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The deep eutectic melt of sorbitol and metformin hydrochloride: Synthesis of 3-substituted 2-aminonaphtho[2,3-*b*]furan-4,9-diones and their photophysical properties

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An efficient and environmentally benign one-pot method is presented for diverse synthesis of 3-substituted 2-aminonaphtho[2,3-*b*]furan-4,9-diones *via* the domino reaction between 2-hydroxy-1,4-naphthoquinone, *β*-nitrostyrenes and ammonium acetate in a new deep eutectic solvent made of sorbitol and metformin.HCl. A pronounced positive solvatochromism was observed for the electron-donor-acceptor conjugated system of these products, resulting in bathochromic and hyperchromic shifts of their visible absorption band in polar and protic solvents. The red-shift of about 30 nm observed on going from non-polar to polar solvents and gave rise to a distinct colour change.

Introduction

Compounds with quinone core are quite ubiquitous in nature and play important physiological roles in animals and plants. For example, ubiquinones are the key quinone-based compounds involving in the respiratory chains of mitochondrial and bacterial membranes. Quinone framework is also spread in nature as naphthoquinones such as lapachol and *β*-lapachone which were isolated from heartwood of lapacho tree and show a wide range of therapeutic activities *viz.*, antitumor, bactericidal, fungicidal, virucidal, antiulcer, anti-inflammatory, antiseptic and antiedimic.[1,2] In addition, certain fused heterocyclic systems embedding an in-built quinone nucleus are very important in view of exhibiting prominent bioactivities and existing in living organisms.[3] Naphthofuroquinones constitute a privileged and more abundant class of such fused systems possessing valuable biological properties of medicinal interest.[4-8] In particular, naphtho[2,3-*b*]furan-4,9-diones are recurring representatives of this class which can be obtained synthetically or from many bioresources displaying diverse bioactivities.[3-9] Maturinone and maturone are two members of this class which were isolated from *Cacalia decomposita* and used as antidiabetic drugs.[10] In addition to its sheer impacts on the bioactivities of molecules, quinone nucleus is also responsible of colours in the quinone-based dyes.[11,12] 2-Hydroxy-1,4-naphthoquinone 1 (HNQ; Lawsone) is the principal natural dye presents in the leaves of Henna, (*Lawsonia inermis*) which has long been used as hair dyeing stuff for personal adornment in Middle East countries. However, despite these fascinating features, quinones and particularly naphthofuroquinoes have limited natural resources. Hence, a surge of interest was directed toward their synthesis and in this regard many efforts have been devoted to extending the diversity of the synthetic analogues.[13-15] The totally synthetic 2-aminonaphtho[2,3-*b*]furan-4,9-diones[16] were recently introduced as promising cytotoxic agents operating through oxidative damage of DNA and alkylation of bioorganic molecules in tumor cells.[17] Conjugation of the amino group with the carbonyls of the quinone moiety in 2-aminonaphtho[2,3-*b*]furan-4,9-diones, through the intervening furan ring, was proved to increase the reduction potential of these compounds resulting in significant stability and facile formation of their radical anions. The generated radical anions cause an oxidative stress to cells and their reaction with molecular oxygen gives some superoxide and peroxide species which induce additional damage to DNA of cells. Teimouri and his coworker were the first who reported the synthesis of 2-(aryl/alkyl)aminonaphtho[2,3-*b*]-furan-4,9-dione derivatives *via* a one-pot three-component reaction between 2-hydroxy-1,4-naphthoquinone, isocyanides and aldehydes under reflux condition in toluene.[18] A modification of this isocyanide based multicomponent route was later developed by Ravelo who carried out the same reaction in refluxing toluene under catalysis of EDDA (ethylenediaminodiacetate, 5 mol%).[17] Although these methods have their own merits, there is still ample room for developing an efficient, rapid and environmentally benign method in which hazardous organic solvents are avoided. Recently Ching-Fa Yao et al. reported an interesting and different route for synthesis of 3-substituted-2-aminonaphtho[2,3-*b*]furan-4,9-diones from the reaction of 2-hydroxy-1,4-naphthoquinone, nitroalkenes, and ammonium acetate in water.[19] However, water is a desirable solvent for chemical reactions mainly because of cost, safety, and environmental concerns; it has limited applications since most organic compounds do not dissolve in pure water. Moreover, many reactions that modern organic syntheses are relied on require water-sensitive catalysts and reagents which either decompose or are

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deactivated on reaction with water. To address these shortcomings, chemists have turned their attentions toward the development of ionic liquids, as the promising solvents with the advantages of no volatility, high polarity, excellent solubility, thermal stability, and ease of recycling.[20-27] Despite these interesting aspects, ionic liquids do not fully comply with the rules of green chemistry and they have limitations for use in the synthesis of organic compounds.[28] Unlike the ionic liquids, their congeners, so called deep eutectic solvents (DES), are not merely mixtures of bioresistant ions but they are typically composed of ionizable and biodegradable compounds. As a result, they have usually additional merits of being readily available from bulk renewable resources, low cost, low toxicity, and biodegradability over those of the ionic liquids.[29-33] In the present work, we describe the preparation of a new low-melting DES denoted as S:MetHCl from sorbitol and metformin.HCl. The thermal properties of the obtained DES and its application as a polar melt medium in the synthesis of 3-substituted 2-aminonaphtho[2,3-*b*]furan-4,9-dione derivatives from one-pot reaction of 2-hydroxy-1,4-naphthoquinone, nitroalkenes and ammonium acetate are also presented here. An investigation regarding the solvatochromic behaviour of the products, on manipulation with solvents of various polarities, displayed a typical wavelength shift of about 30 nm (Fig. 1).

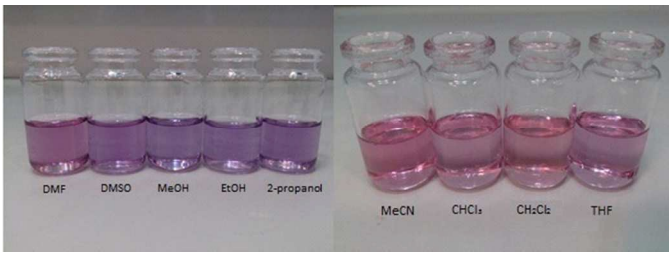


Figure 1. Solvatochromic behaviour of 2-amino-3-phenylnaphtho[2,3-*b*]furan-4,9-dione.

Experimental section

Reagents and materials

All the chemicals and solvents used in the present investigation were of spectral grade products (Merck & Aldrich). Melting points (mp) were recorded on a Barnstead electrothermal instrument. The absorption spectra in the UV and visible regions were recorded by a Perkin Elmer LAMBDA 25 recording spectrophotometer. IR spectra were obtained on a FT-IR Perkin-Elmer (Spectrum One) using KBr wafers. The ^{1}H NMR (400 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker DRX-400 spectrometer using DMSO-d_6 as solvent and the chemical shifts were measured in ppm relative to internal TMS or the deuterated solvent. Thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) studies of the samples were carried out under He atmosphere on a SETARAM (SETSYS-1760) thermal analyzer. PL-fluorescence spectra were recorded in the region of 350-750 nm on a JASCO FP-6200 with standard quartz cuvettes. The dye concentrations were chosen to be about ~9×10^{-5} M for all the liquid solutions. The Onsager's radius was calculated from $a=(3M/4\pi dN)^3$ to be 4.68 Å for **4a**, where M is the molecular weight, d is the density of the solute molecule,[18] and N is the Avogadro's number.

Preparation of 3:1 S:MetHCl deep eutectic melt

A mixture of sorbitol (300 mg, 1.65 mmol) and metformin.HCl (100 mg, 0.6 mmol) was heated in a glass vial (10 mL) at 100 °C with stirring for 45 min until a clear liquid obtained. The resulting eutectic melt was used as homogeneous catalyst for the synthesis of 3-substituted 2-aminonaphtho[2,3-*b*]furan-4,9-dione derivatives without further purification. The ^{1}H- and ^{13}C NMR signals of all the protons and the carbon nuclei of this eutectic mixture were observed at appropriate chemical shifts (Supporting Information, spectra S_{13} and S_{14}). The signals indicate no appreciable displacements of chemical shifts relative to those of pure MetHCl and sorbitol in DMSO-d_6, presumably due to hydrogen bonding and dilution of the eutectic mixture with DMSO-d_6. The two signals appeared at 2.52 ppm and 3.49 ppm are referred to residual solvent and water of DMSO-d_6 respectively.

NMR data for 3:1 S:MetHcl- ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.20 (s, 1/3×2H, -NH- and HCl), 6.67 (s, 1/3×4H, 2 HN= and NH_2), 4.60 (d, *J* 4.4 Hz, 1H, OH), 4.55 (d, *J* 5.6 Hz, 1H, OH), 4.54 (t, *J* 6 Hz, 1H, OH), 4.45 (d, *J* 5.6 Hz, 1H, OH), 4.40 (t, *J* 5.6 Hz, 1H, OH), 4.19 (d, *J* 6.8 Hz, 1H, OH), 3.69-3.33 (m, 8H, C-H), 2.94 (s, 1/3×6H, 2 N-CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 159.7 (C=N), 158.6 (C=N), 74.0 (HC-O), 72.4 (HC-O), 71.8 (HC-O), 69.4 (HC-O), 63.7 (H_2C-O), 62.9 (H_2C-O), 38.0 (2 CH_3) ppm.

Typical procedure for synthesis of 3-phenyl-2-aminonaphtho[2,3-*b*]furan-4,9-dione (4a)

A mixture of 2-hydroxy-1,4-naphthoquinone (0.174 g, 1 mmol) and *β*-nitrostyrene (0.298 g, 2 mmol) in the (sorbitol-metformin hydrochloride) DES (1 mL) was stirred on a magnetic stirrer at 110 °C for nearly 5 min. The progress of the reaction was monitored by TLC (using dichloromethane as the mobile phase). The procedure was followed by addition of ammonium acetate (0.308 g, 4 mmol) and stirring continued at 110 °C for appropriate time until the reaction reached to end. This step takes about 10 min (Fig. 2). After completion of the reaction, water (8 mL) was added to the reaction mixture, while stirring, and the solid separated on cooling the mixture at room temperature was collected by filtration. The filtered crude solid product was purified by flash column chromatography on silica gel 60 (Merck, mesh 70-230) using dichloromethane as the mobile phase and the water-extracted DES remained dissolved in the aqueous filtrate was recovered by evaporation under reduced pressure. The DES collected after evaporation of water is reasonably pure, so can be used in the next cycles of the same synthesis.

The solvatochromic behaviour of these products was explored by measuring the absorptions of 2-amino-3-phenylnaphtho[2,3-*b*]furan-4,9-dione **4a** in various solvents at wavelengths of 200 to 700 nm.

Figure 2. Color changes during synthesis of 2-amino-3-phenylnaphtho [2,3-*b*]furan-4,9-dione **4a**

Selected data for 2-amino-3-(4-nitrophenyl)naphtho[2,3-*b*]furan-4,9-dione (4d): Dark violet solid. Mp 318-320 °C. IR (KBr) cm^{-1}; 3432, 3330, 1646, 1616, 1593, 1550, 1517, 1339, 1248, 1203. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.01 (dd, *J* 7.6 and 1.4 Hz, 1H), 7.94 (dd, *J* 7.6 and 1.2 Hz, 1H), 7.81 (dt, *J* 7.6 and 1.4 Hz, 1H), 7.74 (dt, *J* 7.6 and 1.2 Hz, 1H), 7.72 (s, 2H), 7.62 (d, *J* 8.6 Hz, 2H) 7.46 (d, *J* 8.6 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 181.6, 169.1, 161.7, 161.6, 145.9, 138.2, 134.6, 133.3, 132.9, 131.0, 130.9, 130.4, 126.6, 125.8, 123.6, 95.3. MS (70 eV) m/z (%); 334 (M^+, 10), 319 (22), 289 (MH^+ - NO_2, 5), 264 (14), 236 (9), 218 (17), 176 (20), 150 (46), 114 (51), 76 (100). *Anal. Calcd.* for $C_{18}H_{10}N_2O_5$: C, 64.67; H, 3.02; N, 8.38. Found: C, 64.73; H, 3.11; N, 8.21

Selected data for 2-amino-3-(4-bromophenyl)naphtho[2,3-*b*]furan-4,9-dione (4g): Dark violet solid. Mp 267–269 °C. IR (KBr) cm^{-1}; 3437, 3325, 1654, 1638, 1607, 1540, 1247, 1007. ^{1}H NMR (400 MHz, DMSO-d_6); δ_H 8.27 (d, *J* 8.4 Hz, 2H), 8.01 (dd, *J* 7.6 and 1.2 Hz, 1H), 7.97 (s, 2H), 7.95 (dd, *J* 6.9 and 1.6 Hz, 1H), 7.82 (dt, *J* 7.6 and 1.6 Hz, 1H), 7.78 (d, *J* 8.4 Hz, 2H), 7.77 (dt, *J* 7.4 and 1.2 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6); δ_C 181.7, 168.5, 161.3, 142.4, 134.6, 133.1, 133.1, 133.0, 132.1, 131.4, 131.2, 129.6, 125.8, 120.4, 96.4.MS (70 eV) m/z (%); 369 (M^+, ^{81}Br, 20), 367 (M^+, ^{79}Br, 17), 213 (12), 212 (M^+ - C_6H_4Br, 4), 189 (64), 165 (18), 150 (50). *Anal. Calcd.* for $C_{18}H_{10}BrNO_3$: C, 58.72; H, 2.74; N, 3.80. Found: C, 58.67; H, 2.83; N, 3.77.

Results and discussion

We commenced our investigation with blends of metformin hydrochloride (MetHCl) and sorbitol to obtain a suitable deep eutectic melt of good polarity. Indeed, metformin hydrochloride and sorbitol are expected to establish a network of intense hydrogen bonds in liquid state wherein the formal radius of the solvated chloride ion and consequently its stability is increased. Metformin and sorbitol are polyfunctional hydrogen donors and so both can contribute in solvation of the chloride ions. Therefore, the extent of hydrogen bonding between these constituents considerably depends on their molar ratios. As the extent and strength of hydrogen bonding increase the components gain more and more stabilization energy which serves to partially overcome the lattice energy of each solid component during fusion of their mixture. In the generated eutectic melt the strong proton interactions merge into partial ionization of the components, deepen the eutectic further, and make it an ionic-liquid-like polar solvent.

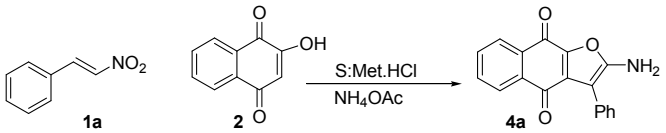
To determine the optimal ratio of MetHCl and sorbitol, three selected mixtures of these compounds were evaluated in terms of melting point depression with respect to the pure ingredients and efficiency to promote the synthesis of 3-aryl-2-aminonaphtho[2,3-*b*]furan-4,9-diones. In this regard, detailed thermal behaviours of 2:1, 3:1, and 4:1 (w/w) mixtures of S:MetHCl were studied by differential scanning calorimetry (DSC) and thermal gravimetric analysis (TGA) techniques. The DSC thermographs of all these mixtures displayed an endothermic trace around 174 °C, which is not corresponding to any mass loose in the relating TGA curves, hence could be ascribed to complete phase transition of the blends to liquid phase. Except for 2:1 mixture of sorbitol and metformin, which does not melt below 160 °C, the other two, namely 3:1 and 4:1 blends, showed one additional endothermic trace centered respectively at 64.5 °C and 55 °C, corresponding to their melting points (Table 1).

Table 1. Melting points of the binary eutectic mixtures with different mass ratio of sorbitol and metformin.HCl (wt %)

S:Met.HCl	1:2	1:3	1:4
T_m(°C)	--	64	55

T_m = Melting points of the eutectic mixtures

Presumably, these peaks are relating to initial fusion of the 3:1 and 4:1 mixtures that leads to depression of their melting points and formation of a rather structured supramolecular melt[39] which on raising the temperature up to 174 °C completely liquifies. Notably, the DSC and TG analyses displayed that these melts remain reasonably unchanged over two cycles of heating up to 140 °C followed by cooling to room temperature. After these two heating cycles, only about 2.7% of the weights of the eutectic melts were lost, which is probably due to loss of the water already adsorbed by the components. In the next phase of this investigation, the suitability of the polar 4:1 and 3:1 S:MetHCl eutectic melts, as the reaction media, for synthesis of 2-amino-3-arylnaphtho[2,3-*b*]furan-4,9-diones was explored. To achieve this goal, an optimized condition was developed by examining the model reaction of 2-hydroxy-1,4-naphthoquinone, *β*-nitrostyrene, and ammonium acetate in various temperatures (Scheme 1).



Scheme 1. The trial synthesis of 2-amino-3-phenylnaphtho[2,3-*b*]furan-4,9-dione.

Table 2. Optimization of the reaction conditions and comparison of the result with those of previous report.

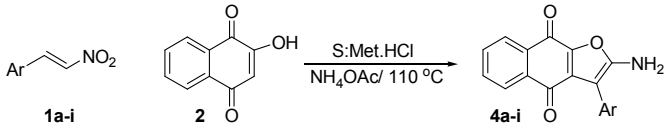
Entry	Catalyst (mmol)	NH_3 source	Temperature (°C)	Time (min)	Yield (%)
1	Solid phase	NH_4OAc	100	300	No prod.
2	Sorbitol	NH_4OAc	110	60	26
3	S:Met.HCl (4:1)	NH_4OAc	110	15	72
4	S:Met.HCl (3:1)	NH_4OAc	25	55	MA[a]
5	S:Met.HCl (3:1)	NH_4OAc	70	15	MA[a]
6	S:Met.HCl (3:1)	NH_4OAc	80	15	MA[a]
7	S:Met.HCl (3:1)	NH_4OAc	100	15	60
8	S:Met.HCl (3:1)	NH_4OAc	110	15	74
9	S:Met.HCl (3:1)	NH_4Cl	110	60	46
10	S:Met.HCl (3:1)	NH_4F	110	15	68
11	S:Met.HCl (3:1)	$(NH_4)_2SO_4$	110	15	70
12	S:Met.HCl (3:1)	$(NH_4)_2CO_3$	110	15	72
13	S:Met.HCl (3:1)	$(NH_4)_2HPO_4$	110	15	69
14	S:Met.HCl (3:1)	Urea	110	15	67
15	Water	NH_4OAc	100	720	65[c]
16	$MetHCl_{(aq)}$ 0.1 M	NH_4OAc	100	240	65
17	Ethylene glycol	NH_4OAc	100	60	29[c]
18	PEG[b]	NH_4OAc	100	300	Trace[c]

[a] Only the Michael adduct is formed. [b] Polyethylene glycol. [c] Reported in Ref. 19.

The results were gathered in Table 2. As this table shows, the best result was obtained at 110 °C using the melt containing 3:1 (w/w)

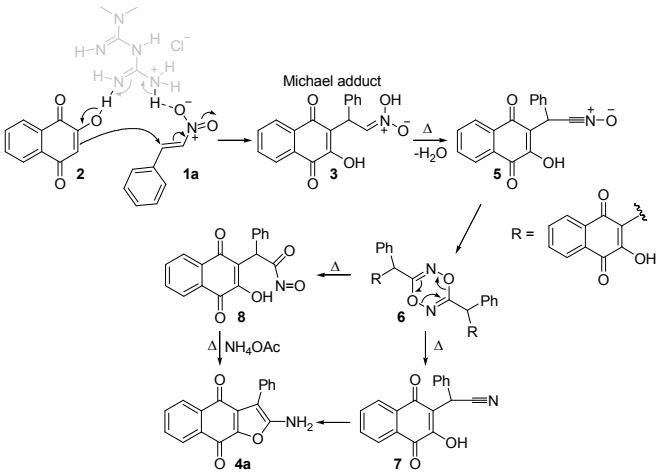
portions of sorbitol and MetHCl. Monitoring of the model reaction by TLC revealed that only the Michael adduct of 2-hydroxy-1,4-naphthoquinone and *β*-nitrostyrene is formed if the reaction mixture is held at temperatures 50 °C to 80 °C. However, at 100 °C a considerable amount of the product 3-phenyl-2-aminonaphtho[2,3-*b*]furan-4,9-dione was formed and reached the maximum yield at 110 °C. Further increase of temperature has almost no effect on the yield of the product. Upon these evaluations, the 3:1 S:MetHCl eutectic melt was selected as the optimal medium, in terms of both catalytic efficiency and melting point depression, for the next experiments. A slight supremacy of this melt over that of the 4:1 mixture in promoting the synthesis may be ascribed to its greater content of Met.HCl which is suggested to act as a proton source in catalysis of the synthesis. Application of some other ammonium sources instead of ammonium acetate afforded similar yields of the model product. Both the acidic and basic ammonium salts tested in this synthetic method appeared slightly less effective and gave lower yields than ammonium acetate (entries 9-13). Noteworthy, urea can play as an amine source in this reaction to give a good yield of the model product (entry 14).

At this end, we set out to explore the substrate scope and specificity of the method under the optimized reaction conditions. Consequently, various substituted *β*-nitrostyrenes **1a-i** were used to react with 2-hydroxy-1,4-naphthoquinone **2** and ammonium acetate under the optimized condition (Scheme 2).



Scheme 2. Synthesis of 2-amino-3-arylnaphtho[2,3-*b*]furan-4,9-dione derivatives under the optimal conditions

As Table 3 shows, both electron-deficient and electron-rich *β*-nitrostyrenes gave fairly higher yields of the desired 3-substituted 2-aminonaphtho[2,3-*b*]furan-4,9-diones in very shorter times with respect to the single earlier report of similar syntheses in water[19] (compare with Table 2 entry 15 for the product **4a**). Very likely, the promoting efficiency of the eutectic melt is partially due to multiple hydrogen-bonding of MetHCl with *β*-nitrostyrenes and 2-hydroxy-1,4-naphthoquinone that brings the two reacting components in close vicinity to each other. Under this situation, *β*-nitrostyrenes gain an enhanced electrophilic character upon accepting a proton from MetHCl at their nitro groups. Hydrogen bonding with MetHCl may also increase the nucleophilic activity of 2-hydroxy-1,4-naphthoquinone, making its Michael addition onto *β*-nitrostyrenes too easy. A significant support of this proposal comes from the fact that MetHCl considerably increases the rate of the reaction in water (Table 2, entry 16), however, to less extent with respect to its eutectic melt with sorbitol. Even in the optimal 3:1 S:MetHCl eutectic melt, the reactions stop at production of the Michael adducts at temperatures below 80 °C. Further progress of the reaction from this point involves thermal dehydration of the Michael adducts that occurs at temperatures above 90 °C to give the intermediate nitrile-*N*-oxides **5**, according to a plausible mechanism suggested by Yao[19] (Scheme 3). These zwitterionic intermediates undergo a dipolar dimerization reaction to yield the intermediate 1,4,2,5-dioxadiazines **6** followed by a chain of thermal demanding reactions involving electrocyclic scission of the dioxadiazine ring and conversion of the resulting two fragments into naphtho[2,3-*b*]furan-4,9-diones. Upon heating, the fragmented intermediate **7** is presumed to undergo a direct cyclization while its twin **8** cyclocondenses with ammonia to deliver the product **4**.



Scheme 3. A plausible mechanism for synthesis of 2-amino-3-phenylnaphtho[2,3-*b*]furan-4,9-dione

Table 3. Synthesis of 2-amino-3-arylnaphtho[2,3-*b*]furan-4,9-diones under optimized conditions.

Entry	Ar	Product	Time (min)	Yield (%)[a]	Mp °C	
					Found	Rep. [Ref.]
1	C_6H_5-	**4a**	15	74	237-239	238-240[19]
2	4-MeC_6H_4-	**4b**	20	68	243-245	242-244[19]
3	4-ClC_6H_4-	**4c**	15	78	255-257	254-256[19]
4	4-$NO_2C_6H_4$-	**4d**[b]	10	67	318-320	--
5	4-MeOC_6H_4-	**4e**	25	64	286-288	288-290[19]
6	4-MeSC_6H_4-	**4f**	20	59	205-207	204-206[19]
7	4-BrC_6H_4-	**4g**[b]	15	79	267-269	--
8	4-FC_6H_4-	**4h**	15	47	232-234	232-234[19]
9	3-BrC_6H_4-	**4i**	15	75	269-271	258-260[19]

[a] Isolated yields. [b] New products.

Table 4. Influence of solvents on λ_{max} of product **4a**.

Solvent	CH_2Cl_2	$CHCl_3$	THF	MeCN	2-propanol	DMSO	DMF	EtOH	MeOH-HCl	MeOH
λ_{max} (Ab)	520nm	520 nm	520nm	520nm	550nm	550nm	540nm	550nm	545nm	545nm
λ_{max} (Em)	602nm	624nm	……	612nm	644nm	655nm	646nm	604nm	605nm	602nm
$\Delta\lambda^a$	82nm	104nm	……	92nm	94nm	105nm	106nm	54nm	60nm	57nm
ε^b	2405	2249	2461	2127	2661	2605	2049	2639	2839	3084

[a] Stocke shift. [b] ($M^{-1}cm^{-1}$).

The physical and spectral data of the known products are well consistent with those reported by Yao et. al.[19] The structures of new products were deduced from their IR, ^{1}H NMR, ^{13}C NMR and MS spectral data as well as their elemental microanalyses. For example, the IR spectrum of **4d** exhibits two absorption bands at 3432 and 3330 cm^{-1}, characteristic of symmetric and asymmetric stretching-vibrations of NH_2 group. Presence of this group in the molecule can also be evidenced to a singlet peak at δ 7.72 in ^{1}H NMR spectrum of **4d**, which completely disappears on exchange with D_2O. All other protons of **4d** resonated in the aromatic region of the spectrum with appropriate coupling constants. The $^{13}C\{^1H\}$ NMR spectrum of **4d** displayed 16 lines corresponding to the number of chemically different carbons in the molecule and the mass spectrum of this compound exhibited the molecular ion peak at m/z = 334.

In continuation, we aimed to explore the recyclability of S:MetHCl. In this regard, preparation of **4a** was chosen as the model. After completion, the reaction was quenched by addition of water to the reaction mixture and cooling to room temperature. The resulting precipitates of the crude solid product were filtered and the filtrate was evaporated under reduced pressure. The DES remained after evaporation of water was collected and used in the next cycles of the same synthesis. As Fig. 3 shows, the catalytic efficiency of 3:1 S:MetHCl was obviously retained even after six times recycling in the synthesis of **4a**.

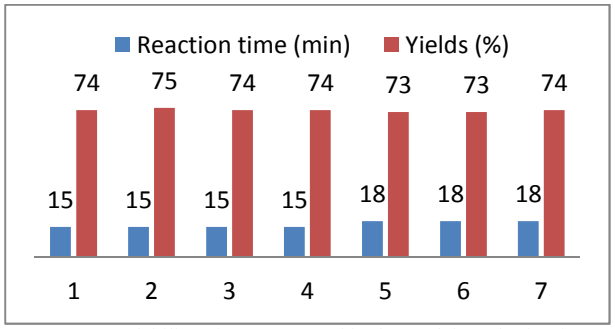


Figure 3. Recyclability of 3:1 S:MetHCl in the model synthesis of **4a**.

Owing to being conjugated systems of the electron-donor amino group and the electron-accepting quinone ring, these products display intense colours. The optical energy associated with the charge transfer in these electron-donor-acceptor dyads falls in the range of visible spectrum and considerably varies by changing their solvents. This dependence is due to polarity of compounds **4** that increases by the intramolecular charge-transfer associated with their photoexcitation and because these electron-donor-acceptors can also play as proton-donor-acceptor systems in interaction with polar and protic solvents. For example, the UV-visible spectra of **4a** in various solvents at ~9×10^{-5} M concentration exhibited a broad absorption band and presented a significant solvatochromism in the visible region (Table 4). Fig. 4 illustrates the effect of solvents on the position of the λ_{max} of **4a**. As could be seen, the absorption maximum of the dye in moderately polar solvents such as acetonitrile, chloroform, dichloromethane and tetrahydrofuran is located at 520 nm but in more polar and protic solvents it shows, as expected, bathochromic shifts. Polar solvents tend to stabilize the highly polar excited state of the dye slightly more than its ground state; leading to a decrease in energy of the charge transfer. This effect can even be enhanced if H-acceptor solvents form hydrogen bonding with the NH_2 termini of the dye and H-donors bind with its quinonoid carbonyl oxygens. These conditions are met in ethanol, methanol, DMSO, DMF, and 2-propanol solutions of **4a**, where they give rise to significant red-shifts of the absorption maxima in the visible region of the spectra. These findings are close to those reported for similar compounds.[17]

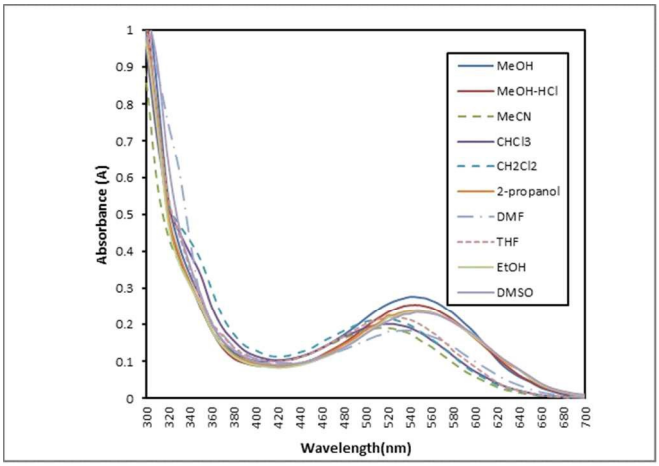


Figure 4. Spectral changes of the product **4a** in different solvents

The solvatochromic behaviour of **4a** is also seen in photoluminescence (PL) fluorescence spectra of this compound in the selected solvents. It is apparent from Table 4 and Fig. 5 that the red shift of the fluorescence spectra becomes larger with increasing polarity of the solvents and that the shifts are slightly larger than those of absorption bands. These Stokes red shifts are attributed to a change in solute-solvent interactions and so reorientation of the surrounding solvents during the life-time of the excited solute molecule.

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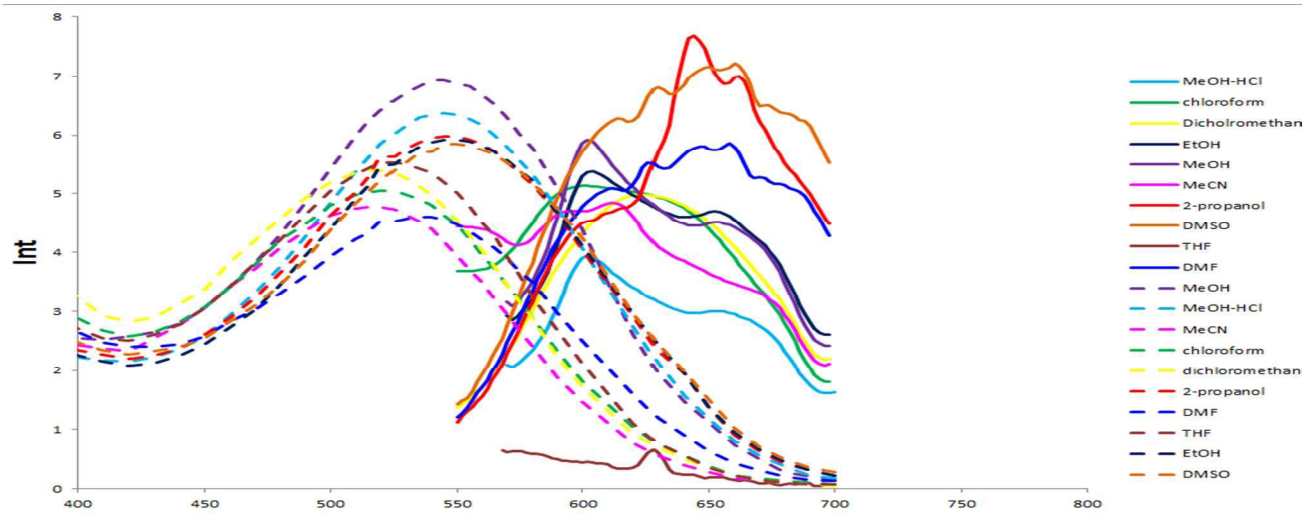

Figure 5. Absorption and emission spectra of the product **4a** in selected solvents

Based on these Stoke's shifts one may calculate the change in dipole moment of the solute as it goes from ground to excited state by using Lippert Mataga's equation. This equation takes the dipole-dipole forces as the main solute-solvent interaction and is defined as follow:

$$\Delta\bar{\nu} = \frac{2(\mu_e - \mu_g)^2}{hca^3} f(\varepsilon, n) + \Delta\bar{\nu}^o$$

where $\Delta\bar{\nu}$ is the Stoke's wavenumber shift (cm^{-1}), $\Delta\bar{\nu}^o$ is the shift in absence of solvent, μ_g and μ_e are, respectively, the dipole moments in the ground state and the excited (fluorescence) state, a is the cavity radius in Onsager's theory of reaction field, and $f(\varepsilon, n)$ is the orientation polarizability of solvent given by the following definition:[40]

$$f(\varepsilon, n) = \left[\frac{\varepsilon - 1}{2\varepsilon + 1} - \frac{n^2 - 1}{2n^2 + 1}\right]$$

where ε and n are solvent dielectric constant and refractive index, respectively. As can be seen in Fig. 6, the Lippert-Mataga's plot for compound **4a** displays an approximately linear relation between $\Delta\bar{\nu}$ and $f(\varepsilon, n)$. The slope of this curve represents the excited state of the molecule **4a** about Δμ= 1.48 Debye more polar than its ground state. Photoexcitation of **4a** to a momentary Franck Condon excited state seems to be associated with an intramolecular charge transfer through the conjugated system from the amino group to one of the quinonyl oxygen atoms of the molecule, whereupon the dipole moment of **4a** is increased. In this excited state, the amino group acquires a positive charge and is tilted to efficiently take part in the conjugation. Hence, as a requirement the polarity and planarity of the molecule is increased.[41] Because of these charge and structural reconfigurations of the molecule at the Franck Condon excited state its near surrounding solvent molecules rearrange to adopt the contribution of their hydrogen bonding, dipole-dipole, and London interactions with the solute.

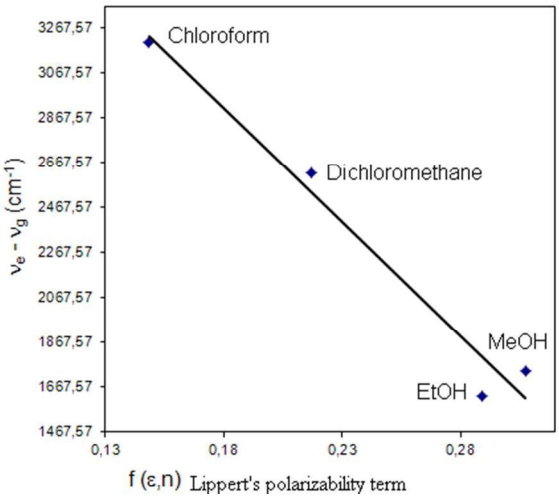

Figure 6. The Lippert-Mataga's plot for **4a**, with correlation quality of R^2= 0.97 and slope of $2\Delta\mu^2/hca^3$ = -10166.87.

Upon reorientation of solvent molecules the solute molecules are relaxed from the Franck Condon excited state to an equilibrium excited state that gives rise to a Stoke's shift.[40] As is evident from Fig. 5, 2-propanol may stabilize the excited state of **4a** by H-donating to the negatively charged oxygen atom of the carbonyl group which takes part in conjugation with the amino group of the solute. However, DMSO and DMF do this job by their high polarity through reorientation during the life time of the excited state. It is noteworthy that excitation of **4a** in THF leads to a small Stoke's shift, presumably due to incomplete or inefficient reorientation of the peripheral solvent molecules during the life time of the Franck Condon excited state. Moreover, the fluorescence emission of **4a** is markedly quenched by THF and appears very weak in this solvent.

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Similar Stoke's shifts and trend of dependence to polarity of solvents were observed for other products **4b-i** (Table 5). Absorption and emission spectra of these products are available in Supplementary Information.

Table 5. Photophysical data of 2-amino-3-arylnaphtho[2,3-*b*]furan-4,9-diones derivatives.

			CH_2Cl_2			DMSO			2-propanol		
Ent.	Ar	ε^a	λ_{max} (ab)^b	λ_{max} (em)^b	$\Delta\lambda^b$	λ_{max} (ab)^b	λ_{max} (em)^b	$\Delta\lambda^b$	λ_{max} (ab)^b	λ_{max} (em)^b	$\Delta\lambda^b$
4b	4-MeC_6H_4-	1164	496	618	122	510	626	116	510	598	88
4c	4-ClC_6H_4-	1350	518	638	120	540	638	98	530	638	108
4d	4-$NO_2C_6H_4$-	2044	494	622	128	518	616	98	518	616	98
4e	4-$MeOC_6H_4$	1219	526	620	94	536	618	82	508	614	106
4f	4-$MeSC_6H_4$-	1338	508	600	92	520	612	92	526	628	102
4g	4-BrC_6H_4-	1405	510	628	118	540	638	98	540	634	94
4h	4-FC_6H_4-	2937	520	612	92	538	610	72	538	628	90
4i	3-BrC_6H_4-	2506	512	630	118	538	634	96	538	634	96

[a] ($M^{-1}cm^{-1}$). [b] nm

Conclusion

In conclusion, the eutectic melt of sorbitol and metformin was found to be an efficient catalytic medium for synthesis of 3-substituted 2-aminonaphtho[2,3-*b*]furan-4,9-diones *via* one-pot reaction of 2-hydroxy-1,4-naphthoquinone, *β*-nitrostyrenes and ammonium acetate. All the products are colored in solid state owing to comprising of an electron-donor-acceptor dyad which displays a remarkable positive solvatochromism in solution phase in the visible region of the spectra. The present method offers a simple experimental procedure and mild reaction conditions for expedient synthesis of the titled products using a readily available, biocompatible, and easily recyclable eutectic melt.

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Graphical Abstract

The deep eutectic melt of sorbitol and metformin hydrochloride: Synthesis of 3-substituted 2-aminonaphtho[2,3-*b*]furan-4,9-diones and their photophysical properties

The low-melting deep-eutectic mixture of sorbitol and metforminHCl was successfully employed as a recyclable solvent for promoting the synthesis of benzofuroquinone dyes