Russian Journal of Organic Chemistry, Vol. 41, No. 11, 2005, pp. 1598–1600. Translated from Zhurnal Organicheskoi Khimii, Vol. 41, No. 11, 2005, pp. 1632–1634.

Cyclopropanation of Alkyl and Aryl 3-Aryl-2-cyanopropenoates with Bromine-containing Zinc Enolates Obtained from 1-Aryl-2,2-dibromoalkanones and Zinc

V.V. Shchepin, P.S. Silaichev, and M.I. Vakhrin

Perm State University, Perm, 614990 Russia

Received July 22, 2004

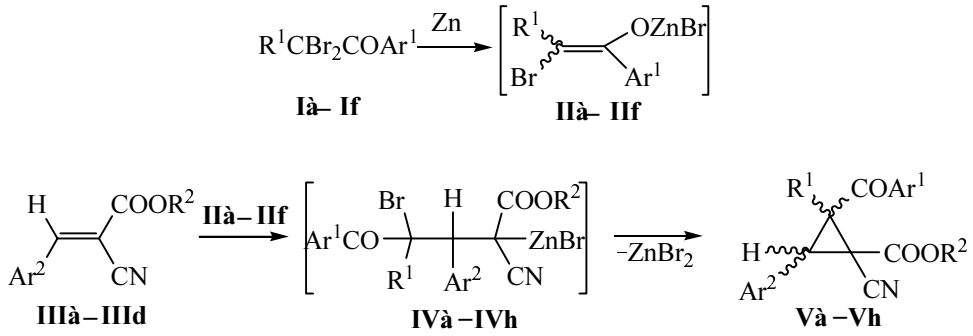
Abstract—Zinc enolates prepared from 1-aryl-2,2-dibromoalkanones and zinc react with alkyl and aryl 3-aryl-2-cyanopropenoates affording alkyl and aryl 2-alkyl-3-aryl-2-aroyl-1-cyanocyclopropane-1-carboxylates.

We showed formerly that 1-aryl-2,2-dibromobutanones react with zinc and dialkyl 2-arylmethylene- or 2-isobutylidenemalonates yielding cyclopropanes with one aroyl and two ester groups [1, 2]. Aiming at extending the synthetic limits of this process we carried out reactions of bromine-containing zinc enolates obtained from 1-aryl-2,2-dibromoalkanones and zinc with electrophilic substrates like alkyl and aryl 3-aryl-2-cyanopropenoates. We were able to establish that the reaction occurred along Scheme 1.

Zinc enolates **II** preliminary prepared from dibromoketones **I** and zinc add to the double bond of electrophilic substrates **IIIa–IIId** providing intermediates **IVa–IVh** which undergo cyclization in the reaction conditions affording cyclopropane derivatives, esters of 2-alkyl-3-aryl-2-aroyl-1-cyanocyclopropane-1-carboxylic acids **Va–Vh**. Compounds **Va–Vh** may arise as four diastereomers. As showed the study, cyclopropanes **Va–Vh** were obtained in 54–72% yield as a single diastereomer by recrystallization from methanol. Compound **Ve** was an exception for according to the ^{1}H NMR spectrum it was isolated as a mixture of two diastereomers in a ratio ~5 : 1. The structure of compounds **Va–Vh** was proved by IR and ^{1}H NMR spectra.

The IR spectra contain the characteristic absorption bands of carbonyls from the keto and ester groups in the region 1680–1695 and 1725–1755 cm^{-1} respectively. In the ^{1}H NMR spectrum, for example, of methyl 2-methyl-

Scheme 1.



I, II, R^1 = Me: Ar^1 = 4-FC_6H_4 (**a**), 4-ClC_6H_4 (**b**), 4-BrC_6H_4 (**c**); R^1 = Et: Ar^1 = 4-FC_6H_4 (**d**), 4-ClC_6H_4 (**e**); **III**, R^2 = Me: Ar^2 = 2,4-$Cl_2C_6H_3$ (**a**), 3-$NO_2C_6H_4$ (**b**); R^2 = Et, Ar^2 = 2,4- $Cl_2C_6H_3$ (**c**); R^2 = 4-BrC_6H_4, Ar^2 = Ph (**d**); **IV, V**, R^1 = R^2 = Me, Ar^1 = 4-ClC_6H_4, Ar^2 = 2,4-$Cl_2C_6H_3$ (**a**); R^1 = Me, R^2 = Et, Ar^1 = 4-FC_6H_4, Ar^2 = 3-$NO_2C_6H_4$ (**b**); R^1 = Et, R^2 = Me; Ar^1 = 4-ClC_6H_4, Ar^2 = 2,4-$Cl_2C_6H_3$ (**c**); R^1 = Me, R^2 = Et; Ar^1 = 4-ClC_6H_4, Ar^2 = 2,4-$Cl_2C_6H_3$ (**d**); R^1 = R^2 = Et, Ar^1 = 4-BrC_6H_4, Ar^2 = 2,4- $Cl_2C_6H_3$ (**e**); R^1 = Me, R^2 = 4-BrC_6H_4; Ar^1 = 4-FC_6H_4, Ar^2 = Ph (**f**); R^1 = Me, R^2 = 4-BrC_6H_4, Ar^1 = 4-ClC_6H_4, Ar^2 = Ph (**g**); R^1 = Et, R^2 = 4-BrC_6H_4, Ar^1 = 4-ClC_6H_4, Ar^2 = Ph (**h**).

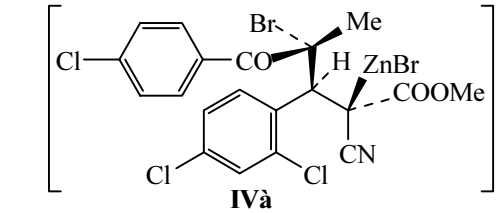
1070-4280/05/4111-1598©2005 Pleiades Publishing, Inc.

3-(2,4-dichlorophenyl)-2-(4-chlorobenzoyl)-1-cyanocyclopropane-1-carboxylate (**Va**) the characteristic proton signals appear at 1.69 s (Me), 3.46 s (CH), 3.91 s (COOMe) ppm. A single set of proton signals indicate that the compound formed as one diastereomer.

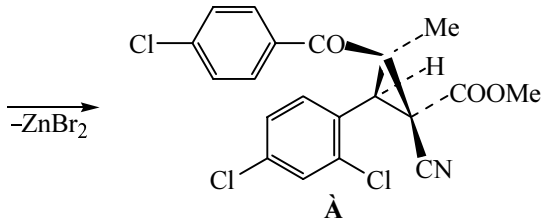
We previously established that similar compounds, dialkyl 2-aroyl-3-R-2-ethylcyclopropane-1,1-dicarboxylates, prepared by analogous procedure also formed as an only main isomer where the aroyl and aryl groups were situated on the same side of the cyclopropane ring (*Z*-position) [1, 2]. Therefore presumably in compound **Va** these groups are also located in the *Z*-position.

For instance, in the ^{1}H NMR spectrum of dimethyl 2-benzoyl-3-phenyl-2-ethylcyclopropane-1,1-dicarboxylate (**VI**) with *Z*-located phenyl and benzoyl groups the following proton signals were observed: 1.13 t, 1.22 m, 2.32 m (5H, Et), 3.33 s, 4.03 s (2COOMe). The two-dimensional spectra revealed that the downfield methoxycarbonyl group at δ 4.03 ppm was situated in the *trans*-position with respect to the benzoyl group. Note also that in the associated isomer arising in 10% amount with respect to the main compound where the phenyl and benzoyl groups were in *E*-position the downfield signals appeared at 3.30 and 3.70 ppm These data show that the proton chemical shift of the most downfield group decreases by ~0.3 ppm in going from the *Z*-isomer to *E*-isomer.

The comparison of the downfield proton chemical shifts from the methoxycarbonyl groups of compounds *Z*-**VI** and **Va** suggests that the latter has a structure of diastereomer **A** where the cyano group, dichlorophenyl, and chlorobenzoyl groups are placed on the same side of the cyclopropane ring.

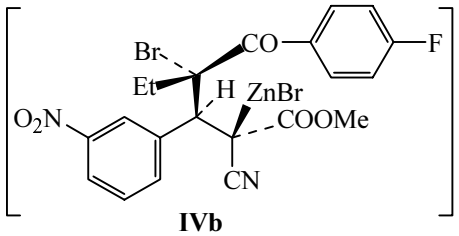


IVà

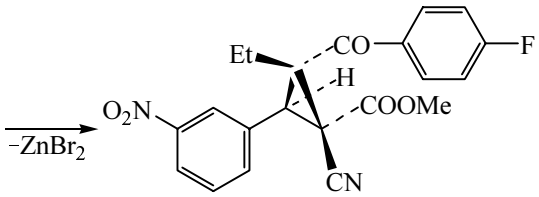


À

On the other hand, in compound **Vb** the resonance of the methoxycarbonyl group in the ^{1}H NMR spectrum appeared at 3.68 ppm, by ~0.2 ppm upfield as compared to compound **Va**. Besides the chemical shift of the methine proton signal is by 0.35 ppm greater that is also characteristic of cyclopropanes with the *E*-position of the phenyl and benzoyl groups. Therefrom it is clear that compound **Vb** exists as diastereomer **B** where on the same side of the cyclopropane ring plane are located the cyano group, aryl, and the R^1 substituent.



IVb



B

This stereochemical result is due apparently, firstly, to the geometry of initial substrates **IIIa–IIIc**, in particular, to the *E*-configuration of their molecules, and, secondly, to close in energy sterical interactions of groups in intermediates **IVa** and **IVb** governing the structure of the final compounds. The assignment to compounds **Va–Vh** the structure of diastereomers either **A** or **B** is reported in EXPERIMENTAL.

Thus, compounds **Va–Vh** can be obtained as a mixture of two diastereomer, and after double recrystallization one of them is isolated, either **A** or **B**.

EXPERIMENTAL

IR spectra of individual compounds were recorded on a spectrophotometer UR-20 from mulls in mineral oil. ^{1}H NMR spectra of compounds **Va–Vh** were registered from solutions in $CDCl_3$ on spectrometer Tesla BS-576A at operating frequency 100 MHz using HMDS as internal reference.

Esters of 2-alkyl-3-aryl-2-aroyl-1-cyanocyclopropane-1-carboxylic acids Va–Vh. To 3 g of fine zinc turnings in 8 ml of ether and 5 ml of ethyl acetate was added 0.013 mol of 1-aryl-2,2-dibromoalkanone in 3 ml of ethyl acetate. The mixture was heated till the reaction started, and then it was self-sustained. On completion of the reaction the mixture was boiled at reflux for 10 min,

cooled, and decanted from zinc. Then to the reaction mixture 0.01 mol of an ester of 3-aryl-2-cyanopropenoic acid was added, the reaction mixture was heated for 30 min, cooled, and hydrolyzed with 5% HCl. The reaction products were extracted into ether, the extract was dried over Na_2SO_4, the solvents were distilled off, and the residue was recrystallized from methanol.

Methyl 2-methyl-3-(2,4-dichlorophenyl)-2-(4-chlorobenzoyl)-1-cyanocyclopropane-1-carboxylate (Va). Diastereomer **A**. Yield 64%, mp 158–159°C. IR spectrum, ν, cm^{-1}: 1680, 1740. ^1H NMR spectrum, δ, ppm: 1.69 s (3H, Me), 3.46 s (1H, CH), 3.91s (3H, COOMe), 6.92–7.68 m (7H, 2,4-$Cl_2C_6H_3$, 4-ClC_6H_4). Found, %: C 56.75; H 3.27; N 3.16. $C_{20}H_{14}Cl_3NO_3$. Calculated, %: C 56.83; H 3.34; N 3.31.

Methyl 2-ethyl-3-(3-nitrophenyl)-2-(4-fluorobenzoyl)-1-cyanocyclopropane-1-carboxylate (Vb). Diastereomer **B**. Yield 54%, mp 149–151°C. IR spectrum, ν, cm^{-1}: 1680, 1740. ^1H NMR spectrum, δ, ppm: 0.89 t (3H, MeCH$_2$), 1.69 m, 2.12 m (2H, MeCH$_2$), 3.68 s (3H, COOMe), 3.81 s (1H, CH), 6.98–8.25 m (8H, 3-$NO_2C_6H_4$, 4-FC_6H_4). Found, %: C 63.50; H 4.24; N 6.91. $C_{21}H_{17}FN_2O_5$. Calculated, %: C 63.63; H 4.32; N 7.07.

Methyl 2-ethyl-3-(2,4-dichlorophenyl)-2-(4-chlorobenzoyl)-1-cyanocyclopropane-1-carboxylate (Vc). Diastereomer **B**. Yield 69%, mp 135–136°C. IR spectrum, ν, cm^{-1}:1680, 1740. ^1H NMR spectrum, δ, ppm: 0.84 t (3H, MeCH$_2$), 2.09 q (2H, MeCH$_2$), 3.72 s (1H, CH), 3.89 s (3H, COOMe), 6.85–7.69 m (7H, 2,4-$Cl_2C_6H_3$, 4-ClC_6H_4). Found, %: C 57.66; H 3.60; N 3.06. $C_{21}H_{16}Cl_3NO_3$. Calculated, %: C 57.76; H 3.69; N 3.21.

Ethyl 2-methyl-3-(2,4-dichlorophenyl)-2-(4-chlorobenzoyl)-1-cyanocyclopropane-1-carboxylate (Vd). Diastereomer **A**. Yield 72%, mp 113–114°C. IR spectrum, ν, cm^{-1}: 1685, 1725. ^1H NMR spectrum, δ, ppm: 1.38 t (3H, MeCH$_2$), 1.70 d (3H, Me), 3.45 d (1H, CH), 4.37 q (2H, MeCH$_2$), 6.97– 7.65 m (7H, 2,4-$Cl_2C_6H_3$, 4-ClC_6H_4). Found, %: C 57.63; H 3.62; N 3.08. $C_{21}H_{16}Cl_3NO_3$. Calculated, %: C 57.76; H 3.69; N 3.21.

Ethyl 2-ethyl-3-(2,4-dichlorophenyl)-2-(4-bromobenzoyl)-1-cyanocyclopropane-1-carboxylate (Ve). Diastereomer **B**. Yield 57%, mp 154–156°C. IR spectrum, ν, cm^{-1}: 1680, 1735. ^1H NMR spectrum, δ, ppm: 0.89 t (3H, MeCH$_2$), 1.37 t (3H, MeCH$_2$O), 2.07 q (2H, MeCH$_2$), 3.82 s (1H, CH), 4.33 q (2H, MeCH$_2$O), 6.88–7.69 m (7H, 2,4-$Cl_2C_6H_3$, 4-BrC_6H_4). Found, %: C 53.28; H 3.26; N 2.70. $C_{22}H_{18}BrCl_2NO_3$. Calculated, %: C 53.36; H 3.66; N 2.83.

4-Bromophenyl 2-methyl-3-phenyl-2-(4-fluorobenzoyl)-1-cyanocyclopropane-1-carboxylate (Vf).

A : **B** ratio = 83 : 17. Yield 68%, mp 154–156°C. IR spectrum, ν, cm^{-1}: 1695, 1755. ^1H NMR spectrum, δ, ppm, **A**: 1.73 s (3H, Me), 3.51 s (1H, CH), 6.57–7.98 m (13H, Ph, 4-FC_6H_4, 4-BrC_6H_4); **B**: 1.63 s (3H, Me), 3.84 s (1H, CH). Found, %: C 62.68; H 3.52; N 2.80. $C_{25}H_{17}BrFNO_3$. Calculated, %: C 62.78; H 3.58; N 2.93.

4-Bromophenyl 2-methyl-3-phenyl-2-(4-chlorobenzoyl)-1-cyanocyclopropane-1-carboxylate (Vg). Diastereomer **B**. Yield 62%, mp 197–198°C. IR spectrum, ν, cm^{-1}: 1685, 1750. ^1H NMR spectrum, δ, ppm: 1.63 s (3H, Me), 3.84 s (1H, CH), 6.62–7.83 m (13H, Ph, 4-ClC_6H_4, 4-BrC_6H_4). Found, %: C 60.56; H 3.39; N 2.72. $C_{25}H_{17}BrClNO_3$. Calculated, %: C 60.69; H 3.46; N 2.83.

4-Bromophenyl 2-ethyl-3-phenyl-2-(4-chlorobenzoyl)-1-cyanocyclopropane-1-carboxylate (Vh). Diastereomer **A**. Yield 61%, mp 179–181°C. IR spectrum, ν, cm^{-1}:1685, 1755. ^1H NMR spectrum, δ, ppm: 0.85 t (3H, Me), 2.00–2.25 m (2H, CH$_2$Me), 3.55 s (1H, CH), 6.89–7.63 m (13H, Ph, 4-ClC_6H_4, 4-BrC_6H_4). Found, %: C 61.25; H 3.67; N 2.62. $C_{26}H_{19}BrClNO_3$. Calculated, %: C 61.38; H 3.76; N 2.75.

The study was carried out under financial support of the Federal Agency on Education (grant A.04-2.11-492) and Russian Foundation for Basic research (grants nos. 04-03-96036, 04-03-97505).

REFERENCES

1. Aliev, Z.G., Shchepin, V.V., Lewis, Scott, B., Shchepin, R.V., and Atovmyan, L.O., *Izv. Akad. Nauk, Ser. Khim.,* 2000, no. 12, p. 2107.
2. Shchepin, V.V., Tryastsin, A.A., Shchepin, R.V., Kalyuzhnyi, M.M., and Lewis, Scott, B., *Zh. Org. Khim*., 2001, vol. 37, p. 1669.