ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 4, pp. 499–502. © Pleiades Publishing, Ltd., 2010. Original Russian Text © V.V. Shchepin, Yu.G. Stepanyan, P.S. Silaichev, M.A. Ezhikova, M.I. Kodess, 2010, published in Zhurnal Organicheskoi Khimii, 2010, Vol. 46, No. 4, pp. 509–513.

Reactions of Bromine-Containing Organozinc Compounds Derived from α,α-Dibromo Ketones with 2-Arylmethylideneindan-1,3-diones and 5-Arylmethylidene-2,2-dimethyl-1,3-dioxane-4,6-diones

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Received December 2, 2008

Abstract—Bromine-containing organozinc compounds generated from 1,1-dibromo-3,3-dimethylbutan-2-one reacted with 2-arylmethylideneindan-1,3-diones and 5-arylmethylidene-2,2-dimethyl-1,3-dioxane-4,6-diones to give 3-aryl-2-(2,2-dimethylpropanoyl)spiro[cyclopropane-1,2'-indan]-1',3'-diones and 1-aryl-6,6-dimethyl-2-(2,2-dimethylpropanoyl)-5,7-dioxaspiro[2.5]octan-4,8-diones, respectively. Reactions of 2-arylmethylidene-indan-1,3-diones with bromine-containing zinc enolates derived from 1-aryl-2,2-dibromopropan-1-ones and 2,2-dibromo-1,2,3,4-tetrahydronaphthalen-1-one resulted in the formation of 2-aroyl-3-aryl-2-methylspiro-[cyclopropane-1,2'-indan]-1',3'-diones and 2,3:8,9-dibenzo-12-phenyldispiro[4.0.5.1]dodecane-1,4,7-trione, respectively.

DOI: 10.1134/S1070428010040081

We previously developed a procedure for the synthesis of spirocyclopropanes via reaction of 3-aryl-2cyanoprop-2-enoic acid derivatives with zinc enolates derived from 2,2-dibromo-1,2,3,4-tetrahydronaphthalen-1-one and 2,2-dibromoindan-1-one [1]. In the present work we made an attempt to find out another synthetic approach to cyclopropane derivatives having one and two spiro carbon atoms. For this purpose, we examined reactions of bromine-containing organozinc compounds derived from α,α -dibromo ketones with 2-arylmethylideneindan-1,3-diones and 5-arylmethylidene-2,2-dimethyl-1,3-dioxane-4,6-diones. In fact, these reactions led to the formation of the corresponding cyclopropanation products as shown in Scheme 1.

Zinc enolate II preliminarily generated from 1,1-dibromo-3,3-dimethylbutan-2-one I added at the double C=C bond in substrates IIIa, IIIb, IVa, and IVb to give intermediates Va, Vb, VIIa, and VIIb which underwent cyclization with formation of cyclopropanation products, 1-aryl-6,6-dimethyl-2-(2,2-dimethylpropanoyl)-5,7-dioxaspiro[2.5]octane-4,8-diones VIa and VIb and 3-aryl-2-(2,2-dimethylpropanoyl)spiro[cyclopropane-1,2'-indan]-1',3'-diones VIIIa and VIIIb (Scheme 1).

The structure of compounds VIa, VIb, VIIIa, and VIIIb was confirmed by their elemental analyses and IR and ¹H NMR spectra. The IR spectra of **VIa** and VIb characteristically contained absorption bands belonging to stretching vibrations of the ketone and ester carbonyl groups at 1700 and 1720–1730 cm⁻¹, respectively. In the ¹H NMR spectra of these compounds we observed a strong signal from 9 protons in the *tert*-butyl group (δ 1.24–1.25 ppm), two methyl proton singlets at δ 1.64–1.67 and 1.73–1.76 ppm, and two protons in the cyclopropane ring at δ 3.90– 3.96 ppm. Compounds VIIIa and VIIIb displayed in the IR spectra absorption bands at 1690 and 1705 cm⁻¹ due to stretching vibrations of carbonyl groups. Protons in the tert-butyl group resonated in the ¹H NMR spectrum of **VIIIa** and **VIIIb** at δ 1.0– 1.01 ppm, and signals from two protons in the cyclopropane rings appeared at δ 3.59 ppm (VIIIa in DMSO- d_6) or at δ 3.51 and 3.54 ppm (VIIIb in CDCl₃). The spin–spin coupling constants for protons







III, V, VI, Ar = 4-ClC₆H₄ (**a**), 4-BrC₆H₄ (**b**); IV, VII, VIII, Ar' = Ph (**a**), 4-FC₆H₄ (**b**).

in the cyclopropane ring in the spectrum of **IIIb** in CDCl₃ (${}^{3}J_{\text{HH}} = 9.9 \text{ Hz}$) indicates their mutual *cis* orientation with respect to the cyclopropane ring plane.

2-Arylmethylideneindan-1,3-diones IVa and IVb reacted with zinc enolates derived from 1-aryl-2,2-dibromopropan-1-ones IXa and IXb and 2,2-dibromo-1,2,3,4-tetrahydronaphthalen-1-one as shown in Scheme 2. The reactions were carried out in diethyl ether-tetrahydrofuran. Primary adducts XIIIa, XIIIb, and XV underwent spontaneous cyclization to give final products, 2-aroyl-3-aryl-2-methylspiro[cyclopropane-1,2'-indan]-1',3'-diones XIVa and XIVb and 2,3,8,9-dibenzo-12-phenyldispiro[4.0.5.1]dodecane-1,4,7-trione (XVI), respectively.

The structure of compounds **XIVa**, **XIVb**, and **XVI** was confirmed by their elemental analyses and IR and



Structure of the 2-(4-bromobenzoyl)-2-methyl-3-phenylspiro-[cyclopropane-1,2'-indan]-1',3'-dione (**XIVa**) molecule with atom numbering.

¹H NMR spectra. In the IR spectra of **XIVa** and **XIVb**, absorption bands typical of carbonyl stretching vibrations appeared at 1660 and 1690 cm⁻¹. Their ¹H NMR spectra contained signals from protons in the methyl group and CH proton in the cyclopropane ring at δ 1.90–1.97 and 3.59–3.70 ppm, respectively. Compounds XIVa and XIVb were isolated as a single stereoisomer, as followed from the presence of only one set of signals in the spectrum. Compound XVI displayed carbonyl absorption bands at 1670 and 1690 cm⁻¹. In the ¹H NMR spectrum of **XVI**, four methylene protons resonated in the region δ 2.57– 3.10 ppm, and the signal at δ 3.85 ppm was assigned to the cyclopropane ring proton. The spectrum of XVI contained only one set of signals, indicating the presence of a single stereoisomer.

Compound **XIVa** was additionally studied by ¹H and ¹³C NMR spectroscopy, including two-dimensional homo- and heteronuclear correlation techniques (¹H–¹³C HSQC, ¹H–¹³C HMBC, ¹H–¹H NOESY; see figure) with a view to determine steric configuration of the isolated products. The arrangement of substituents in the cyclopropane ring of **XIVa** was determined on the basis of the Karplus dependence of the vicinal coupling constant ³*J*_{CH} for the 3-H proton and carbon atom in the substituents. Signals from vicinal carbon atoms in the ¹³C NMR spectrum recorded without decoupling from protons appeared as unresolved multi-



plets, and we succeeded in determining only the coupling constant between 3-H and carbon atom in the methyl group on C²: ${}^{3}J_{CH} = 6.2$ Hz. The other coupling constants were measured using 2D J-spectroscopy with selective inverting pulse [2] acting on 3-H $(\delta 3.71 \text{ ppm})$. Cross-sections of the resulting two-dimensional spectrum that are parallel to the F1 axis and passing through signals of the corresponding carbon atoms give one-dimensional spectra displaying only coupling constants with the 3-H proton: ${}^{3}J(3-H, C^{1'}) =$ $4.2, {}^{3}J(3-H, C^{3'}) = 2.9, {}^{3}J(3-H, Me) = 6.1, {}^{3}J(3-H, CO) =$ 4.6 Hz. Comparison of the vicinal coupling constants for compound XIVa with ${}^{3}J_{CH}$ values found by us previously for substituted cyclopropanes [1, 3] led us to conclude that the 3-H proton and the methyl group on C^2 are arranged at the same side of the cyclopropane ring plane. Among two carbonyl carbon atoms in the indandione fragment, the C^{1'} atom [downfield signal, $\delta_{\rm C}$ 196.87 ppm, ³*J*(3-H, C^{1'}) = 4.2 Hz] is oriented *cis* with respect to 3-H, whereas the $C^{3'}$ atom [upfield signal, $\delta_{\rm C}$ 194.14 ppm, ³J(3-H, C^{3'}) 2.9 Hz] is oriented trans.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer from samples dispersed in mineral oil. The ¹H NMR spectra were measured on a Mercury Plus-300 instrument (300 MHz) from solutions in

CDCl₃ (VIa, VIIIb, XIVb) or DMSO- d_6 (VIIIa, XVI) using hexamethyldisiloxane as internal reference. The one- (1H, ¹³C) and two-dimensional NMR spectra (NOESY, HSQC, HMBC) of compound XIVa were recorded on a Bruker DRX-400 spectrometer (400 MHz for ¹H and 100 MHz for ¹³C) from solutions in CDCl₃ using tetramethylsilane as internal reference, and the spectra of VIb in CDCl₃ were measured on a Tesla BS-567A instrument (100 MHz) using hexamethyldisiloxane as internal reference.

1-Aryl-6,6-dimethyl-2-(2,2-dimethylpropanoyl)-5,7-dioxaspiro[2.5]octane-4,8-diones VIa and VIb (general procedure). 1,1-Dibromo-3,3-dimethylbutan-2-one, 0.015 mol, was added to a mixture of 4 g of metallic zinc prepared as fine turnings, 7 ml of diethyl ether, and 10 ml of tetrahydrofuran. The mixture was heated to initiate the reaction which then occurred spontaneously. When the reaction was complete, the mixture was heated for 15 min under reflux and cooled, the liquid phase was separated by decanting, 0.01 mol of 5-arylmethylidene-2,2-dimethyl-1,3-dioxane-4.6-dione IIIa or IIIb was added, and the mixture was heated for 30-40 min under reflux, cooled, hydrolyzed with 5% acetic acid, and extracted with benzene. The solvent was distilled off from the extract, and the residue was recrystallized from ethyl acetate or methanol.

1-(4-Chlorophenyl)-6,6-dimethyl-2-(2,2-dimethylpropanoyl)-5,7-dioxaspiro[2.5]octane-4,8-dione (VIa). Yield 33%, mp 186–188°C. IR spectrum, v, cm⁻¹: 1700, 1720. ¹H NMR spectrum, δ, ppm: 1.25 s (9H, *t*-Bu), 1.67 s (3H, CH₃), 1.76 s (3H, CH₃), 3.96 s (2H, CH), 7.27–7.32 m (4H, C₆H₄). Found, %: C 62.51; H 5.76. C₁₉H₂₁ClO₅. Calculated, %: C 62.55; H 5.80.

1-(4-Bromophenyl)-6,6-dimethyl-2-(2,2-dimethylpropanoyl)-5,7-dioxaspiro[2.5]octane-4,8-dione (VIb). Yield 36%, mp 197–198°C. IR spectrum, v, cm⁻¹: 1700, 1730. ¹H NMR spectrum, δ, ppm: 1.24 s (9H, *t*-Bu), 1.64 s (3H, CH₃), 1.73 s (3H, CH₃), 3.90 s (2H, CH), 7.06–7.43 m (4H, C₆H₄). Found, %: C 55.71; H 5.13. C₁₉H₂₁BrO₅. Calculated, %: C 55.76; H 5.17.

3-Aryl-2-(2,2-dimethylpropanoyl)spiro[cyclopropane-1,2'-indan]-1',3'-diones VIIIa and VIIIb (general procedure). 1,1-Dibromo-3,3-dimethylbutan-2-one, 0.015 mol, was added to a mixture of 4 g of metallic zinc prepared as fine turnings, 7 ml of diethyl ether, and 10 ml of tetrahydrofuran. The mixture was heated to initiate the reaction which then occurred spontaneously. When the reaction was complete, the mixture was heated for 15 min under reflux and cooled, the liquid phase was separated by decanting, 0.01 mol of 2-arylmethylideneindan-1,3-dione IVa or **IVb** and 5 ml of anhydrous toluene were added, and the mixture was heated for 30-40 min under reflux, cooled, hydrolyzed with 5% acetic acid, and extracted with benzene. The solvent was distilled off from the extract, and the residue was recrystallized from ethyl acetate or methanol.

2-(2,2-Dimethylpropanoyl)-3-phenylspiro[cyclopropane-1,2'-indan]-1',3'-dione (VIIIa). Yield 37%, mp 159–160°C. IR spectrum, v, cm⁻¹: 1990, 1705. ¹H NMR spectrum, δ , ppm: 1.00 s (9H, *t*-Bu), 3.59 s (2H, CH), 7.26–8.00 m (9H, H_{arom}). Found, %: C 79.46; H 6.02. C₂₂H₂₀O₃. Calculated, %: C 79.50; H 6.06.

2-(2,2-Dimethylpropanoyl)-3-(4-fluorophenyl)spiro[cyclopropane-1,2'-indan]-1',3'-dione (VIIIb). Yield 36%, mp 162–163°C. IR spectrum, v, cm⁻¹: 1690, 1750. ¹H NMR spectrum, δ , ppm: 1.01 s (9H, *t*-Bu), 3.51 d (1H, CH), 3.54 d (1H, CH, *J* = 9.9 Hz), 6.96–7.85 m (8H, H_{arom}). Found, %: C 75.36; H 5.41. C₂₂H₁₉FO₃. Calculated, %: C 75.41; H 5.47.

Compounds **XIVa** and **XIVb** were synthesized in a similar way.

2-(4-Bromobenzoyl)-2-methyl-3-phenylspiro-[cyclopropane-1,2'-indan]-1',3'-dione (XIVa). Yield 53%, mp 172–173°C. IR spectrum, v, cm⁻¹: 1690, 1660. ¹H NMR spectrum, δ , ppm: 1.97 s (1H, CH₃), 3.71 s (1H, 3-H), 7.16–7.20 m (3H, 11-H, 12-H), 7.32 m (2H, 10-H), 7.41 d (2H, 7-H, J = 8.8 Hz), 7.64 d (2H, 6-H, J = 8.8 Hz), 7.75–7.85 m (3H, 4'-H, 5'-H, 6'-H), 8.03 d.t (1H, 7'-H, J = 7.3, 1.1 Hz). ¹³C NMR spectrum, δ_{C} , ppm: 19.57 (CH₃), 47.27 (C²), 49.99 (C³), 50.25 (C¹), 122.58 (C⁷), 122.92 (C⁴), 127.47 (C¹²), 127.60 (C¹¹), 130.31 (C⁶), 130.76 (C¹⁰), 131.82 (C⁷), 131.91 (C⁹), 133.65 (C⁵), 135.32 and 134.99 (C^{5'}, C⁶), 141.59 (C^{7a'}), 142.57 (C^{3a'}), 192.72 (C⁴), 194.14 (C^{3'}), 196.87 (C^{1'}). Found, %: C 67.38; H 3.80. C₂₅H₁₇BrO₃. Calculated, %: C 67.43; H 3.85.

2-(4-Fluorobenzoyl)-3-(4-fluorophenyl)-2-methylspiro[cyclopropane-1,2'-indan]-1',3'-dione (XIVb). Yield 51%, mp 148–150°C. IR spectrum, v, cm⁻¹: 1690, 1660. ¹H NMR spectrum, δ , ppm: 1.90 s (3H, CH₃), 3.59 s (1H, CH), 6.82–7.73 m (12H, H_{arom}). Found, %: C 74.60; H 3.39. C₂₆H₁₈F₂O₂. Calculated, %: C 74.62; H 4.01.

2,3:8,9-Dibenzo-12-phenyldispiro[4.0.5.1]dodeca-2,8-diene-1,4,7-trione (XVI). 2,2-Dibromo-1,2,3,4tetrahydronaphthalen-1-one, 0.024 mol, was added to a mixture of 2 g of fine zinc turnings, 7 ml of diethyl ether, and 10 ml of tetrahydrofuran. The mixture was heated to initiate the reaction which then occurred spontaneously. When the reaction was complete, the mixture was heated for 5 min under reflux and cooled, the liquid phase was separated by decanting and transferred into a flask charged with 0.02 mol of 2-phenylmethylideneindan-1,3-dione (IVa), 10 ml of anhydrous toluene was added, and the mixture was heated for 60 min under reflux. The mixture was cooled, hydrolyzed with 5% acetic acid, and extracted with diethyl ether, the extract was dried over Na₂SO₄, the solvent was distilled off, and the residue was recrystallized from ethyl acetate. Yield 58%, mp 189-190°C. IR spectrum, v, cm⁻¹: 1690, 1670. ¹H NMR spectrum, δ , ppm: 2.57–3.10 m (4H, C₆H₄), 3.85 s (1H, CH), 7.19– 8.07 m (13H, H_{arom}). Found, %: C 82.49; H 4.76. C₂₆H₁₈O₃. Calculated, %: C 82.52; H 4.79.

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 07-03-96035).

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