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Reactions of Zinc Enolates Derived from α,α-Dibromo Carbonyl Compounds with 3-(2-oxo-4a,8a-dihydro-2*H*-chromene-3-carbonyl)chromen-2-one

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Abstract — Zinc enolates derived from 1-R-2,2-dibromoethanone reacted with 3-(2-oxo-4a,8a-dihydro-2*H*-chromene-3-carbonyl)chromen-2-one to give the corresponding 1-R-1a-{(1-R-2-oxo-1,7b-dihydrocyclopropa[*c*]chromen-1(2*H*)-yl)carbonyl}-1a,7b-dihydrocyclopropa[*c*]chromen-2(1*H*)-ones as a single diastereoisomer with *cis* arrangement of the hydrogen atoms with respect to the cyclopropane ring plane. Reactions of the same electrophilic substrate with zinc enolates obtained from 1-aryl-2,2-dibromoalkanones led to the formation of 1-alkyl-1a-{(1-alkyl-1-aroyl-2-oxo-1,7b-dihydrocyclopropa[*c*]chromen-1(2*H*)-yl)carbonyl}-1-aroyl-1a,7b-dihydrocyclopropa[*c*]chromen-2(1*H*)-ones as a single diastereoisomer with *trans* arrangement of the alkyl group and hydrogen atom with respect to the cyclopropane ring plane.
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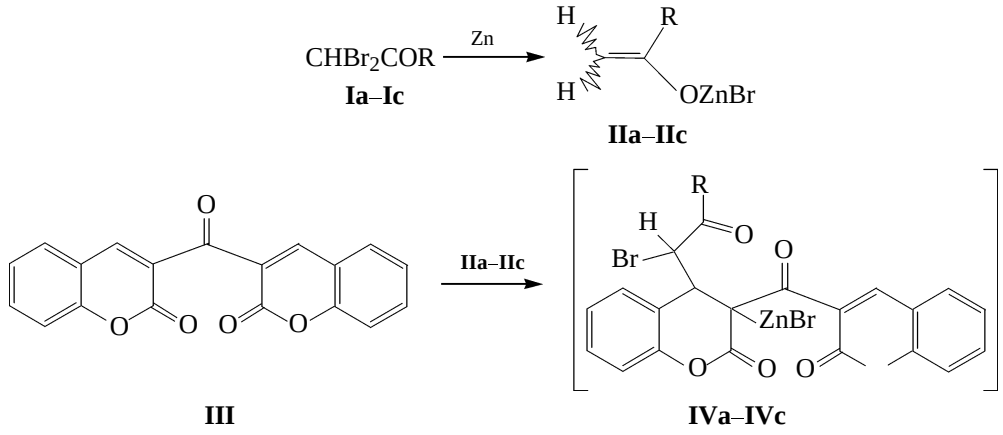
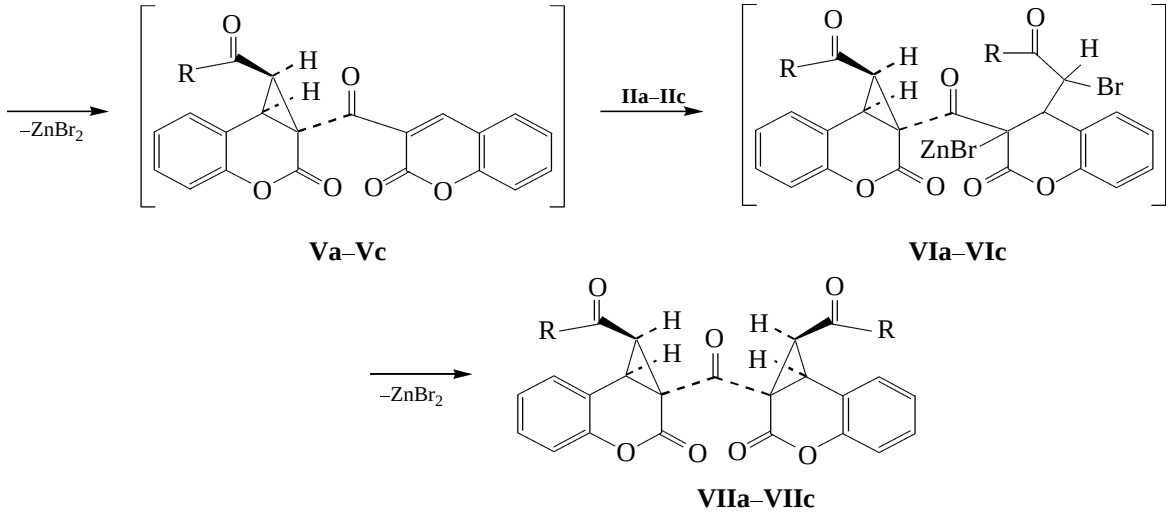
In the preceding communication we showed that bromine-containing zinc enolates derived from 1-aryl-2,2-dibromoalkanones are capable of reacting with 3-(2-oxo-4a,8a-dihydro-2*H*-chromene-3-carbonyl)-chromen-2-one in diethyl ether–ethyl acetate (2:1) to give the corresponding monocyclopropanation products, 1-alkyl-1-aroyl-1a(2-oxo-2*H*-chromene-3-carbonyl)-1a,3a,7a,7b-tetrahydro-1*H*-cyclopropa[*c*]-chromen-2-ones [1].

In the present work we made an attempt to obtain in a similar way dicyclopropanation products. Initially, we examined the reactions of bromine-containing zinc enolates **IIa**–**IIc** proved from 1,1-dibromo-3,3-dimethyl-2-butanone (**Ia**), ethyl 4,4-dibromo-2,2-dimethyl-3-oxobutanoate (**IIb**), and ethyl 4,4-dibromo-2,2-diethyl-3-oxobutanoate **IIc** with 3-(2-oxo-4a,8a-dihydro-2*H*-chromene-3-carbonyl)chromen-2-one (**III**) in the solvent system diethyl ether–ethyl acetate–toluene (8:5:10); during the process, diethyl ether and a part of ethyl acetate were distilled off, so that the reaction temperature rose to ~90°C. The reaction followed Scheme 1.

Zinc enolates **IIa**–**IIc** generated by treatment of 1-R-2,2-dibromoethanones **Ia**–**Ic** with zinc added at the double $C^3=C^4$ bond of one pyran ring in molecule **III** to form intermediates **IVa**–**IVc**. The latter underwent spontaneous cyclization to compounds **Va**–**Vc** which took up the second molecule of zinc enolate

Scheme 1.





Va–Vc **VIa–VIc**

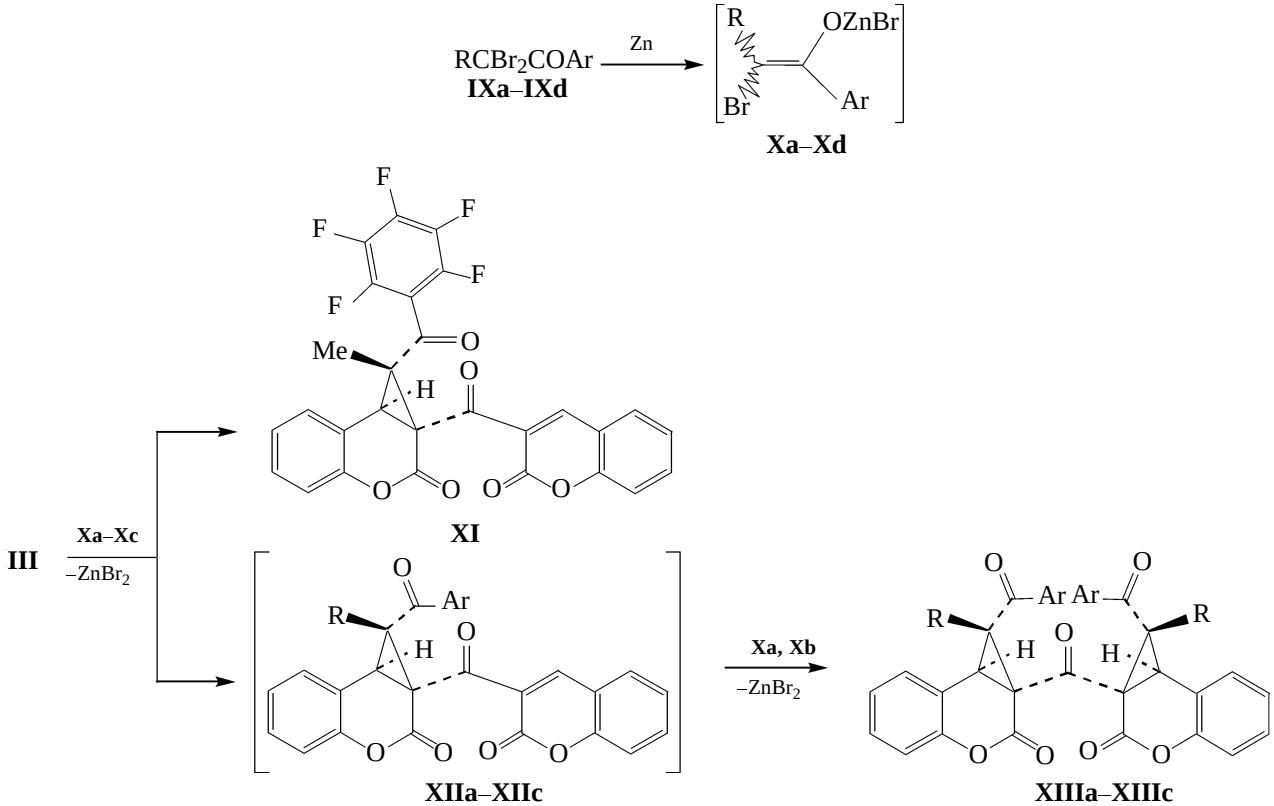
VIIa–VIIc

I, II, IV–VII, R = *t*-Bu (**a**), $EtOCOC(CH_3)_2$ (**b**), $EtOCOC(C_2H_5)_2$ (**c**).

IIa–IIc. Likewise, cyclization of intermediates **VIa–VIc** resulted in the formation of target products **VIIa–VIIc**.

The structure of compounds **VIIa–VIIc** was proved by the analytical data and ^1H NMR and IR spectra. The IR spectra of **VIIa–VIIc** contained absorption bands in the regions 1660–1695 and 1720–1745 cm^{-1} due to stretching vibrations of the ketone, lactone, and ester groups. In the ^1H NMR spectra of these compounds, protons in the cyclopropane ring appeared at δ 3.17–3.21 and 3.63–3.84 ppm. Only one set of sig-

Scheme 2.



XIIa–XIIc **XIIIa–XIIIc**

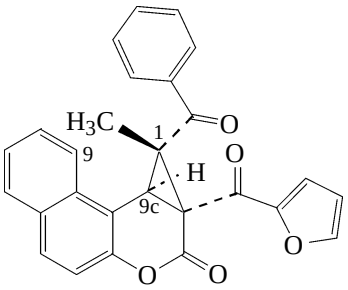
IX, X, R = Me, Ar = 4-BrC_6H_4 (**a**); R = Et, Ar = 4-BrC_6H_4 (**b**); R = Me, Ar = 4-MeC_6H_4 (**c**); R = Me, Ar = C_6F_5 (**d**).
XII, XIII, R = Me, Ar = 4-BrC_6H_4 (**a**); R = Et, Ar = 4-BrC_6H_4 (**b**); R = Me, Ar = 4-MeC_6H_4 (**c**).

nals was present in the ^{1}H NMR spectra, indicating that compounds **VIIa**–**VIIc** were formed as a single diastereoisomer. According to published data, structurally related compounds are characterized by vicinal coupling constants ^3J for protons in the cyclopropane ring of 9.4–9.8 Hz for the *cis* isomers and 5.1–5.5 Hz for the *trans* isomers [2]. The corresponding coupling constant for compounds **VIIa**–**VIIc** was found to be $^3J_{HH}$ = 9.7; therefore, protons in the cyclopropane ring in their molecules are arranged *cis*.

The addition of zinc enolates derived from 1-aryl-2,2-dibromoalkanones **IXa**–**IXc** to ketone **III** followed an analogous pattern; however, we isolated no dicyclopropane derivative in the reaction with the zinc enolate obtained from 2,2-dibromo-1-pentafluorophenylpropan-1-one (**IXc**); presumably the C-nucleophilic center in this reagent is deactivated (Scheme 2).

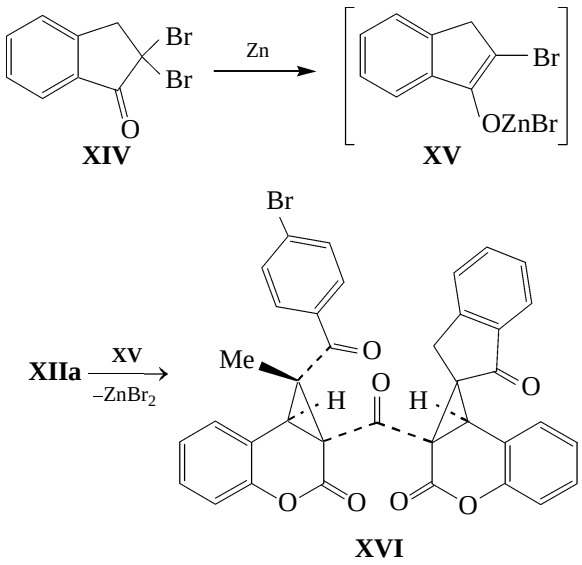
The structure of compounds **XI** and **XIIIa**–**XIIIc** was proved by elemental analysis and ^{1}H NMR and IR spectroscopy. In the IR spectra of **XIIIa**–**XIIIc** absorption bands due to ketone and lactone carbonyl groups characteristically appeared in the regions 1670–1695 and 1735–1745 cm^{-1}, respectively. Compound **XI** showed in the IR spectrum carbonyl absorption bands at 1670–1700 and 1715–1730 cm^{-1}. Singlets from the cyclopropane ring protons were located at δ 3.32–3.56 ppm in the ^{1}H NMR spectra of **XIIIa**–**XIIIc**. The ^{1}H NMR spectrum of **XI** contained a signal at δ 3.76 ppm due to proton in the cyclopropane ring and a signal at δ 8.41 ppm from proton at the double bond. Compounds **XI** and **XIIIa**–**XIIIc** were isolated as a single stereoisomer, as followed from the presence of only one set of signals in their ^{1}H NMR spectra.

Comparison of the relative intensities obtained by volume integration of cross peaks in the 2D-ROESY NMR spectrum of 1-benzoyl-1-methyl-1a-(2-furoyl)-1a,9c-dihydrobenzo[f]cyclopropa[*c*]chromen-2(1*H*)-one, where [(9c-H, 9-H) >> (9c-H, CH_3)] indicated *trans* arrangement of the 9c-H proton and methyl group [3]. Taking into account similar conditions of synthesis and structures of the above compound and compounds **XIIIa**–**XIIIc**, the latter were also assigned *trans* orientation of the 9c-H proton and 1-alkyl group with respect to the cyclopropane ring plane.



We also tried to synthesize a mixed dicyclopropanation product. For this purpose, compound **XIIa** was taken as substrate. The structure of product **XVI** thus obtained (Scheme 3) was confirmed by spectral and analytical data. The IR spectrum of **XVI** absorption bands at 1655 and 1690 cm^{-1} due to ketone carbonyl groups and at 1730–1745 cm^{-1} sue to lactone carbonyl. In the ^{1}H NMR spectrum of this compound, the cyclopropane ring protons appeared as singlets at δ 3.61 ppm, and the methylene protons in the indan fragment gave two doublets at δ 2.51 and 3.05 ppm with a coupling constant $^2J_{HH}$ of 17.6 Hz.

Scheme 3.



EXPERIMENTAL

The IR spectra were recorded on a Specord IR-75 spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra of compounds **VIIb, VIIc, XI, XIIIa, XIIIb**, and **XIIId** were measured from solutions in $CDCl_3$ on a Tesla BS-576A spectrometer, and of **XIIIc**, in $CDCl_3$ on a Mercury Plus-300 instrument (300 MHz) using HMDS as internal reference; the spectrum of **VIIa** was obtained in DMSO-d_6 on a Bruker DRX-500 spectrometer (500 MHz) using TMS as internal reference.

General procedure for the synthesis of compounds **VIIa**–**VIIc**, **XI**, **XIIIa**–**XIIIc**, and **XVI**. A solution of 0.018 mol of the corresponding α,α-dibromocarbonyl compound in 3 ml of ethyl acetate was added to a mixture of 2 g of zinc turnings, 8 ml of diethyl ether, and 5 ml of ethyl acetate, mercury(II) chloride was added to activate zinc, and 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 on a water bath, the solution was separated from zinc by decanting, 0.006 mol of compound **III** and 10 ml of anhydrous toluene were added, and the mixture was heated for 45–60 min with simultaneous removal of diethyl ether and ethyl acetate by distillation; as a result, the temperature of the reaction mixture rose to 85–95°C. The mixture was cooled, treated with 5% hydrochloric acid, and extracted with diethyl ether. The extract was dried over Na_2SO_4, the solvent was distilled off under reduced pressure, and the residue was recrystallized thrice from benzene–methanol (3 : 1). In the synthesis of compounds **VIIa**–**VIIc** and **XVI**, 0.016 and 0.013 mol, respectively, of the dibromo ketone was taken.

1-(2,2-Dimethylpropanoyl)-1a-{(1-(2,2-dimethylpropanoyl)-2-oxo-1,7b-dihydrocyclopropa[*c*]chromen-1(2*H*)-yl)carbonyl}-1a,7b-dihydrocyclopropa[*c*]chromen-2(1*H*)-one (VIIa). Yield 32%, mp 242–245°C. IR spectrum, ν, cm^{-1}: 1660–1680, 1710–1745. ^1H NMR spectrum, δ, ppm: 0.95 s (18H, $6CH_3$); 3.75 d (2H, 2CH, *J* 9.7 Hz); 3.97 d (2H, 2CHCO, *J* 9.7 Hz); 7.09 d, 7.19 t, 7.35 t, and 7.52 d (8H, $2C_6H_4$). Found, %: C 72.30; H 5.85. $C_{31}H_{30}O_7$. Calculated, %: C 72.36; N 5.88.

Ethyl 3-[(1a-{(1-(3-ethoxy-2,2-dimethyl-3-oxopropanoyl)-2-oxo-1,7b-dihydrocyclopropa[*c*]chromen-1(2*H*)-yl)carbonyl}-2-oxo-1,1a,2,7b-tetrahydrocyclopropa[*c*]chromen-1-yl]-2,2-dimethyl-3-oxopropanoate (VIIb). Yield 21%, mp 163–165°C. IR spectrum, ν, cm^{-1}: 1665–1690, 1715–1745. ^1H NMR spectrum, δ, ppm: 1.05–1.19 m (18H, $4CH_3$, $2OCH_2 \cdot CH_3$), 3.18 d (2H, 2CH, *J* 9.7 Hz), 3.68 d (2H, 2CHCO, *J* 9.7 Hz), 3.99–4.09 m (4H, $2OCH_2CH_3$), 6.93–7.18 m (8H, $2C_6H_4$). Found, %: C 66.58; H 5.40. $C_{35}H_{34}O_{11}$. Calculated, %: C 66.66; H 5.43.

Ethyl 2-[(1a-{(1-[2-ethylbutanoyl-(2-ethoxycarbonyl)]-2-oxo-1,7b-dihydrocyclopropa[*c*]chromen-1(2*H*)-yl)carbonyl}-2-oxo-1,1a,2,7b-tetrahydrocyclopropa[*c*]chromen-1-yl)carbonyl]-2-ethylbutanoate (VIIc). Yield 34%, mp 188–191°C. IR spectrum, ν, cm^{-1}: 1665–1695, 1710–1745. ^1H NMR spectrum, δ, ppm: 0.32– 0.61 m (12H, $4CH_2CH_3$), 1.16 t (6H, $2OCH_2CH_3$), 1.73 m (8H, $4CH_2CH_3$), 3.17 d (2H, 2CH, *J* 9.7 Hz), 3.63 d (2H, 2CHCO, *J* 9.7 Hz), 4.07 q (4H, $2OCH_2CH_3$), 6.93–7.19 m (8H, $2C_6H_4$). Found, %: C 68.18; H 6.10. $C_{39}H_{42}O_{11}$. Calculated, %: C 68.21; H 6.16.

1-Methyl-1a-[(2-oxo-2*H*-chromen-3-yl)carbonyl]-1-(2,3,4,5,6-pentafluorobenzoyl)-1a,7b-dihydrocyclopropa[*c*]chromen-2(1*H*)-one (XI). Yield 37%, mp 235–236°C. IR spectrum, ν, cm^{-1}: 1670–1700, 1715–1735. ^1H NMR spectrum, δ, ppm: 1.25 s (3H, CH_3), 3.76 s (1H, CH), 7.04–7.52 m (8H, $2C_6H_4$), 8.41 s (1H, CH=C). Found, %: C 62.20; H 2.43; F 17.50. $C_{28}H_{13}F_5O_6$. Calculated, %: C 62.23; H 2.42; F 17.58.

1-(4-Bromobenzoyl)-1a-{(1-(4-brombenzoyl)-1-methyl-2-oxo-1,7b-dihydrocyclopropa[*c*]chromen-1(2*H*)-yl)carbonyl}-1-methyl-1a,7b-dihydrocyclopropa[*c*]chromen-2(1*H*)-one (XIIIa). Yield 74%, mp 254°C (from DMF). IR spectrum, ν, cm^{-1}: 1680–1695, 1745. ^1H NMR spectrum, δ, ppm: 1.19 s (6H, $2CH_3$), 3.52 s (2H, 2CH), 6.93–7.79 m (16H, $2C_6H_4$, $2BrC_6H_4$). Found, %: C 60.00; H 3.25; Br 21.53. $C_{37}H_{24}Br_2O_7$. Calculated, %: C 60.02; H 3.27; Br 21.58.

1-(4-Bromobenzoyl)-1a-{(1-(4-brombenzoyl)-1-ethyl-2-oxo-1,7b-dihydrocyclopropa[*c*]chromen-1(2*H*)-yl)carbonyl}-1-ethyl-1a,7b-dihydrocyclopropa[*c*]chromen-2(1*H*)-one (XIIIb). Yield 71%, mp 262–264°C. IR spectrum, ν, cm^{-1}: 1670–1685, 1740. ^1H NMR spectrum, δ, ppm: 0.39 t (6H, $2CH_2 \cdot CH_3$), 1.58–1.95 m (4H, $2CH_2CH_3$), 3.32 s (2H, 2CH), 7.06–7.44 m (16H, $2C_6H_4$, $2BrC_6H_4$). Found, %: C 60.90; H 3.65; Br 20.76. $C_{39}H_{28}Br_2O_7$. Calculated, %: C 60.96; H 3.67; Br 20.80.

1-Methyl-1-(4-methylbenzoyl)-1a-{(1-methyl-1-(4-methylbenzoyl)-2-oxo-1,7b-dihydrocyclopropa[*c*]chromen-1(2*H*)-yl)carbonyl}-1a,7b-dihydrocyclopropa[*c*]chromen-2(1*H*)-one (XIIIc). Yield 41%, mp 249–251°C. IR spectrum, ν, cm^{-1}: 1670–1685, 1735. ^1H NMR spectrum, δ, ppm: 1.21 s (6H, $2CH_3$), 2.41 s (6H, $2CH_3C_6N_4$), 3.56 s (2H, 2CH), 7.16–7.67 m (16H, $2C_6H_4$, $2CH_3C_6H_4$). Found, %: C 76.69; H 4.90. $C_{39}H_{30}O_7$. Calculated, %: C 76.71; H 4.95.

1a-(2,1′-Dioxospiro[1a,7b-dihydrocyclopropa[*c*]chromene-1,2′-indan]-3-yl)-1-(4-bromobenzoyl)-1-methyl-1a,7b-dihydrocyclopropa[*c*]chromen-2(1*H*)-one (XVI). Yield 29%, mp 272–274°C (decomp.). IR spectrum, ν, cm^{-1}: 1655, 1690, 1730–1745. ^1H NMR spectrum, δ, ppm: 1.12 s (3H, CH3), 2.51 d (1H, CH_2, *J* 17.6 Hz), 3.05 d (1H, CH_2, *J* 17.6 Hz), 3.61 s (1H, CH), 6.86–7.76 m (16H, $3C_6H_4$, BrC_6H_4). Found, %: C 67.35; H 3.50; Br 12.10. $C_{37}H_{23}BrO_7$. Calculated, %: C 67.39; H 3.52; Br 12.12.

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