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NEW SYNTHESIS OF TETRAHYDROBENZODIFURANS BY ITERATIVE COUPLING OF QUINONE MONOACETALS WITH ALKENE NUCLEOPHILES

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Abstract – A new efficient synthetic strategy of tetrahydrobenzodifurans has been developed by the repetitive [3+2] couplings of quinone monoacetals with alkene nucleophiles. Both the symmetrical and unsymmetrical tetrahydrobenzodifurans can be easily synthesized by this continuous method by altering the type of alkenes. These tetrahydrobenzodifurans have also become a useful precursor of highly-substituted benzofurans by dehydrogenation.

In Celebration of Professor Dr. Lutz F. Tietze *on His 75th Birthday*

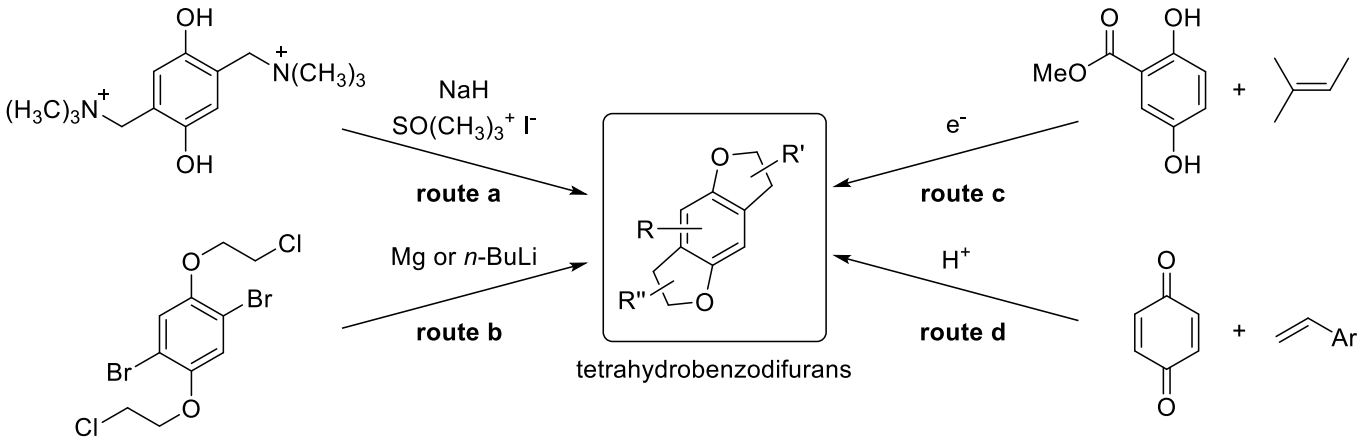
INTRODUCTION

Dihydrobenzofuran skeletons exist in many natural products and biologically-active compounds, showing a wide range of biological activities.[1] In addition, dihydrobenzofurans can be converted into aromatized benzofurans frequently found not only in biologically-active compounds,[2] but also in artificial organic materials,[3] by the treatment with oxidants, such as 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ).[4] Moreover, the tetrahydrobenzodifuran skeletons, which have two dihydrofuran rings fused to one benzene ring, are involved in several biologically-active compounds,[5] and their oxidation products, benzodifurans, are also utilized as biologically-active compounds[6] and organic materials.[7] Therefore, the development of

a concise synthetic method of dihydrobenzofurans and tetrahydrobenzodifurans is an important objective for contributing to the progress of pharmaceutical and material sciences.

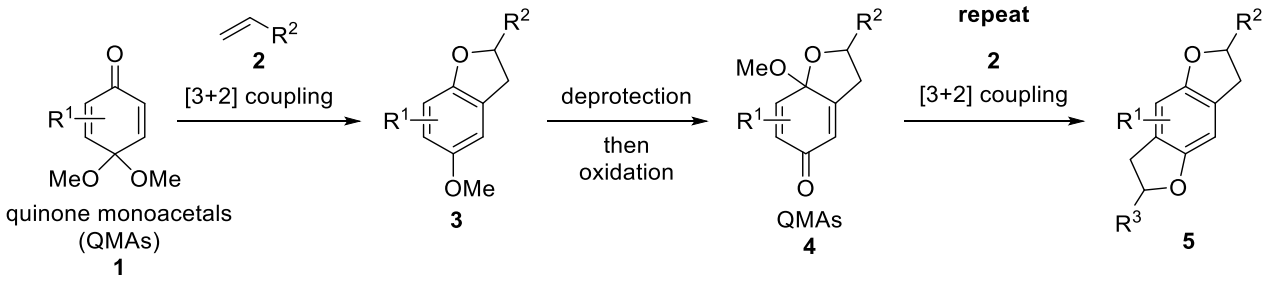
Because of their attractiveness as a synthetic target, many organic chemists have reported the methods for the synthesis of dihydrobenzofurans skeletons.[1] Most of these reported methods featured the construction of the furan ring skeletons, and the intramolecular *O*-alkyl or *O*-aryl bond formations were utilized as the key step of the cyclizations. However, these methods usually involve the pre-functionalization of the reaction site requiring many steps because the bond formations occurred in a step-by-step manner. Although some two-component intermolecular coupling cyclization strategies were reported as the short-step synthesis of these dihydrobenzofurans, the scope and application in natural products syntheses are still limited.

Furthermore, tetrahydrobenzodifuran syntheses are rather rare and few examples are known (Scheme 1),[5a,5c,8] despite their attractive characteristics. In 1982, Bladé-Font *et al.* reported the intermolecular cyclization of the *in situ* generated quinone methide and methiodide (route a).[8a] An efficient cyclization was achieved by the intramolecular nucleophilic substitution of an aryl alkyl ether promoted by butyl lithium[4a] or a Grignard reagent[5c] (route b). The anodic oxidative [3+2] cyclization of a hydroquinone and alkene nucleophile afforded the tetrahydrobenzodifuran in almost quantitative yield (route c).[8b] However, these previous reports did not focus on the synthesis of the tetrahydrobenzodifurans, and only one example of a tetrahydrobenzodifuran synthesis was mentioned in each report. Meanwhile, Lei *et al.* recently reported the synthesis of tetrahydrobenzodifurans by the one-pot sequential [3+2] coupling reactions of quinones and various styrene derivatives (route d).[8c] However, the unsymmetrical tetrahydrobenzodifurans were difficult to obtain by this method, thus the synthetic products were limited to symmetrical benzodifurans and very few examples of unsymmetrical benzodifurans. In addition, only the two quinone compounds, 1,4-benzoquinone and 1,4-naphthoquinone, were applicable for the reactions.



Scheme 1. General approaches to tetrahydrobenzodifurans

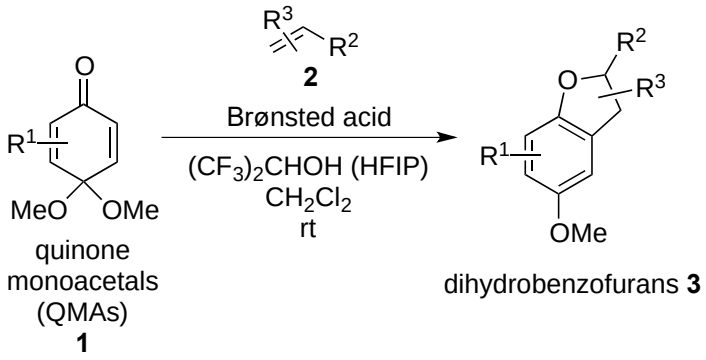
As an improvement of the quinone strategy, we now assume that the synthesis of the tetrahydrobenzodifurans **5** by the repetitive [3+2] coupling reactions of quinone monoacetals (QMAs) **1** and **4** *via* the deprotection of the methoxy group and oxidation of phenols is possible (Scheme 2). We now report the new synthetic strategy of symmetrical and unsymmetrical tetrahydrobenzodifurans by the iterative couplings of QMAs **1** and **4**.



Scheme 2. New approach toward benzodifurans

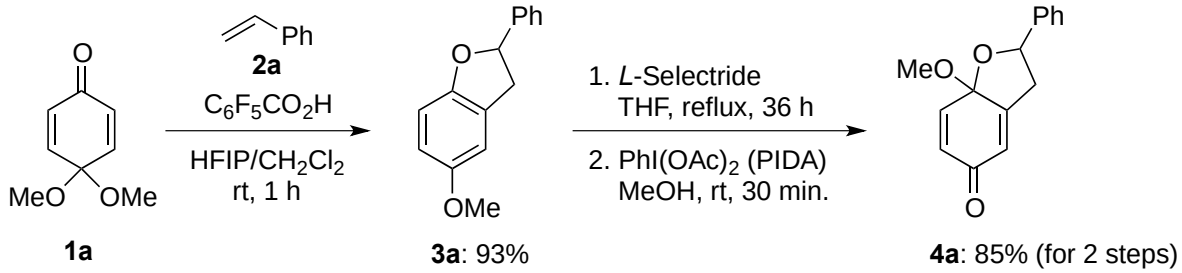
RESULTS AND DISCUSSION

For the synthesis of the tetrahydrobenzodifurans **5**, we focused on the utilization of the QMAs **1**, mono-protected quinones, as versatile precursors of the regio-controlled couplings to the allyl acetalcarbonyl moieties. These QMAs **1** can be effectively obtained by treating phenols with hypervalent iodine reagents, such as phenyl iodine(III) diacetate (PIDA), in methanol.[9,10] Regarding the reactivity, all the ring carbon atoms have an electrophilic nature due to the bifunctional structure, that is, the α,β-unsaturated carbonyl and allyl acetal moieties. Although the 1,2- or 1,4-addition reactions to the enone moiety have been reported,[11,12] only a few examples of substitution reactions at the α-position of the carbonyl group were reported.[13] On the other hand, we have recently realized substitution reactions by the aid of a suitable acid promoter, and various π-nucleophiles, such as aromatic nucleophiles,[14] alkene nucleophiles,[15] and silyl enol ethers[16] can be selectively introduced at the α-position of the carbonyl group of the QMAs **1**. Accordingly, the [3+2] coupling of QMAs **1** and alkene nucleophiles **2**,[15] promoted by a specific Brønsted acid, can afford dihydrobenzofurans **3** in high yields in the mixed solvent of 1,1,1,3,3,3-hexafluoroisopropanol (HFIP)[17] and dichloromethane (Scheme 3).



Scheme 3. Previously reported [3+2] coupling reaction of quinone monoacetals

Our study regarding the tetrahydrobenzodifuran synthesis was thus started with the effective demethylation of dihydrobenzofuran **3a**, which has two types of ether bonds, that is, a methoxy group and a reactive 2-phenyldihydrobenzofuran moiety (Scheme 4). By screening of the reductants, we found that *L*-selectride, a bulky hydride source, effectively afforded the corresponding phenol from **3a**,[18] whereas other deprotection methods did not give good results.[19] The subsequent oxidation of the phenol ring was smoothly proceeded by the standard QMA synthetic procedure using PIDA in methanol,[20] and the desired QMA **4a** was obtained in a very high yield as a diastereo mixture (Scheme 4).

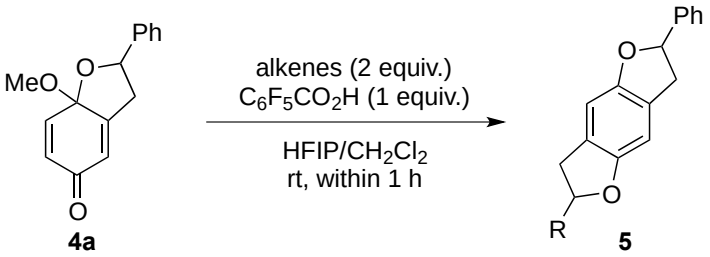


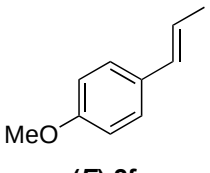
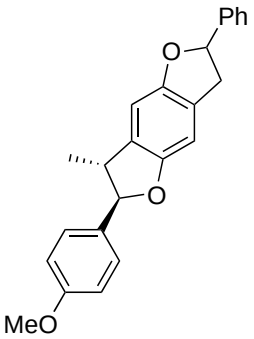
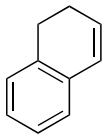
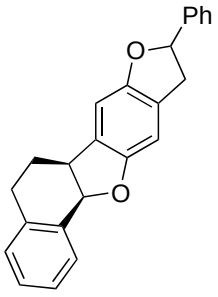
Scheme 4. Synthesis of QMA **4a** from QMA **1a**

For the bicyclic QMA **4a**, the [3+2] coupling reaction with styrene **2a** and various alkene nucleophiles **2b-g** under our previously reported conditions[15a] was then examined (Table 1). As a result, the symmetrical dihydrobenzodifuran **5aa** was successfully obtained as a mixture of two diastereomers[21] (Entry 1). 4-Methyl- and 4-*tert*-butylstyrene (**2b** and **2c**) were similarly transformed into the desired products, **5ab** and **5ac,** in excellent yields, respectively (Entries 2 and 3). 4-Phenyl- and chlorostyrene (**2d** and **2e**) gave the products **5ad** and **5ae** in somewhat lower yields (Entries 4 and 5). The highly-substituted product **5af** was obtained in an excellent yield in which the (*E*)-alkene **2f** selectively produced the vicinal *trans* product (Entry 6).[22] It is possible to construct the highly fused ring system of dihydronaphthalene

2g in a good yield, and this product takes the *cis*-configuration due to its rigid bicyclic structure (Entry 7).[23]

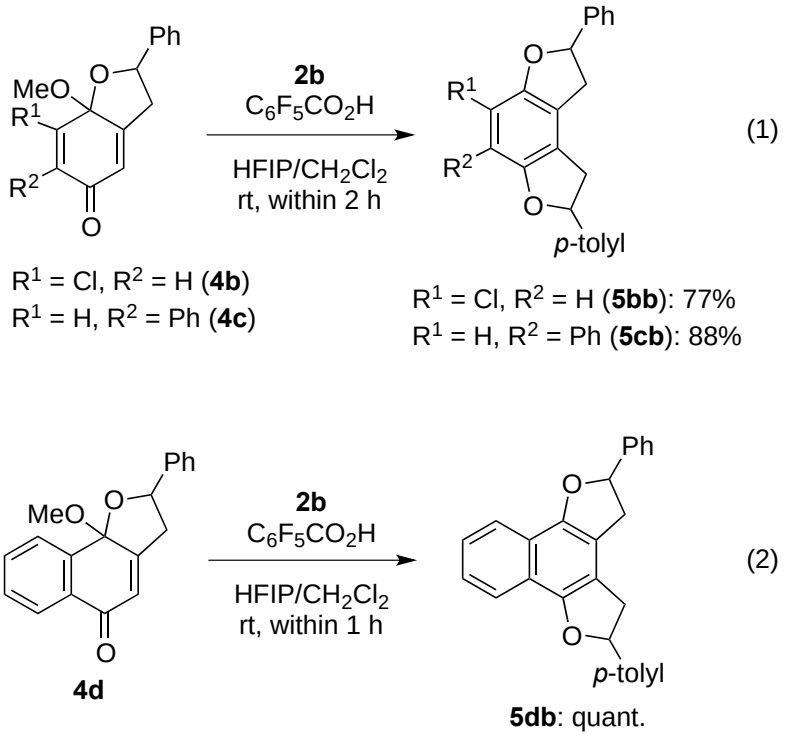
Table 1. Scope of nucleophiles [a]



entry	alkene	product	entry	alkene	product
1	R = H (**2a**)	R = H (**5aa**): 91%	6		
2	Me (**2b**)	Me (**5ab**): 99%		(***E***)-**2f**	***trans*-5af**: 96%
3	*t*-Bu (**2c**)	*t*-Bu (**5ac**): 99%	7		
4	Ph (**2d**)	Ph (**5ad**): 69%		**2g**	**5ag:** 73%
5	Cl (**2e**)	Cl (**5ae**): 67%			

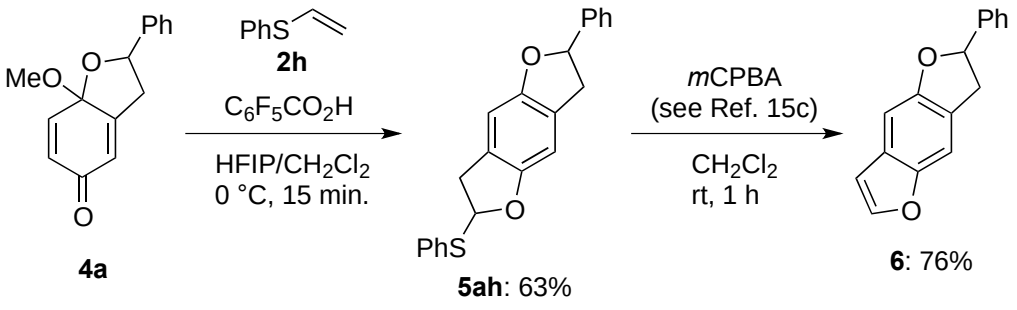
[a] The reactions were carried out using 2 equiv. of alkene nucleophiles **2** and 1 equiv. of pentafluorobenzoic acid at room temperature.

Next, we briefly tested the scope of QMA substrates **4b-d** having different ring substituent patterns (Scheme 5) that were effectively synthesized by our established protocol (see Scheme 4). In QMAs **4b** and **4c** the late-stage [3+2] coupling reactions selectively occurred at the vacant opposite side of the ring substituents, and the unsymmetrical dihydrobenzodifurans **5bb** and **5cb** were thus obtained in high yields (Eq. 1). Similarly, the highly-substituted unsymmetrical naphthalene **5db** was obtained from the naphthoquinone monoacetal **4d** in a quantitative yield (Eq. 2).



Scheme 5. Synthesis of unsymmetrical tetrahydrobenzodifurans by substituted QMAs **4b-d**

Finally, we conducted the transformation of the dihydrobenzofurans **5ah** into the aromatized benzofuran **6** for the synthetic elucidation of our developed strategy (Scheme 6). To obtain the tetrahydrobenzodifuran **5ah**, phenyl vinyl sulfide **2h** was effectively coupled with QMA **4a** under the standard conditions, which showed the effective production of **5ah** due to the mildness of the reaction conditions. Next, the oxidation of sulfide tetrahydrobenzodifuran **5ah** using *m*CPBA[24] caused elimination of the sulfide functionality, and the desired benzofuran **6** was obtained. Therefore, our new synthetic route is useful for the construction of both tetrahydrobenzodifurans **4** and benzofurans, such as the mixed benzofuran **6**.



Scheme 6. Oxidative conversion of tetrahydrobenzodifuran into benzofuran **6**

CONCLUSION

In this study, we have newly developed an efficient synthetic strategy of tetrahydrobenzodifurans by the iterative [3+2] coupling reactions of QMAs with styrene nucleophiles. The symmetrical and unsymmetrical heterocyclic products could be synthesized with perfect regioselectivities by employing QMAs instead of quinone compounds. The synthesized tetrahydrobenzodifuran can be effectively converted into unique mixed benzofuran. Further investigations of the expeditious coupling strategy, such as the asymmetric reaction and expansion of the substrate scope, are ongoing in our research group.

EXPERIMENTAL

Melting point (mp) is uncorrected. All ^{1}H- and ^{13}C-NMR spectra of the obtained products were measured in $CDCl_3$ by NMR spectrometers operating at 400 MHz (100 MHz for ^{13}C-NMR) at 25 ^{o}C. Chemical shifts of ^{1}H-NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ = 0.00 ppm) as an internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (*J*) in Hz, and integration. Chemical shifts of ^{13}C-NMR were reported in ppm with the solvent as reference peak ($CDCl_3$: δ = 77.0 ppm). High resolution mass measurements were performed by the Elemental Analysis Section of Osaka University. Flash column chromatography was performed with Merck Silica-gel 60 (230-400 mesh) eluting with hexane and ethyl acetate for isolation of the products. Analytical thin-layer chromatography (TLC) was carried out on Merck Silica-gel F_{254} plates (0.25 mm). The spots and bands were detected by UV light of irradiation (254, 365 nm) and/or by staining with 5% phosphomolybdic acid followed by heating. Unless otherwise noted, all experiments were carried out at room temperature in open flask without care of moisture.

Materials

QMA **1a** was prepared from 4-methoxyphenol by the conventional oxidation procedure using phenyliodine(III) diacetate (PIDA) in methanol.[8] Other QMAs **1** were also prepared according to the method. All other chemicals including the alkene nucleophiles **2**, pentafluorobenzoic acid, and solvents such as hexafluoroisopropanol (HFIP), for the reactions were obtained from commercial suppliers and used as received without further purification.

Procedure for the synthesis of 7a-methoxy-2-phenyl-2,3-dihydrobenzofuran-5(7a*H*)-one (4a) from QMA 1a (Scheme 4)

To a solution of QMA **1a** (1.54 g, 10 mmol) and syrene **2a** (1.04 g, 20 mmol) in the mixture of HFIP (25 mL) and dichloromethane (25 mL), pentafluorobenzoic acid (2.12 g, 10 mmol) was added in one portion at room temperature. The reaction mixture was stirred for 1 h and then solvent was removed *in vacuo*. The residue was purified by column chromatography on silica-gel (hexane/EtOAc = 10/1) to give 2,3-dihydro-5-methoxy-2-phenylbenzofuran **3a** (2.04 g, 9.0 mmol) in 90% yield.

Then, to a solution of **3a** (2.04 g, 9 mmol) in THF (18 mL), *L*-selectride (1.0 M in THF, 27 mL, 27 mmol) was added dropwise and the reaction mixture was refluxed for 36 h. After completion of the reaction, the reaction mixture was cooled to room temperature, which was diluted with ether and was quenched with water. The organic layer was washed with aqueous 1 M HCl and brine. The organic layer was dried over anhydrous sodium sulfate, then filtered, concentrated, and purified by short column chromatography on silica-gel (hexane/EtOAc = 5/1) to give a corresponding phenol **3'a** (1.91 g, 9.0 mmol) in a quantitative yield.

Finally, to a solution of **3'a** (1.91 g, 9.0 mmol) in methanol (45 mL), PIDA (2.90 g) was added in one portion at room temperature. The reaction mixture was stirred for 30 minutes and then quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc three times. Organic layer was washed with brine and dried over anhydrous sodium sulfate, then filtered, concentrated, and purified by column chromatography on silica-gel (hexane/EtOAc = 5/1) to give QMA **4a** (1.85 g, 7.7 mmol) in 85% yield. QMA **4a** was obtained as the mixture of two diastereomers.

7a-Methoxy-2-phenyl-2,3-dihydrobenzofuran-5(7a*H*)-one (4a) (mixture of two diastereomers)

A yellow-colored solid; mp 65-67 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): 2.62 (dd, J = 17.1, 3.9 Hz, 1H), 3.02-3.14 (m, 2H), 3.27 and 3.31 (s, 6H), 3.46-3.53 (m, 1H), 5.23-5.28 (m, 1H), 5.47 (dd, J = 9.2, 3.9 Hz, 1H), 6.09 (s, 1H), 6.13 (s, 1H), 6.28 (m, 2H), 6.97 (d, J = 10.2 Hz, 1H), 7.05 (d, J = 10.3 Hz, 1H), 7.21-7.49 (m, 10H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 37.0, 37.6, 50.5, 80.0, 82.5, 97.5, 98.3, 121.6, 122.2, 125.8, 126.7, 128.2, 128.3, 128.6, 128.7, 130.1, 130.8, 139.1, 139.8, 141.0, 141.1, 157.8, 158.3, 185.9 ppm; IR (KBr): 3054, 2929, 2828, 1684, 1655, 1287, 1133, 1088, 1033, 960, 765 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{15}H_{15}O_3$ $[M+H]^+$; 243.1021, found 243.1016.

The physical and spectral data of the products **3a** matched those previously reported.[15]

Typical procedure for the coupling of QMA 4a with alkene nucleophiles 2 leading to benzodifurans 5.

To a stirred solution of QMA **4a** (242 mg, 1.0 mmol) and alkene nucleophile **2a** (208 mg, 2.0 mmol) in the mixture of HFIP (2.5 mL) and dichloromethane (2.5 mL), pentafluorobenzoic acid (212 mg, 1.0

mmol) was added in one portion at room temperature. The reaction mixture was stirred for 1 h, then solvent as removed *in vacuo*. The residue was purified by column chromatography on silica-gel (hexane/EtOAc = 10/1) to give 2,6-diphenyl-2,3,6,7-tetrahydrobenzo[1,2-*b*:4,5-*b'*]difuran **5aa** (286 mg, 0.91 mmol) in 91% yield. The product **5aa** was obtained as the mixture of two diastereomers.[21]

2,6-Diphenyl-2,3,6,7-tetrahydrobenzo[1,2-*b*:4,5-*b'*]difuran (5aa)

A colorless solid; mp 153-156 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.14-3.20 (m, 2H), 3.56 (dd, *J* = 16.1, 9.3 Hz, 2H), 3.56 (t, *J* = 8.8 Hz, 2H), 6.68 (s, 2H), 7.27-7.41 (m, 10H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 38.8, 38.9, 84.4, 105.8, 125.7, 125.8, 127.9, 128.6, 142.0, 153.9 ppm; IR (KBr): 3064, 3035, 2906, 2853, 1476, 1449, 1376, 1222, 1199, 1137, 968, 908, 857, 745, 697 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{22}H_{18}O_2$ $[M]^+$; 314.1307, found 314.1301.

2-Phenyl-6-(*p*-tolyl)-2,3,6,7-tetrahydrobenzo[1,2-*b*:4,5-*b'*]difuran (5ab)

A colorless solid; mp 135-137 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): 2.33 (s, 3H), 3.16 (dd, *J* = 15.6, 8.8 Hz, 2H), 3.49-3.58 (m, 2H), 5.66-5.74 (m, 2H), 6.66 (s, 1H), 6.67 (s, 1H), 7.16 (d, *J* = 8.3 Hz, 2H), 7.28-7.40 (m, 7H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 21.1, 38.8 (x 4), 84.4(x 2), 105.8, 125.6, 125.8 (x 3), 127.9, 128.6, 129.2, 137.7, 139.0, 142.0, 153.8, 153.9 ppm; IR (KBr): 3035, 2914, 2851, 1477, 1450, 1223, 1199, 1137, 920, 855, 816, 749, 696 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{23}H_{20}O_2$ $[M]^+$; 328.1463, found 328.1458.

2-(4-(*tert*-Butyl)phenyl)-6-phenyl-2,3,6,7-tetrahydrobenzo[1,2-*b*:4,5-*b'*]difuran (5ac)

A colorless solid; mp 98-102 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): 1.30 (s, 9H), 3.13-3.22 (m, 2H) 3.50-3.58 (m, 2H), 5.67-5.74 (m, 2H), 6.66 (s, 1H), 6.68 (s, 1H), 7.27-7.40 (m, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 31.3, 34.5, 38.5 (x 2), 38.8 (x 2), 84.3 (x 2), 105.8, 125.4, 125.6 (x 2), 125.7, 125.8, 125.9, 127.9, 128.5, 138.8, 142.0, 150.9, 153.8, 153.9 ppm; IR (KBr): 3059, 3030, 2960, 2871, 1482, 1450, 1361, 1310, 1266, 1227, 1194, 1140, 972, 930, 837, 745, 698 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{26}H_{26}O_2$ $[M]^+$; 370.1933, found 370.1927.

2-([1,1'-Biphenyl]-4-yl)-6-phenyl-2,3,6,7-tetrahydrobenzo[1,2-*b*:4,5-*b'*]difuran (5ad)

A colorless solid; mp 183-185 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.14-3.24 (m, 2H), 3.54-3.62 (m, 2H), 5.71-5.79 (m, 2H), 6.70 (s, 2H), 7.29-7.48 (m, 10H), 7.56-7.59 (m, 4H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 38.8, 38.9, 84.2, 84.4, 105.8 (x 2), 125.7, 125.8, 126.3, 127.1, 127.3, 127.4, 128.0, 128.6, 128.8, 140.8, 140.9, 142.0, 153.9 ppm; IR (KBr): 3060, 3032, 2923, 2850, 1475, 1450, 1375, 1199, 1137, 912, 750 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{28}H_{22}O_2$ $[M]^+$; 390.1620, found 390.1614.

2-(4-Chlorophenyl)-6-phenyl-2,3,6,7-tetrahydrobenzo[1,2-*b*:4,5-*b'*]difuran (5ae)

A colorless solid; mp 140-144 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.10 (dd, *J* = 15.6, 7.8 Hz, 1H), 3.16 (dd, *J* = 15.6, 8.3 Hz, 1H), 3.56 (dd, *J* = 14.6, 9.3 Hz, 2H), 5.67-5.74 (m, 2H), 6.67 (s, 2H), 7.28-7.40 (m, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 38.8 (x 3), 38.9, 83.6, 84.4, 105.8, 105.9 (x 3), 125.3, 125.4, 125.7, 125.9, 127.1, 128.0, 128.6, 128.7, 133.6, 140.6, 142.0, 153.7 (x 2), 154.0 ppm; IR (KBr): 3089, 3034, 2907, 1476, 1450, 1374, 1222, 1198, 1137, 1093, 969, 917, 857, 823, 751 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{22}H_{17}O_2Cl$ $[M]^+$; 348.0917, found 348.0912.

2-(4-Methoxyphenyl)-3-methyl-6-phenyl-2,3,6,7-tetrahydrobenzo[1,2-*b*:4,5-*b'*]difuran (5af)

A colorless solid; mp 90-91 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): 1.35 (dd, *J* = 6.8, 2.0 Hz, 3H), 3.13-3.20 (m, 1H), 3.34-3.41 (m, 1H), 3.56 (dd, *J* = 15.6, 9.3 Hz, 1H), 3.80 (s, 3H), 5.06 (d, *J* = 8.8 Hz, 1H), 5.72 (t, *J* = 8.8 Hz, 1H), 6.23 (s, 1H), 6.66 (s, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 7.28-7.43 (m, 7H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 17.6, 17.7, 38.8, 45.6 (x 2), 55.3, 84.4 (x 2), 92.7, 104.7 (x 2), 105.9, 106.0, 113.9, 125.6, 125.7 (x 2), 125.8, 127.6 (x 2), 127.9, 128.6 (x 2), 131.5, 132.7, 142.0, 153.4, 153.9, 159.6 ppm; IR (KBr): 3035, 2956, 2929, 1513, 1443, 1249, 1149, 969, 828, 760, 701 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{24}H_{22}O_3$ $[M]^+$; 358.1569, found 358.1564.

9-Phenyl-6,6a,9,10,12,12a-hexahydro-5*H*-naphtho[7,8-*d*]benzo[1,2-*b*:4,5-*b'*]difuran (5ag)

A colorless solid; mp 213-215 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): 1.76-1.84 (m, 1H), 2.00-2.07 (m, 1H), 2.60-2.67 (m, 1H), 2.71-2.77 (m, 1H), 3.14 (dd, *J* = 15.6, 8.3 Hz, 1H), 3.53 (dd, *J* = 16.1, 9.8 Hz, 1H), 3.58-3.64 (m, 1H), 5.63 (d, *J* = 8.3 Hz, 1H), 5.71 (t, *J* = 8.8 Hz, 1H), 6.60 (s, 1H), 6.74 (s, 1H), 7.14 (d, *J* = 6.8 Hz, 1H), 7.22-7.40 (m, 7H), 7.51 (d, *J* = 6.8 Hz, 1H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 27.6, 27.9, 38.8, 41.6, 82.1, 84.4, 105.3, 106.1, 125.8 (x 2), 126.6, 128.0, 128.2, 128.4, 128.6, 130.1, 130.8, 133.6, 138.8, 142.1, 153.6, 153.8 ppm; IR (KBr): 3060, 3032, 2922, 2882, 1477, 1448, 1120, 1142, 942, 917, 795, 757 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{24}H_{20}O_2$ $[M]^+$; 340.1463, found 340.1458.

4-Chloro-2-phenyl-7-(*p*-tolyl)-1,2,7,8-tetrahydrobenzo[1,2-*b*:4,3,-*b'*]difuran (5bb)

A colorless oily compound; ^{1}H-NMR (400 MHz, $CDCl_3$): 2.34 (s, 3H), 3.17-3.26 (m, 2H), 3.57-3.66 (m, 2H), 5.75 (t, *J* = 8.8 Hz, 1H), 5.81 (t, *J* = 8.8 Hz, 1H), 6.57 (s, 1H), 7.17 (d, J = 7.3 Hz, 2H), 7.27-7.41 (m, 7H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 14.1, 21.1, 22.6, 31.5, 37.96, 38.0, 39.5, 39.6, 84.5, 84.9, 104.19, 104.2, 111.4, 111.5, 124.60, 124.61, 125.7, 127.0, 128.1, 128.6, 129.27, 129.29, 137.9, 137.91, 138.4, 138.5, 141.4, 149.6, 154.13, 154.14 ppm; IR (KBr): 3029, 2919, 2855, 1597, 1516, 1495, 1450, 1356,

1310, 1230, 1196, 1173, 973, 934,911, 816, 754, 699 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{23}H_{19}O_2Cl$ $[M]^+$; 362.1074, found 362.1068.

4,7-Diphenyl-2-(*p*-tolyl)-1,2,7,8-tetrahydrobenzo[1,2-*b*:4,3,-*b'*]difuran (5cb)

A colorless oily compound; ^{1}H-NMR (400 MHz, $CDCl_3$): 2.33 and 2.34 (s, 3H), 3.06-3.15 (m, 2H), 3.46-3.59 (m, 2H), 5.73-5.81 (m, 2H), 6.86 (s, 1H), 7.15-7.18 (m, 2H), 7.26-7.44 (m, 10H), 7.73-7.75 (m, 2H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 21.1, 37.6, 37.7, 84.0, 84.1, 84.20, 84.22, 106.95, 106.97, 121.6, 122.27, 122.28, 123.77, 123.78, 125.6, 125.67, 125.68, 126.9, 127.9, 128.2, 128.3, 128.59, 128.61, 129.2, 137.4, 137.6, 139.2, 139.3, 142.00, 142.03, 151.6, 154.9 ppm; IR (KBr): 3053, 3029, 2920, 2856, 1601, 1514, 1472, 1453, 1407, 1259, 1179, 971, 912, 855, 768, 695 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{29}H_{24}O_2$ $[M]^+$; 404.1776, found 404.1771.

2-Phenyl-5-(*p*-tolyl)-2,3,4,5-tetrahydronaphtho[1,2-*b*:4,3,-*b'*]difuran (5db)

A colorless solid; mp 111-114 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): 2.33 and 2.34 (s, 3H), 3.20-3.31 (m, 2H), 3.63-3.77 (m, 2H), 5.88-5.97 (m, 2H), 7.15-7.17 (m, 2H), 7.32-7.45 (m, 9H), 7.95-7.98 (m, 2H), ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 21.1, 38.6, 38.7, 84.3 (x 3), 115.9, 116.0, 119.4 (x 2), 121.8, 121.9, 125.0 (x 2), 125.7 (x 3), 125.8, 127.9, 128.6 (x 2), 129.2 (x 2), 137.7, 139.4, 142.5, 142.6, 149.3, 149.4 ppm; IR (KBr): 3025, 2924, 2849, 1449, 1394, 1257, 1030, 881, 764 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{27}H_{22}O_2$ $[M]^+$; 378.1620, found 378.1614.

2-Phenyl-6-(phenylthio)-2,3,6,7-tetrahydrobenzo[1,2-*b*:4,5-*b'*]difuran (5ah)

A colorless oily compound; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.10-3.18 (m, 2H), 3.52-3.65 (m, 2H), 5.68-5.74 (m, 1H), 6.16 (dd, J = 8.8, 4.4 Hz, 1H), 6.68-6.69 (m, 2H), 7.25-7.39 (m, 8H), 7.54 (d, J = 6.8 Hz, 2H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 37.2 (x 2), 38.7, 38.8, 84.4, 84.5, 89.6, 89.7, 105.6 (x 2), 106.9 (x 2), 125.2 (x 2), 125.7, 125.8, 126.0, 127.5, 128.0, 128.6, 128.9, 131.7 (x 2), 134.0 (x 2), 141.9, 141.9, 152.1, 154.3 ppm; IR (KBr): 3056, 3033, 2904, 2846, 1584, 1481, 1448, 1312, 1226, 1178, 1143, 913, 744, 695 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{22}H_{18}O_2S$ $[M]^+$; 346.1028, found 346.1022.

Synthesis of benzofuran 6 from tetrahydrobenzodifuran 5ah (Scheme 6)

To the stirred solution of tetrahydrobenzofuran **5ah** (104 mg, 0.3 mmol) in dichloromethane (3 mL), *m*-chloro perbenzoic acid (70%, 74 mg, 0.3 mmol) was added. After consumption of the starting material, it was quenched with saturated aqueous sodium hydrogen carbonate. The organic layer was washed with brine, dried over anhydrous sodium sulfate, then filtered, and concentrated *in vacuo*. The resulting residue was purified by column chromatography on silica-gel (hexane/EtOAc = 25/1) to give benzofuran **6**.

2-Phenyl-2,3-dihydrobenzo[1,2-*b*:4,5-*b'*]difuran (6)

A colorless oily compound; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.29 (dd, J = 15.6, 8.8 Hz, 1H), 3.69 (dd, J = 15.6, 9.3 Hz, 1H), 5.79 (t, J = 8.8 Hz, 1H), 6.67 (dd, J = 2.4, 1.0 Hz, 1H), 6.99 (s, 1H), 7.28-7.43 (m, 6H), 7.54 (d, J = 2.4 Hz, 1H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): 38.6, 84.6, 99.9, 106.8, 107.7, 124.5, 125.7, 127.1, 128.0, 128.6, 141.9, 145.3, 150.5, 155.9 ppm; IR (KBr): 3035, 2920, 2854, 1593, 1527, 1450, 1381, 1189, 1160, 1120, 1030, 984, 865, 750 cm^{-1}; HRMS: (MALDI-TOF) calcd for $C_{16}H_{12}O_2$ $[M]^+$; 236.0837, found 236.0832.

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22. In the case of acyclic *cis*-styrene, both *cis*- and *trans*-products were formed by some isomerization. See Ref. 15c.
23. The configurations of **5af** and **5ag** were determined by coupling-constants of the vicinal protons in ^{1}H-NMR spectrum. These coupling-constant values well match with those of related *trans* and *cis* cyclic compounds reported in our previous literatures. See Ref. 15.
24. We reported the efficient oxidative conversion of dihydrobenzofurans having *O,S*-acetal to benzofurans by employing several reaction conditions. See Ref. 15c.