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FULL-LENGTH PAPER

An efficient and expeditious synthesis of novel 2,2-dialkyl-2,3-dihydrobenzofurans from phenols and 2,2-dialkylacetaldehydes

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Abstract Reactions of 2,2-dialkylaldehydes with electron-rich 2-naphthols and *para*-substituted phenols in presence of catalytic amount of *p*-TSA under closed vessel solvent-free microwave irradiation conditions resulted in formation of corresponding 2,2-dialkyl-1,2-dihydronaphtho[2,1-*b*]furans and 2,2-dialkyl-2,3-dihydrobenzofurans, respectively, in good to excellent yields. The effect of stoichiometry, temperature, and catalyst in reaction progress was systematically investigated. 14-Alkyl-14*H*-dibenzo[*a*, *j*]xanthenes was obtained as minor products when 2-naphthol and 6-bromo-2-naphthols were used as starting phenols. Simple phenols gave a lower yield of the 2,2-dialkyl-2,3-dihydrobenzofurans products than their electron-rich naphthalene counterparts. Also, xanthene-type products were not detected in case of simple phenols by GC–MS or column chromatography.

Keywords Phenols · 2-Naphthol · 2,2-Dialkyl-1,2-dihydronaphtho[2,1-*b*]furans · 2,2-Dialkyl-2,3-dihydrobenzofurans · Microwave-assisted synthesis · Solvent-free

Introduction

New ways to synthesize benzofuran and naphthofuran derivatives are constantly pursued by synthetic chemists worldwide as these frameworks are found abundantly in many natural and synthetic bioactive compounds (Fig. 1) [1–5]. Since this communication deals with the synthesis of 2,2-dialkyl-2,3-dihydrobenzofuran-type compounds, it is pertinent to summarize the variety and virtues (or lack thereof) in the previously reported synthesis of this class of compounds. In 1973, Martini et al. [6] reported the sulfuric acid-catalyzed formation of 2,2-dialkyl-2,3-dihydrobenzofurans from electron-rich phenols and 2,2-dialkylacetaldehydes with toluene as the solvent in 10–62 % yields. A similar procedure reported the formation of 2,2-dimethyl-2,3-dihydrobenzofurans, in trace quantities in most cases, from aryloxymagnesium bromides and isobutyraldehyde [7]. Other procedures leading to 2,2-dialkyl-2,3-dihydrobenzofurans mainly involve employing intramolecular cyclization reactions on non-commercial starting materials [8–20]. Several of these are usual [8,9] or Ir-catalyzed [10] intramolecular Claisen rearrangement followed by cyclo-isomerization. Amberlyst 15-catalyzed cyclo-isomerization of *o*-(2,2-dialkylvinyl)phenols and cyclo-dehydration of *o*-(2,2-dialkyl-1-hydroxyethyl)phenols leading to 2,2-dialkyl-2,3-dihydrobenzofurans have also been reported [11]. Lithium-mediated rearrangement of salicylic alcohol ketals followed by cyclo-dehydration also produces 2,2-dialkyl-2,3-dihydrobenzofurans [12]. Very recently, an efficient and mechanistically interesting synthesis of 2,2-dialkyl-2,3-dihydrobenzofurans has been reported through [3+2] coupling of *p*-quinone monoacetals and alkene catalyzed by Bronsted acids [13,14]. Paladium catalysis has also been used for dehydrohalogenation in 2-(2-bromophenyl)-1,1-dialkylethanol-type molecules to create intramolecular C–O bond by the research groups of Buchwald and co-workers [15] and Hartwig and co-workers [16,17]. A copper(I) version of such cyclization is also reported [18]. Palladium-based reagents have also been used for intramolecular cyclo-dehydrogenation in 1,1-dialkyl-2-arylethanols [19], cyclo-alkane-arylation in 1-halo-2-(1,1-dialkylethoxy)arenes

Dedicated to Professor Virinder Singh Parmar, Department of Chemistry, University of Delhi on his 65th birthday.

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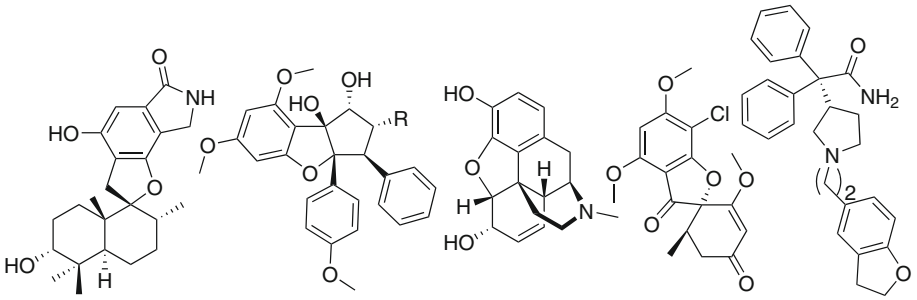


Fig. 1 Natural products and pharmaceuticals containing benzofuran ring

[20], and oxidative-activation of *o*-hydroxyarylcyclopropanes [21] to yield 2,2-dialkyl-2,3-dihydrobenzofurans.

Despite poor to excellent yields of the methodologies discussed above, they suffer from several drawbacks such as long reaction times, complex substrates, multiple reaction steps, and expensive catalysts. Thus, there exists a need for the development of novel, convenient, and greener methods to the prepare this class of compounds.

The use of commercial microwave-irradiating reactors has become very popular over the past few years, owing to numerous advantages such as dramatic decreases in reaction times by reaction rate acceleration, control of temperature and pressure, control of product/side product distribution, use of solvent-free conditions, etc. [9]. Our research group constantly employs this technique in designing environmentally benign synthetic methodologies to prepare important molecular frameworks [22–26].

Results of our preliminary investigation to produce 2,2-dialkyl-1,2-dihydronaphtho[2,1-*b*]furans from electron-rich 2-naphthol analogs and 2,2-dialkylacetaldehydes under microwave irradiation conditions were recently reported [27]. Herein, we wish to report the conclusion of our detailed study on the reaction of phenols with 2,2-dialkylacetaldehydes under microwave-assisted, *p*-TSA catalyzed, solvent-free conditions. Our procedure can be seen as a modification of the procedure reported by Martini et al. [6] with significant improvement in the product yields. The systematic investigation of the effect of temperature, stoichiometry, and catalyst is also being reported.

Results and discussion

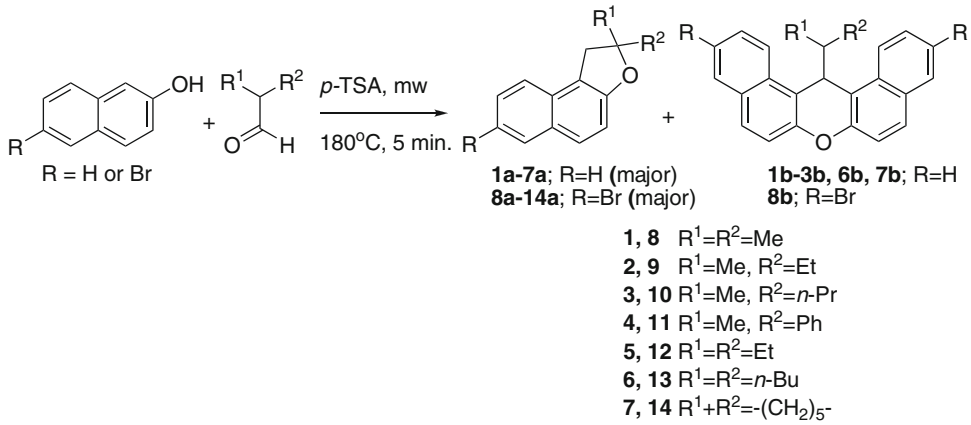
In our preliminary report [27] we disclosed that in a closed vessel, solvent-free, and *p*-TSA catalysis, 2,2-dialkyl-1,2-dihydronaphtho[2,1-*b*]furans (**1a**–**14a**) were formed in 44–92 % yields with trace amounts of 14-alkyl-14*H*-dibenzo[*a*, *j*]xanthenes (**1b**–**3b**, **6b**–**8b**) as by-products. The by-product xanthene appeared to be formed in all cases (by TLC) but was isolated only in six cases (Scheme 1).

We propose that the reaction proceeds via the attack from the nucleophilic C-1 position of 2-naphthol on the 2,2-dialkylacetaldehydes leading to the formation of a secondary alcohol intermediate which under acidic conditions forms a secondary benzylic carbocation. A 1,2-hydride shift leading to a tertiary carbocation followed by nucleophilic attack by the naphthol oxygen produces a stable furan ring. Martini et al. proposed a similar mechanism in their report [6]. Also, attack from the nucleophilic C-1 position of another 2-naphthol molecule on the secondary benzylic carbocation followed by dehydration was proposed for the formation of 14-alkyl-14*H*-dibenzo[*a*, *j*]xanthenes (**1b**–**14b**) as by-products [27]. The syntheses of 14*H*-dibenzo[*a*, *j*]xanthenes have been widely studied most notably from 2-naphthol analogs and aromatic aldehydes [28]; however, several examples from dialkylacetaldehydes and 2-naphthol are also known [29,30]. Being unstable under electron impact conditions, none of the xanthene products showed the molecular ion peak in their respective GC–MS spectra. However, all of the 2-naphthol-based xanthenes invariably showed a signal at *m*/*z* 281 with 100 % intensity. This was obviously due to the highly stabilized xanthene carbocation after the loss of alkyl group from the benzylic position. Consistent with this observation, the sole example of isolated xanthene from 6-bromo-2-naphthol also showed the corresponding set of most intense signals for the isotopomers at *m*/*z* 437/439/441 in appropriate ratio and no signal for the molecular ion. The detailed characterization data for all isolated new compounds are reported in the "Experimental" section.

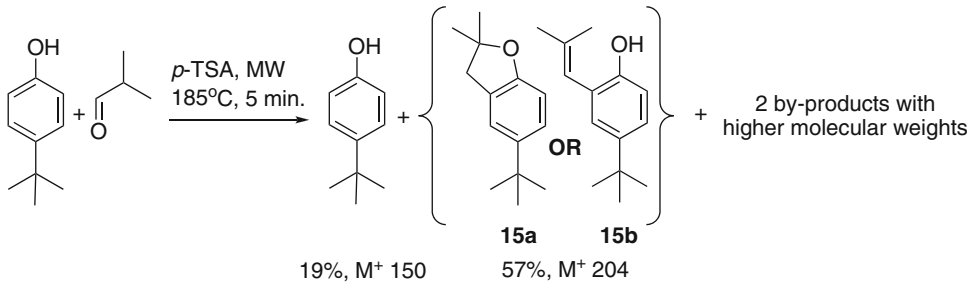
When 4-*tert*-butylphenol was used under similar conditions with isobutyraldehyde, the TLC of the reaction mixture was found to be relatively complicated with multiple and overlapping spots. Based on GC analysis of this reaction mixture, the structure of the major product was tentatively assigned as isomeric 4-*tert*-butyl-2-(2-methylprop-1-enyl)phenol (**15b**, M^+ 204), rather than expected 5-*tert*-butyl-2,2-dimethyl-2,3-dihydrobenzofuran (**15a**) [27].

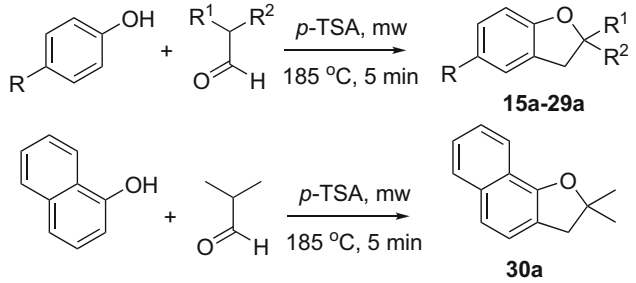
Subsequently, we decided to explore the reactivity of phenols with 2,2-dialkylacetaldehydes in detail. The reaction of 4-*tert*-butylphenol and isobutyraldehyde was repeated using the same reaction conditions as described above with careful chromatographic separation of the reaction mixture.

Scheme 1 The microwave-assisted reaction of 2-naphthol analogs with isobutyraldehyde



Scheme 2 The microwave-assisted reaction of 4-*tert*-butylphenol with isobutyraldehyde





Scheme 3 General microwave-assisted synthesis of 2, 2-dialkyl-2, 3-dihydrobenzofuran-type compounds from phenols and 2, 2-dialkylacetaldehydes

Our repeated attempts to isolate the non-polar by-products in pure form from the reaction mixture were of no avail. However, the relatively polar major product was isolated in pure form (57 % yield based on the starting phenol) and was unambiguously identified as 4-*tert*-butyl-2,2-dimethyl-2,3-dihydrobenzofuran (**15a**) based on ^{1}H and ^{13}C NMR, and MS data. This was contrary to the isomeric alkene structure we previously proposed [27]. This was found to be consistent with similar reactions on 2-naphthol analogs (*vide supra*). Interestingly, no evidence for the formation of 9*H*-xanthene derivative analogous to 2-naphthol reactions was observed in the GC–MS analysis. Also, ~19 % of the starting 4-*tert*-butylphenol was recovered unreacted.

Before examining the generality of this reaction on an array of phenols, we decided to optimize the reaction of 4-*tert*-butylphenol with isobutyraldehyde. This included varying the stoichiometry, reaction temperatures, and Lewis acids catalysts. Looking at the possible products in Schemes 1 and 2, it is clear that reactant stoichiometry plays a role in this reaction; the desired benzofurans require 1:1 phenol to aldehyde ratio whereas the by-products require of a higher ratio of phenol. Thus, it can be safely concluded that employing a higher ratio of aldehyde should lead of higher yield of the desired product and employing higher ratio of phenol should produce more by-products. To test this hypothesis, we selected 4-*tert*-butylphenol and 4-methoxyphenol as phenol representatives to react with isobutyraldehyde. Reactions were conducted with 1:1, 1:2, 1:3, and 2:1 phenol to aldehyde ratio with 2.5 mol% of *p*-TSA as the catalyst, at 185 °C under closed vessel microwave irradiation for 5 min. The major products from both reactions were identified as expected 2,2-dimethyl-2,3-dihydrobenzofurans based on detailed spectral analysis. Best results (62 and 60 % yield of the benzofuran products, respectively, from 4-*tert*-butylphenol and 4-methoxyphenol) were obtained when the ratio of phenol to aldehyde was 1:2. However, the yields from 1:1 ratio of phenol to aldehyde were fairly comparable (~2 % lower). On the other hand, use of 2:1 ratio of phenol to aldehyde understandably led to significant decrease in the yield (~40 %, based on aldehyde). Thus, in the interest of atom economy we chose to use 1:1 ratio of phenol to aldehyde as the optimal ratio for the reaction. Furthermore, to better understand the time needed for optimum reaction outcome, the reaction between 4-*tert*-butylphenol

Table 1 Physical data for compounds **15a**–**30a**

Entry	R	R^1	R^2	% Yield[a] of **15a**–**30a**	Unreacted phenol (%)
15	*t*-Bu	Me	Me	60 (57)	19
16	H	Me	Me	55 (51)	27
17	Me	Me	Me	55 (50)	17
18	OMe	Me	Me	58 (54)	30
19	Ph	Me	Me	48 (42)	49
20	F	Me	Me	33 (28)	62
21	Cl	Me	Me	32 (29)	64
22	Br	Me	Me	0	–
23	NO_2	Me	Me	0	–
24	OMe	Me	Ph	59 (55)	12
25	*t*-Bu	Me	Ph	56 (50)	6
26	H	$-(CH_2)_5-$		29 (22)	4
27	OMe	$-(CH_2)_5-$		56 (51)	21
28	*t*-Bu	$-(CH_2)_5-$		76 (69)	18
29	Ph	$-(CH_2)_5-$		56 (50)	20
30	1-Naphthol	Me	Me	84 (80)	3

All products are liquid at ambient temperature

[a] Yields are based on GC–MS before purification. Isolated yields in the parenthesis

and isobutyraldehyde was run for various lengths of time (5–30 min). Microwave irradiation for 5 and 10 min gave nearly identical and best results in terms of yield of the desired benzofuran (60 %). Also, by conducting reactions at various temperatures from 80 to 195 °C and using previously optimized stoichiometry and reaction time, the optimum temperature was determined to be 185 °C resulting in 60 % yield of the desired benzofuran product. Finally, experiments were carried identify and optimize a suitable Bronsted or Lewis acid catalysts [31] for this apparent hydroxyalkylation cyclo-dehydration sequence. After conducting experiments with varying amount (0, 2.5, 5, 10, 20, and 25 mol%) of *p*-TSA, acetic acid, and four other Lewis acid catalysts ($InCl_3$, $Sc(OTf)_3$, $Y(OTf)_3$, and $La(OTf)_3$), *p*-TSA at 2.5 mol% was found to the best catalyst producing 57–60 % yield of the desired benzofuran. The desired product was formed in all cases except in the negative control reaction.

To assess the generality of the optimized procedure, a number of substituted phenols were reacted with isobutyraldehyde. A few reactions were also carried out on phenols with 2-phenylpropanal and cyclohexane carboxaldehyde (Scheme 3). These results are summarized in Table 1. In all these cases, the expected 2,2-dialkyl-2,3-dihydrobenzofurans were obtained in moderate to excellent yields (29–84 %), except for the starting materials 4-bromophenol (entry 22) and 4-nitrophenol (entry 23), which failed to produce any desired product. The failure of 4-nitrophenol reaction may be attributed to the electron withdrawing effect of the nitro group that reduced the nucleophilicity of the position *ortho* to the phenolic group. The reason for the failure of 4-bromophenol, which reacted violently with sudden increase in the pressure inside the closed reaction vessel, is not yet clear. Among the cases where desired benzofurans products were formed, unsubstituted phenol and somewhat deactivated 4-halophenols gave relatively poor yields. On the other hand, electron-rich phenols appear to perform better presumably due to their stabilizing effect on putative carbocation intermediate. This is further corroborated by the excellent yield (84 %) of 2,2-dimethyl-2,3-dihydronaphtho[1,2-*b*]furan (**30a**) from the reaction between 1-naphthol and isobutyraldehyde (entry 30). Results from the reactions of 2-naphthol analogs with 2,2-dialkylacetaldehydes (Scheme 1) also support this assertion. It should be noted that the yields obtained in this study is significantly higher than those reported by Martini et al. [6] and Casnati et al. [7].

By-products were invariably formed in each of these reactions but unfortunately, attempts to isolate/purify these side products were unsuccessful due to their small amount, instability, and/or inseparability with other side products. Unlike 2-naphthol analogs, the reactions of phenols with 2,2-dialkylacetaldehydes did not appear to form any xanthene side products as corresponding peaks were missing in the GC–MS.

Conclusions

We have devised a novel and green methodology to synthesize 2,2-dialkyl-2,3-dihydronaphtho[2,1-*b*]furans, 2,2-dimethyl-2,3-dihydronaphthol[1,2-*b*]furan, and 2,2-dialkyl-2,3-dihydrobenzofurans from cheaply and abundantly available phenols and 2,2-dialkylacetaldehydes. Generally, naphthols and electron-rich phenols were found to give

better reaction yields. Although the yields of the desired furan products range from low to excellent, there are a number of merits to this one-step conversion such as very short reaction time, solvent-free conditions, and use of an economical catalyst.

Experimental

General

All chemicals were purchased from Aldrich Chemical Co. and were used without further purification. Pre-coated fluorescent silica gel TLC plates were used to monitor the progress of the reactions. Reactions were done in a CEM Discover S-Class microwave reactor. ^{1}H and ^{13}C NMR were recorded on a Bruker AV300 spectrophotometer at 300 and 75 MHz, respectively in $CDCl_3$ where residual $CHCl_3$ ($\delta = 7.27$) served as the *internal standard* for ^{1}H NMR, and $CDCl_3$ was used as the *internal standard* ($\delta = 77.0$) for ^{13}C NMR. Melting points were recorded on a MEL-TEMP II apparatus and are uncorrected. UV–Vis and IR spectra were recorded on Pharmacia Biotech Ultrospec 4000 and Nicolet Avatar 330FT-IR spectrophotometers, respectively. EIMS experiments were performed on an HP 5890 Series II Gas Chromatograph with an HP 5971A Mass Selective Detector, as well as a Varian 450-GC Gas Chromatograph with a Varian 240-MS IT Mass Spectrometer. ESI HRMS were recorded by Mr. Xiao Feng at Dalhousie University, Halifax, Nova Scotia.

General procedure for the synthesis of 2,2-dialkyl-1,2-dihydronaphtho-[2,1-*b*]furans

A mixture of appropriate phenol (10 mmol), aldehyde (10 mmol) and *p*-TSA (2.5 mol%) were heated under stirring in a closed vessel in the cavity of a CEM Discover S-Class microwave reactor at 185 °C for 5 min. The crude mixtures were dissolved in diethyl ether and were dried over sodium sulfate. The ether was removed under reduced pressure and the resulting residue was purified by column chromatography (silica gel mesh size 230–240; eluent 5–10 % EtOAc/hexane).

To study the effect of stoichiometry, temperature, and catalyst, the reaction contents and conditions were accordingly modified.

2,2-Dimethyl-1,2-dihydronaphtho[2,1-b]furan (**1a**)

Yield: 48 %. Its ^{1}H and ^{13}C NMR data were found to be identical to those reported in the literature [20]. FT-IR ν_{max} (NaCl): 3051, 2974, 2925, 1631, 1463, 1363, 1261, 873, 808 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 198 (M^+, 100). ESI HRMS (amu): calcd $C_{14}H_{14}O$ $[M+H]^+$: 199.1117; found $[M+H]^+$: 199.1112.

2-Ethyl-2-methyl-1,2-dihydronaphtho[2,1-b]furan (**2a**)

Yield: 79 %. Its ^{1}H and ^{13}C NMR data were found to be identical to those reported in the literature [21]. FT-IR ν_{max} (NaCl): 2969, 2921, 1631, 1465, 1376, 1260, 980, 808 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 212 (M^+, 100). ESI HRMS (amu): calcd $C_{15}H_{16}O$ $[M+H]^+$: 213.1274; found $[M+H]^+$: 213.1264.

2-Methyl-2-propyl-1,2-dihydronaphtho[2,1-b]furan (**3a**)

Yield: 46 %. ^{1}H NMR: δ 1.22 (t, $J = 7.2$ Hz, 3H), 1.73 (m, 5H), 1.98–2.04 (m, 2H), 3.31–3.53 (AB multiplet, 2H), 7.38 (d, $J = 8.7$ Hz, 1H), 7.55 (t, $J = 7.6$ Hz, 1H), 7.69 (t, $J = 7.1$ Hz, 1H), 7.77 (d, $J = 8.2$ Hz, 1H), 7.89 (d, $J = 8.7$ Hz, 1H), 8.01 (d, $J = 8.3$ Hz, 1H). ^{13}C NMR: δ 14.8, 17.6, 27.1, 40.2, 44.1, 89.9, 112.6, 118.4, 122.8, 122.9, 126.8, 129.0, 129.2, 129.31, 131.4, 156.8. FT-IR ν_{max} (NaCl): 3056, 2958, 2921, 2868, 1629, 1462, 1258, 976, 804 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 226 (M^+, 100). ESI HRMS (amu): calcd $C_{16}H_{18}O$ $[M+H]^+$: 227.1430; found $[M+H]^+$: 227.1419.

2-Methyl-2-phenyl-1,2-dihydronaphtho[2,1-b]furan (**4a**)

Yield: 73 %. Mp: 76–78 °C. ^{1}H NMR: δ 1.93 (s, 3H, CH_3), 3.67–3.79 (AB quartet, $J = 15.4$, 2H, Ar–CH_2), 7.31 (m, 3H, Ar–H), 7.27–7.48 (m, 2H, Ar–H), 7.52 (t, $J = 7.9$, 1H, Ar–H), 7.61 (d, $J = 7.9$, 3H, Ar–H), 7.78 (d, $J = 8.7$, 1H, Ar–H), 7.87 (d, $J = 8.2$, 1H, Ar–H). ^{13}C NMR: δ 29.5, 43.9, 90.1, 112.3, 117.9, 122.7, 122.9, 124.6, 126.7, 127.2, 128.4, 128.8, 129.3, 129.4, 131.0, 147.1, 156.4. UV–Vis (λ_{max}, EtOH): 234 nm. IR (KBr; ν_{max}): 3062, 3021, 2971, 2923, 2897, 2844, 1599, 1465, 1444, 1375, 1254, 821 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 260 (M^+, 100). ESI HRMS (amu): calcd $C_{19}H_{16}O$ $[M+Na]^+$: 283.1093; found $[M+Na]^+$: 283.1102.

2,2-Diethyl-1,2-dihydronaphtho[2,1-b]furan (**5a**)

Yield: 71 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.99 (t, $J = 7.5$, 6H), 1.82–1.89 (m, 4H), 3.27 (s, 2H), 7.10 (d, $J = 8.5$ Hz, 1H), 7.32 (d, $J = 7.4$ Hz, 1H), 7.48 (t, $J = 8.1$ Hz, 1H), 7.59 (d, $J = 8.3$ Hz, 1H), 7.69 (d, $J = 8.8$ Hz, 1H), 7.80 (d, $J = 8.2$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 7.9, 31.8, 36.9, 92.5, 112.1, 118.2, 122.4, 122.6, 126.4, 128.0, 128.2, 128.9, 131.1, 157.0. FT-IR ν_{max} (NaCl): 3058, 2966, 2936, 2878, 1600, 1466, 1376, 1261, 1060, 807 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 226 (M^+, 100). ESI HRMS

(amu): calcd $C_{16}H_{18}O$ $[M+H]^+$: 227.1430; found $[M+H]^+$: 227.1423.

2-Butyl-2-ethyl-1,2-dihydronaphtho[2,1-b]furan (**6a**)

Yield: 44 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93–1.02 (m, 6H), 1.39 (s, 4H), 1.79–1.87 (m, 4H), 3.28 (s, 2H), 7.10 (d, J = 7.7 Hz, 1H), 7.32 (d, J = 7.6 Hz, 1H), 7.48 (t, J = 8.1 Hz, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 8.7 Hz, 1H), 7.82 (d, J = 7.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 7.9, 14.0, 23.1, 25.6, 32.3, 37.4, 39.0, 92.2, 112.1, 118.1, 122.4, 122.5, 126.4, 128.7, 128.8, 128.9, 131.0, 156.9. FT-IR ν_{max} (NaCl): 3058, 2959, 2932, 2860, 1600, 1466, 1376, 1261, 807 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 254 (M^+, 100). ESI HRMS (amu): calcd $C_{18}H_{22}O$ $[M+H]^+$: 255.1743; found $[M+H]^+$: 255.1739.

1′H-Spiro[cyclohexane-1,2′-naphtho[2,1-b]furan] (**7a**)

Yield: 90 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.82–1.90 (m, 10H), 3.26 (s, 2H), 7.11 (d, J = 8.8 Hz, 1H), 7.31 (d, J = 7.9 Hz, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.59 (d, J = 8.2 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.79 (d, J = 8.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.1, 25.3, 37.5, 39.9, 89.5, 112.5, 117.9, 122.5, 124.0, 126.5, 128.0, 128.7, 128.8, 131.2, 156.4. FT-IR ν_{max} (NaCl): 3057, 2926, 2855, 1600, 1465, 1261, 1205, 808 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 238 (M^+, 100). ESI HRMS (amu): calcd $C_{17}H_{18}O$ $[M+H]^+$: 239.1430; found $[M+H]^+$: 239.1422.

7-Bromo-2,2-dimethyl-1,2-dihydronaphtho[2,1-b]furan (**8a**)

Yield: 74 %. Mp: 60–64 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.58 (s, 6H), 3.28 (s, 2H), 7.09 (d, J = 8.7 Hz, 1H), 7.43 (d, J = 8.8 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.96 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.5, 41.6, 87.8, 113.4, 116.0, 118.5, 124.3, 128.1, 129.6, 129.7, 130.1, 130.6, 156.6. FT- IR ν_{max} (NaCl): 2967, 2926, 2854, 1623, 1453, 1367, 1349, 1254, 876, 841 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 276/278 (M^+, 100). EI HRMS (amu): calcd $C_{14}H_{13}BrO$ $[M+H]^+$: 277.0223; found $[M+H]^+$: 277.0233.

7-Bromo-2-ethyl-2-methyl-1,2-dihydronaphtho[2,1-b]furan (**9a**)

Yield: 73 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (t, J = 7.4 Hz, 3H) 1.55 (s, 3H), 1.89 (q, J = 7.3 Hz, 2H), 3.03–3.47 (AB quartet, J = 15.5 Hz, 2H), 7.14 (d, J = 8.7 Hz, 1H), 7.43 (d, J = 8.7 Hz, 1H), 7.55–7.97 (m, 2H), 7.97 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 8.4, 26.3, 34.1, 39.3, 90.42, 113.4, 116.0, 118.5, 124.3, 128.1, 129.6, 129.7, 130.0, 130.6, 156.9. FT-IR ν_{max} (NaCl): 2966, 2925, 2872, 2843, 1621, 1580, 1343, 1250, 980, 878, 804 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 290/292 (M^+, 100). ESI HRMS (amu): calcd $C_{15}H_{15}BrO$ $[M+H]^+$: 291.0379; found $[M+H]^+$: 291.0392.

7-Bromo-2-methyl-2-propyl-1,2-dihydronaphtho[2,1-b]furan (**10a**)

Yield: 65 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (t, J = 7.2 Hz, 3H), 1.57 (m, 5H), 1.86 (t, J = 8.1 Hz, 2H), 3.15–3.36 (AB quartet, J = 15.5 Hz, 2H), 7.16 (d, J = 8.7 Hz, 1H), 7.42 (d, J = 8.7 Hz, 1H), 7.54–7.61 (m, 2H), 7.98 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.6, 17.4, 26.8, 39.8, 43.8, 90.1, 113.4, 116.0, 118.5, 124.4, 128.1, 129.6, 129.7, 130.1, 130.6, 156.9. FT-IR ν_{max} (NaCl): 2959, 2930, 2871, 1626, 1587, 1508, 1350, 1256, 982, 879, 804 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 304/306 (M^+, 100). ESI HRMS (amu): calcd $C_{16}H_{17}BrO$ $[M+H]^+$: 305.0536; found $[M+H]^+$: 305.0527.

7-Bromo-2-methyl-2-phenyl-1,2-dihydronaphtho[2,1-b]furan (**11a**)

Yield: 79 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.89 (s, 3H), 3.63–3.75 (AB quartet, J = 15.4 Hz, 2H), 7.24–7.32 (m, 2H), 7.37–7.44 (m, 3H), 7.51–7.57 (m, 3H), 7.65 (d, J = 8.7 Hz, 1H), 7.98 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.4, 43.6, 90.2, 113.3, 116.2, 118.1, 124.3, 124.4, 124.7, 127.2, 127.8, 128.3, 128.4, 129.8, 130.3, 130.6, 156.7. FT-IR ν_{max} (NaCl): 3064, 2973, 2925, 1628, 1458, 1350, 1255, 879, 806 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 338/340 (M^+, 100). ESI HRMS (amu): calcd $C_{19}H_{15}BrO$ $[M+H]^+$: 339.0379; found $[M+H]^+$: 339.0369.

7-Bromo-2,2-diethyl-1,2-dihydronaphtho[2,1-b]furan (**12a**)

Yield: 83 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 (t, J = 7.4 Hz, 6H), 1.86 (q, 4H), 3.25 (s, 2H), 7.13 (d, J = 8.7 Hz, 1H), 7.45 (d, J = 8.8 Hz, 1H), 7.57 (t, J = 8.8 Hz, 2H), 7.97 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 7.9, 31.7, 36.9, 92.8, 113.1, 115.9, 118.5, 124.3, 128.1, 129.4, 129.7, 130.0, 130.6, 157.4. FT- IR ν_{max} (NaCl): 2967, 2937, 2878, 1626, 1463, 1350, 1256, 879, 805 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 304/306 (M^+, 66). ESI HRMS (amu): calcd $C_{16}H_{17}BrO$ $[M+H]^+$: 305.0536; found $[M+H]^+$: 305.0548.

7-Bromo-2-butyl-2-ethyl-1,2-dihydronaphtho[2,1-b]furan (**13a**)

Yield: 91 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93–1.04 (m, 6H), 1.40 (s, 4H), 1.84 (m, 4H), 3.25 (s, 2H), 7.13 (d, J = 8.8 Hz, 1H), 7.44 (d, J = 8.8 Hz, 1H), 7.56

(t, J = 8.8 Hz, 2H), 7.96 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 7.9, 14.2, 23.1, 25.7, 32.2, 37.3, 38.9, 92.5, 113.1, 115.9, 118.5, 124.3, 128.1, 129.5, 129.7, 130.0, 130.6, 157.3. FT-IR ν_{max} (NaCl): 2960, 2932, 2860, 1627, 1463, 1350, 1256, 879, 805 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 332/334 (M^+, 100). ESI HRMS (amu): calcd $C_{18}H_{21}BrO$ $[M+H]^+$: 333.0849; found $[M+H]^+$: 227.1423.

7′-Bromo-1′H-spiro[cyclohexane-1,2′-naphtho[2,1-b] furan] (**14a**)

Yield: 92 %. Mp: 80–83 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.59 (s, 4H), 1.80–1.95 (m, 6H), 3.23 (s, 2H), 7.11 (d, J = 8.8 Hz, 1H), 7.44 (d, J = 8.8 Hz, 1H), 7.52 (d, J = 8.8 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.95 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.0, 25.1, 37.4, 39.7, 89.7, 113.5, 115.9, 118.2, 124.2, 127.9, 129.4, 129.6, 130.0, 130.5, 156.7. FT-IR ν_{max} (KBr): 2929, 2858, 1624, 1460, 1244, 878, 809 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 316/318 (M^+, 100). ESI HRMS (amu): calcd $C_{17}H_{17}BrO$ $[M+Na]^+$: 339.0355; found $[M+Na]^+$: 339.0353.

14-Isopropyl-14H-dibenzo[a, j]xanthene (**1b**)

Yield: 8 %. Mp: 146–150 °C (Lit. m.p. 152–153 °C) [29]. Its ^{1}H and ^{13}C NMR, and IR data were found to be identical to those reported in the literature [29]. GC–MS (EI): *m/z* (% relative abundance) 324 (M^+, 0), 281 (100). ESI HRMS (amu): calcd $C_{24}H_{20}O$ $[M+H]^+$: 325.1587; found $[M+H]^+$: 325.1576.

14-Sec-butyl-14H-dibenzo[a, j]xanthene (**2b**)

Yield: 2 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.79–0.85 (m, 6H), 1.56–1.68 (m, 2H), 1.98 (m, 1H), 5.51 (bs, 1H), 7.47 (m, 4H), 7.62–7.64 (m, 2H), 7.81 (d, J = 8.6 Hz, 2H), 7.90 (d, J = 7.9 Hz, 2H), 8.33 (d, J = 8.5 Hz, 2H). FT-IR ν_{max} (NaCl): 3067, 2961, 1632, 1591, 1455, 1238, 811. GC–MS (EI): *m/z* (% relative abundance) 338 (M^+, 0), 281 (100). ESI HRMS (amu): calcd $C_{25}H_{22}O$ $[M+Na]^+$: 361.1563; found $[M+Na]^+$: 361.1554.

14-(Pentan-2-yl)-14H-dibenzo[a, j]xanthene (**3b**)

Yield: 2 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.76–0.79 (m, 6H), 0.92–0.96 (m, 4H), 2.06–2.08 (m, 1H), 5.50 (m, 1H), 7.42–7.49 (m, 4H), 7.59–7.66 (m, 2H), 7.80 (d, J = 8.6 Hz, 2H), 7.89 (d, J = 8.2 Hz, 2H), 8.31 (d, J = 8.3 Hz, 2H). FT-IR ν_{max} (NaCl): 2950, 2925, 1632, 1511, 1453, 1438, 1245, 821 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 352 (M^+, 0), 281 (100).

14-(Heptan-3-yl)-14H-dibenzo[a, j]xanthene (**6b**)

Yield: 5 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.83–0.91 (m, 6H), 1.60 (m, 8H), 1.74–1.80 (m, 1H), 5.57 (s, 1H), 7.41–7.49 (m, 4H), 7.59–7.65 (m, 2H), 7.79 (d, J = 8.8 Hz, 2H), 7.88 (d, J = 7.6 Hz, 2H), 8.31 (d, J = 9.2 Hz, 2H). FT-IR ν_{max} (NaCl): 2926, 2852, 1646, 1239, 907, 814 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 380 (M^+, 0), 281 (100).

14-Cyclohexyl-14H-dibenzo[a, j]xanthene (**7b**)

Yield: 5 %. Its ^{1}H and ^{13}C NMR, and IR data were found to be identical to those reported in the literature [30]. GC–MS (EI): *m/z* (%relative abundance) 364 (M^+, 0), 281 (100). ESI HRMS (amu): calcd $C_{27}H_{24}O$ $[M+Na]^+$: 387.1719; found $[M+Na]^+$: 387.1709.

3,11-Dibromo-14-isopropyl-14H-dibenzo[a, j]xanthenes (**8b**)

Yield: 4.3 %. Mp: 188–190 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.80 (d, J = 6.8 Hz, 6H), 2.29–2.25 (m, 1H), 5.32 (d, J = 6.8 Hz), 7.44 (d, J = 8.8 Hz, 2H), 7.69 (t, J = 10.0 Hz, 4H), 8.04 (s, 2H), 8.13 (d, J = 9.1 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.2, 36.4, 37.0, 117.2, 117.9, 118.6, 124.7, 127.2, 129.6, 130.6, 130.6, 132.2, 150.9. FT-IR ν_{max} (KBr): 2945, 1585, 1502, 1251, 955 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 480/482/484 (M^+, 0), 437/439/441 (50/100/48). ESI HRMS (amu): calcd $C_{24}H_{18}Br_2O$ $[M+H]^+$: 480.9797; found $[M+H]^+$: 480.9778.

5-(tert-Butyl)-2,2-dimethyl-2,3-dihydrobenzofuran (**15a**)

Yield: 57 %. Its ^{1}H NMR spectrum was found to be identical to that reported in the literature [11]. ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.7, 32.1, 35.1, 43.4, 86.9, 109.0, 122.5, 125.0, 127.0, 143.3, 159.1. FT-IR ν_{max} (NaCl): 2964, 2875, 1609, 1494, 1261, 814 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 204 (M^+, 27), 189 (100). ESI HRMS (amu): calcd $C_{14}H_{20}O$ $[M+H]^+$: 205.1587; found $[M+H]^+$: 205.1580.

2,2-Dimethyl-2,3-dihydrobenzofuran (**16a**)

Yield: 51 %. Its ^{1}H and ^{13}C NMR spectra were found to be identical to those reported in the literature [19]. FT-IR ν_{max} (NaCl): 2962, 2917, 1740, 1478, 1254, 881 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 148 (M^+, 75), 133 (100), 105 (74). ESI HRMS (amu): calcd $C_{10}H_{12}O$ $[M+H]^+$: 149.0961; found $[M+H]^+$: 149.0968.

2,2,5-Trimethyl-2,3-dihydrobenzofuran (**17a**)

Yield: 50 %. Its ^{1}H and ^{13}C NMR spectra were found to be identical to those reported in the literature [19]. FT-IR ν_{max} (NaCl): 3019, 2972, 2925, 2864, 1614, 1492, 1256, 808 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 162 (M^+, 98), 147 (100), 119 (52). ESI HRMS (amu): calcd $C_{11}H_{14}O$ $[M+H]^+$: 163.1117; found $[M+Na]^+$: 163.1124.

5-Methoxy-2,2-dimethyl-2,3-dihydrobenzofuran (**18a**)

Yield: 54 %. Its ^{1}H and ^{13}C NMR spectra were found to be identical to those reported in the literature [19]. FT-IR ν_{max} (NaCl): 2969, 2959, 1609, 1488, 1255, 1147, 1034, 878 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 178 (M^+, 100), 163 (49), 135 (24). ESI HRMS (amu): calcd $C_{11}H_{14}O_2$ $[M+H]^+$: 179.1067; found $[M+H]^+$: 179.1070.

2,2-Dimethyl-5-phenyl-2,3-dihydrobenzofuran (**19a**)

Yield: 42 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.55 (s, 6H), 3.10 (s, 2H), 6.84 (d, J = 8.1 Hz, 1H), 7.55–7.59 (m, 2H), 7.32–7.44 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.7, 43.2, 87.5, 110.2, 124.4, 126.8, 127.1, 127.5, 128.2, 129.0, 133.9, 141.8, 158.9. FT-IR ν_{max} (NaCl): 3052, 2962, 2925, 2856, 1736, 1609, 1479, 1257, 761 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 224 (M^+, 100), 209 (27). ESI HRMS (amu): calcd $C_{16}H_{16}O$ $[M+H]^+$: 225.1274; found $[M+H]^+$: 225.1276.

5-Fluoro-2,2-dimethyl-2,3-dihydrobenzofuran (**20a**)

Yield: 28 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.49 (s, 6H), 3.01 (s, 2H), 6.62–6.66 (m, 1H), 6.84–7.29 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.4, 43.4, 87.6, 112.7, 114.5, 116.5, 128.8, 156.0, 159.1. FT-IR ν_{max} (NaCl): 2956, 2913, 2869, 1732, 1486, 1252, 858 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 166 (M^+, 100), 151 (96), 123 (68). ESI HRMS (amu): calcd $C_{10}H_{11}FO$ $[M+H]^+$: 167.0867; found $[M+H]^+$: 167.0870.

5-Chloro-2,2-dimethyl-2,3-dihydrobenzofuran (**21a**)

Yield: 29 %. Its ^{1}H and ^{13}C NMR spectra were found to be identical to those reported in the literature [19]. FT-IR ν_{max} (NaCl): 2957, 2921, 2851, 1740, 1475, 1370, 1258, 811 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 182/184 (M^+, 100/31), 167/169 (91/29), 139/137 (51/18). ESI HRMS (amu): calcd $C_{10}H_{11}ClO$ $[M+H]^+$: 183.0571; found $[M+H]^+$: 183.0572.

5-Methoxy-2-methyl-2-phenyl-2,3-dihydrobenzofuran (**24a**)

Yield: 55 %. Its ^{1}H and ^{13}C NMR spectra were found to be identical to those reported in the literature [13]. GC–MS (EI): *m/z* (% relative abundance) 240 (M^+, 100), 225 (24). ESI HRMS (amu): calcd $C_{16}H_{16}O_2$ $[M+Na]^+$: 263.1043; found $[M+Na]^+$: 263.1048.

5-(tert-Butyl)-2-methyl-2-phenyl-2,3-dihydrobenzofuran (**25a**)

Yield: 50 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.51 (s, 9H), 1.97 (s, 3H), 3.58 (AB quartet, J = 15.2 Hz, 2H), 7.05 (d, J = 8.0 Hz, 1H), 7.38–7.52 (m, 5H), 7.69 (d, J = 7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.0, 32.4, 34.8, 45.6, 89.6, 109.3, 122.6, 125.1, 125.4, 126.6, 127.5, 128.9, 1439, 147.7, 157.2. FT-IR ν_{max} (NaCl): 3064, 3023, 2963, 2864, 1739, 1494, 1242, 1049, 820 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 266 (M^+, 46), 251 (100). ESI HRMS (amu): calcd $C_{19}H_{22}O_2$ $[M+Na]^+$: 289.1563; found $[M+Na]^+$: 289.1558.

3H-Spiro[benzofuran-2, 1′-cyclohexane] (***26a***)

Yield: 22 %. Its ^{1}H and ^{13}C NMR spectra were found to be identical to those reported in the literature [19]. FT-IR ν_{max} (NaCl): 3035, 2931, 2854, 1732, 1481, 1239, 873 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 188 (M^+, 100). ESI HRMS (amu): calcd $C_{13}H_{16}O$ $[M+H]^+$: 189.1274; found $[M+H]^+$: 189.1271.

5-Methoxy-3H-spiro[benzofuran-2, 1′-cyclohexane] (**27a**)

Yield: 51 %. Its ^{1}H and ^{13}C NMR spectra were found to be identical to those reported in the literature [13]. GC–MS (EI): *m/z* (% relative abundance) 218 (M^+, 100). ESI HRMS (amu): calcd $C_{14}H_{18}O_2$ $[M+Na]^+$: 241.1199; found $[M+Na]^+$: 241.1197.

5-(tert-Butyl)-3H-spiro[benzofuran-2, 1′-cyclohexane] (**28a**)

Yield: 69 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 9H), 1.74–2.09 (m, 10H), 3.00 (s, 2H), 6.88 (d, J = 8.0 Hz, 1H), 7.27 (m, 1H), 7.31 (d, J = 8.0 Hz, 1H). ^{13}C NMR (75 MHz $CDCl_3$): δ 23.5, 25.6, 32.1, 34.6, 37.6, 41.5, 88.9, 109.0, 122.5, 124.9, 126.8, 143.1, 157.0. FT-IR ν_{max} (NaCl): 2934, 2891, 1736, 1496, 1240, 812 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 244 (M^+, 44), 229 (100). ESI HRMS (amu): calcd $C_{17}H_{24}O$ $[M+Na]^+$: 267.1719; found $[M+Na]^+$: 267.1710.

5-Phenyl-3H-spiro[benzofuran-2, 1′-cyclohexane] (**29a**)

Yield: 50 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.74–1.88 (m, 10H), 3.05 (s, 2H), 6.84 (d, $J = 7.2$ Hz, 1H), 7.28–7.45 (m, 5H), 7.55 (d, $J = 7.4$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 27.3, 37.6, 41.3, 89.4, 110.0, 124.4, 126.7, 127.1, 127.4, 127.9, 129.0, 133.7, 141.9, 159.0. FT-IR ν_{max} (NaCl): 3031, 2930, 2853, 1740, 1609, 1479, 1240, 761 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 264 (M^+, 100). ESI HRMS (amu): calcd $C_{19}H_{20}O$ $[M+H]^+$: 265.1587; found $[M+H]^+$: 265.1591.

2,2-Dimethyl-2,3-dihydronaphtho[1,2-b]furan (**30a**)

Yield: 80 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.62 (s, 6H), 3.23 (s, 2H), 7.35–7.50 (m, 4H), 7.84–7.87 (m, 1H), 8.00–805 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.9, 44.1, 87.8, 119.9, 120.0, 121.1, 122.0, 123.6, 125.4, 125.8, 128.2, 134.4, 154.6. FT-IR ν_{max} (NaCl): 3056, 2970, 2925, 1527, 1454, 1313, 800 cm^{-1}. GC–MS (EI): *m/z* (% relative abundance) 198 (M^+, 100), 183 (42), 155 (12). ESI HRMS (amu): calcd $C_{14}H_{14}O$ $[M+H]^+$: 199.1117; found $[M+H]^+$: 199.1111.

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References

1. Varanda EA, Raddi MSG, Dias FLP, Araujo MCS, Gibran SCA, Takahashi CS, Vilegas W (1997) Mutagenic and cytotoxic activity of an isocoumarin (paepalantine) isolated from *Paepalanthus vellozioide*. Teratogen Carcinog Mutagen 17:85–95. doi:10.1002/(SICI)1520-6866(1997)17:2<85:AID-TCM4>3.0.CO;2-A
2. Apers S, Vlietinck A, Pieters L (2003) Lignans and neolignans as lead compounds. Phytochem Rev 2:201–217. doi:10.1023/B:PHYT.0000045497.90158.d2
3. Hussein AA, Barberena I, Capson TL, Kursar TA, Coley PD, Solis PN, Gupta MP (2004) New cytotoxic naphthopyrane derivatives from *Adenaria floribunda*. J Nat Prod 67:451–453. doi:10.1021/np030223d
4. Gravot A, Larbat R, Hehn A, Lievre K, Gontier E, Goergen J, Bourgaud F (2004) Cinnamic acid 4-hydroxylase mechanism-based inactivation by psoralen derivatives: cloning and characterization of a C4H from a psoralen producing plant—*Ruta graveolens*—exhibiting low sensitivity to psoralen inactivation. Arch Biochem Biophys 422:71–80. doi:10.1016/j.abb.2003.12.013
5. Marumoto S, Miyazawa M (2011) Microbial reduction of coumarin, psoralen, and xanthyletin by *Glomerella cingulata*. Tetrahedron 67:495–500. doi:10.1016/j.tet.2010.10.089
6. Martini JC, Franke NW, Singerman GM (1970) New preparation of coumarins. J Org Chem 35:2904–2907. doi:10.1021/jo00834a011
7. Casnati G, Pochini A, Terenghi MG, Ungaro R (1983) *O*-Quinonemethide intermediates and their role in coordinated reactions of magnesium phenoxides with α-branched aliphatic aldehydes. J Org Chem 48:3783–3787. doi:10.1021/jo00169a036
8. Bartz QR, Miller RF, Adams R (1935) The introduction of isobutyl groups into phenols, cresols and homologous compounds. J Am Chem Soc 57:371–376. doi:10.1021/ja01305a044
9. Bagnell L, Cablewski T, Strauss CR, Trainor RW (1996) Reactions of allyl phenyl ether in high-temperature water with conventional and microwave heating. J Org Chem 61:7355–7359. doi:10.1021/jo961095j
10. Grant VH, Liu B (2005) Iridium(III)-catalyzed tandem Claisen rearrangement-intramolecular hydroaryloxylation of aryl allyl ethers to form dihydrobenzofurans. Tetrahedron Lett 46:1237–1239. doi:10.1016/j.tetlet.2005.01.006
11. Arduini A, Pochini A, Ungaro R (1984) Selective synthesis of 2-alkenylphenols and 2,2-dialkyl-2,3-dihydrobenzofurans from 2-hydroxybenzyl alcohols. Synthesis 1984:950–953. doi:10.1055/s-1984-31033
12. Choudhury PK, Almena J, Foubelo F, Yus M (1997) New homologation of 2-hydroxy and 2-mercapto benzylic alcohols. Tetrahedron 53:17373–17382. doi:10.1016/S0040-4020(97)10161-2
13. Dohi T, Hu Y, Kamitanaka T, Washimi N, Kita Y (2011) [3+2] Coupling of quinone monoacetals by combined acid-hydrogen bond donor. Org Lett 13:4814–4817. doi:10.1021/ol201886r
14. Dohi T, Hu Y, Kamitanaka T, Kita Y (2012) Controlled coupling of quinone monoacetals using reusable polystyrene-anchored specific proton catalyst. Tetrahedron 68:8424–8530. doi:10.1016/j.tet.2012.07.089
15. Palucki M, Wolfe JP, Buchwald SL (1996) Synthesis of oxygen heterocycles via a palladium-catalyzed C–O bond-forming reaction. J Am Chem Soc 118:10333–10334. doi:10.1021/ja962408v
16. Mann G, Incarvito C, Rheingold AL, Hartwig JF (1999) Palladium-catalyzed C–O coupling involving unactivated aryl halides. sterically induced reductive elimination to form the C–O bond in diaryl ethers. J Am Chem Soc 121:3224–3225. doi:10.1021/ja984321a
17. Kataoka N, Shelby Q, Stambuli JP, Hartwig JF (2002) Air stable, sterically hindered ferrocenyl dialkylphosphines for palladium-catalyzed C–C, C–N, and C–O bond-forming cross-couplings. J Org Chem 67:5553–5566. doi:10.1021/jo025732j
18. Niu J, Guo P, Kang J, Li Z, Xu J, Hu S (2009) Copper(I)-catalyzed aryl bromides to form intermolecular and intramolecular carbon–oxygen bonds. J Org Chem 74:5075–5078. doi:10.1021/jo900600m
19. Wang X, Lu Y, Dai H-X, Yu J-Q (2010) Pd(II)-catalyzed hydroxyl-directed C–H activation/C–O cyclization: expedient construction of dihydrobenzofurans. J Am Chem Soc 132:12203–12205. doi:10.1021/ja105366u
20. Lafrance M, Gorelsky SI, Fagnou K (2007) High-yielding palladium-catalyzed intramolecular alkane arylation: reaction development and mechanistic studies. J Am Chem Soc 129:14570–14571. doi:10.1021/ja076588s
21. He Z, Yudin AK (2006) Palladium-catalyzed oxidative activation of arylcyclopropanes. Org Lett 8:5829–5832. doi:10.1021/ol062476e
22. Huang P-JJ, Stanley Cameron T (2009) Novel synthesis of 2,2-dialkyl-3-dialkylamino-2,3-dihydro-1*H*-naphtho[2,1-*b*]pyrans. Tetrahedron Lett 50:51–54. doi:10.1016/j.tetlet.2008.10.083
23. Jha A, Paul NK, Trikha S, Cameron TS (2006) Novel synthesis of 2-naphthol Mannich bases and their NMR behaviour. Can J Chem 84:843–853. doi:10.1139/v06-081
24. Paul NK, Dietrich L, Jha A (2007) Convenient synthesis of 1-arylmethyl-2-naphthols. Synth Commun 37:877–888. doi:10.1080/00397910601163547
25. Huang P-JJ, Youssef D, Cameron TS, Jha A (2008) Microwave-assisted synthesis of novel 2-naphthol bis-Mannich bases. Arkivoc 16:165–177
26. Mukherjee C, MacLean ED, Cameron TS, Jha A (2010) Enzyme-assisted kinetic resolution of novel 2-naphthol Mannich bases.

J Mol Catal B Enzym 62:46–53. doi:10.1016/j.molcatb.2009.09.001

27. Vaughan D, Jha A (2009) Convenient synthesis of novel 2,2-dialkyl-1,2-dihydronaphtho[2,1-*b*]furans. Tetrahedron Lett 50:5709–5712. doi:10.1016/j.tetlet.2009.07.087
28. Vaughan D, Naidu AB, Jha A (2012) One-pot annulation of 2-naphthol analogs to heterocycles. Curr Org Synth 9:613–649. doi:10.2174/157017912803251747
29. Kumar R, Nandi GC, Verma RK, Singh MS (2010) A facile approach for the synthesis of 14-aryl- or alkyl-14*H*-dibenzo[*a*,*j*] xanthenes under solvent-free condition. Tetrahedron Lett 51:442–445. doi:10.1016/j.tetlet.2009.11.064
30. Urinda S, Kundu D, Majee A, Hajra A (2009) Indium triflate-catalyzed one-pot synthesis of 14-alkyl or aryl-14*H*-dibenzo[*a*,*j*] xanthenes in water. Heteroatom Chem 20:232–234. doi:10.1002/hc.20539
31. Kobayashi S, Sugiura M, Kitagawa H, Lam WWL (2002) Rare-earth metal triflates in organic synthesis. Chem Rev 102:2227–2302. doi:10.1021/cr010289i