Synthesis of Tetracyclic System of 2,4-Di(*tert*-Butyl)-6,7-dihydrofuro[2′,3′:3,4]cyclohepta[1,2-*b*]indole

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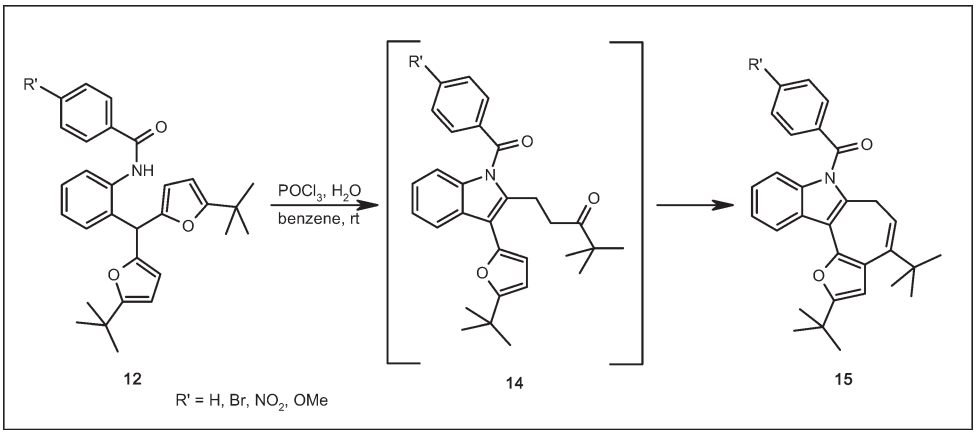

For the first time, tetracyclic compounds, namely, furo[2′,3′:3,4]cyclohepta[1,2-b]indoles were synthesized by recyclization of *ortho*-substituted aryldifurylmethanes containing *tert*-butyl groups at C5 positions of the furan rings. It was shown that [2-(benzoylamino)phenyl]bis(5-*tert*-butyl-2-furyl)methanes **12** are transformed into tetracycles **15** at room temperature under treatment with $POCl_3$ in benzene solution containing some drops of water. The reaction proceeds *via* the intermediate formation of 1-benzoylamino-3-(5-*tert*-butyl-2-furyl)-2-(4,4-dimethyl-3-oxopentyl)indoles **14** which can be isolated from the reaction mixture. The method is very simple but its application is restricted due to side reactions if electron-releasing groups are present in **12**. On the other hand, the decrease of electron density on furan ring in the starting compounds (for example, the use of [2-X-phenyl]difurylmethanes (where X = tosylamino or hydroxy group) prevents cyclization under the studied reaction conditions. As a result, corresponding ketones are formed as products of recyclization.

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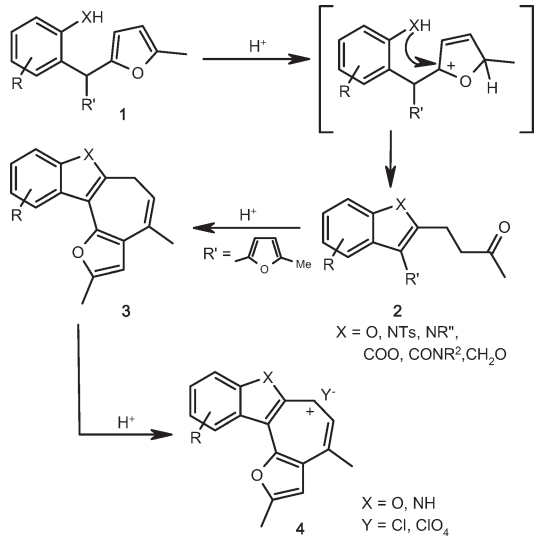
INTRODUCTION

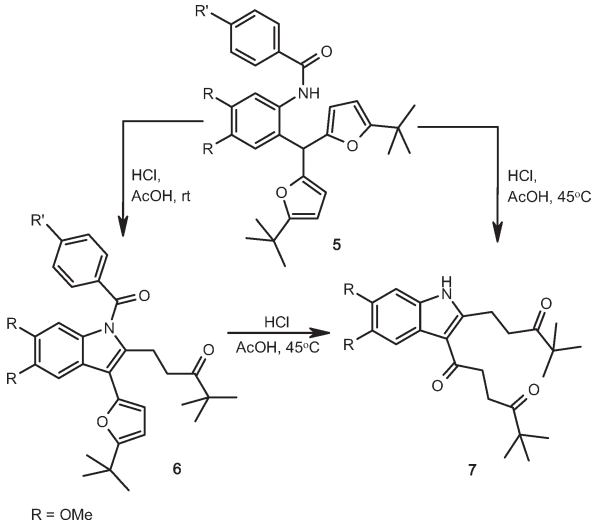
It is well known that 2,5-dialkylfurans undergo ring opening into 1,4-dicarbonyl compounds under treatment with Broensted acids [1]. We have used this kind of furan reactivity for the development of new approach to benzannulated heterocyclic compounds **2**, such as benzofurans [2], indoles [3], isochromones [4], isoquinolones [5], isochromenes [6], *via* acid-catalyzed recyclization of 2-(*ortho*-substituted benzyl)furans **1** (Scheme 1).

This approach is based on the idea that furan ring can be considered as synthetic equivalent of 1,4-diketone. Under treatment with acids, one of these masked carbonyl functions reacts with nucleophilic center in *ortho*-position of benzyl group leading to new heterocycles; the transformation proceeds with liberation of the second carbonyl group, which might participate in some one pot transformations. For example, acid-catalyzed recyclization of 2-[2-(hydrazinocarbonyl)benzyl]furans yields the corresponding pyridazino[1,6-*b*]isoquinolin-10-ones [7]. Similarly, recyclization of arylbis(5-methyl-2-furyl)methanes is accompanied by the secondary cyclization due to the attack of carbonyl group onto furan ring with the formation of tetracyclic compounds **3** (Scheme 1). Such cycloheptatriene derivatives were obtained by us during synthesis of isochromones [4],

Scheme 1. Acid-catalyzed recyclization of 2-(*ortho*-substituted benzyl)furans **1** into benzannulated heterocycles **2** and tetracyclic compounds **3** and **4**.



Scheme 2. Transformation of [2-(benzoylamino)phenyl]bis(5-*tert*-butyl-2-furyl)methanes **5** into 3-(2-furyl)indoles **6** and triketoindoles **7**.



isoquinolones [5], and isochromenes [6]. In contrast, similar benzofuran- and indole-based tetracyclic compounds are unstable under the reaction conditions. These substances disproportionate resulting in the corresponding tropylium salts **4** easily (Scheme 1) [8,9].

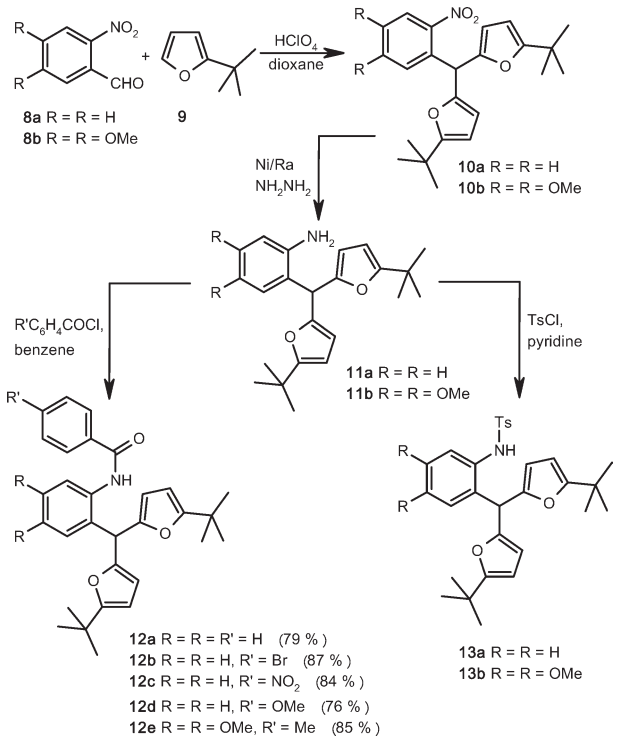
At the same time, during our study of recyclization of 2-(2-furylmethyl)benzoic acids and their amides, we have found that *tert*-butyl group at the C5 atom of furan ring prevents the secondary cyclization and allows us to isolate the corresponding ketones [4,5]. We used this windfall for the synthesis of 3-(2-furyl)indoles. In particular, we have shown that the treatment of [2-(benzoylamino)phenyl]bis(5-*tert*-butyl-2-furyl)methanes **5** with HCl/AcOH at room temperature leads to ketones **6**. However, at 45°C, this reaction is accompanied by debenzoylation followed by the second furan ring opening resulting in triketoindoles **7** (Scheme 2) [10].

In continuation of our study of [2-(benzoylamino)-phenyl]bis(5-*tert*-butyl-2-furyl)methanes recyclization, we have found that their treatment with $POCl_3$ in benzene in the presence of one drop of water yields earlier unknown furo[2′,3′:3,4]cyclohepta[1,2-*b*]indoles [11]. Herein, we describe the full results of this investigation.

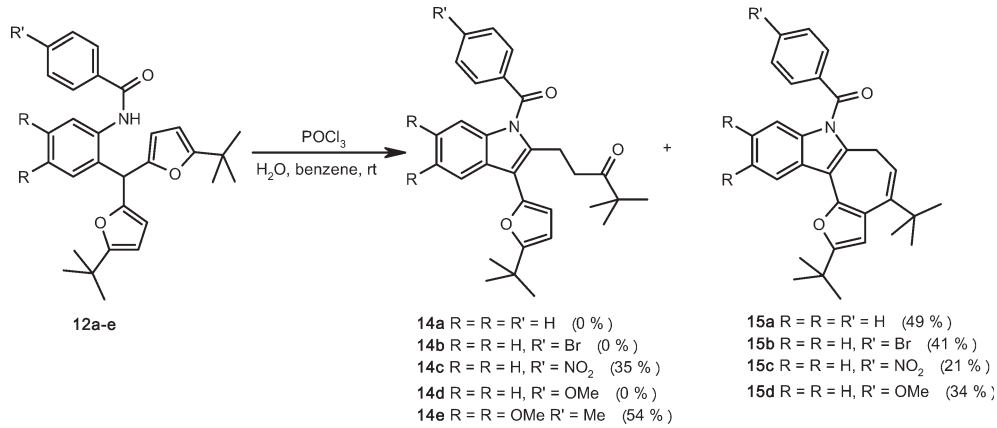
RESULTS AND DISCUSSION

The starting (2-aminoaryl)bis(2-furyl)methanes were synthesized from the commercially available *ortho*-nitrobenzaldehydes **8a,b** and 2-(*tert*-butyl)furan (**9**) [12] according to Scheme 3. Condensation of these reagents in dioxane in the presence of catalytic quantity of perchloric acid gave rise to (2-nitroaryl)bis(5-*tert*-butyl-2-furyl)methanes **10a,b**, which were further reduced by the treatment with hydrazine hydrate in the presence of Raney nickel [10]. The resulting anilines **11a,b** were acylated with the corresponding benzoyl chlorides leading to benzamides **12a–e** (Scheme 3). The reactions of **11** with tosyl chloride in pyridine yielded the corresponding *N*-tosylanilines **13a,b** (Scheme 3) [10].

Scheme 3. Synthesis of benzamides **12** and *p*-toluenesulfamides **13**.



Scheme 4. Synthesis of furo[2′,3′:3,4]cyclohepta[1,2-*b*]indoles **15a–d**.



The treatment of amides **12a-d** with $POCl_3$ in benzene in the presence of one drop of water at room temperature for 24 h produced tetracyclic compounds **15a–d** (Scheme 4). Structures of these compounds were established on the basis of ^1H and ^{13}C NMR spectra and elemental analysis data. This assessment was unambiguously proved by single-crystal X-ray data for furo[2′,3′:3,4]cyclohepta[1,2-*b*]indole **15b** (Fig. 1).

Reactions of amide **12c** resulted in both tetracyclic compound **15c** and 1-acyl-3-(5-*tert*-butyl-2-furyl)-2-(3-oxoalkyl)indole **14c**. It can be explained by decrease of nucleophilic reactivity of furan ring in **14c** due to the presence of nitro group in benzoyl moiety and efficient electronic conjugation between this group and furan ring through indole scaffold.

On the other hand, we failed to isolate cycloheptatriene **15** in reaction of amide **12e** containing electron-releasing methoxy groups. Instead of the target product, the complex reaction mixture was formed in this case. Methoxy groups make furan ring to be more reactive in cyclization of intermediate **14e**. However, these groups accelerate also some by-processes, for example, disproportionation reaction discussed above. As a result, the product **15e** cannot be isolated under the studied reaction conditions, if it is formed. We performed the careful optimization of reaction conditions for transformation of **12e** and have found that significant decrease of $POCl_3$ concentration in the reaction mixture allows us to obtain ketone **14e** in 54% yield after 15 h. Any attempts to increase yield of this compound by exposure of **12e** for phosphorus oxychloride for a longer time gave rise to formation of the unidentified and unseparable products and, finally, to the tarring of the reaction mixture.

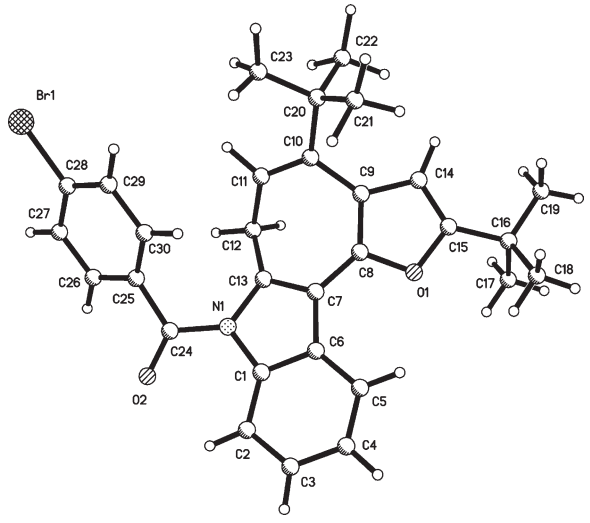
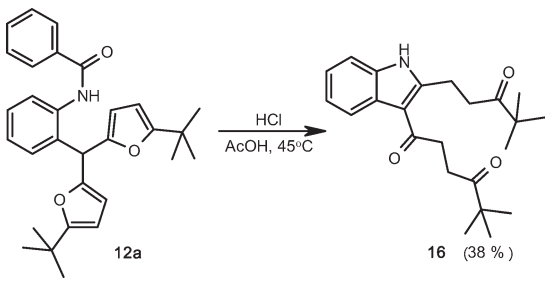


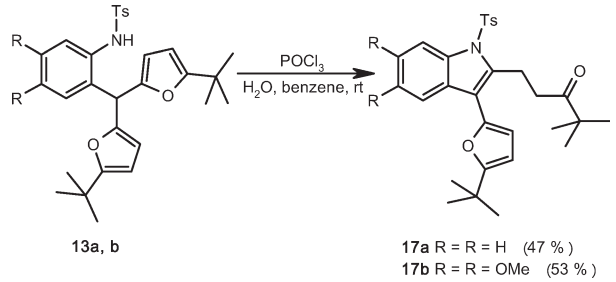
Figure 1. Single-crystal X-ray structure of compound **15b**.

The obtained results stimulated us to investigate carefully recyclization of [2-(benzoylamino)phenyl]bis(5-*tert*-butyl-2-furyl)methanes **12** in the mixture of acetic and hydrochloric acids [10]. We used compound **12a** as a model substrate. We have found that this substrate was converted into ketone **14a** under treatment with the aforementioned acids at room temperature for 24 h. When reaction was performed at 45°C, the full conversion was achieved only after 3 h. However, in this case, reaction mixture contains both **14a** and some quantity of tetracyclic product **15a**. The increase of reaction time leads, however, to triketone **16** but not to **15a** (Scheme 5). This triketone was a single isolated product when

Scheme 5. Synthesis of triketoindole **16**.



Scheme 6. Transformation of *N*-tosylanilines **13a,b** into indoles **17a,b**.

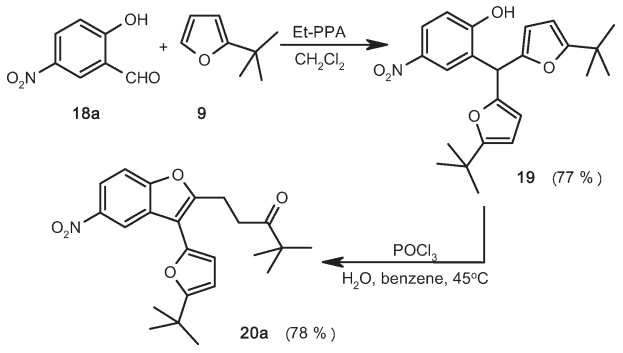


reaction was performed for 9 h what is in a good accordance with the earlier obtained data [10].

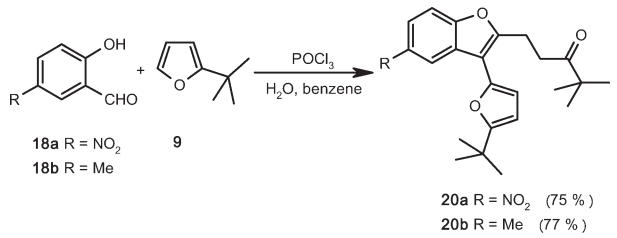
On the contrary to benzanilides **12**, the corresponding *N*-tosylanilines **13a,b** gave no tetracyclic products **15** under treatment with $POCl_3$ at the same reaction conditions. Instead of it, 3-(5-*tert*-butyl-2-furyl)-2-(3-oxoalkyl)-1-tosylindoles **17a,b** were formed (Scheme 6). The increase of process duration or refluxing the reaction mixture for 6 h did not result in formation of **15**. Some tarring of reaction mixture was only found in both cases. This behavior of *N*-tosylanilines **13** can be explained analogously to that of **14c**. Tosyl group is more efficient electron-withdrawing substituent than benzoyl moiety. Therefore, electron density on furan ring in **17** is decreased relatively to that in **14** what hampers the secondary cyclization of **17**.

(2-Acylaminophenyl)bis(5-methyl-2-furyl)methanes behave differently in reactions with $POCl_3$ depending on the substituent at nitrogen atom. At the same time, it was found earlier that reactivity of (2-hydroxyphenyl)-bis(5-methyl-2-furyl)methanes toward acids is similar to that of (2-aminophenyl)bis(5-methyl-2-furyl)methanes [8,9]. Therefore, it would be interesting to study $POCl_3$-induced recyclization of (2-hydroxyphenyl)bis(5-*tert*-butyl-2-furyl)methanes for comparison with the results obtained for recyclizations of **12** and **13**. So, we synthesized aryldifurylmethane **19** by reaction of 2-(*tert*-butyl)-furan (**9**) with 5-nitrosalicylic aldehyde **18a**. Treatment

Scheme 7. Synthesis of benzofuran **20a** from aryldifurylmethane **19**.



Scheme 8. Synthesis of benzofurans **20** from salicylic aldehydes **18** and 2-(*tert*-butyl)furan **9**.



of **19** with phosphorus oxychloride in the moist benzene at 45°C for 2 h yields benzofuran **20a** exclusively (Scheme 7). Similarly to the reactions of **13**, the increase of reaction temperature or duration did not lead to formation of tetracyclic products.

Also, we have found that benzofuran **20a** can be easily obtained directly from 2-(*tert*-butyl)furan **9** and aldehyde **18a** under the same reaction conditions (Scheme 8). Benzofuran **20b** was synthesized analogously.

In conclusion, we have found that [2-(benzoylamino)-phenyl]bis(5-*tert*-butyl-2-furyl)methanes are transformed into furo[2′,3′:3,4]cyclohepta[1,2-*b*]indoles in the presence of phosphorus oxychloride and traces of moisture. It is the first example of synthesis of such tetracyclic compounds by recyclization of furan derivatives with *tert*-butyl group at C5 position.

The application of this reaction is restricted as both electron-withdrawing and electron-releasing groups prevent formation of tetracyclic products. Acceptor substituents decrease reactivity of furan ring what hampers secondary cyclization. As a result, 3-(5-*tert*-butyl-2-furyl)-2-(3-oxoalkyl)indoles were the major or single products. Similarly, (2-hydroxyphenyl)bis(5-*tert*-butyl-2-furyl)methanes yield the corresponding 2-(3-furylbenzofuran-2-yl)ethyl *tert*-butyl ketones. On the other hand, the donor substituents stimulate both cyclization to furo[2′,3′:3,4]cyclohepta[1,2-*b*]indoles and their disproportionation.

EXPERIMENTAL

NMR spectra were recorded with a ''Bruker DPX 300'' (300 MHz for ^1H and 75 MHz for ^{13}C NMR) spectrometer at room temperature; the chemical shifts (δ) were measured in ppm with respect to the solvent ($CDCl_3$, ^1H: δ = 7.26 ppm, ^{13}C: δ = 77.13 ppm). Coupling constants (*J*) are given in Hz. Multiplicities of signals are described as follows: s = singlet, d = doublet, dd = double doublet, t = triplet, and m = multiplet. 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. Melting points (uncorrected) were determined in capillaries with Electrothermal 9100 capillary melting point apparatus. Column chromatography was performed on silica gel KSK (50−160 μm, LTD Sorbpolymer).

(2-Nitrophenyl)difurylmethanes **10a,b**, (2-aminophenyl)difurylmethanes **11a,b**, and [2-(tosylamino)phenyl]difurylmethanes **13a,b** were synthesized according to procedures described earlier [10].

General procedure of the synthesis of [2-(benzoylamino)-phenyl]difurylmethanes 12a-e (procedure A). A solution of benzoyl chloride (0.015 mol) in benzene (25 mL) was added dropwise to the solution of compound **11** (0.01 mol) in benzene (30 mL) under stirring. The reaction mixture was stirred at room temperature for 1 h (TLC control) and poured into water (100 mL). The mixture was neutralized with $NaHCO_3$ and kept for 2 h. Benzene fraction was separated. Aqueous phase was extracted with ethyl acetate (2 × 30 mL). The combined organic fractions were dried with anhydrous Na_2SO_4 and filtered. The solvent was evaporated under the reduced pressure. Residue was dissolved in methylene chloride/petroleum ether (1:8) mixture. The solution was passed through pad of silica gel, solvent was evaporated. All products were recrystallized from the specified solvents.

[2-(Benzoylamino)phenyl]bis(5-tert-butyl-2-furyl)methane (12a). This compound was obtained according to the general procedure **A** in 79% yield as colorless needles (CH_2Cl_2–petroleum ether); M.p. 144–145°C; IR (potassium bromide): 3244, 2968, 1644, 1580, 1528, 1456, 1324, 1312, 1184, 1128, 1016, 784, 748, 696 cm^{-1}; ^1H NMR (300 MHz, deuteriochloroform): δ 1.19 (s, 18H, *t*-Bu), 5.52 (s, 1H, CH), 5.87 (d, J = 3.0 Hz, 2H, H_{Fur}), 5.89 (d, J = 3.0 Hz, 2H, H_{Fur}), 7.01–7.05 (m, 1H, H_{Ar}), 7.11–7.16 (m, 1H, H_{Ar}), 7.32–7.41 (m, 3H, H_{Ar}), 7.46–7.52 (m, 1H, H_{Ar}), 7.62–7.65 (m, 2H, H_{Ar}), 8.10–8.13 (m, 2H, H_{Ar} + NH); ^{13}C NMR (75 MHz, deuteriochloroform): δ 28.9 (6C), 32.6 (2C), 42.4, 102.5 (2C), 108.5 (2C), 124.0, 125.1, 127.0 (2C), 127.9, 128.5 (2C), 129.4, 130.8, 131.7, 134.8, 135.5, 150.4 (2C), 164.3 (2C), 165.2; ms: *m*/*z* 455 (25) [M^+], 399 (41), 398 (40), 352 (24), 350 (100), 105 (82), 77 (15), 57 (72), 43 (53). *Anal*. Calcd. for $C_{30}H_{33}NO_3$: C, 79.09; H, 7.30; N, 3.07. Found: C, 79.30; H, 7.37; N, 3.10.

{2-[(4-Bromobenzoyl)amino]phenyl}bis(5-tert-butyl-2-furyl)-methane (12b). This compound was obtained according to the general procedure **A** in 87 % yield as pale-yellow cubes (CH_2Cl_2–petroleum ether); mp 155–156°C; IR (potassium bromide): 3428, 2964, 1680, 1588, 1520, 1488, 1452, 1312, 1276, 1188, 1124, 1016, 804, 784, and 756 cm^{-1}; ^1H NMR (300 MHz, deuteriochloroform): δ 1.19 (s, 18H, *t*-Bu), 5.51 (s, 1H, CH), 5.88 (d, J = 3.3 Hz, 2H, H_{Fur}), 5.90 (d, J = 3.3 Hz, 2H, H_{Fur}), 7.06–7.09 (m, 1H, H_{Ar}), 7.12–7.18 (m, 1H, H_{Ar}), 7.32–7.38 (m, 1H, H_{Ar}), 7.47–7.54 (m, 4H, H_{Ar}), 8.01–8.14 (m, 2H, H_{Ar} + NH); ^{13}C NMR (75 MHz, deuteriochloroform): δ 28.9 (6C), 32.6 (2C), 42.7, 102.6 (2C), 108.5 (2C), 123.9, 125.3, 126.3, 128.0, 128.7 (2C), 129.7, 130.7, 131.7(2C), 133.6, 135.4, 150.3 (2C), 164.4 (3C); ms: *m*/*z* 536/534 (65/64) [M^+], 479/477 (39/41), 478/476 (94/96), 351 (34), 350 (100), 246 (47), 185/183 (97/99), 155 (26), 105 (94), 77 (28), 59 (22), 57 (66), 43 (70). *Anal*. Calcd. for $C_{30}H_{32}BrNO_3$: C, 67.42; H, 6.03; N, 2.62. Found: C, 67.27; H, 6.10; N, 2.51.

Bis(5-tert-butyl-2-furyl){2-[(4-nitrobenzoyl)amino]-phenyl}methane (12c). This compound was obtained according to the general procedure **A** in 84% yield as colorless needles (CH_2Cl_2–petroleum ether); M.p. 159–160°C; IR (potassium bromide): 3284, 2964, 1648, 1600, 1520, 1492, 1344, 1296, 1128, 1013, 780, 756, and 716 cm^{-1}; ^1H NMR (300 MHz, deuteriochloroform): δ 1.17 (s, 18H, *t*-Bu), 5.50 (s, 1H, CH), 5.88 (d, J = 3.0 Hz, 2H, H_{Fur}), 5.92 (d, J = 3.0 Hz, 2H, H_{Fur}), 7.11–7.15 (m, 1H, H_{Ar}), 7.16–7.22 (m, 1H, H_{Ar}), 7.35–7.40 (m, 1H, H_{Ar}), 7.76 (d, J = 9.0 Hz, 2H, H_{Ar}), 8.11–8.14 (m, 1H, H_{Ar}), 8.21–8.25 (m, 3H, H_{Ar} + NH); ^{13}C NMR (75 MHz, deuteriochloroform): δ 28.9 (6C), 32.6 (2C), 43.1, 102.6 (2C), 108.5 (2C), 123.7 (2C), 124.0, 125.8, 128.1, 128.2 (2C), 130.1, 130.6, 135.1, 140.4, 149.5, 150.2 (2C), 163.1, 164.6 (2C); ms: *m*/*z* 500 (34) [M^+], 443 (100), 350 (27), 332 (16), 150 (23), 120 (22), 57 (16), 43 (13). *Anal*. Calcd. for $C_{30}H_{32}N_2O_5$: C, 71.98; H, 6.44; N, 5.60. Found: C, 71.85; H, 6.49; N, 5.55.

Bis(5-tert-butyl-2-furyl){2-[(4-methoxybenzoyl)amino]-phenyl}methane (12d). This compound was obtained according to the general procedure **A** in 76% yield as white solid (CH_2Cl_2–petroleum ether); M.p. 134–135°C; IR (potassium bromide): 3276, 2964, 1636, 1608, 1504, 1300, 1252, 1184,1028, 1016, 844, 780, and 752 cm^{-1}; ^1H NMR (300 MHz, deuteriochloroform): δ 1.20 (s, 18H, *t*-Bu), 3.84 (s, 3H, OCH_3), 5.52 (s, 1H, CH), 5.88 (d, J = 3.3 Hz, 2H, H_{Fur}), 5.89 (d, J = 3.3 Hz, 2H, H_{Fur}), 6.87 (d, J = 8.7 Hz, 2H, H_{Ar}), 7.00–7.03 (m, 1H, H_{Ar}), 7.09–7.14 (m, 1H, H_{Ar}), 7.31–7.36 (m, 1H, H_{Ar}), 7.59 (d, J = 8.7 Hz, 2H, H_{Ar}), 8.00 (br.s, 1H, NH), 8.08–8.11 (m, 1H, H_{Ar}); ^{13}C NMR (75 MHz, deuteriochloroform): δ 28.9 (6C), 32.6 (2C), 42.3, 55.4, 102.5 (2C), 108.5 (2C), 113.7 (2C), 124.0, 124.9, 127.0, 127.8, 128.9 (2C), 129.3, 130.7, 135.7, 150.4 (2C), 162.3, 164.3 (2C), 164.7; ms: *m*/*z* 485 (33) [M^+], 429 (15), 428 (37), 351 (31), 350 (70), 183 (19), 152 (17), 135 (100), 77 (24), 59 (16), 57 (33), 43 (44). *Anal*. Calcd. for $C_{31}H_{35}NO_4$: C, 76.67; H, 7.26; N, 2.88. Found: C, 76.92; H, 7.39; N, 2.82.

Bis(5-tert-butyl-2-furyl){4,5-dimethoxy-2-[(4-methyl-benzoyl)amino]phenyl}methane (12e). This compound was obtained according to the general procedure **A** in 85% yield as white solid. For analytical data of **12e**, see [10].

General procedure of the recyclization of arylbis(5-tert-butyl-2-furyl)methanes into indoles 14c,e and furo[2′,3′:3,4]-cyclohepta[1,2-b]indoles 15a-d (Procedure B). Phosphorus oxychloride was added to the solution of compound **12** (2 mmol) in benzene (40 mL) containing one drop of water. The reaction mixture was stirred at room temperature for 1 d, poured into water (200 mL), and neutralized with 5 M NaOH (150 mL). Product was extracted with methylene chloride (3 × 50 mL). The combined organic fractions were dried with Na_2SO_4, filtered and evaporated under reduced pressure. For **12a,d,e**, the residue was dissolved in petroleum ether and passed through pad of silica gel. The solvent was evaporated. All products were recrystallized from the specified solvents. For **12b,c**, the residue was purified by preparative column chromatography on silica gel (eluent: benzene–petroleum ether, 1:8).

1-[3-(5-tert-Butyl-2-furyl)-1-(4-nitrobenzoyl)-1H-indol-2-yl]-4,4-dimethylpentan-3-one (14c). This compound was obtained from **12c** according to the general procedure **B** using 10 mL of $POCl_3$ in 35% yield as red solid (CH_2Cl_2–petroleum ether); M.p. 126–127°C; IR (potassium bromide): 2968, 1696, 1604, 1520, 1476, 1456, 1408, 1344, 1304, 1208, 1160, 1104, 1080, 996, 852, 776, 736, and 716 cm^{-1}; ^1H NMR (300 MHz, deuteriochloroform): δ 1.12 (s, 9H, *t*-Bu), 1.35 (s, 9H, *t*-Bu), 3.06–3.11 (m, 2H, CH_2), 3.29–3.34 (m, 2H, CH_2), 6.14 (d, J = 3.3 Hz, 1H, H_{Fur}), 6.55 (d, J = 3.3 Hz, 1H, H_{Fur}), 6.57–6.59 (m, 1H, H_{Ar}), 6.99–7.05 (m, 1H, H_{Ar}), 7.20–7.26 (m, 1H, H_{Ar}), 7.87–7.89 (m, 1H, H_{Ar}), 7.94 (d, J = 9.0 Hz, 2H, H_{Ar}),

8.35 (d, J = 9.0 Hz, 2H, H_{Ar}); ^{13}C NMR (75 MHz, deuteriochloroform): δ 22.2, 26.4 (3C), 29.1 (3C), 32.7, 36.9, 44.0, 103.8, 108.4, 112.8, 113.8, 120.5, 123.3, 123.6, 124.0 (2C), 127.5, 131.0 (2C), 135.9, 137.5, 140.7, 146.0, 150.3, 163.7, 167.4, 214.7; ms: *m/z* 500 (100) [M^+], 485 (26), 352 (15), 336 (18), 276 (25), 266 (25), 250 (26), 236 (21), 150 (36), 120 (67), 104 (15), 92 (17), 84 (16), 57 (75), 43 (25). *Anal*. Calcd. for $C_{30}H_{32}N_2O_5$: C, 71.98; H, 6.44; N, 5.60. Found: C, 71.83; H, 6.58; N, 5.55.

1-[3-(5-tert-Butyl-2-furyl)-5,6-dimethoxy-1-(4-methyl-benzoyl)-1H-indol-2-yl]-4,4-dimethylpentan-3-one (14e). This compound was obtained from **12e** according to the general procedure **B** (2 mL of $POCl_3$, reaction time 15 h) in 54% yield as white solid. For spectral data of **14e**, see [10].

7-Benzoyl-2,4-di(tert-butyl)-6,7-dihydrofuro[2′,3′:3,4]-cyclohepta[1,2-b]indole (15a). This compound was obtained from **12a** according to the general procedure **B** using 5 mL of $POCl_3$ in 49% yield as yellow needles (petroleum ether), M.p. 202–203°C; IR (potassium bromide): 2964, 1680, 1448, 1376, 1360, 1328, 1312, 1208, 1152, 744, 720, and 700 cm^{-1}; ^{1}H NMR (300 MHz, deuteriochloroform): δ 1.20 (s, 9H, *t*-Bu), 1.43 (s, 9H, *t*-Bu), 2.83 (d, J = 7.2 Hz, 2H, CH_2), 5.18 (t, J = 7.2 Hz, 1H, ═CH), 6.45 (s, 1H, H_{Fur}), 7.18–7.23 (m, 1H, H_{Ar}), 7.28–7.33 (m, 1H, H_{Ar}), 7.50–7.61 (m, 3H, H_{Ar}), 7.63–7.69 (m, 1H, H_{Ar}), 7.79–7.83 (m, 2H, H_{Ar}), 7.97–8.00 (m, 1H, H_{Ar}); ^{13}C NMR (75 MHz, deuteriochloroform): δ 25.8, 29.1 (3C), 30.8 (3C), 32.7, 35.9, 104.1, 112.7, 112.8, 114.9, 119.9, 122.2, 123.4, 123.7, 126.4, 128.7 (2C), 129.9 (2C), 132.2, 133.0, 135.5, 137.2, 144.2, 147.3, 161.9, 169.0; ms: *m/z* 437 (37) [M^+], 422 (44), 381 (82), 380 (100), 302 (15), 276 (32), 260 (15), 135 (66), 105 (65), 76 (32), 59 (18), 45 (12), 43 (58). *Anal*. Calcd. for $C_{30}H_{31}NO_2$: C, 82.35; H, 7.14; N, 3.20. Found: C, 82.41; H, 6.97; N, 3.18.

7-(4-Bromobenzoyl)-2,4-di(tert-butyl)-6,7-dihydrofuro-[2′,3′:3,4]cyclohepta[1,2-b]indole (15b). This compound was obtained from **12b** according to the general procedure **B** using 10 mL of $POCl_3$ in 41% yield as yellow needles (CH_2Cl_2–petroleum ether); M.p. 206–207°C; IR (potassium bromide): 2952, 1680, 1592, 1544, 1448, 1324, 1268, 1204, 1016, 976, 832, and 756 cm^{-1}; ^{1}H NMR (300 MHz, deuteriochloroform): δ 1.20 (s, 9H, *t*-Bu), 1.43 (s, 9H, *t*-Bu), 2.87 (d, J = 7.2 Hz, 2H, CH_2), 5.22 (t, J = 7.2 Hz, 1H, ═CH), 6.45 (s, 1H, H_{Fur}), 7.18–7.24 (m, 1H, H_{Ar}), 7.29–7.34 (m, 1H, H_{Ar}), 7.51–7.53 (m, 1H, H_{Ar}), 7.65–7.72 (m, 4H, H_{Ar}), 7.97–7.99 (m, 1H, H_{Ar}); ^{13}C NMR (75 MHz, deuteriochloroform): δ 25.7, 29.1 (3C), 30.8 (3C), 32.7, 35.9, 104.0, 112.5, 112.9, 114.8, 120.0, 122.4, 123.6, 123.9, 126.3, 128.1, 131.4 (2C), 131.8, 132.1 (2C), 134.2, 137.0, 144.3, 147.1, 161.9, 167.9; ms: *m/z* 518/516 (100/100) [M^+], 460/458 (91/89), 331 (24), 316 (23), 276 (44), 260 (53), 185/183 (50/52), 76 (62), 57 (70), 43 (46). *Anal*. Calcd. for $C_{30}H_{30}BrNO_2$: C, 69.77; H, 5.85; N, 2.71. Found: C, 69.79; H, 5.92; N, 2.57.

2,4-Di(tert-butyl)-7-(4-nitrobenzoyl)-6,7-dihydrofuro-[2′,3′:3,4]cyclohepta[1,2-b]indole (15c). This compound was obtained from **12c** according to the general procedure **B** using 10 mL of $POCl_3$ in 21% yield as orange solid (CH_2Cl_2–petroleum ether); M.p. 191–192°C; IR (potassium bromide): 2964, 1680, 1524, 1452, 1348, 1324, 1208, 1156, 1092, 980, 860, 836, 752, 728, and 708 cm^{-1}; ^{1}H NMR (300 MHz, deuteriochloroform): δ 1.20 (s, 9H, *t*-Bu), 1.43 (s, 9H, *t*-Bu), 2.83 (d, J = 7.2 Hz, 2H, CH_2), 5.17 (t, J = 7.2 Hz, 1H, ═CH), 6.46 (s, 1H, H_{Fur}), 7.19–7.24 (m, 1H, H_{Ar}), 7.31–7.37 (m, 1H, H_{Ar}), 7.47–7.51 (m, 1H, H_{Ar}), 7.97–8.01 (m, 1H, H_{Ar}), 7.98 (d, J = 9.0 Hz, 2H, H_{Ar}), 8.39 (d, J = 9.0 Hz, 2H, H_{Ar}); ^{13}C NMR (75 MHz, deuteriochloroform): δ 25.8, 29.1 (3C), 30.8 (3C), 32.7, 35.9, 104.1, 112.2, 113.7, 114.9, 120.3, 122.9, 124.0 (2C), 124.1, 124.3, 126.6, 130.7 (2C), 131.0, 136.8, 141.0, 144.6, 146.8, 150.2, 162.3, 166.8; ms: *m/z* 482 (66) [M^+], 467 (26), 425 (100), 331 (46), 316 (31), 276 (32), 260 (37), 57 (21), 43 (24). *Anal*. Calcd. for $C_{30}H_{30}N_2O_4$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.44; H, 6.38; N, 5.72.

2,4-Di(tert-butyl)-7-(4-methoxybenzoyl)-6,7-dihydrofuro-[2′,3′:3,4]cyclohepta[1,2-b]indole (15d). This compound was obtained from **12d** according to the general procedure **B** using 5 mL of $POCl_3$ in 34% yield as beige solid (petroleum ether); M.p. 148–149°C; IR (potassium bromide): 2964, 1676, 1608, 1512, 1452, 1364, 1308, 1260, 1212, 1172, 1028, 976, 852, 820, 760, and 748 cm^{-1}; ^{1}H NMR (300 MHz, deuteriochloroform): δ 1.20 (s, 9H, *t*-Bu), 1.43 (s, 9H, *t*-Bu), 2.90 (d, J = 7.2 Hz, 2H, CH_2), 3.91 (s, 3H, OCH_3) 5.26 (t, J = 7.2 Hz, 1H, ═CH), 6.45 (s, 1H, H_{Fur}), 6.99 (d, J = 8.7 Hz, 2H, H_{Ar}), 7.16–7.22 (m, 1H, H_{Ar}), 7.26–7.31 (m, 1H, H_{Ar}), 7.51–7.55 (m, 1H, H_{Ar}), 7.80 (d, J = 8.7 Hz, 2H, H_{Ar}), 7.96–7.99 (m, 1H, H_{Ar}); ^{13}C NMR (75 MHz, deuteriochloroform): δ 25.8, 29.2 (3C), 30.8 (3C), 32.7, 35.9, 55.6, 104.0, 112.1, 112.7, 114.0 (2C), 114.6, 119.9, 121.9, 123.1, 123.5, 126.2, 127.5, 132.5 (2C), 132.7, 137.2, 144.1, 147.5, 161.7, 163.7, 168.3; ms: *m/z* 467 (83) [M^+], 410 (100), 276 (14), 261 (23), 136 (41), 135 (64), 107 (80), 92 (38), 76 (32), 57 (76), 43 (39). *Anal*. Calcd. for $C_{31}H_{33}NO_3$: C, 79.63; H, 7.11; N, 3.00. Found: C, 79.77; H, 6.97; N, 3.01.

Synthesis of 5,5-dimethyl-1-[2-(4,4-dimethylpentan-3-on-1-yl)-1H-indol-3-yl]hexane-1,4-dione (16). A total of 35% hydrochloric acid (7 mL) was added to the cooled solution (10–12°C) of compound **12a** (1.0 g, 2.2 mmol) in AcOH (25 mL). The reaction mixture was kept at 45°C for 9 h. After completion of the reaction (TLC monitoring), the mixture was poured into water, neutralized with $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 50 mL). The extract was dried with anhydrous Na_2SO_4 and evaporated to dryness. Compound **16** was isolated by column chromatography (eluent: petroleum ether–acetone–CH_2Cl_2, 15:5:3) in 38% yield as a white solid. For spectral data of **16**, see [10].

1-[3-(5-tert-Butyl-2-furyl)-1-(4-toluenesulfonyl)-1H-indol-2-yl]-4,4-dimethylpentan-3-one (17a). This compound was synthesized from **13a** according to general procedure **B** using 5 mL of $POCl_3$ in 47% yield. For spectral data of **17a**, see [10].

1-[3-(5-tert-Butyl-2-furyl)-5,6-dimethoxy-1-(4-toluene-sulfonyl)-1H-indol-2-yl]-4,4-dimethylpentan-3-one (17b). This compound was synthesized from **13b** according to general procedure **B** using 5 mL of $POCl_3$ in 53% yield. For spectral data of **17b**, see [10].

Synthesis of bis(5-*tert*-butyl-2-furyl)(2-hydroxy-5-nitrophenyl)methane (19). 2-(*tert*-Butyl)furan (3.76 mL, 26.4 mmol) and 1 N solution of PPA ethyl ester (20 mL) were added to the solution of aldehyde **18a** (2 g, 12 mmol) in methylene chloride (100 mL). The reaction mixture was stirred at 40–45°C for 3 h and poured into water (150 mL). Organic layer was separated; aqueous fraction was extracted with methylene chloride (2 × 30 mL). The combined organic fractions were dried with Na_2SO_4 and filtered. The solvent was evaporated under reduced pressure. Residue was dissolved in methylene

chloride–petroleum ether (1:20) mixture and passed through pad of silica gel. The obtained solution was evaporated under reduced pressure. Product was obtained as pale-yellow prisms after crystallization from petroleum ether.

The yield is 3.66 g (77%); M.p. 123–124°C; IR (potassium bromide): 3456, 2964, 1592, 1532, 1488, 1328, 1292, 1208, 1124, 1080, 1016, 796, and 776 cm^{-1}; ^1H NMR (300 MHz, deuteriochloroform): δ 1.23 (s, 18H, *t*-Bu), 5.54 (s, 1H, CH), 5.90 (d, $J = 3.0$ Hz, 2H, H_{Fur}), 5.98 (d, $J = 3.0$ Hz, 2H, H_{Fur}), 6.92 (d, $J = 9.0$ Hz, 1H, H_{Ar}), 8.06 (d, $J = 2.1$ Hz, 1H, H_{Ar}), 8.08 (dd, $J = 2.1$, 9.0 Hz, 1H, H_{Ar}); ^{13}C NMR (75 MHz, deuteriochloroform): δ 28.9 (6C), 32.6 (2C), 40.6, 102.6 (2C), 108.5 (2C), 117.0, 124.8, 126.3, 126.9, 141.4, 149.3 (2C), 159.8, 164.6 (2C); ms: *m/z* 397 (100) [M^+], 382 (37), 341 (34), 340 (99), 259 (43), 245 (34), 229 (33), 216 (77), 200 (22), 186 (31), 109 (29), 95 (21), 57 (84), 43 (56). *Anal.* Calcd. for $C_{23}H_{27}NO_5$: C, 69.50; H, 6.85; N, 3.52. Found: C, 69.43; H, 6.76; N, 3.54.

Synthesis of 1-[3-(5-tert-Butyl-2-furyl)-5-nitrobenzofuran-2-yl]-4,4-dimethylpentan-3-one (20a).

Method A. $POCl_3$ (2.5 mL) and one drop of water were added to the solution of compound **19** (0.5 g, 1.26 mmol) in benzene (40 mL). The reaction mixture was stirred at 40–45°C for 2 h, poured into water (100 mL), and neutralized with 2.5 M NaOH solution (50 mL). Products were extracted with methylene chloride (3 × 40 mL). The combined organic fractions were dried with Na_2SO_4, filtered and evaporated under reduced pressure. The residue was dissolved in methylene chloride–petroleum ether (3:20) mixture and passed through pad of silica gel. The obtained solution was evaporated under reduced pressure. Crystallization from methylene chloride–petroleum ether mixture gave 0.39 g (78%) of compound **20a**.

Method B. 2-(*tert*-Butyl)furan **9** (5.76 mL, 40 mmol), $POCl_3$ (20 mL), and two drops (0.1 mL) of water were added to the solution of compound **18a** (2.5 g, 18.4 mmol) in benzene (140 mL). The reaction mixture was stirred at room temperature for 2.5 h, poured into water (250 mL), and neutralized with 5 M NaOH (150 mL). Products were extracted with methylene chloride (3 × 50 mL). The combined organic fractions were dried with Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was dissolved in petroleum ether and passed through pad of silica gel. Crystallization from petroleum ether in refrigerator gave 3.64 g (75%) of compound **20a**. M.p. 166–167°C; IR (potassium bromide): 2972, 1696, 1520, 1456, 1340, 1264, 1196, 1080, and 768 cm^{-1}; ^1H NMR (300 MHz, deuteriochloroform): δ 1.17 (s, 9H, *t*-Bu), 1.36 (s, 9H, *t*-Bu), 3.00–3.05 (m, 2H, CH_2), 3.30–3.35 (m, 2H, CH_2), 6.13 (d, $J = 3.3$ Hz, 1H, H_{Fur}), 6.57 (d, $J = 3.3$ Hz, 1H, H_{Fur}), 7.48 (d, $J = 9.0$ Hz, 1H, H_{Ar}), 8.21 (dd, $J = 2.1$, 9.0 Hz, 1H, H_{Ar}),. 8.72 (d, $J = 2.1$, Hz, 1H, H_{Ar}); ^{13}C NMR (75 MHz, deuteriochloroform): δ 22.6, 26.4 (3C), 29.1 (3C), 32.8, 34.3, 44.2, 103.8, 108.0, 109.5, 111.1, 117.2, 119.9, 127.3, 143.8, 144.2, 156.5, 156.7, 164.1, 213.7; ms: *m/z* 397 (83) [M^+], 382 (75), 296 (17), 283 (24), 282 (32), 252 (14), 236 (18), 57 (100), 43 (68). *Anal.* Calcd. for $C_{23}H_{27}NO_5$: C, 69.50; H, 6.85; N, 3.52. Found: C, 69.48; H, 6.90; N, 3.60.

1-[3-(5-tert-Butyl-2-furyl)-5-methylbenzofuran-2-yl]-4,4-dimethylpentan-3-one (20b). This compound was obtained analogously to **20a** using method **B** in 77% yield as white solid (petroleum ether); M.p. 77–78°C; IR (potassium bromide): 2960, 1700, 1576, 1476, 1356, 1280, 1200, 1148, 1084, 1032, 980, 800, and 772 cm^{-1}; ^1H NMR (300 MHz, deuteriochloroform): δ 1.15 (s, 9H, *t*-Bu), 1.34 (s, 9H, *t*-Bu), 2.46 (s, 3H, CH_3), 2.96–3.01 (m, 2H, CH_2), 3.26–3.31 (m, 2H, CH_2), 6.08 (d, $J = 3.3$ Hz, 1H, H_{Fur}), 6.47 (d, $J = 3.3$ Hz, 1H, H_{Fur}), 7.06 (dd, $J = 1.8$, 8.2 Hz, 1H, H_{Ar}), 7.28 (d, $J = 8.2$ Hz, 1H, H_{Ar}), 7.54 (d, $J = 1.8$ Hz, 1H, H_{Ar}); ^{13}C NMR (75 MHz, deuteriochloroform): δ 21.5, 22.6, 26.4 (3C), 29.1 (3C), 32.7, 34.9, 44.1, 103.4, 106.7, 108.2, 110.3, 120.2, 125.0, 126.7, 132.2, 145.7, 152.4, 153.8, 163.1, 214.2; ms: *m/z* 366 (61) [M^+], 351 (73), 267 (37), 251 (100), 238 (14), 197 (21), 165 (17), 145 (14), 57 (80), 43 (44). *Anal.* Calcd. for $C_{24}H_{30}O_3$: C, 78.65; H, 8.25. Found: C, 79.02; H, 8.16.

SUPPLEMENTARY CRYSTALLOGRAPHIC DATA

CCDC 776889 (**19b**) contains the supplementary crystallographic data for this article. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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