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A convenient access to 1,3-disubstituted furo[3,4-*b*]indoles by acid ion-exchange resin-catalyzed furan formation

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ABSTRACT

Efficient synthesis of furo[3,4-*b*]indoles starting from the corresponding indole is reported. The first route involves derivatization, protection, and deprotection steps, which stretch the syntheses. The second method provides a shorter and more efficient strategy to accessing the furoindole. The innovation starts with alkylation at C-2 of the indole presenting at the C-3 position a ketone-acetal, followed by the cycloaromatization catalyzed by polymeric ion-exchange resins. The second route represents a significant improvement over other methods previously described.

1. Introduction

Furoindole dienes have been the subject of intense research for many years and they are valuable tools in organic chemistry. These intermediates have been applied in diverse inter- and intramolecular cycloaddition reactions. Substituted furoindoles may be used as the starting material for the synthesis of drugs with a wide range of pharmaceutical effects.[1,2,9]

Cycloaddition reactions from furoindoles offer rapid access to polycyclic systems. Isobenzofuran derivatives are molecules of great synthetic utility.[3] Many of these rather reactive molecules have been found to act as versatile precursors and to participle promptly in a variety of reactions including cycloadditions.[4]

Due to their value as synthetic intermediates, furo[3,4-*b*]indoles have attracted increasing attention.[1,2,9] Many different routes have been published for the preparation of these dienes, which in several cases have only been prepared in situ. In general, these interesting molecules are short-lived. A few years ago, we reported the synthesis of tetracyclic compounds containing the 1,4-benzodioxin from the appropriate furo[3,4-*b*][1,4]benzodioxan.[5] Other authors worked on the synthesis of furoindoles from distinct starting materials. In general, the synthesis involved lithiation of protected indoles followed by quenching with aldehydes, oxidation and cyclization of the corresponding hydroxyketone.[6] Gribble has reported a route to formylation of the *N*-protected hydroxymethylindole via metalation and alkylation of the 2-formyl group by Grignard reagents. This is followed by oxidation of the primarily alcohol and intramolecular cyclization. The alkylation of the indole at the C-2 position of a hindered 3-imino group prepared from the corresponding aldehyde was also studied.[7]

In 2002, Gribble et al. described a synthesis of 1,3-dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole from the 3-acetyl-1-(phenylsulfonyl)indole in 49% overall yield. The key intermediate was an enol ether formed by treatment of the methylketone with LDA followed by the addition of TBSOTf (*tert*-butyldimethylsilyl triflate).[8] For the preparation of ellipticine and isoellipticine, the 1,3-dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole was prepared from 3-ethylindole in six steps (46% yield) or from the corresponding indole-3-carboxaldehyde in four steps (21% yield).[9] In all the methods mentioned so far the group linked to the C-3 of the indole was an alcohol, an aldehyde or an alkyl and there was no evidence of alkylation of ketone acetal.[10] More recently,[11] the 1,3-unsubstituted furo[3,4-*b*]indoles was synthesized from the *N*-sulfonyl-indole-3-carboxaldehyde by a more efficient route with 48% overall yield. A key intermediate of this original method was an ethylene acetal of the 3-indole carbaldehyde, which unfortunately was not conducive to a general synthesis of 1,3-disubstituted furoindoles because of the steric hindrance. Although these routes allow us to obtain a wide range of derivatives, they involve complex synthesis, which limits their applicability and reduce their field of application.

Results of our previous experiments indicated that the furoindole formation occurs only if the 1-position of the indole is substituted by a withdrawing group, such as phenylsulfonyl, which is a classical protecting and activating group. Pursuant to our interest in novel indole chemistry, we have developed two distinct routes to general 1,3-disubstitued furoindoles from the commercial indole compounds.

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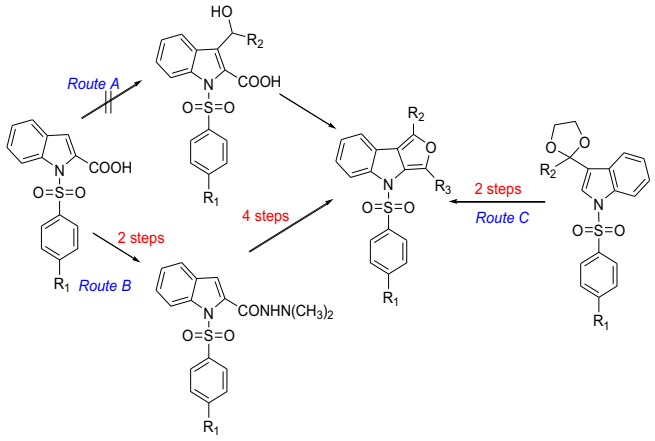
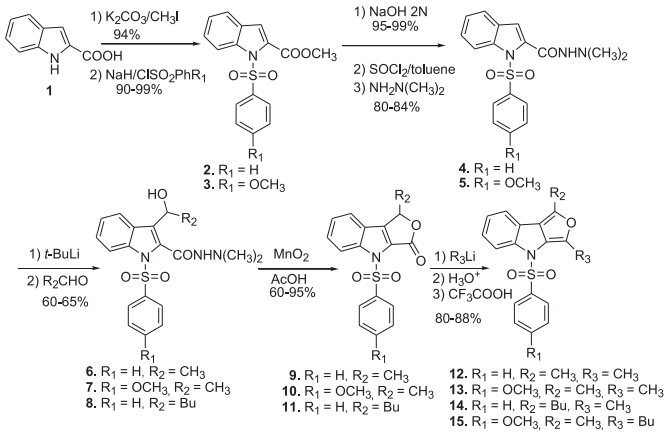
2. Results and discussion

As in our previous studies the synthesis of furodienes could be accomplished by indole alkylation and subsequent intramolecular cyclization (Scheme 1).



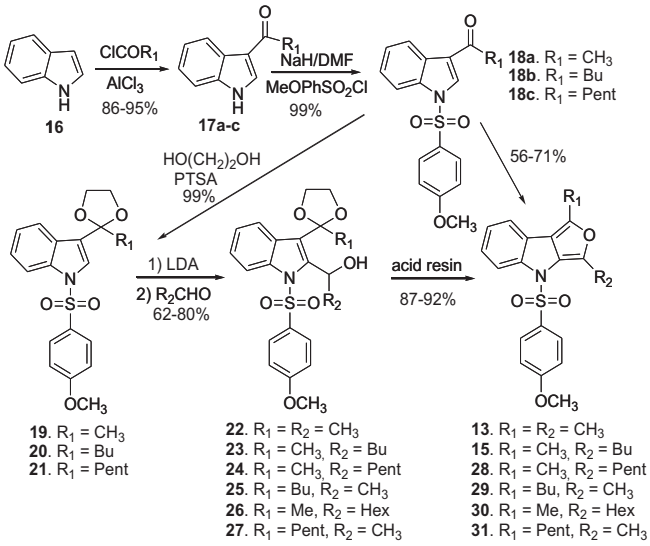
Scheme 1. Synthesis of 1,3-disubstituted furo[3,4-*b*]indoles.

First we attempted to repeat a route we had established earlier for the preparation of 1,3-disusbstituted furobenzodioxan compounds, but with indoles this procedure was unsuccessful (Scheme 1, *route A*).[5d] Our failure to synthesize similar compounds can be attributed to the carboxylic group at the 2 position of the indole.[12] For this reason the derivatisation of indole-2-carboxylic acid was attempted (Scheme 1, *route B*). The hydrazides **4** and **5** were prepared as follows from the indole-2-carboxylic acid (**1**) (Scheme 2). Several attempts were made to convert the indole-carboxylic acid **1** to the corresponding hydrazide and the results demonstrated that the protection of the carboxylic acid is necessary for the N-protection of the indole. Metalation at the position 3, accomplished with *t*-BuLi in THF, was followed by oxidation of the hydrazide, affording the tricyclic lactones **9**–**11**.[11] This procedure requires additional alkylation and dehydration from the intermediate lactone to the furoindole (*route B*).



Scheme 2. Synthesis of furo[3,4-*b*]indoles using *route B*.

Subsequently our attention has been directed to alkylation at the C-2 or C-3 position of indoles and cyclization to the expected furoindoles. We attempted the alkylation of ketone ethylene acetals (*route C*), which to our knowledge has not been reported. Compounds **17a**–**c** are available from acylation of indole **16** under classical conditions (Scheme 3).[13] N-protection of **17a**–**c** with 4-methoxyphenylchlorosulfonyl chloride gave **18a**–**c**. The carbonyl group of the resulting *N*-sulfonylindoles, without further purification, was protected by formation of the acetal (**19**–**21**).



Scheme 3. Synthesis of furo[3,4-*b*]indoles by *route C*.

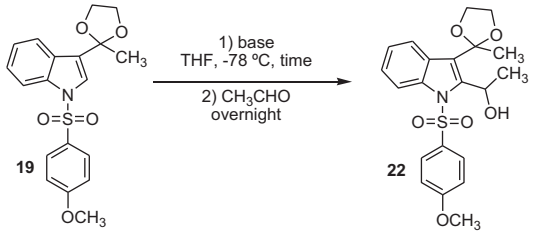
The 4-methoxyphenylsulfonic and the phenylsulfonic groups were chosen because their withdrawing character is suitable for diene formation. The alkylation at position 2 of the indole (**19**–**21**) was accomplished using *t*-BuLi or LDA as a base and a variety of aldehydes were used. Alcohols **22**–**27** were obtained as unstable compounds joined to the acetal. On treatment of non-purified hydroxyketals **22**–**27** with acid resin in polar solvent, dienes **13**, **15**, and **28**–**31** were obtained.

The second method reduces the number of steps in the synthesis of 1,3-disubstituted furoindoles and, moreover, it permits the isolation of the ethylene glycol ketals intermediates but no its purification because of the instability. Acid ion-exchange resin as solid catalyst plays a key role in this route. The acid resin mediated the ketal hydrolysis and intramolecular cyclization followed by dehydration. The use of a solid acid ion-exchange resin (Amberlyst-15) instead of a classical acid is strong economic driving and environmentally friendly, since it is inexpensive and a recyclable heterogeneous catalyst.[14]

We established that the indole ketals can be converted into the corresponding hydroxy derivatives by alkylation. Several bases and conditions were tested for the 2-indole alkylation (see Table 1). For example the use of *t*-BuLi and TMEDA gave mixtures of the desired compound in low yield, together with unreacted starting material (Table 1, entries 2–4). Use of LDA in THF at −78 °C gave the corresponding alcohol in acceptable yields (Table 1, entries 6 and 7). Small amounts of base (<3 equiv) led to low yields of product (Table 1, entry 5). Addition of TMEDA did not significantly affect the yield of alkylation (Table 1, entry 8).

The cyclization reaction did not occur in certain conditions. The use of trifluoroacetic acid in toluene at reflux did not give the diene. Although the use of PTSA in toluene afforded degradation products of the starting hydroxyketal (Table 2, entry 3), the mixture of trifluoroacetic acid and sodium sulfate at room temperature in CH_2Cl_2 led predominantly to the recovery of unreacted starting material (Table 2, entry 1). The use of HCl in isopropanol provided the diene in 52% yield. Moreover, the intermediate hydroxyketal was converted directly, in a one-pot reaction, to the diene by treatment with acid resin in isopropanol, without previous hydrolysis to the corresponding aryl alkyl ketone. Thus, stirring the hydroxyketal in isopropanol/H_2O (99:1) in

Table 1
Alkylation of the indoleketal **19**



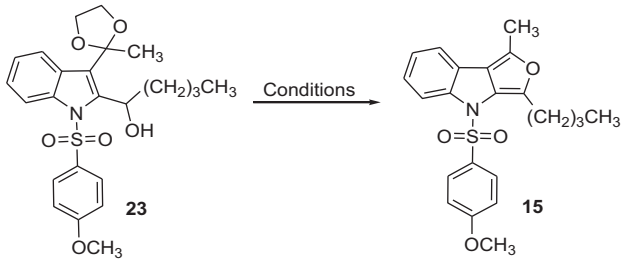
Entry	Base	Time (h)	Yield[a] (%)
1	LiHMDS 3.0 equiv	3	—
2	*t*-BuLi 1.5 equiv+TMEDA 1.5 equiv	1	—
3	*t*-BuLi 3.0 equiv+TMEDA 3.0 equiv	1	5
4	*t*-BuLi 3.0 equiv+TMEDA 3.0 equiv	3	33
5	LDA 1.5 equiv	3	18
6	LDA 3.0 equiv	3	62
7	LDA 4.0 equiv	3	63
8	LDA 3.0 equiv+TMEDA 3.0 equiv	3	68

[a] Isolated yield.

the presence of acid resin afforded the diene in 92% yield (Table 2, entry 5). Acid ion-exchange resins are effective catalysts for furan formation from hydroxyketals, such as **23**. The diene **13** was up-scaled, and 20 g was easily prepared using the method described above.

Finally, to show the synthetic interest of the dienes obtained, we synthesized the ellipticine, a natural compound with anticancer properties.[15,16] The optimized process route is shown in Scheme 4. The diene **13** was successfully converted to the mixture of isomeric Diels–Alder adducts **32a** and **32b** (100% conversion) by cycloaddition with 3,4-pyridyne as the dienophile, obtained from 3-bromopyridine. These adducts were deoxygenated with $Fe_2(CO)_9$ without previous purification as described elsewhere.[17]

Table 2
Intramolecular cyclization of hydroxylketals



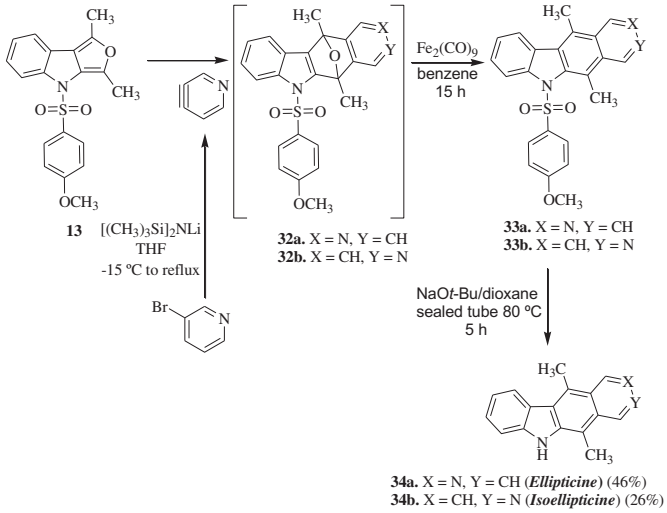
Entry	Conditions	Solvent	Products (yield)[a]
1	CF_3COOH, Na_2SO_4	CH_2Cl_2	**15** (<10%)
2	CF_3COOH, $(CF_3CO)_2O$	Toluene	Trace
3	PTSA	Toluene	—
4	HCl	Isopropanol	**15** (52%)
5	Acid resin	*i*-PrOH/1% H_2O	**15** (92%)

[a] Isolated yield.

The last step, basic desulfonylation using NaO*t*-Bu in dioxane in a sealed tube,[18] afforded the ellipticine (**34a**) in 46% overall yield and the regioisomer isoellipticine (**34b**) was obtained in 26% after separation by column chromatography over silica gel (hexane/ethyl acetate). These compounds were identical with commercial samples purchased from Sigma–Aldrich.

3. Conclusions

In summary, we report two synthetic routes to furoindoles. In particular, the shorter route proved to be of value for the synthesis of 1,3-disubstituted furo[3,4-*b*]indoles from the corresponding 3-alkylketones. The dienes obtained are more stable and less reactive than the corresponding benzo[*c*]furans. These furoindoles could be synthesized by alkylation of protected ketones and subsequent intramolecular cyclization. This is a mild efficient method for the synthesis of furoindoles, and different alkyl substituents were tolerated. This procedure is simple and broadly applicable. *Route B*, starting from the indole-2-carboxylic acid, led to the diene in eight steps with yields between 24 and 40%, while *route C* provide the same dienes in four steps from the corresponding ketone-indole in overall yields of 65–70%. This furo[3,4-*b*]indole may be a versatile precursor for the preparation of molecules with high biological activity. More detailed applications are under investigation in our laboratory and will be reported in due course.



Scheme 4. Synthesis of ellipticine.

4. Experimental section

4.1. Materials

Commercial reagents and solvents were purchased from Sigma–Aldrich and SDS-Carlo Erba.

4.2. General methods

Melting points were obtained on an MFB-595010M Gallenkamp apparatus with digital thermometer in open capillary tubes and are uncorrected. IR spectra were obtained using an FTIR Perkin–Elmer 1600 Infrared Spectrophotometer. Only noteworthy IR absorptions are listed (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 (200 and 50.3 MHz, respectively) or Varian Gemini-300 (300 and 75.5 MHz) instrument using $CDCl_3$ as solvent with tetramethylsilane as internal standard, $(CD_3)_2CO$ or $(CD_3)_2SO$. Other ^1H, ^{13}C NMR spectra and heterocorrelation ^1H–^{13}C (HSQC and HMBC) experiments were recorded on a Varian Gemini-400 (400 MHz and 100.6 MHz). Chemical shifts (δ scale) are reported in parts per million (ppm) relative to the central peak of the solvent (δ=7.26 ppm for $CDCl_3$ in ^1H NMR and δ=77.16 ppm for $CDCl_3$ in ^{13}C NMR). Mass spectra were taken on a Hewlett–Packard 5988-A. Column chromatography was performed with silica gel (E. Merck, 70–230 mesh). Reactions were monitored by TLC using 0.25 mm silica gel F_{254} (E. Merck). Elemental analysis for C, H, and N were determined on a Carlo Erba-1106 analyzer. All reagents were of commercially quality or were purified before use. Organic solvents were of analytical grade or were purified by standard procedures. Commercial products were obtained from Sigma–Aldrich. Reactions were carried out under argon.

4.3. Preparation of 1,3-disubstituted furo[3,4-*b*]indoles. *Route B*

4.3.1. Preparation of methyl indole-2-carboxylate. Indole-2-carboxylic acid (1.99 g, 12.3 mmol) was dissolved in a flask by distilled DMF. Then, 2 equiv of both, $NaHCO_3$ (1.59 g) and CH_3I (3 mL), were added to the flask. The mixture was stirred overnight at room temperature. The crude product was extracted with ether/purified water (3×20 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. This procedure gave the ester as white solid in 94% of average yield. The analytical data is in agreement with the reported data.[2,9]

*4.3.2. Preparation of methyl N-benzenesulfonylindole-2-carboxylate (**2**) and methyl N-(4-methoxybenzenesulfonyl)indole-2-carboxylate (**3**).* Methyl indole-2-carboxylate (1.86 g, 10.6 mmol) was dissolved in a flask by distilled DMF. NaH (0.50 g, 1.1 equiv) and $PhSO_2Cl$ (1.6 mL, 1.2 equiv) or $MeOSO_2Cl$ (2.62 g, 1.2 equiv) were slowly added to the flask on a pre-cooled bath of ice. The mixture was stirred overnight at room temperature. The crude product was extracted with ethyl ether/purified water (3×20 mL), the organic layer was dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure to obtain the desired product as a white solid in 90–99% of average yield. Compounds (**2**)[19] and (**3**) mp: 116–118 °C (methanol). IR (KBr) ν cm^{-1}: 1731 (C=O); 1594 (C=C); 1260 (Ar–O); 1205 (Ar–S); 1087 (C–O). NMR ^1H ($CDCl_3$, 200 MHz) δ (ppm): 3.71 (s, 3H CH_3–OC_6H_4); 3.92 (s, 3H, CH_3–OOC); 6.85 (d, *J*=9.0 Hz, 2H, H-3′, H-5′); 7.12 (s, 1H, H-3); 7.22 (t, *J*=7.8 Hz, 1H, H-5); 7.39 (t, *J*=7.0 Hz, 1H, H-6); 7.51 (d, *J*=7.6 Hz, 1H, H-4); 7.96 (d, *J*=9.0 Hz, 2H, H-2′, H-6′); 8.10 (d, *J*=8.4 Hz, 1H, H-7). NMR ^{13}C ($CDCl_3$, 50.3 MHz) δ (ppm): 52.6 (CH_3–OOC); 55.4 (CH_3–OC_6H_4); 113.9 (CH, C-3′, C-5′); 115.1 (CH, C-3); 116.4 (CH, C-7); 122.3 (CH, C-6); 123.8 (CH, C-5); 126.7 (CH, C-4); 127.1 (C, C-2); 127.9 (C, C-1′); 129.5 (C, C-2′, C-6′); 131.2 (C, C-3a); 137.8 (C, C-7a); 161.6 (C, C-4′); 163.5 (C, C=O). $C_{17}H_{15}NO_5S$ (345.07): calcd C 59.12, H 4.38, N 4.06; found C 59.43, H 4.68, N 3.87.

*4.3.3. Preparation of N-benzenesulfonylindole-2-carboxylic acid and N-(4-methoxybenzenesulfonyl)indole-2-carboxylic acid. Preparation of N-benzenesulfonyl-2-chlorocarbonylindole, N-benzenesulfonyl-2-(N,N-dimethylhydrazinecarbonyl)indole (**4**), 2-chlorocarbonyl-N-(4-methoxybenzenesulfonyl)indole, and 2-(N,N-dimethylhydrazinecarbonyl)-N-(4-methoxybenzenesulfonyl)indole (**5**).* The *N*-protected ester (6.37 mmol) dissolved in ethanol (20 mL) was treated with NaOH 2 N (30 mL). The resulting mixture was stirred overnight at room temperature. Then, ethanol was removed under reduced pressure and the remaining ester was extracted with a mixture of ethyl ether and drops of ethyl acetate (3×20 mL). Finally, the addition of HCl 1 N let us extract the *N*-protected acid with the same solvent mixture indicated above. The latter organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. This gave the desired carboxylic acid as a white solid in 95–99% of average yield. Alternatively, these carboxylic acids can be crystallized from MeOH. The carboxylic acid (2.34 mmol) and an excess of $SOCl_2$ (1.2 mL) were added in a flask dissolved in toluene (20 mL). The mixture was heated at reflux temperature and stirred for 2 h. After removing the toluene under reduced pressure, the obtained solid was dissolved in CH_2Cl_2 and *N*,*N*-dimethylhydrazine (1.5 equiv) was added. The mixture was stirred overnight at room temperature. The crude product was washed with NaOH 2 N (3×10 mL), the organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. Purification by silica gel column chromatography, using hexane/ethyl acetate as eluent gave the desired compound as a white solid in 80–84% of average yield. Compound (**4**) mp: 170–173 °C (hexane/AcOEt). IR (KBr) ν cm^{-1}: 1658 (C=O); 1455; 1174 (C–N); 1191 (Ar–S). NMR ^1H ($CDCl_3$, 300 MHz) δ (ppm): 2.74 (s, 6H, CH_3N); 6.93 (s, 1H, H-3); 7.28–7.52 (m, 8H, Ar); 8.04 (s, 1H, NH); 8.10 (d, *J*=8.9 Hz, 1H, H-4). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 46.2 (CH_3); 47.4 (CH_3); 111.5 (CH, C-3); 114.4 (CH, C-7); 122.3 (CH, C-6); 124.2 (CH, C-5); 126.0 (CH, C-4); 127.3 (CH, C-2′, C-6′); 129.4 (CH, C-4′); 129.6 (CH, C-3′, C-5′); 134.5 (CH, C-3a); 134.6 (C, C-1′); 135.0 (C, C-2); 135.4 (C, C-7a); 158.7 (C, C=O). $C_{17}H_{17}N_3O_3S$ (343.09): calcd C 59.46, H 4.99, N 12.24; found C 59.88, H 4.78, N 11.98. Compound (**5**) mp 126–128 °C (hexane/AcOEt). IR (KBr) ν cm^{-1}: 3202 (NH); 1664 (C=O); 1594 (C=C); 1265 (Ar–O); 1211 (Ar–S); 1169 (C–O); 1092 (C–O). NMR ^1H ($CDCl_3$, 200 MHz) δ (ppm): 2.76 (s, 6H, CH_3–N); 3.77 (s, 3H, CH_3–O); 6.87 (s, 3H, H-3); 6.86 (d, *J*=9.0 Hz, 2H, H-3′, H-5′); 6.97 (s, 1H, NH); 7.23 (t, *J*=7.4 Hz, 1H, H-5); 7.38 (t, *J*=7.0 Hz, 1H, H-6); 7.47 (d, *J*=7.8 Hz, 1H, H-4); 7.99 (d, *J*=9.0 Hz, 2H, H-2′, H-6′); 8.08 (d, *J*=8.2 Hz, 1H, H-7). $C_{18}H_{19}N_3O_4S$ (373.11): calcd C 57.89, H 5.13, N 11.25; found C 58.34, H 5.09, N 11.43.

*4.3.4. Preparation of N-benzenesulfonyl-2-(N,N-dimethylhydrazinecarbonyl)-3-(1-hydroxyalkyl)-indoles (**6**, **8**) and 3-(1-hydroxymethyl)-2-(N,N-dimethylhydrazinecarbonyl)-N-(4-methoxybenzenesulfonyl)indole (**7**).* The compound (1.5 mmol) dissolved in THF (10 mL) was transferred to a three-necked anhydrous flask equipped with stirrer and cooled to −78 °C by a solid carbon dioxide–acetone bath. Then, 3 equiv of TMEDA (0.7 mL, 4.5 mmol) and *t*-BuLi 1.5 M (3.0 mL, 4.5 mmol) were added dropwise. The mixture was stirred at controlled temperature for 3 h. After that, 5 equiv of the corresponding aldehyde (7.5 mmol) were added. The mixture was stirred overnight at room temperature. The crude product was treated with NH_4Cl and then extracted with purified water/mixture of ethyl ether and drops of ethyl acetate (3×15 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure, giving the desired compound as yellow oil in 60–65% of gross average yield. Compound (**6**) oil. IR (KBr) ν cm^{-1}: 3512 (OH, NH); 1653 (C=O); 1202 (C–O); 1175 (C–N). NMR ^1H ($CDCl_3$, 300 MHz) δ (ppm): 1.53 (d, *J*=8.5 Hz, 3H, CH_3N); 2.71 and 2.78 (s, 3H, CH_3); 5.20 (q, *J*=8.5 Hz, 1H, CH–O); 7.27–7.53 (m, 7H, Ar); 7.98 (d, *J*=9 Hz, 1H, H-7); 8.17 (d, *J*=9.0 Hz, 1H, H-4). 9.42 (br s, 1H, NH). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 23.1 (CH_3); 46.9 (CH_3 (×2)); 105.4 (CH, C-7); 115.8 (CH, C-4); 121.4 (CH, C-6); 124.5 (CH, C-5); 127.5 (CH, C-2′ and C-6′); 128.8 (CH, C-3′, C-5′); 129.0 (C, C-3); 132.1 (C, C-3); 137.0 (C, C-1′); 145.5 (C, C-7a); 160.8 (C, C=O). $C_{19}H_{21}N_3O_4S$ (387.13): calcd C 58.90, H 5.46, N 10.85; found C 59.88, H 5.78, N 10.65. Compound (**7**) mp: 144–146 °C (hexane/AcOEt). IR (KBr) ν cm^{-1}: 3268 (OH, NH); 1645 (C=O); 1594 (C=C); 1265 (Ar–O); 1210 (Ar–S); 1170 (C–O); 1070 (C–O). NMR ^1H ($CDCl_3$, 200 MHz) δ (ppm): 1.51 (d, *J*=6.8 Hz, 3H, CH_3–C); 2.70 (s, 6H, CH_3–N); 3.70 (s, 3H, CH_3–O); 5.13 (q, *J*=6.6 Hz, 1H, CH–O); 6.80 (d, *J*=9.0 Hz, 2H, H-3′, H-5′); 7.19 (t, *J*=8.0 Hz, 1H, H-5); 7.34 (t, *J*=8.0 Hz, 1H, H-6); 7.70 (d, *J*=7.8 Hz, 1H, H-4); 7.91 (d, *J*=9.0 Hz, 2H, H-2′, H-6′); 8.02 (d, *J*=7.8 Hz, 1H, H-7); 9.81 (s, 1H, NH). $C_{20}H_{23}N_3O_5S$ (417.14): calcd C 57.54, H 5.55, N 10.97; found C 57.32, H 5.89, N 10.76. Compound (**8**) oil. IR (KBr) ν cm^{-1}: 3299 (OH, NH); 1657 (C=O); 1175 (C–N). NMR ^1H ($CDCl_3$, 300 MHz) δ (ppm): 0.97 (t, *J*=7.8 Hz, 3H, CH_3N); 1.20–1.34 (m, 4H, CH_2); 2.53 (s, 6H, CH_3–N); 4.62 (t, *J*=7.8 Hz, 1H, CH–O); 5.24 (br s, 1H, OH); 7.27–7.62 (m, 4H, Ar); 7.70–7.82 (m, 2H, Ar); 7.99 (d, *J*=8.2 Hz, 2H, H-2′, H-6′). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 16.2 (CH_2); 22.1 (CH_2); 24.1 (CH_2); 30.2 (CH_2); 46.9 (CH_3); 68.9 (CH, CH–O); 113.9 (CH, C-7); 126.3 (CH, C-4); 127.4 (CH, C-6); 127.7 (CH, C-5); 128.4 (CH, C-2′ and C-6′); 128.9 (CH, C-3′, C-5′); 123.8 (C, C-4a); 133.9 (C, C-3); 136.1 (C, C-1′); 136.9 (C, C-2); 137.2 (C, C-7a); 162.1 (C, C=O). $C_{22}H_{27}N_3O_4S$ (429.17): calcd C 61.52, H 6.34, N 9.78; found C 61.23, H 6.68, N 9.55.

*4.3.5. Preparation of 1-alkyl-N-benzenesulfonyl-3-oxo-(1H)-furo[3,4-b]indoles (**9**, **11**) and N-(4-methoxybenzenesulfonyl)-1-methyl-3-oxo-(1H)-furo[3,4-b]indole (**10**).* The starting material (2.24 mmol), dissolved in anhydrous CH_2Cl_2 (20 mL), 10 equiv of

MnO_2 (2.51 g, 28.87 mmol) and 10 equiv of glacial acetic acid (1.4 mL, 22.4 mmol) were added in an anhydrous flask and stirred overnight at room temperature. The crude product was filtered and washed with $NaHCO_3/CH_2Cl_2$ (3×10 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. Purification by silica gel column chromatography, using hexane/ethyl acetate as eluent, allowed us to obtain the intermediate lactone as yellow oil in 60–95% of average yield. Compound (**9**) mp=164–166 °C (hexane/AcOEt). IR (KBr) ν cm^{-1}: 1762 (C=O); 1377; 1183 (C–N); 1039 (C–O). NMR ^1H ($CDCl_3$, 200 MHz) δ (ppm): 1.67 (d, J=6.6 Hz, 3H, CH_3N); 5.59 (q, J=6.6 Hz, 1H, CH–CH_3); 7.27–7.45 (m, 3H, Ar); 7.48 (d, J=7.8 Hz, 1H, H-7); 7.54 (d, J=7.4 Hz, 2H, H-3′, H-5′); 8.12 (d, J=7.4, 2H, H-2′, H-6′); 8.42 (d, J=7.8 Hz, 1H, H-4). NMR ^{13}C ($CDCl_3$, 50.4 MHz) δ (ppm): 19.9 (CH_3); 73.9 (CH–O); 115.7 (CH, C-5); 120.9 (CH, C-8); 121.4 (C, C-8b); 124.5 (CH, C-6); 127.3 (C, C-8a); 127.4 (CH, C-3′ and C-5′); 128.9 (CH, C-7); 129.4 (CH, C-2′, C-6′); 134.4 (C, C-4′); 137.9 (C, C-1′); 142.4 (C, C-3a); 148.0 (C, C-4a); 160.7 (C, C=O). $C_{17}H_{13}NO_4S$ (327.06): calcd C 62.37, H 4.00, N 4.28; found C 62.12, H 4.44, N 3.98. Compound (**10**) mp: 139–141 °C (hexane/AcOEt). IR (KBr) ν cm^{-1}: 1768 (C=O); 1594 (C=C); 1263 (Ar–O); 1221 (Ar–S); 1171 (C–O); 1084 (C–O). NMR ^1H ($CDCl_3$, 200 MHz) δ (ppm): 1.67 (d, J=6.8 Hz, 3H, CH_3–C); 3.81 (s, 3H, CH_3–O); 5.56 (q, J=6.8 Hz, 1H, CH–O); 6.92 (d, J=9.0 Hz, 2H, H-3′, H-5′); 7.37 (t, J=7.0 Hz, 1H, H-5); 7.58 (m, 2H, H-4, H-6); 8.10 (d, J=9.0 Hz, 2H, H-2′, H-6′); 8.36 (d, J=8.8 Hz, 1H, H-7). NMR ^{13}C ($CDCl_3$, 50.3 MHz) δ (ppm): 19.9 (CH_3–C); 55.7 (CH_3–O); 73.8 (CH, CH–O); 114.5 (CH, C-3′, C-5′); 115.7 (CH, C-5); 120.8 (CH, C-6); 121.3 (C, C-8b); 123.3 (C, C-1′); 124.2 (CH, C-7); 127.3 (C, C-8a); 128.7 (C, C-8); 129.8 (CH, C-2′, C-6′); 142.8 (C, C-3a); 147.5 (C, C-4′); 143.2 (C, C-3a); 149.3 (C, C-4a); 164.1 (C, C=O). $C_{18}H_{15}NO_5S$ (357.07): calcd C 60.49, H 4.23, N 3.92; found C 60.34, H 4.54, N 3.76. Compound (**11**) oil. IR (KBr) ν cm^{-1}: 1764 (C=O); 1379; 1187 (C–N); 1064 (C–O). NMR ^1H ($CDCl_3$, 300 MHz) δ (ppm): 0.85 (t, J=6.7 Hz, 3H, CH_3N); 1.29 (m, 4H, CH_2); 1.97 (m, 4H, CH_2–); 5.41 (q, J=6.7 Hz, 1H, CH–O); 7.21–7.61 (m, 5H, Ar); 8.05 (d, J=6.9 Hz, 2H, H-2′, H-6′); 8.21 (d, J=6.9 Hz, 1H, H-8). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 13.8 (CH_3); 22.3 (CH_2); 26.6 (CH_2); 33.8 (CH_2); 77.4 (CH, CH–O); 115.5 (CH, C-7); 121.1 (CH, C-8); 121.8 (CH, C-8b); 124.5 (CH, C-6); 127.5 (CH, C-3′ and C-5′); 128.9 (CH, C-7); 129.3 (C, C-8a); 129.9 (CH, C-2′, C-6′); 134.3 (C, C-4′); 138.1 (C, C-1′); 143.0 (C, C-3a); 147.2 (C, C-4a); 158.2 (C, C=O). $C_{20}H_{19}NO_4$ (369.11): calcd C 65.02, H 5.18, N 3.79; found C 65.34, H 4.99, N 3.65.

4.3.6. Preparation of N-benzenesulfonyl-1,3-dialkyl-3-hydroxyfuro[3,4-b]indoles and 1,3-dialkyl-3-hydroxy-N-(4-methoxybenzenesulfonyl) furo[3,4-b]indoles. The compound (0.40 mmol) dissolved in THF (5 mL) was transferred to a three-necked anhydrous flask equipped with stirrer and cooled to −78 °C by a bath of solid carbon dioxide–acetone. Then, 2.5 equiv of alkyllithium (1.00 mmol) were added. The mixture was stirred at fixed temperature for 2 h. Then, the crude product was treated with NH_4Cl and extracted with purified water/mixture of ethyl ether and drops of ethyl acetate (3×10 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure, obtaining the crude compound as yellow oil.

*4.3.7. Preparation of N-benzenesulfonyl-1,3-dialkylfuro[3,4-b]indoles (**12**, **14**) and 3-alkyl-N-(4-methoxybenzenesulfonyl)-1-methylfuro [3,4-b]indoles (**13**, **15**).* The starting material (0.27 mmol) was dissolved in anhydrous CH_2Cl_2 (15 mL) and some drops of CF_3COOH (0.1 mL, 1.35 mmol), dried over Na_2SO_4, and stirred at room temperature for 4 h. The crude product was filtered and washed with $NaHCO_3/CH_2Cl_2$ (3×10 mL), the organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. Purification by silica gel column chromatography, using hexane/ethyl acetate as eluent, allowed us to obtain the desired dienes as yellow oil in 80–88% of average yield (24–40% global yields from indole-2-carboxylic acid). Compounds (**12**)[10] and (**13**). Mp: 166–168 °C (hexane/AcOEt). IR (ATR) ν cm^{-1}: 1594 (C=C); 1262 (Ar–O); 1184 (Ar–S); 1167 (C–O). NMR ^1H ($CDCl_3$, 400 MHz) δ (ppm): 2.43 (s, 3H, CH_3–Ar); 2.68 (s, 3H, CH_3–Ar); 3.74 (s, 3H, CH_3–O); 6.75 (d, J=9.0 Hz, 2H, H-3′, H-5′); 7.13–7.32 (m, 2H, H-6, H-7); 7.40 (d, J=7.5 Hz, 1H, H-5); 7.56 (d, J=9.0 Hz, 2H, H-2′, H-6′); 8.03 (d, J=8.4 Hz, 1H, H-8). NMR ^{13}C ($CDCl_3$, 100.6 MHz) δ (ppm): 13.1 (CH_3, CH_3–Ar); 14.3 (CH_3, CH_3–Ar); 55.6 (CH_3, CH_3–O); 114.1 (CH, C-3′, C-5′); 116.8 (CH, C-5); 118.7 (C, C-8b); 121.1 (CH, C-8); 123.8 (C, C-3a); 124.6 (CH, C-6); 126.5 (CH, C-7); 128.2 (C, C-1′); 128.4 (C, C-8a); 129.3 (CH, C-2′, C-6′); 132.6 (C, C-4a); 138.1 (C, C-3); 145.2 (C, C-1); 163.6 (C, C-4′). $C_{19}H_{17}NO_4S$ (355.09): calcd C 64.21, H 4.82, N 3.94; found C 64.45, H 4.78, N 3.65. Compound (**14**) mp: 110–112 °C (hexane/AcOEt). IR (KBr) ν cm^{-1}: 1678 (C=C); 1455; 1362 (Ar–O); 1180 (Ar–S). NMR ^1H ($CDCl_3$, 300 MHz) δ (ppm): 0.98 (t, J=7.3 Hz, 3H, $CH_3CH_2CH_2CH_2$–Ar); 1.44 (sext, J=7.3 Hz, 2H, $CH_3CH_2CH_2CH_2$–Ar); 1.75 (qt, J=7.3 Hz, 2H, $CH_3CH_2CH_2CH_2$–Ar); 2.44 (s, 3H, CH_3–Ar); 3.11 (t, J=7.3 Hz, 2H, $CH_3CH_2CH_2CH_2$–Ar); 7.18 (dt, J_1=1.1 Hz, J_2=7.5 Hz, 1H, H-6); 7.20–7.24 (m, 1H, H-7); 7.25–7.33 (dt, J_1=1.3 Hz, J_2=7.3 Hz, 2H, H-3′, H-5′); 7.39 (dd, J_1=1.1 Hz, J_2=7.5 Hz, 1H, H-5); 7.44 (m, 1H, H-4′); 7.64 (dd, J_1=1.4 Hz, J_2=8.4, 2H, H-2′, H-6′); 8.03 (dt, J_1=0.4 Hz, J_2=8.3 Hz, 1H, H-8). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 13.5 (CH_3, $CH_3CH_2CH_2CH_2$–Ar); 14.0 (CH_3, CH_3–Ar); 22.5 (CH_2, $CH_3CH_2CH_2CH_2$–Ar); 26.6 (CH_2, $CH_3CH_2CH_2CH_2$–Ar); 31.0 (CH_2, $CH_3CH_2CH_2CH_2$–Ar); 116.7 (CH, C-5); 118.3 (C, C-8b); 120.9 (CH, C-8); 123.7 (C, C-3a); 124.6 (CH, C-6); 126.3 (CH, C-7); 126.9 (CH, C-2′, C-6′); 127.5 (C, C-4a); 128.7 (CH, C-3′, C-5′); 133.4 (CH, C-4′); 136.6 (C, C-8a); 137.2 (C, C-1′); 138.1 (C, C-1); 144.9 (C, C-3). Compound (**15**) mp: 94–96 °C (hexane/AcOEt). IR (ATR) ν cm^{-1}: 1594 (C=C); 1264 (Ar–O); 1180 (Ar–S); 1161 (C–O). NMR ^1H ($CDCl_3$, 200 MHz) δ (ppm): 0.98 (t, J=7.2 Hz, 3H, $CH_3CH_2CH_2CH_2$–Ar); 1.41–1.43 (m, 2H, $CH_3CH_2CH_2CH_2$–Ar); 1.72–1.76 (m, 2H, $CH_3CH_2CH_2CH_2$–Ar); 2.44 (s, 3H, CH_3–Ar); 3.10 (t, J=7.3 Hz, 2H, $CH_3CH_2CH_2CH_2$–Ar); 3.73 (s, 3H, CH_3–O); 6.74 (d, J=9.0 Hz, 2H, H-3′, H-5′); 7.17 (td, J_1=1.3 Hz, J_2=7.4 Hz, 1H, H-7); 7.27 (td, J_1=1.5 Hz, J_2=7.5 Hz, 1H, H-6); 7.39 (dd, J_1=1.0 Hz, J_2=7.2 Hz, 1H, H-5); 7.55 (d, J=9.0 Hz, 2H, H-2′, H-6′); 8.02 (d, J=7.5 Hz, 1H, H-8). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 13.7 (CH_3, $CH_3CH_2CH_2CH_2$–Ar); 14.1 (CH_3, CH_3–Ar); 22.7 (CH_2, $CH_3CH_2CH_2CH_2$–Ar); 26.8 (CH_2, $CH_3CH_2CH_2CH_2$–Ar); 31.1 (CH_2, $CH_3CH_2CH_2CH_2$–Ar); 55.6 (CH_3, CH_3–O); 114.0 (CH, C-3′, C-5′); 117.0 (CH, C-5); 118.6 (C, C-8b); 121.1 (CH, C-8); 123.9 (C, C-3a); 124.7 (CH, C-6); 126.4 (CH, C-7); 127.9 (C, C-1′); 128.5 (C, C-8a); 129.3 (CH, C-2′, C-6′); 137.4 (C, C-4a); 138.2 (C, C-3); 145.3 (C, C-1); 163.5 (C, C-4′). $C_{22}H_{23}NO_4S$ (397.13): calcd C 66.48, H 5.83, N 3.52; found C 66.78, H 5.98, N 3.67.

4.4. Preparation of 1,3-disubstituted furo[3,4-b]indoles. *Route C*

*4.4.1. Preparation of 1,3-disubstituted furo[3,4-b]indoles. Route C. Preparation of 3-acylindoles (**17a–c**).* For the preparation of 3-acylindoles, we followed the method described by Stalick.[13] Using butyryl chloride and valeroyl chloride as reagents, we obtained the 3-acyl derivatives in good yields (86–95%). Note that 3-acetylindole was purchased from Sigma–Aldrich.

*4.4.2. Preparation of 1-[N-(4-methoxybenzenesulfonyl)indol-3-yl]alkanones (**18a–c**).* Indol-3-yl-alkanone (12.6 mmol) was dissolved in dry DMF. NaH (0.67 g, 16.4 mmol) was slowly added and stirred at room temperature for 30 min. Then, the flask was cooled down on a bath of ice and $MeOPhSO_2Cl$ (3.38 g, 16.4 mmol) dissolved in DMF was slowly added to the flask. The mixture was stirred at room temperature overnight. Then, the crude product was extracted with AcOEt/water (20:20 mL), the organic layers were dried over Na_2SO_4, and the solvent was removed under reduced pressure to

give the desired compound as a white solid in quantitative yield (99%). Compounds (**18a**),[20] (**18b**), and (**18c**).

*4.4.3. Preparation of 3-(2-alkyl-1,3-dioxolan-2-yl)-N-(4-methoxybenzene sulfonyl)-1H-indoles (**19**–**21**).* The 3-indolylalkanone (4.5 mmol), ethylene glycol (1.7 mL; 30.5 mmol) and a catalytic amount of PTSA were added in a flask containing toluene as a solvent. The mixture was heated at reflux temperature and stirred for 3–4 h. At the end of the reaction, the mixture was diluted with ethyl acetate (20 mL) and washed with $NaHCO_3$ 0.5 N aqueous solution (20 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure to give the crude ketal in quantitative yield (99%). Ketals are not purified due to its lack of stability. The reaction was monitored by TLC and ^1H NMR.

*4.4.4. Preparation of 3-(2-alkyl-1,3-dioxolan-2-yl)-2-(1-hydroxyalkyl)-N-(4-methoxybenzenesulfonyl)-1H-indoles (**22**–**27**).* The crude ketal (1.14 mmol) was dissolved in distilled THF in an anhydrous flask under argon atmosphere and was transferred to a three-necked anhydrous flask equipped with stirrer, cooled and maintained at −78 °C by a solid carbon dioxide–acetone bath. Then 3.5 equiv of LDA (2.2 mL; 3.96 mmol) were added. The mixture was stirred at controlled temperature for 3 h. After that, an excess of acetaldehyde (0.5 mL, 8.96 mmol) were added. The mixture was stirred at room temperature overnight. The crude product was treated with a saturated aqueous solution of NH_4Cl and then extracted with ethyl acetate (3×25 mL). The organic layer was dried over Na_2SO_4, the solvent was removed in vacuum to give the crude product (62–80%), which is not purified due to its lack of stability. The quality control of the reaction was monitored by TLC and ^1H NMR. Hydroxyketals are not purified due to its lack of stability.

*4.4.5. Preparation of N-(4-methoxybenzenesulfonyl)-1,3-dialkylfuro[3,4-b]indole (**28**–**31**).* 1.0 g of acid resin (Amberlyst-15) was added to the crude hydroxyketal compound (1.80 mmol) dissolved with a mixture of 1% purified water in *i*-PrOH and the solution was stirred at room temperature for 2 h. The mixture was filtered and the solvent was removed in vacuum to give the crude product. The obtained residue was purified by silica gel column chromatography using hexane/ethyl acetate as eluent to obtain the desired diene as a white solid in 87–92% yield (65–70% global yields from the *N*-protected alkanones).

*4.4.6. N-(4-Methoxybenzenesulfonyl)-1-methyl-3-pentylfuro[3,4-b]indole (**28**).* Yellow oil. IR (ATR) ν cm^{-1}: 1594 (C=C); 1262 (Ar–O); 1180 (Ar–S); 1166 (C–O). NMR ^1H ($CDCl_3$, 300 MHz) δ (ppm): 0.89–0.92 (m, 3H, $CH_3CH_2CH_2CH_2CH_2$–Ar); 1.27–1.32 (m, 2H, $CH_3CH_2CH_2CH_2CH_2$–Ar); 1.40–1.42 (m, 2H, $CH_3CH_2CH_2CH_2CH_2$–Ar); 1.74–1.78 (m, 2H, $CH_3CH_2CH_2CH_2CH_2$–Ar); 2.39 (s, 3H, CH_3–Ar); 3.10 (t, J=7.3 Hz, 2H, $CH_3CH_2CH_2CH_2CH_2$–Ar); 3.60 (s, 3H, CH_3–O); 6.64 (d, J=9.0 Hz, 2H, H-3′, H-5′); 7.12 (t, J=7.5 Hz, 1H, H-7); 7.23 (t, J=8.3 Hz, 1H, H-6); 7.34 (d, J=7.6 Hz, 1H, H-5); 7.53 (d, J=8.6 Hz, 2H, H-2′, H-6′); 8.01 (d, J=8.3 Hz, 1H, H-8). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 13.4 (CH_3, $CH_3CH_2CH_2CH_2CH_2$–Ar); 14.1 (CH_3, CH_3–Ar); 22.5 (CH_2, $CH_3CH_2CH_2CH_2CH_2$–Ar); 26.9 (CH_2, $CH_3CH_2CH_2CH_2CH_2$–Ar); 28.6 CH_2, ($CH_3CH_2CH_2CH_2CH_2$–Ar); 31.7 (CH_2, $CH_3CH_2CH_2CH_2CH_2$–Ar); 55.3 (CH_3, CH_3–O); 113.8 (CH, C-3′, C-5′); 116.7 (CH, C-5); 118.4 (C, C-8b); 120.9 (CH, C-8); 123.7 (C, C-3a); 124.5 (CH, C-6); 126.2 (CH, C-7); 127.7 (C, C-1′); 128.2 (C, C-8a); 129.1 (CH, C-2′, C-6′); 137.2 (C, C-4a); 138.1 (C, C-3); 145.1 (C, C-1); 163.4 (C, C-4′). $C_{22}H_{25}NO_4S$ (411.15): calcd C 67.13, H 6.12, N 3.40; found C 67.38, H 5.99, N 3.59.

*4.4.7. 1-Butyl-N-(4-methoxybenzenesulfonyl)-3-methylfuro[3,4-b]indole (**29**).* Mp: 87–89 °C (hexane/AcOEt). IR (ATR) ν cm^{-1}: 1594 (C=C); 1261 (Ar–O); 1184 (Ar–S); 1163 (C–O). NMR ^1H ($CDCl_3$, 300 MHz) δ (ppm): 0.90 (t, J=7.4 Hz, 3H, $CH_3CH_2CH_2CH_2$–Ar); 1.28–1.32 (m, 2H, $CH_3CH_2CH_2CH_2$–Ar); 1.65–1.69 (m, 2H, $CH_3CH_2CH_2CH_2$–Ar); 2.68 (s, 3H, CH_3–Ar); 2.77 (t, J=7.5 Hz, 2H, $CH_3CH_2CH_2CH_2$–Ar); 3.74 (s, 3H, CH_3–O); 6.75 (d, J=9.0 Hz, 2H, H-3′, H-5′); 7.18 (t, J=7.5 Hz, 1H, H-7); 7.28 (t, J=7.5 Hz, 1H, H-6); 7.40 (d, J=7.5 Hz, 1H, H-5); 7.55 (d, J=9.0 Hz, 2H, H-2′, H-6′); 8.03 (d, J=8.3 Hz, 1H, H-8). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 13.2 (CH_3, CH_3–Ar); 13.9 (CH_3, $CH_3CH_2CH_2CH_2$–Ar); 22.4 (CH_2, $CH_3CH_2CH_2CH_2$–Ar); 28.0 (CH_2, $CH_3CH_2CH_2CH_2$–Ar); 30.5 (CH_2, $CH_3CH_2CH_2CH_2$–Ar); 55.6 (CH_3, CH_3–O); 114.1 (CH, C-3′, C-5′); 116.9 (CH, C-5); 118.4 (C, C-8b); 121.4 (CH, C-8); 124.0 (C, C-3a); 124.7 (CH, C-6); 126.4 (CH, C-7); 128.2 (C, C-1′); 128.3 (C, C-8a); 129.3 (CH, C-2′, C-6′); 132.6 (C, C-4a); 142.7 (C, C-3); 145.3 (C, C-1); 163.5 (C, C-4′). $C_{22}H_{23}NO_4S$ (397.13): calcd C 66.48, H 5.83, N 3.52; found C 66.76, H 6.03, N 3.43.

*4.4.8. 3-Hexyl-N-(4-methoxybenzenesulfonyl)-1-methylfuro[3,4-b]indole (**30**).* Mp: 92–94 °C (hexane/AcOEt). IR (ATR) ν cm^{-1}: 1593 (C=C); 1256 (Ar–O); 1183 (Ar–S); 1169 (C–O). NMR ^1H ($CDCl_3$, 300 MHz) δ (ppm): 0.90 (t, J=6.9 Hz, 3H, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 1.21–1.45 (m, 6H, $CH_3CH_2(CH_2)_4$–Ar, $CH_3CH_2CH_2(CH_2)_3$–Ar, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 1.76 (q, J=7.6 Hz, 2H, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 2.42 (s, 3H, CH_3–Ar); 3.10 (t, J=7.5 Hz, 2H, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 3.68 (s, 3H, CH_3–O); 6.70 (d, J=9.0 Hz, 2H, H-3′, H-5′); 7.15 (td, J_1=1.1 Hz, J_2=7.5 Hz, 1H, H-7); 7.25 (td, J_1=1.4 Hz, J_2=7.5 Hz, 1H, H-6); 7.37 (dd, J_1=1.0 Hz, J_2=7.5 Hz, 1H, H-5); 7.55 (d, J=9.0 Hz, 2H, H-2′, H-6′); 8.02 (d, J=8.2 Hz, 1H, H-8). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 13.5 (CH_3, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 14.2 (CH_3, CH_3–Ar); 22.7 (CH_2, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 27.0 (CH_2, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 28.9 (CH_2, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 29.2 (CH_2, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 31.8 (CH_2, $CH_3CH_2CH_2CH_2CH_2CH_2$–Ar); 55.5 (CH_3, CH_3–O); 113.9 (CH, C-3′, C-5′); 116.8 (CH, C-5); 118.5 (C, C-8b); 121.0 (CH, C-8); 123.8 (C, C-3a); 124.6; 126.3 (CH, C-7); 127.8 (C, C-1′); 128.4 (C, C-8a); 129.2 (CH, C-2′, C-6′); 137.3 (C, C-4a); 138.1 (C, C-3); 145.2 (C, C-1); 163.5 (C, C-4′). $C_{24}H_{27}NO_4S$ (425.17): calcd C 67.74, H 6.40, N 3.29; found C 67.84, H 6.13, N 3.06.

*4.4.9. N-(4-Methoxybenzenesulfonyl)-3-methyl-1-pentylfuro[3,4-b]indole (**31**).* Yellow oil. IR (ATR) ν cm^{-1}: 1594 (C=C); 1261 (Ar–O); 1181 (Ar–S); 1165 (C–O). NMR ^1H ($CDCl_3$, 300 MHz) δ (ppm): 0.85 (t, J=7.0 Hz, 3H, $CH_3CH_2CH_2CH_2CH_2$–Ar); 1.25–1.31 (m, 4H, $CH_3CH_2CH_2CH_2CH_2$–Ar, $CH_3CH_2CH_2CH_2CH_2$–Ar); 1.66–1.69 (m, 2H, $CH_3CH_2CH_2CH_2CH_2$–Ar); 2.69 (s, 3H, CH_3–Ar); 2.76 (t, J=7.4 Hz, 2H, $CH_3CH_2CH_2CH_2CH_2$–Ar); 3.71 (s, 3H, CH_3–O); 6.73 (d, J=9.1 Hz, 2H, H-3′, H-5′); 7.17 (td, J_1=1.1 Hz, J_2=7.5 Hz, 1H, H-7); 7.28 (td, J_1=1.4 Hz, J_2=7.5 Hz, 1H, H-6); 7.40 (dd, J_1=0.9 Hz, J_2=7.5 Hz, 1H, H-5); 7.48 (d, J=9.0 Hz, 2H, H-2′, H-6′); 8.03 (d, J=8.3 Hz, 1H, H-8). NMR ^{13}C ($CDCl_3$, 75.5 MHz) δ (ppm): 13.1 (CH_3, CH_3–Ar); 14.1 (CH_3, $CH_3CH_2CH_2CH_2CH_2$–Ar); 22.5 (CH_2, $CH_3CH_2CH_2CH_2CH_2$–Ar); 28.1 (CH_2, $CH_3CH_2CH_2CH_2CH_2$–Ar); 28.2 (CH_2, $CH_3CH_2CH_2CH_2CH_2$–Ar); 31.4 (CH_2, $CH_3CH_2CH_2CH_2CH_2$–Ar); 55.6 (CH_3, CH_3–O); 114.0 (CH, C-3′, C-5′); 116.8 (CH, C-5); 118.4 (C, C-8b); 121.4 (CH, C-8); 123.9 (C, C-3a); 124.7 (CH, C-6); 126.4 (CH, C-7); 128.1 (C, C-1′); 128.3 (C, C-8a); 129.3 (CH, C-2′, C-6′); 132.5 (C, C-4a); 142.8 (C, C-3); 145.2 (C, C-1); 163.5 (C, C-4′); (CH, C-6); 126.3 (CH, C-7); 127.8 (C, C-1′); 128.4 (C, C-8a); 129.2 (CH, C-2′, C-6′); 137.3 (C, C-4a); 138.1 (C, C-3); 145.2 (C, C-1); 163.5 (C, C-4′). $C_{22}H_{25}NO_4S$ (411.15): calcd C 67.13, H 6.12, N 3.40; found C 67.34, H 6.32, N 3.76.

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Supplementary data

These data include copies of the NMR spectra. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.10.022.

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