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ORIGINAL RESEARCH PAPER

KETONIC MANNICH BASES DERIVED FROM 1-(5-BROMOBENZOFURAN-2-YL)ETHAN-1-ONE[#]

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Abstract: 1-(5-Bromobenzofuran-2-yl)ethan-1-one has been employed as substrate in a direct Mannich reaction with common secondary amines to generate several *β*-aminoketones hydrochlorides. Alkylation of *S*- and *N*-nucleophiles (4-chlorothiophenol, piperazine, sulfanilamide, 3,5-dimethylpyrazole) with the dimethylamine-containing β-aminoketone derived from the aforementioned substrate has also been investigated. Reaction of the same ketonic Mannich base with phenylhydrazine afforded the corresponding 1,3-disubstituted pyrazoline, whose UV-Vis absorption has been measured in dimethylsulfoxide, toluene and chloroform at room temperature to give similar spectra having a maximum at approximately 390 nm. The fluorescence spectrum of this pyrazoline in toluene is more intense and blue-shifted compared to its emission spectrum in dimethylsulfoxide.

Keywords: *alkylation, amine exchange, aminomethylation, benzofuran, fluorescence, pyrazoline*

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INTRODUCTION

Benzofuran is a heterocyclic ring system that is present in the structure of a large number of naturally occurring compounds with significant biological properties [1 – 3]. Another reason for the widespread attention that benzofuran derivatives have attracted throughout the years is the plethora of interesting properties and practical applications that have been associated with synthetic compounds featuring a fully aromatic or a partially reduced benzofuran scaffold. Benzofuran derivatives have found multiple uses in medicinal chemistry as anti-tubercular and antibacterial candidates [4], for development of drugs for Alzheimer's disease [5], as inhibitors of protein kinases in the treatment of cancer or viral infections [6] or as radioligands useful in positron emission tomography and single-photon emission computer tomography [7]. Several more general reviews that provide accounts of miscellaneous pharmacological activities of benzofuran derivatives are also available [8, 9]. In the field of optical applications, symmetrical and non-symmetrical diarylethene derivatives having a benzofuran ring exhibit remarkable photochromism [10, 11], while benzofuran trimers with luminescent properties were theoretically investigated [12] and the electro-optic properties of benzofuran-terminated dyes as guest molecules in polymer matrices have been determined [13]. Synthesis and characterization of polymers containing benzofuran in their backbone or as pendant moieties, as well as the relationship between the presence of benzofuran in polymers with various structures and their specific properties have been reported [14 – 17].

The synthetic approaches leading to benzofurans and the chemistry of this heterocyclic ring system have also been systematically reviewed [18 – 22]. A careful and detailed analysis of the available information has revealed that, despite the efforts of several research groups, very little is still known on the aminomethylation of 2-acetylbenzofurans. Several ketonic Mannich bases of 2-acetylbenzofuran itself as substrate and common secondary dialkylmines (morpholine, piperidine, dimethylamine, pyrrolidine) as amine reagents have been obtained with yields ranging from moderate to good as compounds involved in studies concerning their behavior under reductive conditions [23], in reports dealing with their stability [24], or in investigations of various biological activities of the amino ketones themselves [25] or of the secondary amino alcohols [26, 27], tertiary amino alcohols [27, 28] and unsaturated amines [27] obtained from them. Other *β*-aminoketones derived from 2-acetylbenzofurans and having diverse substitution patterns in the benzene ring (*e.g.* 7-methoxy [28, 29], 5-chloro [24], 5-methoxy [24], 5-methyl [28], 5,6-, 4,5- and 5,7-dimethyl [28]) have also been disclosed. Although 2-acetyl-5-bromobenzofuran is accessible in a straightforward manner [30] from commercially available 5-bromosalicylaldehyde, the data on *β*-amino ketones derived from this substrate is scarce. To the best of our knowledge, only the hydrochlorides of the dimethylamine-containing ketonic Mannich base and its diethylamine-containing analog [24], along with the hydrochloride of the piperidine-derived ketonic Mannich base [31] have been reported in the literature so far, but they have not been fully characterized. Aiming to revisit the issue and to further expand the existing knowledge on these particular compounds, the present study examines the aminomethylation of 2-acetyl-5-bromobenzofuran using various secondary dialkylamines in order to obtain and properly characterize the resulting ketonic Mannich bases, whose reactivity in selected alkylation and ring closure

reactions is subsequently investigated with the view to obtain hitherto unknown benzofuran derivatives.

EXPERIMENTAL SECTION

Materials

The reagents used in this study (5-bromosalicylaldehyde, chloroacetone, paraformaldehyde, dimethylamine hydrochloride, morpholine hydrochloride, piperidine hydrochloride, 4-methylpiperidine, 4-chlorothiophenol, piperazine, sulfanilamide, 3,5-dimethylpyrazole and phenylhydrazine) were purchased from Merck–Sigma–Aldrich, and were used without prior purification. The solvents were obtained from Merck–Sigma–Aldrich or VWR International, and were used without prior purification. 2-Acetyl-5-bromobenzofuran **1** was synthesized from 5-bromosalicylaldehyde and chloroacetone as previously reported [30]. 4-Methylpiperidine hydrochloride was prepared by treating a solution of 4-methylpiperidine in anhydrous diethyl ether with a solution of hydrogen chloride in anhydrous diethyl ether.

Methods

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. 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. UV–Vis absorption spectra were recorded on a SPECORD 210 Plus spectrophotometer at room temperature, using 10 mm quartz cells. For UV-Vis absorption measurements, stock solutions of pyrazoline **10** (100 µL, 1×10^{-3} M) in the required solvent were diluted with the same solvent (3 mL). Emission spectra were measured on a Perkin-Elmer LS 55 spectrofluorometer at room temperature. For the fluorescence measurements, stock solutions of pyrazoline **10** (100 µL, 1×10^{-3} M) in the required solvent were diluted with the same solvent (10 mL).

Synthesis

***General procedure for the synthesis of ketonic Mannich bases of 2-acetyl-5-bromobenzofuran* 2 – 5**

A mixture of 1-(5-bromobenzofuran-2-yl)ethan-1-one **1** (1195 mg, 5 mmol), paraformaldehyde (300 mg, 10 mmol), amine hydrochloride (6 mmol) and aq. 36 % HCl (5 drops) in 2-propanol (10 mL) was heated at reflux temperature for 4 h. The mixture was allowed to reach 50 °C, then it was diluted with acetone (30 mL) under efficient stirring. Overnight refrigeration gave a solid material, which was filtered, washed with acetone (2×10 mL), air-dried and recrystallized from abs. ethanol to afford the pure ketonic Mannich bases **2** – **5** as hydrochlorides.

1-(5-Bromobenzofuran-2-yl)-3-(dimethylamino)propan-1-one hydrochloride **2**
Colorless crystals, yield 63 %; mp 187–188 °C (lit. mp 191 °C [24]); ^{1}H NMR (DMSO-d_6): δ 2.79 (s, 6H), 3.42 (t, J = 7.2 Hz, 2H), 3.60 (t, J = 7.2 Hz, 2H), 7.67–7.79 (m, 2H), 7.94 (s, 1H), 8.11 (s, 1H), 10.88 (br s, 1H, exchangeable with D); ^{13}C NMR (DMSO-d_6): δ 33.3, 42.2, 51.0, 113.6, 114.4, 116.3, 126.1, 128.9, 131.3, 152.3, 153.7, 186.9.

1-(5-Bromobenzofuran-2-yl)-3-(morpholin-4-yl)propan-1-one hydrochloride **3**
Off-white crystals, yield 50 %; mp 214–215 °C; ^{1}H NMR (DMSO-d_6): δ 3.05–3.22 (m, 2H), 3.42–3.57 (m, 4H), 3.67 (t, J = 7.2 Hz, 2H), 3.82 (t, J = 8.0 Hz, 2H), 3.99 (d, J = 11.6 Hz, 2H), 7.72 (dd, J = 2.0 and 8.8 Hz, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.93 (s, 1H), 8.15 (d, J = 1.6 Hz, 1H), 11.38 (br s, 1H, exchangeable with D); ^{13}C NMR (DMSO-d_6): δ 32.7, 50.3, 51.2, 63.4, 113.6, 114.5, 116.4, 126.2, 128.9, 131.3, 152.3, 153.7, 186.8.

1-(5-Bromobenzofuran-2-yl)-3-(piperidin-1-yl)propan-1-one hydrochloride **4**
Off-white crystals, yield 30 %; mp 199–200 °C (lit. mp 218 °C [31]); ^{1}H NMR (DMSO-d_6): δ 1.32–1.48 (m, 1H), 1.64–1.89 (m, 5H), 2.84–3.03 (m, 2H), 3.30–3.54 (m, 4H), 3.66 (t, J = 7.2 Hz, 2H), 7.72 (dd, J = 2.0 and 8.8 Hz, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.94 (s, 1H), 8.14 (d, J = 2.0 Hz, 1H), 10.60 (br s, 1H, exchangeable with D); ^{13}C NMR (DMSO-d_6): δ 21.3, 22.4, 33.0, 50.2, 52.1, 113.5, 114.4, 116.3, 126.1, 128.8, 131.3, 152.3, 153.7, 187.0.

1-(5-Bromobenzofuran-2-yl)-3-(4-methylpiperidin-1-yl)propan-1-one hydrochloride **5**
Colorless crystals, yield 34 %; mp 172–173 °C; ^{1}H NMR (DMSO-d_6): δ 0.93 (d, J = 6.4 Hz, 3H), 1.43–1.70 (m, 3H), 1.79 (d, J = 13.2 Hz, 2H), 2.87–3.03 (m, 2H), 3.36–3.47 (m, 2H), 3.49 (d, J = 12.4 Hz, 2H), 3.66 (t, J = 7.2 Hz, 2H), 7.71 (dd, J = 2.0 and 8.8 Hz, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.94 (s, 1H), 8.13 (d, J = 1.6 Hz, 1H), 10.69 (br s, 1H, exchangeable with D); ^{13}C NMR (DMSO-d_6): δ 21.1, 28.1, 30.7, 33.1, 50.3, 52.0, 113.6, 114.5, 116.4, 126.1, 128.9, 131.3, 152.4, 153.7, 187.0.

***Synthesis of 1-(5-bromobenzofuran-2-yl)-3-[(4-chlorophenyl)thio]propan-1-one* 6**
Mannich base **2** (332.5 mg, 1 mmol) and 4-chlorothiophenol (144.5 mg, 1 mmol) were heated at reflux temperature in a mixture of ethanol–water (10 mL, 1:1 *v*/*v*) for 1 h. On cooling, a solid separated, which was filtered, washed with ethanol–water (2×6 mL, 1:1 *v*/*v*), air-dried and recrystallized from 96 % ethanol to give beige crystals, yield 83 %; mp 120–121 °C; ^{1}H NMR ($CDCl_3$): δ 3.24–3.35 (m, 4H), 7.27 (d, J = 8.8 Hz, 2H), 7.31 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 0.8 Hz, 1H), 7.44 (d, J = 8.8 Hz, 1H), 7.57 (dd, J = 2.0 and 8.8 Hz, 1H), 7.84 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 28.1, 38.7, 112.1, 114.1, 117.3, 126.0, 128.9, 129.4, 131.3, 131.6, 132.7, 134.1, 153.2, 154.3, 189.0.

***Synthesis of 3,3'-(piperazine-1,4-diyl)bis[1-(5-bromobenzofuran-2-yl)propan-1-one]* 7**
To the solution of Mannich base **2** (332.5 mg, 1 mmol) in water (20 mL), a solution of piperazine (43 mg, 0.5 mmol) in water (5 mL) was added in one portion. The resulting mixture was stirred at room temperature for 24 h, then the solid material was filtered, washed with water (2×15 mL), air-dried, and recrystallized from ethyl acetate–ethanol (1:1, *v*/*v*) to afford a yellowish powder, yield 32 %; mp 167–168 °C; ^{1}H NMR ($CDCl_3$): δ 2.55 (br s, 8H), 2.86 (t, J = 7.2 Hz, 4H), 3.15 (t, J = 7.2 Hz, 4H), 7.41–7.48 (m, 4H),

7.56 (dd, J = 2.0 and 8.8 Hz, 2H)), 7.84 (d, J = 1.6 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ 36.7, 52.7, 53.0, 111.6, 114.0, 117.0, 125.8, 128.9, 131.2, 153.4, 154.2, 190.0.

Synthesis of 4-{[3-(5-bromobenzofuran-2-yl)-3-oxopropyl]amino}benzenesulfonamide 8

A mixture of Mannich base **2** (665 mg, 2 mmol) and 4-aminobenzenesulfonamide (344 mg, 2 mmol) was heated at reflux temperature in a mixture of 96 % ethanol (5 mL) and water (2.5 mL) for 1 h. The solid that separated was filtered, washed sequentially with 96 % ethanol (2×10 mL) and water (2×10 mL), and air-dried. The material was heated at reflux temperature with 96 % ethanol (20 mL) for 5 min, then the solid was filtered and air-dried to give an off-white powder, yield 74 %; mp 209–211 °C; ^{1}H NMR (DMSO-d_6): δ 3.28 (t, J = 6.4 Hz, 2H), 3.43–3.53 (m, 2H), 6.45 (t, J = 5.6 Hz, 1H), 6.65 (d, J = 8.4 Hz, 2H), 6.92 (s, 2H), 7.53 (d, J = 8.8 Hz, 2H), 7.64–7.77 (m, 2H), 7.84 (s, 1H), 8.06 (s, 1H); ^{13}C NMR (DMSO-d_6): δ 37.3, 37.7, 110.8, 113.0, 114.4, 116.2, 126.0, 127.4, 129.0, 130.3, 131.0, 151.1, 152.9, 153.7, 189.0.

Synthesis of 1-(5-bromobenzofuran-2-yl)-3-(3,5-dimethyl-1H-pyrazol-1-yl)propan-1-one 9

A solution of Mannich base **2** (332.5 mg, 1 mmol) and 3,5-dimethylpyrazole (96 mg, 1 mmol) in water (10 mL) was heated at reflux temperature for 1 h. During this interval, a dense oil separated gradually. At the end of the reaction time, the mixture was cooled in an ice bath under efficient stirring, when the oil solidified. The solid was filtered, washed with thoroughly with water, and air-dried. Recrystallization from cyclohexane afforded colorless crystals, yield 63 %; mp 117–118 °C; ^{1}H NMR ($CDCl_3$): δ 2.18 (s, 3H), 2.28 (s, 3H), 3.54 (t, J = 6.8 Hz, 2H), 4.38 (t, J = 6.8 Hz, 2H), 5.73 (s, 1H), 7.43 (d, J = 7.6 Hz, 2H), 7.55 (dd, J = 2.0 and 8.8 Hz, 1H), 7.83 (d, J = 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 11.0, 13.5, 39.1, 42.5, 104.9, 112.3, 114.0, 117.0, 125.8, 128.8, 131.4, 139.3, 147.9, 152.9, 154.3, 188.5.

Synthesis of 3-(5-bromobenzofuran-2-yl)-1-phenyl-4,5-dihydro-1H-pyrazole 10

Mannich base **2** (332.5 mg, 1 mmol) and phenylhydrazine (108 mg, 1 mmol) were heated at reflux temperature in a mixture of ethanol–water (10 mL, 3:2, *v*/*v*) for 3 h. The material that separated was filtered, washed with a cold mixture of ethanol–water (2×10 mL, 3:2, *v*/*v*), air-dried and recrystallized from 96 % ethanol to afford yellow microcrystals, yield 46 %; mp 164–165 °C; ^{1}H NMR (DMSO-d_6): 3.33 (t, J = 10.8 Hz, 2H), 3.96 (t, J = 10.8 Hz, 2H), 6.87 (t, J = 7.2 Hz, 1H), 7.12 (d, J = 7.2 Hz, 2H), 7.14 (s, 1H), 7.31 (dd, J = 7.2 and 8.4 Hz, 2H), 7.49 (dd, J = 2.0 and 8.8 Hz, 1H), 7.65 (d, J = 8.8 Hz, 1H), 7.88 (d, J = 2.0 Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 31.2, 47.9, 105.4, 112.9, 113.1, 115.6, 119.4, 123.6, 127.7, 129.1, 130.5, 140.3, 144.5, 151.1, 153.4.

RESULTS AND DISCUSSION

Under generic reaction conditions for a direct Mannich reaction, 1-(5-bromobenzofuran-2-yl)ethan-1-one **1** has been aminomethylated at the methyl group α to the carbonyl function employing paraformaldehyde and hydrochlorides of secondary amines, in the

presence of catalytic amounts of HCl, by heating the reactants in 2-propanol for several hours (Figure 1). Aminomethylation of substrate **1** using dimethylamine hydrochloride proceeded smoothly to afford ketonic Mannich base **2** as hydrochloride in good yields. Although the reaction product usually separated as a solid after 2-3 hours of refluxing, the reaction mixture is slightly cooled and diluted with acetone in order to ensure a thorough removal of any unreacted substrate (soluble in acetone) while improving the recovery of the desired product **2** (insoluble in acetone). Aminomethylation of substrate **1** with other secondary amine hydrochlorides (morpholine hydrochloride, piperidine hydrochloride and 4-methylpiperidine hydrochloride) afforded under the same reaction conditions and work-up only moderate to low yields of the corresponding ketonic Mannich bases **3** – **5**, which suggests that the reactivity of the aforementioned amine hydrochlorides towards substrate **1** is inferior to that of dimethylamine hydrochloride. *β*-Amino ketones **2** – **5** are stable in solid state, but in aqueous and DMSO solutions they have a tendency for decomposition through loss of the amine moiety. Thus, a perfectly clear aqueous solution of compound **3** gradually developed into a slightly cloudy emulsion overnight. Also, as the structure of Mannich bases **2** – **5** was being established by NMR spectroscopy, reexamination of a one-day old sample of Mannich base **5** in DMSO-d_6 clearly showed the presence in the proton spectrum of peaks associated with the vinyl protons from the *α*,*β*-unsaturated ketone, which is the normal product of deamination of **5**. As for the structural characterization of compounds **2** – **5**, their proton NMR spectra in DMSO-d_6 exhibited the same pattern in the aromatic region, while the pattern comprising two triplets, which is typical for ketonic Mannich bases derived from methyl aryl/heteroaryl ketones and is associated with the protons in the two neighboring methylene groups, was easily noticeable in the aliphatic region of the proton spectra of compounds **2** and **3**. In the case of *β*-amino ketones **4** and **5**, these triplets and the signals of other aliphatic protons were partially superimposed. A slightly broad peak in the off-set, which was present in all the proton spectra of Mannich bases **2** – **5** and disappeared after D_2O had been added to the NMR sample, was indicative for the presence of the labile proton at the quaternized nitrogen atom. Two sets of signals were partially discernable for the 4-methylpiperidin-1-yl moiety in the aliphatic region of the proton NMR spectra of compounds **5**, which suggests the co-existence in the structure of Mannich base **5** of the two possible chair conformations for the piperidine ring in which the methyl group is either equatorial or axial. Decomposition of the sample, as previously mentioned, during NOE experiments precluded the determination beyond any doubt of the conformation for the major stereoisomer, but literature precedents indicate that the equatorial conformer is preferred [32]. For the sake of clarity, only the spectra of the major stereoisomer are presented in Experimental section.

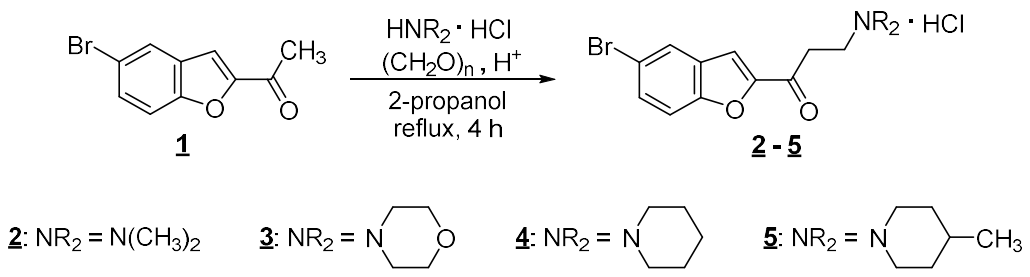

Figure 1. *Aminomethylation of 1-(5-bromobenzofuran-2-yl)ethan-1-one* **2**

The well-known reactivity of *β*-amino ketones could be exploited for generation of many structurally diverse novel compounds [33]. As the most important reactions of ketonic Mannich bases (*e.g.* alkylations, ring closure) rely on their ability to eliminate the easily leaving dialkylamino group, *β*-amino ketones **2** – **5** are excellent candidates for preparation of benzofuran derivatives otherwise difficult to obtain. Due to the its synthesis in conveniently high yield compared to the yields recorded for analogs **3** – **5**, compound **2** was selected as the starting material for the investigation of the reactivity of these benzofuran-containing *β*-amino ketones. Thus, *S*-alkylation of 4-chlorothiophenol led to *β*-(arylmercapto) ketone **6**, while *N*-alkylation of piperazine as an example of aliphatic secondary afforded bis-derivative **7** (Figure 2). For the representative *N*-alkylation of a primary aromatic amine by ketonic Mannich base **2**, pharmacologically relevant sulfanilamide was chosen as substrate, whereas 3,5-dimethylpyrazole served as substrate for the model *N*-alkylation of an *NH*-heterocycle by *β*-amino ketone **2** (Figure 2). In addition, ring closure of ketonic Mannich base **2** with phenylhydrazine yielded pyrazoline **10** (Figure 2). Under the general conditions employed for the replacement of the easily leaving dimethylamino group by nucleophiles (heating at reflux temperature in the solvent of choice for 1 h) [34], the yields of compounds **6**, **8** and **9** were good. *N*-Alkylation of bifunctional nucleophile piperazine with Mannich base **2** under a different set of conditions [35, 36] also led to the isolation of a fair amount (272 mg) of solid material at the end of the reaction time, but substantial loss incurred during recrystallization, and that led to a low recovery of the pure benzofuran derivative **7**.

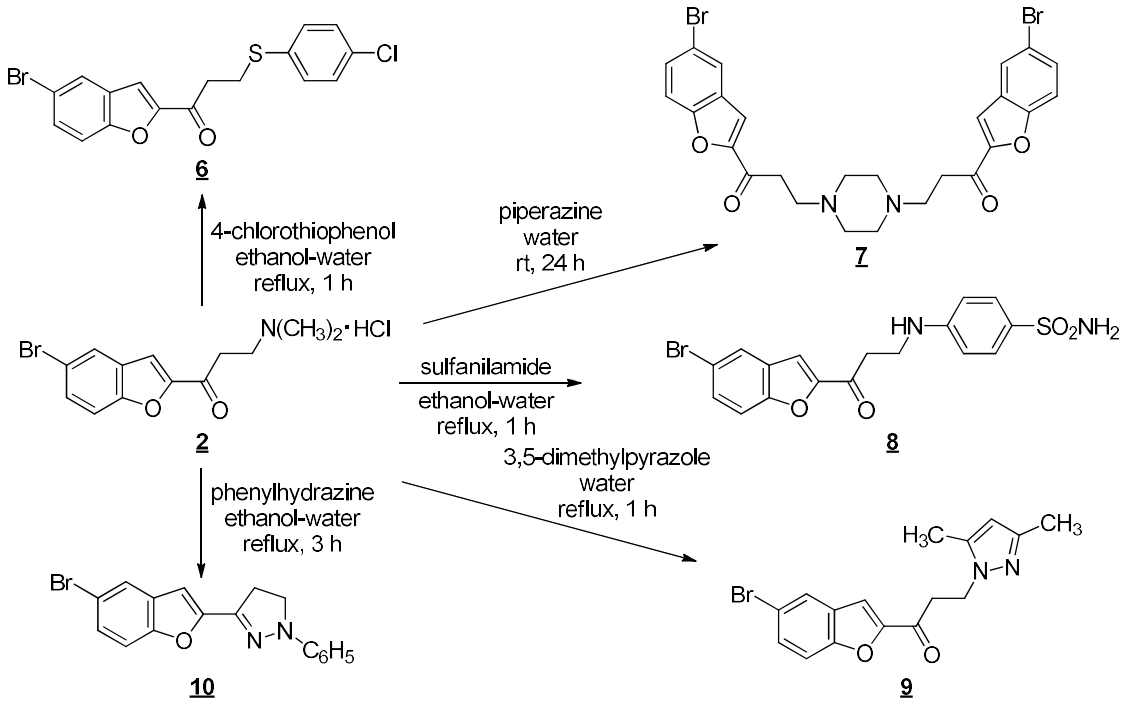

Figure 2. *Synthesis of benzofuran derivatives* ***6*** *–* ***10*** *using ketonic Mannich base* ***2*** *as starting material*

The structure of these benzofuran derivatives has been determined using NMR spectroscopy. The protons in the benzofuran ring in the structure of compounds **6** – **10** appear above 7.40 ppm in $CDCl_3$ and above 7.60 ppm in DMSO-d_6. Apart from the aromatic protons, whose number and signal pattern in corresponding region of the proton NMR spectra is different for each particular structure in this collection, the protons from the two methylene groups bridging the benzofuran and nucleophile moieties in the acyclic structure of compounds **6** – **9** can be easily identified in the aliphatic region of these spectra. In the case of compound **6**, the signals of these four protons are superimposed in a very narrow range of the chemical shift value, but they can be easily discerned as separate triplets in the spectra of compounds **7** and **9**. In the case of compound **8**, the signals of the protons in the methylene adjacent to carbonyl appear as a typical triplet, but the triplet associated with the protons in the methylene group adjacent to secondary nitrogen atom undergoes additional splitting. In the structure of compound **10**, the same two methylene groups belong to the pyrazoline ring, and while their protons also appear as two triplets in the proton spectrum of this compound, the coupling constant for these signals is higher (10.8 Hz) than that recorded for the acyclic structures **6** – **9** (approximately 6-7 Hz).

1,3,5-Triarylpyrazolines are a class of compounds whose photophysical properties have been extensively studied for various applications [37, 38]. However, considerable little information on the photophysical properties of 1,3-diarylpyrazolines is available in literature, and the existing data has been garnered mostly from the study of common 1,3-diphenylpyrazoline [39, 40]. Therefore, the photophysical study of the 3-(5-bromobenzofuran-2-yl)-1-phenylpyrazoline **10** was undertaken. In order to evaluate the influence of the polarity of the solvent on the photophysical properties of **10**, a polar solvent (DMSO) and a less polar solvent (chloroform) were initially chosen to record the UV-Vis absorption spectra. It was noticed that the strong fluorescence of pyrazoline **10** in chloroform gradually disappears in time, while the initial yellow color of the solution slowly changes to orange and then light brown, which was interpreted as a lack of chemical stability of compound **10** in chloroform. Therefore, chloroform was replaced with toluene as the less polar solvent in the subsequent studies. In DMSO and toluene, the absorption maximum for pyrazoline **10** was at 390 nm (Figure 3A), while in chloroform, the maximum shifted to a slightly lower wavelength (λ_{abs} = 387 nm), presumably owing to the onset of degradation of compound **10**. Taking into account the available literature data for 1,3-diphenylpyrazoline (λ_{abs} = 363 nm in benzene) [39], it appears that replacement of the phenyl at position 3 of the pyrazoline ring with a benzofuran-2-yl moiety results in a bathochromic shift of the absorption maximum. The fluorescence spectrum of pyrazoline **10** in toluene presented an intense emission with a maximum at 452 nm and a shoulder at 467 nm, while the maximum for the emission spectrum of **10** in DMSO is red-shifted (λ_{em} = 480 nm) and less intense (Figure 3B).

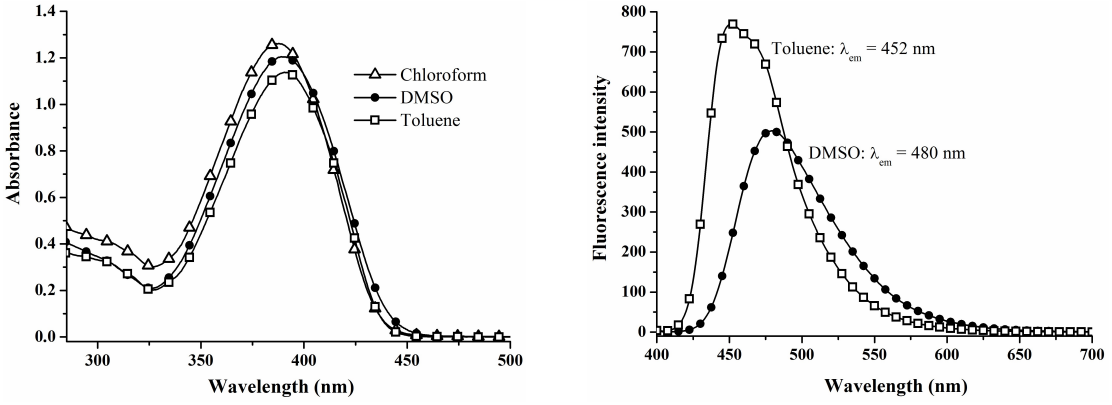

Figure 3. *UV-Vis absorption (**A**) and fluorescence (**B**) spectra of pyrazoline **10** in different solvents*

CONCLUSIONS

Four ketonic Mannich bases derived from 2-acetyl-5-bromobenzofuran have been synthesized and structurally characterized. A series of successful amine exchange reactions with *S*- and *N*-nucleophiles has been performed with one of these β-amino ketones to provide access to structurally diverse benzofurans. Reaction of a benzofuran-containing ketonic Mannich base with phenylhydrazine afforded a 1,3-disubtituted pyrazoline, whose solvent-dependent fluorescence spectra showed that the emission maximum is red-shifted compared to that of 1,3-diphenylpyrazoline.

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