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NOVEL PHENOLIC 1-ARYL-3-ARYLAMINO-1-PROPANONES: SYNTHESIS AND CHARACTERIZATION*

Gheorghe Roman[a†]

[a]*Department of Inorganic Polymers, Petru Poni Institute of Macromolecular Chemistry, 41A Aleea Gr. Ghica Vodă, Iaşi 700487, Romania*

Abstract: A small collection of 1-aryl-3-arylamino-1-propanones having a phenolic moiety in their structure has been obtained by the replacement of the tertiary amino group in ketonic Mannich bases with (hetero)aromatic amines. The installment of the phenolic moiety took place either through the *N*-alkylation of 4-aminophenol with ketonic Mannich base hydrochlorides, or via amine exchange in ketonic Mannich bases derived from either 2′-hydroxyacetophenone or 4′-hydroxyacetophenone.

***Keywords*:** Amino ketones; Mannich reaction; Aminomethylation; Amine exchange; *N*-Alkylation

Introduction

1-Aryl-3-arylamino-1-propanones (also known as β-arylamino ketones) are valuable synthetic reagents, as well as compounds with practical uses. For example, these compounds may serve as starting materials in the synthesis of quinoline derivatives. Treatment of such β-

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† Gheorghe Roman, *e-mail*: gheorghe.roman@icmpp.ro

arylamino ketones with polyphosphoric acid[1,2] or hydrochloric acid[2] in ethanol afforded a mixture of quinoline and the corresponding 1,2,3,4-tetrahydroquinoline through disproportionation of the intermediate 1,2-dihydroquinoline; however, only quinolines were isolated when an oxidant such as trityl chloride was added.[1] The use of tin(IV) chloride (either alone,[3] or in the presence of zinc chloride[4]) or iron(III) chloride[5] in similar reactions also led to quinoline derivatives. In addition, in the presence of a mixture of acetic and sulfuric acids, various analogous 2-[(phenylamino)-(phenyl)methyl]cycloalkanones gave quinolines having saturated rings of variable size fused onto the *c* side of the heterocyclic system.[6] More recently, the reaction of 1-aryl-3-arylamino-1-propanones with arylhydrazines and formaldehyde under mild conditions provided easy access to 3,4,5,6-tetrahydro-2,4,7-triaryl-2*H*-1,2,4-triazepines.[7] Furthermore, several biological activities of β-arylamino ketones have been recently reported. Thus, a small number of 1-aryl-3-arylamino-1-propanones exhibited a higher binding affinity to androgen receptor than its endogen ligand (5α-dihydrotestosterone).[8] Owing to the importance of the androgen receptor as a molecular target for the treatment of prostate cancer, these compounds could be leads for the development of drugs for prostate cancer therapy. In addition, these compounds have been disclosed as selective non-steroidal antagonists of progesterone receptor, which makes these small molecules useful candidates for the treatment of breast cancer.[9] Evaluation of 3-(arylamino)-1-ferrocenyl-1-propanones against both Gram-positive and Gram-negative bacteria showed that these compounds inhibited especially the growth of *Staphylococcus aureus*.[10] Several 6-(arylaminomethyl)-2-arylidenecyclohexanones have also been claimed to have anti-inflammatory and pain-relieving activity superior to that of

ibuprofen.[11] Finally, analogous 1,2-diaryl-3-arylamino-1-propanones have been evaluated as inhibitors of intestinal α-glucosidase with potential antidiabetic action,[12] or as antioxidant agents.[13]

Taking into consideration the potential of β-arylamino ketones in organic synthesis and in medicinal chemistry, the current study investigates the preparation and presents the structural characterization of several novel 1-aryl-3-arylamino-1-propanones. Because information on members of this class of compounds having a phenolic moiety (either at position 1 or at position 3 of the oxopropylidene linker between the two aromatic rings) is scarce,[7,14,15] this report focuses on this particular type of β-arylamino ketones.

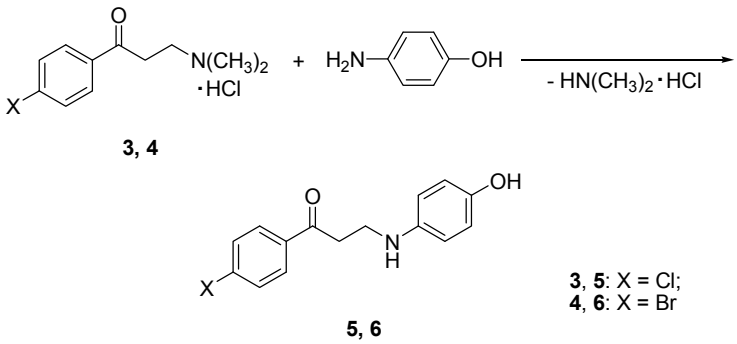
Results and Discussion

In contrast to 1,2-diaryl-3-arylamino-1-propanones, which are conveniently obtained through the direct condensation of a aryl methyl ketone, an aromatic aldehyde and an arylamine in the presence of various catalysts,[16-18] β-arylamino ketones lacking any substituent at position 2 of the oxopropylidene linker are usually prepared by replacing the quaternized, easily leaving dialkylamino group in ketonic Mannich base hydrochlorides with an arylamino moiety.[19] Using the latter synthetic approach, two different types of phenolic 1-aryl-3-arylamino-1-propanones can be prepared. The first type presents a phenolic amino moiety, which is introduced via an amine exchange between a ketonic Mannich base hydrochloride and an aminophenol (structure (**1**) in Figure 1), whereas the second type retains the phenolic moiety from the starting Mannich base hydrochloride, in whose structure the initial dialkylamino group has been replaced by a (hetero)arylamino function (structure (**2**) in Figure 1).

1 **2**

Figure 1. Types of phenolic Mannich bases.

In this study, phenolic 1-aryl-3-arylamino-1-propanones of type (**1**) are represented by compounds (**5**) and (**6**), which were obtained starting from ketonic Mannich bases (**3**) and (**4**), respectively (Scheme 1).

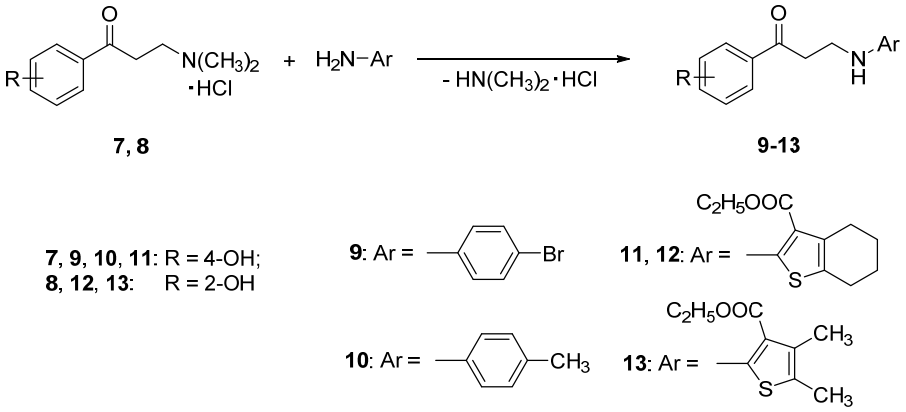


3, 4 **5, 6**

3, **5**: X = Cl;
4, **6**: X = Br

Scheme 1. Synthetic approach for the preparation of phenolic 1-aryl-3-arylamino-1-propanones (**5**) and (**6**).

On the other hand, phenolic 1-aryl-3-arylamino-1-propanones of type (**2**) were obtained from ketonic Mannich bases (**7**) and (**8**) derived from hydroxyacetophenones and various (hetero)aromatic amines (Scheme 2).



Scheme 2. Synthetic pathway for the preparation of phenolic 1-aryl-3-arylamino-1-propanones (**9**)–(**13**).

The ketonic Mannich bases (**3**), (**4**), (**7**) and (**8**) required as starting materials were prepared via a direct Mannich condensation between the appropriately substituted acetophenones, paraformaldehyde and dimethylamine hydrochloride, as previously reported.[20] Besides the readily available and more common 4-aminophenol, 4-bromoaniline and *para*-toluidine, two 2-aminothiophene derivatives have been used, to the best of our knowledge, for the first time as nucleophiles in this type of amine exchange reaction. The replacement of the amino moiety in the starting materials (**3**), (**4**), (**7**) and (**8**) proceeds smoothly in a mixture of ethanol and water at reflux temperature. The former solvent is employed with the view to ensure the solubility of the aromatic amine in the reaction mixture both as the reaction proceeds at reflux temperature, and afterwards, when the reaction mixture is cooled to the room temperature. On the other hand, ketonic Mannich base hydrochlorides dissolve easily in water. As a result, the reactants either form a solution at the outset of the reaction, or the mixture gradually becomes homogenously with the increase of the reaction temperature from the room temperature to the solvent's reflux temperature. In most cases, as the reaction advances, the reaction product separates from the solution either as an emulsion or as a solid. However, phenolic 1-aryl-3-arylamino-1-propanones (**9**)–(**11**) derived from 4′-hydroxyacetophenone only separate when the reaction mixture is cooled to room temperature. Several slightly different reaction conditions have been tried for the synthesis of these phenolic 1-aryl-3-arylamino-1-propanones. Thus, the ratio ethanol–water has been marginally adjusted from 2:3 in the synthesis of phenolic 1-aryl-3-arylamino-1-propanones of type (**1**) to 1:1 in the synthesis of phenolic 1-aryl-3-arylamino-1-propanones of type (**2**) in order to account for the higher solubility in the solvent mixture of 4-aminophenol

compared to the solubility of the other (hetero)aromatic employed in the preparation of β-arylamino ketones (**9**)–(**13**). Also, the reaction has been extended from one hour in the case of phenolic 1-aryl-3-arylamino-1-propanones of type (**1**) to 90 minutes for 1-aryl-3-arylamino-1-propanones (**9**) and (**11**) derived from 4′-hydroxyacetophenone in an attempt to improve the low yields recorded in initial experiments for the latter compounds. The reaction time has been further extended to two hours when sterically hindered 2-aminothiophene derivatives have been employed in the amine exchange reaction. Under the experimental conditions detailed above, all the phenolic 1-aryl-3-arylamino-1-propanones [with the exception of (**13**)], separate as solid materials and can be easily isolated through filtration. Analysis of each crude material isolated from reaction by NMR showed that 1-aryl-3-arylamino-1-propanones (**9**) and (**11**) derived from 4′-hydroxyacetophenone were practically pure, whereas all other β-arylamino ketones incorporated small amounts of the arylamine employed in the amine exchange reaction, which could be removed through recrystallization. The yields of the pure phenolic 1-aryl-3-arylamino-1-propanones range from good (78%) to moderate (47%).

The IR spectra of phenolic 1-aryl-3-arylamino-1-propanones (**5**), (**6**) and (**9**)–(**11**) exhibit an intense and sharp peak at approximately 1660–1680 cm^{-1} attributed to the carbonyl group stretching band. In compounds (**12**) and (**13**), this absorption band is shifted towards lower wavenumbers (approximately 1650 cm^{-1}) owing to the intramolecular hydrogen bond formed with the adjacent phenolic hydroxyl. Two significant absorption bands can also be found in the region of N-H and O-H stretching absorptions (3200 to 3600 cm^{-1}) of these spectra. They are both usually of medium intensity, and one of them is visibly broader than the other. These

peaks can be associated with the presence of the secondary amino group and of phenolic hydroxyl in the structure of these compounds.

NMR analysis has confirmed the structure assigned to each phenolic 1-aryl-3-arylamino-1-propanones. Thus, ^{1}H NMR spectra contain the corresponding signals for each type of proton, and the integration of these signals is in agreement with the proposed structure. In the case of β-arylamino ketones (**5**) and (**6**), the signals of the protons of the methylene groups in the oxopropylidene linker between the aromatic rings merge into a multiplet. At least one well-defined triplet, situated between 3.16 and 3.40 ppm and assigned to the protons of the methylene group adjacent to the carbonyl function, could be observed in the case of other phenolic 1-aryl-3-arylamino-1-propanones, while the multiplet in the range 3.27–3.58 ppm was associated with the protons of the methylene group adjacent to the secondary amino function. The signal owing to the proton of the secondary amino function has been also identified in the ^{1}H NMR spectra of each newly synthesized phenolic 1-aryl-3-arylamino-1-propanones. Thus, for β-arylamino ketones (**5**) and (**6**), the aforementioned proton gives a sharp singlet at 4.90 ppm. In the case of 1-aryl-3-arylamino-1-propanones (**9**) and (**10**) derived from *para*-substituted anilines, the signal corresponding to the proton in the >NH function appears as a triplet at chemical shift values between 5 and 6 ppm. In *N*-alkylated 2-aminothiophenes (**11**)–(**13**), the signal associated with the same proton is even more deshielded, and has been identified with the triplet at approximately 7.80 ppm in the ^{1}H NMR spectra of compounds (**11**) and (**12**) (which were recorded in DMSO-d_6), and with the very broad singlet at 6.77 ppm in the proton spectrum of compound (**13**) (which was recorded in $CDCl_3$). In addition, the characteristic singlet owing to the proton of the phenolic hydroxyl has been

easily discriminated in the ^{1}H NMR spectra of these novel phenolic 1-aryl-3-arylamino-1-propanones. Thus, the sharp singlets at 8.42 ppm (for β-arylamino ketones (**5**) and (**6**) derived from 4-aminophenol) and at approximately 10.4 ppm (for 1-aryl-3-arylamino-1-propanones (**9**)–(**11**) derived from 4′-hydroxyacetophenone) have been attributed to the phenolic proton in these compounds' structure. In the case of 1-aryl-3-arylamino-1-propanones (**12**) and (**13**) derived from 2′-hydroxyacetophenone, because of the intramolecular hydrogen bond between the phenolic hydrogen and the oxygen atom in the neighbouring carbonyl function, the phenolic hydrogen appears as a singlet at even higher δ values (11.7 ppm and 12 1 ppm, respectively).

The ^{13}C NMR spectra of the newly synthesized 1-aryl-3-arylamino-1-propanones support their structure. The assignment of the peaks corresponding to the carbon atoms in the methylene groups of the oxopropylidene linker were sometimes difficult to assign, as they mingled with the signals of the carbon atoms in residual dimethylsulfoxide. In the aromatic region of the ^{13}C NMR spectra of β-arylamino ketones (**5**) and (**6**), the peaks at approximately 141 ppm, 148 ppm and 198 ppm were assigned to the aromatic carbon atom adjacent to nitrogen, to the aromatic carbon atom adjacent to oxygen, and to the carbon atom of the carbonyl function, respectively. The same three types of carbon atoms have been assigned the peaks at approximately 147 ppm, 162 ppm, and 197 ppm in the ^{13}C NMR spectra of β-arylamino ketones (**9**) and (**10**). The peak of the carbon atom of the carbonyl function of 1-aryl-3-arylamino-1-propanones (**12**) and (**13**) derived from 2′-hydroxyacetophenone can be found at δ values (above 200 ppm) that are higher than those recorded for β-arylamino ketones (**9**) and (**10**) derived from 4′-hydroxyacetophenone.

Experimental

Melting points were taken on a Mel-Temp II apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400-MHz spectrometer. The signals owing to residual protons in the deuterated solvents were used as internal standards for the ^{1}H NMR spectra.[21] The chemical shifts for the carbon atoms are given relative to residual chloroform (δ = 77.16 ppm) or dimethyl sulfoxide (δ = 39.52 ppm) in the corresponding deuterated solvents. The chemical reagents and solvents were obtained from Sigma–Aldrich, Alfa Aesar or Merck, and were used without prior purification. Ethyl 2-amino-4,5-tetramethylenethiophene-2-carboxylate and ethyl 2-amino-4,5-dimethylthiophene-2-carboxylate were synthesized from ethyl cyanoacetate, sulfur and the corresponding carbonyl compound through the Gewald synthesis, using previously reported procedures.[22]

1-(4-Chlorophenyl)-3-(4-hydroxyphenylamino)propan-1-one (**5**). A mixture of 1-(4-chlorophenyl)-3-(dimethylamino)propan-1-one hydrochloride[23] (744 mg, 3 mmoles) and 4-aminophenol (327 mg, 3 mmoles) in 96% ethanol (4 mL) and water (6 mL) was heated at reflux temperature for one hour. After a solid had separated upon cooling to room temperature, the mixture was further refrigerated for 3 h, then the precipitate was filtered, washed with a mixture of 96% ethanol–water (10 mL, 2:3, v/v), and air-dried. Recrystallization from 96% ethanol (8 mL) gave tan leaflets (645 mg, 78%), mp = 144–145 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.20–3.33 (m, 4H), 4.90 (s, 1H), 6.45 (d, J = 8.8 Hz, 2H), 6.56 (d, J = 8.8 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.96 (d, J = 8.4 Hz, 2H), 8.42 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 38.0, 39.3, 113.6, 115.7, 128.8, 129.9, 135.4, 138.1, 141.5, 148.5, 198.2.

1-(4-Bromophenyl)-3-(4-hydroxyphenylamino)propan-1-one (**6**). To a mixture of 96% ethanol (4 mL) and water (6 mL) were added 1-(4-bromophenyl)-3-(dimethylamino)propan-1-one hydrochloride[24] (585 mg, 2 mmoles) and 4-aminophenol (218 mg, 2 mmoles), and the mixture was then heated at reflux temperature for one hour. Upon slow cooling to room temperature, a solid separated, and afterwards the mixture was kept in a refrigerator for 3 h. The resulting precipitate was filtered, washed with a mixture of 96% ethanol–water (10 mL, 2:3, v/v), and air-dried. Recrystallization from 96% ethanol (10 mL) afforded beige crystals (397 mg, 62%), mp = 150–151 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.20–3.33 (m, 4H), 4.90 (s, 1H), 6.45 (d, J = 8.8 Hz, 2H), 6.55 (d, J = 8.8 Hz, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 8.4 Hz, 2H), 8.42 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 38.0, 39.3, 113.6, 115.7, 127.2, 130.0, 131.8, 135.7, 141.5, 148.5, 198.4.

3-(4-Bromophenylamino)-1-(4-hydroxyphenyl) propan-1-one (**9**). To the solution of 3-(dimethylamino)-1-(4-hydroxyphenyl)propan-1-one hydrochloride[25] (459 mg, 2 mmoles) in a mixture of 96% ethanol–water (16 mL, 1:1, v/v) was added 4-bromoaniline (344 mg, 2 mmoles), and the resulting mixture was heated at reflux temperature for 90 min. The solid that separated upon cooling in a refrigerator for 3 h was filtered, washed with a mixture of 96% ethanol–water (9 mL, 1:2, v/v), and air-dried. Colorless crystals (314 mg, 49%), mp = 157–158 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.17 (t, J = 6.8 Hz, 2H), 3.32 (t, J = 6.4 Hz, 2H), 5.83 (t, J = 5.6 Hz, 2H), 6.53 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 7.19 (d, J = 8.8 Hz, 2H), 7.84 (d, J = 8.8 Hz, 2H), 10.36 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 36.8, 38.2, 106.1, 113.9, 115.2, 128.3, 130.5, 131.4, 148.0, 162.1, 196.7.

1-(4-Hydroxyphenyl)-3-(4-methylphenylamino)propan-1-one (**10**). 3-(Dimethylamino)-1-(4-hydroxyphenyl)propan-1-one hydrochloride[25] (459 mg, 2 mmoles) and 4-methylaniline (214 mg, 2 mmoles) were heated at reflux temperature in a mixture of 96% ethanol–water (16 mL, 1:1, v/v) for 90 min. The solid that separated upon in a refrigerator for 3 h was filtered, washed with a mixture of 96% ethanol–water (9 mL, 1:2, v/v), and air-dried. Off-white crystals (296 mg, 58%), mp = 154–155 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 2.14 (s, 3H), 3.16 (t, J = 6.8 Hz, 2H), 3.27–3.36 (m, 2H), 5.30 (s, 1H), 6.49 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.8 Hz, 2H), 10.35 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 20.1, 37.1, 38.7, 112.3, 115.2, 124.1, 128.4, 129.4, 130.5, 146.4, 162.1, 197.0.

Ethyl 2-(3-(4-hydroxyphenyl)-3-oxopropylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**11**). A mixture of 3-(dimethylamino)-1-(4-hydroxyphenyl)propan-1-one hydrochloride[25] (689 mg, 3 mmoles) and ethyl 2-amino-4,5-tetramethylenethiophene-2-carboxylate (675 mg, 3 mmoles) in 96% ethanol (12 mL) and water (12 mL) was heated at reflux temperature for 2 h. The solid obtained upon cooling under efficient stirring was filtered, washed with a mixture of 96% ethanol–water (10 mL, 1:1, v/v), and air-dried. Recrystallization from 96% ethanol (8 mL) afforded yellowish crystals (526 mg, 47%), mp = 167–168 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.22 (t, J = 7.2 Hz, 3H), 1.58–1.76 (m, 4H), 2.42–2.51 (m, 2H), 2.55–2.66 (m, 2H), 3.30 (t, J = 6.4 Hz, 2H), 3.42–3.53 (m, 2H), 4.12 (q, J = 7.2 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 7.78 (t, J = 6.0 Hz, 1H), 7.86 (d, J = 8.8 Hz, 2H), 10.40 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 14.3, 22.4, 22.8, 24.0, 26.5, 36.9, 42.6, 56.8, 101.7, 115.3, 115.7, 128.0, 130.6, 132.5, 162.3, 163.9, 165.2, 196.6.

Ethyl 2-(3-(2-hydroxyphenyl)-3-oxopropylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**12**). To a mixture of 96% ethanol (12 mL) and water (12 mL) were added 3-(dimethylamino)-1-(2-hydroxyphenyl)propan-1-one hydrochloride[26] (689 mg, 3 mmoles) and ethyl 2-amino-4,5-tetramethylenethiophene-2-carboxylate (675 mg, 3 mmoles). The solution was heated at reflux temperature for 2 h, and then it was allowed to slowly reach room temperature, when a solid precipitated. The material was filtered, washed with a mixture of 96% ethanol–water (10 mL, 1:1, v/v), and air-dried. Recrystallization from 96% ethanol (8 mL) gave yellowish crystals (674 mg, 60%), mp = 109–110 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.23 (t, J = 7.2 Hz, 3H), 1.59–1.76 (m, 4H), 2.43–2.51 (m, 2H), 2.57–2.66 (m, 2H), 3.41–3.58 (m, 4H), 4.13 (q, J = 7.2 Hz, 2H), 6.91–7.02 (m, 2H), 7.47–7.57 (m, 1H), 7.79 (t, J = 6.0 Hz, 1H), 7.88 (dd, J = 0.8 and 8.0 Hz, 1H), 11.66 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 14.3, 22.4, 22.8, 24.0, 26.5, 38.9, 42.3, 58.8, 101.8, 115.8, 117.6, 119.3, 120.6, 130.7, 132.5, 136.1, 160.4, 163.8, 165.2, 203.8.

Ethyl 2-(3-(2-hydroxyphenyl)-3-oxopropylamino)-4,5-dimethylthiophene-3-carboxylate (**13**). 3-(Dimethylamino)-1-(2-hydroxyphenyl)-propan-1-one hydrochloride[26] (689 mg, 3 mmoles) and ethyl 2-amino-4,5-dimethylthiophene-2-carboxylate (597 mg, 3 mmoles) were heated at reflux temperature in a mixture of 96% ethanol–water (24 mL, 1:1, v/v) for 2 h. A semi-solid material separated upon slow cooling to room temperature. The supernatant was decanted, and the semi-solid was redissolved in boiling 96% ethanol (25 mL). The solution was allowed to reach room temperature, and then it was kept in a refrigerator overnight. The separated solid was filtered, washed with 96% ethanol (5 mL), and air-dried to afford light orange crystals (520 mg, 50%), mp = 151–152 °C; ^{1}H NMR ($CDCl_3$, 400

MHz): δ 1.33 (t, J = 7.2 Hz, 3H), 2.18 (s, 3H), 2.19 (s, 3H), 3.40 (t, J = 6.4 Hz, 2H), 3.67 (t, J = 6.4 Hz, 2H), 4.25 (q, J = 7.2 Hz, 2H), 6.77 (br s, 1H), 6.89 (superimposed dd, J = 8.0 Hz, 1H), 6.98 (dd, J = 8.4 Hz, 1H), 7.47 (superimposed dd, J = 7.6 Hz, 1H), 7.71 (dd, J = 7.6 Hz, 1H), 12.09 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.6, 14.6, 14.9, 37.5, 42.5, 59.7, 105.9, 114.0, 118.8, 119.2, 119.3, 129.9, 131.7, 136.8, 162.2, 162.5, 166.3, 204.1.

Conclusions

Facile access to novel phenolic 1-aryl-3-arylamino-1-propanones has been provided by the replacement of the dimethylamino group in ketonic Mannich base hydrochlorides. *N*-Alkylation of 4-aminophenol with β-amino ketones derived from halogen-substituted acetophenones afforded 1-aryl-3-arylamino-1-propanones having the phenolic hydroxyl in the aromatic moiety at position 3, while exchange of the dimethylamino group in ketonic Mannich base hydrochlorides derived from 2′-hydroxyacetophenone or 4′-hydroxyacetophenone with (hetero)aromatic primary amines gave 1-aryl-3-arylamino-1-propanones having the phenolic hydroxyl in the aromatic moiety at position 1. The reaction has been conducted in mixtures of ethanol–water, which ensured a homogenous reaction medium and allowed simple and straightforward separation of the reaction product at the end of the reaction time. Structural characterization by IR and NMR spectroscopy of the obtained products supports their chemical identity.

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