REACTION OF METHYL DICHLOROACETATE WITH SUBSTITUTED BENZALDEHYDES UNDER THE CONDITIONS OF THE DARZENS CONDENSATION

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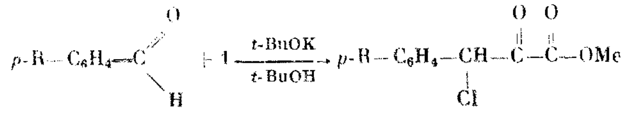
We have found that condensation of methyl dichloroacetate (1 with benzaldehyde, p-chloro- and p-bromobenzaldehyde in t-BuOH in the presence of t-BuOK yields methyl 3-aryl-3-chloro-2-oxopropionates (3-5). In the case of nitrobenzaldehydes the reaction products are α-chloro-ketones (6, 7) and mainly methyl 2-chloro-3-aryl-2,3-epoxypropionates (8, 9). α-Chloroepoxide (10) is formed in the reaction with 2,4-dichlorobenzaldehyde.

Keywords: methyl dichloroacetate, condensation, substituted benzaldehydes, Darzens condensation.

Martynov and Titov [1] were the first who studied the reaction of methyl dichloroacetate with benzaldehyde under the conditions of the Darzens condensation with the aim of preparing methyl 2-chloro-3-phenyl-2,3-epoxypropionate (**2**). However, it has been shown in [2] by means of spectral methods (IR, PMR) and also by retrosynthesis that the result of the reaction of ester (**1**) with benzaldehyde under the conditions of the Darzens condensation is methyl 3-phenyl-3-chloro-2-oxopropionate (**3**), the isomerization product of (**2**). Probably, the stability of the α-chloroepoxide may be influenced by introduction of electron-accepting substituents in benzaldehyde. Therefore it was interesting to investigate reactions of methyl dichloroacetate with different benzaldehydes under the conditions of the Darzens condensation.

It has been shown that condensation of compound **1** with benzaldehyde, *p*-chloro- and *p*-bromobenzaldehyde in *t*-BuOH in the presence of *t*-BuOK yields methyl 3-aryl-3-chloro-2-oxopropionates (**3-5**).



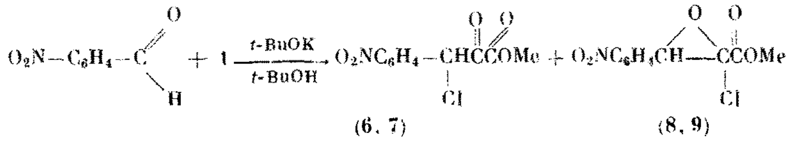
$$p\text{-R}-C_6H_4-CHO + 1 \xrightarrow[t\text{-BuOH}]{t\text{-BuOK}} p\text{-R}-C_6H_4-CH(Cl)-C(=O)-C(=O)-OMe$$

R=H(3), Cl(4), Br(5).

(3—5)

PMR spectral data of compound (**3**) are identical with those given in [2]. PMR spectra of compounds (**4**) and (**5**) have singlet signals in the regions 3.46 and 3.47 ppm of the protons of CH_3O, and 5.96 and 5.93 ppm of the methyne protons. IR spectra of these compounds contain an intensive absorption band in the region 1750 cm^{-1}, characteristic of vibration of the C(=O) − C(=O) group.

PMR spectra of crude products from reactions of ester **1** with *m*- and *p*-nitrobenzaldehyde contain, in addition to the signal of the methyne proton in the region ~6 ppm, a several times more-intensive singlet signal in the region ~4.8 ppm, corresponding with the epoxy proton.



$$O_2N-C_6H_4-CHO + 1 \xrightarrow[t\text{-BuOH}]{t\text{-BuOK}} O_2NC_6H_4-CH(Cl)C(=O)C(=O)OMe + O_2NC_6H_4\overset{O}{CH-C}(Cl)C(=O)OMe$$

(6, 7) (8, 9)

R=*m*-O_2N(6, 8), *p*-O_2N(7, 9).

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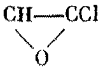
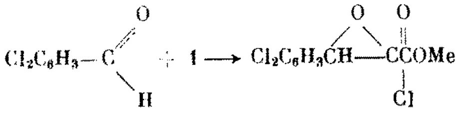
TABLE 1. Physicochemical and Spectral Data of Compounds (**3-10**)

Compound	Bp, °C (mm Hg) or mp, °C	n_D^{20}	Yield, %	Found/Calculated, % C	H	Hal	N	Empirical formula	C=O in IR spectrum, cm^{-1}	PMR spectrum (δ, ppm, solvent)
3	105-106 (0.02)	1.5295 (1.5300 [2])	65	56.47 56.60	4.22 4.23	16.52 16.67	–	$C_{10}H_9ClO_3$	1750	3.63s (3H, CH_3O), 5.93s (1H, CHCl), 7.30s (5H, C_6H_5), CCl_4
4	120-125 (0.01)	1.5385	63	48.71 48.60	3.32 3.23	29.91 28.69	–	$C_{10}H_8Cl_2O_3$	1750	3.46s (3H, CH_3O), 5.96s (1H, CHCl), 7.26s (4H, ClC_6C_4), CCl_4
5	Not distilled	1.5660	66	41.90 41.19	3.02 2.74	40.11 39.59	–	$C_{10}H_8BrClO_5$	1745	3.76 s (3H, CH_3O), 6.21s (1H, CHCl), 7.13—7.70m (4H, C_6H_4), $(CD_3)_2CO$
6	170-172 (0.02)	1.5605	8	45.65 45.20	3.41 3.30	13.76 13.36	6.01 5.81	$C_{10}H_8NClO_5$	1750	3.80 s (3H, CH_3O), 6.43s (1H, CHCl), 7.40—8.33 m (4H, m-$O_2NC_6H_4$), $(CD_3)_2CO$
7	170-174 (0.02)	1.5625	10	45.60 45.20	3.57 3.30	13.68 13.36	5.98 5.81	$C_{10}H_8NClO_5$	1755	3.83 s (3H, CH_3O), 6.23s (1H, CHCl), 7.43—8.26 m (4H, p-$O_2NC_6H_4$), $CDCl_3$
8	88-90	–	62	45.11 45.20	3.23 3.30	13.43 13.36	5.75 5.81	$C_{10}H_8NClO_5$	1745	3.83s (3H, CH_3O), 4.83 s (1H, $\underset{\diagdown O \diagup}{CH—CCl}$) 7.53—8.26m (4H, m-$O_2NC_6H_4$), $(CD_3)_2CO$
9	108-109	–	56	45.09 45.20	3.30 3.30	13.40 13.36	5.78 5.81	$C_{10}H_8NClO_5$	1750	3.86 s (3H, CH_2O), 4.83s (1H, $\underset{\diagdown O \diagup}{CH—CCl}$) 7.50—8.36m (4H, p-$O_2NC_6H_4$), $(CD_3)_2CO$
10	Not distilled	–	76	43.10 42.67	2.76 2.49	38.25 37.79	...	$C_{10}H_7Cl_3O_3$	1755	3.90 s (3H, CH_3O), 4.60 s (1H, $\underset{\diagdown O \diagup}{CH—CCl}$) 7.15—7.35m (3H, $Cl_2C_6H_3$), $CDCl_3$

Separation of α-chloroketones (**6**, **7**) and α-chloroepoxides (**8**, **9**) does not offer difficulty. Compounds **8** and **9** are crystalline, and **6** and **7** are viscous liquids. Location of the NO_2 group at different positions of the benzene ring has no influence on the ratio of products (**6**, **7**:**8**, **9** ∼ 1:7). The presence in the IR spectra of a narrow absorption band of C═O vibrations in the regions 1740 and 1755 cm^{-1}, respectively, and absorption bands of vibration of the epoxide proton in the regions 3000 and 3050 cm^{-1} do not contradict the assigned structure. The most exhaustive information on the structure of compounds **8** and **9** is provided by ^{13}C NMR spectra, which contain signals of all ten C atoms and were interpreted with the help of available data [4]. The PMR spectrum of the crude product from the reaction of 2,4-dichlorobenzaldehyde with **1** does not contain signals that relate to methyl 3-(2,4-dichlorophenyl)-3-chloro-2-oxopropionate. Singlet signals at 5.90 and 4.60 ppm and multiplet signals at 7.10-7.40 ppm relating to protons of $CH_3OC(O)$  and the 2,4-dichlorophenyl group, respectively, in the PMR spectrum, and absorption bands of C═O and C−H bonds in the regions 1755 and 2950 cm^{-1} in the IR spectra are evidence of the formation of methyl 2-chloro-3-(2′,4′-dichlorophenyl)-2,3-epoxypropionate (**10**). This is also confirmed by ^{13}C NMR spectra.


(10)

Formation of only α-chloroepoxide **10** in the case of 2,4-dichlorobenzaldehyde is probably not only explained by the electronegativity of the substituents, but also by steric factors.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrometer, PMR spectra on a Varian T-60 spectrometer (internal standard TMS), and ^{13}C NMR spectra on a Bruker M-250 spectrometer.

Methyl 3-Phenyl-3-chloro-2-oxopropionate (3). Under an atmosphere of dry argon, to a mixture of 19.0 g (0.18 mole) of benzaldehyde and 15.7 g (0.18 mole) of compound **1** is added at 0 to −5°C over 1.5 h a solution of 7.0 g (0.18 g-atom) K in 150 ml of *t*-BuOH. The mixture is stirred for another 8 h. Then it is stored at ∼20°C for 24 h and *t*-BuOH is evaporated under vacuum. To the residue is added a 5% aqueous NaCl solution, the mixture is extracted with diethyl ether (3 × 100 ml), and the extract is dried over $MgSO_4$. The solvent is evaporated under vacuum and the residue is distilled.

In much the same way compounds (4) and (5) are prepared from *p*-chloro- and *p*-bromobenzaldehyde.

Reaction of Ester 1 with *m*-Nitrobenzaldehyde. The reaction is carried out in much the same way as described for the synthesis of compound **3**. The mixture is extracted with chloroform. From the residue obtained after evaporation of the chloroform, crystals are formed on storing. The crystals are filtered off and washed with ether. Compound **8** is obtained. ^{13}C NMR spectrum ($CHCl_3$, δ, ppm): 56.70 (CH_3O), 63.83 (CH), 76.34 (CCl), 118.68, 120.19, 124.92, 128.44, 128.56, 141.85 (phenyl C), 157.00 (C═O). From the filtrate the solvent is evaporated and the residue is distilled under vacuum to yield compound **6**.

In much the same way, compounds **7** and **9** are obtained from *p*-nitrobenzaldehyde. ^{13}C NMR spectrum ($CHCl_3$, δ, ppm): 36.67 (CH_3O), 63.88 (CH), 76.25 (CCl), 119.35, 124.05, 133.77, 142.15 (phenyl C; the signals of two *ortho* and two *meta* C atoms are superimposed), 156.94 (C═O).

Methyl 2-chloro-3-(2,4-dichlorophenyl)-2,3-epoxypropionate (10) is prepared in much the same way from 2,4-dichlorobenzaldehyde. ^{13}C NMR spectrum ($CHCl_3$, δ, ppm): 56.64 (CH_3O), 62.99 (CH), 75.96 (CCl), 122.80, 125.75, 126.46, 127.45, 130.29, 130.61 (phenyl C), 157.06 (C═O).

Physicochemical and spectral data of compounds **3-10** are given in Table 1.

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2. R. N. McDonald and P. A. Schwab, *J. Org. Chem.*, **29**, No. 8, 2459 (1964).
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