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SYNTHESIS OF BENZOFURANS FROM ISOVANILLIN *VIA* *C*-PROPENYLATION-*O*-VINYLATION AND RING-CLOSING METATHESIS

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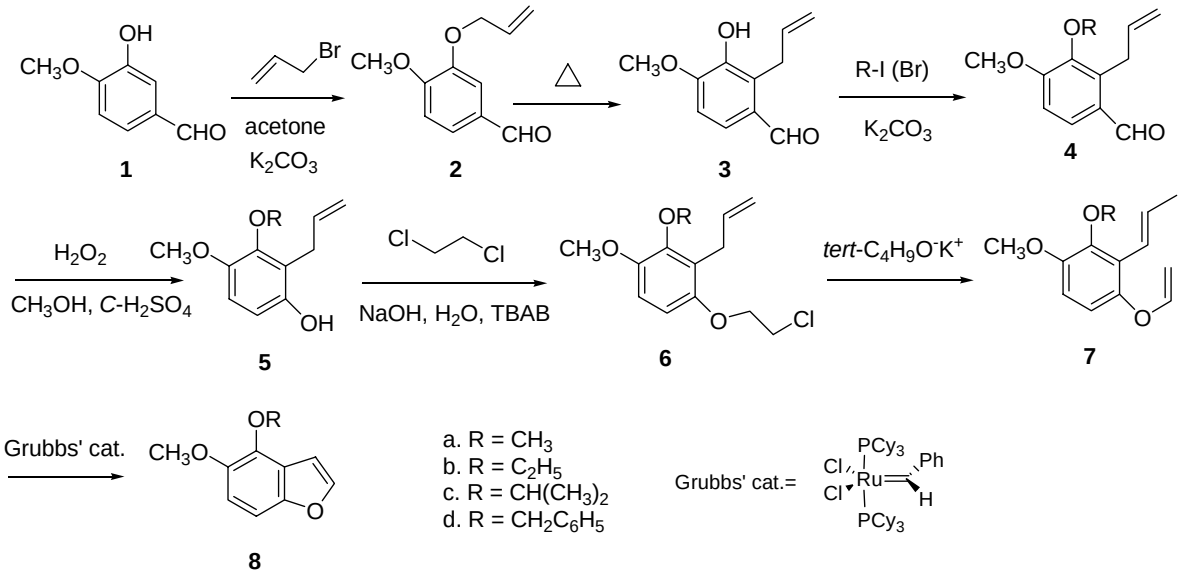
Abstract –Substituted benzofurans derived from isovanillin were synthesized. 2-Allyl-3-alkoxy-4-methoxyphenol, prepared from isovanillin *via* the Claisen rearrangement, *O*-alkylation and Baeyer-Villiger oxidation, were chloroethylated by two-phase reaction to furnish 1-allyl-3-alkoxy-(2-chloroethoxy)-4-methoxy-benzenes. The given compounds were treated with potassium *tert*-butoxide to undergo the isomerization of *O*-allyl group and dehydrochlorination of 2-chloroethoxy group to efficiently construct the precursors with *C*-propenyl-*O*-vinyl function for the ring-closing metathesis (RCM) in one pot. Then, then precursors were subjected to RCM to furnish 4,5-*O*-difunctionalized benzofurans in good over-all yield, respectively.

INTRODUCTION

In recent years, benzofurans become an important target compounds in organic synthesis because of their various pharmacological activities.[1a-f] In addition, RO-094879 and its related benzofurans were synthesized and shown significant antifungal activities.[2] However, the strategies for the construction of benzofurans are various. Such as by the coupling of conjugated dienynes with Fisher carbene complexes,[3] using an intramolecular cross-coupling of vinyl halides with phenols,[4] by a cyclofragmentation-release pathway to 3-arylbenzofuran,[5] utilizing of *O*-hydroxyphenyl ketones or

O-(1-hydroxy-2,2-dimethylpropyl)phenol with 1-benzo-triazol-1-ylalkyl chloride,[6] and by the oxidative cyclization of 2-allylphenols with palladium (II) salts[7] were reported. Recently Grubbs *et al*.[8] reported use of titanium reagents to convert the esters to acyclic olefinic enol ethers which were further transferred to 2-substituted benzofurans with a molybdenum alkylidene catalyst. However, those methods still have some disadvantages including the tedious reaction condition for the preparation of the precursor for ring-closing metathesis (RCM), limited substituents on the benzofuran ring, and commercial unavailable key intermediates which are difficult to prepare. Thus, it is necessary to develop more practical and efficient methods for the preparation of multi-substituted benzofurans. Until present, no attention has been paid to apply the RCM to the chemistry of 4,5-*O*-functionalized benzofurans. Herein we disclose a facile strategy for the construction of dienes, the precursor of RCM for the synthesis of substituted benzofurans. Thus, isovanillin was transformed into 4,5-*O*-functionalized benzofurans through a sequence of reactions such as *O*-allylation, Claisen rearrangement, *O*-alkylation, Bayer-Villiger oxidation, the phase transfer catalyzed *O*-chloroethylation, and double bond isomerization of allyl group and concomitant with dehydrochlorination of 2-chloroethoxy group by potassium *tert*-butoxide, and finally by RCM. All reactions involved are easily to handle, and are high yields. Furthermore, the 4,5-*O*-functionalized disubstituted benzofurans prepared in this report are all new compounds (**Scheme 1**).



RESULTS AND DISCUSSION

3-Alkoxy-2-allyl-3-methoxyphenols (**5a-d**), prepared from isovanillin through 4 steps, were described in our previous study.[9] *O*-Chloroethylation of compounds (**5a-d**) were achieved by two phases reaction utilization of excess 1,2-dichloroethane as organic phase, 20% NaOH as aqueous phase, and tetrabutylammonium bromide (TBAB) as catalyst gave compounds (**6a-d**) in yields of 82-84%. In this

reaction condition, it gave exclusively chloroethylated product, compounds (**6a-d**) and no dialkylated product was observed. The structure elucidation of compounds (**6a-d**) can be easily made by EI-MS and ^{1}H-NMR spectra. For example compound (**6b**), it not only has correct *m/z* 270 (M^+) but also has a correct ratio of relative intensity of M^+/M^{+2} in 3/1 in EI-MS spectrum, indicating one chlorine atom in the molecule. Furthermore, it exhibited two two-proton signals with triplet at δ 3.78 and 4.02 having same coupling constant 5.8 Hz, clearly indicating the protons of $OCH_2C\underline{H}_2Cl$, and $OC\underline{H}_2CH_2Cl$ in the molecule, respectively.[10] It also exhibited one allyl group with chemical shifts at δ 3.49 (d, *J* = 6.8 Hz, 2H, $ArC\underline{H}_2CH=CH_2$), 5.05 (dd, *J* = 16.8 Hz, 1.6 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), 4.98 (dd, *J* = 10.2 Hz, 1.6 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), and 6.01 (ddt, *J* = 16.8 Hz, 10.2 Hz, 6.8 Hz, 1H, $ArCH_2C\underline{H}=CH_2$). One methoxy signal at δ 3.80 (s, 3H, $OC\underline{H}_3$), and one ethoxy signal at δ 1.39 (t, *J* = 7.2 Hz, 3H, $OCH_2C\underline{H}_3$), and 4.13 (q, *J* = 7.2 Hz, 2H, $OC\underline{H}_2CH_3$) were also found. In ^{13}C-NMR spectra, it revealed fourteen carbons matched the structure of **6b**. Furthermore, the HRMS (EI) spectral value of 270.1014 was observed, which is coincident with the calculated one for **6b**, $C_{14}H_{19}O_3Cl$. The results of yields and selected signals of ^{1}H-NMR spectra were summarized in **Table 1**.

Table 1. The Yield (%) of Chloroethylation of Compound (**5**) to Give **6** by Utilization of Two Phases Reaction, and Selected Signals of ^{1}H-NMR Spectra*

Compd	Yield (%)	Selected signals of ^{1}H-NMR ($CDCl_3$, 200 MHz) δ		
		Allylic-H	2-Chloroethoxy-H	Aromatic-H
6a	84	3.46 (dt, *J* = 6.2, 1.6 Hz) 4.96 (dq, *J* = 10.2, 1.6 Hz) 5.02 (dq, *J* = 17.2, 1.6 Hz) 5.99 (ddt, *J* = 17.2, 10.2, 6.2 Hz)	3.79 (t, *J* = 5.8 Hz) 4.17 (t, *J* = 5.8 Hz)	6.55 (d, *J* = 8.8 Hz) 6.72 (d, *J* = 8.8 Hz)
6b	82	3.49 (d, *J* = 6.8 Hz) 4.98 (dd, *J* = 10.2, 1.6 Hz) 5.05 (dd, *J* = 16.8, 1.6 Hz) 6.01 (ddt, *J* = 16.8, 10.2, 6.8 Hz)	3.78 (t, *J* = 5.8 Hz) 4.02 (t, *J* = 5.8 Hz)	6.53 (d, *J* = 8.8 Hz) 6.71 (d, *J* = 8.8 Hz)
6c	83	3.38 (dt, *J* = 6.2, 1.4 Hz) 4.86 (dq, *J* = 10.0, 1.6 Hz) 4.93 (dq, *J* = 16.8, 1.6 Hz) 5.88 (ddt, *J* = 16.8, 10.0, 6.2 Hz)	3.70 (t, *J* = 5.8 Hz) 4.07 (t, *J* = 5.8 Hz)	6.42 (d, *J* = 9.0 Hz) 6.61 (d, *J* = 9.0 Hz)
6d	84	3.45 (dt, *J* = 6.4, 1.6 Hz) 4.94 (dq, *J* = 10.4, 1.6 Hz) 4.98 (dq, *J* = 16.8, 1.6 Hz) 5.95 (ddt, *J* = 16.8, 10.4, 6.4 Hz)	3.78 (t, *J* = 6.0 Hz) 4.16 (t, *J* = 6.0 Hz)	6.57 (d, *J* = 8.8 Hz) 6.75 (d, *J* = 8.8 Hz) 7.32 (d, *J* = 7.2 Hz) 7.38 (t, *J* = 7.2 Hz) 7.48 (d, *J* = 7.2 Hz)

*Other chemical shifts are described in EXPERIMENTAL.

Followed by treating **6a-d** with potassium *tert*-butoxide in THF at reflux, it underwent the isomerization of allylic double, together with 1,2-elimination of 2-chloroethoxy group to generate an *C*-propenyl-*O*-vinyl functions to produce compounds (**7a-d**) as precursor for RCM. The structure of **7a-d** elucidated based on ^{1}H-NMR spectral and other spectral data. For instances, compound (**7c**) revealed one double doublet signal with three protons at δ 1.90 indicating one methyl group, and the two

olefinic protons, one at δ 6.58 (dq, J = 14.8, 6.4 Hz, 1H, ArCH=C<u>H</u>CH$_3$), and the other one at δ 6.50 (dq, J = 14.8, 1.2 Hz, 1H, ArC<u>H</u>=CHCH$_3$), indicating the allylic double bond has been isomerized. The elucidation of structure (**7a-d**) can be made by their spectra data. One isopropyl group at δ 1.26 (d, J = 6.4 Hz, 6H, ArOCH(C<u>H</u>$_3$)$_2$), and 4.42 (sept, J = 6.4 Hz, 1H, ArOC<u>H</u>(CH$_3$)$_2$) were also found. Furthermore, one vinyl group of three protons was observed at δ 4.30 (dd, J = 6.4 Hz, 1.8 Hz, 1H, OCH=C<u>H</u>$_2$), 4.56 (dd, J = 14.0 Hz, 1.8 Hz, 1H, OCH=C<u>H</u>$_2$), and 6.52 (dd, J =14.0, 6.4 Hz, 1H, OC<u>H</u>=CH$_2$), respectively. On the other hand, fourteen carbons were found in ^{13}C-NMR, and *m/z* 248 was observed in EI-MS that all match the structure of compound (**7c**). The yields and selected ^{1}H-NMR spectra of **7a-d** were compiled in **Table 2**.

Table 2. The Yields and Selected ^{1}H-NMR Spectra of **7a-d** Obtained from **6a-d** by Treating with Potassium *tert*-Butoxide

Compd	Yield (%)	Selected signals* of ^{1}H-NMR ($CDCl_3$, 200 MHz) δ		
		Propenyl -H	*O*-Vinyl-H	Aromatic-H
7a	87	1.92 (dd, J = 6.4, 1.6 Hz), 6.49 (dq, J = 16.0, 1.6 Hz), 6.62 (dq, J = 16.0, 6.4 Hz)	4.31 (dd, J = 6.4, 1.6 Hz), 4.57 (dd, J = 14.0, 1.6 Hz), 6.51 (dd, J = 14.0, 6.4 Hz).	6.68 (d, J = 8.8Hz), 6.71 (d, J = 8.8 Hz)
7b	88	1.91 (dd, J = 6.4, 1.6 Hz), 6.53 (dq, J = 15.8, 6.4 Hz), 6.70 (dq, J = 15.8, 6.4 Hz)	4.30 (dd, J = 6.0, 1.6 Hz), 4.56 (dd, J = 14.0, 1.6 Hz), 6.54 (dd, J = 14.0, 6.0 Hz).	6.65 (d, J = 8.8 Hz), 6.69 (d, J = 8.8 Hz)
7c	87	1.90 (dd, J = 6.4, 1.2 Hz), 6.50 (dq, J = 14.8, 1.2 Hz), 6.58 (dq, J = 14.8, 6.4 Hz)	4.30 (dd, J = 6.4, 1.8 Hz), 4.56 (dd, J = 14.0, 1.8 Hz), 6.52 (dd, J = 14.0, 6.4 Hz).	6.65 (d, J = 8.8 Hz), 6.69 (d, J = 8.8 Hz)
7d	87	1.86 (dd, J = 6.4, 1.6 Hz), 6.49 (dq, J = 16.0, 1.6 Hz), 6.58 (dq, J = 16.0, 6.4 Hz)	4.30 (dd, J = 6.4, 1.6 Hz), 4.56 (dd, J = 14.0, 1.6 Hz), 6.51 (dd, J = 14.0, 6.4 Hz).	6.69 (d, J = 8.8 Hz), 6.72 (d, J = 8.8 Hz)

*****Other signals are described in EXPERIMENTAL

Finally, we utilized of Grubbs' catalyst to undergo RCM, and compounds (**7a-d**) were converted successfully into a series of benzofurans (**8a-d**) in yields of 95-96%. The structures of benzofuran (**8a-d**) were assigned basically by their ^{1}H-NMR and ^{13}C-NMR spectra. For instance, ^{1}H-NMR spectra of compound (**8c**) exhibited a two-methyl doublet signal with coupling constant J = 6.0 Hz at δ 1.34, and one proton septet signal with coupling constant J = 6.0 Hz at δ 4.57 indicating the presence of one isopropyl group, and at δ 3.87 exhibited a singlet of three protons signal indicating the presence of one methoxy group. Furthermore, two protons on furan ring, one at δ 6.79 exhibited double doublet signal with coupling constant, $J_{2,3}$ = 2.2, and $J_{3,7}$ = 0.8 Hz, revealing the proton of H-3, which coupled with H-2, and H-7, the other one at δ 7.50 showed a doublet signal with coupling constant $J_{2,3}$ = 2.2 Hz indicating the presence of H-2, which coupled with H-3, were found. Thus, the remaining two aromatic protons can be easily assigned by their coupling constants, the proton with the doublet signal by coupling constant J

= 8.8 Hz at δ 6.93 indicating H-6, and the other proton with the double-doublet signal by coupling constant *J* = 8.8, and 0.8 Hz at δ 7.15 indicating H-7. Furthermore the molecular ion, *m/z* 206 observed, is coincident with the calculated one for **8c**, $C_{12}H_{14}O_3$. The yields, and selected ^{1}H-NMR spectra of **8a-d** are summarized in **Table 3**.

Table 3. The Yield and Selected ^{1}H-NMR ($CDCl_3$, 200 MHz) Spectra* of Benzofurans (**8a-d**)

Compd	Yield (%)	Selected signals of ^{1}H-NMR ($CDCl_3$, 200 MHz) δ			
		H-2	H-3	H-6	H-7
8a	96	7.50 (d, *J* = 2.2 Hz)	6.85 (dd, *J* = 2.2, 1.0 Hz)	6.92 (d, *J* = 8.8 Hz)	7.13 (dd, *J* = 8.8, 1.0 Hz)
8b	95	7.52 (d, *J* = 2.2 Hz)	6.83 (dd, *J* = 2.2, 1.0 Hz)	6.95 (d, *J* = 8.8 Hz)	7.16 (dd, *J* = 8.8, 1.0 Hz)
8c	96	7.50 (d, *J* = 2.2 Hz)	6.79 (dd, *J* = 2.2, 0.8 Hz)	6.93 (d, *J* = 8.8 Hz)	7.15 (dd, *J* = 8.8, 0.8 Hz)
8d	96	7.46 (d, *J* = 2.2 Hz)	6.71 (dd, *J* = 2.2, 0.8 Hz)	6.96 (d, *J* = 8.8 Hz)	7.17 (dd, *J* = 8.8, 0.8 Hz)

* Other signals are described in EXPERIMENTAL.

CONCLUSION

A concise, and practical method for the preparation of 4,5-*O*-functional disubstituted benzofurans from isovanillin was established in high over-all yields. Furthermore, our strategy to generate the dienes, the precursor for ring-closing matathesis is simple, efficient, and advantageous.

EXPERIMENTAL

Melting points (Yanaco micro melting-point apparatus) were uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were obtained on a Varian Gemini-200 or Varian Unity plus 400 Spectrometer. Chemical shifts were measured in parts per million with respect to TMS. Elemental analyses were recorded on a Heraeus CHN-O Rapid analyzer. MS spectra were recorded on a Chem/hp/middle spectrometer connected to a Hewlett Packard series II model gas-liquid chromatograph. HRMS spectra were performed on a JEOL JMS SX/SX 102A instrument. Silica gel (230-400 mesh) for column chromatography and precoated silica gel plates (60 F-254) for TLC was purchased from E. Merck Co. UV light (254 nm) was used to detect spots on TLC plates after development.

Isovanillin (**1**) was purchased from TCI Co., Japan, and compounds (**2a-d** to **5a-d**) were prepared, by the procedure we previously reported.[9]

General procedure for the preparation of 1-allyl-2-(2-chloroethoxy)benzene (6a-d).

To the solution of allyl phenol (**5a-d**) (10 mmol) in dichloroethane (15 mL) was added NaOH solution (2.4 M, 15 mL), and TBAB (10% mol) at rt. The reaction mixture was stirred, and heated to the reflux for 8 h. Then, the organic layer was separated, dried under anhydrous $MgSO_4$, and filtered. The filtrate was concentrated to remove the excess dichloroethane *in vacuo*, and the resulting residue was purified by column chromatography on silical gel (ethyl acetate: *n*-hexane = 1: 12) to give pale yellow to colorless liquids (**6a-d**) in good yields.

2-Allyl-1-(2-chloroethoxy)-3, 4-dimethoxylbenzene (**6a**).

6a (84%) was obtained as a colorless liquid, R_f = 0.60 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) 2937, 1635, 1592, 1487, 1455, 1257, 1122, 912, 790, 734, 673 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.46 (dt, *J* = 6.2 Hz, 1.6 Hz, 2H, $ArC\underline{H}_2CH=CH_2$), 3.79 (t, *J* = 5.8 Hz, 2H, $ArOCH_2C\underline{H}_2Cl$), 3.82 (s, 6H, $ArOC\underline{H}_3$), 4.17 (t, *J* = 5.8 Hz, 2H, $ArOC\underline{H}_2CH_2Cl$), 4.96 (dq, *J* = 10.2 Hz, 1.6 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), 5.02 (dq, *J* = 17.2 Hz, 1.6 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), 5.99 (ddt, *J* = 17.2 Hz, 10.2 Hz, 6.2 Hz, 1H, $ArCH_2C\underline{H}=CH_2$), 6.55 (d, *J* = 8.8 Hz, 1H, H-6), 6.72 (d, *J* = 8.8 Hz, 1H, H-5); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 28.28, 42.12, 56.14, 60.83, 69.05, 107.27, 110.25, 114.62, 123.93, 137.03, 147.81, 148.12, 150.70; EI-MS (70 eV), *m/z* 258 (M^{+2}, 33), 256 (M^+, 100), 241 (16), 227 (16), 178 (27), 165 (36), 151 (18), 91 (14); HRMS: Calcd for $C_{13}H_{17}O_3Cl$: 256.0861. Found: 256.0862. Anal. Calcd for $C_{13}H_{17}O_3Cl$: C, 60.82; H, 6.67. Found: C, 60.83; H, 6.70.

2-Allyl-1-(2-chloroethoxy)-3-ethoxy-4-methoxylbenzene (**6b**).

6b (82%) was obtained as a pale yellow liquid, R_f = 0.67 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) 2976, 1636, 1593, 1487, 1455, 1257, 1212, 1122, 911, 789, 735, 669 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.39 (t, *J* = 7.2 Hz, 3H, $OCH_2C\underline{H}_3$), 3.49 (d, *J* = 6.8 Hz, 2H, $ArC\underline{H}_2CH=CH_2$), 3.78 (t, *J* = 5.8 Hz, 2H, $OCH_2C\underline{H}_2Cl$), 3.80 (s, 3H, $OC\underline{H}_3$), 4.02 (t, *J* = 5.8 Hz, 2H, $OC\underline{H}_2CH_2Cl$), 4.13 (q, *J* = 7.2 Hz, 2H, $OC\underline{H}_2CH_3$), 4.98 (dd, *J* = 10.2 Hz, 1.6 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), 5.05 (dd, *J* = 16.8 Hz, 1.6 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), 6.01 (ddt, *J* = 16.8 Hz, 10.2 Hz, 6.8 Hz, 1H, $ArCH_2C\underline{H}=CH_2$), 6.53, 6.71 (each, d, *J* = 8.8 Hz, 2H, H-6 and H-5); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 15.50, 28.36, 42.07, 55.89, 68.62, 68.77, 106.78, 109.93, 114.28, 123.70, 136.85, 147.02, 147.66, 150.48; EI-MS (70 eV), *m/z* 272 (M^{+2}, 34), 270 (M^+, 100), 241 (26), 201 (33), 175 (16), 159 (49), 147 (50), 119 (17); HRMS: Calcd for $C_{14}H_{19}O_3Cl$: 270.1017. Found: 270.1014. Anal. Calcd for $C_{14}H_{19}O_3Cl$: C, 62.10; H, 7.07. Found: C, 62.13; H, 7.10.

2-Allyl-1-(2-chloroethoxy)-3-isopropoxy-4-methoxylbenzene (**6c**).

6c (83%) was obtained as a pale yellow liquid, R_f = 0.68 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) 2975, 1638, 1593, 1486, 1455, 1257, 1108, 913, 788, 738, 674 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.18 (d, *J* = 6.0 Hz, 6H, ArOCH$\underline{Me}_2$), 3.38 (dt, *J* = 6.2 Hz, 1.4 Hz, 1H, ArC$\underline{H}_2$CH=CH_2), 3.69 (s, 3H, ArOC$\underline{H}_3$), 3.70 (t, *J* = 5.8 Hz, 2H, ArOCH_2C$\underline{H}_2$Cl), 4.07 (t, *J* = 5.8 Hz, 2H, ArOC$\underline{H}_2$CH_2Cl), 4.45 (sept, *J* = 6.0 Hz, 1H, ArOC$\underline{H}$Me$_2$), 4.86 (dq, *J* = 10.0 Hz, 1.6 Hz, 1H, ArCH_2CH=C$\underline{H}_2$), 4.93 (dq, *J* = 16.8 Hz, 1.6 Hz, 1H, ArCH_2CH=C$\underline{H}_2$), 5.88 (ddt, *J* = 16.8 Hz, 10.0 Hz, 6.2 Hz, 1H, ArCH_2C$\underline{H}$=CH_2), 6.42 (d, *J* = 9.0 Hz, 1H, H-6), 6.61 (d, *J* = 9.0 Hz, 1H, H-5); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 22.60, 28.89, 42.13, 56.12, 68.91, 74.60, 106.54, 110.14, 114.54, 124.27, 136.84, 145.90, 147.95, 150.94; EI-MS (70 eV), *m/z* 286 (M^{+2}, 24), 284 (M^+, 65), 242 (100), 227 (33), 180 (56), 165 (29), 147 (77), 119 (19), 91 (24); HRMS: Calcd for $C_{15}H_{21}O_3Cl$: 284.1174. Found: 284.1171. Anal. Calcd for $C_{15}H_{21}O_3Cl$: C, 63.26; H, 7.43. Found: C, 63.23; H, 7.40.

2-Allyl-1-(2-chloroethoxy)-3-benzyloxy-4-methoxylbenzene (**6d**).

6d (84%) was obtained as a pale yellow liquid, R_f = 0.63 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) 2936, 1635, 1592, 1487, 1455, 1372, 1258, 1211, 1122, 912, 790, 735, 697 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.45 (dt, *J* = 6.4 Hz, 1.6 Hz, 2H, ArC$\underline{H}_2$CH=CH_2), 3.78 (t, *J* = 6.0 Hz, 2H, ArOCH_2C$\underline{H}_2$Cl), 3.83 (s, 3H, ArOC$\underline{H}_3$), 4.16 (t, *J* = 6.0 Hz, 2H, ArOC$\underline{H}_2$CH_2Cl), 4.94 (dq, *J* = 10.4 Hz, 1.6 Hz, 1H, ArCH_2CH=C$\underline{H}_2$), 4.98 (dq, *J* = 16.8 Hz, 1.6 Hz, 1H, ArCH_2CH=C$\underline{H}_2$), 4.99 (s, 2H, ArOC$\underline{H}_2$C$_6$H$_5$), 5.95 (ddt, *J* = 16.8 Hz, 10.4 Hz, 6.4 Hz, 1H, ArCH_2C$\underline{H}$=CH_2), 6.57 (d, *J* = 8.8 Hz, 1H, H-6), 6.75 (d, *J* = 8.8 Hz, 1H, H-5), 7.32 (d, *J* = 7.2 Hz, 1H, ArOCH_2C$_6\underline{H}_5$), 7.38 (t, *J* = 7.2 Hz, 2H, ArOCH_2C$_6\underline{H}_5$), 7.48 (d, *J* = 7.2 Hz, 2H, ArOCH_2C$_6\underline{H}_5$) ; ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 28.48, 42.13, 56.21, 68.99, 74.72, 107.38, 110.23, 114.69, 124.16, 127.77, 127.95, 128.31, 136.96, 137.87, 146.87, 147.87, 150.72; EI-MS (70 eV), *m/z* 334 (M^{+2}, 9), 332 (M^+, 26), 241 (31), 209 (21), 177 (15), 163 (10), 147 (10), 91 (100), 65 (17); HRMS: Calcd for $C_{19}H_{21}O_3Cl$: 332.1174. Found: 332.1177. Anal. Calcd for $C_{19}H_{21}O_3Cl$: C, 68.57; H, 6.36. Found: C, 68.59; H, 6.40.

General Procedure for the Preparation of Propenyl vinyloxybenzenes (**7a-d**)

To a stirred solution of 1-(1-propenyl)-2-chloroethoxybenzenes (**6a-d**) (5 mmol) in anhydrous THF (30 mL) was added potassium *tert*-butoxide (0.62 g, 5.5 mmol) at rt, and the reaction mixture was under reflux for 30 min. THF was removed from the reaction mixture in *vacuo*, and the residue was extracted with ethyl acetate (20 mL x 5). The extracted solution was dried from anhydrous $MgSO_4$. After filtration, the filtrate was concentrated in *vacuo*, and the resulting residue was purified by column chromatography

on silica gel (ethyl acetate: *n*-hexane = 1: 20) to give **7a-d**, respectively.

1,2-Dimethoxy-3-(1-propenyl)-4-vinyloxybenzene (**7a**).

7a (87%) was obtained as a colorless liquid, R_f = 0.73 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) 2936, 2835, 2359, 2341, 1644, 1471, 1417, 1243, 1157, 1088, 1048, 974, 843, 799 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.92 (dd, *J* = 6.4 Hz, 1.6 Hz, 3H, ArCH=CHC$\underline{H}_3$), 3.78 (s, 3H, ArOC$\underline{H}_3$), 3.84 (s, 3H, ArOC$\underline{H}_3$), 4.31 (dd, *J* = 6.4 Hz, 1.6 Hz, 1H, ArOCH=C$\underline{H}_2$), 4.57 (dd, *J* = 14.0 Hz, 1.6 Hz, 1H, ArOCH=C$\underline{H}_2$), 6.49 (dq, *J* = 16.0 Hz, 1.6 Hz, 1H, ArC$\underline{H}$=CHCH$_3$), 6.51 (dd, *J* = 14.0 Hz, 6.4 Hz, 1H, ArOC$\underline{H}$=CH$_2$), 6.62 (dq, *J* = 16.0 Hz, 6.4 Hz, 1H, ArCH=C$\underline{H}$CH$_3$), 6.68 (d, *J* = 8.8 Hz, 1H, H-6), 6.71 (d, *J* = 8.8 Hz, 1H, H-5); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 20.03, 56.13, 60.20, 93.09, 110.21, 113.59, 120.85, 123.49, 132.16, 147.47, 148.24, 149.48, 149.86; EI-MS (70 eV), *m/z* 220 (M^+, 14), 191 (83), 178 (53), 163 (33), 115 (44), 107 (76), 91 (100), 77 (62); HRMS: Calcd for $C_{13}H_{16}O_3$: 220.1094. Found: 220.1094. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.90; H, 7.30.

2-Ethoxy-1-methoxy-3-(1-propenyl)-4-vinyloxybenzene (**7b**).

7b (88%) was obtained as a liquid: R_f = 0.8 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) 2976, 2836, 1643, 1470, 1384, 1157, 1088, 1047, 973, 843, 799 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.38 (t, *J* = 7.2 Hz, 3H, OCH$_2$C$\underline{H}_3$), 1.91 (dd, *J* = 6.4 Hz, 1.6 Hz, 3H, ArCH=CHC$\underline{H}_3$), 3.82 (s, 3H, OC$\underline{H}_3$), 3.98 (q, *J* = 7.2 Hz, 2H, OC$\underline{H}_2$CH$_3$), 4.30 (dd, *J* = 6.0 Hz, 1.6 Hz, 1H, OCH=C$\underline{H}_2$), 4.56 (dd, *J* = 14.0 Hz, 1.6 Hz, 1H, OCH=C$\underline{H}_2$), 6.53 (dq, *J* = 15.8 Hz, 6.4 Hz, 1H, ArCH=C$\underline{H}$CH$_3$), 6.54 (dd, *J* =14.0 Hz, 6.0 Hz, 1H, OC$\underline{H}$=CH$_2$), 6.58, 6.65 (each d, *J* = 8.0 Hz, 2H, H-5 and H-6), 6.70 (dq, *J* = 15.8 Hz, 1.6 Hz, 1H, ArC$\underline{H}$=CHCH$_3$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 15.65, 20.02, 56.18, 68.58, 93.02, 110.21, 113.35, 121.18, 123.79, 131.94, 146.55, 148.26, 149.60, 149.84; EI-MS (70 eV), *m/z* 234 (M^+, 32), 205 (100), 192 (77), 177 (54), 164 (48), 149 (27), 119 (14), 103 (12), 91 (38); HRMS: Calcd for $C_{14}H_{18}O_3$: 234.1256. Found: 234.1255. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.80; H, 7.75.

2-Isopropoxy-1-methoxy-3-(1-propenyl)-4-vinyloxybenzene (**7c**).

7c (87%) was obtained as a liquid: R_f = 0.8 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) IR (KBr) 2974, 1644, 1471, 1440, 1372, 1243, 1157, 1109, 1036, 972, 796 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.26 (d, *J* = 6.4 Hz, 6H, ArOCH$\underline{Me}_2$), 1.90 (dd, *J* = 6.4, 1.2 Hz, 3H, ArCH=CHC$\underline{H}_3$), 3.80 (s, 3H, ArOC$\underline{H}_3$), 4.30 (dd, *J* = 6.4, 1.8 Hz, 1H, ArOCH=C$\underline{H}_2$), 4.42 (sept, *J* = 6.4 Hz, 1H, ArOC$\underline{H}$Me$_2$), 4.56 (dd, *J* = 14.0, 1.8 Hz, 1H, ArOCH=C$\underline{H}_2$), 6.50 (dq, *J* = 14.8, 1.2 Hz, 1H, ArC$\underline{H}$=CHCH$_3$), 6.52 (dd, *J* = 14.0, 6.4 Hz, 1H,

ArOC<u>H</u>=CH_2), 6.58 (dq, *J* = 14.8, 6.4 Hz, 1H, ArCH=C<u>H</u>CH_3), 6.65 (d, *J* = 8.8 Hz, 1H, H-6), 6.69 (d, *J* = 8.8 Hz, 1H, H-5); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 19.86, 22.39, 56.03, 75.32, 92.89, 110.07, 112.98, 121.80, 124.41, 131.81, 145.38, 148.29, 149.70, 149.83; EI-MS (70 eV), *m/z* 248 (M^+, 14), 206 (15) 191 (19), 177 (100), 164 (38), 149 (39), 91 (24); HRMS: Calcd for $C_{15}H_{20}O_3$: 248.1407. Found: 248.1409. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.57; H, 8.15.

2-Benzyloxy-1-methoxy-3-(1-propenyl)-4-vinyloxybenzene (**7d**).

7d (87%) was obtained as a liquid, R_f = 0.78 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) 2936, 1644, 1471, 1455, 1372, 1243, 1156, 1088, 1039, 976, 799, 697 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.86 (dd, *J* = 6.4 Hz, 1.6 Hz, 1H, ArCH=CHC<u>H</u>$_3$), 3.83 (s, 3H, ArOC<u>H</u>$_3$), 4.30 (dd, *J* = 6.4 Hz, 1.6 Hz, 1H, ArOCH=C<u>H</u>$_2$), 4.56 (dd, *J* = 14 Hz, 1.6 Hz, 1H, ArOCH=C<u>H</u>$_2$), 4.93 (s, 2H, ArOC<u>H</u>$_2$$C_6$<u>H</u>$_5$), 6.49 (dq, *J* = 16.0 Hz, 1.6 Hz, 1H, (ArC<u>H</u>= CHCH_3), 6.51 (dd, *J* = 14.0 Hz, 6.4 Hz, 1H, ArOC<u>H</u>=CH_2), 6.58 (dq, *J* = 16.0 Hz, 6.4 Hz, 1H, ArCH=C<u>H</u>CH_3), 6.69 (d, *J* = 8.8 Hz, 1H, H-6), 6.72 (d, *J* = 8.8 Hz, 1H, H-5), 7.32 (d, *J* = 7.2 Hz, 1H, ArOC$H_2$$C_6$<u>H</u>$_5$), 7.37 (t, *J* = 7.2 Hz, 2H, ArOC$H_2$$C_6$<u>H</u>$_5$), 7.46 (d, *J* = 7.2 Hz, 2H, ArOC$H_2$$C_6$<u>H</u>$_5$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 19.92, 56.19, 74.54, 93.04, 110.30, 113.71, 121.06, 123.97, 127.86, 128.25, 128.30, 132.30, 137.57, 146.27, 148.19, 149.60, 149.84; EI-MS (70 eV), *m/z* 296 (M^+, 4), 254 (4), 205 (11), 103 (9), 91 (100), 77 (16), 65 (22); HRMS: Calcd for $C_{19}H_{20}O_3$: 296.1405. Found: 296.1407. Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 77.01; H, 6.83.

General Procedure for the Preparation of Benzofurans (**8a-d**)

To a stirred solution of 1-(1-propenyl)-2-vinyloxybenzenes (**7a-d**) (1.15 mmol) in dichloromethane (23 mL) was added Grubbs' catalyst (50 mg, 5% mmol) at rt, and the reaction mixture was stirred for 8 h. Excess dichloromethane was removed from the reaction mixture in *vacuo*, and the resulting residue was purified by column chromatography on silica gel (ethyl acetate: *n*-hexane = 1: 50) to give **8a-d.**

4,5-Dimethoxyfuran (**8a**).

8a (96%) was obtained as a colorless crystals, mp 35-36 ^{o}C (ethyl acetate + *n*-hexane), R_f = 0.68 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) 2941, 2834, 1594, 1538, 1487, 1434, 1345, 1281, 1226, 1140, 1062, 1026, 969, 871, 780, 742, 686, 636 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.87 (s, 3H, OC<u>H</u>$_3$), 4.04 (s, 3H, OC<u>H</u>$_3$), 6.85 (dd, *J* = 2.2 Hz, 0.8 Hz, 1H, H-3), 6.92 (d, *J* = 8.8 Hz, 1H, H-6), 7.13 (dd, *J* = 8.8 Hz, 0.8 Hz, 1H, H-7), 7.50 (d, *J* = 2.2 Hz, 1H, H-2); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 57.41, 60.34, 104.27, 105.31, 111.34, 120.56, 141.83, 144.71, 146.42, 151.02; EI-MS (70 eV), *m/z* 178 (M^+, 100); 163 (64), 107(72), 77 (29); Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.41; H, 5.66. Found: C, 67.41; H, 5.70.

4-Ethoxy-5-methoxyfuran (**8b**).

Pure **8b** (95%) was obtained as a liquid: R_f = 0.75 (ethyl acetate: *n*-hexane = 1: 4), IR (KBr) 2931, 1599, 1538, 1487, 1428, 1341, 1279, 1239, 1219, 1139, 1059, 941, 856, 779, 742, 635 cm^{-1}, ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.41 (t, *J* = 7.2 Hz, 3H, $OCH_2C\underline{H}_3$), 3.90 (s, 3H, $OC\underline{H}_3$), 4.28 (q, *J* = 7.2 Hz, 2H, $OC\underline{H}_2CH_3$), 6.83 (dd, *J* = 2.2 Hz, 0.8 Hz, 1H, H-3), 6.95 (d, *J* = 8.8 Hz, 1H, H-6), 7.16 (dd, *J* = 8.8 Hz, 0.8 Hz, 1H, H-7), 7.52 (d, *J* = 2.2 Hz, 1H, H-2); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 15.74, 57.65, 68.73, 104.50, 105.65, 111.70, 121.94, 140.93, 144.82, 147.17, 151.05; EI-MS (70 eV), *m/z* 192 (M^+, 73); 164 (41), 149 (100); HRMS: Calcd for $C_{11}H_{12}O_3$: 192.0781. Found: 192.0779. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.75; H, 6.30.

4-Isopropoxy-5-methoxyfuran (**8c**).

8c (96 %) was obtained as a pale yellow liquid; R_f = 0.75 (ethyl acetate: *n*-hexane = 1: 4); IR (KBr) 2974, 2833, 1599, 1538, 1487, 1427, 1331, 1279, 1220, 1138, 1108, 1083, 1052, 1014, 944, 873, 780, 742 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.34 (d, *J* = 6.0 Hz, 6H, $OCH\underline{Me}_2$), 3.87 (s, 3H, $OC\underline{H}_3$), 4.57 (sept, *J* = 6.0 Hz, 1H, $OC\underline{H}Me_2$), 6.79 (dd, *J* = 2.2 Hz, 0.8 Hz, 1H, H-3), 6.93 (d, *J* = 8.8 Hz, 1H, H-6), 7.15 (dd, *J* = 8.8 Hz, 0.8 Hz, 1H, H-7), 7.50 (d, *J* = 2.2 Hz, 1H, H-2); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 22.73, 57.51, 75.26, 104.64, 105.80, 111.58, 123.26, 139.95, 144.82, 147.81, 150.86; EI-MS (70 eV), *m/z* 206 (M^+, 22); 164 (56), 149 (100); HRMS: Calcd for $C_{12}H_{14}O_3$: 206.0937. Found: 206.0938. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.85; H, 6.83.

4-Benzyloxy-5-methoxyfuran (**8d**).

8d (96%) was obtained as a pale yellow liquid; R_f = 0.73 (ethyl acetate: *n*-hexane = 1: 4); IR (KBr) 2937, 2834, 1599, 1538, 1487, 1455, 1428, 1342, 1280, 1238, 1139, 1084, 1056, 1019, 740, 697 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.90 (s, 3H, $OC\underline{H}_3$), 5.21 (s, 2H, $ArOC\underline{H}_2C_6H_5$), 6.71 (dd, *J* = 2.2 Hz, 0.8 Hz, 1H, H-3), 6.96 (d, *J* = 8.8 Hz, 1H, H-6), 7.17 (dd, *J* = 8.8 Hz, 0.8 Hz, 1H, H-7), 7.33 (td, *J* = 7.6, 1.0 Hz, 2H, $ArOCH_2C_6\underline{H}_5$); 7.34 (dd, *J* = 7.6, 1.0 Hz, 1H, $ArOCH_2C_6\underline{H}_5$), 7.46 (dd, *J* = 7.6, 1.0 Hz, 2H, $ArOCH_2C_6\underline{H}_5$), 7.46 (dd, *J* = 2.2 Hz, 1H, H-2); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 57.70, 75.02, 104.42, 106.13, 111.72, 122.30, 127.91, 128.05, 128.32, 137.72, 140.81, 144.91, 147.35, 150.91; EI-MS (70 eV), *m/z* 254 (M^+, 66); 239 (10), 163 (17), 127 (15), 107 (31), 91 (100), 85 (21); HRMS: Calcd for $C_{16}H_{14}O_3$: 254.0937. Found: 254.0938. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.59; H, 5.56.

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