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ORIGINAL PAPER

Acid-catalyzed cascade rearrangement of 4-acetoxy-9-furylnaphtho[2,3-*b*]furans

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Abstract Acid-catalyzed recyclization of 4-acetoxy-9-furylnaphtho[2,3-*b*]furans efficiently produced naphtho[1,2-*b*:3,4-*b'*]difurans. On the other hand, 4-aminonaphtho[2,3-*b*]furans failed to undergo the analogous recyclization into benzo[*g*]furo[2,3-*e*]indoles. The difference in behavior of these two types of substrates was explained by employing density functional theory calculations.

Keywords Heterocycles · Protonation · Recyclization · Reaction mechanisms · Density functional theory

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Introduction

The isomeric naphthofuran core omnipresent in various natural and synthetic biologically active compounds is an increasingly attractive target for synthetic and medicinal chemists [1–10]. Naphthodifurans have been studied less, but they have potential pharmaceutical utility. For many years the single reported example of naphtho[1,2-*b*:3,4-*b'*]difuran **1** was tetraphenyl derivative **2** synthesized by condensation of benzoin with 1,3-dihydroxynaphthalene (Scheme 1a) [11]. We recently reported the acid-catalyzed transformation of 4-acetoxy-9-furylnaphtho[2,3-*b*]furans **3** into naphthodifurans **4** (Scheme 1b) [12]. This reaction represents a simple approach to an array of functionalized naphthodifurans **4**, which can be further modified to access a large diversity of naphtho[1,2-*b*:3,4-*b'*]difurans **1**. This simple idea inspired us to study this transformation in detail aiming for extension of the reaction applicability and elucidation of the mechanism of reaction. Herein we provide a full account of this investigation.

Results and discussion

9-Furylnaphthofurans **3** were synthesized by treatment of (2-carboxyaryl)difurylmethanes **5** [13, 14] with a mixture of acetic anhydride and acetic acid in the presence of $ZnCl_2$ (Table 1) [15].

In our preliminary report we demonstrated that naphthofurans **3** undergo recyclization into naphthodifurans **4** in only moderate yields. So, we opted to optimize this transformation by screening various reaction conditions typically applied for furan recyclizations. Specifically, we treated compounds **3** with a mixture of acetic and hydrochloric acids either at room temperature [16, 17] or under

moderate heating [18, 19]. Alternatively, the mixture was refluxed in benzene solution in the presence of TsOH [20] or $HClO_4$/AcOH combination [21]. However, these attempts did not improve the reaction yields from what was obtained under the earlier described conditions, i.e., when naphthofurans **3** were heated under reflux with ethanolic HCl for 20–40 min (Table 1).

TLC monitoring demonstrated that the reaction proceeds through the formation of an unstable intermediate. Shortened reaction time and decreased quantity of HCl allowed for its accumulation in the reaction mixture. Any attempts to isolate this intermediate, however, were unsuccessful. It is believed that the described rearrangement proceeded as a cascade process involving deacylation of **3**, followed by protonation of linear naphthofuran **6** at the C(2) position resulting in its isomerization into angular isomer **7**, which further isomerized into the final naphthodifuran **4** (Scheme 2).

This mechanistic rationale is supported by our DFT calculations, which were performed by employing the B3LYP functional and 6-311G** basis set. This modeling showed 4-hydroxy-5-(2-furyl)naphtho[1,2-*b*]furan (**7′**, Fig. 1) to be 24.3 kJ/mol more stable than the isomeric naphtho[2,3-*b*]furan **6′**. In its turn, **7′** is 9.1 kJ/mol less stable than the corresponding naphthodifuran **4′** ($R^1 = R^2 = R^3 = H$).

Isomerization of *ortho*-(2-furyl)phenols **7** into the corresponding benzofuran moiety is analogous to recyclization of *ortho*-(2-furyl)anilines into indoles [21]. So, we suppose that the mechanisms of these two processes are the same.

Recyclization of **6** into **7** has, to the best of our knowledge, a single analogue in the literature, namely, recyclization of 4-aminobenzofurans into 4-hydroxyindoles [22]. This precedent prompted us to believe that 4-amino-9-furylnaphtho[2,3-*b*]furans **8** could undergo a related rearrangement into 5-furyl-4-hydroxybenz[*g*]indoles **9**, followed by the corresponding transformation of **9** into benzo[*g*]furo[2,3-*e*]indoles **10** (Scheme 3).

To evaluate this assumption and extend the applicability of the discussed transformation, we attempted to synthesize 4-aminonaphtho[2,3-*b*]furans from the same starting compounds **5** (Scheme 4). Carboxylic acids **5** were reduced to the corresponding benzyl alcohols **11** with $LiAlH_4$. Oxidation of these alcohols with pyridinium chlorochromate (PCC) gave aldehydes **12** which were transformed into 9-furylnaphtho[2,3-*b*]furans **13** by treatment with $HClO_4$.

Scheme 1

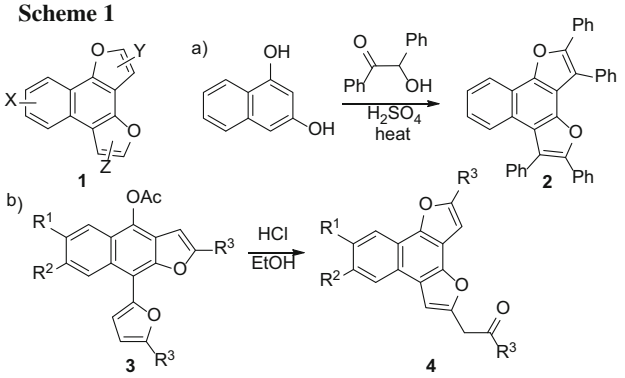
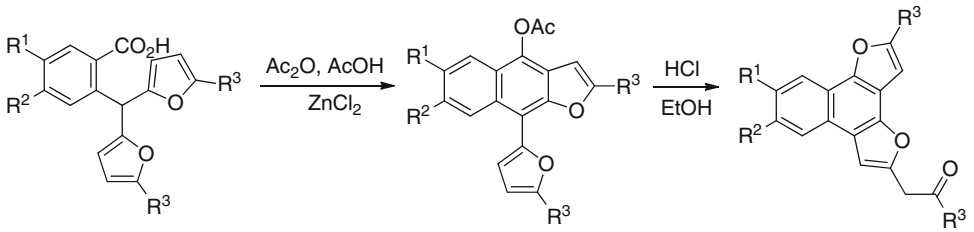


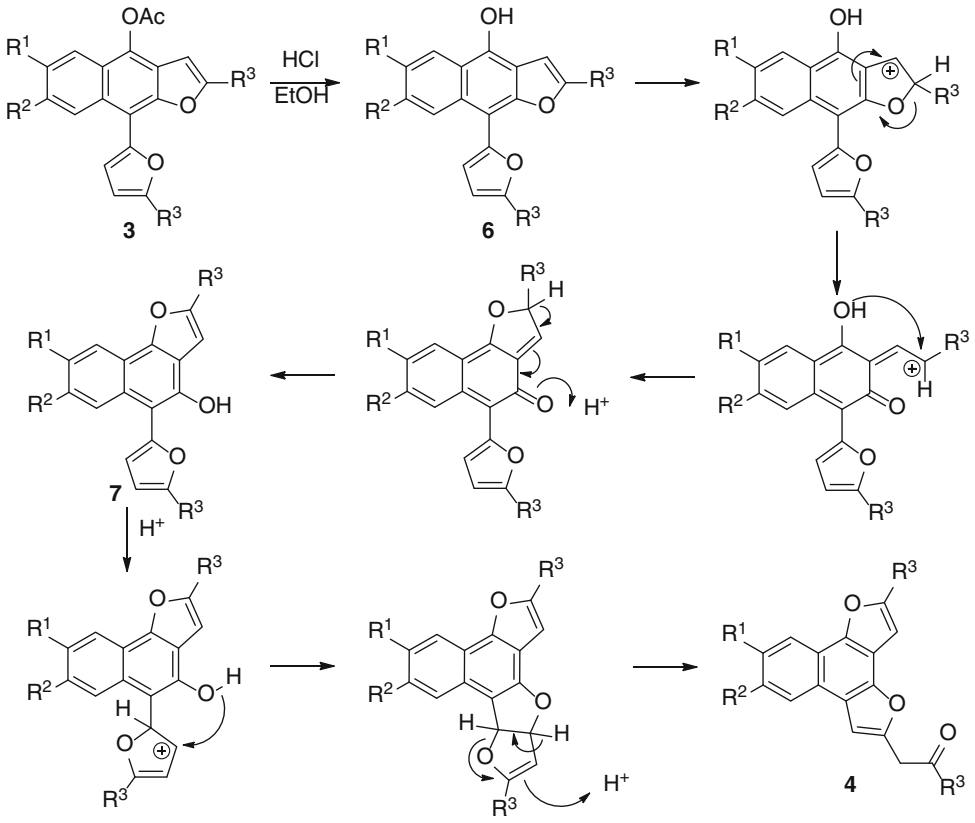
Table 1 Synthesis and acid-catalyzed rearrangement of 4-acetoxy-9-furylnaphtho[2,3-*b*]furans **3**



5a-5g **3a-3g** **4a-4g**

Entry	R^1	R^2	R^3	Yield of **3**/%	Yield of **4**/%
a	H	H	Me	31	40
b	Cl	H	Me	31	42
c	Br	H	Me	33	42
d	Br	H	Et	28	37
e	H	Cl	Me	31	41
f	OMe	H	Me	40	48
g	OMe	OMe	Me	37	55

Scheme 2



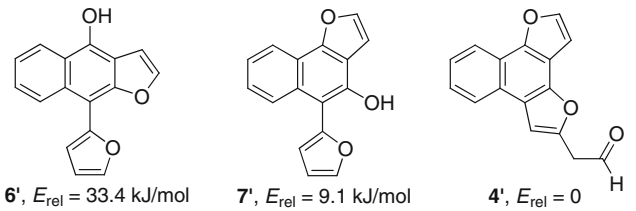


Fig. 1 Relative energies of model compounds **4′**, **6′**, and **7′** determined at B3LYP/6-311G** level

Nitration of **13** produced 4-nitro derivatives **14** [15]. Unexpectedly, common reducing agents like Raney Ni/N_2H_4, Zn/NaOH, Fe/AcOH, and Zn/AcOH failed to give 4-aminonaphthofurans **8** (R^4 = H) owing to the formation of either a complex mixture of unidentified products or polymeric resins (the related reduction of 9-nitroanthracene was shown to proceed efficiently affording 9-aminoanthracene [23–26]). This observation advocates for rather low stability of amines **8** (R^4 = H). To avoid this issue we decided to convert amines in situ into much more stable amide derivatives. To this end, reduction of **14** with Zn in Ac_2O was performed to afford 4-(diacetylamino)naphthofurans **15** in good yields (Table 2).

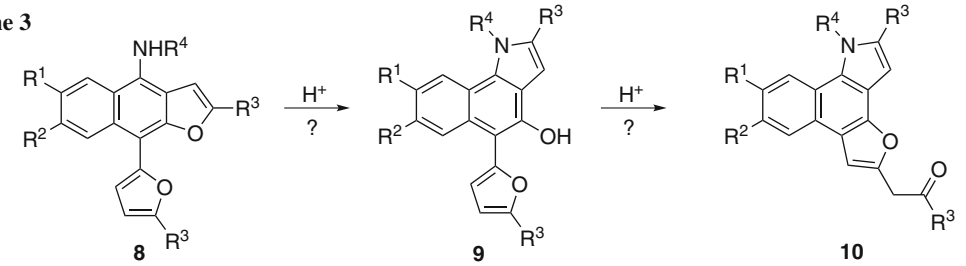
The structures of compounds **15** were determined by a combination of spectral methods and proved unambiguously for **15b** by single-crystal X-ray analysis (Fig. 2).

Heating of compounds **15** under reflux in ethanolic HCl for a short time led to the formation of monoacylated products **8** (Table 3). This partial hydrolysis of **15** was found to be more efficient under alkaline conditions wherein compounds **8** are formed in 70–88 % yields.

Compounds **8** could serve as substrates for an acid-induced rearrangement. Accordingly, we expected that prolonged treatment of **15** with ethanolic HCl would afford either the corresponding benzindoles **9** or benzo[*g*]furo[2,3-*e*]indoles **10**. Indeed, **15** disappeared after heating under reflux for 30–40 min. However, the expected products **9** and/or **10** were not detected in the reaction mixture; instead only tar was obtained. Similarly, when pure compounds **8a** and **8b**, isolated after alkaline hydrolysis of **15a** and **15b**, were heated with ethanolic HCl until full conversion, significant tarring of the reaction mixture precluded isolation of any product.

On the basis of our previous experience [19, 27], we supposed that these negative results are caused by competing deacylation of *N*-acylindoles **9** (R^4 = Ac) leading to NH-indoles **9′** which undergo oligomerization in ethanolic HCl. This problem can be avoided by utilization of the corresponding *N*-tosyl derivatives as both *N*-tosylanilines and *N*-tosylindoles are stable under the utilized reaction conditions. Therefore, we transformed compound **8a** into

Scheme 3



Scheme 4

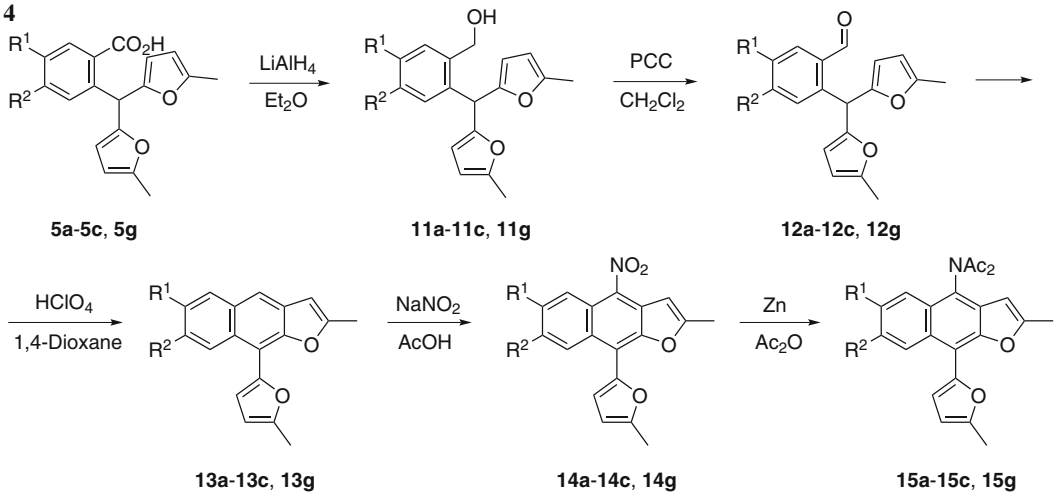


Table 2 Yields of compounds **11–15**

Entry	R^1	R^2	Yield/%				
			11	**12**	**13**	**14**	**15**
a	H	H	92	70	59	30	67
b	Cl	H	98	68	63	33	72
c	Br	H	93	66	60	32	71
g	OMe	OMe	90	65	55	24	60

its *N*-tosyl analogue **17** in 78 % yield via tosylation/deacylation sequence (Scheme 5).

To our great disappointment, neither prolonged heating of **16** nor refluxing of isolated compound **17** with ethanolic HCl afforded the desired recyclization product. The complete consumption of starting compounds was achieved at ca. 45 min; however, no formation of isolable products was observed. Therefore, the above explanation of decomposition is inappropriate for compound **17**.

To understand the difference in behaviors of 4-acetoxynaphthofurans **3** and their 4-acetylamino analogues **8**, we studied the protonation of a model compounds **6′** and **8′** ($R^1 = R^2 = R^3 = R^4 = H$) using DFT calculations employing the B3LYP functional with the 6-311G** basis set (Fig. 3). It was found that the most stable cation **B** is formed by protonation of **6′** at the C(5′) atom of the 9-furyl group. Cation **A**, which was proposed as a key intermediate, is significantly less stable than **B**. Moreover, protonation of **6′** at the C(4) and C(9) atoms produces cations **C** and **D**, respectively, which are also more stable than **A**. Fortunately, the main transformation of cations **B**–**D** is their reversed deprotonation. Nevertheless, moderate yields of naphthodifurans **4** can be explained by side reactions via formation of these cations.

Similar results were obtained by protonation of **8′** (Fig. 4). However, cation **G** formed by protonation of C(9) can be stabilized in two ways. First, it can form N,O-acetal **18** which is known to be relatively stable even in the presence of anhydrous acids (Scheme 6) [28–32]. Second, *N*-deprotonation can lead to iminoanthracene **19**. These compounds are also compatible with acids [33, 34]. Furan rings in both **18** and **19** are not conjugated or fused to another arene; therefore, they are susceptible to facile hydrolysis. Even if the lifetime of **18** and **19** is small, it is enough for decomposition of the starting compound. As a result, tar is only formed in reactions of **8** and **17**.

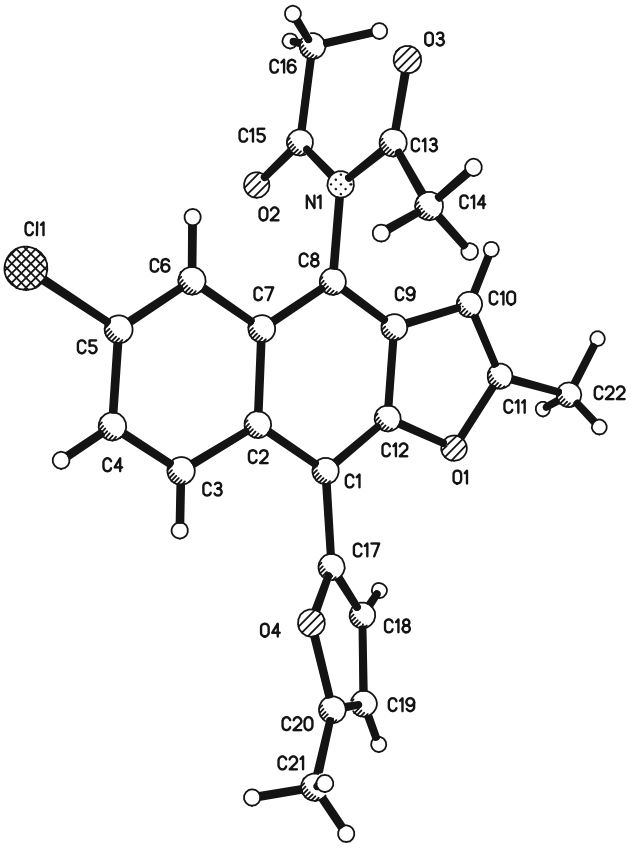


Fig. 2 Single-crystal X-ray structure of **15b**

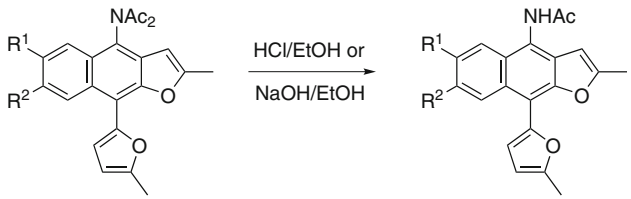
Conclusion

4-Acetoxy-9-furylnaphtho[2,3-*b*]furans undergo cascade rearrangement into naphtho[1,2-*b*:3,4-*b*′]difurans under heating with ethanolic HCl. On the contrary, the related 4-acetylamino and 4-tosylamino derivatives do not form the corresponding benzo[*g*]furo[2,3-*e*]indoles under these reaction conditions but produce tar instead. Density functional theory calculations on model compounds were employed to explain the obtained results.

Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX 300 spectrometer at room temperature; the chemical shifts δ were measured in parts per million with respect to the solvent ($CDCl_3$, ^{1}H: $\delta = 7.25$ ppm, ^{13}C: $\delta = 77.2$ ppm; DMSO-d_6, ^{1}H: $\delta = 2.50$ ppm, ^{13}C: $\delta = 39.7$ ppm). Coupling constants (J) are given in Hertz. Multiplicities of signals are described as follows: s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet, dd = double doublet, br = broadened. IR spectra were measured as KBr plates on InfraLUM FT-02 and InfraLUM FT-801 instruments. Mass spectra were recorded on a Kratos MS-30 instrument with 70 eV electron impact ionization at 200 °C. Elemental

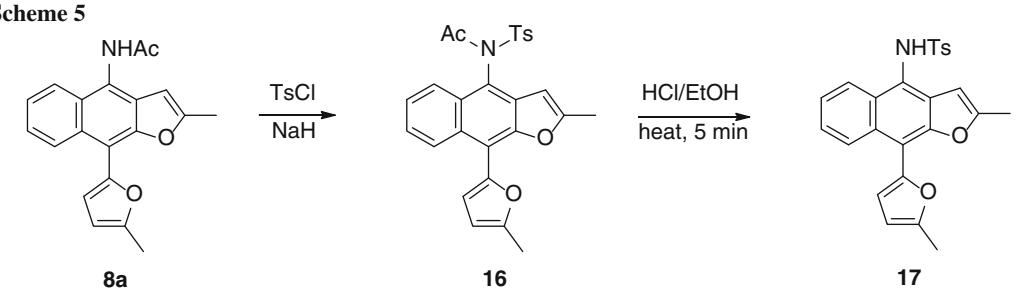
Table 3 Partial hydrolysis of **15**



15a-15c, 15g **8a-8c, 8g**

Entry	R^1	R^2	Yield of **8**/%	
			HCl/EtOH, 1–2 min	NaOH/EtOH
a	H	H	62	88
b	Cl	H	70	75
c	Br	H	65	78
g	OMe	OMe	45	70

Scheme 5



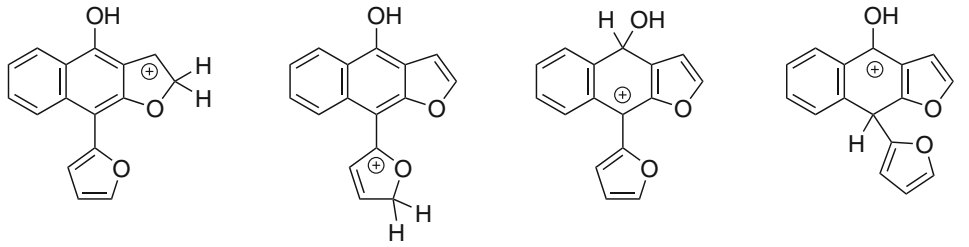


Fig. 3 Results of B3LYP/6-311G** calculations of protonated 9-furyl-4-hydroxynaphtho[2,3-*b*]furan **6′**

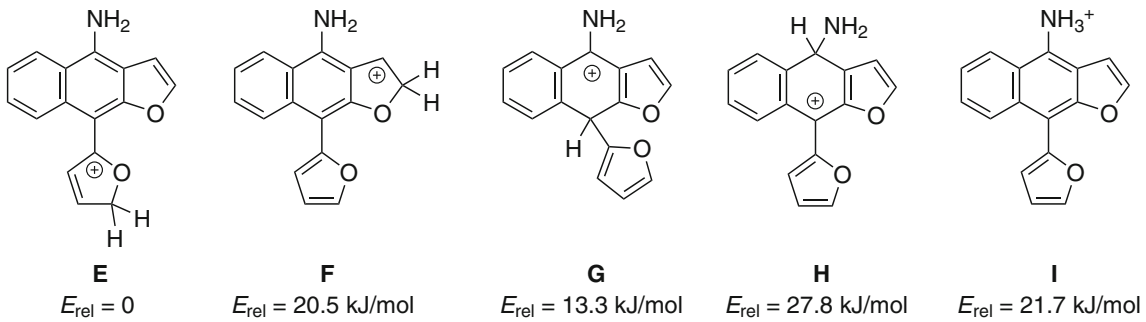
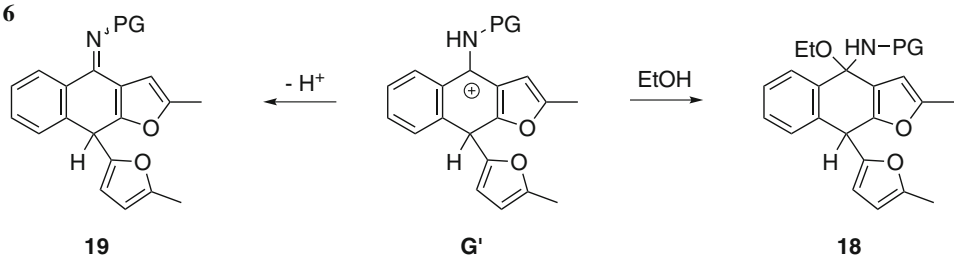


Fig. 4 Results of calculations of protonated forms of model compound **8′**

Scheme 6



analyses were performed with a Fisons EA-1108 CHNS elemental analyzer instrument. Melting points were determined in capillaries with an Electrothermal 9100 capillary melting point apparatus. Column chromatography was performed on silica gel KSK (50–160 μm, LTD Sorbpolymer). All the reactions were carried out using freshly distilled and dry solvents. Compounds **5** were synthesized according to reported procedures [13, 14]. Crystallographic data (excluding structure factors) for compound **15b** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication number CCDC 924197. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

General procedure for synthesis of 4-acetoxy-9-furylnaphtho[2,3-b]furans ***3***

Compound **5** (5.0 mmol) was refluxed with 10 cm^3 acetic acid, 10 cm^3 acetic anhydride, and 10 mg $ZnCl_2$ until completion of the reaction (TLC control). The reaction mixture was poured into 50 cm^3 cold water, neutralized with $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 25 cm^3). The combined organic extracts were dried with Na_2SO_4, treated with charcoal, and filtered. The solvent was removed under reduced pressure. Product was isolated by column chromatography on silica gel with petroleum ether/CH_2Cl_2 (4:1) as eluent and recrystallized from petroleum ether/CH_2Cl_2.

2-Methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl acetate (**3a**)
Starting from **5a**, 0.5 g **3a** (31 %) was isolated as pale yellow needles. M.p.: 146–147 °C (Ref. [15] 145–147 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [15].

6-Chloro-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]-furan-4-yl acetate (**3b**)
Starting from **5b**, 0.55 g **3b** (31 %) was isolated as pale yellow needles. M.p.: 141–142 °C (Ref. [15] 140–143 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [15].

6-Bromo-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]-furan-4-yl acetate (**3c**)
Starting from **5c**, 0.66 g **3c** (33 %) was isolated as pale yellow needles. M.p.: 149–150 °C (Ref. [15] 148–150 °C). IR, ^{1}H and ^{13}C NMR data are identical to theose described in Ref. [15].

6-Bromo-2-ethyl-9-(5-ethylfuran-2-yl)naphtho[2,3-b]-furan-4-yl acetate (**3d**)
Starting from **5d**, 0.6 g **3d** (28 %) was isolated as yellow needles. M.p.: 84–86 °C (Ref. [15] 84–86 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [15].

7-Chloro-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]-furan-4-yl acetate (**3e**)
Starting from **5e**, 0.55 g **3e** (31 %) was isolated as pale yellow needles. M.p.: 166–168 °C (Ref. [15] 166–168 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [15].

6-Methoxy-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]-furan-4-yl acetate (**3f**, $C_{21}H_{18}O_5$)
Starting from **5f**, 0.70 g **3f** (40 %) was isolated as pale yellow needles. M.p.: 140–141 °C; R_f = 0.75 (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.51 (1H, d, J = 9.8 Hz, H_{Ar}), 7.21 (1H, dd, J = 2.7, 9.8 Hz, H_{Ar}), 7.18 (1H, d, J = 2.7 Hz, H_{Ar}), 6.89 (1H, d, J = 3.1 Hz, H_{Fur}), 6.35 (1H, s, H_{Fur}), 6.26 (1H, d, J = 3.1 Hz, H_{Fur}), 3.94 (3H, s, OCH_3), 2.53 (3H, s, CH_3), 2.49 (6H, s, $2CH_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.8, 158.3, 156.5, 152.4, 149.9, 146.3, 135.2, 128.0, 124.6, 124.3, 122.8, 118.3, 112.9, 108.4, 107.4, 99.7, 98.5, 55.1, 20.8, 14.4, 13.9 ppm; IR (KBr): $\bar{\nu}$ = 1,762, 1,605, 1,431, 1,231, 1,189, 1,037, 794 cm^{-1}; MS (70 eV): m/z = 350 (M^+, 12), 308 (100), 293 (15), 265 (11), 43 (16).

6,7-Dimethoxy-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl acetate (**3g**, $C_{22}H_{20}O_6$)
Starting from **5g**, 0.70 g **3g** (37 %) was isolated as pale yellow needles. M.p.: 146–147 °C; R_f = 0.70 (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99 (1H, s, H_{Ar}), 7.15 (1H, s, H_{Ar}), 6.89 (1H, d, J = 3.2 Hz, H_{Fur}), 6.31 (1H, s, H_{Fur}), 6.25 (1H, d, J = 3.2 Hz, H_{Fur}), 4.01 (3H, s, OCH_3), 3.99 (3H, s, OCH_3), 2.52 (3H, s, CH_3), 2.48 (3H, s, CH_3), 2.47 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9, 157.3, 152.0, 150.7, 149.5, 148.7, 146.9, 135.5, 124.8, 120.8, 119.5, 112.7, 107.6, 107.3, 105.2, 99.8, 99.2, 55.8 (2C), 21.0, 14.5, 14.0 ppm; IR (KBr): $\bar{\nu}$ = 1,756, 1,613, 1,507, 1,481, 1,432, 1,369, 1,265, 1,210, 1,179, 1,162, 1,015, 783 cm^{-1}; MS (70 eV): m/z = 380 (M^+, 22), 338 (67), 322 (100), 307 (29), 279 (50), 264 (23), 236 (35), 43 (15).

General procedure for synthesis of naphthodifurans ***4a–4g***

A suspension of compound **3** (5.0 mmol) in 130 cm^3 33 % ethanolic HCl was refluxed until complete dissolution of the starting compound. Then the reaction mixture was poured into 500 cm^3 of water and neutralized with sodium carbonate to pH 7. The resulting precipitate was filtered, dried, dissolved in benzene/hexane (1:1), and passed through a pad of silica gel. The refined solution was evaporated under reduced pressure; the residue was recrystallized from ethanol.

1-(2-Methylnaphtho[1,2-b:3,4-b']difuran-5-yl)-2-propanone (**4a**, $C_{18}H_{14}O_3$)
Starting from **3a**, 0.56 g **4a** (40 %) was isolated as a pale yellow solid. M.p.: 94–96 °C; R_f = 0.62 (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.35–8.32 (1H, m, H_{Ar}), 8.12–8.08 (1H, m, H_{Ar}), 7.59–7.51 (2H, m, H_{Ar}), 7.08 (1H, s, H_{Fur}), 6.71 (1H, s, H_{Fur}), 3.95 (2H, s, CH_2), 2.59 (3H, s, CH_3), 2.26 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.5, 154.9, 149.3, 149.0, 145.8, 125.0 (2C), 124.7, 124.4, 123.8, 120.7, 119.0, 113.3, 104.9, 100.1, 43.8, 29.3, 14.2 ppm; IR (KBr): $\bar{\nu}$ = 1,720, 1,588, 1,566, 1,530, 1,440, 1,390, 1,159, 1,108, 981, 948, 815, 764 cm^{-1}; MS (70 eV): m/z = 278 (M^+, 27), 235 (100), 207 (17), 179 (18), 178 (30), 149 (10), 55 (16), 43 (19).

1-(9-Chloro-2-methylnaphtho[1,2-b:3,4-b']difuran-5-yl)-2-propanone (**4b**, $C_{18}H_{13}ClO_3$)
Starting from **3b**, 0.66 g **4b** (42 %) was isolated as yellow crystals. M.p.: 113–115 °C; $R_f = 0.61$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.27$ (1H, s, H_{Ar}), 8.01 (1H, d, $J = 8.7$ Hz, H_{Ar}), 7.44 (1H, d, $J = 8.7$ Hz, H_{Ar}), 7.07 (1H, s, H_{Fur}), 6.70 (1H, s, H_{Fur}), 3.96 (2H, s, CH_2), 2.59 (3H, s, CH_3), 2.28 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 203.5$, 155.5, 149.3, 148.3, 145.6, 130.4, 125.3, 125.1, 122.3, 119.7, 119.4, 118.8, 114.1, 104.7, 100.1, 43.6, 29.5, 14.2 ppm; IR (KBr): $\bar{\nu} = 1{,}716$, 1,566, 1,355, 1,136, 1,116, 1,079, 944, 860, 808, 777 cm^{-1}; MS (70 eV): $m/z = 314/312$ (M^+, 10/30), 271/269 (33/100), 234 (32), 205 (10), 178 (17), 163 (21), 152 (13), 43 (14).

1-(9-Bromo-2-methylnaphtho[1,2-b:3,4-b']difuran-5-yl)-2-propanone (**4c**)
Starting from **3c**, 0.75 g **4c** (42 %) was isolated as yellow crystals. M.p.: 135–136 °C (Ref. [12] 135–137 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [12].

1-(9-Bromo-2-ethylnaphtho[1,2-b:3,4-b']difuran-5-yl)-butan-2-one (**4d**, $C_{20}H_{17}BrO_3$)
Starting from **3d**, 0.71 g **4d** (37 %) was isolated as yellow crystals. M.p.: 123–124 °C; $R_f = 0.65$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.43$ (1H, d, $J = 1.5$ Hz, H_{Ar}), 7.91 (1H, d, $J = 8.7$ Hz, H_{Ar}), 7.55 (1H, dd, $J = 1.5$, 8.7 Hz, H_{Ar}), 7.03 (1H, s, H_{Fur}), 6.70 (1H, s, H_{Fur}), 3.96 (2H, s, CH_2), 2.93 (2H, q, $J = 7.2$ Hz, CH_2), 2.60 (2H, q, $J = 7.2$ Hz, CH_2), 1.43 (3H, t, $J = 7.2$ Hz, CH_3), 1.11 (3H, t, $J = 7.2$ Hz, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 206.2$, 161.3, 149.6, 148.0, 145.9, 128.0, 125.6, 123.1, 122.7, 120.1, 118.9, 118.5, 114.1, 104.7, 98.7, 42.6, 35.5, 22.0, 12.1, 7.7 ppm; IR (KBr): $\bar{\nu} = 1{,}714$, 1,562, 1,519, 1,384, 1,356, 1,109, 1,038, 925, 806, 753 cm^{-1}; MS (70 eV): $m/z = 386/384$ (M^+, 13/13), 329/327 (100/100), 248 (13), 232 (16).

1-(8-Chloro-2-methylnaphtho[1,2-b:3,4-b']difuran-5-yl)-2-propanone (**4e**, $C_{18}H_{13}ClO_3$)
Starting from **3e**, 0.64 g **4e** (41 %) was isolated as a white solid. M.p.: 154–155 °C; $R_f = 0.60$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.20$ (1H, d, $J = 8.7$ Hz, H_{Ar}), 8.04 (1H, d, $J = 2.1$ Hz, H_{Ar}), 7.46 (1H, dd, $J = 2.1$, 8.7 Hz, H_{Ar}), 7.03 (1H, s, H_{Fur}), 6.67 (1H, s, H_{Fur}), 3.95 (2H, s, CH_2), 2.57 (3H, s, CH_3), 2.27 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 203.5$, 155.1, 149.2, 148.8, 146.2, 130.6, 125.1, 124.9, 123.0, 122.0, 118.2, 117.0, 113.3, 104.6, 100.0, 43.6, 29.3, 14.1 ppm; IR (KBr): $\bar{\nu} = 1{,}714$, 1,605, 1,393, 1,166, 1,086, 940, 892, 814, 763 cm^{-1}; MS (70 eV): $m/z = 314/312$ (M^+, 5/15), 271/269 (32/96), 234 (30), 176 (33), 163 (17), 151 (13), 126 (11), 88 (14), 75 (15), 43 (100).

1-(9-Methoxy-2-methylnaphtho[1,2-b:3,4-b']difuran-5-yl)-2-propanone (**4f**, $C_{19}H_{16}O_4$)
Starting from **3f**, 0.74 g **4f** (48 %) was isolated as yellow crystals. M.p.: 138–139 °C; $R_f = 0.54$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.96$ (1H, d, $J = 9.0$ Hz, H_{Ar}), 7.60 (1H, d, $J = 2.4$ Hz, H_{Ar}), 7.16 (1H, dd, $J = 2.4$, 9.0 Hz, H_{Ar}), 6.98 (1H, s, H_{Fur}), 6.67 (1H, s, H_{Fur}), 3.98 (3H, s, OCH_3), 3.91 (2H, s, CH_2), 2.57 (3H, s, CH_3), 2.24 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 203.8$, 156.9, 154.7, 148.8, 148.6, 144.4, 125.3, 119.6, 119.0, 118.9, 116.6, 113.5, 104.6, 100.1, 99.9, 55.3, 43.7, 29.2, 14.1 ppm; IR (KBr): $\bar{\nu} = 1{,}714$, 1,570, 1,535, 1,360, 1,220, 1,165, 1,001, 834 cm^{-1}; MS (70 eV): $m/z = 308$ (M^+, 78), 265 (100), 222 (21), 165 (14), 43 (22).

1-(8,9-Dimethoxy-2-methylnaphtho[1,2-b:3,4-b']difuran-5-yl)-2-propanone (**4g**, $C_{20}H_{18}O_5$)
Starting from **3g**, 0.93 g **4g** (55 %) was isolated as yellow crystals. M.p.: 167–168 °C; $R_f = 0.47$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.60$ (1H, s, H_{Ar}), 7.38 (1H, s, H_{Ar}), 7.02 (1H, s, H_{Fur}), 6.55 (1H, s, H_{Fur}), 4.07 (3H, s, OCH_3), 4.04 (3H, s, OCH_3), 3.94 (2H, s, CH_2), 2.57 (3H, s, CH_3), 2.26 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 204.1$, 154.2, 149.0, 148.7, 148.6, 148.4, 128.4, 119.3, 118.5, 113.6, 111.7, 104.7, 104.0, 100.6, 100.1, 56.1, 56.0, 43.9, 29.5, 14.3 ppm; IR (KBr): $\bar{\nu} = 1{,}713$, 1,579, 1,528, 1,492, 1,462, 1,371, 1,281, 1,246, 1,213, 1,157, 1,006, 844, 798 cm^{-1}; MS (70 eV): $m/z = 338$ (M^+, 36), 295 (100), 280 (14), 251 (16), 59 (18), 43 (16).

Synthesis of [2-(difuranylmethyl)phenyl]methanols ***11***

Lithium aluminum hydride (100.0 mmol) was added portionwise to an ice-cooled suspension of benzoic acid **5** (50.0 mmol) in 150 cm^3 anhydrous Et_2O and stirred for 5 h. Then mixture was poured into ice water (**caution!**) and neutralized with 6 M hydrochloric acid. The product was extracted with Et_2O (3 × 100 cm^3). The extract was dried with Na_2SO_4, treated with charcoal, and filtered. The solvent was removed under reduced pressure; the residue was recrystallized from petroleum ether.

[2-[Bis(5-methylfuran-2-yl)methyl]phenyl]methanol (**11a**)
Starting from **5a**, 13.65 g **11a** (92 %) was isolated as a white solid. M.p.: 65–67 °C (Ref. [15] 65–67 °C). IR and ^{1}H NMR data are identical to those described in Ref. [15].

[5-Chloro-2-[bis(5-methylfuran-2-yl)methyl]phenyl]methanol (**11b**)
Starting from **5b**, 12.6 g **11b** (98 %) was isolated as a white solid. M.p.: 71–72 °C (Ref. [15] 71–72 °C). IR and ^{1}H NMR data are identical to those described in Ref. [15].

[5-Bromo-2-[bis(5-methylfuran-2-yl)methyl]phenyl]methanol (**11c**)
Starting from **5c**, 14.8 g **11c** (93 %) was isolated as a white solid. M.p.: 75–76 °C (Ref. [15] 75–76 °C). IR and ^{1}H NMR data are identical to those described in Ref. [15].

[2-[Bis(5-methylfuran-2-yl)methyl]-4,5-dimethoxyphenyl]methanol (**11g**, $C_{20}H_{22}O_5$)
Starting from **5g**, 15.39 g **11g** (90 %) was isolated as a white solid. M.p.: 96–97 °C; $R_f = 0.38$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.92$ (1H, s, H_{Ar}), 6.71 (1H, s, H_{Ar}), 5.86 (2H, d, $J = 3.2$ Hz, H_{Fur}), 5.84 (2H, d, $J = 3.2$ Hz, H_{Fur}), 5.63 (1H, s, CH), 4.66 (2H, s, CH_2), 3.87 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 2.23 (6H, s, $2CH_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 152.8$ (2C), 151.7 (2C), 148.7, 148.1, 130.9, 130.4, 112.5, 112.4, 108.5 (2C), 106.2 (2C), 63.0, 56.1, 56.0, 40.6, 13.8 (2C) ppm; IR (KBr): $\bar{\nu} = 3{,}508$, 1,609, 1,516, 1,462, 1,279, 1,216, 1,165, 1,091, 1,018, 783, 756 cm^{-1}; MS (70 eV): $m/z = 324$ ($M^+ - H_2O$, 49), 281 (40), 264 (89), 224 (100), 209 (29), 193 (28), 181 (60), 165 (28), 152 (26), 119 (25), 91 (28), 77 (26), 65 (25), 51 (28), 43 (27).

General procedure for synthesis of 2-(difuranylmethyl)benzaldehydes ***12***

A solution of alcohol **11** (35.0 mmol) in 100 cm^3 dry CH_2Cl_2 was added dropwise to a suspension of pyridinium chlorochromate (70.0 mmol) in 100 cm^3 dry CH_2Cl_2. The mixture was stirred for 6 h at room temperature. The precipitate was filtered and washed with hot CH_2Cl_2 (3 × 100 cm^3). The combined solvent was concentrated under reduced pressure. Product was purified by column chromatographically on silica gel with petroleum ether/CH_2Cl_2 (10:1) as eluent. The fraction containing benzaldehyde was concentrated to 20 cm^3 and left to crystallize overnight.

2-[Bis(5-methylfuran-2-yl)methyl]benzaldehyde (**12a**)
Starting from **11a**, 8.17 g **12a** (70 %) was isolated as colorless prisms. M.p.: 63–65 °C (Ref. [15] 63–65 °C). IR and ^{1}H NMR data are identical to those described in Ref. [15].

5-Chloro-2-[bis(5-methylfuran-2-yl)methyl]benzaldehyde (**12b**)
Starting from **11b**, 7.06 g **12b** (68 %) was isolated as pale yellow prisms. M.p.: 75–77 °C (Ref. [15] 75–77 °C). IR and ^{1}H NMR data are identical to those described in Ref. [15].

5-Bromo-2-[bis(5-methylfuran-2-yl)methyl]benzaldehyde (**12c**)
Starting from **11c**, 7.92 g **12c** (66 %) was isolated as pale yellow prisms. M.p.: 85–87 °C (Ref. [15] 85–87 °C). IR and ^{1}H NMR data are identical to those described in Ref. [15].

2-[Bis(5-methylfuran-2-yl)methyl]-4,5-dimethoxybenzaldehyde (**12g**, $C_{20}H_{20}O_5$)
Starting from **11g**, 7.74 g **12g** (65 %) was isolated as a white solid. M.p.: 94–95 °C; $R_f = 0.68$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 10.22$ (1H, s, CHO), 7.40 (1H, s, H_{Ar}), 6.74 (1H, s, H_{Ar}), 6.29 (1H, s, CH), 5.88 (4H, s, H_{Fur}), 3.93 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 2.24 (6H, s, $2CH_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 189.8$, 153.7, 152.0 (2C), 151.9 (2C), 148.3, 137.0, 126.8, 112.2, 111.8, 109.1 (2C), 106.3 (2C), 56.2, 56.1, 39.6, 13.7 (2C) ppm; IR (KBr): $\bar{\nu} = 1{,}684$, 1,596, 1,563, 1,512, 1,442, 1,268, 788, 755 cm^{-1}; MS (70 eV): $m/z = 340$ (M^+, 48), 322 (24), 297 (100), 283 (43), 258 (16), 254 (10), 175 (10), 106 (10), 59 (10), 43 (36).

General procedure for synthesis of 9-furanylnaphtho[2,3-b]furans ***13***

To a solution of **12** (18.0 mmol) in 50 cm^3 1,4-dioxane, 0.5 cm^3 70 % $HClO_4$ was added. Reaction mixture was stirred at 40 °C for 20 min. The reaction mixture was poured into 250 cm^3 water, neutralized with $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 100 cm^3). The combined organic fractions were dried with Na_2SO_4, treated with charcoal, and filtered. The solvent was removed under reduced pressure. Product was isolated by flash chromatography on silica gel with petroleum ether/benzene (5:1) as eluent and recrystallized from petroleum ether/benzene.

2-Methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan (**13a**)
Starting from **12a**, 612 mg **13a** (59 %) was isolated as colorless crystals. M.p.: 59–61 °C (Ref. [15] 59–61 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [15].

6-Chloro-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan (**13b**)
Starting from **12b**, 605 mg **13b** (63 %) was isolated as pale yellow crystals. M.p.: 94–95 °C (Ref. [15] 94–96 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [15].

6-Bromo-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]-furan (**13c**)
Starting from **12c**, 555 mg **13c** (60 %) was isolated as pale yellow crystals. M.p.: 119–121 °C (Ref. [15] 119–121 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [15].

6,7-Dimethoxy-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan (**13g**, $C_{20}H_{18}O_4$)
Starting from **12g**, 3.19 g **13g** (55 %) was isolated as a white solid. M.p.: 93–94 °C; $R_f = 0.54$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.01$ (1H, s, H_{Ar}), 7.70 (1H, s, H_{Ar}), 7.16 (1H, s, H_{Ar}), 6.95 (1H, d, $J = 3.0$ Hz, H_{Fur}), 6.43 (1H, s, H_{Fur}), 6.27 (1H, d, $J = 3.0$ Hz, H_{Fur}), 4.00 (6H, s, 2OCH_3), 2.50 (3H, s, CH_3), 2.48 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 157.1$, 151.9, 150.5, 149.1, 148.1, 147.5, 128.4, 127.1, 123.8, 116.4, 112.6, 107.6, 106.5, 104.9, 102.3, 97.4, 55.9, 55.7, 14.6, 14.0 ppm; IR (KBr): $\bar{\nu} = 1{,}620$, 1,503, 1,465, 1,400, 1,260, 1,145, 1,029, 872, 783 cm^{-1}; MS (70 eV): $m/z = 322$ (M^+, 100), 307 (24), 279 (50), 264 (27), 236 (34), 165 (15), 149 (20), 101 (16), 59 (44), 43 (37).

General procedure for nitration of 9-furanylnaphtho[2,3-b]furans ***13***

Sodium nitrite (1.59 g, 23.0 mmol) was added to a solution of **13** (17.0 mmol) in 100 cm^3 glacial acetic acid and stirred at room temperature for 0.5 h. The reaction mixture was poured into 500 cm^3 water, neutralized with $NaHCO_3$, and filtered. Product was recrystallized from acetone.

2-Methyl-9-(5-methylfuran-2-yl)-4-nitronaphtho[2,3-b]-furan (**14a**)
Starting from **13a**, 350 mg **14a** (30 %) was isolated as a dark yellow solid. M.p.: 157–158 °C (Ref. [15] 157–159 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [15].

6-Chloro-2-methyl-9-(5-methylfuran-2-yl)-4-nitronaphtho[2,3-b]furan (**14b**)
Starting from **13b**, 430 mg **14b** (33 %) was isolated as a dark orange solid. M.p.: 211–213 °C (Ref. [15] 211–213 °C). IR, ^{1}H and ^{13}C NMR data are identical to those described in Ref. [15].

6-Bromo-2-methyl-9-(5-methylfuran-2-yl)-4-nitronaphtho[2,3-b]furan (**14c**, $C_{18}H_{12}BrNO_4$)
Starting from **13c**, 2.10 g **14c** (32 %) was isolated as a dark orange solid. M.p.: 222–223 °C; $R_f = 0.57$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 8.89$ (1H, d, $J = 2.0$ Hz, H_{Ar}), 8.64 (1H, d, $J = 9.0$ Hz, H_{Ar}), 7.83 (1H, dd, $J = 2.0$, 9.0 Hz, H_{Ar}), 7.28 (1H, d, $J = 3.2$ Hz, H_{Fur}), 7.19 (1H, s, H_{Fur}), 6.54 (1H, d, $J = 3.2$ Hz, H_{Fur}), 2.63 (3H, s, CH_3), 2.54 (3H, s, CH_3) ppm; IR (KBr): $\bar{\nu} = 1{,}616$, 1,596, 1,572, 1,504, 1,492, 1,320, 1,308, 1,264, 1,236, 800, 792 cm^{-1}; MS (70 eV): $m/z = 387/385$ (M^+, 48/48), 357/355 (100/99), 314/312 (19/19), 189 (16), 149 (13), 55 (14), 43 (25).

6,7-Dimethoxy-2-methyl-9-(5-methylfuran-2-yl)-4-nitronaphtho[2,3-b]furan (**14g**, $C_{20}H_{17}NO_6$)
Starting from **13g**, 1.50 g **14g** (24 %) was isolated as a red-orange solid. M.p.: 231–232 °C; $R_f = 0.59$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.27$ (1H, s, H_{Ar}), 8.10 (1H, s, H_{Ar}), 7.12 (1H, d, $J = 3.3$ Hz, H_{Fur}), 7.01 (1H, s, H_{Fur}), 6.32 (1H, d, $J = 3.3$ Hz, H_{Fur}), 4.05 (3H, s, OCH_3), 4.00 (3H, s, OCH_3), 2.55 (3H, s, CH_3), 2.50 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 169.1$, 161.3, 153.9, 151.0, 149.1, 148.8, 145.7, 126.9, 124.0, 121.2, 116.3, 115.4, 108.4, 105.7, 103.8, 102.3, 56.0, 55.7, 14.7, 14.0 ppm; IR (KBr): $\bar{\nu} = 1{,}603$, 1,514, 1,476, 1,437, 1,270, 1,238, 1,216, 1,023, 802 cm^{-1}; MS (70 eV): $m/z = 367$ (M^+, 55), 337 (100), 321 (32), 310 (12), 294 (25), 279 (17), 251 (21), 235 (10), 178 (11), 169 (15), 57 (13), 43 (33).

General procedure for synthesis of 4-(diacetylamino)-9-(5-methylfuran-2-yl)-naphtho[2,3-b]furans ***15***

To a solution of **14** (4.0 mmol) in 40 cm^3 acetic anhydride, 4.55 g zinc dust (70.0 mmol) was added in small portions. The reaction mixture was refluxed for 3 h, poured into 250 cm^3 water, neutralized with $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 50 cm^3). The combined organic fractions were dried with Na_2SO_4, treated with charcoal, and filtered. The solvent was evaporated under reduced pressure. The residue was recrystallized from ethanol.

N-Acetyl-N-[2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl]acetamide (**15a**, $C_{22}H_{19}NO_4$)
Starting from **14a**, 0.97 g **15a** (67 %) was isolated as a yellow solid. M.p.: 166–167 °C; $R_f = 0.50$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.68$–8.65 (1H, m, H_{Ar}), 7.78–7.74 (1H, m, H_{Ar}), 7.54–7.51 (2H, m, H_{Ar}), 6.97 (1H, d, $J = 3.0$ Hz, H_{Fur}), 6.41 (1H, s, H_{Fur}), 6.31 (1H, d, $J = 3.0$ Hz, H_{Fur}), 2.54 (3H, s, CH_3), 2.52 (3H, s, CH_3), 2.32 (6H, s, 2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 173.2$ (2C), 160.6, 153.1, 150.8, 145.9, 129.3, 129.0, 127.9, 127.1, 126.0, 125.6, 124.4, 121.1, 114.0, 111.3, 107.7, 99.8, 26.3 (2C), 14.7, 14.0 ppm; IR (KBr): $\bar{\nu} = 1{,}704$, 1,605, 1,554, 1,419, 1,366, 1,234, 983, 945, 813, 766 cm^{-1}; MS (70 eV): $m/z = 361$ (M^+, 45), 319 (72), 277 (71), 260 (15), 234 (17), 95 (16).

N-Acetyl-N-[6-chloro-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl]acetamide
(**15b**, $C_{22}H_{18}ClNO_4$)
Starting from **14b**, 1.14 g **15b** (72 %) was isolated as a yellow solid. M.p.: 191–192 °C; $R_f = 0.53$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 8.56$ (1H, d, $J = 9.2$ Hz, H_{Ar}), 7.90 (1H, d, $J = 2.1$ Hz, H_{Ar}), 7.58 (1H, dd, $J = 2.1$, 9.2 Hz, H_{Ar}), 7.06 (1H, d, $J = 3.2$ Hz, H_{Fur}), 6.81 (1H, s, H_{Fur}), 6.45 (1H, d, $J = 3.2$ Hz, H_{Fur}), 2.54 (3H, s, CH_3), 2.47 (3H, s, CH_3), 2.24 (6H, s, $2CH_3$) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 172.4$ (2C), 161.4, 153.2, 150.0, 144.4, 131.0, 130.3, 128.6, 128.5, 126.2, 126.1, 124.2, 120.3, 114.5, 110.2, 108.1, 100.4, 26.0 (2C), 14.1, 13.5 ppm; IR (KBr): $\bar{\nu} = 1{,}724$, 1,709, 1,599, 1,389, 1,369, 1,337, 1,273, 1,244, 1,227, 1,105, 1,024, 988, 903, 789 cm^{-1}; MS (70 eV): $m/z = 397/395$ (M^+, 16/48), 355/353 (33/100), 313/311 (23/70), 297 (10), 268 (13), 43 (24).

N-Acetyl-N-[6-bromo-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl]acetamide
(**15c**, $C_{22}H_{18}BrNO_4$)
Starting from **14c**, 1.25 g **15c** (71 %) was isolated as a yellow solid. M.p.: 208–210 °C; $R_f = 0.54$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 8.48$ (1H, d, $J = 9.6$ Hz, H_{Ar}), 8.06 (1H, d, $J = 2.4$ Hz, H_{Ar}), 7.69 (1H, dd, $J = 2.4$, 9.6 Hz, H_{Ar}), 7.05 (1H, d, $J = 3.3$ Hz, H_{Fur}), 6.82 (1H, s, H_{Fur}), 6.44 (1H, d, $J = 3.3$ Hz, H_{Fur}), 2.54 (3H, s, CH_3), 2.46 (3H, s, CH_3), 2.24 (6H, s, $2CH_3$) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 172.8$ (2C), 161.8, 153.6, 150.5, 144.8, 130.6, 129.4, 129.1, 129.0, 126.7, 124.5, 123.9, 120.0, 115.0, 110.7, 108.5, 100.8, 26.4 (2C), 14.5, 13.9 ppm; IR (KBr): $\bar{\nu} = 1{,}724$, 1,596, 1,392, 1,368, 1,276, 1,244, 1,236, 1,228, 792 cm^{-1}; MS (70 eV): $m/z = 441/439$ (M^+, 10/10), 399/397 (17/17), 357/355 (30/30), 317 (15), 232 (14), 203 (24), 189 (13), 175 (19), 151 (14), 51 (12), 43 (100).

N-Acetyl-N-[6,7-dimethoxy-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl]acetamide
(**15g**, $C_{24}H_{23}NO_6$)
Starting from **14g**, 1.01 g **15g** (60 %) was isolated as a pale yellow solid. M.p.: 179–181 °C; $R_f = 0.44$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 7.97$ (1H, s, H_{Ar}), 7.06 (1H, d, $J = 3.0$ Hz, H_{Fur}), 7.01 (1H, s, H_{Ar}), 6.67 (1H, s, H_{Fur}), 6.42 (1H, d, $J = 3.0$ Hz, H_{Fur}), 3.90 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 2.50 (3H, s, CH_3), 2.46 (3H, s, CH_3), 2.24 (6H, s, $2CH_3$) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 172.5$ (2C), 158.7, 152.3, 149.4, 149.3, 149.1, 145.6, 127.0, 123.7, 123.5, 113.5, 108.8, 107.9, 104.9, 100.1, 100.0 (2C), 55.4, 55.1, 25.8 (2C), 14.0, 13.4 ppm; IR (KBr): $\bar{\nu} = 1{,}708$, 1,508, 1,486, 1,261, 1,227, 1,213, 782 cm^{-1}; MS (70 eV): $m/z = 421$ (M^+, 43), 379 (55), 336 (34), 43 (100).

*Synthesis of 4-(acetylamino)-9-furanylnaphtho[2,3-b]-furans **8***

Method **A**
A suspension of **15** (4.0 mmol) in 130 cm^3 33 % ethanolic HCl was refluxed for 1–2 min. The reaction mixture poured into 500 cm^3 water, neutralized with $NaHCO_3$, and extracted with CH_2Cl_2 (3×50 cm^3). The combined organic fractions were dried with Na_2SO_4, treated with charcoal, and filtered. The solvent was removed under reduced pressure. Product was isolated by flash chromatography on silica gel with petroleum ether/benzene (1:1) as eluent and recrystallized from petroleum ether/benzene.

Method **B**
Compound **15** (4.0 mmol) was added to a solution of 4.0 g NaOH (100.0 mmol) in 20 cm^3 EtOH. The reaction mixture was heated for 10 min (TLC monitoring), poured into 200 cm^3 water, and extracted with CH_2Cl_2 (3×50 cm^3). The combined organic fractions were dried with Na_2SO_4, treated with charcoal, and filtered. The solvent was removed under reduced pressure. Product was isolated by flash chromatography on silica gel with petroleum ether/benzene (1:1) as eluent and recrystallized from petroleum ether/benzene.

N-[2-Methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl]acetamide (**8a**, $C_{20}H_{17}NO_3$)
Compound **8a** was obtained from **15a** as a beige solid using method A (0.79 g, 62 %) or B (1.12 g, 88 %). M.p.: 239–240 °C; $R_f = 0.39$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 10.13$ (1H, br s, NH), 8.41–8.39 (1H, m, H_{Ar}), 8.11–8.07 (1H, m, H_{Ar}), 7.55–7.47 (2H, m, H_{Ar}), 6.89 (1H, d, $J = 3.3$ Hz, H_{Fur}), 6.56 (1H, s, H_{Fur}), 6.39 (1H, d, $J = 3.3$ Hz, H_{Fur}), 2.51 (3H, s, CH_3), 2.45 (3H, s, CH_3), 2.25 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 168.4$, 157.4, 152.0, 150.3, 145.4, 127.9, 126.3, 126.1, 125.3, 125.1, 124.4, 123.8, 123.1, 112.9, 107.5, 107.3, 102.1, 22.8, 13.8, 13.3 ppm; IR (KBr): $\bar{\nu} = 3{,}219$, 1,651, 1,529, 1,388, 1,281, 1,254, 1,028, 943, 791, 764 cm^{-1}; MS (70 eV): $m/z = 319$ (M^+, 53), 276 (100), 234 (26), 203 (11), 149 (22), 69 (12), 59 (17), 55 (24), 43 (37).

N-[6-Chloro-2-methyl-9-(5-methylfuran-2-yl)naphtho-[2,3-b]furan-4-yl]acetamide (**8b**, $C_{20}H_{16}ClNO_3$)
Compound **8b** was obtained from **15b** as a beige solid using method A (0.99 g, 70 %) or B (1.06 g, 75 %). M.p.: 247–248 °C; $R_f = 0.44$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 10.18$ (1H, br s, NH), 8.46 (1H, d, $J = 9.2$ Hz, H_{Ar}), 8.10 (1H, d,

$J = 2.1$ Hz, H_{Ar}), 7.51 (1H, dd, $J = 2.1$, 9.2 Hz, H_{Ar}), 6.94 (1H, d, $J = 3.2$ Hz, H_{Fur}), 6.57 (1H, s, H_{Fur}), 6.40 (1H, d, $J = 3.2$ Hz, H_{Fur}), 2.51 (3H, s, CH_3), 2.45 (3H, s, CH_3), 2.27 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 168.8$, 158.5, 152.6, 150.5, 145.1, 129.2, 128.0, 127.6, 126.9, 126.2, 125.7, 123.7, 122.0, 113.7, 108.0, 107.6, 102.6, 23.1, 14.1, 13.6 ppm; IR (KBr): $\bar{\nu} = 3{,}249$, 1,660, 1,603, 1,527, 1,389, 1,279, 1,098, 1,030, 943, 897, 794 cm^{-1}; MS (70 eV): $m/z = 355/353$ (M^+, 13/38), 313/311 (33/100), 295 (25), 268 (24), 234 (16), 149 (27), 69 (18), 57 (40), 43 (41).

N-[6-Bromo-2-methyl-9-(5-methylfuran-2-yl)naphtho-[2,3-b]furan-4-yl]acetamide (**8c**, $C_{20}H_{16}BrNO_3$)

Compound **8c** was obtained from **15c** as a beige solid using method A (1.03 g, 65 %) or B (1.24 g, 78 %). M.p.: 249–251 °C; $R_f = 0.42$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 10.22$ (1H, br s, NH), 8.37 (1H, d, $J = 9.3$ Hz, H_{Ar}), 8.25 (1H, d, $J = 1.8$ Hz, H_{Ar}), 7.61 (1H, dd, $J = 1.8$, 9.3 Hz, H_{Ar}), 6.91 (1H, d, $J = 3.3$ Hz, H_{Fur}), 6.56 (1H, s, H_{Fur}), 6.39 (1H, d, $J = 3.3$ Hz, H_{Fur}), 2.50 (3H, s, CH_3), 2.44 (3H, s, CH_3), 2.26 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 168.7$, 158.4, 152.5, 150.4, 145.0, 128.1, 128.0, 127.4, 127.3, 126.3, 125.1, 123.6, 117.7, 113.6, 107.9, 107.5, 102.6, 23.1, 14.0, 13.6 ppm; IR (KBr): $\bar{\nu} = 3{,}248$, 1,664, 1,600, 1,528, 1,392, 1,280, 1,092, 892, 784 cm^{-1}; MS (70 eV): $m/z = 399/397$ (M^+, 46/46), 357/355 (42/42), 312 (13), 232 (10), 204 (12), 176 (9), 151 (11), 51 (12), 43 (100).

N-[6,7-Dimethoxy-2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl]acetamide (**8g**, $C_{22}H_{21}NO_5$)

Compound **8g** was obtained from **15g** as a white solid using method A (0.68 g, 45 %) or B (1.06 g, 70 %). M.p.: 265–267 °C; $R_f = 0.34$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 10.06$ (1H, br s, NH), 7.87 (1H, s, H_{Ar}), 7.35 (1H, s, H_{Ar}), 6.94 (1H, d, $J = 3.0$ Hz, H_{Fur}), 6.45 (1H, s, H_{Fur}), 6.38 (1H, d, $J = 3.0$ Hz, H_{Fur}), 3.92 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 2.49 (3H, s, CH_3), 2.45 (3H, s, CH_3), 2.25 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 168.5$, 155.9, 151.7, 149.5, 149.0, 147.8, 146.2, 124.6, 123.5, 123.0, 122.0, 112.6, 107.7, 106.2, 104.3, 102.4, 102.1, 55.2, 55.1, 23.1, 13.9, 13.5 ppm; IR (KBr): $\bar{\nu} = 3{,}244$, 1,656, 1,532, 1,508, 1,488, 1,472, 1,372, 1,264, 1,216, 1,196, 1,168, 1,044, 1,028, 784 cm^{-1}; MS (70 eV): $m/z = 379$ (M^+, 68), 336 (58), 292 (10), 43 (100).

N-[2-Methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl]-N-[(4-methylphenyl)sulfonyl]acetamide (**16**, $C_{27}H_{23}NO_5S$)

Ice-cooled solution of 1.21 g **8a** (3.8 mmol) in 25 cm^3 dry THF was treated with 0.36 g 60 % NaH (15.0 mmol) and then 1.50 g TsCl (7.9 mmol). The mixture was stirred at 0–5 °C for 30 min, poured into 100 cm^3 water, neutralized with NH_4Cl, and extracted with ethyl acetate (3×50 cm^3). The combined organic fractions were dried with Na_2SO_4, treated with charcoal, and filtered. The solvent was removed under reduced pressure. Product was isolated by flash chromatography on silica gel with petroleum ether/CH_2Cl_2 (3:1) as eluent. Recrystallization from petroleum ether/CH_2Cl_2 afforded 1.22 g (68 %) **16** as a dark yellow solid. M.p.: 186–187 °C; $R_f = 0.60$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 8.70$–8.68 (1H, m, H_{Ar}), 8.05 (2H, d, $J = 8.4$ Hz, H_{Ts}), 7.83–7.80 (1H, m, H_{Ar}), 7.57–7.46 (2H, m, H_{Ar}), 7.36 (2H, d, $J = 8.4$ Hz, H_{Ts}), 7.01 (1H, d, $J = 3.3$ Hz, H_{Fur}), 6.49 (1H, s, H_{Fur}), 6.31 (1H, d, $J = 3.3$ Hz, H_{Fur}), 2.55 (3H, s, CH_3), 2.51 (3H, s, CH_3), 2.48 (3H, s, CH_3), 1.71 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 170.9$, 160.8, 153.2, 150.4, 145.6, 145.3, 135.9, 131.2, 130.1 (2C), 129.2, 129.1 (2C), 128.7, 127.0, 126.0, 125.5, 122.1, 121.5, 114.4, 112.1, 107.8, 100.8, 24.0, 21.7, 14.7, 13.9 ppm; IR (KBr): $\bar{\nu} = 1{,}709$, 1,594, 1,354, 1,243, 1,208, 1,168, 1,084, 1,011, 947, 792, 760 cm^{-1}; MS (70 eV): $m/z = 318$ ($M^+ - Ts$, 18), 303 (10), 276 (60), 260 (22), 203 (12), 176 (11), 91 (56), 65 (34), 51 (14), 43 (100).

4-Methyl-N-[2-methyl-9-(5-methylfuran-2-yl)naphtho[2,3-b]furan-4-yl]benzenesulfonamide (**17**, $C_{25}H_{21}NO_4S$)

Compound **17** was obtained as a beige solid from **16** by methods applied for the synthesis of **8**—method A (1.34 g, 78 %) or B (1.50 g, 87 %). M.p.: 199–200 °C; $R_f = 0.56$ (acetone/CH_2Cl_2/petroleum ether = 1:1:2); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 8.53$–8.50 (1H, m, H_{Ar}), 7.68–7.65 (1H, m, H_{Ar}), 7.50 (2H, d, $J = 8.4$ Hz, H_{Ts}), 7.41–7.35 (1H, m, H_{Ar}), 7.24–7.19 (1H, m, H_{Ar}), 7.10 (2H, d, $J = 8.4$ Hz, H_{Ts}), 6.90 (1H, d, $J = 3.3$ Hz, H_{Fur}), 6.68 (1H, s, NH), 6.41 (1H, s, H_{Fur}), 6.26 (1H, d, $J = 3.3$ Hz, H_{Fur}), 2.47 (3H, s, CH_3), 2.44 (3H, s, CH_3), 2.33 (3H, s, CH_3) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): $\delta = 158.7$, 152.7, 150.6, 146.0, 143.6, 136.4, 129.8, 129.5 (2C), 128.5, 128.0, 127.3 (2C), 126.1, 125.0, 124.4, 122.1, 120.2, 113.6, 110.0, 107.5, 101.5, 21.4, 14.4, 13.9 ppm; IR (KBr): $\bar{\nu} = 3{,}276$, 1,601, 1,409, 1,379, 1,330, 1,161, 1,090, 946, 787, 756 cm^{-1}; MS (70 eV): $m/z = 431$ (M^+, 5), 227 (78), 234 (15), 204 (34), 190 (15), 178 (18), 91 (94), 77 (15), 65 (67), 51 (24), 43 (100).

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