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A NEW SYNTHESIS OF SUBSTITUTED 2,5-DIHYDRO[*b*]-OXEPINES

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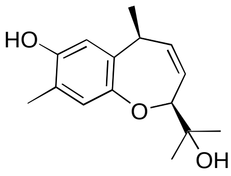
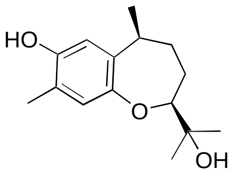
Abstract- Based on Claisen rearrangement, Baeyer-Villiger oxidation, and ring-closing metathesis (RCM), a series of substituted 2,5-dihydrobenzo[*b*]-oxepines were synthesized from isovanillin in good over-all yields. Other appropriate substituted 2,5-dihydrobenzo[*b*]oxepines prepared from corresponding phenol derivatives were also described.

INTRODUCTION

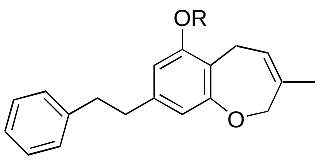
Benzo[*b*]oxepine, a structural unit of some natural occurring sesquiterpines, attracts the attention of either synthetic or natural product chemists for their activities. Just as heliannuol B isolated from *Helianthus annuus* var. *SH-222 and VYP* exhibited allelopathic activity in the cultivated sunflower to make a defense against dicotyledon species.[1] Heliannuols D,[1] a reduced form of heliannuol B, synthesized by Takabatake, *et al.*[2] has also revealed an alleochemical activity. Radulanin A, and its methyl ether isolated from *Radula complanata* by Asakawa, *et al.*,[3a] and synthesized *via* Mitsunobu's reaction by Yamaguchi, *et al.*,[3b] have shown 5-lipoxygenase and calmodulin inhibitory activity, and vasopressin antagonist activity.[3a] However those synthetic methods still have disadvantages including tedious reaction conditions, multi-synthetic steps, low over-all yields, and commercial unavailable intermediate, which difficulty to prepared. Thus, to build-up a brief and rationale synthetic method for those title compounds is requisite.



heliannuol B



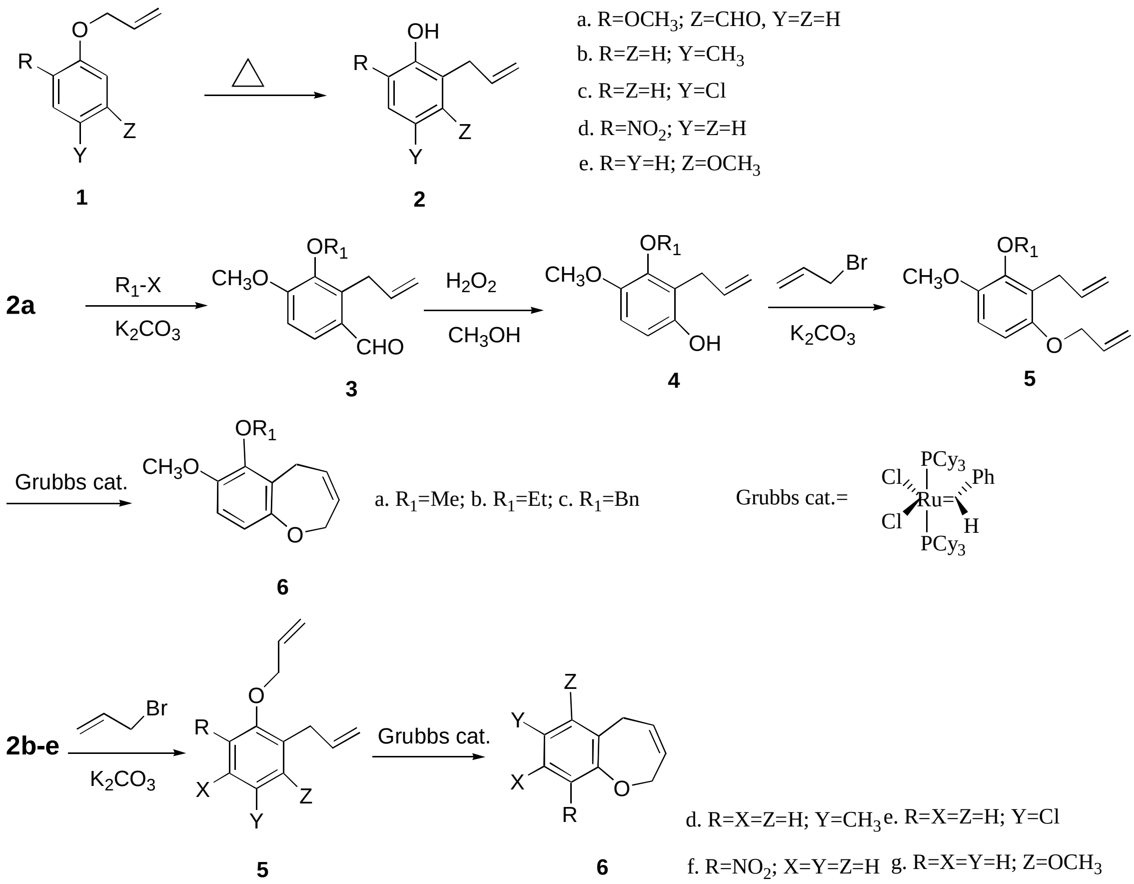
heliannuol D



radulanin A, R=H
radulanin A methyl ether, R=CH$_3$

Since 1995 Grubbs et al.[4] discovered a novel alkylidene-ruthenium complex as a catalyst for ring-closing metathesis (RCM), it has been widely applied in organic synthesis in many aspects.[5] Based on this chemistry, we have recently reported a new route to *N*-aryl α,β-unsaturated lactams,[6] substituted

*Correponding author: Eng-Chi Wang, Fax: 886-7-3125339; e-mail: enchwa@kmu.edu.tw naphthalenes.[7] Although ring-closing metathesis has been preliminarily applied for the synthesis 2,5-dihydrobenzo[*b*]oxepines by Fuerstner, *et al.*,[8a] and Miyaki, *et al.*,[8b] but for their substituted derivatives is only paid a little attention.[8c] In this our continuing studies, based on Claisen reaction, Baeyer-Villiger oxidation and RCM, we herein reported a versatile synthesis of some new substituted 2,5-dihydrobenzo[*b*]oxepines, which started from isovanillin. Furthermore other appropriate new substituted 2,5-dihydrobenzo[*b*]oxepines prepared from corresponding phenol derivatives were also described. The synthetic scheme was shown in **Scheme 1**.



Scheme 1

RESULTS AND DISCUSSION

According to the general procedure,[9] by the reflux of the corresponding phenols (**1a-f**) with allyl bromide in the presence of anhydrous K_2CO_3 in acetone, it gave phenyl ethers (**2a-f**) in good yields. These phenyl ethers were respectively heated to boil as previous study[7, 10] to undergo Claisen rearrangement to give 2-allylphenols (**2a-e**) in good yields. The migration of allyl group to the *ortho*-position of corresponding phenol was confirmed by ^{1}H-NMR spectra. For example chemical shifts of **2a** showed two aromatic signals with doublet at δ 7.0, and 7.5 having coupling constant, J = 8.8 Hz, indicated *ortho*-couple of each other. Thus, the evidence of the migration of allyl group from allyloxy to the *ortho*-position of phenolic OH of **2a** was confirmed.[7] As the procedure previously described,[7] these 2-allylphenols (**2a**) were respectively alkylated with various alkyl iodide or bromide to give 2-allyl-3-alkoxy-4-methoxybenzaldehydes (**3a-c**) in good yields. Followed by undergoing Baeyer-Villiger oxidation,[11] **3a-c** was respectively converted into corresponding phenols (**4a-c**) in yields of 71-75 %. The structure of **4a-c** was confirmed by ^{1}H-NMR and ^{13}C-NMR spectrometry. For example, **4a** exhibited a phenolic proton at δ 4.89 (D_2O exchangeable), no formyl proton or carbon observed either in ^{1}H-NMR or ^{13}C-NMR spectra, indicated the work of oxidation. Furthermore the molecular ion of **4a** in EI-MS is *m/z* 194, which is coincident with the calculated one for **4a**, $C_{11}H_{14}O_3$. Then, allylation of **4a-c** and **2b-e** was smoothly carried out as general procedure[10] to lead **5a-g** in yields of 82-88 %. The structure of **5a-g** was confirmed by spectral data such as ^{1}H-NMR, ^{13}C-NMR, and EI-MS. For instance, **5b** revealed two sets of allyl group in ^{1}H-NMR, one at δ 3.47 (dt, *J* 6.3, 1.9 Hz, 2H, $ArC\underline{H_2}CH{=}CH_2$), 4.94 (ddt, *J* 10.2, 1.9, 1.9 Hz, 1H, $ArCH_2CH{=}C\underline{H_2}$), 5.01 (ddt, *J* 17.5, 1.9, 1.9 Hz, 1H, $ArCH_2CH{=}C\underline{H_2}$), and 5.99 (ddt, *J* 17.5, 10.2, 6.3 Hz, 1H, $ArCH_2C\underline{H}{=}CH_2$), the other one at δ 4.46 (dt, *J* 5.0, 1.8 Hz, 2 H, $ArOC\underline{H_2}CH{=}CH_2$), 5.23 (ddt, *J* 10.5, 1.8, 1.8 Hz, 1H, $ArCH_2CH{=}C\underline{H_2}$), 5.40 (ddt, *J* 17.2, 1.8, 1.8 Hz, 1H, $ArCH_2CH{=}C\underline{H_2}$), and 6.03 (ddt, *J* 17.2, 10.5, 5.0 Hz, 1H, $ArCH_2C\underline{H}{=}CH_2$). Furthermore fifteen lines were found in ^{13}C-NMR spectra, matched the carbon numbers for **5b**. On the other hand, the molecular ion, *m/z* 248 was found in EI-MS, which is coincident with the calculated one for **5b**, $C_{15}H_{20}O_3$. Finally **5a-f** was respectively treated with Grubbs' catalyst in dichloromethane to undergo RCM reaction, it furnished substituted benzo[*b*]oxepines (**6a-g**) in yields of 80-88 % yields. The structure of **6a-g** was supported by the data of ^{1}H-NMR, ^{13}C-NMR, and EI-MS spectra. Such as **6c**, two *cis*-olefinic protons at δ 5.36 (*J* 14.4, 5.3, 2.4 Hz, 1H, H-4), and 5.68 (*J* 14.4, 8.1, 2.0 Hz, 1H, H-3) in ^{1}H-NMR spectrum, and two olefinic carbons at δ 110.09 and 116.28 in ^{13}C-NMR spectrum were found, respectively. The molecular ion, *m/z* 282 was found in EI-MS spectrum, which is coincident with the calculated one for **6c**, $C_{18}H_{18}O_3$.

In conclusion, besides 6-methoxybenzo[*b*]oxepines (**6g**),[8c] such as 6-alkoxy-7-methoxybenzo[*b*]oxepines (**6a-c**) 7-methyl or 7-chlorobenzo[*b*]oxepines (**6d-e**), and 9-nitrobenzo[*b*]oxepines (**6f**), which are all new compounds, were synthesized in good over-all yields. Thus, our study gave a new and versatile route to substituted benzo[*b*]oxepines from isovanillin, and various phenols. Furthermore the ^{1}H-NMR, ^{13}C-NMR, EI-MS, and HRMS spectral data for those substituted benzo[*b*]oxepines (**6a-g**) were also established. The synthesis of other new substituted benzo[*b*]oxepines is currently in progress in our lab.

EXPERIMENTAL

Melting points (Yanaco micro melting-point apparratus) are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were obtained on a Varian Gemini-200 or Varian Unity plus 400 or Bruker Avance 600 Spectrometer. Chemical shifts are 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 Chem/hp/middle instrument, and HRMS were recorded on JEOL, JMSD-200 or on JEOL, JMS-SX. Silica gel (230-400 mesh) for column chromatography, and precoated silica gel plates (60F-254) for TLC was purchased from E. Merck. UV light (254 nm) was used to detect spots on TLC plates after development.

General procedure for *o*-allylation of corresponding phenolic compound to give allyloxyl

compounds (**1a-e**)

The corresponding phenols (20 mmol) were respectively reacted with allyl bromide as the known procedure[10] to give allyloxyl compounds (**1a-e**).

3-allyloxy-4-methoxybenzaldehyde (**1a**)[12]

Pure **1a** (3.34 g, 87%) was obtained as colorless liquid, R_f 0.36 (ethyl acetate/*n*-hexane = 1/3); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.96 (s, 3H, $OC\underline{H}_3$), 4.67 (dt, *J* = 5.2 Hz, 1.2 Hz, 2H, $OC\underline{H}_2CH{=}CH_2$), 5.32 (ddt, *J* = 10.4 Hz, 1.2 Hz, 1.2 Hz, 1H, $OCH_2CH{=}C\underline{H}_2$), 5.45 (ddt, *J* = 17.2 Hz, 1.2 Hz, 1.2 Hz, 1H, $OCH_2CH{=}C\underline{H}_2$), 6.09 (ddt, *J* = 17.2, 10.4, 5.2 Hz, 1H, $OCH_2C\underline{H}{=}CH_2$), 6.99, 7.46 (each d, *J* = 8.0 Hz, 1H, $Ar\underline{H}$), 7.41 (s, 1H, $Ar\underline{H}$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 56.08, 69.64, 110.62, 110.82, 118.51, 126.72, 129.94, 132.44, 148.45, 154.77, 190.76.

1-Allyloxy-4-methylbenzene (**1b**)[13]

Pure **9a** (2.58 g, 87%) was obtained as colorless liquid, R_f =0.89 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.25 (s, 3H, $ArC\underline{H}_3$), 4.46 (dt, *J* = 5.2 Hz, 1.6 Hz, 2H, $ArOC\underline{H}_2CH{=}CH_2$), 5.24 (dd, *J* = 10.4 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 5.37 (dd, *J* = 17.2 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 6.02 (ddt, *J* = 17.2 Hz, 10.4 Hz, 5.2 Hz, 1H, $ArOCH_2C\underline{H}{=}CH_2$), 6.79 (d, *J* = 8.4 Hz, 2H, $Ar\underline{H}$), 7.04 (d, *J* = 8.6 Hz, 2H, $Ar\underline{H}$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 20.35, 68.73, 114.51, 117.25, 129.77, 129.88, 133.49, 156.43; EI-MS (70 eV) *m/z* 148 (M^+, 100), 133 (65), 131 (4), 120 (5), 107 (76), 91 (17), 80 (6), 77 (54), 65 (12), 51 (12); HRMS calcd for $C_{10}H_{12}O$: 148.0888. Found: 148.0888.

Allyloxy-4-chlorobenzene (**1c**)[14]

Pure **1c** (3.04 g, 90 %) was obtained as colorless liquid, R_f =0.87 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.47 (dt, *J* = 5.2 Hz, 1.6 Hz, 2H, $ArOC\underline{H}_2CH{=}CH_2$), 5.27 (ddt, *J* = 10.0 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 5.38 (ddt, *J* = 17.2 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 6.01 (ddt, *J* = 17.2 Hz, 10.0 Hz, 5.2 Hz, 1H, $ArOCH_2C\underline{H}{=}CH_2$), 6.81 (d, *J* = 8.8 Hz, 2H, $Ar\underline{H}$), 7.20 (d, *J* = 8.8 Hz, 2H, $Ar\underline{H}$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 68.94, 115.95, 117.72, 125.58, 129.21, 132.87, 157.13; EI-MS (70 eV) *m/z* 168 (M^+, 100), 153 (13), 140 (4), 133 (81), 111 (12), 99 (60), 91 (4), 75 (31), 63 (26), 50 (14); HRMS calcd for C_9H_9ClO: 168.0342. Found: 168.0339.

1-Allyloxy-2-nitrobenzene (**1d**)[15]

Pure **1d** (3.19 g, 89%) was obtained as yellow liquid, R_f =0.41 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.68 (dt, *J* = 4.8 Hz, 1.6 Hz, 2H, $ArOC\underline{H}_2CH{=}CH_2$), 5.31 (ddt, *J* = 10.8 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 5.49 (ddt, *J* = 17.2 Hz, 1.6 Hz , 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 6.03 (ddt, *J* = 17.2 Hz, 10.8 Hz, 4.8 Hz, 1H, $ArOCH_2C\underline{H}{=}CH_2$), 7.02 (td, *J* = 8.0 Hz, 1.6 Hz, 1H, $Ar\underline{H}$), 7.08 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H, $Ar\underline{H}$), 7.51 (td, *J* = 8.0 Hz, 1.6 Hz, 1H, $Ar\underline{H}$), 7.82 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H, $Ar\underline{H}$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 69.81, 114.76, 118.07, 120.35, 125.43, 131.62, 133.96, 139.91, 151.74; EI-MS (70 eV) *m/z* 179 (M^+, 12), 139 (6), 123 (100), 106 (46), 92 (9), 78 (11), 63 (22), 51 (15); HRMS calcd for $C_9H_9NO_3$: 179.0582. Found: 179.0585.

1-Allyloxy-3-methoxybenzene (1e)[16]

Pure **1e** (2.82 g, 86%) was obtained as colorless liquid, R$_f$ = 0.59 (ethyl acetate/*n*-hexane=1/12), ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.75 (s, 3H, $OC\underline{H}_3$), 4.49 (dt, *J* = 5.3 Hz, 1.6 Hz, 2H, $C\underline{H}_2CH{=}CH_2$), 5.26 (ddt, *J* = 10.5 Hz, 1.6 Hz, 1.6 Hz, 1H, $CH_2CH{=}C\underline{H}_2$), 5.39 (ddt, *J* = 17.3 Hz, 1.6 Hz, 1.6 Hz, 1H, $CH_2CH{=}C\underline{H}_2$), 6.04 (ddt, *J* = 17.3 Hz, 10.5 Hz, 5.3 Hz, 1H, $CH_2C\underline{H}{=}CH_2$), 6.48 (s, 1H, Ar$\underline{H}$), 6.50 (dt, *J* = 7.6 Hz, 2.1 Hz, 2H, Ar$\underline{H}$), 7.15 (t, *J* = 7.6 Hz, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 55.11, 68.70, 101.17, 106.34, 106.79, 117.50, 129.76, 133.22, 159.78, 160.76; EI-MS (70 eV) *m/z* 164 (M^+, 100), 149 (23), 136 (22), 121 (30), 109 (12), 105 (13), 95 (39), 77 (13), 64 (11), 52 (12); HRMS: Calcd for $C_{10}H_{12}O_2$: 164.0837. Found: 164.0835.

General procedure for the preparation of 2a-e *via* the Claisen rearrangement of 1a-e

The corresponding allyloxyl compounds **1a-e** (15 mmol) were respectively heated to undergo Claisen reaction as the known procedure[7, 8, 10] to give **2a-e**.

2-Allyl-3-hydroxy-4-methoxybenzaldehyde (2a)[7, 8]

Pure **2a** (2.7 g, 94%) was obtained as pale yellow liquid; R$_f$ 0.47 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.75 (dt, *J* = 6.0 Hz, 1.6 Hz, 2H, $ArC\underline{H}_2CH{=}CH_2$), 3.77 (s, 3H, $OC\underline{H}_3$), 4.84 (dt, *J* = 18.8 Hz, 1.6 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 4.88 (dt, *J* = 10.0 Hz, 1.6 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.89 (ddt, *J* = 18.8 Hz, 10.0 Hz, 6.0 Hz, 1H, $ArCH_2C\underline{H}{=}CH_2$), 6.28 (br s, 1H, O$\underline{H}$), 6.71, 7.27 (each d, *J* = 8.4 Hz, 1H, Ar$\underline{H}$), 9.90 (s, 1H, C$\underline{H}$O); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.08 ($ArC\underline{H}_2CH{=}CH_2$), 55.76 ($O\underline{C}H_3$), 107.91, 114.96, 125.28, 127.31, 127.74, 136.07, 143.61, 150.80, 191.40 ($\underline{C}HO$); EI-MS (70 eV) *m/z* (rel. intensity, %) 192 (M^+, 54), 177 (100), 159 (24), 149 (23), 143 (19), 131 (29), 115 (19), 103 (28), 91 (20), and 77 (23); HRMS calcd for $C_{11}H_{12}O_3$: 192.0786. Found: 192.0789.

2-Allyl-4-methylphenol (2b)[15]

Pure **2b** (1.96 g, 88%) was obtained as colorless liquid, R$_f$ =0.32 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 2.25 (s, 3H, $ArC\underline{H}_3$), 3.63 (d, *J* = 6.4 Hz, 2H, $ArC\underline{H}_2CH{=}CH_2$), 4.98 (s, 1H, ArO$\underline{H}$), 5.13 (dd, *J* = 11.6 Hz, 1.6 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.14 (dd, *J* = 15.6 Hz, 1.6 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 6.01 (ddt, *J* = 17.6 Hz, 9.7 Hz, 6.4 Hz, 1H, $ArCH_2C\underline{H}{=}CH_2$), 6.69 (d, *J* = 8.7 Hz, 1H, Ar$\underline{H}$), 6.90 (s, 1H, Ar$\underline{H}$), 6.91 (d, *J* = 8.6 Hz, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 20.42, 35.03, 115.60, 116.24, 125.07, 128.17, 130.08, 130.92, 136.52, 151.69; EIMS (70 eV) *m/z* 148 (M^+, 100), 133 (83), 131 (15), 105 (53), 91 (28), 77 (15), 65(6), 51(6); HRMS: Calcd for $C_{10}H_{12}O$: 148.0888. Found: 148.0890.

2-Allyl-4-chlorophenol (2c)[15]

Pure **2c** (2.15 g, 85%) was obtained as colorless liquid, R$_f$ =0.79 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.37 (dt, *J* = 6.4 Hz, 1.6 Hz, 2H, $ArC\underline{H}_2CH{=}CH_2$), 5.11 (ddt, *J* = 10.4 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.18 (ddt, *J* = 17.5 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.65 (br s, 1H, ArO$\underline{H}$), 5.98 (ddt, *J* = 17.5 Hz, 10.4 Hz, 6.4 Hz, 1H, $ArCH_2C\underline{H}{=}CH_2$), 6.74, 7.04 (each d, *J* = 8.8 Hz, 1H, Ar$\underline{H}$), 7.09 (s, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 34.57, 116.00, 116.82, 125.28, 127.37, 129.95, 130.20, 135.55, 152.69; EI-MS (70 eV) *m/z* 168(M^+, 100), 153(36), 141(13), 133(98), 115(33), 105(79), 89(14), 77(62), 66(16), 51(47); HRMS: Calcd for C_9H_9OCl: 168.0342. Found: 168.0344.

2-Allyl-6-nitrophenol (2d)[15]

Pure **2d** (2.07 g, 77%) was obtained as yellow liquid, R_f =0.77 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.48 (dt, *J* = 6.6 Hz, 1.3 Hz, 2H, $ArC\underline{H}_2CH=CH_2$), 5.12 (ddt, *J* = 15.0 Hz, 1.3 Hz, 1.3 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), 5.11 (ddt, *J* = 17.7 Hz, 1.3 Hz, 1.3 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), 5.98 (ddt, *J* = 17.7 Hz, 15.0 Hz, 6.6 Hz, 1H, $ArCH_2C\underline{H}=CH_2$), 6.92 (t, *J* = 8.0 Hz, 1H, $Ar\underline{H}$), 7.46 (dd, *J* = 8.0 Hz, 1.0 Hz, 1H, $Ar\underline{H}$), 7.97 (dd, *J* = 8.0 Hz, 1.0 Hz, $Ar\underline{H}$), 10.93 (s, 1H, $ArO\underline{H}$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 33.55, 116.75, 119.42, 123.02, 131.34, 133.56, 135.05, 137.42, 153.20; EI-MS (70 eV) *m/z* 179 (M^+, 56), 162(11), 132(12), 116(14), 103(61), 89(11), 77(46), 65(7.0), 51(17); HRMS: Calcd for $C_9H_9NO_3$: 179.0582. Found: 179.0582.

2-Allyl-3-methoxyphenol (2e)[17]

Pure **2e** (1.85 g, 75%) was obtained as colorless liquid, R_f =0.47 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.48 (dt, *J* = 6.3 Hz, 1.8 Hz, 1.7 Hz, 2H, $ArC\underline{H}_2CH=CH_2$), 3.80 (s, 3H, $OC\underline{H}_3$), 5.07 (br s, 1H, $O\underline{H}$), 5.08 (ddt, *J* = 10.4 Hz, 1.8 Hz, 1.8 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), 5.10 (ddt, *J* = 18.0 Hz, 1.8 Hz, 1.8 Hz, 1H, $ArCH_2CH=C\underline{H}_2$), 5.98 (ddt, *J* = 18.0 Hz, 10.4 Hz, 6.3 Hz, 1H, $ArCH_2C\underline{H}=CH_2$), 6.49 (dd, *J* = 8.5 Hz, 2.0 Hz, 2 H, $Ar\underline{H}$), 7.08 (t, *J* = 8.5 Hz, 1H, $Ar\underline{H}$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 27.32, 55.80, 103.33, 108.79, 113.61, 115.36, 127.51, 136.30, 155.14, 158.21; EI-MS (70 eV) *m/z* 164 (M^+, 100), 149 (34), 135 (42), 121 (34), 107 (39), 103 (23), 91 (20), 77 (21), 65 (7), 51 (7); HRMS: Calcd for $C_{10}H_{12}O_2$: 164.0837. Found: 164.0837.

General procedure for the preparation of 3a-c from 2a-c

The corresponding *o*-allylphenols (**2a-c**) (10 mmol) were respectively reacted with methyl iodide, ethyl bromide, and benzyl bromide as the known procedure[7, 8] to give allylalkoxy compounds (**3a-c**).

2-Allyl-3,4-dimethoxybenzaldehyde (3a)[7, 18]

Pure **3a** (1.81 g, 88%) was obtained as pale yellow liquid, R_f 0.62 (ethyl acetate/*n*-hexane = 1/3); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.73, 3.85 (each s, 3H, $OC\underline{H}_3$), 3.78 (dt, *J* = 5.8, 1.8 Hz, 2H, $CH_2=CHC\underline{H}_2Ar$), 4.84 (ddd, *J* = 17.0, 3.3, 1.8 Hz, 1H, $C\underline{H}_2=CHCH_2Ar$), 4.93 (ddd, *J* = 10.3, 3.3, 1.8 Hz, 1H, $C\underline{H}_2=CHCH_2Ar$), 5.94 (dtd, *J* = 17.0, 10.3, 5.8 Hz, 1H, $CH_2=C\underline{H}CH_2Ar$), 6.85 (d, *J* = 8.6 Hz, 1H, $Ar\underline{H}$), 7.54 (d, *J* = 8.6 Hz, 1H, $Ar\underline{H}$), 9.95 (s, 1H, $C\underline{H}O$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 28.41 ($CH_2=CH\underline{C}H_2Ar$), 55.50, 60.60 (each, $O\underline{C}H_3$), 109.64, 115.24, 127.62, 128.88, 135.72, 136.91, 146.98, 157.22, 190.59 ($\underline{C}HO$); EI-MS (70 eV) *m/z* (rel. intensity, %) 206 (M^+, 58), 191 (100), 175 (39), 174 (19), 163 (22), 147 (23), 131 (28), 103 (33), 91 (33); HRMS calcd for $C_{12}H_{14}O_3$: 206.0943. Found: 206.0935.

2-Allyl-3-ethoxy-4-methoxybenzaldehyde (3b)[7]

Pure **3b** (1.76 g, 80%) was obtained as pale yellow liquid; R_f 0.55 (ethyl acetate/*n*-hexane=1/3); ^{1}H-

NMR ($CDCl_3$, 200 MHz) δ 1.36 (t, *J* = 7.0 Hz, 3H, $OCH_2C\underline{H}_3$), 3.84 (dt, *J* = 5.8, 1.8 Hz, 2H, $CH_2{=}CHC\underline{H}_2Ar$), 3.89 (s, 3H, $OC\underline{H}_3$), 3.96 (q, *J* = 7.0 Hz, 2H, $OC\underline{H}_2CH_3$), 4.88 (ddd, *J* = 17.0, 3.3, 1.8 Hz, 1H, $C\underline{H}_2{=}CHCH_2Ar$), 4.98 (ddd, *J* = 10.3, 3.3, 1.8 Hz, 1H, $C\underline{H}_2{=}CHCH_2Ar$), 5.99 (dtd, *J* = 17.0, 10.3, 5.8 Hz, 1H, $CH_2{=}C\underline{H}CH_2Ar$), 6.88 (d, *J* = 8.5 Hz, 1H, $Ar\underline{H}$), 7.57 (d, *J* = 8.5 Hz, 1H, $Ar\underline{H}$), 10.02 (s, 1H, $C\underline{H}O$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 16.09 ($OCH_2\underline{C}H_3$), 29.33 ($CH_2{=}CH\underline{C}H_2Ar$), 56.27 ($O\underline{C}H_3$), 110.26, 115.98, 128.43, 129.34, 136.69, 137.68, 146.96, 158.11, 191.47($\underline{C}HO$); EI-MS (70 eV) *m/z* (rel. intensity, %) 220 (M^+, 68), 205 (100), 192 (32), 191 (38), 177 (99), 164 (31), 159 (38), 143 (35), 135 (46), 131 (57), 103 (73), 91 (53); HRMS calcd for $C_{13}H_{16}O_3$: 220.1099. Found: 220.1104.

2-Allyl-3-benzyloxy-4-methoxybenzaldehyde (**3c**)[7, 19]

Pure **3c** (2.76 g, 98%) was obtained as pale yellow liquid, R_f 0.56 (ethyl acetate/*n*-hexane=1/3); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.88 (dt, *J* = 5.8, 1.8 Hz, 2H, $CH_2{=}CHC\underline{H}_2Ar$), 3.92 (s, 3H, $OC\underline{H}_3$), 4.91 (ddd, *J* = 17.0, 3.3, 1.8 Hz, 1H, $C\underline{H}_2{=}CHCH_2Ar$), 4.99 (s, 2H, $OC\underline{H}_2C_6H_5$), 5.02 (ddd, *J* = 10.3, 3.3, 1.8 Hz, 1H, $C\underline{H}_2{=}CHCH_2Ar$), 6.01 (dtd, *J* = 17.0, 10.3, 5.8 Hz, 1H, $CH_2{=}C\underline{H}CH_2Ar$), 6.94 (d, *J* = 8.5 Hz, 1H, $Ar\underline{H}$), 7.34 (d, *J* = 7.5 Hz, 2H, $OCH_2C_6\underline{H}_5$), 7.42 (d, *J* = 7.5 Hz, 2H, $OCH_2C_6\underline{H}_5$), 7.48 (d, *J* = 7.5 Hz, 1H, $OCH_2C_6\underline{H}_5$), 7.67 (d, *J* = 8.5 Hz, 1H, $Ar\underline{H}$), 10.06 (s, 1H, $C\underline{H}O$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 29.41 ($CH_2{=}CH\underline{C}H_2Ar$), 56.37 ($O\underline{C}H_3$), 75.41 ($O\underline{C}H_2C_6H_5$), 110.49, 116.21, 128.57, 128.72, 128.85, 128.96, 129.69, 136.90, 137.71, 137.96, 146.59, 158.12, 191.42 ($\underline{C}HO$); EI-MS (70 eV) *m/z* (rel. intensity, %) 282 (M^+, 0.3), 192 (2), 191 (20), 177 (9), 163 (2), 159 (2), 135 (3), 131 (3), 105 (3), 103 (5), 92 (10), 91 (100); HRMS calcd for $C_{18}H_{18}O_3$: 282.1256. Found: 282.1259.

General procedure for the preparation of 4a-e from 3a-e *via* Baeyer-Villiger oxidation[11]

Compound (**3a-e**) (15 mmol) dissolved in methanol (45 mL) was added with 35% H_2O_2 (3 mL, 35 mmol), and *conc.* H_2SO_4 (3 drops), and stirred at rt by monitoring with TLC until the disappearance of starting material for 1.5 h. The solution was concentrated under *vacuo* to remove methanol. And then the residue was suspended in water (20 mL), and extracted with ethyl acetate (20 mL x 3). The mixture of organic phases was washed with brine (10 mL x 2), and then dried with anhydrous $MgSO_4$. After filtration, the filtrate was concentrated in *vacuo* to give the crude **4a-e**. When subjected to chromatographic column (ethyl acetate/*n*-hexane=1/6), it gave pure **4a-e** in yields of 71-74 %.

2-Allyl-3,4-dimethoxyphenol (**4a**)[20]

Pure **4a** (2.16 g, 74%) was obtained as colorless liquid, R_f =0.57 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.48 (ddd, *J* = 6.0 Hz, 1.6 Hz, 1.6 Hz, 2H, $ArC\underline{H}_2CH{=}CH_2$), 3.80 (s, 3H, $ArOC\underline{H}_3$), 3.81 (s, 3H, $ArOC\underline{H}_3$), 4.89 (br s, 1H, $ArO\underline{H}$), 5.10 (ddt, *J* = 10.6 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.11 (ddt, *J* = 17.6 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 6.01 (ddt, *J* = 17.6 Hz, 10.6 Hz, 6.0 Hz, 1H, $ArCH_2C\underline{H}{=}CH_2$), 6.56, 6.71 (each d, *J* = 8.8 Hz, 1H, $Ar\underline{H}$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 28.33, 56.32, 61.01, 110.56, 111.37, 115.75, 120.29, 136.37, 147.10, 147.80, 148.77; EI-MS (70 eV) *m/z* 194 (M^+, 87), 179 (100), 163 (9), 147 (73), 123 (18), 119 (34), 107 (7), 91 (22), 77 (6), 55 (3); HRMS: Calcd for $C_{11}H_{14}O_3$: 194.0943. Found: 194.0941.

2-Allyl-3-ethoxy-4-methoxyphenol (4b)

Pure **4b** (2.22 g, 71%) was obtained as white solid, R_f =0.60 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($\mathrm{CDCl_3}$, 200 MHz) δ 1.35 (t, *J* = 7.1 Hz, 3H, $\mathrm{ArOCH_2C\underline{H}_3}$), 3.49 (ddd, *J* = 6.0 Hz, 1.6 Hz, 1.6 Hz, 2H, $\mathrm{ArC\underline{H}_2CH{=}CH_2}$), 3.79 (s, 3H, $\mathrm{ArOC\underline{H}_3}$), 4.00 (q, *J* = 7.1 Hz, 2H, $\mathrm{ArOC\underline{H}_2CH_3}$), 4.91 (br s, 1H, $\mathrm{ArO\underline{H}}$), 5.10 (ddt, *J* = 10.6 Hz, 1.6 Hz, 1.6 Hz, 1H, $\mathrm{ArCH_2CH{=}C\underline{H}_2}$), 5.11 (ddt, *J* = 17.6 Hz, 1.6 Hz, 1.6 Hz, 1H, $\mathrm{ArCH_2CH{=}C\underline{H}_2}$), 6.00 (ddt, *J* = 17.6 Hz, 10.6 Hz, 6.0 Hz, 1H, $\mathrm{ArCH_2C\underline{H}{=}CH_2}$), 6.54 (d, *J* = 8.8 Hz, 1H, $\mathrm{Ar\underline{H}}$), 6.7 (d, *J* = 8.8 Hz, 1H, $\mathrm{Ar\underline{H}}$); ^{13}C-NMR ($\mathrm{CDCl_3}$, 50 MHz) δ 15.62, 28.57, 56.37, 69.10, 110.42, 111.39, 115.74, 120.42, 136.40, 146.95, 147.19, 148.82; EI-MS (70eV) *m/z* 208 (M^+, 100), 193 (28), 165 (85), 147 (23), 137 (67), 119 (33), 109 (16), 91 (13), 77 (4), 53 (3); HRMS: Calcd for $C_{12}H_{16}O_3$: 208.1099. Found: 208.1098; Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 79.51; H, 7.56.

2-Allyl-3-benzyloxy-4-methoxyphenol (4c)

Pure **4c** (3.04 g, 75%) was obtained as colorless liquid, R_f =0.45 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($\mathrm{CDCl_3}$, 400 MHz) δ 3.43 (ddd, *J* = 6.0 Hz, 1.6 Hz, 1.6 Hz, 2H, $\mathrm{ArC\underline{H}_2CH{=}CH_2}$), 3.83 (s, 3H, $\mathrm{ArOC\underline{H}_3}$), 4.89 (s, 1H, $\mathrm{ArO\underline{H}}$), 4.99 (s, 2H, $\mathrm{ArOC\underline{H}_2C_6H_5}$), 5.07 (ddt, *J* = 10.6 Hz, 1.6 Hz, 1.6 Hz, 1H, $\mathrm{ArCH_2CH{=}C\underline{H}_2}$), 5.08 (ddt, *J* = 17.6 Hz, 1.6 Hz, 1.6 Hz, 1H, $\mathrm{ArCH_2CH{=}C\underline{H}_2}$), 5.87 (ddt, *J* = 17.6 Hz, 10.6 Hz, 6.0 Hz, 1H, $\mathrm{ArCH_2C\underline{H}{=}CH_2}$), 6.57, 6.74 (each d, *J* = 8.8 Hz, 1H, $\mathrm{Ar\underline{H}}$), 7.29 (d, *J* = 7.8 Hz, 1H, $\mathrm{ArCH_2C_6\underline{H}_5}$), 7.36 (t, *J* = 7.8 Hz, 2H, $\mathrm{ArCH_2C_6\underline{H}_5}$), 7.48 (d, *J* = 7.8 Hz, 2H, $\mathrm{ArCH_2C_6\underline{H}_5}$); ^{13}C-NMR ($\mathrm{CDCl_3}$, 100 MHz) δ 26.62, 56.46, 75.03, 110.77, 111.58, 115.90, 120.47, 127.89, 128.24, 128.34, 136.32, 137.69, 146.48, 147.17, 148.87; EI-MS (70 eV) *m/z* 270 (M^+, 16), 179 (25), 147 (16), 119 (8), 91 (100); HRMS (EI, *m/z*): Calcd for $C_{17}H_{18}O_3$: 270.1256. Found: 270.1254; Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.88; H, 6.56.

General procedure for the preparation of 5a-g from 4a-c, and 2b-e *via o*-allylation

The corresponding phenols (**4a-e**) or (**2b-e**) (10 mmol) were respectively reacted with allyl bromide (10.5 mmol) to give **5a-g** as the same process described for the preparation of **1a-e**.

2-Allyl-1-allyloxy-3,4-dimethoxybenzene (5a)

Pure **5a** (1.94 g, 83%) was obtained as colorless liquid, R_f =0.76 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($\mathrm{CDCl_3}$, 400 MHz) δ 3.46 (ddd, *J* = 6.2 Hz, 1.6 Hz, 1.6 Hz, 2H, $\mathrm{ArC\underline{H}_2CH{=}CH_2}$), 3.80 (s, 3H, $\mathrm{ArOC\underline{H}_3}$), 3.81 (s, 3H, $\mathrm{ArOC\underline{H}_3}$), 4.47 (ddd, *J* = 5.6 Hz, 1.6, Hz 1.6 Hz, 2H, $\mathrm{ArOC\underline{H}_2CH{=}CH_2}$), 4.95 (ddt, *J* = 10.5 Hz, 1.6 Hz, 1.6 Hz, 1H, $\mathrm{ArCH_2CH{=}C\underline{H}_2}$), 5.02 (ddt, *J* = 16.6 Hz, 1.6 Hz, 1.6 Hz, 1H, $\mathrm{ArCH_2CH{=}C\underline{H}_2}$), 5.23 (ddt, *J* = 10.4 Hz, 1.6 Hz, 1.6 Hz, 1H, $\mathrm{ArOCH_2CH{=}C\underline{H}_2}$), 5.40 (ddt, *J* = 16.9 Hz, 1.6 Hz, 1.6 Hz, 1H, $\mathrm{ArOCH_2CH{=}C\underline{H}_2}$), 5.98 (ddt, *J* = 16.6 Hz, 10.5 Hz, 6.2 Hz, 1H, $\mathrm{ArCH_2C\underline{H}{=}CH_2}$), 6.03 (ddt, *J* = 16.9 Hz, 10.4 Hz, 5.6 Hz, 1H, $\mathrm{ArOCH_2C\underline{H}{=}CH_2}$), 6.55, 6.70 (each d, *J* = 8.8 Hz, 1H, $\mathrm{Ar\underline{H}}$); ^{13}C-NMR ($\mathrm{CDCl_3}$, 100 MHz) δ 28.27, 56.08, 60.77, 69.41, 107.04, 110.14, 114.45, 116.57, 123.53, 133.67, 137.05, 147.29, 147.98, 151.07; EI-MS (70 eV) *m/z* 234 (M^+, 80), 219 (8), 193 (100), 178 (68), 162 (37), 150 (18), 135 (16), 107 (9), 105 (15), 79 (6); HRMS (EI, *m/z*) : 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, 72.04; H, 7.58.

2-Allyl-1-allyloxy-3-ethoxy-4-methoxybenzene (**5b**)

Pure **5b** (2.04 g, 82%) was obtained as colorless liquid, R_f =0.74 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 1.37 (t, *J* = 7.1 Hz, 3H, ArOCH$_2$C$\underline{H}_3$), 3.47 (ddd, *J* = 6.2 Hz, 1.6 Hz, 1.6 Hz, 2H, ArC$\underline{H}_2$CH=CH$_2$), 3.79 (s, 3H, ArOC$\underline{H}_3$), 4.01 (q, *J* = 7.1 Hz, 2H, ArOC$\underline{H}_2$CH$_3$), 4.46 (ddd, *J* = 5.6 Hz, 1.6, Hz 1.6 Hz, 2H, ArOC$\underline{H}_2$CH=CH$_2$), 4.94 (ddt, *J* = 10.5 Hz, 1.6 Hz, 1.6 Hz, 1H, ArCH$_2$CH=C$\underline{H}_2$), 5.01 (ddt, *J* = 16.6 Hz, 1.6 Hz, 1.6 Hz, 1H, ArCH$_2$CH=C$\underline{H}_2$), 5.23 (ddt, *J* = 10.4 Hz, 1.6 Hz, 1.6 Hz, 1H, ArOCH$_2$CH=C$\underline{H}_2$), 5.40 (ddt, *J* = 16.9 Hz, 1.6 Hz, 1.6 Hz, 1H, ArOCH$_2$CH=C$\underline{H}_2$), 5.99 (ddt, *J* = 16.6 Hz, 10.5 Hz, 6.2 Hz, 1H, ArCH$_2$C$\underline{H}$=CH$_2$), 6.03 (ddt, *J* = 16.9 Hz, 10.4 Hz, 5.6 Hz, 1H, ArOCH$_2$C$\underline{H}$=CH$_2$), 6.53, 6.69 (each d, *J* = 8.8 Hz, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 15.64, 28.51, 56.16, 68.80, 69.41, 106.84, 110.12, 114.32, 116.56, 123.68, 133.73, 137.10, 147.21, 147.45, 151.15; EI-MS (70 eV) *m/z* 248 (M^+, 100), 207 (63), 192 (68), 178 (54), 163 (22), 147 (81), 119 (41), 91 (28), 79 (10); HRMS: Calcd for $C_{15}H_{20}O_3$: 248.1412. Found: 248.1415; Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.90; H, 8.48.

2-Allyl-1-allyloxy-3-benzyloxy-4-methoxybenzene (**5c**)

Pure **5c** (2.64 g, 85%) was obtained as colorless liquid, R_f =0.75 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.46 (ddd, *J* = 6.2 Hz, 1.6 Hz, 1.6 Hz, 2H, ArC$\underline{H}_2$CH=CH$_2$), 3.81 (s, 3H, ArOC$\underline{H}_3$), 4.46 (ddd, *J* = 5.6 Hz, 1.6, Hz 1.6 Hz, 2H, ArOC$\underline{H}_2$CH=CH$_2$), 4.93 (ddt, *J* = 10.5 Hz, 1.6 Hz, 1.6 Hz, 1H, ArCH$_2$CH=C$\underline{H}_2$), 4.94 (ddt, *J* = 16.6 Hz, 1.6 Hz, 1.6 Hz, 1H, ArCH$_2$CH=C$\underline{H}_2$), 4.99 (s, 2H, ArOC$\underline{H}_2$C$_6$H$_5$), 5.23 (ddt, *J* = 10.4 Hz, 1.6 Hz, 1.6 Hz, 1H, ArOCH$_2$CH=C$\underline{H}_2$), 5.39 (ddt, *J* = 16.9 Hz, 1.6 Hz, 1.6 Hz, 1H, ArOCH$_2$CH=C$\underline{H}_2$), 5.95 (ddt, *J* = 16.6 Hz, 10.5 Hz, 6.2 Hz, 1H, ArCH$_2$C$\underline{H}$=CH$_2$), 6.02 (ddt, *J* = 16.9 Hz, 10.4 Hz, 5.6 Hz, 1H, ArOCH$_2$C$\underline{H}$=CH$_2$), 6.57, 6.73 (each d, *J* = 8.8 Hz, 1H, Ar$\underline{H}$), 7.30 (d, *J* = 7.8 Hz, 1H, ArCH$_2$C$_6\underline{H}_5$), 7.36 (t, *J* = 7.8 Hz, 2H, ArCH$_2$C$_6\underline{H}_5$), 7.48 (d, *J* = 7.8 Hz, 2H, ArCH$_2$C$_6\underline{H}_5$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 28.49, 56.23, 69.43, 74.69, 107.21, 110.27, 114.52, 116.62, 123.82, 127.71, 127.92, 128.27, 133.68, 137.02, 137.99, 146.87, 147.43, 151.16; EI-MS (70eV) *m/z* 310 (M^+, 46), 269 (6), 219 (93), 191 (14), 178 (29), 131 (11), 105 (10), 91 (100), 65 (8); HRMS (EI, *m/z*): Calcd for $C_{20}H_{22}O_3$: 310.1569. Found: 310.1567; Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.55; H, 7.40.

3-Allyl-4-allyloxytoluene (**5d**)

Pure **5d** (1.62 g, 86%) was obtained as colorless liquid, R_f =0.91 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.25 (s, 3H, ArC$\underline{H}_3$), 3.38 (ddt, *J* = 6.4 Hz, 2.0 Hz, 2.0 Hz, 2H, ArC$\underline{H}_2$CH=CH$_2$), 4.49 (ddt, *J* = 6.8 Hz, 1.6 Hz, 1.6 Hz, 2H, ArOC$\underline{H}_2$CH=CH$_2$), 5.02 (ddt, *J* = 10.4 Hz, 2.0 Hz, 2.0 Hz, 1H, ArCH$_2$CH=C$\underline{H}_2$), 5.06 (ddt, *J* = 16.6 Hz, 2.0 Hz, 2.0 Hz, 1H, ArCH$_2$CH=C$\underline{H}_2$), 5.23 (ddt, *J* = 10.4 Hz, 1.6 Hz, 1.6 Hz, 1H, ArOCH$_2$CH=C$\underline{H}_2$), 5.40 (ddt, *J* = 17.2 Hz, 1.6 Hz, 1.6 Hz, 1H, ArOCH$_2$CH=C$\underline{H}_2$), 5.99 (ddt, *J* = 16.6 Hz, 10.4 Hz, 6.4 Hz, 1H, ArCH$_2$C$\underline{H}$=CH$_2$), 6.03 (ddt, *J* = 17.2 Hz, 10.4 Hz, 6.8 Hz, 1H, ArOCH$_2$C$\underline{H}$=CH$_2$), 6.71, 6.94 (each d, *J* = 7.0 Hz, 1H, Ar$\underline{H}$), 6.95 (s, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 20.53, 34.49, 69.02, 111.85, 115.31, 116.77, 127.49, 128.81, 129.95, 130.65, 133.81, 137.22, 154.21; EI-MS, (70 eV) *m/z* 188 (M^+, 63), 147 (85), 132 (27), 119 (100), 91 (84), 77 (22),; HRMS (EI, *m/z*): Calcd for $C_{13}H_{16}O$: 188.1201. Found: 188.1202; Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.23; H, 8.89.

2-Allyl-1-allyloxy-4-chlorobenzene (**5e**)

Pure **5e** (1.82 g, 87%) was obtained as colorless liquid, R_f =0.90 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.42 (ddt, *J* = 6.4 Hz, 2.0 Hz, 2.0 Hz, 2H, $ArC\underline{H}_2CH{=}CH_2$), 4.55 (ddt, *J* = 6.8 Hz, 1.6 Hz, 1.6 Hz, 2H, $ArOC\underline{H}_2CH{=}CH_2$), 5.12 (ddt, *J* = 10.4 Hz, 2.0 Hz, 2.0 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.13 (ddt, *J* = 16.6 Hz, 2.0 Hz, 2.0 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.31 (ddt, *J* = 10.4 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 5.45 (ddt, *J* = 17.2 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 5.99 (ddt, *J* = 16.6 Hz, 10.4 Hz, 6.4 Hz, 1H, $ArCH_2C\underline{H}{=}CH_2$), 6.07 (ddt, *J* = 17.2 Hz, 10.4 Hz, 6.8 Hz, 1H, $ArOCH_2C\underline{H}{=}CH_2$), 6.78, 7.13 (each d, *J* = 7.0 Hz, 1H, Ar$\underline{H}$), 7.17 (s, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 34.10, 69.01, 112.73, 116.15, 117.18, 125.46, 126.78, 129.62, 130.83, 133.07, 135.99, 154.78; EI-MS (70 eV) *m/z* 210 (M^{+2}, 11), 208 (M^+, 33), 167 (50), 132 (51), 115 (15), 103 (100), 89 (12), 77 (55), 51 (24); HRMS: Calcd for $C_{12}H_{13}OCl$: 208.0655. Found: 208.0655; Anal. Calcd for $C_{12}H_{13}OCl$: C, 69.07; H, 6.28. Found: C, 69.36; H, 6.50.

1-Allyl-2-allyloxy-3-nitrobenzene (**5f**)

Pure **5f** (1.86 g, 85%) was obtained as yellow liquid, R_f =0.71 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.49 (ddt, *J* = 6.4 Hz, 2.0 Hz, 2.0 Hz, 2H, $ArC\underline{H}_2CH{=}CH_2$), 4.49 (ddt, *J* = 6.8 Hz, 1.6 Hz, 1.6 Hz, 2H, $ArOC\underline{H}_2CH{=}CH_2$), 5.09 (ddt, *J* = 10.4 Hz, 2.0 Hz, 2.0 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.13 (ddt, *J* = 16.6 Hz, 2.0 Hz, 2.0 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.27 (ddt, *J* = 10.4 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 5.39 (ddt, *J* = 17.2 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 5.97 (ddt, *J* = 16.6 Hz, 10.4 Hz, 6.4 Hz, 1H, $ArCH_2C\underline{H}{=}CH_2$), 6.07 (ddt, *J* = 17.2 Hz, 10.4 Hz, 6.8 Hz, 1H, $ArOCH_2C\underline{H}{=}CH_2$), 7.16 (t, *J* = 8.0 Hz, 1H, Ar$\underline{H}$), 7.44 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H, Ar$\underline{H}$), 7.67 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 33.61, 75.94, 116.97, 118.60, 123.28, 123.93, 132.72, 134.94, 135.70, 136.58, 144.48, 149.99; EI-MS (70 eV) *m/z* 219(M^+, 94), 202 (64), 172 (74), 129 (77), 128 (100), 77 (42), 65 (20); HRMS (EI, *m/z*) : Calcd for $C_{12}H_{13}NO_3$: 219.0895. Found: 219.0897; Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98. Found: C, 65.95; H, 6.31.

2-Allyl-1-allyloxy-3-methoxybenzene (**5g**)

Pure **5g** (1.80 g, 88%) was obtained as colorless liquid, R_f =0.68 (ethyl acetate/*n*-hexane=1/12), ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 3.45 (ddt, *J* = 6.4 Hz, 2.0 Hz, 2.0 Hz, 2H, $ArC\underline{H}_2CH{=}CH_2$), 3.80 (s, 3H, $OC\underline{H}_3$), 4.53 (ddt, *J* = 6.8 Hz, 1.6 Hz, 1.6 Hz, 2H, $ArOC\underline{H}_2CH{=}CH_2$), 4.92 (ddt, *J* = 10.4 Hz, 2.0 Hz, 2.0 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 4.99 (ddt, *J* = 16.6 Hz, 2.0 Hz, 2.0 Hz, 1H, $ArCH_2CH{=}C\underline{H}_2$), 5.24 (ddt, *J* = 10.4 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 5.41 (ddt, *J* = 17.2 Hz, 1.6 Hz, 1.6 Hz, 1H, $ArOCH_2CH{=}C\underline{H}_2$), 5.96 (ddt, *J* = 16.6 Hz, 10.4 Hz, 6.4 Hz, 1H, $ArCH_2C\underline{H}{=}CH_2$), 6.07 (ddt, *J* = 17.2 Hz, 10.4 Hz, 6.8 Hz, 1H, $ArOCH_2C\underline{H}{=}CH_2$), 6.53 (d, *J* = 8.3 Hz, 1H, Ar$\underline{H}$), 6.54 (d, *J* = 8.3 Hz, 1H, Ar$\underline{H}$), 7.11 (t, *J* = 8.3 Hz, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 27.37, 55.78, 69.08, 103.97, 105.18, 114.04, 116.67, 117.03, 126.99, 133.63, 136.87, 157.18, 158.29; EI-MS (70 eV) *m/z* 204 (M^+, 74), 189 (13), 161 (40), 147 (41), 131 (26), 115 (16.26, 105 (46), 91 (45), 77 (31), 51 (8); HRMS (EI, *m/z*): Calcd for $C_{13}H_{16}O_2$: 204.1150. Found: 204.1149; Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.80; H, 8.03.

General procedure for the preparation of substituted 2,5-dihydrobenzo[*b*]oxepine (6a-g)

Compound (**5a-g)** (1 mmol) dissolved in anhydrous CH_2Cl_2 (20 mL), was added with Grubbs catalyst (5mol %). The mixture was stirred for 12 h at ambient temperature under dry argon. Finally dichloromethane was removed under reduced pressure, and the residue was subjected to a silica gel column (3/1: hexane/MTBE) or to distill under vacuum to give **6a-g**, respectively.

6,7-Dimethoxy-2,5-dihydrobenzo[*b*]oxepine (**6a**)

Pure **6a** (0.2 g, 85%) was obtained as colorless liquid, R_f =0.64 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 3.55 (dd, *J* = 5.3 Hz, 2.0 Hz, 2H, $ArC\underline{H}_2CH{=}CH$), 3.77 (s, 3H, $ArOC\underline{H}_3$), 3.83 (s, 3H, $ArOC\underline{H}_3$), 4.54 (dd, *J* = 8.1 Hz, 2.4 Hz, 2H, $ArOC\underline{H}_2CH{=}CH_2$), 5.44 (dtt, *J* = 14.4 Hz, 5.3 Hz, 2.4 Hz, 1H, $ArCH_2C\underline{H}{=}CH$), 5.84 (dtt, *J* = 14.4 Hz, 8.1 Hz, 2.0 Hz, 1H, $ArOCH_2C\underline{H}{=}CH$), 6.69, 6.80 (each d, *J* = 8.8 Hz, 1H, $Ar\underline{H}$); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 22.98, 56.01, 61.99, 71.82, 109.93, 116.24, 125.56, 127.81, 130.89, 145.73, 149.59, 152.96; EI-MS (70eV) *m/z* 206 (M^+, 75), 191 (100), 175 (34), 159 (18), 131 (22), 115 (12), 103 (21), 91 (13), 77 (4), 55 (2); HRMS (EI, *m/z*): Calcd for $C_{12}H_{14}O_3$: 206.0943. Found: 206.0940; Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 70.14; H, 7.06.

6-Ethoxy-7-methoxy-2,5-dihydrobenzo[*b*]oxepine (**6b**)

Pure **6b** (2.21 g, 82%) was obtained as colorless liquid, R_f =0.71 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.36 (t, *J* = 7.2 Hz, 3H, $ArOCH_2C\underline{H}_3$), 3.55 (dd, *J* = 5.3 Hz, 2.0 Hz, 2H, $ArC\underline{H}_2CH{=}CH$), 3.81 (s, 3H, $ArOC\underline{H}_3$), 3.97 (q, *J* = 7.2 Hz, 2H, $ArC\underline{H}_2CH_3$), 4.54 (dd, *J* = 8.1 Hz, 2.4 Hz, 2H, $ArOC\underline{H}_2CH{=}CH$), 5.43 (dtt, *J* = 14.4 Hz, 5.3 Hz, 2.4Hz, 1H, $ArCH_2C\underline{H}{=}CH$), 5.83 (dtt, *J* = 14.4 Hz, 8.1 Hz, 2.0 Hz, 1H, $ArOCH_2C\underline{H}{=}CH$), 6.68, 6.78 (each d, *J* = 8.8 Hz, 1H, $Ar\underline{H}$); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 15.53, 23.26, 56.05, 69.12, 71.82, 109.93, 116.02, 125.64, 127.74, 131.30, 144.74, 149.72, 152.91; EI-MS (70 eV) *m/z* 220 (M^+, 100), 205 (96), 191 (20), 177 (84), 159 (17), 131 (15), 115 (8), 103 (18), 77 (11), 65 (5); HRMS: Calcd for $C_{13}H_{16}O_3$: 220.1099. Found: 220.1098; Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.22; H, 7.58.

6-Benzyloxy-7-methoxy-2,5-dihydrobenzo[*b*]oxepine (**6c**)

Pure **6c** (2.28 g, 88%) was obtained as colorless liquid, R_f =0.72 (ethyl acetate/*n*-hexane=1/3); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.45 (dd, *J* = 5.3 Hz, 2.0 Hz, 2H, $ArC\underline{H}_2CH{=}CH$), 3.83 (s, 3H, $ArOC\underline{H}_3$), 4.52 (dd, *J* = 8.1 Hz, 2.4 Hz, 2H, $ArOC\underline{H}_2CH{=}CH$), 4.94 (s, 2H, $ArC\underline{H}_2C_6H_5$), 5.36 (dtt, *J* = 14.4 Hz, 5.3 Hz, 2.4 Hz, 1H, $ArCH_2C\underline{H}{=}CH$), 5.68 (dtt, *J* = 14.4 Hz, 8.1 Hz, 2.0 Hz, 1H, $ArOCH_2C\underline{H}{=}CH$), 6.72, 6.80 (each d, *J* = 8.8 Hz, 1H, $Ar\underline{H}$), 7.32 (tt, *J* = 6.8 Hz, 2.0 Hz, 2H, $ArCH_2C_6\underline{H}_5$), 7.36 (tt, *J* = 6.8 Hz, 2.0 Hz, 2H, $ArCH_2C_6\underline{H}_5$), 7.42 (d, *J* = 8.0 Hz, 1H, $ArCH_2C_6\underline{H}_5$); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 23.24, 56.11, 71.77, 75.23, 110.09, 116.28, 125.60, 127.51, 127.95, 128.34, 128.37, 131.30, 137.54, 144.49, 149.63, 152.94; EI-MS (70 eV) *m/z* 282 (M^+, 36), 192 (4), 191 (33), 159 (20), 131 (7), 103 (9), 91 (100), 65 (11); HRMS:

Calcd for $C_{18}H_{18}O_3$: 282.1256. Found: 282.1259; Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 72.04; H, 7.58.

7-Methyl-2,5-dihydrobenzo[*b*]oxepine (**6d**)

Pure **6d** (0.15 g, 80%) was obtained as colorless liquid, R_f =0.83 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.27 (s, 3H, ArC$\underline{H}_3$), 3.43 (ddt, *J* = 4.8 Hz, 1.6 Hz, 1.6 Hz, 2H, ArC$\underline{H}_2$CH=CH), 4.54 (ddt, *J* = 5.0 Hz, 1.6 Hz, 1.6 Hz, 2H, ArOC$\underline{H}_2$CH=CH), 5.44 (ddt, *J* = 11.6 Hz, 4.8 Hz, 1.6 Hz, 1H, ArCH$_2$C$\underline{H}$=CH), 5.83 (ddt, *J* = 11.6 Hz, 5.0 Hz, 1.6 Hz, 1H, ArOCH$_2$C$\underline{H}$=CH), 6.89 (d, *J* = 8.4 Hz, 1H, Ar$\underline{H}$), 6.94 (s, 1H, Ar$\underline{H}$), 6.96 (d, *J* = 8.4 Hz, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 20.65, 31.73, 71.25, 121.08, 125.73, 127.40, 128.15, 129.42, 133.35, 135.75, 156.50; EI-MS (70 eV) *m/z* 160 (M^+, 76), 146 (11), 145 (100), 131 (19), 127 (31), 115 (35), 105 (8), 91 (23), 77 (12); HRMS: Calcd for $C_{11}H_{12}O$: 160.0888. Found: 160.0891; Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.80; H, 7.38.

7-Chloro-2,5-dihydrobenzo[*b*]oxepine (**6e**)

Pure **6e** (0.17 g, 83%) was obtained as colorless liquid, R_f =0.79 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.44 (ddt, *J* = 4.8 Hz, 1.6 Hz, 1.6 Hz, 2H, ArC$\underline{H}_2$CH=CH), 4.56 (ddt, *J* = 5.0 Hz, 1.6 Hz, 1.6 Hz, 2H, ArOC$\underline{H}_2$CH=CH), 5.47 (ddt, *J* = 11.6 Hz, 4.8 Hz, 1.6 Hz, 1H, ArCH$_2$C$\underline{H}$=CH), 5.82 (ddt, *J* = 11.6 Hz, 5.0 Hz, 1.6 Hz, 1H, ArOCH$_2$C$\underline{H}$=CH), 6.97 (d, *J* = 8.4 Hz, 1H, Ar$\underline{H}$), 7.08 (s, 1H, Ar$\underline{H}$), 7.13 (d, *J* = 8.4 Hz, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 31.47, 71.25, 122.79, 125.17, 127.42, 127.62, 128.68, 128.83, 137.81, 157.34; EI-MS (70eV) *m/z* 182 (M^{+2}, 21), 180 (M^+, 65), 165 (100), 145 (50), 115 (67), 114 (5), 89 (13), 63 (8); HRMS: Calcd for : $C_{10}H_9OCl$ 180.0342. Found: 180.0345; Anal. Calcd for $C_{10}H_9OCl$: C, 66.49; H, 5.02. Found: C, 66.77; H, 5.26.

9-Nitro-2,5-dihydrobenzo[*b*]oxepine (**6f**)

Pure **6f** (0.18 g, 80%) was obtained as yellow liquid; R_f =0.86 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.54 (ddt, *J* = 4.8 Hz, 1.6 Hz, 1.6 Hz, 2H, ArC$\underline{H}_2$-CH=CH), 4.79 (ddt, *J* = 5.0 Hz, 1.6 Hz, 1.6 Hz, 2H, ArOC$\underline{H}_2$CH=CH), 5.53 (ddt, *J* = 11.6 Hz, 4.8 Hz, 1.6 Hz, 1H, ArCH$_2$C$\underline{H}$=CH), 5.86 (ddt, *J* = 11.6 Hz, 5.0 Hz, 1.6 Hz, 1H, ArOCH$_2$C$\underline{H}$=CH), 7.11 (t, *J* = 8.2Hz, 1H, Ar-$\underline{H}$), 7.33 (d, *J* = 8.2 Hz, 1H, Ar-$\underline{H}$), 7.65 (d, *J* = 8.2 Hz, 1H, Ar-$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 31.38, 71.54, 122.90, 123.88, 124.46, 127.37, 127.49, 132.73, 140.39, 151.09; EI-MS (70 eV) *m/z* 191 (M^+, 33), 174 (57), 144 (100), 135 (11), 115 (93), 91 (13), 89 (16), 63 (11), 51 (11); HRMS: Calcd for $C_{10}H_9NO_3$: 191.0582. Found: 191.0581; Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74. Found: C, 63.02; H, 4.52.

6-Methoxy-2,5-dihydrobenzo[*b*]oxepine (**6g**)

Pure **6g** (0.17 g, 82%) was obtained as colorless liquid, R_f = 0.59 (ethyl acetate/*n*-hexane=1/12); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.55 (ddt, *J* = 4.8 Hz, 1.6 Hz, 1.6 Hz, 2H, ArC$\underline{H}_2$CH=CH$_2$), 3.77 (s, 3H, ArOC$\underline{H}_3$), 4.55 (ddt, *J* = 5.0 Hz, 1.6 Hz, 1.6 Hz, 2H, ArOC$\underline{H}_2$CH=CH), 5.45 (ddt, *J* = 11.6 Hz, 4.8 Hz, 1.6 Hz, 1H, ArCH$_2$C$\underline{H}$=CH), 5.83 (ddt, *J* = 11.6 Hz, 5.0 Hz, 1.6 Hz, 1H, ArOCH$_2$C$\underline{H}$=CH), 6.63 (d, *J* = 8.3 Hz, 1H, Ar$\underline{H}$), 6.70 (d, *J* =8.3 Hz, 1H, Ar$\underline{H}$), 7.10 (t, *J* = 8.3 Hz, 1H, Ar$\underline{H}$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 22.17, 55.70, 71.10, 106.66, 113.98, 124.66, 126.02, 127.22, 127.49, 156.47, 159.87; EI-MS (70 eV) *m/z* 176 (M^+, 96), 161 (100), 146 (27), 144 (19), 127 (79), 115 (35), 105 (16), 91 (17), 77 (83), 65 (15), 63 (14), 51 (32); HRMS: Calcd for $C_{11}H_{12}O_2$: 176.0837. Found: 176.0838; Anal. Calcd for $C_{11}H_{22}O_2$: C, 74.98; H, 6.86. Found: C, 75.21; H, 7.16.

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