HETEROCYCLES, Vol. 55, No. 6, 2001, pp. 1113 - 1119, Received, 7th March, 2001

REDUCTIVE AMINATION OF 1-[3-(2-ALKYLBENZOFURANYL)]-2-PHENYLETHANONES. SYNTHESIS OF 1-[3-(2-ALKYLBENZOFURANYL)-2-PHENYLETHYLAMINES

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Abstract - 1-[3-(2-Alkylbenzofuranyl)]-2-phenylethylamines were prepared by reduction of 1-[3-(2-alkylbenzofuranyl)]-2-phenylethanone azines with amalgamated aluminum. Two isomeric azines were separated from products of reaction of 1-[3-(2-alkylbenzofuranyl)]-2-phenylethanones with hydrazine hydrate in ethanol solution. On the other hand, instead of desired amine, aziridine derivative was obtained by reduction of the mixture of (*Z*)- and (*E*)-1-[3-(2-butylbenzofuranyl)-2-(4-methoxyphenyl)]ethanone oximes with lithium aluminum hydride. The reduction of 1-[3-(2-butylbenzofuranyl)]-2-phenylethanone hydrazone with aluminium lead up to the corresponding imine.

Many substituted benzofurans show marked pharmacological activity. In particular, acyl- and alkylamine derivatives of benzofurans are used in medicine as antiarrhythmic [1a-c] and antihypertensive agents.[1d-f] Benzofuran derivative of 3-aminopyridin-2-one has been shown to be a potent and selective inhibitor of a human immunodeficiency virus type 1 reverse transcriptase (HIV-1RT).[1h]

Our previous research of new biological active benzofuran derivatives carried out to find an efficient route to the 1-[3-(2-alkylbenzofuranyl)]-2-phenylethanones allowed us to develop a demethylation reaction, a reduction as well as selective halogenation and *O*-alkylamination of their corresponding hydroxy derivatives.[2a,b] In this report are presented attempts to obtain new 1-[3-(2-alkylbenzofuranyl)]-2-phenylethylamines from 1-[3-(2-alkylbenzofuranyl)]-2-phenylethanones based on a reduction of their oximes and azines. Acyl derivatives of such amines have proved to be valuable materials in the synthesis of 3-benzofuranyl-3,4-dihydroisoquinolines, by modified Bischler-Napieralski method.[3]

RESULTS AND DISCUSSION

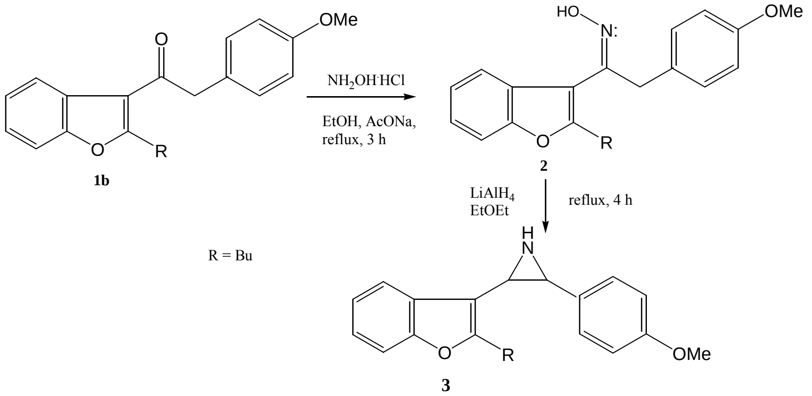
In order to obtain the oxime (**2**) a reaction of 1-[3-(2-butylbenzofuranyl)]-2-(4-metoxyphenyl)ethanone (**1**) with hydroxylamine hydrochloride in alcohol in the presence of sodium acetate was carried out (Scheme 1). This reaction gave a liquid mixture of (*Z*) and (*E*)- ketoximes in ratio *ca.* 4:1, which was analysed with the ^{1}H NMR spectral data. Pure (*E*)- oxime was separated from the mixture of two isomers, by crystallization with n-hexane, as solid melting at 55-57°C, but it has been impossible to isolate (*Z*)-isomer in a pure form.

According to early reports[4a-d] 2- or 3-acylbenzofurans react with hydroxylamine yielding either the expected oxime or the corresponding isoxazoles. The ratio of the two products depends on the structure of the benzofuran used and the reaction conditions, particularly pH of the reaction medium.[4a] In this work no products of the benzofuran ring conversion or rearrangement has been found.

The mixture of (*E*)- and (*Z*)- stereoisomers as well as separated *E*-isomer were reduced with lithium aluminum hydride in ether for 4 h to yield in each case an oil, the ^{1}H NMR and IR spectral analyses of which have shown it to be aziridine (**3**), instead of the expected amine. ^{1}HNMR spectrum taken in $CDCl_3$ shows typical aziridine signals at 3.69 and 3.41. An N-H absorption at 3180 cm^{-1} is observed in the IR spectrum.

The results of experiments were consistent with those reported earlier, which showed that reduction of some benzyl ketoximes with $LiAlH_4$ afforded corresponding aziridines.[5] On the other hand one paper[6] has reported the reduction of 2-ethyl-3-formylbenzofuran oxime with $LiAlH_4$ resulting in 2-aminomethyl-3-methylbenzofuran with 37% yield.

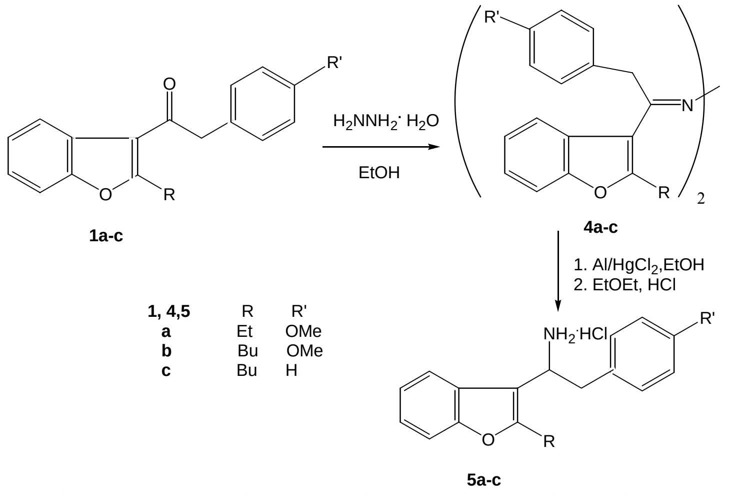
Scheme 1



A useful method to prepare alkyl and aryl ketone azines is reaction of hydrazine hydrate with 2 equivalents of a carbonyl compound.[7a-c] Two papers have reported that reaction of 2-acetylbenzofurans [8a] and 3-formylbenzofuran[8b] with hydrazine leads to the corresponding azines. In one report, 2-ethyl-3-acyl-benzofuran reacts with hydrazine yielding pyrazoles.[8c]

In this work azines (**4a-c**) were prepared by reaction of 1-[3-(2-alkylbenzofuranyl)]-2-phenylethanones (**1a-c**) with hydrazine hydrate in absolute ethanol in the presence of a catalytic amount of acetic acid (Scheme 2 and Table).

Scheme 2



When reaction was carried out for 2 h in refluxing ethanol without acetic acid 1-[3-(2-alkyl-benzofuranyl)]-2-phenylethanone hydrazones (**6a-b**) were the main products. Required azines (**4a-c**) were obtained in best yield when a mixture of hydrazine hydrate and ketone **(1)** (1.5 equivalents) in acidic absolute ethanol was heated for 30 min and then left at room temperature for a few days. Azines (**4a-c**) precipitated from solution in form of yellow crystals. After separation and drying, each showed a broad melting point. These solids were recrystallized from ethanol giving two isomers. For each case of **4a-c**, two products were isolated. The first, sparingly soluble in ethanol, was obtained in *ca.* 52-62% yield in the form of yellow prisms. These had a melting points of 126-128, 116-118 and 99-101°C for **4a, 4b,** and **4c**, respectively. A secondproduct, readily soluble in ethanol, was separated as pale yellow needles in 7-11% yield after cooling for several days. These had melting points of 114-116, 103-105 and 92-94 ^{0}C for **4a, 4b** and **4c,** respectively. The ^{1}H and ^{13}C NMR spectra such pair of isomers performed at -30^0 C to room temperature show the same chemical shift values. It seems likely, that have been isolated two symmetrical isomers for **4a-c**: the higher melting isomer being the (*E*), (*E)* isomer and the other being the (*Z*), (*Z*) isomer. Azines of unsymmetrical substituted ketones are subject to *syn, anti* imine isomerism with the possibility for one unsymmetrical and two symmetrical isomers.[7a]

Table

Azines (**4a-c**), and amines (**5a-c**) produced *via* Scheme 2

Entry	Conditions	yield (%)
4a	14 days, rt	62[a]
4b	16 days, rt	71[a]
4c	15 days, rt	69[a]
5a	ethanol, reflux, 5.0 h	78
5b	ethanol, reflux, 5.0 h	70
5c	ethanol, reflux, 5.0 h	73

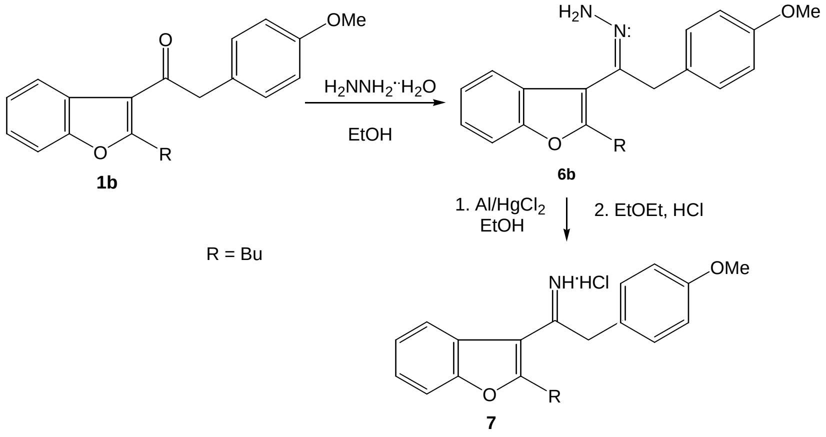
[a] Yield of the isomers mixture.

It is noteworthy that the same azines (**4a,b**) were obtained in good yields from related hydrazones (**6a,b),** after reaction in acidic ethanol solution at room temperature for a few days.

Reductions of azines were carried out using aluminum activated with mercuric chloride in aqueous ammonia/alcohol solution. The reduction of each of the two azine isomers or their mixture gave a dark red oily substance. IR and ^{1}H NMR spectra show that the obtained product is the desired amine (**5a-c**). The amine was then converted into its hydrochloride by treatment with ethereal HCl. The structure of the hydrochloride has unequivocally been established by elementary analysis, as well as ^{1}H, ^{13}C and ^{1}H, ^{13}C COSY correlation NMR spectra.

On the other hand the reduction of hydrazone (**6b**) with amalgamated aluminum yielded imine (**7**) (Scheme 3). The ^{1}H NMR spectrum of its hydrochloride in $CDCl_3$ shows broad singlet at 15.47 ppm which corresponds to the two protons of imine cation, and a two broad singlets

Scheme 3



at 4.03 and 3.95 ppm attributable to the two protons of CH_2 group, which is connected with a imine group. In the ^{1}H NMR spectrum of this compound in DMSO, the protons signal of CH_2 group appears at 3.90 as an singlet. ^{13}C NMR DEPT and ^{1}H NMR COSY experimental data provide evidence for the structure of the imine hydrochloride (see experimental part).

SUMARRY

A successful route to the 1-[3-(2-alkylbenzofuranyl)]-2-phenylethylamine was found involving preparation of 1-[3-(2-alkylbenzofuranyl)]-2-phenylethanone azines and their reduction with activated aluminum. This route offers mild reaction conditions and overcomes the problems of destruction of the benzofuran ring *via* reaction of starting acylbenzofurans with hydrate hydrazine in room temperature. Two isomeric azines were isolated from products of reaction of 1-[3-(2-alkylbenzofuranyl)]-2-phenylethanones with hydrazine hydrate. The reduction of 1-[3-(2-butylbenzofuranyl)]-2-phenylethanone hydrazone with aluminium lead up to the imine, however lithium aluminum hydride reduction of (*Z*)- and (*E*)-1-[3-(2-butylbenzofuranyl)-2-(4-methoxyphenyl)]ethanone oxime give aziridine derivative instead of desired amine.

EXPERIMENTAL

General. ^{1}H NMR and ^{13}C spectra were recorded with TM Bruker DPX 400 spectrometer for solution in $CDCl_3$ or DMSO-d_6 with TMS as internal standard. IR spectra were measured with a Specord M. 80 Carl Zeiss (Jena) spectrophotometer. Melting points were determined with a Boetius apparatus and are uncorrected. 1-[3-(2-Alkylbenzofuranyl)]-2-phenylethanones (**1a-c**) were prepared as described previously.[2a]

(*E, Z*)-1- [3-(2-Butylbenzofuranyl)]-2-(4-methoxyphenyl)ethanone oxime (**2**). A mixture of **1b** (6.4 g, 20 mmol), hydroxylamine hydrochloride (2.8 g, 40.0 mmol) and sodium acetate (3.2 g, 40.0 mmol) in ethanol (40 mL) and water (10 mL) was refluxed for 3 h. After cooling, the mixture was concentrated to remove ethanol and residue was extracted with ether. The ethereal layer was washed with water, dried over Na_2SO_4 and evaporated. The residue dark oil was dried under reduced press to give a mixture of *Z* and *E* oximes (4.2 g, 60%), in the ratio of *ca.*1:4, analysed by the ^{1}H NMR spectrum. ^{1}H NMR ($CDCl_3$) δ 8.66 (br s., 1H, OH), 7.42 (d, *J* =7.4, 1H, Ar, *E*+*Z*), 7.32-7.25 (m, 1H, Ar, *E* + *Z*), 7.14-7.08 (m, 2H, Ar, *E*+*Z*), 6.99 (d, *J* = 8.4, 2H, Ar, *E*), 6.93 (d, *J* = 8.3, 2H, Ar, *Z*), 6.64 (d, *J*= 8.4, 2H, Ar, *E*), 6.62 (d, *J*= *8.3*, 2H, Ar), 4.04 (s, 2H, CH_2, *E*), 3.77 (s, 2H, CH_2, *Z*), 3.62 (s, 3H, CH_3, *E*), 3.61 (s, 3H, CH_3, *Z*), 2.57 (t, *J*=7.62, 2H, CH_2, *E*), 2.39 (t, *J* =7.64, 2H, CH_2, *Z*), 1.43-1.36 (m, 2H, CH_2, *E*), 1.31-1.28 (m, 2H, CH_2, *Z*), 1.12-1.04 (m, 2H, CH_2, *E*+*Z*), 0.72 (t, *J* =7.2, 3H, CH_3 *E*+*Z*) ppm. IR (hexachlorobutadiene), ν 3400-3120, 1610 cm^{-1}. The mixture of oximes was recrystallized from hexane to give *E* isomer (*ca.* 2.2 g) mp. 55-57°C, IR (hexachlorobutadiene) ν 3600-3120, 1610 cm^{-1}. Anal. Calcd for $C_{21}H_{23}NO_3$: C 74.7, H 6.9, N 4.1. Found: C 74.4, H 7.1, N 3.8.

1-[3-(2-Butylbenzofuranyl)]-2-(4-metoxyphenyl)aziridine (3). A solution of **2** (1.8g, 5.33 mmol) in ether (25 mL) was added with stirring to a suspension of $LiAlH_4$ (1.2 g, 32 mmol) in ether (25 mL) at a rt over a period of 15 min. The mixture was refluxed with stirring for 4 h. After cooling, a small amount of water was added to the mixture to decompose an excess $LiAlH_4$ and the inorganic substance was separated by filtration and washed with ether. The filtrate was combined with the washings and evaporated to dryness *in vacuo* to afford aziridine **3**, pale yellow oil (1.1 g, 65 %). IR (hexachlorobutadiene) ν 3350 - 3200 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.39 -6.86 (m, 8H, Ar), 3.77-3.63 (m, 1H, CH), 3.43 -3.39 (m, 1H, CH), 3.72 (s, 3H, CH_3), 2.59-2.54 (m, 2H, CH_2), 1.36-1.34 (m, 1H, NH), 1.32-1.325 (m, 2H, CH_2), 0.93 (t, *J* =7.3, 3H, CH_3) ppm.

General procedure for 4: 1-[3-(2-ethylbenzofuranyl)]-2-(4-methoxyphenyl)ethanone azine (4a). A mixture of **1** (2.9 g, 10 mmol), 98% hydrazine hydrate (0.37 g, 7 mmol) and acetic acid (0.1 mL) was warmed in dry ethanol (25 mL) on a steam bath for 30 min. The solution was allowed to stand in a closed flask at rt for 7 days. The yellow solid of **4a** (1.8 g, 62 %) was filtered and dried. A second crop of **4a** (0.3 g, 10%) was obtained from the ethanol filtrate after standing for a week in a closed flask. The crude azine (2.1 g) was dissolved in warm ethanol (60 mL). After cooling at rt the yellow crystals were obtained (1.5 g, 52%); mp 126-128°C. ^{1}HNMR ($CDCl_3$) δ 7.74 (d, *J* = 7.8, 1H, Ar), 7.40 (d, *J* = 8.1, 1H, Ar), 7.25-7.20 (m, 1H, Ar), 7.18 - 7.13 (m, 1H, Ar), 7.00 (d, *J* = 8.6, 2H, Ar), 6.71 (d, *J* = 8.6, 2H, Ar), 4.38 (s, 2H, CH_2), 3.73 (s, 3H, OCH_3), 2.80 (q, *J*= 7.5, 2H, CH_2), 1.14 (t, *J* = 7.5, 3H, CH_3) ppm; ^{13}C NMR δ($CDCl_3$) 161.15, 159.99, 157.94, 153.85, 129.40, 128.94, 127.49, 123.71, 122.92, 121.73, 114.70, 113.90, 110.71, 55.18, 36.12, 21.70, 12.70 ppm. IR (KBr) ν 3000-2840, 1612, 1592, 1585, 1560, 1512, 1465, 1452, 1245, 1235, 1180, 1105, 1038, 1005, 820, 785, 755, 610, 520 cm^{-1}; UV (ethanol) λ_{max} 230, 277.5, 284.4, 333.8 nm. The ethanol filtrate was kept overnight in a refrigerator and pale yellow needles was separated

(0.3 g, 10%) mp 114-116°C; ^{1}HNMR ($CDCl_3$) δ 7.74 (d, *J* = 7.7, 1H, Ar), 7.40 (d, *J* = 8.1, 1H, Ar), 7.25-7.21 (m, 1H, Ar), 7.16 - 7.13 (m, 1H, Ar), 7.00 (d, *J* = 8.6, 2H, Ar), 6.71 (d, *J* = 8.6, 2H, Ar), 4.37 (s, 2H, CH_2), 3.74 (s, 3H, OCH_3), 2.80 (q, *J*= 7.5, 2H, CH_2), 1.14 (t, *J* = 7.5, 3H, CH_3) ppm; UV (ethanol) λ_{max} 230, 278.1, 285.5, 333.8 nm. Anal. Calcd for $C_{38}H_{36}N_2O_4$: C, 78.06, H 6.21, N 4.79. Found: C, 77.9, H, 6.2, N 4.6.

1-[3-(2-Butylbenzofuranyl)]-2-(4-methoxyphenyl)ethanone azine (**4b**) Yellow crystals (2.0 g, 60%) mp 116-118°C and pale yellow crystals (0.36 g, 11%) mp 103-105°C. ^{1}H NMR ($CDCl_3$) δ 7.76 (d, *J* =7.7, 1H,Ar), 7.39 (d, *J* = 8.1, 1H, Ar), 7.25 -7.21 (m, 1H, Ar), 7.16-7.13 (m, 1H, Ar), 7.00 (d, *J* = 8.5,2H, Ar), 6.71 (d, *J* = 8.5, 2H, Ar), 4.38 (s, 2H, CH_2), 3.73 (s, 3H, OCH_3), 2.79 (t, *J* =7.6,2H, CH_2), 1.58-1.51(m, 2H, CH_2), 1.22-1.13 (m, 2H, CH_2), 0.81 (t, *J* = 7.3, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$) δ 160.33, 159.94, 157,98, 153.83, 129.44, 128.91, 127.52, 123.68, 122.90, 121.78, 115.06, 113.90, 110.68, 55.16, 36.10, 30.55, 28.08, 22.50, 13.86 ppm. IR (KBR) ν 2985-2840, 1615, 1595, 1582, 1575, 1510, 1470, 1445, 1440, 1390, 1305, 1035, 1020, 1005, 910, 815, 770, 750, 610, 520 cm^{-1}. Anal. Calcd for $C_{42}H_{44}N_2O_4$: C 78.72, H 6.92, N 4.37. Found: C, 78.5, H, 6.7, N 4.1

1-[3-(2-Butylbenzofuranyl)]-2-phenylethanone azine (**4c**). Yellow crystals mp 99-101°C (1.8 g, 62%) and 92-94°C (0.2 g, 7%).^{1}H NMR ($CDCl_3$) δ 7.75 (d, *J* = 7.6, 1H, Ar), 7.33 (d, *J* = 7.8, 1H, Ar), 7.27-6.94 (m, 7H, Ar), 4.42 (s, 2H, CH_2), 2.71 (t, *J* = 6.9, 2H, CH_2), 1.46 (m, 2H, CH_2), 1.10-1.07(m, 2H, CH_2), 0.72 (t, *J* = 7.1, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$) δ 160.42, 159.86, 153.83, 136.92, 128.54, 128.45, 127.48, 126.16, 123.70, 122.92, 121.81, 115.06, 110.63, 36.99, 30.50, 28.09, 22.46, 13.83 ppm. Anal. Calcd for $C_{40}H_{40}N_2O_2$: C 82.72, H 6.94, N 4.82. Found: C 82. 5, H 6.8, N 4.6.

General procedure for 5: 1-[3-(2-ethylbenzofuranyl)]-2-(4-methoxyphenyl)ethylamine (**5a**).

To a stirred mixture of aluminum amalgamate (1.12 g Al) in ethanol (40 mL) a suspension of azine (**4a**) (1.7 g, 2.7 mmol) in ethanol (30 mL) containing 20% ammonia solution (5 mL) was added dropwise. The mixture was refluxed for 5.0 h, cooled and inorganic solid filtered, and washed with ethanol. The residue, after evaporation, was extracted with ether. The ether solution was extracted with 10% hydrochloric acid. Chilled acid solution was neutralized carefully with cold 20% NaOH solution and the amine again extracted with ether. The ether solution was evaporated and dark red oil residue dried in *vacuo* to yield amine (**5a**). The corresponding hydrochloride, obtained from the amine with etheric HCl, was recrystallized from ethyl acetate giving colorless crystals 1.3 g (78 %), mp 123-124°C. ^{1}H NMR ($CDCl_3$) δ 8.95 (s, 3H, NH_3^+), 8.13 (d, *J* = 6.3, 1H, Ar), 7.31 - 7.26 (m, 1H, Ar), 7.18-7.13 (m, 2H, Ar), 6.75 (d, *J* = 7.8, 2H, Ar), 6.60 (d, *J* = 7.8, 2H, Ar), 4.42 (m, 1H, CH), 3.67 (s, 3H, OCH_3), 3.38-3.27 (m, 2H, CH_2), 2.45-2.40 (m, 1H, CH_2), 2.30-2.25 (m, 1H, CH_2), 0.83 (t, *J* = 6.8, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$) δ 159.47, 158.55, 154.10, 130.18, 127.88, 125.50, 123.87, 122.86, 120.30, 113.77, 111.14, 108.19, 55.18, 50.35, 37.60, 19.70, 12.17 ppm. Anal. Calcd for $C_{19}H_{22}NO_2Cl$: C, 68.77, H 6.68, N 4.22, Cl 10.68. Found; C 68.5, H 6.7, N 4.0, Cl 10.3.

1-[3-(2-Butylbenzofuranyl)]-2-(4-methoxyphenyl)ethylamine (**5b**). The free amine was obtained as red oil, (2.0 g, 70%). IR (KBr) ν 3300-3200 cm^{-1}, ^{1}H NMR ($CDCl_3$) δ 7.95-7.92 (m, 1H, Ar), 7.37-7.34 (m, 1H, Ar), 7.25-7.18 (m, 2H. Ar), 6.89 (d, *J* = 8.58, 2H, Ar), 6.69 (d, *J* =8.59, 2H, Ar), 4.33-4.29 (m, 1H, CHN), 3.71 (s, 3H, CH_3), 3.19-3.16 (m, 2H, CH_2), 2.49-2.40 (m, 2H, CH_2), 1.39 (2H, CH_2), 1.20-1.12 (m, 4H, $2CH_2$), 0.81 (t, *J* = 7.05, 3H, CH_2) ppm. The hydrochloride was isolated as colorless crystals (1.8 g, 70%) mp 105-108°C, ^{1}H NMR ($CDCl_3$) δ 8.89 (s, 3H, NH_3^+), 8.09 (d, *J* = 7.36, 1H, Ar), 7.23 -7.21 (m, 1H, Ar), 7.13 - 7.05 (m, 2H, Ar), 6.67 (d, *J* =8.41, 2H, Ar), 6.52 (d, *J* =8.53, 2H, Ar), 4.33- 4.32 (m., 1H, CHN), 3.60 (s, 3H, OCH_3), 3.29-3.21 (m, 2H, CH_2), 2.39-2.32 (m, 1H, CH_2), 2.24-2.17 (m, 1H, CH_2), 1.20-1.18 (m, 1H, CH_2), 0.97-0.85 (m, 1H+1H, CH_2), 0.65 (t, *J* = 7.06, 3H,CH_3) ppm. ^{13}C NMR ($CDCl_3$) δ 158.53, 157.43, 152.93, 129.10, 126.70, 124.28, 122.71, 121.70, 119.15, 112.58, 109.98, 107.48, 53.95, 49.37, 36.45, 28.77, 24.93, 21.10, 12.58 ppm. ^{13}C, ^{1}H, COSY ($CDCl_3$) 129.10, 6.67, CH, Ar; 122.71, 7.13-7.05, CH, Ar; 121.70, 7.23-7.21, CH, Ar; 119.15, 8.09, CH, Ar; 112.58, 6.52, CH, Ar; 109.98, 7.23-7.21 CH, Ar; 53.95, 3.60, OCH_3; 49.37, 4.32, CHN; 36.45, 3.29-3.21, CH_2; 28.77, 1.20-

1.18, CH_2; 24.93, 2.39-2.32 and 2.24-2.17, CH_2; 21.10, 0.97-0.85, CH_2, 12.58, 0.65, CH_3 ppm. Anal. Calcd for $C_{21}H_{26}NO_2Cl$: C 70.08, H 7.28, N 3.89, Cl 9.85. Found: C 69.85, H 7. 3, N 4.0, Cl 9.5.

1-[3-(2-Butylbenzofuranyl)-2-phenylethylamine (**5c**). Hydrochloride, colorless crystals, mp 116-118°C, (1.2 g, 73%). ^{1}H NMR ($CDCl_3$) δ 8.50 (br s, 3H, NH_3), 8.17 (d, *J* = 7.0, 1H, Ar), 7.30-7.07 (m, 6H, Ar), 6.85 (d, *J* = 6.6, 2H, Ar), 4.45-4.44 (m, 1H, CHN), 3.39-3.34 (m, 2H, CH_2), 2.44-2.39 (m, 1H, CH_2), 2.29-2.24 (m, 1H, CH_2), 1.24-1.20 (m, 1H, CH_2), 1.01-0.91 (m, 3H, CH_2), 0.73 (t, *J* = 7.0, 3H, CH_3) ppm. Anal. Calcd for $C_{20}H_{24}NOCl$: C 72.8, H 7.33, N 4.25, Cl 10.75. Found: C 72.6, H 7.3, N 4.0, Cl 10,9.

General procedure for 6: 1-[3-(2-ethyllbenzofuranyl)]-2-(4-methoxyphenyl)ethanone hydrazone (**6a**). Ketone **1a** (1.9 g 6.5 mmol) and 98% hydrazine hydrate (0.65 g, 13 mmol) were dissolved in dry ethanol (20 mL) and refluxed for 2 h. The solution was evaporated to dryness and the resulting viscous residue was recrystallized from methanol. The pale brown crystals (1.6 g, 85%) had mp 56-58 °C. ^{1}H NMR ($CDCl_3$) δ 7.26-7.22 (m, 1H, Ar), 7.02-6.88 (m, 5H, Ar), 6.71 (d, *J* = 8.4, 2H, Ar), 3.75 (s, 2H, CH_2), 3.72 (s. 3H, OCH_3), 2.50 (q, *J* = 7.4, 2H, CH_2), 1.08 (t, *J* = 7.5, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$) δ 158.10, 154.23, 149.17, 147.33, 131.82, 130.52, 129.61, 129.34, 120.26, 118.98, 115.33, 113.90, 111.41, 55.21, 31.19, 19.16, 13.34 ppm.

1-[3-(2-Butylbenzofuranyl)]-2-(4-methoxyphenyl)ethanone hydrazone (**6b**). The pale brown crystals obtained from ethanol (1.7g, 80) had mp 37-40 °C. IR (KBr) ν 3400-3200, 1615 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.27- 7.22 (m, 1H, Ar), 7.01-6.89 (m, 5H, Ar), 6.72 (d, *J* = 8.6, 2H, Ar), 6.30 (br s, 2H, NH_2) 3.77 (s, 2H, CH_2), 3.72 (s, 3H, OCH_3), 2.47 (t, *J* =7.6, 2H, CH_2), 1.49 -1.41 (m, 2H, CH_2), 1.26-1.18 (m 2H, CH_2), 0.78 (t, *J* = 7.4, 3H, CH_3) ppm. Anal. Calcd for $C_{21}H_{24}N_2O_2$: C 74.97, H 7.19, N 8.33. Found: C, 74.7, H 7.3, N 8.1.

1-[3-(2-Butylbenzofuranyl)-2-(4-methoxyphenyl)]ethylimine (**7**). To a stirred mixture of aluminum amalgamate (1.0 g Al) in ethanol (20 mL) a solution of hydrazone (**6b**) (3.40 g, 10 mmole) in ethanol (15 mL) containing 20% ammonia solution (5 mL) was added dropwise. The mixture was refluxed for 5.0 h, cooled, the inorganic solid filtered, and washed with ethanol. The filtrate was evaporated and dark brown oil residue dried in *vacuo*, dissolved in ether and treated with etheric solution of HCl. A precipitated solid was filtered off and recrystallized from ethyl acetate. Colorless crystals (2.0 g, 60%) had mp 143-145° C. IR (KBr) ν 3400, 3100-2500, 1615 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 15.47 (s, 2H, NH_2^+), 7.29-7.25 (m, 1H, Ar), 7.10 (d, *J* = 8.15, 1H, Ar), 6.98 (d, *J* = 8.6, 2H, Ar), 6.91 (d, *J* = 4.35, 2H, Ar), 6.66 (d, *J* = 8.6, 2H, Ar), 4.03 and 3.95 (2br s, 2H, CH_2), 3.73 (s, 3H, OCH_3), 2.67 (br s, 2H, CH_2), 1.60-1.55 (m, 2H, CH_2), 1.22-1.17 (m, 2H, CH_2), 0.75 (t, *J* = 7.05, 3H, CH_3) ppm**.** ^{13}C NMR ($CDCl_3$) δ 158.4, 154.7, 148.1, 146.8, 131.7, 130.5, 130.0, 127.9, 120.3, 116.4, 115.8, 115.3, 114.0, 55.2, 30.2, 29.8, 24.3, 22.1, 13.4 ppm. ^{13}C NMR DEPT ($CDCl_3$) δ negative values for CH_2: 30.2, 29.8, 24.3, 22.1; positive values for CH_3: 13.4, 55.2 and CH: 114.0, 116.4, 120.3, 130.0, 130.5, 131.7 ppm. ^{1}H NMR (DMSO-d_6) δ 9.78 (s, 2H, NH_2^+), 7.35 (m, 1H, Ar)7.26-7.22 (m, 2H, Ar), 7.07-7.00 (m., 2H, Ar), 6.95 (d, *J* = 8.4, 1H, Ar), 6.89-6.76 (m., 2H, Ar) 3.90 (s, 2H, CH_2), 3.68 (s, 3H, OCH_3), 2.61 (t, *J* = 7.3, 2H, CH_2), 1.51-1.44 (m, 2H, CH_2), 1.22-1.12 (m, 2H, CH_2), 0.75 (t, *J* = 7.4, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6) δ 158.1, 155.5, 146.7, 145.6, 131.8, 129.8, 129.5, 129.1, 119.3, 116.6, 116.1, 115.9, 114.0, 55.2, 29.7, 29.5, 24.1, 21.6, 13.5 ppm. ^{13}C, ^{1}H COSY (DMSO-d_6) δ 131.8, 7.07-7.00, CH Ar; 129.8, 6.89 - 6.76, CH, Ar, 129.5, 6.89-6.76, CH, Ar; 119.3, 6.95, CH, Ar, 116.1, 7.26-7.22, CH, Ar; 114.0, 6.89-6.76, CH, Ar; 55.2, 3.68 OCH_3; 29.7, 3.90, CH_2; 29.5, 1.51-1.44 CH_2; 24.1, 2.61, CH_2; 21.6, 22-1.17, CH_2; 13.5, 0.75, CH_3, ppm. Anal. Calcd for $C_{21}H_{25}NO_2Cl$: C 70.28, H, 7.02, N 3.90, Cl 9.88. Found: C 70.1, H 7.2, N 3.6, Cl 9.6.

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