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Synthesis of Ethyl 2-Hydroxy-3-[aryl(2-naphthylamino)methyl]-2-cyclopentenecarboxylates and Ethyl 3-Arylmethylene-2-(2-naphthylamino)-1-cyclopentenecarboxylates

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Abstract—Condensation of *N*-arylmethylene-2-naphthylamines with ethyl 2-oxocycopentanecarboxylate in the presence of HCl or CH_3COOH yields ethyl 2-hydroxy-3-[aryl(2-naphthylamino)methyl]-2-cyclopentenecarboxylates and ethyl 3-arylmethylene-2-(2-naphthylamino)-1-cyclopentenecarboxylates, respectively.

Schiff bases are known to react with cyclic ketones to give derivatives of benzo[*f*]quinoline or cyclic enamines [1, 2]. We previously found [3] that reactions of ethyl 2-oxocyclopentanecarboxylate with *N*-arylmethylene-2-naphthylamines occur under mild conditions (on heating for a short time in the presence of a catalytic amount of HCl), leading to formation of 4-aryl-1-ethoxycarbonyl-2,3,4,5-tetrahydro-1*H*-cyclopenta[*c*]benzo[*f*]quinolines. When the reaction was performed under more severe conditions in the presence of nitrobenzene, 4-aryl-1-ethoxycarbonyl-2,3-dihydro-1*H*-cyclopenta[*c*]benzo[*f*]quinolines were obtained. The same reaction carried out in the presence of nitrobenzene and excess HCl was accompanied by decarboxylation of intermediate 4-aryl-1-ethoxycarbonyl-2,3-dihydro-1*H*-cyclopenta[*c*]benzo[*f*]quinolines to afford 4-aryl-2,3-dihydro-1*H*-cyclopenta[*c*]benzo[*f*]-quinolines.

The goal of the present work was to synthesize ethyl 2-hydroxy-3-[aryl(2-naphthylamino)methyl]-2-cyclopentenecarboxylates and ethyl 3-arylmethylene-2-(2-naphthylamino)-1-cyclopentenecarboxylates by reaction of ethyl 2-oxocyclopentanecarboxylate (**I**) with *N*-benzylidene-, *N*-(4-chlorobenzylidene)-, *N*-(4-methoxybenzylidene)-, *N*-(4-nitrobenzylidene)-, *N*-(3,4-dimethoxybenzylidene)-, and *N*-(3,4-methylenedioxybenzylidene)-2-naphthylamines **IIa**–**IIf**. The latter were prepared from 2-naphthylamine and the corresponding aromatic aldehydes. We were the first to reveal that the condensation of Schiff bases **IIa**–**IIc** with ester **II** occurs under mild conditions (at room temperature in the absence of HCl). In several minutes previously unknown ethyl 2-hydroxy-3-[aryl-(2-naphthylamino)methyl]-2-cyclopentenecarboxylates **IIIa**–**IIIc** were obtained in 27–41% yield (Scheme 1). It should be emphasized that the substituent in the aldehyde moiety of the Schiff base has no appreciable effect on the yield of the target product. As expected, electron-acceptor substituents slightly increase the yield of benzo[*f*]quinolines (compound **IIIa**), while electron-donor substituents exert the reverse effect (**IIIb** and **IIIc**). This is explained by different degrees of polarization of the C=N bond in Schiff bases **II** [4, 5]. Raising the temperature and reaction time leads to formation of hitherto unknown ethyl 4-aryl-2,3,4,5-tetrahydro-1*H*-cyclopenta[*c*]benzo[*f*]quinoline-1-carboxylates **IVa** and **IVb**. Compounds **IVa** and **IVb** were also synthesized by heating of solutions of **IIIb** and **IIIc** in ethanol at 60°C in the presence of HCl.

The reaction of ester **I** with Schiff bases **II** in the presence of acetic acid involves intermediate formation of esters **III** which undergo decomposition into the corresponding primary amine and α,β-unsaturated ketone. The reaction between the decomposition products yields enamines **Va**–**Ve**. These reactions were carried out by heating ester **I** and Schiff base **II** in boiling ethanol containing glacial acetic acid. The yields of products **V** were 57–70%. Esters **Vb**–**Ve** can also be obtained by heating compounds **IIIa** and **IIIb** in boiling ethanol in the presence of glacial acetic acid. The yields, melting points, and elemental analyses of the newly synthesized compounds are given in Table. Their structure was confirmed by the IR, ^1H and ^{13}C NMR, and mass spectra.

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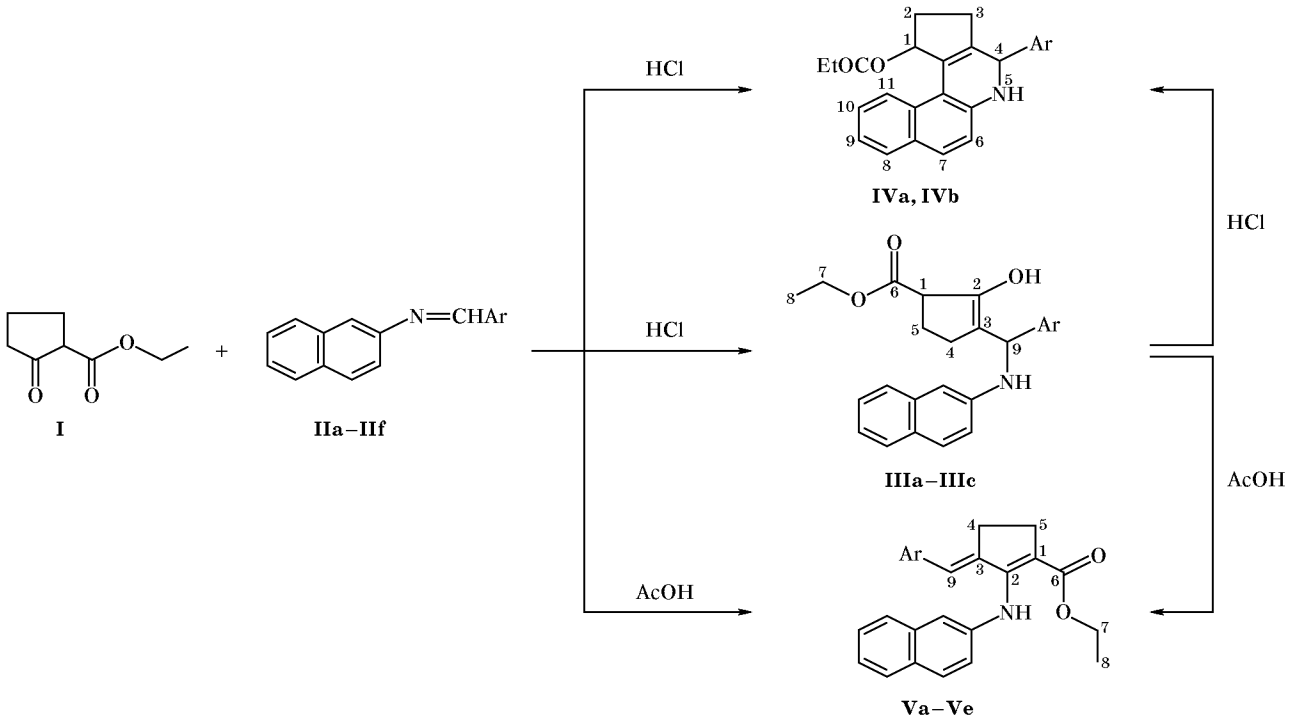
Scheme 1.



II, Ar = C_6H_5 (**a**), 4-ClC_6H_4 (**b**), 4-$CH_3OC_6H_4$ (**c**), 4-$NO_2C_6H_4$ (**d**), 3,4-$(CH_3O)_2C_6H_3$ (**e**), 3,4-$OCH_2OC_6H_3$ (**f**); **III**, Ar = 4-ClC_6H_4 (**a**), 3,4-$(CH_3O)_2C_6H_3$ (**b**), 3,4-$OCH_2OC_6H_3$ (**c**); **IV**, Ar = 3,4-$(CH_3O)_2C_6H_3$ (**a**), 3,4-$OCH_2OC_6H_3$ (**b**); **V**, Ar = C_6H_5 (**a**), 4-ClC_6H_4 (**b**), 4-$CH_3OC_6H_4$ (**c**), 4-$NO_2C_6H_4$ (**d**), 3,4-$(CH_3O)_2C_6H_3$ (**e**).

The IR spectra of esters **IIIa**–**IIIc** contain absorption bands belonging to stretching vibrations of O–H (3420–3450 cm^{-1}), N–H (3390 cm^{-1}), C=O (1690 cm^{-1}), and C–O–C bonds (1220–1230 cm^{-1}). Compounds **IVa** and **IVb** show in the IR spectra strong absorption bands at 3400 (N–H), 1695–1700 (C=O), and 1210–1220 cm^{-1} (C–O–C). Esters **Va**–**Ve** are characterized by strong IR bands at 1670 (C=O, chelated) and 1610 cm^{-1} (C=C, conjugated). A band at 3300 cm^{-1} arises from stretching vibrations of the N–H bond [6, 7].

The mass spectra of compounds **III**–**V** characteristically contain a little of fragment ions. The molecular ion peaks of **III**–**V** have the following relative intensities: **III**, ~15%; **IV**, ~30%; **V**, ~12%. Also, the $[M-C_2H_5]^+$ (60–70%) and $[M-COOC_2H_5]^+$ (15–20%) ion peaks are present.

In the ^{1}H NMR spectra signals from aromatic protons of the naphthalene and benzene rings appear as a multiplet in the region δ 7.10–7.70 ppm (compounds **III** and **IV**). The 9-H signal of **III** and 4-H signal of **IV** are observed as singlets at δ 6.60–6.80 and 6.65–6.75 ppm, respectively. The methoxy group in compounds **IIIb** and **IVa** gives a singlet at δ 3.90 and 3.89 ppm, respectively. The signal from the OCH_2O group in **IIIc** and **IVb** is observed as a singlet at δ 5.95 ppm. The downfield shift of this signal relative to the usual position of signals from such aliphatic protons [8] is likely to be caused by anisotropic effect of the two oxygen atoms, in keeping with our previous data [5]. The ethoxy group in esters **III** and **IV** gives rise to a triplet at δ 0.70 ppm (CH_3) and a quartet at δ 3.87 ppm (CH_2). Signals from the methylene protons on C^4 and C^5 in compounds **III** and on C^2 and C^3 in compounds **IV** appear as multiplets centered at δ 3.00 and 1.95 ppm. The NH proton of **III** and **IV** gives a singlet at δ 4.42 ppm.

Compound **Ve** shows in the ^{1}H NMR spectrum a triplet signal from C**H**$_3$CH$_2$O at δ 1.12 ppm, two multiplets from the cyclopentene CH_2 protons (4H) at δ 2.70 and 2.90 ppm, and a 6H-singlet at δ 3.70 ppm from the two methoxy groups. Methylene protons of the ethoxy group appear as a quartet at δ 4.05 ppm. The singlet at δ 6.50 ppm belongs to 9-H. Aromatic protons of the benzene and naphthalene rings give three multiplets centered at δ 6.87 (3H), 7.32 (4H), and 7.73 ppm (3H). The NH proton signal is observed as a singlet at δ 8.70 ppm.

Yields, melting points, and elemental analyses of compounds **III**–**V**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IIIa	41	220–221	71.1	5.9	3.3	$C_{25}H_{24}ClNO_3$[a]	71.2	5.7	3.3
IIIb	27	161–162	72.3	6.5	3.0	$C_{27}H_{29}NO_3$	72.5	6.5	3.1
IIIc	32	205–206	70.7	6.1	3.2	$C_{26}H_{25}NO_5$	70.7	6.0	3.1
IVa	52	164–165	75.7	6.6	3.3	$C_{27}H_{27}NO_4$	75.5	6.3	3.3
IVb	44	208–209	77.6	6.0	3.4	$C_{26}H_{23}NO_4$	77.4	5.7	3.5
Va	70	130–131	81.3	6.2	3.8	$C_{25}H_{23}NO_2$	81.3	6.2	3.8
Vb	69	146–147	74.1	5.8	3.4	$C_{25}H_{22}ClNO_2$[b]	74.4	5.5	3.5
Vc	64	123–124	78.5	6.2	3.5	$C_{26}H_{25}NO_3$	78.2	6.3	3.5
Vd	58	117–118	72.4	5.3	6.5	$C_{25}H_{22}N_2O_4$	72.5	5.3	6.8
Ve	57	138–139	75.5	6.4	3.3	$C_{27}H_{27}NO_4$	75.5	6.3	3.2

[a] Found Cl: 8.4%. Calculated Cl: 8.3%.
[b] Found Cl: 8.9%. Calculated Cl: 8.8%.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer in KBr. The mass spectra were obtained om an MKh-1320 instrument (energy of ionizing electrons 70 eV; vaporizer temperature 130–200°C). The NMR spectra were measured on BS-567A (^{1}H) and BS-587A spectrometers (^{13}C) using $CDCl_3$ or DMCO-d_6 as solvent and TMS as internal reference.

Ethyl 2-oxocyclopentanecarboxylate (**I**) was synthesized by the procedure reported in [9]; yield 72%, bp 102–103°C (13 mm), n_D^{20} = 1.4515.

Schiff bases IIa–IIf. A mixture of 0.05 mol of 2-naphthylamine and 0.05 mol of appropriate aromatic aldehyde in 50 ml of ethanol was heated for 15–20 min to 75–80°C. After cooling, the crystalline precipitate was filtered off and recrystallized from ethanol.

Ethyl 2-hydroxy-3-[aryl(2-naphthylamino)-methyl]-2-cyclopentenecarboxylates IIIa–IIIc. To a solution of 0.01 mol of Schiff base **IIIa**–**IIIc** in 25–30 ml of ethanol we added one drop of concentrated hydrochloric acid and 0.01 mol of ester **I**, and the mixture was stirred at room temperature. After 2–3 min, a crystalline solid precipitated and was filtered off, treated with an aqueous solution of ammonia, and recrystallized from ethanol. ^{13}C NMR spectra, δ_C, ppm: **IIIa**: 17.22 t (C^8), 27.43 t (C^4), 37.23 t (C^5), 53.04 t (C^1), 63.31 t (C^7), 67.25 d (C^9), 120.79 d (C^{17}), 128.64 s (C^{10}), 130.0 s (C^3), 143.9 s (C^{13}), 147.87 s (C^2), 148.09 s (C^{16}), 169.54 s (C^6); **IIIb**: 17.31 t (C^8), 27.72 t (C^4), 37.29 t (C^5), 52.9 s (C^1), 59.48 s (C^{16}), 59.48 s (C^{17}), 63.26 t (C^7), 67.93 d (C^9), 110.48 s (C^{10}), 115.1 d (C^{14}), 115.57 d (C^{11}), 120.95 d (C^{19}), 148.16 s (C^2), 148.72 d (C^{18}), 152.30 s (C^{12}), 152.60 s (C^{13}), 169.70 s (C^6); **IIIc**: 17.03 t (C^8), 27.54 t (C^4), 37.2 t (C^5), 52.9 s (C^1), 63.26 t (C^7), 67.82 d (C^9), 104.68 s (C^{16}), 110.53 s (C^{10}), 111.52 d (C^{14}), 111.67 d (C^{11}), 120.08 d (C^{18}), 148.06 s (C^2), 148.61 s (C^{17}), 150.53 s (C^{13}), 152.07 s (C^{12}), 169.97 s (C^6).

Ethyl 4-aryl-2,3,4,5-tetrahydro-1*H*-cyclopenta-[*c*]benzo[*f*]quinoline-1-carboxylates IVa and IVb. *a*. To a solution of 0.003 mol of ester **IIIa** and **IIIb** in 10 ml of ethanol we added 2 drops of concentrated hydrochloric acid, and the mixture was heated for 3 min at 60°C. After cooling, a crystalline solid precipitated and was filtered off, treated with an aqueous solution of ammonia, and recrystallized from ethanol.

b. To a solution of 0.01 mol of Schiff base **IIe** or **IIf** in 25–30 ml of ethanol we added 3 drops of concentrated hydrochloric acid and 0.01 mol of ester **I**, and the mixture was heated for 5 min at 60°C. After cooling, the precipitate was filtered off and treated as described above in *a*.

Ethyl 3-arylmethylene-2-(2-naphthylamino)-1-cyclopentenecarboxylates Va–Ve. *a*. A mixture of 0.01 mol of Schiff base **IIa**–**IIe**, 0.012 mol of ester **I**, 7 ml of glacial acetic acid, and 7 ml of anhydrous ethanol was refluxed for 15–20 min. The mixture was cooled, and the precipitate was filtered off and recrystallized from ethanol. ^{13}C NMR spectrum of **Ve**, δ_C, ppm: 18.13 t (C^8), 31.35 t (C^4), 32.04 t (C^5), 59.35 s (C^{16}), 59.35 s (C^{17}), 63.03 t (C^7), 115.5 d (C^{14}),

115.9 d (C^1), 117.7 d (C^9), 151.9 s (C^{12}), 152.2 s (C^{13}), 169.5 s (C^6).

b. Esters **Vb** and **Ve** were synthesized by the same procedure, starting from compounds **IIIa** and **IIIb**.

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