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Cyclopropanation of N-Substituted 2-Oxochromene-3-carboxamides and 3-Oxobenzo[*f*]chromene-2-carboxamides with Bromine-containing Zinc Enolate Prepared from α,α -Dibromopinacolin and Zinc

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Abstract—Zinc enolate obtained from 1,1-dibromo-3,3-dimethylbutan-2-one reacted with N-substituted 2-oxochromene-3-carboxamides and 3-oxobenzo[*f*]chromene-2-carboxamides affording 1-(2,2-dimethyl-propanoyl)-2-oxo-1a,7b-dihydrocyclopropa[*c*]chromene-1a-carboxamides and 1-(2,2-dimethylpropanoyl)-2-oxo-1a,9C-dihydrobenzo[*f*]cyclopropa[*c*]chromene-1a-carboxamide as single isomers.

In extension of studies on the cyclopropanation of 2-oxochromene-3-carboxylic acid derivatives [1, 2] we investigated the reaction of N-substituted amides of this acid and its analogs with a bromine-containing zinc enolate **II** generated from α,α-dibromopinacolin (**I**) and zinc.

It was established that zinc enolate **II** was highly reactive toward electrophilic substrates **IIIa–IIIc** and **IV**. The reaction occurred along the following scheme.

First the treating with organozinc reagent **II** converts substrates **IIIa–IIIc** and **IV** into the corresponding salts, and then zinc enolate **II** regiospecifically adds with its C-nucleophilic center to the C^4 atom of the heterocycle providing intermediates **Va–Vc** and **VI**. The latter spontaneously undergo cyclization transforming into intermediates **VIIa–VIIc** and **VIII** which on hydrolysis afford the target products, N-substituted 1-(2,2-dimethylpropanoyl)-2-oxo-1*a*,7*b*-dihydrocyclopropa[*c*]chromene-1*a*-carboxamides **IXa–IXc**, and 1-(2,2-dimethylpropanoyl)-2-oxo-1*a*,9*C*-dihydrobenzo[*f*]cyclopropa[*c*]chromene-1*a*-carboxylic acid *p*-toluidide (**X**) (see Scheme).

The structure of obtained compounds **IXa–IXc** and **X** was proved by the data of IR and ^{1}H NMR spectroscopy. In the IR spectra appear characteristic absorption bands (ν) of amide carbonyl at 1670–1680, ketone and lactone carbonyls at 1725–1755, and NH group at 3325–3390 cm^{-1}. In the ^{1}H NMR spectra a single set of proton signals is observed evidencing that the compounds synthesized formed as one geometrical isomer. It is known that in cyclopropa[*c*]chromene derivatives of similar structures the value of coupling constant J_{HH}^{cis} is 9.4–9.8, and J_{HH}^{trans} is 5.1–5.5 Hz [3].

To gain more information on the configuration of such compounds we performed by the above procedure a synthesis of ethyl 1-(2,2-dimethylpropanoyl)-2-oxo-1*a*,7*b*-dihydrocyclopropa[*c*]chromene-1*a*-carboxylate (**XI**) using as starting compound ethyl 2-oxochromene-3-carboxylate.

In the ^{1}H NMR spectrum of compound **XI** $J_{H^1C-CH^{7b}}$ is equal to 10.0 Hz. In the ^{1}H NMR spectra of compounds **IXa–IXc** and **X** $J_{H^1C-CH^{7b}}$ is 10.2 and $J_{H^1C-CH^{9c}}$ is 9.8 Hz respectively, i.e, very close to J_{HH}^{cis} of cyclopropa[*c*]-chromene derivatives [3]. These data are a reliable proof of compounds **IXa–IXc** and **X** formation as a single diastereomer with pivaloyl and amide (or alkoxycarbonyl) groups situated on the different sides with respect to the plane of the cyclopropane ring.

EXPERIMENTAL

IR spectra were recorded on a spectrometer UR-20 from samples as mulls in mineral oil. ^{1}H NMR spectra of compounds **IXa–IXc, X,** and **XI** were registered from solutions in $CDCl_3$ on Tesla BS-576 A instrument at operating frequency 100 MHz using HMDS as internal reference.

1-(2,2-Dimethylpropanoyl)-2-oxo-1*a*,7*b*-dihydrocyclopropa[*c*]chromene-1*a*-carboxamides IXa–IXc and 1-(2,2-dimethylpropanoyl)-2-oxo-1*a*,9*C*-di-

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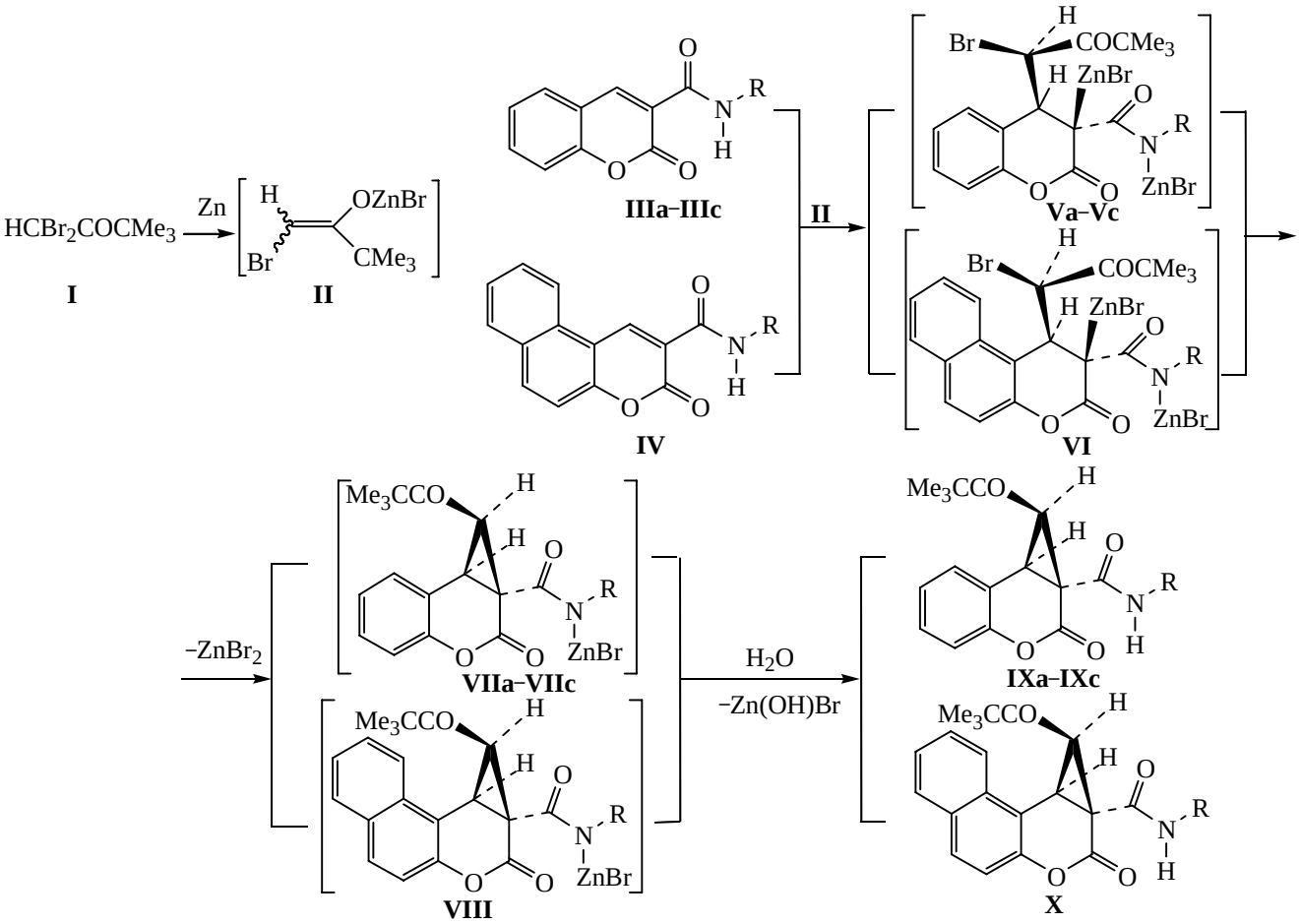
Scheme.



III, V, VII, IX, R = CH_2Ph (**a**), 4-MeC_6H_4 (**b**), C_6H_{11} (**c**); **IV, VI, VIII, X**, R = 4-MeC_6H_4.

hydrobenzo[*f*]cyclopropa[*c*]-chromene-1*a*-carboxylix acid *p*-toluidide (X). To 4 g of fine zinc turnings in 7 ml of ether and 10 ml of ethyl acetate was added 0.03 mol of α,α-dibromopinacolin. The mixture was heated till the reaction started, and then it proceeded spontaneously. On completion of the reaction the mixture was boiled for 15 min, cooled, and decanted from zinc. Then to the solution was added 0.01 mol of compound **IIIa–IIIc** or **IV**, the mixture was boiled for 30–40 min, cooled, and hydrolyzed with 5% acetic acid. The product was extracted into benzene, the solvent was distilled off, and the residue was recrystallized from ethyl acetate or methanol.

1-(2,2-Dimethylpropanoyl)-2-oxo-1*a*,7*b*-dihydrocyclopropa[*c*]chromene-1*a*-carboxylic acid benzylamide (IXa). Yield 65%, mp 125–127°C. IR spectrum, ν, cm^{-1}: 1680, 1735, 1745, 3390. ^1H NMR spectrum, δ, ppm: 0.95 s (9H, *t*-Bu), 3.35 d , 3.67 d (2H, CH, $J_{H^1C-CH^{7b}}$ 10.2 Hz), 4.39 d (2H, CH_2, *J* 5.6 Hz), 6.83–7.25 m (9H, C_6H_4, Ph), 8.53 t (1H, NH). Found, %: C 7.07; H 6.05; N 3.58. $C_{23}H_{23}NO_4$. Calculated, %: C 73.19; H 6.14; N 3.71.

1-(2,2-Dimethylpropanoyl)-2-oxo-1*a*,7*b*-dihydrocyclopropa[*c*]chromene-1*a*-carboxylic acid *p*-toluidide (IXb). Yield 52%, mp 179–180°C. IR spectrum, ν, cm^{-1}: 1680, 1735, 1755, 3325. ^1H NMR spectrum, δ, ppm: 0.97 s (9H, *t*-Bu), 2.24s (3H, Me), 3.38 d, 3.74 d (2H, CH, $J_{H^1C-CH^{7b}}$ 10.2 Hz), 6.89–7.35 m (8H, C_6H_4, 4-$MeC_6\underline{H_4}$), 10.09 s (1H, NH). Found, %: C 73.04; H 6.03; N 3.60. $C_{23}H_{23}NO_4$. Calculated, %: C 73.19; H 6.14; N 3.71.

1-(2,2-Dimethylpropanoyl)-2-oxo-1*a*,7*b*-dihydrocyclopropa[*c*]chromene-1*a*-carboxylic acid cyclohexylamide (IXc). Yield 63%, mp 192– 193°C. IR spectrum, ν, cm^{-1}: 1670, 1735, 1745, 3375. ^1H NMR spectrum, δ, ppm: 0.95 s (9H, *t*-Bu), 1.16–1.92 m (10H, C_6H_{11}), 3.29 d, 3.40 d (2H, CH, $J_{H^1C-CH^{7b}}$ 10.2 Hz), 3.45 m (1H, C_6H_{11}), 6.85–7.20 m (4H, C_6H_4), 8.09 d (1H,

NH). Found, %: C 72.40; H 7.29; N 3.65. $C_{22}H_{27}NO_4$. Calculated, %: C 72.51; H 7.37; N 3.79.

1-(2,2-Dimethylpropanoyl)-2-oxo-1*a*,9*C*-dihydrobenzo[*f*]cyclopropa[*c*]chromene-1*a*-carboxylic acid *p*-toluidide (X). Yield 41%, mp 99–101°C. IR spectrum, ν, cm^{-1}: 1665, 1725,1740, 3330. ^1H NMR spectrum, δ, ppm: 0.87 s (9H, *t*-Bu), 2.24 s (3H, Me), 3.58 d, 4.21 d (2H, CH, $J_{H^1C-CH^{9c}}$ 9.8 Hz), 6.95–7.93 m (10H, $C_{10}H_6$, 4-$MeC_6\underline{H}_4$), 10.07 s (1H, NH). Found, %: C 75.73; H 5.80; N 3.17. $C_{27}H_{25}NO_4$. Calculated, %: C 75.86; H 5.89; N 3.28.

Ethyl 1-(2,2-dimethylpropanoyl)-2-oxo-1*a*,7*b*-dihydrocyclopropa[*c*]chromene-1*a*-carboxylate (XI). To 2 g of fine zinc turnings in 7 ml of ether and 10 ml of ethyl acetate was added 0.03 mol of α,α-dibromopinacolin. The mixture was heated till the reaction started, and then it proceeded spontaneously. On completion of the reaction the mixture was boiled for 5 min, cooled, and decanted from zinc. Then 0.01 mol of ethyl 2-oxochromene-3-carboxylate was added, the mixture was boiled for 30–40 min, cooled, and hydrolyzed with 5% acetic acid. The product was extracted into benzene, the solvent was distilled off, and the residue was recrystallized from methanol. Yield 78%, mp 155°C. IR spectrum, ν, cm^{-1}: 1690, 1730, 1760. ^1H NMR spectrum, δ, ppm: 1.00 s (9H, *t*-Bu), 1.22 t (3H, Me), 3.07 d, 3.59 d (2H, CH, $J_{H^1C-CH^{7b}}$ 10.0 Hz), 4.17 q (2H, CH_2), ~7.05 m (4H, C_6H_4). Found, %: C 68.22; H 6.30. $C_{18}H_{20}O_5$. Calculated, %: C 68.34; H 6.37.

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