

Reactions of Zinc Enolates Derived from 1-Aryl-2-bromoalkanes and 1-Aryl-2-bromo-2-phenylethanone with 3-Aroyl-6-bromochromen-2-ones and 2-Benzoylbenzo[*f*]chromen-3-one

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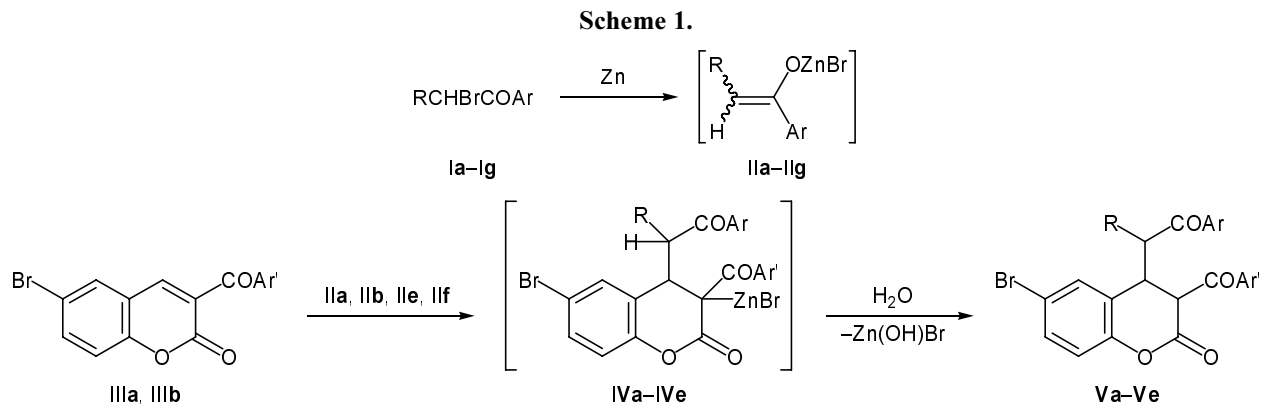
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Abstract—3-Aroyl-6-bromochromen-2-ones and 2-benzoylbenzo[*f*]chromen-3-one reacted with zinc enolates derived from 1-aryl-2-bromoalkanes and 1-aryl-2-bromo-2-phenylethanone to give, respectively, 4-(1-alkyl-2-aryl-2-oxoethyl)-3-aryol-6-bromochroman-2-ones and 1-(2-aryol-1-methyl-2-oxoethyl)-2-benzoyl-1,2-dihydrobenzo[*f*]chromen-3-ones as a single stereoisomer. Treatment with acetic anhydride of the intermediate product obtained from 3-benzoyl-6-bromochromen-2-one and [1-(4-chlorophenyl)-2-phenylethen-1-yloxy]-zinc(II) bromide resulted in the formation of 3-(1-acetoxy-1-phenylmethylidene)-6-bromo-4-[2-(4-chlorophenyl)-2-oxo-1-phenylethyl]chroman-2-one.

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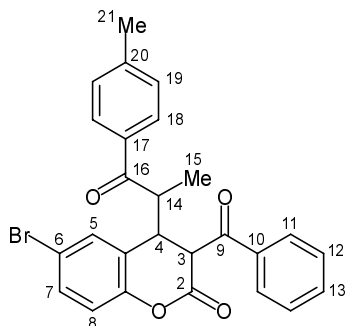
In continuation of our studies on reactions of zinc enolates with chromen-2-one derivatives [1], in the present work we examined reactions of zinc enolates **IIa**, **IIb**, **IIe**, and **IIf** generated from α -bromo ketones **Ia**, **Ib**, **Ie**, and **If**, respectively, with 3-benzoyl- and 3-(4-bromobenzoyl)-6-bromochromen-2-ones **IIIa** and **IIIb**. The reaction involved regioselective attack by enolate **II** on the electrophilic C⁴ atom in substrate **III** to give intermediates **IVa–IVe**; hydrolysis of the latter

gave 4-(1-alkyl-2-aryl-2-oxo-ethyl)-3-aryol-6-bromochroman-2-ones **Va–Ve** as final products (Scheme 1). The IR spectra of **Va–Ve** contained absorption bands in the regions 1660–1675 and 1760–1775 cm⁻¹, which are typical of stretching vibrations of ketone and lactone carbonyl groups. The coupling constant $J_{3,4}$ in the ¹H NMR spectra of these compounds was less than 2 Hz. The steric structure of the products was determined by detailed analysis of the ¹H and ¹³C NMR

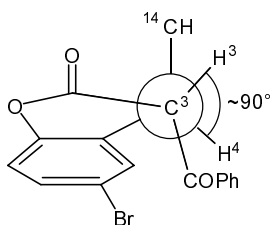


I, II, R = Me, Ar = Ph (**a**), 4-MeC₆H₄ (**b**), 4-ClC₆H₄ (**c**), 4-BrC₆H₄ (**d**), 4-MeOC₆H₄ (**e**); R = *i*-Pr, Ar = 4-BrC₆H₄ (**f**); R = Ph, Ar = 4-ClC₆H₄ (**g**); **III**, Ar' = Ph (**a**), 4-BrC₆H₄ (**b**); **IV, V**, R = Me, Ar = Ar' = Ph (**a**), Ar = 4-MeC₆H₄, Ar' = Ph (**b**), Ar = 4-MeC₆H₄, Ar' = 4-BrC₆H₄ (**d**), Ar = 4-MeOC₆H₄, Ar' = Ph (**e**); R = *i*-Pr, Ar = 4-BrC₆H₄, Ar' = Ph (**c**).

spectra of 3-benzoyl-6-bromo-4-[1-methyl-2-oxo-2-(4-tolyl)ethyl]chroman-2-one (**Vb**) (see Experimental). Signals from carbon atoms having hydrogen atoms attached thereto were assigned using two-dimensional heteronuclear HSQC technique.



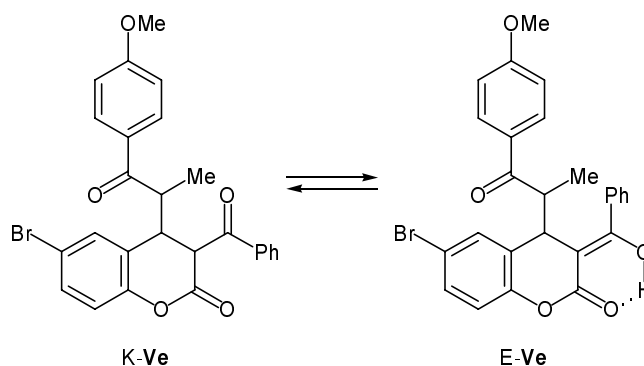
The ^1H NMR spectrum of **Vb** in $\text{DMSO-}d_6$ (400 MHz) contained the following CH signals, δ , ppm: 3.79 d.d (1H, 4-H, $J_{4,14} = 8.2$, $J_{4,3} = 1.4$ Hz), 3.98 d.q (1H, 14-H, $J_{14,4} = 8.2$, $J_{14,15} = 7.1$ Hz), 5.03 d (1H, 3-H, $J_{3,4} = 1.4$ Hz), $J_{3,4} = 1.4$ Hz. Judging by the $J_{3,4}$ value equal to 1.5 Hz, Bojilova [2] assigned *trans* arrangement of the substituents on C^3 and C^4 in methyl 2-oxo-4-trichloromethylchromene-3-carboxylate which is structurally related to **Vb**. Therefore, we presumed that compounds **Va–Ve** are also characterized by *trans* configuration of 3-H and 4-H which occupy equatorial or pseudoequatorial positions in the pyran ring, the dihedral angle $\text{HC}^3\text{C}^4\text{H}$ approaching 90 deg.



3-Benzoyl-6-bromo-4-[1-methyl-2-(4-methoxyphenyl)-2-oxoethyl]chroman-2-one (**Ve**) was isolated as ketone (**K-Ve**) and enol tautomers (**E-Ve**) (Scheme 2). The latter displayed the following signals in the ^1H NMR spectrum (CDCl_3), δ , ppm: 0.80 d (3H, CHMe , $J = 7$ Hz), ~ 3.35 m (1H, CHMe), 3.73 s (3H, OMe), 4.24 d (1H, 4-H, $J = 5.5$ Hz), 12.85 s (1H, OH). After 2 months, the ^1H NMR spectrum of the same solution (CDCl_3) of **Ve** corresponded to an equilibrium mixture of tautomers **K-Ve** and **E-Ve** at a ratio of 1:2.

Zinc enolate **Ilg** prepared from 1-(4-chlorophenyl)-2-bromo-2-phenylethanone is also capable of adding at the double bond of substrate **IIIa** with formation of intermediate **VI**. The subsequent treatment with acetic

Scheme 2.



anhydride gave the corresponding O-acylation product, 6-bromo-4-[2-(4-chlorophenyl)-2-oxo-1-phenylethyl]-2-oxochroman-3-ylidene(phenyl)methyl acetate (**VII**) as a single stereoisomer with respect to the exocyclic double bond (Scheme 3).

Likewise, zinc enolates **Iic** and **Iid** reacted with 2-benzoylbenzo[*f*]chromen-3-one (**VIII**) through intermediates **IXa** and **IXb** to give 1-(2-aroylethyl)-2-benzoyl-1,2-dihydrobenzo[*f*]chromen-3-ones **Xa** and **Xb**, respectively (Scheme 4).

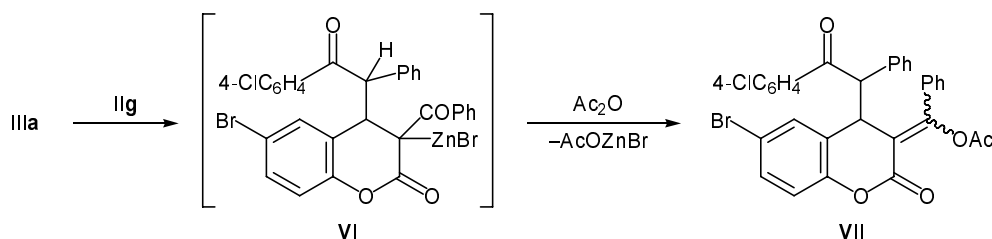
The analytical data, and IR and ^1H NMR spectra of the prepared compounds are given in Experimental. According to the ^1H NMR data, compounds **Xa** and **Xb** were formed exclusively in the ketone form. In particular, this follows from the presence of a singlet at δ 4.70 ppm from the 3-H proton. The coupling constant $J_{3,4} < 2$ Hz indicates *trans* arrangement of the 3-H and 4-H protons.

EXPERIMENTAL

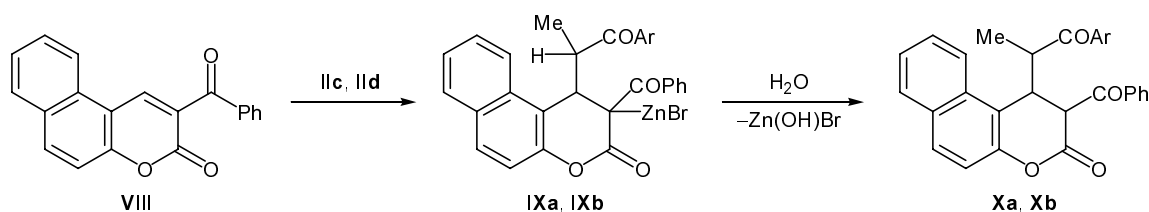
The IR spectra were recorded on a UR-20 spectrometer from samples dispersed in mineral oil. The ^1H NMR spectra were measured on RYa-2310 (60 MHz; **K-Ve**, **Xa**, **Xb**; $\text{CDCl}_3/\text{HMDS}$), Tesla BS-567A (100 MHz; **Vd**, **E-Ve**; $\text{CDCl}_3/\text{HMDS}$), Mercury Plus 300 (300 MHz; **VII**; CDCl_3/TMS), Bruker DRX-500 (500 MHz; **Va**, **Vc**; $\text{DMSO-}d_6\text{-CCl}_4/\text{TMS}$), and Bruker DRX-400 spectrometers (400 MHz; **Vb**; $\text{DMSO-}d_6/\text{TMS}$). The ^{13}C NMR spectrum of **Vb** was obtained on a Bruker DRX-400 instrument (100 MHz).

4-(1-Alkyl-2-aryl-2-oxoethyl)-3-aroyle-6-bromochroman-2-ones Va–Ve (general procedure). 3-Aroyle-6-bromochromen-2-one **IIIa** or **IIIb**, 0.01 mol, and 1-aryl-2-bromoalkanone **Ia**, **Ib**, **Ie**, or **If**, 0.015 mol, were added to a mixture of 3 g of metallic zinc (prepared as fine turnings), 8 ml of diethyl ether, and 8 ml of ethyl acetate. The mixture was heated to initiate the

Scheme 3.



Scheme 4.



Ar = 4-ClC₆H₄ (a), 4-BrC₆H₄ (b).

reaction which then occurred spontaneously. When the exothermic reaction was complete, the mixture was heated for 15 min under reflux, cooled, treated with 10% hydrochloric acid, and extracted with diethyl ether. The extract was washed with a 10% solution of sodium hydrogen carbonate to neutral reaction and dried over sodium sulfate, the solvent was distilled off, and the residue was purified by double recrystallization from methanol.

3-Benzoyl-6-bromo-4-(1-methyl-2-oxo-2-phenylethyl)chroman-2-one (Va). Yield 69%, mp 151–153°C. IR spectrum, ν , cm⁻¹: 1675 (C=O, ketone), 1760 (C=O, lactone). ¹H NMR spectrum, δ , ppm: 1.13 d (3H, CH₃, J = 7 Hz), 3.78 d (1H, 4-H, J = 7 Hz), 3.90 m (1H, α -H), 4.86 s (1H, 3-H), 7.05–8.05 m (13H, C₆H₅, BrC₆H₃). Found, %: C 64.82; H 4.15; Br 17.23. C₂₃H₁₉BrO₄. Calculated, %: C 64.81; H 4.13; Br 17.25.

3-Benzoyl-6-bromo-4-[1-methyl-2-(4-methylphenyl)-2-oxoethyl]chroman-2-one (Vb). Yield 71%, mp 181–183°C. IR spectrum, ν , cm⁻¹: 1660 (C=O, ketone), 1765 (C=O, lactone). ¹H NMR spectrum, δ , ppm: 1.10 d (3H, 15-H, J = 7.1 Hz), 2.39 s (3H, 21-H), 3.79 d.d (1H, 4-H, $J_{4,14}$ = 8.2, $J_{4,3}$ = 1.4 Hz), 3.98 d.q (1H, 14-H, $J_{14,4}$ = 8.2, $J_{14,15}$ = 7.1 Hz), 5.03 d (1H, 3-H, $J_{3,4}$ = 1.4 Hz), 7.15 d (1H, 8-H, J = 8.7 Hz), 7.37 d (2H, 19-H, J = 8.1 Hz), 7.46 d (1H, 5-H, J = 2.4 Hz), 7.52 d.d (1H, 7-H, J = 8.7, 2.4 Hz), 7.63 d.d (2H, 12-H, J = 8.4, 7.4 Hz), 7.75 t.t (1H, 13-H, J = 7.4, 1.2 Hz), 7.96 d (2H, 18-H, J = 8.1 Hz), 8.06 d.d (2H, 11-H, J = 8.4, 1.2 Hz). ¹³C NMR spectrum (DMSO-*d*₆), δ _C, ppm: 16.21 (C¹⁵), 21.14 (C²¹), 41.10 (C⁴), 43.99 (C¹⁴), 52.76

(C³), 115.98 (C^{4a}), 118.79 (C⁸), 123.47 (C⁶), 128.61 (C¹⁸), 128.99 and 129.12 (C¹¹, C¹²), 129.55 (C¹⁹), 132.02 and 132.15 (C⁵, C⁷), 132.79 and 133.23 (C¹⁰, C¹⁷), 134.55 (C¹³), 144.55 (C²⁰), 150.35 (C^{8a}), 164.46 (C⁹), 194.55 (C²), 201.57 (C¹⁶). Found, %: C 63.45; H 4.45; Br 16.77. C₂₆H₂₁BrO₄. Calculated, %: C 65.42; H 4.43; Br 16.74.

3-Benzoyl-6-bromo-4-[1-(4-bromobenzoyl)-2-methylpropyl]chroman-2-one (Vc). Yield 82%, mp 180–181°C. IR spectrum, ν , cm⁻¹: 1670 (C=O, ketone), 1755 (C=O, lactone). ¹H NMR spectrum, δ , ppm: 0.83 d and 0.86 d [6H, CH(CH₃)₂, J = 7 Hz], 2.08 m [1H, CH(CH₃)₂], 3.81 m (2H, 4-H, α -H), 4.81 s (1H, 3-H), 6.90–8.00 m (12H, BrC₆H₄, C₆H₅, BrC₆H₃). Found, %: C 56.86; H 3.87; Br 28.05. C₂₇H₂₂Br₂O₄. Calculated, %: C 56.87; H 3.89; Br 28.02.

6-Bromo-3-(4-bromobenzoyl)-4-[1-methyl-2-(4-methylphenyl)-2-oxoethyl]chroman-2-one (Vd). Yield 43%, mp 168–170°C. IR spectrum, ν , cm⁻¹: 1660 (C=O, ketone), 1775 (C=O, lactone). ¹H NMR spectrum, δ , ppm: 1.06 d (3H, CH₃, J = 7 Hz), 2.33 s (3H, 4-MeC₆H₄), 3.50 m (2H, 4-H, α -H), 4.52 s (1H, 3-H), 6.80–7.90 m (11H, MeC₆H₄, BrC₆H₄, BrC₆H₃). Found, %: C 56.15; H 3.65; Br 28.75. C₂₆H₂₀Br₂O₄. Calculated, %: C 56.14; H 3.62; Br 28.73.

3-Benzoyl-6-bromo-4-[2-(4-methoxyphenyl)-1-methyl-2-oxoethyl]chroman-2-one (K-Ve). Yield 40%, mp 156–158°C. IR spectrum, ν , cm⁻¹: 1670 (C=O, ketone), 1770 (C=O, lactone). ¹H NMR spectrum, δ , ppm: 1.10 d (3H, CH₃, J = 7 Hz), 3.70 m (2H, 4-H, α -H), 3.80 s (3H, OMe), 4.58 s (1H, 3-H), 6.70–

8.10 m (12H, MeOC₆H₄, C₆H₅, BrC₆H₃). Found, %: C 63.32; H 4.27; Br 16.23. C₂₆H₂₁BrO₅. Calculated, %: C 63.30; H 4.29; Br 16.20.

6-Bromo-3-hydroxyphenylmethylidene-4-[2-(4-methoxyphenyl)-1-methyl-2-oxoethyl]chroman-2-one (E-Ve). Yield 45%, mp 168–171°C. IR spectrum, ν , cm⁻¹: 1600–1620 (C=C–C=O, enol), 1675 (C=O, ketone). ¹H NMR spectrum, δ , ppm: 0.80 d (3H, CH₃, J = 7 Hz), 3.37 m (1H, α -H), 3.73 s (3H, OMe), 4.24 d (1H, 4-H, J = 5.5 Hz), 6.50–7.60 m (12H, MeOC₆H₄, C₆H₅, BrC₆H₃), 12.85 s (1H, OH). Found, %: C 63.30; H 4.31; Br 16.21. C₂₆H₂₁BrO₅. Calculated, %: C 63.30; H 4.29; Br 16.20.

6-Bromo-4-[2-(4-chlorophenyl)-2-oxo-1-phenylethyl]-2-oxochroman-3-ylidene(phenyl)methyl acetate (VII). Compound IIIa, 0.01 mol, and ketone Ig, 0.012 mol, were added to a mixture of 3 g of metallic zinc (prepared as fine turnings), 8 ml of diethyl ether, and 8 ml of ethyl acetate. The mixture was heated to initiate the reaction which then occurred spontaneously. When the exothermic reaction was complete, the mixture was heated for 15 min under reflux. The solution was separated by decanting, 0.01 mol of acetic anhydride was added, and the mixture was heated for 10 min under reflux and treated as described above in the synthesis of compounds Va–Ve. Yield 85%, mp 210–211°C. IR spectrum, ν , cm⁻¹: 1680 (C=O, ketone), 1775 (C=O, lactone). ¹H NMR spectrum, δ , ppm: 2.03 s (3H, CH₃), 4.59 m (2H, 4-H, α -H), 6.71–7.91 m (17H, ClC₆H₄, C₆H₅, BrC₆H₃). Found, %: C 63.86; H 3.65; Br 13.25. C₃₂H₂₂BrClO₅. Calculated, %: C 63.86; H 3.68; Br 13.28.

2-Benzoyl-1-[2-(4-chlorophenyl)-1-methyl-2-oxoethyl]-1,2-dihydrobenzo[*f*]chromen-3-one (Xa). Compound VIII, 0.01 mol, and propanone Ic, 0.015 mol, were added at room temperature to a mixture of 1.3 g of fine zinc turnings with 10 ml of tetrahydrofuran. The mixture was stirred for 2 h, heated for 1 h at 35°C, and treated as described above for compounds Va–Ve. Yield 60%, mp 177–179°C. IR spectrum, ν , cm⁻¹: 1670 (C=O, ketone), 1765 (C=O, lactone). ¹H NMR spectrum, δ , ppm: 0.94 d (3H, CH₃, J = 7 Hz), 3.73 m (1H, α -H), 4.61 d (1H, 4-H, J = 7 Hz), 4.70 s (1H, 3-H), 7.10–8.00 m (15H, H_{arom}). Found, %: C 74.30; H 4.54; Cl 7.55. C₂₉H₂₁ClO₄. Calculated, %: C 74.28; H 4.51; Cl 7.56.

2-Benzoyl-1-[2-(4-bromophenyl)-1-methyl-2-oxoethyl]-1,2-dihydrobenzo[*f*]chromen-3-one (Xb) was synthesized in a similar way from 2-bromo-1-(4-bromophenyl)propan-1-one (Id). Yield 65%, mp 175–177°C. IR spectrum, ν , cm⁻¹: 1690 (C=O, ketone), 1785 (C=O, lactone). ¹H NMR spectrum, δ , ppm: 0.97 d (3H, CH₃, J = 7 Hz), 3.70 m (1H, α -H), 4.65 d (1H, 4-H, J = 7 Hz), 4.70 s (1H, 3-H), 7.00–8.00 m (15H, H_{arom}). Found, %: C 67.81; H 4.10; Br 15.58. C₂₉H₂₁BrO₄. Calculated, %: C 67.85; H 4.12; Br 15.56.

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