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Synthesis of Unsymmetrical β-Arylaminoketones

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Abstract—Azomethines derived from aniline were condensed with acetophenone derivatives to obtain new unsymmetrical β-arylaminoketones.

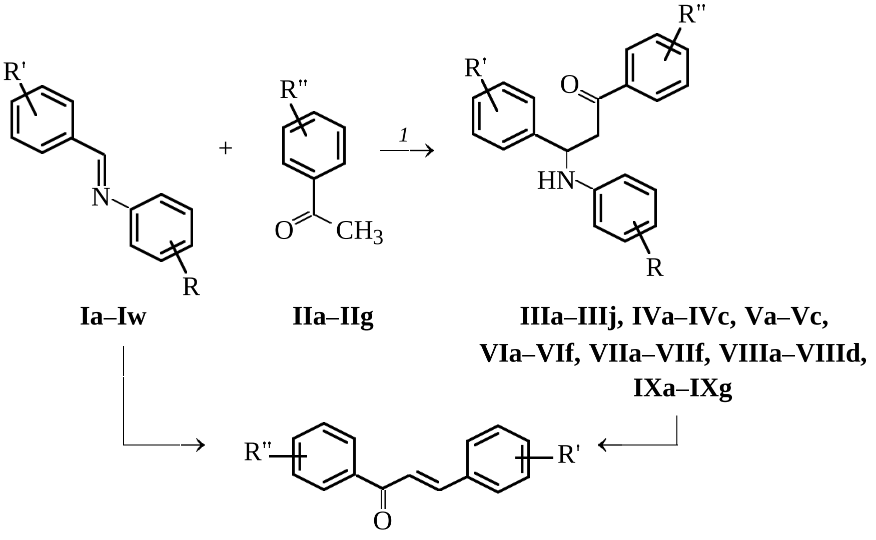
It follows from published data that β-arylaminoketones are quite active local anesthetics [1]. They serve as starting materials in the synthesis of pyrazolines [2] and compounds that exhibit bronchodilatating and hypotensive properties [3]. As known, biological activity of compounds is closely related to their steric structure. Therewith, asymmetry is an indispensable attribute of most biomolecules [4].

The present work reports on the synthesis of aminoketones by condensation of azomethines derived aniline and substitutes anilines with acetophenone and halo-, hydroxy-, and nitro-substituted acetophenones in alcoholic solution under heating.

Aminoketones has first been prepared by reactions of benzylideneaniline, benzylidene-*p*-toluidine, and benzylidene-*p*-nitroaniline with dibenzyl ketone and deoxybenzoine [5]. Later on benzylideneaniline was condensed with acetophenone and *p*-methoxyacetophenone [6]. All the cited reactions were performed in the absence of alkali.

Kozlov *et al*. [7–9] has synthesized β-arylaminoketones from hydrochlorides of primary amines incorporated into Schiff bases, in sealed ampules.

In the present work we have synthesized new unsymmetrical β-arylaminoketones in alcoholic solutions at atmospheric pressure in the presence of a catalytic amount of hydrochloric acid.

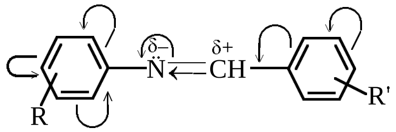


Ia–Iw **IIa–IIg** **IIIa–IIIj, IVa–IVc, Va–Vc, VIa–VIf, VIIa–VIIf, VIIIa–VIIId, IXa–IXg**

Xa–Xg

I, R = H (**a–e**), R' = H (**a**), 4-F (**b**), 4-Cl (**c**), 4-OCH_3 (**d**), 4-N $(CH_3)_2$ (**e**); R = 4-F (**f, g**), R' = H (**f**), 4-OCH_3 (**g**); R = 2-CH_3, R' = H (**h**); R = 4-CH_3 (**i–k**), R' = H (**i**), 4-Cl (**j**), 4-OH (**k**); R = 4-OCH_3, R' = H (**l**); R = 4-COOH (**m–o**), R' = H (**m**), 4-Br (**n**), 4-NO_2 (**o**); R = 4-CH_3OCO (**p, q**), R' = H (**p**), 4-OCH_3 (**q**); R = 4-C_2H_5OCO (**r–v**), R' = H (**r**), 4-Br (**s**), 4-OH (**t**), 2-OCH_3 (**u**), 2,4-di-OH (**v**). **II**, R'' = H (**a**), 4-Cl (**b**), 4-Br (**c**), 4-OH (**d**), 2-OH (**e**), 4-NO_2 (**f**), 3-NO_2 (**g**). **X**, R' = H (**a–c**), R'' = 4-Cl (**a**), 4-Br (**b**), 4-NO_2 (**c**); R' = 4-Br (**d, e**), R'' = H (**d**), 4-NO_2 (**e**); R' = 4-NO_2 (**f, g**), R'' = H (**f**), 4-NO_2 (**g**).

Presunably, the action of the catalyst consists in that its proton adds to the nitrogen atom of the Schiff base, thus polarizing the azomethine bond and increasing the positive charge on the carbon atom. Apparently, simultaneous protonation of the acetophenone molecule takes place, resulting in a typical nucleophilic addition [reaction (*1*)].



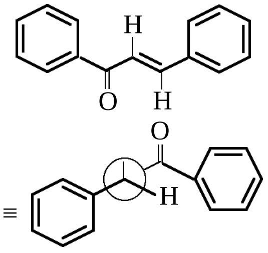
We made use of the following aniline derivatives: *p*-fluoroaniline, *o*- and *p*-toluidines, *p*-anisidine, and *p*-aminobenzoic acid and its methyl and ethyl (anesthesin) esters. The electron density distributions in azomethines **Ia**–**Iv** show that the activity of the azomethine bond is directly related to the nature of substitution in the benzene ring of the amine or aldehyde. As the electron-donor power of the substituent in the aniline moiety increases (in going from CH_3 to OCH_3 and C_2H_5OCO), the yield of condensation products decreases. Thus, the reaction of acetophenone (**IIa**) with *N*-benzylidene-*p*-toluidine (**Ii**) provides 68% of phenyl β-phenyl-β-(*p*-toluidino)ethyl ketone (**Va**), whereas the yield of phenyl β-phenyl-β-[*p*-(ethoxycarbonyl)phenylamino]ethyl ketone (**IXa**) in the reaction of acetophenone with benzylidene[*p*-(ethoxycarbonyl)phenyl]amine (**Ir**) is 43%. Strong electron-donor substituents, donating electrons to the benzene ring and entering in conjugation with the whole system, affect slightly the steady-state electron density by decreasing the additional positive charge on the carbon atom. The yield of β-arylaminoketones also decreases with increasing electron-donor power of R'. Attempted condensation of *N*-[*p*-(dimethylamino)-benzylidene]aniline (**Ie**) with acetophenone under the conditions studied failed. By the same reason, we failed to effect condensation of ethyl *N*-(*p*-hydroxybenzylidene)-*p*-aminobenzoate (**It**) and *N*-(*p*-hydroxybenzylidene)-*p*-toluidine (**Ik**) with *p*-hydroxyacetophenone (**IId**), *N*-(2,4-dihydroxybenzylidene)-*p*-anesthesin (**Iv**) with *p*-chloro- and *p*-bromoacetophenones (**IIb**, **IIc**). The latter reactions resulted in the recovery of the starting azomethines.

Electron-donor substituents in the *ortho* position of the aniline or acetophenone benzene rings act in a direction opposite to the direction of C=N polarization, and the positive charge on the carbon atom decreases so as to prevent condensation of *N*-benzylidene-*o*-toluidine (**Ih**) with acetophenone and its derivatives.

Electron-acceptor substituents withdraw electrons, and the resulting electron density distribution favors the strongest C=N polarization. In this case, the synthesis of β-arylaminoketones occurs under heating within 5–15 min. The yield of the final product of the reaction depends on its duration. The reactions of *N*-(*p*-bromobenzylidene)anesthesin (**Is**) with acetophenone (**IIa**) or *p*-nitroacetophenone (**IIf**) give β-arylaminoketones **IXb** or **IXc** after 15-min heating. In the same reagent mixtures heated for 30 min, 4-bromochalcones **Xd** or **Xe** are formed [reaction (*2*)]. The reactions of *N*-benzylidene-*p*-carboxyaniline (**Im**) with 4-Cl- or 4-Br-acetophenones (**IIb**, **IIc**) are even more sensitive: They yield β-arylaminoketones after 5-min heating and result in exclusive formation of unsaturated ketones **Xa** or **Xb** after 15-min heating.

Thus, we found that the synthesis of β-arylaminoketones from azomethines and acetophenone and its derivatives occurs in mild conditions and good yields if the starting compounds contain electron-acceptor substituents. If the starting compounds contain electron-donor substituents, longer heating of the reaction mixture is required, the yield of final products is reduced, or the reaction fails to occur at all.

The structure of α,β-unsaturated ketones **Xa**–**Xg** was determined by ^1H NMR and IR spectroscopy. The IR spectra of these compounds contain characteristic absorption bands at 1690–1670 and 1600–1580 cm^{-1}, belonging to C=O and C=C stretching vibrations. The ^1H NMR spectra of chalcones **Xa**–**Xg** show signals of protons at C^1=C^2, appearing as doublets at 7.6 and 7.7 ppm, respectively (^3J 15 Hz). Such coupling constant points to a *trans* structure of the CH=CH fragment in **Xa**–**Xg**, since in the *cis* isomer it should not be higher than 6 Hz [10].



Theoretically, chalcones can be formed by two absolutely independent reactions. First, if the initially formed β-arylaminoketone, provided it contains in the α position to carbonyl an aryl radical which decreases the electron density on the NH–CH bond, undergoes hydramine cleavage and converts into amine and chalcone [11]. As also known, in acid medium β-aminoketone takes up proton by the nitrogen lone electron pair to form an ammonium-like compound, thus favoring displacement of the electron density to nitrogen and, as a consequence, cleavage of the NH–CH bond [12]. Second, it can be admitted that

Schiff bases are hydrolyzed under the reaction conditions, and the aldehyde that forms reacts with ketone to give the corresponding chalcone whose reaction with amine yields β-arylaminoketone [13]. As shown in [14], benzalacetone reacts with methyl and ethyl *p*-aminobenzoates to form β-arylaminoketones whose physicochemical properties proved identical to those of β-arylaminoketones obtained from Schiff bases and acetone.

In our conditions, the reactions of *N*-(*p*-nitrobenzylidene)-*p*-carboxyaniline (**Ip**) with acetophenone (**IIa**) and *p*-nitroacetophenone (**IIf**) are the only that provide nitrochalcones **Xf** and **Xg**, respectively, at any reaction duration.

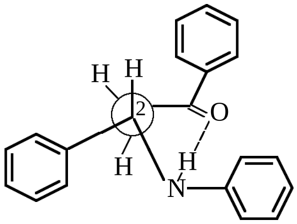
At the same time, β-arylaminoketones are stabilized by electron-donor substituents or hydrogen in the aromatic nuclei of the aldehyde and acetophenone moieties, which is explained by the positive inductive effect [15]. Therefore, in the syntheses of phenyl β-phenyl-β(phenylamino)ethyl ketone (**IIIa**), phenyl β-phenyl-β-(*p*-toluidino)ethyl ketone (**Va**), or *p*-(hydroxyphenyl) β-(*p*-anisidino)-β-phenylethyl ketone (**IVc**) no α,β-unsaturated ketones do not form even on prolonged heating of the reaction mixture.

The structure of β-arylaminoketones **IIIa**–**IIIj**, **IVa**–**IVc**, **Va**–**Vc**, **VIa**–**VIf**, **VIIa**–**VIIf**, **VIIIa**–**VIIId**, and **IXa**–**IXg** was proved by ^{1}H NMR and IR spectroscopy and GC–MS. The melting points, yields, and elemental analyses are given in Table 1.

The IR spectra revealed an H-bonded secondary amino group (band near 3450–3220 cm^{-1} with fine structure) and a carbonyl group (band near 1650–1620 cm^{-1}). Compounds **IIId** and **IVa**–**IVc** give a strong absorption band at 1120–1100 cm^{-1}, belonging to stretching vibrations of the C–F bond, compounds **IIIc**, **IIIe**, **IIIg**, **Vb**, **VIb**, and **VIIb**, a C–Cl band at 860–830 cm^{-1}, and compounds **IIIb**, **IIIh, VIc, VIIc, VIIf, IXb, IXc, IXe**, and **IXg**, a C–Br band at 580–570 cm^{-1}. A strong OCH_3 absorption band at 2880–2840 cm^{-1} is observed in the spectra of compounds **IIIf**–**IIIj, IVb, IVc, VIa**–**VIf, VIIId, IXf**, and **IXg**, and compounds **IIIi, IIIj, Vc, VIe, VIf, VIId, VIIIb**, and **IXc** give bands at 1380–1360 and 1550–1530 cm^{-1}, assignable to symmetric and antisymmetric N–O stretching vibrations. Compounds **VIIIa**–**VIIId** and **IXa**–**IXg** give a strong band at 1600–1530 cm^{-1}, associated with asymmetric vibrations of $CH_3CO_2^-$ or $C_2H_5CO_2^-$ carboxylate ions.

The mass spectra of alkylphenyl β-(alkylanilino)-β-(alkylphenyl)ethyl ketones **IIIa**–**IIIj, IVa**–**IVc, Va**–**Vc, VIa**–**VIf, VIIa**–**VIIf, VIIIa**–**VIIId**, and **IXa**–**IXg** show that these compounds are unstable under electron impact. The base peak (100%) at *m/e* 105 belong to the $[C_6H_5CO]^+$ ion. The spectra contain $[M - C_6H_5COCH_2]^+$ (26–30%) and $[C_6H_4]^+$ (40–50%) fragment ions, as well as molecular ions M^+ (10–15%).

The ^{1}H NMR spectra of the alkylphenyl β-(alkylanilino)-β-(alkylphenyl)ethyl ketones (Table 2) display signals of protons at C^1 and C^2, whose multiplicity and coupling constants relate to the steric structure of these compounds. The signals of protons at C^1 are a doublet of doublets at 2.90–3.58 and 3.20–3.80 ppm, respectively. The common geminal coupling constant ^2J of these compounds is 16.6 Hz. Moreover, the synthesized β-arylaminoketones have by one vicinal coupling constant with the proton at C^2 (4.50–5.40 ppm, d.d), equal to 5.0 and 10.0 Hz. As judged from the magnitudes of these constants, the molecules have a staggered molecular conformation [10] with slightly distorted dihedral angles. Such molecular geometry is associated with intramolecular hydrogen bonding between the carbonyl and amino groups, which brings them closer together (below is shown the Newman projection along the C^2–C^1 bond).



EXPERIMENTAL

The IR spectra were registered on a Nicolet Protege-460 spectrophotometer. The ^{1}H NMR spectra were run on Bruker DRX-500 (500 Hz) or Tesla BS-567A (100 MHz) spectrometers for 2–5% solutions in DMSO-d_6, internal reference TMS. The mass spectra were run on a FINNIGAN-MAT INCOS-50 instrument (electron impact, 70 eV).

Methyl and ethyl *p*-aminobenzoates were prepared from *p*-aminobenzoic acid and corresponding alcohol in the presence of sulfuric acid with isolation of *p*-alkoxycarbonylphenylammonium sulfate [17].

Arylidenealkylanilines Ia–**Iv** were prepared by the reaction of aniline derivatives with benzaldehyde derivatives in alcohol by the standard procedure [18].

β-Anilino-β-phenylethyl phenyl ketone (IIIa). A solution of 0.01 of acetophenone (**IIa**) in 10 ml of alcohol and 3 drops of conc. HCl acid were added to a solution of 0.01 mol of benzylideneaniline (**IIa**) in 15 ml of alcohol heated on a water bath. The reaction mixture was heated for 30 min. After cooling, the

Table 1. Yields, melting points, and elemental analyses of alkylphenyl β-(alkylanilino)-β-(alkylphenyl)ethyl ketones **IIIa**–**IIIj**, **IVa**–**IVc**, **Va**–**Vc**, **VIa**–**VIf**, **VIIa**–**VIIf**, and **IXa**–**IXg**

Comp. no	R	R'	R"	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
						C	H	N (Hlg)		C	H	N (Hlg)
IIIa	H	H	H	54	170–171[a]	83.70	6.28	4.67	$C_{21}H_{19}NO$	83.72	6.31	4.65
IIIb	H	H	4-Br	62	140–141	66.30	4.70	3.70 (21.00)	$C_{21}H_{18}BrNO$	66.32	4.74	3.68 (21.05)
IIIc	H	H	4-Cl	65	112–113[a]	75.21	5.38	4.15 (10.53)	$C_{21}H_{18}ClNO$	75.22	5.36	4.18 (10.57)
IIId	H	4-F	H	60	111–112	–	–	4.32 (5.94)	$C_{21}H_{18}FNO$	78.99	5.64	4.38 (5.96)
IIIe	H	4-Cl	H	67	116–117[a]	75.22	5.34	4.19 (10.60)	$C_{21}H_{18}ClNO$	75.22	5.36	4.18 (10.57)
IIIf	H	4-OCH_3	H	63	160	79.80	6.32	4.28	$C_{22}H_{21}NO_2$	79.76	6.34	4.23
IIIg	H	4-OCH_3	4-Cl	66	135[a]	72.20	5.42	3.80 (9.80)	$C_{22}H_{20}ClNO_2$	72.13	5.46	3.83 (9.84)
IIIh	H	4-OCH_3	4-Br	65	133	64.42	4.91	3.38 (19.47)	$C_{22}H_{20}BrNO_2$	64.40	4.88	3.41 (19.51)
IIIi	H	4-OCH_3	4-NO_2	60	169–170	70.20	5.34	7.45	$C_{22}H_{20}N_2O_4$	70.21	5.32	7.45
IIIj	H	4-OCH_3	3-NO_2	58	142–144	70.23	5.31	7.42	$C_{22}H_{20}N_2O_4$	70.21	5.32	7.45
IVa	4-F	H	H	80	250–252	–	–	4.35 (6.01)	$C_{21}H_{18}FNO$	78.99	5.64	4.38 (5.96)
IVb	4-F	4-OCH_3	H	75	125	–	–	4.00 (5.43)	$C_{22}H_{20}FNO_2$	75.64	5.73	4.01 (5.44)
IVc	4-F	4-OCH_3	2-OH	52	230	–	–	3.84 (5.16)	$C_{22}H_{20}FNO_3$	72.32	5.48	3.84 (5.20)
Va	4-CH_3	H	H	68	171[a]	83.78	6.63	4.47	$C_{22}H_{21}NO$	83.80	6.66	4.45
Vb	4-CH_3	4-Cl	H	70	152–153	75.40	5.60	4.98 (10.25)	$C_{22}H_{20}ClNO$	75.43	5.71	4.00 (10.28)
Vc	4-CH_3	H	4-NO_2	53	161–162	73.30	5.55	7.80	$C_{22}H_{20}N_2O_3$	73.33	5.56	7.78
VIa	4-OCH_3	H	H	45	149[a]	79.74	6.30	4.25	$C_{22}H_{21}NO_2$	79.76	6.34	4.23
VIb	4-OCH_3	H	4-Cl	59	127	72.10	5.42	3.80 (9.80)	$C_{22}H_2OClNO_2$	72.13	5.46	3.83 (9.84)
VIc	4-OCH_3	H	4-Br	52	136	64.44	4.85	3.40 (19.48)	$C_{22}H_2OBrNO_2$	64.40	4.88	3.41 (19.51)
VId	4-OCH_3	H	4-OH	42	153	76.05	6.03	4.06	$C_{22}H_{21}NO_3$	76.08	6.05	4.03
VIe	4-OCH_3	H	4-NO_2	48	138–140	70.20	5.29	7.47	$C_{22}H_2ON_2O_4$	70.21	5.32	7.45
VIf	4-OCH_3	H	3-NO_2	51	144–145	70.23	5.30	7.44	$C_{22}H_2ON_2O_4$	70.21	5.32	7.45
VIIa	4-COOH	H	H	60	212	76.50	5.49	4.03	$C_{22}H_{19}NO_3$	76.52	5.51	4.06
VIIb	4-COOH	H	4-Cl	65	200–201	69.44	4.78	3.65 (9.43)	$C_{22}H_{18}ClNO_3$	69.47	4.74	3.68 (9.47)
VIIc	4-COOH	H	4-Br	61	180	62.25	4.23	3.28 (18.85)	$C_{22}H_{18}BrNO_3$	62.26	4.25	3.30 (18.87)
VIId	4-COOH	H	4-NO_2	50	131–132	67.69	4.61	7.16	$C_{22}H_{18}N_2O_5$	67.69	4.62	7.18
VIIe	4-COOH	H	2-OH	43	172–173	73.25	5.24	3.90	$C_{22}H_{19}NO_4$	73.13	5.26	3.88
VIIf	4-COOH	4-Br	H	47	165–166	62.26	4.25	3.32 (18.86)	$C_{22}H_{18}BrNO_3$	62.26	4.25	3.30 (18.87)
VIIIa	4-CH_3OCO	H	H	51	186[a]	76.87	5.83	3.90	$C_{23}H_{21}NO_3$	76.88	5.85	3.89
VIIIb	4-CH_3OCO	H	4-NO_2	43	160–161	68.31	4.93	6.92	$C_{23}H_{20}N_2O_5$	68.32	4.95	6.93
VIIIc	4-CH_3OCO	H	2-OH	38	153	73.59	5.57	3.73	$C_{23}H_{21}NO_4$	73.60	5.60	3.73
VIIId	4-CH_3OCO	4-CH_3O	H	45	163[a]	74.01	5.92	3.61	$C_{24}H_{23}NO_4$	74.04	5.91	3.60
IXa	4-C_2H_5OCO	H	H	43	149–150[a]	77.20	6.15	3.78	$C_{24}H_{23}NO_3$	77.21	6.17	3.75
IXb	4-C_2H_5OCO	4-Br	H	62	145[a]	63.73	4.90	3.10 (17.69)	$C_{24}H_{22}BrNO_3$	63.72	4.87	3.09 (17.70)
IXc	4-C_2H_5OCO	4-Br	4-NO_2	40	169–170	57.95	4.21	5.62 (16.09)	$C_{24}H_{21}BrN_2O_5$	57.94	4.23	5.63 (16.10)
IXd	4-C_2H_5OCO	4-OH	H	35	178	74.00	5.92	3.58	$C_{24}H_{23}NO_4$	74.04	5.91	3.60
IXe	4-C_2H_5OCO	4-OH	4-Br	37	147–148	61.52	4.71	2.96 (17.10)	$C_{24}H_{22}BrNO_4$	61.54	4.70	2.99 (17.09)
IXf	4-C_2H_5OCO	2-OCH_3	H	39	123	74.47	6.23	3.42	$C_{25}H_{25}NO_4$	74.44	6.21	3.46
IXg	4-C_2H_5OCO	2-OCH_3	4-Br	41	165–166	62.10	5.19	2.93 (16.58)	$C_{25}H_{25}BrNO_4$	62.11	5.17	2.90 (16.56)

[a] The melting points are consistent with those reported in [7] (**IIIa, Va, VIa**), [14] (**IIIa, Va, VIa**), [16] (**IIIc, IIIe, IIIg**), and [11] (**IXb**).

precipitate that formed was filtered off, treated with aqueous ammonia for neutralization, and recrystallized from alcohol–toluene. Alkylphenyl β-(alkylanilino)-β-(alkylphenyl)ethyl ketones **IIIb**–**IIIj**, **IVa**–**IVc**, **Va**–**Vc**, **VIa**–**VIf**, **VIIa**, **VIIe**, **VIIf**, **VIIIa**–**VIIId**, **IXa**, and **IXd**–**IXg** were prepared in a similar way.

β-(*p*-Carboxyanilino)-β-phenylethyl *p*-chloro-

Table 2. ^{1}H NMR spectra of alkylphenyl β-(alkylanilino)-β-(alkylphenyl)ethyl ketones **IIIa–IIIj, IVa–IVc, Va–Vc, VIa–VIf, VIIa–VIIf**, and **IXa–IXg**, δ, ppm (*J*, Hz)

Comp. no	C^1–H, d.d (^3J 5.0, (^2J 16.6)	C^1–H, d.d (^3J 10.0, (^2J 16.6)	$C^2$1–H, d.d (^3J 5.0, (^2J 10.0)	Aromatic and R, R', R" protons	NH
IIIa	3.23	3.50	5.00	6.40 t, 6.52 d (9.6), 7.00 d (8.3), 7.20–7.50 m, 7.80–8.00 m	6.30 d (8.4)
IIIb	3.23	3.60	4.97	6.42 t, 6.45 d (9.7), 6.93 d (9.9), 7.25 t, 7.65 d (10.0), 7.48 d (9.8), 7.80 t, 7.85 d (9.7), 8.03 d (10.0)	6.45 d (8.6)
IIIc	3.18	3.45	4.85	6.40 t, 6.50 d (9.8), 6.90 d (8.0), 7.20 t, 7.65 d (9.8), 7.80 d (9.8), 7.85 t, 7.90 d (9.6), 8.00 d (9.8)	6.35 d (8.0)
IIId	3.20	3.60	5.00	6.40–6.60 m, 6.90–7.20 m, 7.40–7.60 m, 7.90 d (9.6), 8.00 d (10.1)	6.20 d (9.8)
IIIe	3.25	3.53	4.96	6.40 t, 6.50 d (9.6), 7.05 d (8.0), 7.20–7.45 m, 7.70–8.00 m	6.25 d (8.2)
IIIf	3.28	3.60	4.95	3.75 s (3H, OCH_3), 6.45 t, 6.50 d (10.0), 6.80 d (10.0), 6.95 t, 7.35 d (9.0), 7.50 t, 7.70 t, 7.95 d (13.3)	6.00 d (8.8)
IIIg	3.58	3.65	4.40	3.70 s (3H, OCH_3), 6.50 d (7.9), 6.80 d (8.0), 6.95 t, 7.35 d (8.2), 7.55 t, 7.90 d (10.0), 8.15 d (11.3)	6.03 d (8.1)
IIIh	3.55	3.70	4.90	3.75 s (3H, OCH_3), 6.50 t, 6.85 d (8.0), 7.00 t, 7.35 d (8.2), 7.70 t, 7.85 d (9.3), 8.05 d (10.8)	5.98 d (8.7)
IIIi	2.90	3.30	4.90	3.65 s (3H, OCH_3), 6.40–6.60 m, 6.85–7.20 m, 7.45 t, 7.60 t, 8.00 d (9.6)	6.20 d (8.9)
IIIj	3.15	3.50	4.80	3.85 s (3H, OCH_3), 6.50 d (9.7), 6.70 d (8.1), 7.00 t, 7.30 d (8.8), 7.75 t, 8.10 t, 8.25 d (9.6)	6.10 d (9.1)
IVa	3.27	3.63	5.00	6.30 t, 6.52 d (9.8), 6.90 t, 7.05 t, 7.40–7.50 m, 7.60 t, 7.93 d (10.2)	6.18 d (8.9)
IVb	3.30	3.67	4.90	3.70 s (3H, OCH_3), 6.40 t, 6.50 d (10.0), 6.70–6.90 m, 7.30–7.50 m, 7.90 d (9.7), 8.00–8.10 m	6.05 d (8.6)
IVc	3.40	3.58	4.96	3.70 s (3H, OCH_3), 6.20–6.50 m, 6.70–7.00 m,7.50 t, 7.70 t, 8.05 d (9.0), 9.30 s (1H, OH)	6.15 d (8.3)
Va	3.20	3.57	4.95	2.10 s (3H, CH_3), 6.40 t, 6.58 d (9.8), 6.80 d (9.8), 6.90 t, 7.30 d (9.2), 7.50 t, 7.95 d (13.0)	6.0 d (8.8)
Vb	3.50	3.60	4.50	2.05 s (3H, CH_3), 6.45 t, 6.52 d (9.6), 6.70 d (9.5), 6.85 t, 7.25 d (9.0), 7.55 t, 7.90 d (13.0)	6.15 d (8.0)
Vc	3.40	3.70	4.60	2.15 s (3H, CH_3), 6.30–6.60 m, 6.70–7.10 m, 7.30 d (9.0), 7.60 t, 7.90 d (13.0)	6.00 d (8.0)
VIa	3.30	3.65	4.50	3.70 s (3H, OCH_3), 6.50 t, 6.58 d (10.0), 6.75 d (10.0), 6.90 t, 7.40 d (9.0), 7.50 t, 7.60 t, 7.90 d (13.0)	6.05 d (8.2)
VIb	3.25	3.60	4.75	3.65 s (3H, OCH_3), 6.40 t, 6.50 d (10.0), 6.70 d (10.0), 6.90 t, 7.40 d (9.0), 7.50 t, 7.60 t, 7.85 d (12.8)	6.10 d (8.3)
VIc	3.20	3.65	4.65	3.70 s (3H, OCH_3), 6.40–6.70 m, 6.90–7.50 m, 7.65 t, 7.90 d (12.0)	6.05 d (8.5)
VId	3.10	3.50	4.95	3.75 s (3H, OCH_3), 6.10–6.40 m, 6.60–7.10 m, 7.40 t, 7.70 t, 8.00 d (9.0), 9.20 s (1H, OH)	6.00 d (8.0)
VIe	2.90	3.30	4.90	3.65 s (3H, OCH_3), 6.40–6.60 m, 6.85–7.20 m, 7.45 t, 7.60 t, 8.00 d (9.0)	6.20 d (8.7)
VIf	3.00	3.20	4.90	3.60 s (3H, OCH_3), 6.30–6.55 m, 6.80–7.10 m, 7.40 t, 7.65 t, 8.40 d (9.0)	6.10 d (8.5)
VIIa	3.30	3.80	5.20	7.20–7.60 m, 7.90 d (9.7), 8.00–8.10 m, 11.90 br.s (1H, COOH)	6.50 d (9.0)
VIIb	3.25	3.60	5.10	6.48 d (9.7), 7.10 t, 7.30 t, 7.40 d (8.0), 7.48 d (8.3), 7.53–7.60 m, 7.90 d (8.0), 12.00 br.s (1H, COOH)	6.30 d (8.6)

Table 2. (Contd.)

Comp. no	C^1–H, d.d (^3J 5.0, (^2J 16.6)	C^1–H, d.d (^3J 10.0, (^2J 16.6)	C^{2}1–H, d.d (^3J 5.0, (^2J 10.0)	Aromatic and R, R', R" protons	NH
VIIc	3.30	3.60	5.10	6.45 d (9.5), 7.00 t, 7.25 t,7.40 d (8.0), 7.50 d (8.0), 7.50–7.60 m, 7.90 d (8.0), 12.00 br.s (1H, COOH)	6.50 d ‘(8.4)
VIId	3.43	3.80	5.20	6.45 d (9.3), 7.20 t, 7.40 t, 7.48 d (8.7), 7.60 d (6.0), 8.10 t, 8.30 d (8.0), 11.50 br.s (1H, COOH)	6.70 d (9.2)
VIIa	3.30	3.70	5.10	6.60 d (9.8), 7.20 t, 7.30–8.00 m, 10.0 s (1H, OH), 11.2 br.s (1H, COOH)	6.30 d (9.7)
VIIb	3.20	3.50	4.30	6.30 d (9.0), 6.50 t, 5.90–6.30 m, 6.45 d (8.8), 7.10–7.30 m, 10.20 br.s (1H, COOH)	6.20 d (8.8)
VIIIa	3.35	3.70	5.10	3.70 s (3H, OCH$_3$), 6.55 d (13.2), 7.20 t, 7.30 t, 7.45 d (7.8), 7.50 t, 7.60 d (9.5), 7.95 d (10.0)	6.95 d (10.0)
VIIIb	3.40	3.55	5.10	3.70 s (3H, OCH$_3$), 6.55 d (8.6), 7.10 t, 7.40 t, 7.60 d (8.0), 7.90 d (8.4), 8.18 d (8.8), 8.35 d (9.0)	6.95 d (8.3)
VIIIc	3.30	3.60	5.20	3.70 s (3H, OCH$_3$), 6.50 d (8.5), 7.10 t, 7.35 t, 7.60 d (8.0), 7.90 d (8.0), 8.20 d (8.7), 8.35 d (9.0), 9.8 s (1H, OH)	6.90 d (8.7)
VIIId	3.40	3.50	5.00	3.60 s (6H, 2OCH3), 6.40 d (8.3), 7.00 t, 7.40 t, 7.65 d (8.0), 7.90 d (8.0), 8.20 d (8.5), 8.30 d (9.0)	6.60 d (8.4)
IXa	3.40	3.60	5.10	1.30 t (3H, $\mathrm{OCH_2C}H_3$), 4.15 q (2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 6.60 d (9.0), 7.20–7.40 m, 7.90–8.05 m	6.48 d (8.0)
IXb	3.35	3.50	5.00	1.30 t (3H, $\mathrm{OCH_2C}H_3$), 4.10 q (2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 6.50 d (9.0), 7.10–7.50 m, 7.90–8.10 m	6.57 d (8.4)
IXc	3.20	3.50	5.10	1.32 t (3H, $\mathrm{OCH_2C}H_3$), 4.30 q (2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 6.50 t, 7.20–7.50 m, 7.70–7.90 m	6.47 d (8.2)
IXd	3.40	3.60	5.40	1.30 t (3H, $\mathrm{OCH_2C}H_3$), 4.18 q (2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 6.70 t, 6.80–7.00 m, 7.10–7.40 m, 7.50–7.70 m, 7.90 t, 7.98 d (9.0), 9.05 s (1H, OH)	6.30 d (8.1)
IXe	3.22	3.60	5.35	1.30 t (3H, $\mathrm{OCH_2C}H_3$), 4.20 q (2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 6.50 d (7.40), 6.65 d (9.3), 7.20 d (5.6), 7.60–7.75 m, 7.85 d (7.4), 8.90 s (1H, OH)	6.50 d (8.0)
IXf	3.25	3.40	5.30	1.25 t (3H, $\mathrm{OCH_2C}H_3$), 4.18 q (2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 3.90 s (3H, OCH$_3$), 6.60 d (8.1), 6.85 t, 6.93 d (9.5), 7.18 t, 7.35 d (9.1), 7.48 t, 7.57 d (9.0), 7.60 d (10.0)	6.45 d (8.6)
IXg	3.30	3.65	5.40	1.20 t (3H, $\mathrm{OCH_2C}H_3$), 4.20 q (2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 3.65 s (3H, OCH$_3$), 6.85 t, 6.92 d (8.0), 7.18 t, 7.40 d (8.2), 7.60–7.70 m, 7.90 d (9.0)	6.40 d (8.6)

phenyl ketone (VIIb). A solution of 0.01 of acetophenone (**IIa**) in 10 ml of alcohol and 3 drops of conc. HCl acid were added to a solution of 0.01 mol of *N*-benzylidene-*p*-carboxyaniline (**Im**) in 15 ml of alcohol. The reaction mixture was heated for 5 min. After cooling, the crystals that formed were filtered off, treated with aqueous ammonia, and recrystallized from alcohol–toluene (1 : 2).

The reaction mixture of the same composition was heated on a water bath for 15 min. After cooling, the crystals that formed were filtered off and recrystallized from alcohol to isolate 4'-chlorochalcone (**Xa**), mp 101°C (consistent with published data [9]). *p*-Bromophenyl β-(*p*-carboxyanilino)-β-phenylethyl ketone (**VIIc**) and 4'-bromochalcone (**Xb**) (mp 104°C, coincides with that reported in [9]) were obtained in a similar way.

β-(*p*-Bromophenyl)-β-[*p*-(ethoxycarbonylphenylamino)]ethyl *p*-nitrophenyl ketone (IXc). A solution of 0.01 mol of *p*-nitroacetophenone (**IIf**) in 10 ml of alcohol and 3 drops of conc. HCl were added to alcohol solution of 0.01 mol of ethyl *N*-(*p*-bromobenzylidene)-*p*-aminobenzoate (**Is**). The reaction mixture was heated on a boiling water bath for 15 min. After cooling, the precipitate that formed was filtered off, treated with aqueous ammonia, and recrystallized from alcohol–toluene. Phenyl β-(*p*-bromophenyl)-β-[*p*-(ethoxycarbonylphenylamino)]ethyl ketone (**IXb**) and *p*-nitrophenyl β-(*p*-carboxyanilino)-β-phenylethyl ketone (**VIId**).

The reaction mixture of the same composition was heated on a boiling water bath for 30 min. After cooling, the precipitate that formed was filtered off and recrystallized from alcohol–toluene to isolate 4-bromo-4'-nitrochalcone (**Xe**), mp 125°C. 4-Bromochalcone (**Xd**), mp 114°C, and 4'-nitrochalcone (**Xc**), mp 107°C, were isolated in a similar way.

By the above procedure, from the reaction mixture of 0.01 mol of *N*-benzylidene-*p*-carboxyaniline (**Im**) and *p*-nitroacetophenone (**IIf**) after 15-min heating we isolated *p*-nitrophenyl β-(*p*-carboxyanilino)-β-phenylethyl ketone (**VIId**) and after 30-min heating, 4-nitrochalcone (**Xc**), mp 98°C.

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