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Reaction of Organozinc Reagents Formed in Reaction of Dibromomalonic Acid Dialkyl Esters and Zinc, with 2-Arylmethylenemalonic Acid Dinitriles and 3-Aryl-2-cyanopropenoic Acid Methyl Esters

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Abstract—Organozinc compounds, obtained from dibromomalonic acid dialkyl esters and zinc, react with 2-arylmethylmalonic acid dinitriles and 3-aryl-2-cyanopropenoic acid methyl esters forming 3-aryl-2,2-dicyanocyclopropane-1,1-dicarboxylic acid dialkyl esters and 3-aryl-2-cyanocyclopropane-1,1,2-tricarboxylic acid trimethyl esters. ^{1}H and ^{13}C NMR, $^3J_{CH}$ constants are considered.

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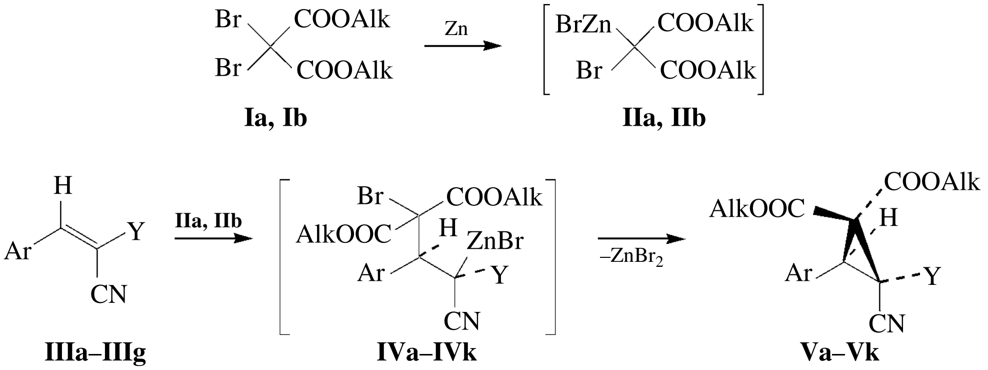
Earlier the organozinc reagents obtained from dialkyl esters of dibromomalonic acid have been applied for cyclopropanation of arylidenmalonic acid alkyl esters [1].

In the present work we have studied an interaction of organozinc reagents **IIa** and **IIb**, formed of dibromomalonic acid dialkyl esters **Ia** and **Ib** and zinc, with electrophilic substrates **IIIa**–**IIIg**, in order to obtain cyclopropane compounds containing in the ring two geminal alkoxycarbonyl or cyano groups and simultaneously another cyano- or ester group. The reaction is found to proceed according to the following scheme:



I, **II**, Alk = CH_3 (**a**), CH_2CH_3 (**b**). **III**, Y = CN, Ar = C_6H_5 (**a**), 4-BrC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 4-$CH_3OC_6H_4$ (**d**), Y = $COOCH_3$, Ar = 4-BrC_6H_4 (**e**), 3-BrC_6H_4 (**f**), 2,4-$Cl_2C_6H_3$ (**g**). **IV, V**, Y = CN, Alk = CH_3, Ar = C_6H_5 (**a**), 4-BrC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 4-MeOC_6H_4 (**d**), Alk = CH_2CH_3, Ar = C_6H_5 (**e**), 4-BrC_6H_4 (**f**), 4-ClC_6H_4 (**g**), 4-MeOC_6H_4 (**h**), Y = $COOCH_3$, Alk = CH_3, Ar = 4-BrC_6H_4 (**i**), 3-BrC_6H_4 (**j**), 2,4-$Cl_2C_6H_3$ (**k**).

In the ether–tetrahydrofuran–HMPTA medium, organozinc compounds **IIa** and **IIb** react regiospecifically with electrophilic substrates **IIIa**–**IIIg**, attacking C^3 carbon atom and giving intermediate compounds **IVa**–**IVk**. Under the reaction conditions, intermediates **IVa**–**IVk** spontaneously undergo cyclization forming corresponding products of cyclopropanation **Va**–**Vk**, dialkyl 3-aryl-2,2-dicyanocyclopropane-

1,1-dicarboxylates and trimethyl 3-aryl-2-cyanocyclopropane-1,1,2-triicarboxylates.

The structure of compounds **Va**–**Vk** was proven by analytical data and IR and ^{1}H NMR spectroscopy. The IR spectra of compounds **Va**–**Vk** contain characteristic absorption bands of the ester carbonyl groups (1720–1725 cm^{-1}) and nitrile groups (2240–2245 cm^{-1}). In ^{1}H NMR spectra of compounds **Va**–**Vh** we observed characteristic signals at 3.84–4.91 ppm, belonging to methine proton (CH), as well as proton signals of methyl- and ethyl-substituents of two ester groups. In ^{1}H NMR spectra of compounds **Vi**–**Vk** we observed characteristic signals belonging to methine proton (CH) at 3.80–3.87 ppm, and there were also proton signals of methyl substituents of three ester groups. The same set of proton signals indicates the formation of these substances as the same diastereoisomer.

The structure of compounds **Vc** and **Vk** was confirmed also by ^{13}C NMR spectra recorded both with and without decoupling from protons. The ^{1}H and ^{13}C signals assignment was made on the basis of two-dimensional HSQC, HMBC and NOESY experiments. Signals of two nitrile and two carbonyl carbons in structure **Vc** were identified according to spin–spin coupling constants $^3J_{CH}$ with cyclopropane ring proton H^3. The constants of the carbons located in *cis*-position to a proton (δ_{CO} 163.26 ppm, $^3J_{CH}$ 6.3 Hz; δ_{CN} 111.45 ppm, $^3J_{CH}$ 6.1 Hz) are larger than for *trans*-carbons (δ_{CO} 161.23 ppm, $^3J_{CH}$ 4.1 Hz; δ_{CN} 109.36 ppm, $^3J_{CH}$ 4.6 Hz). Signals of methoxy groups protons are assigned according to the cross peaks with corresponding carbonyls in HMBC spectrum: protons at 3.98 ppm give cross peak with carbon at 163.26 ppm, and protons at 3.80 ppm with carbon at 161.23 ppm. Carbons of methoxy groups are assigned according to the cross peaks with corresponding protons in HSQC spectrum (due to direct constants). These conclusions are confirmed by the 2D NOESY data for compound **Vc**: *cis*-OMe protons give cross peak with proton H^3, and *trans*-OMe protons with *ortho*-protons of the aromatic substituent. In compound **Vk** the value of vicinal coupling constant between H^3 proton and carbon of nitrile group $^3J_{CH}$ 4.4 Hz allows to assume that in this structure interacting atoms occupy trans-position relative to the cyclopropane plane.

EXPERIMENTAL

IR spectra were recorded on a Specord IR-75 spectrometer for individual compounds dispersed in mineral oil. ^{1}H NMR spectra were measured from solutions of compounds **Va**, **Vd**–**Vj** in CDCl$_3$ on Tesla BS-567A spectrometer at 100 MHz, and for compound **Vb** from solution in CDCl$_3$ on a Mercury–Plus-300 spectrometer at 300 MHz using HMDS as internal reference. 1D- and 2D-NMR spectra of compounds **Vc** and **Vk** from solutions in CDCl$_3$ were taken on a Bruker DRX-400 instrument (400 MHz for ^{1}H and 100 MHz for ^{13}C) relative to TMS as internal reference.

Dialkyl 3-aryl-2,2-dicyanocyclopropane-1,1-dicarboxylates (VIa–VIh). A dibromomalonic acid dialkyl ester 0.024 mol was added to 2 g of zinc crushed in a fine shavings in 7 ml of ether and 10 ml of tetrahydrofuran. Thr mixture was heated up to the beginning of reaction, then reaction continued spontaneously. After the end of reaction the mixture was refluxed for 5 min, then cooled and poured off from zinc into a flask containing 0.02 mol of 2-arylmethylenemalonic dinitrile and 1,5 ml of HMPTA, and refluxed for 60 min. After cooling, the mixture was hydrolyzed with 5% acetic acid and reaction product was extracted with benzene, the solvents were evaporated and the residue was recrystallized from methanol.

Dimethyl 3-phenyl-2,2-dicyanocyclopropane-1,1-dicarboxylate (Va). Yield 76%, mp 125–126°C. IR spectrum (mineral oil), ν, cm^{-1}: 1720, 2240. ^{1}H NMR spectrum, δ, ppm: 3.72 s (3H, COOCH$_3$), 3.91 s (1H, CH), 3.95 s (3H, COOCH$_3$), 7.11–7.44 m (5H, C$_6$H$_5$). Found, %: C 63.29; H 4.20; N 9.74. $C_{15}H_{12}N_2O_4$. Calculated, %: C63.38; H 4.25; N 9.85.

Dimethyl 3-(4-bromophenyl)-2,2-dicyanocyclopropane-1,1-dicarboxylate (Vb). Yield 70%, mp 100–102°C. IR spectrum (mineral oil), ν, cm^{-1}: 1725, 2245. ^{1}H NMR spectrum, δ, ppm: 3.79 s (3H, COOCH$_3$), 3.90 s (1H, CH), 3.97 s (3H, COOCH$_3$), 7.23–7.56 m (4H, BrC$_6$H$_4$). Found, %: C 49.54; H 2.98; N 7.63. $C_{15}H_{11}BrN_2O_4$. Calculated, %: C 49.61; H 3.05; N 7.71.

Dimethyl 3-(4-chlorophenyl)-2,2-dicyanocyclopropane-1,1-dicarboxylate (Vc). Yield 77%, mp 103–104°C. IR spectrum (mineral oil), ν, cm^{-1}: 1720, 2245. ^{1}H NMR spectrum: (400 MHz, δ, ppm, *J*, Hz): 3.80 s (3H, OMe-*trans*); 3.93 t (1H, H^3, 4*J* 0.8); 3.98 s (3H, OMe-*cis*); 7.31 dd (2H, H$_o$, *J* 8.8, 0.8); 8.74 d (2H, H$_m$, *J* 8.8). ^{13}C NMR spectrum (100 MHz, δ, ppm, *J*, Hz): 16.46 d (C^2, *J* 2.8); 39.51 d.t (C^3, *J* 170.4, 4.6); 46.32 d (C^1, *J* 3.4); 54.11 q (OMe-*trans*, *J* 149.3); 54.99 q (OMe-*cis*, *J* 149.4); 109.36 d (CN-*trans*, *J* 4.6); 111.45 d (CN-*cis*, *J* 6.1); 125.58 t.d (C$_i$, *J* 8.0, 2.3); 129.48 d.d (C$_m$, *J* 168.1, 5.1); 130.08 d.d.d (C$_o$, *J* 162.3, 6.8, 2.7); 136.08 t.t (C$_p$, *J* 10.3, 3.4); 161.23 q.d (CO-*trans*, *J* 4.1); 163.26 d.q (CO-*cis*, *J* 6.3, 4.0). Found, %: 56.43; H 3.42; N 8.72.

$C_{15}H_{11}ClN_2O_4$. Calculated, %: C 56.53; H 3.48; N 8.79.

Dimethyl 3-(4-methoxyphenyl)-2,2-dicyanocyclopropane-1,1-dicarboxylate (Vd). Yield 67%, mp 101–102°C. IR spectrum (mineral oil), ν, cm^{-1}: 1725, 2245. ^{1}H NMR spectrum, δ, ppm: 3.75 s (6H, CH_3O, $COOCH_3$), 3.91 s (1H, CH), 3.95 s (3H, $COOCH_3$), 6.78–7.22 m (4H, $MeOC_6H_4$). Found, %: C 61.07; H 4.43; N 8.84. $C_{16}H_{14}N_2O_5$.Calculated, %: C 61.14; H 4.49; N 8.91.

Diethyl 3-phenyl-2,2-dicyanocyclopropane-1,1-dicarboxylate (Ve). Yield 69%, mp 71–72°C. IR spectrum (mineral oil), ν, cm^{-1}: 1720, 2240. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.16 t, 1.36 t (6H, $COOCH_3CH_2$, *J* 7.4), 3.91 s (1H, CH), 4.14 q, 4.40 q (4H, $COOCH_3CH_2$, *J* 7.4), 7.16–7.29 m (5H, C_6H_5). Found, %: C 65.30; H 5.11; N 8.89. $C_{17}H_{16}N_2O_4$. Calculated, %: C65.38; H 5.16; N 8.97.

Diethyl 3-(4-bromophenyl)-2,2-dicyanocyclopropane-1,1-dicarboxylate (Vf). Yield 70%, mp 86–87°C. IR spectrum (mineral oil), ν, cm^{-1}: 1725, 2240. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.20 t, 1.42 t (6H, $COOCH_3CH_2$, J 7.4), 3.84 s (1H, CH), 4.16 q, 4.40 q (4H, $COOCH_3CH_2$, *J* 7.4), 7.12–7.49 m (4H, BrC_6H_4). Found, %: C 52.12; H 3.77; N 7.09. $C_{17}H_{15}BrN_2O_4$. Calculated, %: C 52.19; H 3.86; N 7.16.

Diethyl 3-(4-chlorophenyl)-2,2-dicyanocyclopropane-1,1-dicarboxylate (Vg). Yield 69%, mp 85–87°C. IR spectrum (mineral oil), ν, cm^{-1}: 1725, 2240. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.19 t, 1.43 t (6H, $COOCH_3CH_2$, *J* 7.4), 3.86 s (1H, CH), 4.16 q, 4.40 q (2H, $COOCH_3CH_2$, *J* 7.4), 7.17–7.26 m (4H, ClC_6H_4). Found, %: C 58.79; H 4.30; N 8.02. $C_{17}H_{15}ClN_2O_4$. Calculated, %: C 58.88; H 4.36; N 8.08.

Diethyl 3-(4-methoxyphenyl)-2,2-dicyanocyclopropane-1,1-dicarboxylate (Vh). Yield 67%, mp 75–77°C. IR spectrum (mineral oil), ν, cm^{-1}: 1725, 2240. ^{1}H NMR spectrum, δ, ppm, (*J*, Hz): 1.20 t, 1.42 t (6H, $COOCH_3CH_2$, *J* 7.4), 3.75 s (3H, CH_3O), 3.85 s (1H, CH), 4.16 q, 4.39 q (4H, $COOCH_3CH_2$, *J* 7.4), 6.76–7.23 m (4H, $MeOC_6H_4$). Found, %: C 63.04; H 5.24; N 8.11. $C_{18}H_{18}N_2O_5$. Calculated, %: C 63.15; H 5.30; N 8.18.

3-Aryl-2-cyanocyclopropane-1,1,2-tricarboxylic acid trialkyl esters (Vi–Vk). The procedure is similar to a technique used for preparation of compounds **VIa–VIh** except that instead of 2-arylmethylenemalonic acid dinitrile methyl ester of a 2-aryl-3-cyanopropenoic acid has been used.

Trimethyl 3-(4-bromophenyl)-2-cyanocyclopropane-1,1,2-tricarboxylate (Vi). Yield 68%, mp 92–93°C. IR spectrum (mineral oil), ν, cm^{-1}: 1730, 2235. ^{1}H NMR spectrum, δ, ppm: 3.66 s (3H, $COOCH_3$), 3.77 s (3H, $COOCH_3$), 3.83 s (1H, CH), 3.87 s (3H, $COOCH_3$), 7.15 d (2H, 4-BrC_6H_4), 7.45 d (2H, 4-BrC_6H_4). Found, %: C 48.47; H 3.50; N 3.49. $C_{16}H_{14}BrNO_6$. Calculated, %: C 48.50; H 3.56; N 3.54.

Trimethyl 3-(3-bromophenyl)-2-cyanocyclopropane-1,1,2-tricarboxylate (Vj). Yield 65%, mp 104–106°C. IR spectrum (mineral oil), ν, cm^{-1}: 1730, 2245. ^{1}H NMR spectrum, δ, ppm: 3.68 s (3H, $COOCH_3$), 3.75 s (3H, $COOCH_3$), 3.82 s (1H, CH), 3.87 s (3H, $COOCH_3$), 7.08–7.45 m (4H, 3-BrC_6H_4). Found, %: C 48.40; H 3.48; N 3.47. $C_{16}H_{14}BrNO_6$. Calculated, %: C 48.50; H 3.56; N 3.54.

Trimethyl 3-(2,4-dichlorophenyl)-2-cyanocyclopropane-1,1,2-tricarboxylate (Vk). Yield 66%, mp 116–117°C. IR spectrum (mineral oil), ν, cm^{-1}: 1735, 2245. ^{1}H NMR spectrum.: (400 MHz), δ, ppm (*J*, Hz): 3.78 s (3H, $COOCH_3$); 3.81 d (1H, CH, *J* 1.0); 3.83 s (3H, $COOCH_3$); 3.94 s (3H, $COOCH_3$); 7.29 dd (1H, $H^{5'}$, *J* 8.4, 2.0); 7.34 d.d (1H, $H^{6'}$, *J* 8.4, 1.0); 7.46 d (1H, $H^{3'}$, *J* 2.0). ^{13}C NMR (100 MHz, δ, ppm, *J*, Hz): 31.32 d (C^2, *J* 2.5); 37.90 d.d (C^3, *J* 169.7, 4.6); 47.34 d (C^1, *J* 3.0); 53.72 q (MeO, *J* 148.4); 53.85 q (MeO, *J* 149.0); 54.81 q (MeO, *J* 149.2); 112.03 d (CN, *J* 4.4); 126.28 d.d.d ($C^{1'}$, *J* 7.9, ($C^{4'}$, *J* 10.4, 3.9, 2.5); 162.81 d.q (CO, *J* 5.0, 4.1); 163.87 d.q (CO, *J* 5.7, 4.0); 164.55 d.q (CO, *J* 5.2, 4.0). Found, %: C 49.73; H 3.3.35; N 3.59. $C_{16}H_{13}Cl_2NO_6$. Calculated, %: C 49.76; H 3.3.39; N 3.63.

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