

Reaction of Zinc Enolates Derived from 1-Aryl-2,2-dibromoalkan-1-ones with Tetramethyl 2,2'-(1,4-Phenylenedimethylidene)dimalonate, Dimethyl 3,3'-(1,4-Phenylene)bis(2-cyanoacrylate), and 2,2'-(1,4-Phenylenedimethylidene)-bis(malononitrile)

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Abstract—Zinc enolates derived from 1-aryl-2,2-dibromoalkanones reacted with tetramethyl 2,2'-(1,4-phenylenedimethylidene)dimalonate, dimethyl 3,3'-(1,4-phenylene)bis(2-cyanoacrylate), and 2,2'-(1,4-phenylenedimethylidene)bis(malononitrile) to give, respectively, tetramethyl 3,3'-(1,4-phenylene)bis(2-alkyl-2-aroylecyclopropane-1,1-dicarboxylates), dimethyl 3,3'-(1,4-phenylene)bis(2-alkyl-2-aroylecyclopropane-1,1-dicarboxylates), and 3,3'-(1,4-phenylene)bis(2-alkyl-2-aroylecyclopropane-1,1-dicarbonitriles) as a single stereoisomer.

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1-Aryl-2,2-dibromobutan-1-ones are known to react with zinc and alkyl or aryl 3-aryl-2-cyanoprop-2-enoates, 2-arylmethylidenemalononitriles, and dialkyl 2-arylmethylidenemalonates to give the corresponding cyclopropanation products [1–3]. With a view to extend the synthetic scope of this transformation, we examined reactions of bromine-containing zinc enolates **IIa–IIg** (generated from 1-aryl-2,2-dibromoalkanones **Ia–Ig**) with tetramethyl 2,2'-(1,4-phenylenedimethylidene)dimalonate (**IIIa**), dimethyl 3,3'-(1,4-phenylene)bis(2-cyanoacrylate) (**IIIb**), and 2,2'-(1,4-phenylenedimethylidene)bis(malononitrile) (**IIIc**).

The reactions were carried out in diethyl ether–ethyl acetate; under these conditions, zinc enolates **IIa–IIg** preliminarily prepared from dibromo ketones **Ia–Ig** added at one double bond of unsaturated substrate **IIIa–IIIc** to give intermediates **IVa–IVj** which underwent spontaneous cyclization to cyclopropane derivatives **Va–Vj**. The subsequent addition of zinc enolates **IIa–IIg** at the remaining double bond in **Va–Vj**, followed by cyclopropane ring closure, led to the formation of final products **VIa–VIj** (Scheme 1).

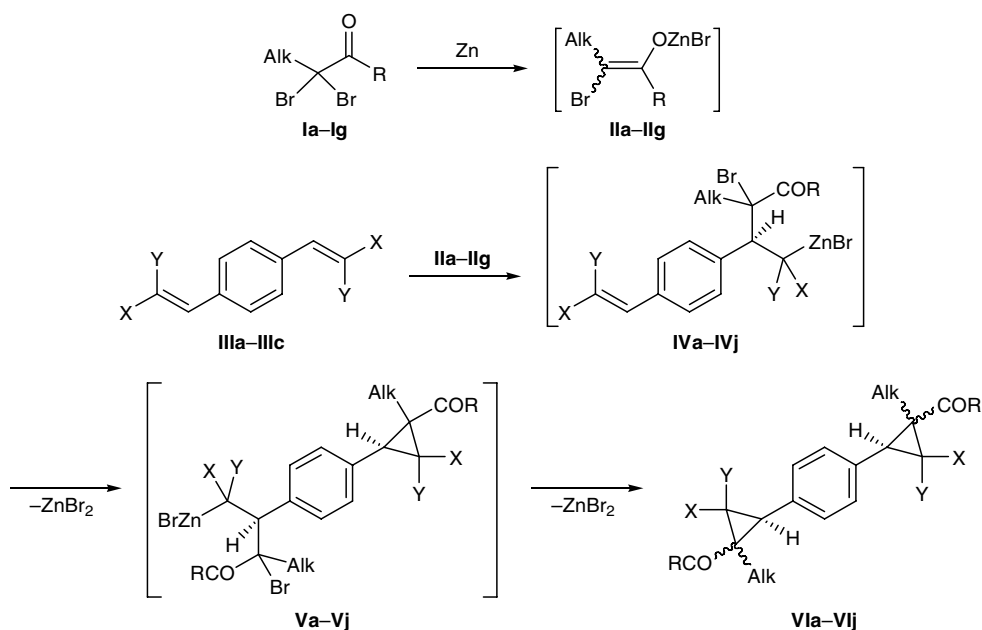
The structure of compounds **VIa–VIj** was proved by elemental analysis and IR and ¹H NMR spectroscopy.

The IR spectra of **VIa–VIg** contained absorption bands due to stretching vibrations of aroyl carbonyl groups at 1675–1680 (**VIa–VIc**) and 1655–1680 cm^{−1} (**VIId–VIg**), ester carbonyl groups at 1730–1740 cm^{−1}, and cyano groups at 2230–2265 cm^{−1} (**VIId–VIg**). In the IR spectra of **VIh–VIj** we observed absorption bands belonging to aroyl carbonyl and cyano groups at 1680 and 2240–2245 cm^{−1}, respectively. Compounds **VIa–VIg** showed in the ¹H NMR spectra singlets from the ester methyl groups at δ 3.25–3.35 (**VIa–VIc**) and 3.40–3.92 ppm (**VIId–VIg**) and CH proton in the cyclopropane ring at δ 3.19–3.20 (**VIa–VIc**) and 3.40 ppm (**VIId–VIg**). The ¹H NMR spectra of **VIh–VIj** contained signals from the methyl protons at δ 1.74–1.80 ppm and CH proton at δ 4.03–4.16 ppm.

We previously showed that structurally related compounds, e.g., dimethyl 2-benzoyl-2-ethyl-3-phenylcyclopropane-1,1-dicarboxylate, are formed as a single stereoisomer with *cis* arrangement of the benzoyl and phenyl groups [1]. It was found that protons of the methoxycarbonyl group in the *cis* position with respect to 3-H resonate in a weaker field (δ 3.88 ppm) than those of the ester group in the *trans* position (δ 3.18 ppm). Comparison of the ¹H NMR spectra of dimethyl 2-benzoyl-2-ethyl-3-phenylcyclopropane-1,1-dicarboxylate and bis-cyclopropane derivatives **VIa–**

[†] Deceased.

Scheme 1.



I, II, Alk = Me, R = Ph (**a**), 4-ClC₆H₄ (**b**), 4-BrC₆H₄ (**c**), 4-FC₆H₄ (**d**), 4-MeC₆H₄ (**e**); Alk = Et, R = 4-BrC₆H₄ (**f**); Alk = H, R = *i*-Pr (**g**); **III**, X = Y = COOMe (**a**); X = CN, Y = COOMe (**b**); X = Y = CN (**c**); **IV-VI**, X = Y = COOMe, Alk = Me, R = 4-BrC₆H₄ (**a**), 4-FC₆H₄ (**b**); Alk = Et, R = 4-BrC₆H₄ (**c**); X = CN, Y = COOMe, Alk = Me, R = Ph (**d**), 4-BrC₆H₄ (**e**), 4-FC₆H₄ (**f**), 4-MeC₆H₄ (**g**); X = Y = CN, Alk = Me, R = 4-ClC₆H₄ (**h**), 4-BrC₆H₄ (**i**), 4-FC₆H₄ (**j**).

VIc (see Experimental) indicates analogous configuration of the cyclopropane fragments in the latter.

We also showed that cyclopropane derivatives in which ester and cyano groups are attached to the same carbon atom, namely methyl 2-(4-chlorobenzoyl)-1-cyano-3-(2,4-dichlorophenyl)-2-methylcyclopropane-1-carboxylate and methyl 2-(4-chlorobenzoyl)-1-cyano-3-(2,4-dichlorophenyl)-2-ethylcyclopropane-1-carboxylate, are formed as mixtures of two diastereoisomers. In the ¹H NMR spectrum of the isomer with *cis* arrangement of the cyano, aryl, and aroyl groups [methyl 2-(4-chlorobenzoyl)-1-cyano-3-(2,4-dichlorophenyl)-2-methylcyclopropane-1-carboxylate], the 3-H proton and protons of the methoxycarbonyl group resonate at δ 3.46 and 3.91 ppm, respectively (CDCl₃). The ester and aroyl groups and 3-H in methyl 2-(4-chlorobenzoyl)-1-cyano-3-(2,4-dichlorophenyl)-2-ethylcyclopropane-1-carboxylate are oriented at the same side of the cyclopropane ring, and the chemical shifts of 3-H and CH₃O are 3.72 and 3.89 ppm, respectively (CDCl₃) [2]. Comparison of these data with the ¹H NMR spectra of compounds **VId-VIj** (see Experimental) led us to conclude that the configuration of the cyclopropane fragments in the latter is analogous to methyl 2-(4-chlorobenzoyl)-1-cyano-3-(2,4-dichlorophenyl)-2-methylcyclopropane-1-carboxylate.

As shown in [3], 2-alkyl-3-aryl-2-arylcyclopropane-1,1-dicarbonitriles are formed as mixtures of two diastereoisomers with *cis* and *trans* orientation of the aroyl and aryl groups with respect to the three-membered ring plane. The chemical shift of 3-H in *r*-2-(4-bromobenzoyl)-2-methyl-*c*-3-phenylcyclopropane-1,1-dicarbonitrile is 4.22 ppm (DMSO-*d*₆). As follows from the ¹H NMR data (see Experimental), the cyclopropane rings in compounds **VIh-VIj** have analogous stereoconfiguration, i.e., the aroyl and aryl substituents therein are arranged *cis* with respect to each other.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer from samples dispersed in mineral oil. The ¹H NMR spectra were measured from solutions in CDCl₃ (**VIa-VIc**, **VIe**, **VIg**) or DMSO-*d*₆ (**VId**, **VIe**, **VIh-VIj**) on a Varian Mercury Plus-300 spectrometer (300 MHz) using hexamethyldisiloxane as internal reference.

General procedure for the synthesis of bicyclopentane derivatives VIa-VIj. A solution of 0.065 mol of dibromo ketone **Ia-Ig** in 3 ml of ethyl acetate was added to a mixture of 2 g of fine zinc

turnings, 5 ml of diethyl ether, and 5 ml of ethyl acetate. The mixture was heated to initiate the reaction which then occurred spontaneously. When the reaction was complete, the mixture was heated for 15–20 min and cooled, and the solution was separated by decanting. Compound **IIIa–IIIc**, 0.05 mol, and ethyl acetate, 2 ml, were added to the solution, and the mixture was heated for 30–40 min, cooled, treated with 5% acetic acid, and extracted with benzene. The solvent was distilled off, and the residue was recrystallized from methanol–acetone.

Tetramethyl 3,3'-(1,4-phenylene)bis[2-(4-bromobenzoyl)-2-methylcyclopropane-1,1-dicarboxylate] (VIa). Yield 65%, mp 212–214°C. IR spectrum, ν , cm^{-1} : 1680, 1735. ^1H NMR spectrum, δ , ppm: 1.55 s (6H, CH_3), 3.20 s (2H, CH), 3.26 s (6H, OCH_3), 3.96 s (6H, OCH_3), 7.37–7.99 m (12H, H_{arom}). Found, %: C 55.10; H 3.95. $\text{C}_{36}\text{H}_{32}\text{Br}_2\text{O}_{10}$. Calculated, %: C 55.12; H 4.11.

Tetramethyl 3,3'-(1,4-phenylene)bis[2-(4-fluorobenzoyl)-2-methylcyclopropane-1,1-dicarboxylate] (VIb). Yield 67%, mp 212–213°C. IR spectrum, ν , cm^{-1} : 1675, 1740. ^1H NMR spectrum, δ , ppm: 1.56 s (6H, CH_3), 3.20 s (2H, CH), 3.25 s (6H, OCH_3), 3.96 s (6H, OCH_3), 7.10–8.16 m (12H, H_{arom}). Found, %: C 65.10; H 4.85. $\text{C}_{36}\text{H}_{32}\text{F}_2\text{O}_{10}$. Calculated, %: C 65.25; H 4.87.

Tetramethyl 3,3'-(1,4-phenylene)bis[2-(4-bromobenzoyl)-2-ethylcyclopropane-1,1-dicarboxylate] (VIc). Yield 69%, mp 232–234°C. IR spectrum, ν , cm^{-1} : 1680, 1735. ^1H NMR spectrum, δ , ppm: 1.06–1.19 m (6H, CH_3CH_2), 2.14–2.15 m (4H, CH_3CH_2), 3.12 s (2H, CH), 3.35 s (6H, OCH_3), 3.95 s (6H, OCH_3), 7.38–7.57 m (12H, H_{arom}). Found, %: C 56.10; H 4.43. $\text{C}_{38}\text{H}_{36}\text{Br}_2\text{O}_{10}$. Calculated, %: C 56.17; H 4.47.

Dimethyl 3,3'-(1,4-phenylene)bis[2-(benzoyl)-1-cyano-2-methylcyclopropane-1-carboxylate] (VIId). Yield 63%, mp 260–262°C. IR spectrum, ν , cm^{-1} : 1655, 1730, 2230. ^1H NMR spectrum, δ , ppm: 1.60 s (6H, CH_3), 3.65 s (2H, CH), 3.85 s (6H, OCH_3), 7.02–7.77 m (12H, H_{arom}). Found, %: C 72.81; H 4.97; N 4.98. $\text{C}_{34}\text{H}_{28}\text{N}_2\text{O}_6$. Calculated, %: C 72.84; H 5.03; N 5.00.

Dimethyl 3,3'-(1,4-phenylene)bis[2-(4-bromobenzoyl)-1-cyano-2-methylcyclopropane-1-carboxylate] (VIe). Yield 65%, mp 260–261°C. IR spectrum, ν , cm^{-1} : 1680, 1735, 2245. ^1H NMR spectrum, δ , ppm: 1.61 s (6H, CH_3), 3.63 s (2H, CH), 3.86 s (6H, OCH_3), 6.99–7.73 m (12H, H_{arom}). Found, %: C 56.83; H 3.62; N 3.78. $\text{C}_{34}\text{H}_{26}\text{Br}_2\text{N}_2\text{O}_6$. Calculated, %: 56.84; H 3.65; N 3.90.

Dimethyl 3,3'-(1,4-phenylene)bis[1-cyano-2-(4-fluorobenzoyl)-2-methylcyclopropane-1-carboxylate] (VIf). Yield 61%, mp 257–258°C. IR spectrum, ν , cm^{-1} : 1670, 1740, 2265. ^1H NMR spectrum, δ , ppm: 1.68 s (6H, CH_3), 3.41 s (2H, CH), 3.92 s (6H, OCH_3), 6.97–7.80 m (12H, H_{arom}). Found, %: C 68.43; H 4.35; N 4.67. $\text{C}_{34}\text{H}_{26}\text{F}_2\text{N}_2\text{O}_6$. Calculated, %: C 68.45; H 4.39; N 4.70.

Dimethyl 3,3'-(1,4-phenylene)bis[1-cyano-2-methyl-2-(4-methylbenzoyl)cyclopropane-1-carboxylate] (VIg). Yield 67%, mp 257–258°C. IR spectrum, ν , cm^{-1} : 1665, 1740, 2245. ^1H NMR spectrum, δ , ppm: 1.68 s (6H, CH_3), 2.40 s (6H, $\text{CH}_3\text{C}_6\text{H}_4$), 3.40 s (2H, CH), 3.91 s (6H, OCH_3), 7.01–7.66 m (12H, H_{arom}). Found, %: C 73.43; H 5.40; N 4.72. $\text{C}_{36}\text{H}_{32}\text{N}_2\text{O}_6$. Calculated, %: C 73.45; H 5.48; N 4.76.

3,3'-(1,4-Phenylene)bis[2-(4-chlorobenzoyl)-2-methylcyclopropane-1,1-dicarbonitrile] (VIh). Yield 65%, mp 274–275°C. IR spectrum, ν , cm^{-1} : 1680, 2245. ^1H NMR spectrum, δ , ppm: 1.80 s (6H, CH_3), 4.10 s (2H, CH), 6.99–7.78 m (12H, H_{arom}). Found, %: C 68.20; H 3.56; N 3.74. $\text{C}_{32}\text{H}_{20}\text{Cl}_2\text{N}_4\text{O}_2$. Calculated, %: C 68.21; H 3.58; N 3.94.

3,3'-(1,4-Phenylene)bis[2-(4-bromobenzoyl)-2-methylcyclopropane-1,1-dicarbonitrile] (VIi). Yield 65%, mp 350°C (decomp.). IR spectrum, ν , cm^{-1} : 1680, 2245. ^1H NMR spectrum, δ , ppm: 1.74 s (6H, CH_3), 4.03 s (2H, CH), 6.92–7.64 m (12H, H_{arom}). Found, %: C 58.90; H 2.89; N 8.54. $\text{C}_{32}\text{H}_{20}\text{Br}_2\text{N}_4\text{O}_2$. Calculated, %: C 58.92; H 3.09; N 8.59.

3,3'-(1,4-Phenylene)bis[2-(4-fluorobenzoyl)-2-methylcyclopropane-1,1-dicarbonitrile] (VIj). Yield 65%, mp 350°C (decomp.). IR spectrum, ν , cm^{-1} : 1680, 2240. ^1H NMR spectrum, δ , ppm: 1.81 s (6H, CH_3), 4.13 s (2H, CH), 6.97–7.80 m (12H, H_{arom}). Found, %: C 72.43; H 3.76; N 10.51. $\text{C}_{32}\text{H}_{20}\text{F}_2\text{N}_4\text{O}_2$. Calculated, %: C 72.45; H 3.80; N 10.56.

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