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Reaction of Ethyl α,α-Dichloroacetoacetate with Aldehydes

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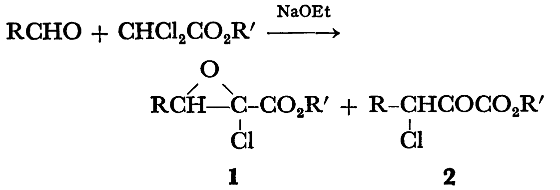
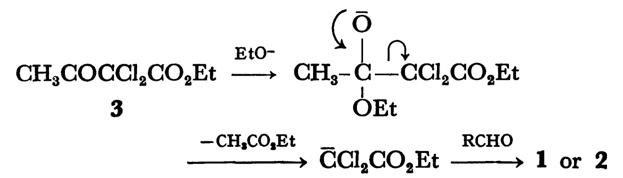
Synopsis. Ethyl α,α-dichloroacetoacetate reacted with aldehydes in the presence of sodium ethoxide to give α-chloropyruvate and/or α-chloroglycidate. 2,5-Bis(1′-chloroalkylidene)-1,4-cyclohexanedione (**4**) was obtained as a by-product in a low yield.

Previously, one of the present authors (A. T.) has reported the base-catalyzed condensation of dichloroacetate with aldehydes to give α-chloropyruvate (**1**) and/or α-chloroglycidate (**2**), which are useful synthetic intermediates.[1)]


$$\mathrm{RCHO + CHCl_2CO_2R' \xrightarrow{NaOEt} RCH{-}C(Cl)(O){-}CO_2R' + R{-}CHCl{-}COCO_2R'}$$

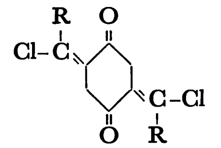
1 **2**

As an extension of the previous work, we carried out the base-catalyzed condensation of ethyl dichloroacetoacetate (**3**) with aldehydes to give esters **1** and **2**. This reaction can be well explained by assuming the formation of enolate anion of dichloroacetate, since the ester **3** is known to undergo retro acetoacetate reaction to afford dichloroacetate in the presence of alkoxide.[2)] The yields and boiling points of the products **1** and **2** are listed in Table 1.


$$\mathrm{CH_3COCCl_2CO_2Et \xrightarrow{EtO^-} CH_3{-}C(O^-)(OEt){-}CCl_2CO_2Et \xrightarrow{-CH_3CO_2Et} \bar{C}Cl_2CO_2Et \xrightarrow{RCHO} 1\ or\ 2}$$

3

The identification of the products was done by comparison of spectral data with those of authentic samples.[1,3)] In contrast with the reaction of dichloroacetate, the present reaction afforded a small amount of crystalline by-products, which were identified as 2,5-bis(1′-chloroalkylidene)-1,4-cyclohexanedione (**4**) or its geometrical isomers on the basis of IR, NMR, MS spectral data, and elemental analyses (see Tables 2 and 3). The mass spectra of these products as well as their analyses supported the composition of $C_8H_4Cl_2O_2R_2$.

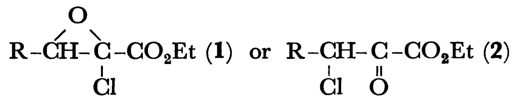


4 (R = alkyl or aryl)

IR spectra exhibited absorptions due to conjugated C=O stretching at 1692—1705 cm^{-1} and those due to C=C stretching at 1660—1665 cm^{-1}.

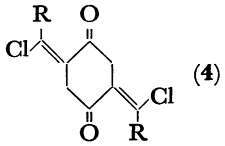
Possible route of the formation of dione **4** can be explained by the following mechanism, involving the condensation of two molecules of **6**, which may be derived from the reaction of dichloroacetonyl anion (**5**) with the aldehyde.

Table 1. Products from the reaction of **3** with aldehydes


$$\mathrm{R{-}CH{-}C(Cl){-}CO_2Et\ (\mathbf{1})\ \text{or}\ R{-}CH(Cl){-}C(=O){-}CO_2Et\ (\mathbf{2})}$$

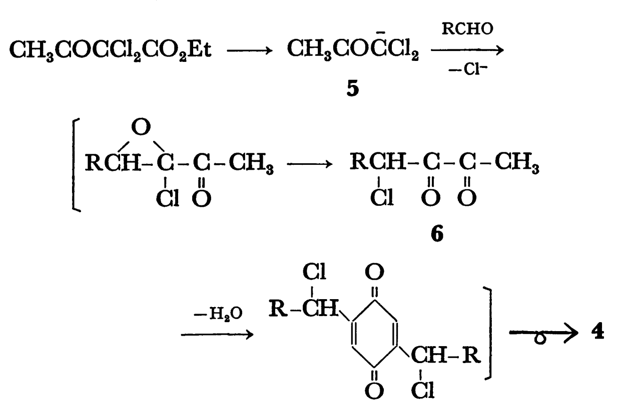
Compound Code	R	Yield, %	Bp(lit,), °C/mmHg
1a	C_2H_5	69	99—105/17 (94—98/18[1)])
1b	$(CH_3)_2CH$	25	76—86/6 (104—106/20.5[1)])
2c	n-C_6H_{13}	15	120—130/7 (134—136/13[1)])
2d	C_6H_5	17	130—136.5/8 (165—167/18.5[3)])

Table 2. By-products from the reaction of **3** with aldehydes



(**4**)

Compound Code	R	Yield, %	Mp, °C	Found (%) (Calcd (%)) C	H
4a	C_2H_5	6.1	141—142	54.93 (55.19	5.46 5.40)
4b	$(CH_3)_2CH$	3.7	197	58.13 (58.14	6.36 6.27)
4c	n-C_6H_{13}	7.9	105.5—106	64.55 (64.33	8.25 8.10)
4d	C_6H_5	5.9	218	67.41 (67.24	3.78 3.95)


$$\mathrm{CH_3COCCl_2CO_2Et \longrightarrow CH_3CO\bar{C}Cl_2 \xrightarrow[-Cl^-]{RCHO} [RCH{-}C(Cl)(O){-}C(=O){-}CH_3 \longrightarrow RCH(Cl){-}C(=O){-}C(=O){-}CH_3] \xrightarrow{-H_2O} [\ ] \longrightarrow 4}$$

5 **6**

TABLE 3. SPECTRAL DATA OF COMPOUND **4**.

Compound	IR (Nujol) cm^{-1}	NMR, δ (solvent)	MS (70 eV) *m/e* (rel. intensity)
4a	1700 (C=O), 1660 (C=C), 1150, 930, 900, 880, 795	($CDCl_3$) 1.12 (br. t, 6H, *J*=6 Hz, $2CH_3$), 1.50—2.90 (m, 8H, $4CH_2$)	260 (12, M$^+$, 2Cl), 231 (14), 225 (100, M$^+$-Cl, 1Cl), 197 (57), 183 (50), 155 (30), 115 (32)
4b	1705 (C=O), 1668 (C=C), 1293, 1180, 1156,1103, 1030, 882, 695	($CDCl_3$) 1.06 (d, 6H, *J*=5.5 Hz, $2CH_3$), 1.16 (d, 6H, *J*=5.5 Hz, $2CH_3$), 1.30—1.80 $\left[\text{m, 4H, 2C}\underline{\mathrm{H}}\text{-}(CH_3)_2 \text{ and } 2{}^{\mathrm{H}}_{\underline{\mathrm{H}}}{>}\overset{\vert}{\mathrm{C}}\text{–CO–}\right]$, 2.25 $\left(\text{d, 2H } J\text{=6 Hz, } 2\frac{\mathrm{H}}{\mathrm{H}}{>}\overset{\vert}{\mathrm{C}}\text{–CO–}\right)$	288 (1, M$^+$, 2Cl), 253 (14, M$^+$-Cl, 1Cl), 245 (4), 233 (21), 211 (12),197 (100)
4c	1692 (C=O), 1660 (C=C), 1100, 940, 880, 730, 680	(CCl_4) 0.9 (br. t, 6H, *J*=6 Hz, $2CH_3$), 1.10—2.11 (m, 24H, $12CH_2$)	372 (7, M$^+$, 2Cl), 337 (30, M$^+$-Cl, 1Cl), 253 (73), 239 (30), 191 (100), 157 (60), 115 (47), 97 (50)
4d[a)]	1703 (C=O), 1665 (C=C), 1603 (benzene ring), 945, 866, 760, 700, 680		356 (18, M$^+$, 2Cl), 321 (82, M$^+$-Cl, 1Cl), 293 (23), 285 (23, M$^+$-2Cl), 258 (45, M$^+$-2Cl-CO), 178 (100), 105 (98)

a) NMR spectrum of this compound could not be measured, because it was almost insoluble in usual solvents such as acetone, chloroform, methanol, and dimethyl sulfoxide.

Experimental

The melting points and boiling points are uncorrected. Elemental analyses were carried out by Mr. Eiichiro Amano. We are indebted to Mr. Hiroshi Ooyama of Hokko Chemical Industry Co., Ltd. for the NMR measurements, and also to Mr. Shinichi Ninomiya for technical assistance. Ethyl α,α-dichloroacetoacetate (**3**) was obtained by the reaction of ethyl acetoacetate with sulfuryl chloride, yield 63%: bp 91.5—92 °C/13 mmHg (lit,[4]) 106—108 °C/30 mmHg). Aldehydes were distilled just before use.

The following experiment is shown as a typical run.

*Reaction of **3** with 2-Methylpropanal.* To a solution of 103 g (0.52 mol) of **3** and 37.3 g (0.52 mol) of 2-methylpropanal in 104 ml of dry ether was added 40.8 g (0.6 mol) of dry, powdered sodium ethoxide in several portions at 0—5 °C. After complete addition, the mixture was allowed to warm up at room temperature and then refluxed for 2 hr. It was poured into a large excess of water. Precipitated crystals collected by filtration were washed with water and ether successively, and dried. Recrystallization of the white crystals from ethanol gave 2.8 g (3.7%) of **4b**: mp 197 °C.

The ethereal layer was washed with water several times, and dried over $MgSO_4$. After removal of the solvent, the residue was distilled to give 24.6 g (25%) of **1b**: bp 76—86 °C/6 mmHg (lit.[1]) 104—106 °C/20.5 mmHg). Its IR and NMR spectra were identical with those of the authentic sample.[1])

References

1) A. Takeda, S. Wada, M. Fujii, and H. Tanaka, This Bulletin, **43**, 2997 (1970).

2) This mechanism was substantiated by Gupta's work. In the course of our study on the reaction of **3** with aldehyde, he has reported that ester **3** reacts with base to give ethyl dichloroacetate: S. K. Gupta, *J. Org. Chem.*, **38**, 4081 (1973).

3) A. Takeda, S. Wada, and T. Uno, *Memoirs of the School of Engineering Okayama Univ.*, **2**, 80 (1967).

4) D. P. Wyman, *J. Org. Chem.*, **29**, 2709 (1964).