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New Synthesis of 2-Aryl-3-Substituted Benzo[*b*]furans from Benzyl 2-Halophenyl Ethers†

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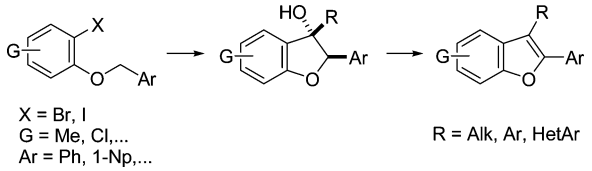
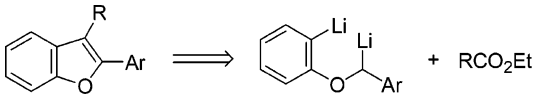


Treatment of benzyl 2-halophenyl ethers with 3 equiv of *t*-BuLi results in Li−halogen exchange and lithiation at benzylic methylene simultaneously. These dianions do not undergo Wittig rearrangement and can be trapped with electrophiles. Their reactions with carboxylic esters afford the corresponding 2-aryl-3-hydroxy-2,3-dihydrobenzo[*b*]-furans as a mixture of diastereoisomers. Subsequent acid-catalyzed or mediated dehydration gives moderate to good overall yield of a variety of 2-aryl-3-substituted benzo[*b*]-furans.

Benzo[*b*]furans have attracted considerable attention as a result of their biological activity and their presence in a variety of significant natural products.[1] So, there is a growing interest in developing general and versatile synthetic methods for the preparation of this kind of compound.[2] In this area, we have recently reported a practical and efficient route to 4-halo and 4-functionalized benzo[*b*]furans from 3-halophenols based on a tandem Sonogashira coupling/5-*endo*-*dig* cyclization of 3-halo-2-iodophenols with alkynes.[3] In contrast to the vast array of methods for benzo[*b*]furan synthesis based on the construction of furan rings from various arene derivatives by formation of one O−C, one C−C or one O−C, and one C−C bonds,[4] there are a limited number of methodologies available based on simultaneous two C−C bond formations, that is, C_2-C_3 and C_3-C_{3a} bonds.[5] In this context, we envisaged that if we were able to prepare α-lithiobenzyl 2-lithiophenyl ethers, the subsequent reaction with carboxylic esters[6] and further dehydration would provide us the corresponding 2-aryl-3-substituted benzo-[*b*]furans (Scheme 1). We believe that this disconnection would represent one efficient strategy for benzo[*b*]furan formation, because starting benzyl ethers are readily accessible, and the C_3 substituent could be easily selected from the huge pool of available esters.

SCHEME 1. Retrosynthetic Analysis of 2-Aryl-3-Substituted Benzo[*b*]furans



However, whereas 3-substituted benzo[*b*]thiophene derivatives have been synthesized by reaction of acyl chlorides with the dianion of thioanisole,[7] it is well-known that α-oxygen carbanions are unstable and usually undergo protophilic cleavage (elimination) or [1,2]-Wittig rearrangement.[8] In our studies on the reactivity of *o*-lithioaryl ethers, we have found that benzyl *o*-lithioaryl ethers, generated by halogen−lithium exchange with *t*-BuLi (2 equiv), undergo in THF a tandem anion translocation/Wittig rearrangement to afford diarylcarbinols.[9] We reasoned that if a benzylic hydrogen atom is removed in that process by an aryllithium moiety, an excess of base could give rise to an α-lithiobenzyl *o*-lithiophenyl ether. Although this kind of organolithium could undergo the Wittig rearrangement, the high anionic character of the *o*-lithiophenoxy ring could inhibit the rearrangement.[10]

In this paper, we wish to report a novel one-step synthesis of 2-aryl-3-substituted benzo[*b*]furans by condensation of carboxylic esters with the dianions generated from benzyl 2-halophenyl ethers.

† Dedicated to Professor Francisco J. Arnáiz on the occasion of his 60th birthday.

(1) (a) Keay, B. A.; Dibble, P. W. Furans and their Benzo Derivatives: Applications. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 2, pp 395−436. (b) Hou, X.-L.; Yang, Z.; Wong, H. N. C. Furans and Benzofurans. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Gilchrist, T. L., Eds.; Pergamon: Oxford, 2002; Vol. 14, pp 139−179. Some 2-arylbenzo[*b*]furans are inhibitors of cell proliferation and the platelet-activating factor, and some of them show fungicidal and cytotoxic activities: Ward, R. S. *Nat. Prod. Rep.* **1997**, *14*, 43−74.

(2) For recent reports on the synthesis of 2,3-disubstituted benzo[*b*]furans, see: (a) Miyata, O.; Takeda, N.; Naito, T. *Org. Lett.* **2004**, *6*, 1761−1763. (b) Zhang, H.; Ferreira, E. M.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 6144−6148. (c) Kim, K.-O.; Tae, J. *Synthesis* **2005**, 387−390. (d) Colobert, F.; Castanet, A.-S.; Abillard, O. *Eur. J. Org. Chem.* **2005**, 3334−3341. (e) Liao, Y.; Smith, J.; Fathi, R.; Yang, Z. *Org. Lett.* **2005**, *7*, 2707−2709. (f) Chen, C.; Dormer, P. G. *J. Org. Chem.* **2005**, *70*, 6964−6967.

(3) Sanz, R.; Castroviejo, M. P.; Fernández, Y.; Fañanás, F. J. *J. Org. Chem.* **2005**, *70*, 6548−6551.

(4) 3-Arylbenzofurans have been prepared by the formation of the C_3-C_{3a} bond through a halogen−metal exchange/cyclization process from iodoketones: (a) Kraus, G. A.; Kim, I. *Org. Lett.* **2003**, *5*, 1191−1192. (b) Kraus, G. A.; Schroeder, J. D. *Synlett* **2005**, 2504−2506.

(5) Katritzky has designed a one-pot, four-step preparation of benzofurans using benzotriazole chemistry: Katritzky, A. R.; Serdyuk, L.; Xie, L. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1059−1064.

(6) We have reported that 1,4-dianions, like 3,4-bis(lithiomethyl)-dihydropyrroles, efficiently react with carboxylic esters to afford hydroxy cyclic derivatives: Barluenga, J.; Fañanás, F. J.; Sanz, R.; Ignacio, J. M. *Eur. J. Org. Chem.* **2003**, 771−783. Also, 2-substituted 6-azaindoles have been synthesized by the condensation of the dianion derived from 3-amino-4-picoline with carboxylic esters: Song, J. J.; Tan, Z.; Gallou, F.; Xu, J.; Yee, N. K.; Senanayake, C. H. *J. Org. Chem.* **2005**, *70*, 6512−6514.

(7) (a) Campaigne, E.; Rogers, R. B.; Donelson, A.; Bosin, T. R. *J. Heterocycl. Chem.* **1973**, *10*, 979−981. (b) Campaigne, E.; Homfeld, R.; Mais, D. E. *J. Heterocycl. Chem.* **1978**, *15*, 1351−1359. (c) Cabiddu, S.; Cancelu, D.; Floris, C.; Gelli, G.; Melis, S. *Synthesis* **1988**, 888−890.

(8) (a) Wittig, G.; Löhmann, L. *Justus Liebigs Ann. Chem.* **1942**, *550*, 260−268. (b) Marshall, J. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, pp 975−1014. (c) Tomooka, K.; Yamamoto, H.; Nakai, T. *Liebigs Ann./Recl.* **1997**, 1275−1281.

(9) Barluenga, J.; Fañanás, F. J.; Sanz, R.; Marcos, C.; Trabada, M. *Org. Lett.* **2002**, *4*, 1587−1590.

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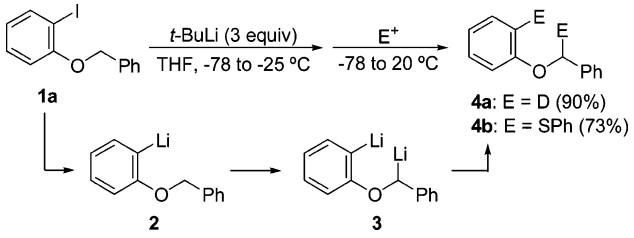
SCHEME 2. Lithiation Conditions for 1-(Benzyloxy)-2-iodobenzene 1a

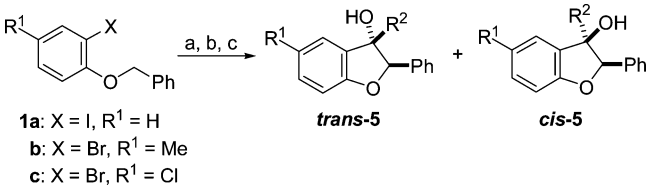


First, benzyl *o*-iodophenyl ether[11] **1a** was chosen to perform an initial set of experiments to determine the optimum reaction conditions for the generation of the dilithiated ether **3**. We had shown that the reaction of **1a** with 2 equiv of *t*-BuLi in THF afforded organolithium **2**, which is stable at low temperature and could be trapped with deuterium oxide.[9] Treatment of **1a** with 3 equiv of *t*-BuLi in THF at −78 °C led to complete lithiation at the ortho position but only partial lithiation at the benzylic methylene, as determined by a deuterium-labeling experiment. An increase of the temperature up to −60 °C resulted in an increase of deuterium incorporation (55%) at the benzylic position. Finally, we found that at −25 °C the dilithiation was complete, allowing the isolation of dideuterated ether **4a** in almost quantitative yield (Scheme 2).[12] Gratifyingly, diphenylmethanol, the expected product from a [1,2]-Wittig rearrangement, was not detected under these conditions. Moreover, dianion **3** was stable for at least 1 h at 0 °C but, at room temperature, slowly underwent Wittig rearrangement (10% of diphenylmethanol was generated after 1 h). At this time, it seems clear that the lithium atom on the phenoxy ring is playing a pivotal role in the inhibition of the Wittig rearrangement, because it is well-known that benzyl phenyl ether affords diphenylmethanol in almost quantitative yield on treatment with *n*-BuLi.[10] Dianion **3** could also be trapped with other electrophiles such as diphenyl disulfide giving rise to the difunctionalized ether **4b** in good yield (Scheme 2).

However, it was not possible to selectively funtionalize one of the metalated positions of **3**. The reaction of **1a** with *t*-BuLi (3 equiv) from −78 to −25 °C, further addition of 1 equiv of MeOD, and subsequent hydrolysis gave rise to **4a** with partial incorporation of deuterium at both lithiated positions of intermediate **3**. This fact points out a similar reactivity for the two anionic centers of dianion **3**.

Once we had found the conditions for the selective double lithiation of ether **1a**, we decided to investigate the reaction of this dianion with carboxylic esters to get the benzo[*b*]furan skeleton (Scheme 3). Thus, as shown in Table 1 (entries 1−6), a wide range of aliphatic or aromatic carboxylic esters[13] were useful electrophiles for the trapping of dianion **3**, and dihydrobenzofuranols **5a**−**f** were isolated in moderate to good yields as mixtures of the corresponding cis and trans diastereoisomers.

SCHEME 3. Preparation of 2-Aryl-3-hydroxy-2,3-dihydrobenzo[*b*]furans 5[a]



[a] Reagents and conditions: (a) *t*-BuLi (3 equiv), THF, −78 to −25 °C, 1 h; (b) R^2CO_2Et, −78 to 20 °C; (c) H_2O.

TABLE 1. Synthesis of 2,3-Dihydrobenzo[*b*]furan Derivatives 5

entry	starting ether	R^1	X	product	R^2	dr[a]	yield[b] (%)
1	**1a**	H	I	**5a**	Me[c]	1.3:1	65
2	**1a**	H	I	**5b**	Pr	5:1	64[d]
3	**1a**	H	I	**5c**	*i*-Pr	5:1	40[d]
4	**1a**	H	I	**5d**	*i*-Bu	7:1	47[d]
5	**1a**	H	I	**5e**	*t*-Bu	1:2.5	63[e]
6	**1a**	H	I	**5f**	2-Th[f]	2.5:1	65
7	**1b**	Me	Br	**5g**	Me[c]	2:1	62[g]
8	**1c**	Cl	Br	**5h**	*i*-Bu	5:1	53
9	**1c**	Cl	Br	**5i**	Ph	1:1.5	55[h]

[a] Diastereoisomeric ratio (trans/cis) calculated from the ^{1}H NMR of the crude of the reaction. [b] Isolated yield based on the starting ether **1**. [c] *tert*-Butyl acetate was used. [d] Yields for the isolated trans isomers. [e] The trans isomer was isolated in 15% yield, and the cis isomer was isolated in 48% yield. [f] 2-Th = 2-thienyl. [g] The trans isomer was isolated in 43% yield and the cis isomer was isolated in 19% yield. [h] The trans isomer was isolated in 23% yield and the cis isomer was isolated in 32% yield.

The use of sterically demanding esters (butyrate, isobutyrate, or isovalerate esters) led to an increase in the stereoselectivity of the reaction, favoring the formation of the trans diastereoisomer. It is important to remark that both diastereoisomers could be easily separated, allowing in most cases the isolation of the major diastereoisomer in a practical yield. Surprisingly, when ethyl pivalate was employed, the opposite stereoselectivity was observed with the *cis*-dihydrobenzofuranol being the major isomer (Table 1, entry 5). An ester derived from 2-thiophene carboxylic acid also condensed with **3** to afford the corresponding dihydrobenzofuranol **5f** with moderate trans selectivity (Table 1, entry 6). The stereochemistry of the cis and trans isomers of **5** was determined by NMR 2D-NOESY experiments and by considering the anisotropic effect of the C_2-phenyl group for the C_3 substituent in the ^{1}H NMR spectra.[14] Also, our assignment was in agreement with reported data for some of these compounds previously prepared with moderate cis selectivity by photocyclization reactions of *o*-alkoxy phenyl ketones.[15] Two other different starting ethers, **1b**,**c**, were prepared, and we checked that their double lithiation took place under the same reaction conditions as the parent ether **1a**. It is interesting to note that even the occurrence of a chlorine atom in **1c** does not interfere in the lithiation of the benzylic position. The reaction of **1b**,**c** with some of the above used organic carboxylates

(10) Schöllkopf, U. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 763−773. Eisch et al. reported that treatment of benzyl 2-bromo-4-*tert*-butylphenyl ether with PhLi (2 equiv) in THF gave rise mainly to α-elimination along with biphenyl and polymeric products. Eisch, J. J.; Kovacs, C. A.; Rhee, S.-G. *J. Organomet. Chem.* **1974**, *65*, 289−301.

(11) See Supporting Information for the detailed preparation of the starting ethers.

(12) At this temperature in Et_2O/TMEDA, complete lithiation at the ortho position, but only partial lithiation (40%) at the benzylic position, took place, as determined by deuteration experiments.

(13) In the case of esters derived from acetic acid, the use of ethyl acetate led to a complex mixture of products.

(14) See Supporting Information for NOESY experiments and for a comparison of the NMR data of cis and trans diastereoisomers.

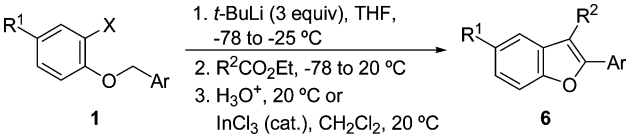
(15) Dihydrobenzofuranols **5a**,**c** have yet been prepared as a mixture of diastereoisomers by photocyclization of the corresponding *o*-alkoxy phenyl ketones: (a) Wagner, P. J.; Meador, M. A.; Scaiano, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 7988−7989. (b) Wagner, P. J.; Meador, M. A.; Park, B.-S. *J. Am. Chem. Soc.* **1990**, *112*, 5199−5211. (c) Sharshira, E. M.; Okamura, M.; Hasegawa, E.; Horaguchi, T. *J. Heterocycl. Chem.* **1997**, *34*, 861−869. (d) Sharshira, E. M.; Horaguchi, T. *J. Heterocycl. Chem.* **1997**, *34*, 1837−1849.

TABLE 2. Synthesis of 2-Aryl-3-Substituted Benzo[*b*]furans 6

starting ether	X	R^1	Ar	R^2	product	yield[a] (%)
1a	I	H	Ph	Me[b]	**6a**	58
1a	I	H	Ph	Pr	**6b**	73
1a	I	H	Ph	*i*-Pr	**6c**	71
1a	I	H	Ph	*i*-Bu	**6d**	46
1a	I	H	Ph	*c*-C_3H_5	**6e**	64
1a	I	H	Ph	2-Th[c]	**6f**	54
1b	Br	Me	Ph	Me[b]	**6g**	53
1b	Br	Me	Ph	*c*-C_3H_5	**6h**	45
1c	Br	Cl	Ph	Me[b]	**6i**	64
1c	Br	Cl	Ph	*i*-Pr	**6j**	61
1d	I	H	*p*-Tol	*i*-Pr	**6k**	70
1d	I	H	*p*-Tol	2-Th[c]	**6l**	58
1d	I	H	*p*-Tol	2-Fu[d]	**6m**	60
1e	I	H	1-Np[e]	*i*-Pr	**6n**	70
1f	Br	H	2-FC_6H_4	*i*-Pr	**6o**	35
1g	I	H	2-(MeO)C_6H_4	2-Fu[d]	**6p**	47

[a] Isolated yield based on the starting ether **1**. [b] $MeCO_2t$-Bu was used as carboxylate. [c] 2-Th = 2-thienyl. [d] 2-Fu = 2-furyl. [e] 1-Np = 1-naphthyl.

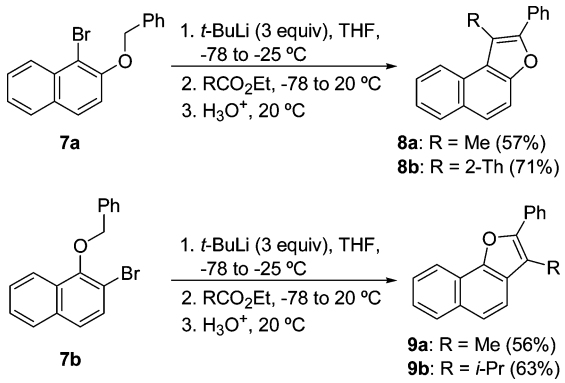
SCHEME 4. Synthesis of 2-Aryl-3-Substituted Benzo[*b*]furans 6



afforded the corresponding 2,3-dihydrobenzo[*b*]furans **5g**,**h** in similar yields and stereoselectivities as those reported for **1a** (Scheme 3 and Table 1, entries 7 and 8).

After we had shown that carboxylic esters behave as useful C_1 synthons for the generation of the benzo[*b*]furan skeleton, we tried to synthesize the targeted 2-aryl-3-substituted benzo[*b*]furans. This goal was easily accomplished by in situ acid-mediated dehydration with concentrated hydrochloric acid of the intermediates dihydrobenzo[*b*]furans **5**.[16] Thus, treatment of starting benzyl ethers **1** with *t*-BuLi, followed by the addition of the carboxylic ester and final treatment with hydrochloric acid, afforded the corresponding 2-aryl-3-substituted benzo[*b*]furans **6** in overall moderate to good yields (Scheme 4 and Table 2). Alternatively, we found that the dehydration process could be carried out with similar overall yields but in milder conditions under Lewis acid-catalyzed conditions by treatment of dihydrobenzofuranols **5** with $InCl_3$ (5 mol %) in CH_2Cl_2.[17] Several aliphatic and aromatic carboxylic esters were treated with different dianions **3** to evaluate the scope of this new method. The results are shown in Table 2. Easily enolizable esters (*tert*-butyl acetate) or sterically demanding ones (ethyl pivalate) are useful substrates, showing that the dianion acts as a typical nucleophile but not as a base. With regard to the starting ether moiety, besides the benzyl ethers **1a**−**c**, 2-halophenyl ethers **1d**,**e** with different aryl groups as the benzylic component also resulted to be useful substrates for the synthesis of benzo[*b*]furans **6k**−**n** (Scheme 4 and Table 2). It is worth pointing out that benzyl ethers **1f**,**g** with fluorine and methoxy substituents, respectively, on the aromatic ring of the benzyl moiety are also selectively lithiated at the benzylic position after the initial halogen−lithium exchange. So, functionalized benzo[*b*]furans **6o**,**p** could be prepared in moderate, not optimized, yields (Table 2).

SCHEME 5. Synthesis of 2-Aryl-3-Substituted Naphtho[2,1-*b*]furans 8 and Naphtho[1,2-*b*]furans 9



Finally, we decided to check if this methodology could be applied to the preparation of naphthofurans starting from benzyl halonaphthyl ethers. So, the reaction of benzyl 1-bromo-2-naphthyl ether **7a**, under the same reaction conditions used for the phenyl ethers **1**, gave rise to the expected naphtho[2,1-*b*]furans **8** in good yields (Scheme 5). In the same way, double lithiation of benzyl 2-bromo-1-naphthyl ether **7b**[18] and subsequent condensation with carboxylic esters furnished the desired naphtho[1,2-*b*]furans **9** (Scheme 5).

In summary, we have developed a practical and efficient route to 2-aryl-3-substituted benzo[*b*]furans and related naphthofurans from readily available starting materials, benzyl 2-haloaryl ethers and carboxylic esters. The key step is the selective double lithiation of the starting ethers at the benzylic and *ortho*-positions and further trapping of these dianions with several esters. Moreover, in most cases, intermediate 2-aryl-3-hydroxy-2,3-dihydrobenzo[*b*]furans could be isolated as pure diastereoisomers. We believe that this methodology constitutes a synthetically competitive alternative to the existing strategies for the construction of the benzo[*b*]furan motif.

Experimental Section

General Procedure for the Synthesis of 2-Aryl-3-hydroxy-2,3-dihydrobenzo[*b*]furans 5. Synthesis of *trans*-3-Hydroxy-3-isopropyl-2-phenyl-2,3-dihydrobenzo[*b*]furan (5c; Table 1, Entry 3). *t*-BuLi (2 mL of a 1.5 M solution in pentane, 3 mmol) was added to a solution of ether **1a** (0.310 g, 1 mmol) in THF (2 mL) at −78 °C. The resulting solution was stirred for 30 min at −78 °C, and then the reaction mixture was allowed to warm to −25 °C and stirred for 40 min. After cooling to −78 °C, ethyl isobutyrate (0.116 g, 1 mmol) was added, and stirring continued at low temperature for an additional 30 min. The reaction mixture was then allowed to warm to room temperature, quenched with water, and extracted with EtOAc (3 × 25 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was purified by column chromatography (eluent: hexane/EtOAc, 5/1) on silica gel to afford the major trans diastereoisomer, ***trans*-5c** (0.102 g, 40%): colorless oil;[15d] R_f 0.44

(16) Treatment of 3-hydroxy-2,3-dihydrobenzofurans with HCl induced dehydration, as previously observed: Pappas, S. P.; Blackwell, J. E., Jr. *Tetrahedron Lett.* **1966**, 1171−1175.

(17) Related with this process, Baba et al. have reported the deoxygenation of aryl ketones and *sec*-benzylic alcohols to the corresponding hydrocarbons with chlorodimethylsilane catalyzed by $InCl_3$: Miyai, T.; Ueba, M.; Baba, A. *Synlett* **1999**, 182−184.

(18) Synthesized from 2-bromo-1-naphthol, which was prepared by selective *o*-bromination with NBS of 1-naphthol following a reported procedure: Fujisaki, S.; Eguchi, H.; Omura, A.; Okamoto, A.; Nishida, A. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1576−1579.

(hexane/EtOAc, 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 7.6 Hz, 2H), 7.45−7.31 (m, 5H), 7.04−6.96 (m, 2H), 5.56 (s, 1H), 2.45 (br s, 1H), 1.81 (sept, J = 6.6 Hz, 1H), 0.97 (d, J = 6.6 Hz, 3H), 0.42 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 159.3 (C), 136.1 (C), 130.4 (C), 129.9 (CH), 128.2 (CH), 127.7 (CH), 126.0 (CH), 125.0 (CH), 121.1 (CH), 110.9 (CH), 94.4 (CH), 86.0 (C), 33.0 (CH), 16.6 (CH_3), 16.4 (CH_3); EI-LRMS *m*/*z* 254 (M^+, 4), 211 (100). HRMS calcd for $C_{17}H_{18}O_2$, 254.1307; found, 254.1316.

General Procedure for the Synthesis of 2-Aryl-3-substituted Benzo[*b*]furans 6. Synthesis of 3-Isopropyl-2-phenylbenzo[*b*]-furan (6c; Table 2). A solution of the corresponding dihydrobenzofuranol **5c**, prepared as described above, in CH_2Cl_2 (2 mL) was treated with $InCl_3$ (5 mol %) at room temperature for 1−2 h. The disappearance of the starting alcohol was monitored by TLC and GC-MS analysis. The solvent was evaporated under reduced pressure, and the crude product was purified by column chromatography (eluent: hexane) on silica gel to afford **6c** (0.168 g, 71%). Alternatively, after the addition of the carboxylic ester and evolution to room temperature, concentrated HCl was added to the THF solution of **5c**, and the stirring was maintained at room temperature until complete dehydration was determined by GC-MS analysis. **6c**: white solid; mp 63−65 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88−7.83 (m, 1H), 7.83−7.77 (m, 2H), 7.64−7.52 (m, 3H), 7.50−7.43 (m, 1H), 7.42−7.28 (m, 2H), 3.59 (sept, J = 7.1 Hz, 1H), 1.59 (d, J = 7.1 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 154.6 (C), 150.1 (C), 131.5 (C), 128.68 (CH), 128.65 (C), 128.4 (CH), 128.1 (CH), 124.0 (CH), 122.1 (CH), 121.8 (C), 121.5 (CH), 111.5 (CH), 25.7 (CH), 22.5 (CH_3); EI-LRMS *m*/*z* 236 (M^+, 54), 221 (100). HRMS calcd for $C_{17}H_{16}O$, 236.1201; found, 236.1208. Anal. Calcd for $C_{17}H_{16}O$: C, 86.40; H, 6.82. Found: C, 86.17; H, 6.81.

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Supporting Information Available: Typical experimental procedures and spectroscopic details for all compounds and a copy of ^{1}H, ^{13}C, and 2D-NOESY NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org

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