acidified with 10% HCl, the mixture was extracted with ether. The ethereal solution was washed with water, dried over Na_2SO_4 and evaporated. The residual oil was distilled at 100—125°C/0.05 mmHg to give 4.4 g (18% yield) of **17**: mp 62°C (*n*-hexane); IR (cm^{-1}, nujol) 1715 (C=O), 1610 and 1577 (furan C=C), 785 (C–Cl); NMR (CCl_4) δ 1.33 (t, 3H, $-CH_2C\underline{H}_3$), 2.12 (s, 3H, $-COCH_3$), 2.55 (s, 3H, furan $-CH_3$), 3.61 (s, 2H, $-C\underline{H}_2CO-$), 4.29 (q, 2H, $-C\underline{H}_2CH_3$); mass spectrum (80 eV) *m/e* (relative intensity) 246 (4.3), 244 (13), 204 (11), 203 (33), 202 (33), 201 (83), 175 (17), 173 (47), 156 (46), 43 (100).

Found: C, 54.30; H, 5.39%. Calcd for $C_{11}H_{13}ClO_4$: C, 54.00; H, 5.35%.