Dimethyl dichloromalonate as a new synthetic equivalent of methyl dichloroacetate in the Darzens condensation

E. A. Berdnikov[a] *and V. A. Mamedov*[b]*

[a] *V. I. Ul'yanov-Lenin Kazan' State University,*
18 ul. Lenina, 420008 Kazan', Russian Federation
[b] *A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan' Scientific Center*
of the Russian Academy of Sciences, 8 ul. Akad. Arbuzova, 420083 Kazan', Russian Federation.
Fax: +7 (843 2) 752 253

Dimethyl dichloromalonate reacts with aldehydes in the presence of sodium methoxide to form α-chloropyruvates, α-chloroglycidates, or α,α-dichlorohydrins, depending on the nature of the aldehyde.

Key words: dimethyl dichloromalonate, Darzens reaction, α-chloroketones, -chloroepoxides, α,α-dichlorohydrins.

Functionalized α-chloroketones and -chloroepoxides can be prepared by the reactions between esters of dichloroacetic acid and aldehydes under conditions of the Darzens reaction.[1,2] These products are formed in low yields from esters of dichloroacetic acid.[3–5] The attempt to involve 3,3-dichloropentanedione in a similar reaction failed because of the change in the direction of the reaction.[6,7]

A new method for preparing functionalized α-chloroketones and -chloroepoxides in reactions between dimethyl dichloromalonate and various aldehydes in the presence of MeONa (Scheme 1) is presented in this work.

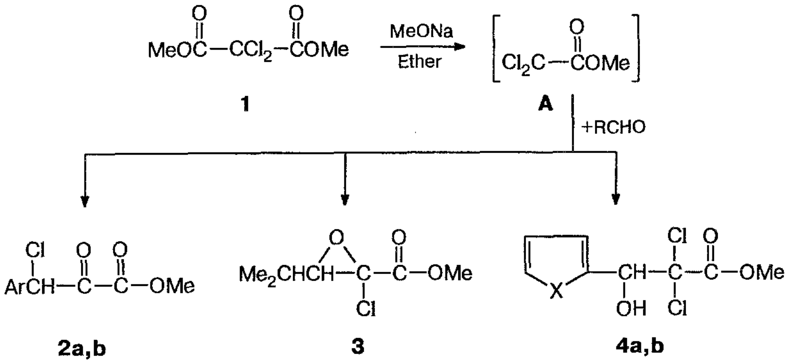
The nature of radical R in the aldehyde RCHO determines the structure of the reaction product. As in the reaction between dichloroacetates and aldehydes, diester **1** with aromatic aldehydes forms methyl 3-aryl-3-chloropyruvates **2** under conditions of the Darzens condensation.[1,2,8,9] Epoxide **3** is formed in the reaction with isobutyric aldehyde, and the products **4** of the first stage of the Darzens reaction are formed in the reactions with heteroaromatic aldehydes. The fairly low yields of compounds **4a** and **4b** can be explained by their decomposition to give the initial aldehyde and methyl dichloroacetate under condensation conditions.[8]

Thus, dimethyl dihloromalonate **1** in the presence of MeONa in the reverse Claisen condensation forms the anion **A**, which reacts with aldehydes to give the products of the Darzens reaction.

Experimental

IR spectra were recorded on a UR-20 spectrophotometer. An ^{1}H NMR spectrum of compound **4a** was recorded on a Bruker MSL-400 instrument (400.13 MHz) in CD_3CN, and ^{1}H NMR spectra of **3** and **4b** were recorded on a Varian 60 instrument (60 MHz).

Scheme 1



Ar = Ph (**2a**), *p*-BrC_6H_4 (**2b**); X = O (**4a**), S (**4b**)

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1544—1545, August, 1995.

Standard procedure. A powder of MeONa (0.1 mol) was added to a mixture of diester **1** (0.1 mol) and benzaldehyde (0.1 mol) in ether in an argon atmosphere with stirring and cooling to −5 to −10 °C. Then the mixture was stirred for 2 h at 0 °C and 10 h at 20 °C, treated with water, acidified with a dilute solution of HCl, extracted with ether (3×50 mL), and dried over $MgSO_4$. After evaporating *in vacuo* the residue was distilled. Methyl 3-phenyl-3-chloropyruvate (**2a**) was obtained in a 72 % yield, b.p. 105 to 107 °C (0.02 Torr), n_D^{20} = 1.5295 (*cf.* Ref. 1: n_D^{20} = 1.5300, yield 65 %).

Compounds **2b**, **3**, and **4a,b** were synthesized by a similar procedure.

Methyl 3-(4′-bromophenyl)-3-chloropyruvate (2b). Yield 55 %, b.p. 140 to 142 °C (0.02 Torr), n_D^{20} = 1.5670 (*cf.* Ref. 2: n_D^{20} = 1.5660, yield 66 %).

Methyl 2-chloro-4-methyl-2,3-epoxypentanoate (3). Yield 98 %, b.p. 83 to 85 °C (14 Torr). ^{1}H NMR ($CDCl_3$, δ): 1.05 (d, 3 H, Me, $^3J_{CH-Me}$ = 6.5 Hz); 1.16 (d, 3 H, Me, $^3J_{CH-Me}$ = 6.5 Hz); 1.26 to 2.16 (m, 1 H, $\underline{CH}$(Me)); 2.97 (d, 1 H, CHO, $^3J_{CH-CH}$ = 8.4 Hz); 3.73 (s, 3 H, Me).

Methyl 3-(2′-furyl)-3-hydroxy-2,2-dichloropropionate (4a). Yield 35 %, b.p. 120 to 122 °C (0.02 Torr). ^{1}H NMR ($CDCl_3$, δ): 3.91 (s, 3 H, OMe); 5.45 (s, 1 H, HCO); 6.39 (dd, 1 H, H-4, $^3J_{3-4}$ = 3.3 Hz, $^3J_{4-5}$ = 1.8 Hz); 6.53 (dd, 1 H, H-3, $^3J_{3-4}$ = 3.3 Hz, $^4J_{3-5}$ = 0.8 Hz); 7.43 (dd, 1 H, H-5, $^3J_{4-5}$ = 1.8 Hz, $^4J_{3-5}$ = 0.8 Hz). IR (ν/cm^{-1}): 3490, 3160, 3130, 2965, 2880, 1760, 1615.

Methyl 3-(2′-thienyl)-3-hydroxy-2,2-dichloropropionate (4b). Yield 33 %, b.p. 112 to 114 °C (0.02 Torr), n_D^{20} = 1.5515 (*cf.* Ref. 2: n_D^{20} = 1.5500, 43.9 %).

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Received November 23, 1994;
in revised form January 12, 1995