

Article

Preparation of Key Intermediates for the Syntheses of Coenzyme Q₁₀ and Derivatives by Cross-Metathesis Reactions

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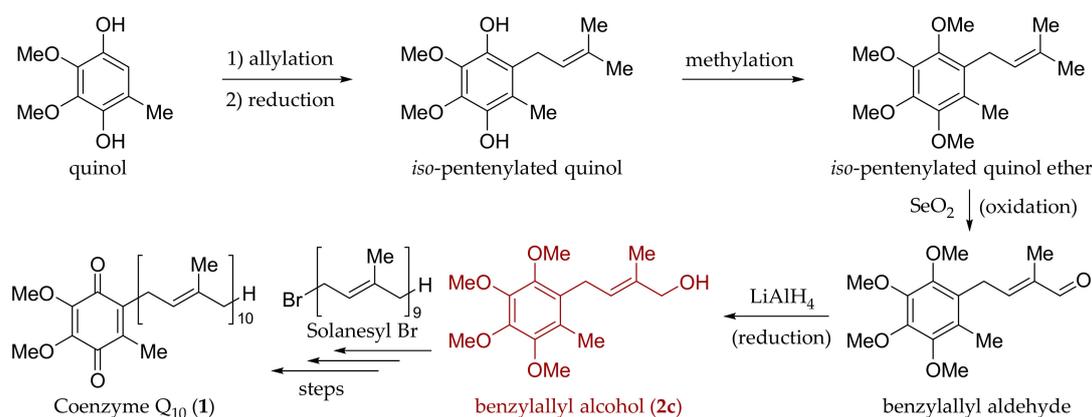
Abstract: An alternative catalytic strategy for the preparation of benzylmethacrylate esters, key intermediates in the synthesis of coenzyme Q₁₀ and derivatives, was reported. This strategy avoided undesirable stoichiometric reduction/oxidation processes by utilizing the catalytic formation of allylarenes and then cross-metathesis to selectively form *E*-benzylmethacrylate esters with good yields (58–64%) and complete *E*-selectivity. The ester intermediates were reduced to common key benzylallylic alcohols (90–92% yield), which were subsequently used in the formal syntheses of coenzyme Q₁₀ and one derivative.

Keywords: coenzyme Q₁₀; solanesol; claisen rearrangement; stille coupling; cross-metathesis.

1. Introduction

Coenzyme Q₁₀ (**1**), an isoprenylated quinone, is a critical electron-transfer compound found in all respiring eukaryotic cells [1–3]. The demand for commercial coenzyme Q₁₀ calls for efficient artificial syntheses of this compound [4–11]. The frame of coenzyme Q₁₀ can be viewed as a combination of terpenyl and aromatic fragments. Therefore, the simplest terpenyl moiety from solanesol, found in tobacco leaves, and the common aromatic moiety benzylallyl alcohol (**2c**) were utilized to build up coenzyme Q₁₀ molecule [11]. In particular, previous studies [11] have utilized a Friedel–Craft allylation of a quinol derivative with 2-methylbut-3-en-2-ol followed by a series of oxidation/reduction reactions to achieve the desired target (**2c**). Alcohol (**2c**) was then used in transformations with the solanesyl bromide obtained from the bromination of solanesol to achieve coenzyme Q₁₀ (Scheme 1). This strategy served as the framework for the synthesis of coenzyme Q₁₀ based on the terpenyl chain from solanesol.

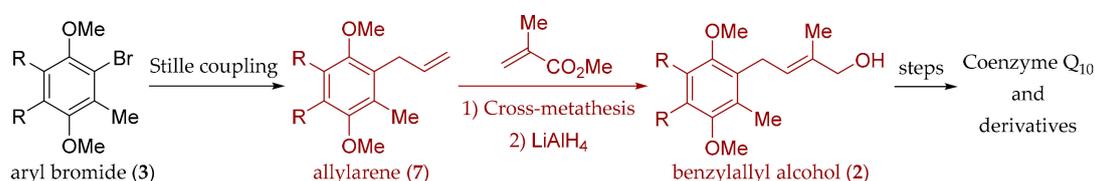
However, the preparation of the *iso*-pentenylated quinol in the reported work unexpectedly required an additional reduction step. Re-examining the transformation, we found that quinone, the oxidized form of the desired *iso*-pentenylated quinol, was in fact the major product in an inseparable mixture of the two compounds. Indeed, upon exposure to air, all the amount of expected quinol was oxidized to its corresponding quinone after 45 min. A similar unexpected oxidation was also observed by the Hecht group [12]. This result led to an undesirable stoichiometric reduction step being added to the synthesis. The *iso*-pentenylated quinol was stoichiometrically oxidized by SeO₂ to aldehyde, not alcohol, and therefore required an extra reduction step to obtain the benzylallyl alcohol (**2c**). The whole procedure to prepare the aromatic moiety was, therefore, accompanied by unenviable stoichiometric oxidation/reduction reactions. With the advantages of known catalytic processes, we anticipated that suitable catalytic transformations such as Claisen rearrangement, Stille coupling, and cross-metathesis could offer additional strategies and allow for catalytic access of coenzyme Q₁₀ and derivatives.



Scheme 1. A previous stoichiometric approach to coenzyme Q₁₀ through benzylallyl alcohol (2c).

Design Plan

We hypothesized that extra reduction/oxidation steps for preparing benzylallyl alcohol (2c) quinol were required because the previous research used readily oxidizable quinol, and unfunctionalized *iso*-pentenyl group. We envisioned that allylarene (7) (Scheme 2) could be prepared from commercially available aryl bromides (3) by Stille coupling. This allylarene could then undergo a cross-metathesis reaction with the methyl methacrylate to offer the desired *E*-cross-metathesis products [13–16], which could be further reduced to the key synthetic intermediate benzyl alcohols (2). This catalytic strategy would allow for alternative access to common key intermediates in the syntheses of coenzyme Q₁₀ and derivatives.



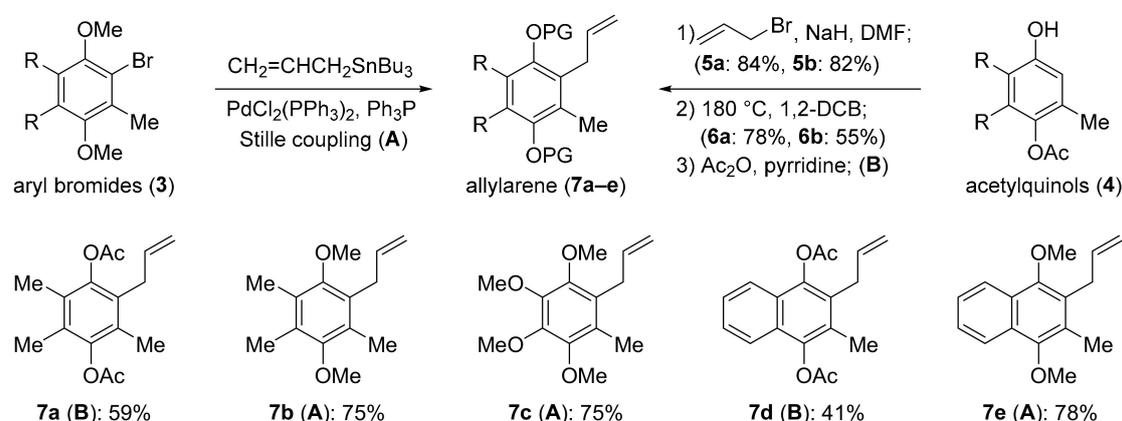
Scheme 2. Our catalytic approach to benzylallyl alcohols (2).

2. Results and Discussion

To examine the proposed idea, five allylated arenes (7a–e) were prepared. These allylarenes were synthesized either from commercially available aryl bromide 3 (path A) [17–19] or monoacetylquinol 4 (path B) [20–24]. (Scheme 3) The Stille coupling of corresponding (MeO)₂ aryl bromides with allyltributylstannane directly afforded allylarenes 7b–c and 7e with high yields (75%–78%). Diacetate allylarenes 7a and 7d were prepared from corresponding quinol derivatives (4). First, quinols 4(a and d) were allylated to provide allyl ethers 5a (84%), and 5b (82%), which then participated in the Claisen rearrangement to furnish allylated quinols 6a (78%) and 6d (55%). Allylated quinols 6a and 6d were then acetylated with Ac₂O to afford 7a (59% overall yield) and 7d (41% overall yield).

Next, the cross-metathesis of allylated arenes with methyl methacrylate was studied. The results are shown in Table 1. Initially, the cross-metathesis reaction of 7a was carried out in neat methyl methacrylate (Table 1, Entry 1). However, only a trace amount of the desired product was obtained. The reaction was then conducted in dichloromethane with a ratio of one equivalent of allylarene 7a and five equivalents of methyl methacrylate. In this case, we mostly obtained the homo-coupling of allylarene (Table 1, Entry 2). Increasing the amount of methyl methacrylate to 20 equivalents, we were able to isolate desired the product 8a with 56% yield and exclusive *E*-configuration based on NOESY NMR spectroscopy analysis. This result was consistent with the previous studies [13–16]. The reaction condition was also applied to allylarenes 7b–e. All cross-metathesis reactions generated desired *E*

isomers with moderate to good yields (**8b–e**, 58–65% yields) providing the key intermediates for the syntheses of coenzyme Q₁₀ and derivatives (**8a–e**).



Scheme 3. Preparation of allylarenes.

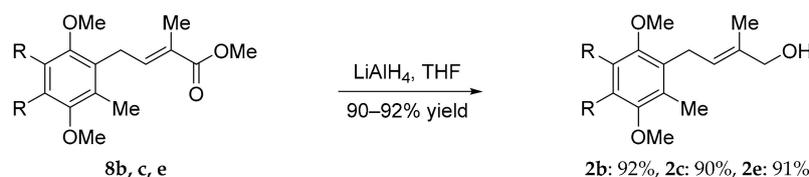
Table 1. Cross-metathesis products.

Table 1 details the cross-metathesis products. Allylarenes (**7a–e**) react with methyl methacrylate in the presence of Grubb's 2nd catalyst (10 mol%) under conditions a, b, or c to yield allyl esters (**8a–e**).

Entries	Allylarene	Allyl Ester	Yields (%)
1			inseparable mixture ^a
2	7a		Dimer ^b
3			56% (all <i>E</i>) ^c
4			7b
5	7c		
6			7d
7	7e		

^a The reaction was conducted using methyl methacrylate as solvent at $50\text{ }^\circ\text{C}$; ^b methyl methacrylate, 5.0 equivalent, CH_2Cl_2 , refluxed; ^c methyl methacrylate, 20 equivalent, dichloromethane, refluxed.

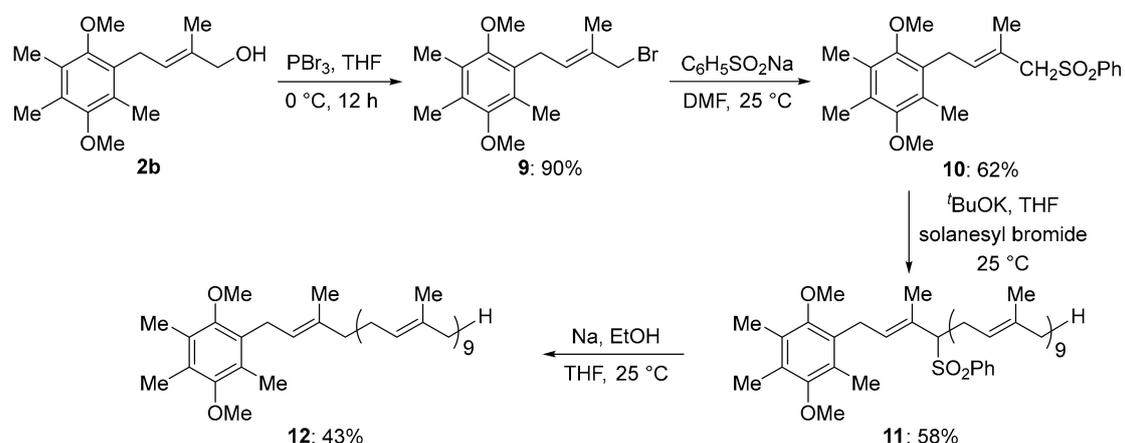
We then reduced esters **8b,c,e** by LiAlH_4 to corresponding alcohols **2b,c,e** with very good yields (90%–92% yield) (Scheme 4). These alcohols could be used in well-established synthetic paths to furnish coenzyme Q₁₀ [25] (from **2c**) and its derivatives.



Scheme 4. Reduction of allylesters.

Synthesis of a Coenzyme Q₁₀'s Derivative

Following a similar procedure for the formal synthesis of coenzyme Q₁₀ [25], we obtained derivative **12** from the corresponding key alcohol (**2b**) (Scheme 5). First, the alcohol (**2b**) was converted into allyl bromide (**9**) (crude yield: 90%). The bromide (**9**, without purifying) was then treated with PhSO₂Na to obtain the phenylsulfinate (**10**: 62%). The sulfinate (**10**) was then subjected to an allylation event with solanesyl bromide in the presence of *t*BuOK to form **11** with a moderate yield (58%). Finally, the de-sulfination of **11** afforded the coenzyme Q₁₀'s derivative (**12**: 43%)

Scheme 5. Synthesis of coenzyme Q₁₀ derivative (**12**).

3. Materials and Methods

3.1. General Information

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego [26]. All solvents were redistilled before using. Reactions under N₂ atmosphere were performed with a Schlenk apparatus or simple dry-box (Laboratory build, Hanoi, Vietnam). Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an ice-water bath for volatile compounds. Chromatographic purification of products was accomplished by flash chromatography on silica gel according to the method of Still [27]. Thin-layer chromatography (TLC) was performed on Merk silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching, *p*-anisaldehyde, ceric ammonium molybdate, or potassium permanganate stains. ¹H and ¹³C NMR spectra were recorded on a Bruker Advance-III 500 (500 and 125 MHz) instrument (Bruker Corp., Billerica, MA, USA) in the Faculty of Chemistry, VNU University of Science, Vietnam National University, Hanoi, Vietnam, and were internally referenced to residual protic solvent signals (note: CDCl₃ referenced at δ 7.27 and 77.0 ppm respectively). ¹³C NMR spectra were recorded in J-MOD (J-modulated spin-echo) mode, which were the combination of ¹³C and DEPT without losing quaternary ¹³C signals. Data for ¹H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, b = broad), integration, coupling constant (Hz), and assignment. Data for ¹³C NMR are reported in terms of chemical shift and multiplicity; no special nomenclature has been used for equivalent carbons. The

IR spectrum (Supplementary Materials) of alcohol **4** was recorded on the Shimadzu FTIR Affinity-1S (Shimadzu Corp., Kyoto, Japan) in the Department of Inorganic Chemistry, Faculty of Chemistry, VNU University of Science, Vietnam National University and has been reported in terms of frequency of absorption. High-resolution mass spectra were obtained via ESI method on Agilent 6530 Accurate-Mass Q-TOP LC/MS (Agilent Technology Inc., Santa Clara, CA, USA) in the Institute of Marine Biochemistry, Vietnam Academy of Science and Technology Hanoi, Vietnam.

3.2. General Procedure for Allylation Reaction

NaH (0.78 g, 32.5 mmol) was slowly added to the solution of phenol (16 mmol) in DMF (60 mL) at 0 °C under an N₂ atmosphere. The reaction mixture was stirred vigorously for 30 min to evaporate the gas in solution. After that, allyl bromide (2.18 mL, 25.2 mmol) was slowly added to the reaction flask and refluxed at 40 °C for 12 h. The mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄, and evaporated under vacuum. The residue was purified via flash column chromatography with silica gel as the stationary phase (0%–2% ethyl acetate/*n*-hexane) to yield the titular allyl aryl ether.

4-(Allyloxy)-2,3,6-trimethylphenyl acetate (5a): clear oil, 84% yield. IR (film) 2976, 2918, 2864, 1759, 1744, 1599, 1584, 1404, 1357, 1211, 1161, 1111, 1084, 937, 895, 839, 768, 745 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.58 (s, 1H), 6.14–6.02 (m, 1H), 5.44 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.28 (dq, *J* = 10.5, 1.5 Hz, 1H), 4.50 (dt, *J* = 5.0, 1.6 Hz, 2H), 2.34 (s, 3H), 2.18 (s, 3H), 2.13 (s, 3H), 2.07 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.5, 154.2, 141.8, 133.8, 129.8, 127.1, 124.3, 116.9, 111.6, 69.4, 20.6, 16.7, 13.1, 12.1; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₄H₁₉O₃) requires *m/z* 235.1334, found *m/z* 235.1329.

4-(allyloxy)-2-methylnaphthalen-1-yl acetate (5d): clear oil, 82% yield. IR (film) 3073, 2918, 2862, 1759, 1744, 1632, 1599, 1506, 1462, 1404, 1356, 1269, 1202, 1159, 1111, 1084, 937, 895, 839, 768, 745 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.26 (d, *J* 8.3 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.52–7.48 (m, 1H), 7.45–7.42 (m, 1H), 6.65 (s, 1H), 6.20–6.14 (m, 1H), 5.53 (dd, *J* = 17.3, 1.5 Hz, 1H), 5.34 (dd, *J* = 6.8, 1 Hz, 1H), 4.70 (d, *J* 5.1 Hz, 2H), 2.46 (s, 3H), 2.30 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.6, 152.3, 137.8, 133.2, 127.9, 127.2, 126.3, 124.9, 122.6, 120.6, 117.6, 107.7, 69.3, 20.7, 16.9; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₆H₁₇O₃) requires *m/z* 257.1178, found *m/z* 257.1172.

3.3. General Procedure for Claisen Rearrangement

A solution of allyl aryl ether (11 mmol) in 1,2-dichlorobenzene (50 mL) was stirred for 24 h at 180 °C under an N₂ atmosphere. The mixture was purified by column chromatography with silica gel as the stationary phase (0%–5% ethyl acetate/*n*-hexane) to yield the titular allylphenol.

3-allyl-4-hydroxy-2,5,6-trimethylphenyl acetate (6a): yellow solid, 78% yield, mp = 119–120 °C. IR 3485, 2924, 1728, 1639, 1574, 1458, 1365, 1300, 1225, 1192, 1070, 993, 905 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.01–5.88 (m, 1H), 5.11–5.02 (m, 2H), 4.79 (s, 1H), 3.41 (dt, *J* = 10.0, 3 Hz, 2H), 2.34 (d, *J* = 0.5 Hz, 2H), 2.15 (s, 5H), 2.05 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 169.8, 150.1, 141.8, 135.5, 127.6, 126.4, 121.7, 121.4, 116.1, 31.5, 20.7, 13.3, 12.8, 12.3; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₄H₁₉O₃) requires *m/z* 235.1334, found *m/z* 235.1329.

3-allyl-4-hydroxy-2-methylnaphthalen-1-yl acetate (6d): light yellow crystal, 55% yield, mp = 117–118 °C. IR 3485, 3441, 3063, 2976, 2924, 1726, 1634, 1595, 1574, 1454, 1389, 1364, 1290, 1233, 1080, 1047, 1015, 982, 914, 768, 737 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.11 (d, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.49–7.43 (m, 2H), 6.07–6.00 (m, 1H), 5.36 (s, 1H), 5.17 (dq, *J* = 10.1, 1.6 Hz, 1H), 5.11 (dq, *J* = 18.9, 1.7 Hz, 1H), 3.59 (dt, *J* = 5.6, 1.7 Hz, 2H), 2.47 (s, 3H), 2.25 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.7, 147.7, 138.4, 135.0, 126.7, 126.5, 126.5, 125.3, 124.0, 121.7, 120.8, 118.2, 116.7, 31.4, 20.8, 13.5; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₆H₁₇O₃) requires *m/z* 257.1178, found *m/z* 257.1172.

3.4. General Procedure for Acetylation

Acetic anhydride (1 mL, 10 mmol) was added to the mixture of allylphenol (5 mmol) and pyridine (10 mL) at 0 °C under an N₂ atmosphere. After that, 4-dimethyl pyridine (0.15 g, 1 mmol) was added as catalyst. The reaction mixture was stirred for 1 h at room temperature. After completion, the mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with water, saturate aqueous CuSO₄ and brine, dried over Na₂SO₄, and evaporated under vacuum. The residue was purified by column chromatography with silica gel as the stationary phase (0%–5% ethyl acetate/*n*-hexane) to yield the titular allyl ester.

2-allyl-3,5,6-trimethyl-1,4-phenylene diacetate (7a): light yellow crystal, 90% yield, mp = 108–109 °C. IR 3458, 3074, 2976, 2927, 1728, 1639, 1573, 1460, 1366, 1225, 1192, 1070, 993, 905, 860, 827, 706, 683 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.81–5.76 (m, 1H), 5.00 (dq, *J* = 10.1, 1.6, 1H), 4.94 (dd, *J* = 17.1, 1H), 3.27 (bd, *J* = 39.5 Hz, 2H), 2.34 (s, 3H), 2.31 (s, 3H), 2.06 (b, 6H, 2CH₃), 2.04 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.1 (b, 2 × C=O), 145.8, 145.6, 134.9, 128.4, 127.9, 127.7, 127.6, 127.4, 115.7, 31.8 (b, 2CH₃CO), 20.5, 13.3, 12.7; HRMS (ESI) exact mass calculated for [M + Na]⁺ (C₁₆H₂₀NaO₄) requires *m/z* 299.1259, found *m/z* 299.1257.

Our above NMR data for prepared compound (7a) were comparable with the NMR data of 2-allyl-1,4-diacetoxy-3,5,6-trimethylbenzen in Reference [28]: ¹H NMR (90 MHz, CDCl₃) δ 5.7–5.9 (m, 1H), 5.0 (d, *J* = 11, 1 H), 4.94 (d, *J* = 18, 1H), 3.28 (br s, 2H), 2.32 and 2.34 (s, 6H), 2.04 and 2.06 (s, 9H); ¹³C NMR δ 168.90, 168.70, 145.97, 145.72, 134.97, 128.47, 127.92, 127.53, 127.36, 115.4, 31.78, 20.42, 20.29, 13.07, 12.47.

2-allyl-3-methylnaphthalene-1,4-diyl diacetate (7d): brown solid, 90% yield, mp = 107–108 °C. IR 3069, 2982, 2928, 2870, 1753, 1639, 1599, 1427, 1354, 1198, 1169, 1092, 1049, 1011, 895, 773, 742 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.72–7.71 (m, 1H), 7.67–7.65 (m, 1H), 7.48–7.46 (m, 2H), 5.91–5.86 (m, 1H), 5.06 (dq, *J* = 10.2, 1.6, 1H), 4.99 (dq, *J* = 17.1, 1.7, 1H), 3.48 (b, 2H), 2.49 (s, 3H), 2.47 (s, 3H), 2.27 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.6 (2 × C=O) 142.9, 142.8, 134.7, 128.4, 127.1, 126.7, 126.6, 126.5, 126.3, 121.6, 121.4, 116.3, 32.1, 20.9, 20.8, 13.2. HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₈H₁₉O₄) requires *m/z* 299.1283, found *m/z* 299.1282.

3.5. General Procedure for Stille Coupling

Bromoaryl (1.0 mmol), (PPh₃)₂PdCl₂ (0.025 mmol) allylSnBu₃ (1.1 mmol), and PPh₃ (0.1 mmol) were dissolved in DMF (10 mL), and then the mixture was heated at 110 °C for 4 h under an N₂ atmosphere. The reaction mixture was diluted with H₂O, extracted five times with Et₂O, and the combined extracts were dried over Na₂SO₄ and evaporated under vacuum. The residue was purified by column chromatography with silica gel as the stationary phase (10%–20% ethyl acetate/*n*-hexane) to yield the titular allylated arene.

1-allyl-2,5-dimethoxy-3,4,6-trimethylbenzene (7b): clear oil, 75% yield. IR (film) 2994, 2936, 2845, 1638, 1558, 1454, 1383, 1223, 1084, 1038, 1002, 937, 837, 758 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.97–5.92 (m, 1H), 5.00 (dq, *J* = 10.0, 1.9 Hz, 1H), 4.90 (dq, *J* = 17.5, 2.0 Hz, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.43 (dt, *J* = 4.0 Hz, 1.7 Hz, 2H), 2.19 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 153.2, 153.0, 136.9, 129.3, 128.9, 128.2, 128.1, 114.9, 61.2, 60.3, 31.4, 12.9, 12.8, 12.0; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₄H₂₁O₂) requires *m/z* 221.1542, found *m/z* 221.1537.

1-allyl-2,3,4,5-tetramethoxy-6-methylbenzene (7c): clear oil, 75% yield. IR (film) 2934, 2829, 1728, 1638, 1464, 1404, 1350, 1292, 1257, 1196, 1105, 1036, 1009, 978, 908, 871, 743 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.93–5.86 (m, 1H), 5.00 (dd, *J* = 10.1, 1.4 Hz, 1H), 4.91 (dd, *J* = 17.1, 1.6 Hz, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.38 (d, *J* = 5.8 Hz, 2H), 2.14 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 147.9 (2 × C-OMe), 145.4, 144.8, 136.7 (–CH=CH₂), 127.0, 125.8, 114.9 (=CH₂), 61.4, 61.3, 61.2, 60.8, 31.0, 11.7; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₄H₂₁O₄) requires *m/z* 253.1440, found *m/z* 253.1436.

2-allyl-1,4-dimethoxy-3-methylnaphthalene (7e): off-white crystal, 78% yield, mp = 83–84 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.09–8.04 (m, 2H), 7.49–7.45 (m, 2H), 6.08–6.00 (m, 1H), 5.05 (dq, *J* = 10.2,

1.8 Hz, 1H), 4.91 (dq, $J = 17.2, 1.9$ Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.64 (dt, $J = 5.5, 1.9$ Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 150.3, 150.2, 136.7, 128.6, 127.9, 127.3, 125.7, 125.4, 122.5, 122.2, 115.2, 62.5, 61.5, 31.4, 12.4; HRMS (ESI) exact mass calculated for $[\text{M} + \text{H}]^+$ ($\text{C}_{16}\text{H}_{19}\text{O}_2$) requires m/z 243.1385, found m/z 243.1380.

Our above NMR data for prepared compound (**7e**) were comparable with the NMR data of compound **5** in Reference [29]: ^1H NMR (80 MHz, CDCl_3) δ 8.40–8.25 (m, 2H), 7.82–7.76 (m, 2H), 6.50–6.00 (m, 1H), 5.40–4.98 (m, 2H), 4.11 (s, 3H), 4.07 (s, 3H), 3.85 (d, $J = 6$, 2H), 2.62 (s, 3H).

3.6. General Procedure for Key Cross Metathesis Reaction

Methyl methacrylate (200.0 mg, 2.0 mmol) and allylarene (0.1 mmol) were dissolved in dichloromethane (100 mL), and Grubbs 2nd (42.1 mg, 0.05 mmol) was added. The reaction mixture was refluxed for 24 h at 40 °C under an N_2 atmosphere. The mixture was then concentrated under vacuum and the residue was purified by column chromatography with silica gel as the stationary phase (5%–10% ethyl acetate/*n*-hexane) to yield the titular key ester intermediate. The *E*-configuration of the cross-coupling products was determined by NOESY NMR spectroscopy analysis.

(*E*)-2-(4-methoxy-3-methyl-4-oxobut-2-en-1-yl)-3,5,6-trimethyl-1,4-phenylene diacetate (**8a**): clear oil, 56% yield. IR (film) 2927, 2926, 1740, 1639, 1495, 1445, 1373, 1238, 1045, 935, 878, 841, 731 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.58 (td, $J = 6.8, 1.4$ Hz, 1H), 3.69 (s, 3H), 3.36 (b, 2H), 2.35 (s, 3H), 2.31 (s, 3H), 2.06 (s, 3H), 2.04 (s, 6H), 1.96 (d, $J = 1.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 168.4, 168.2, 146.1, 145.7, 139.5, 128.7, 128.3, 127.9, 127.4, 112.9, 51.9, 27.6, 20.7, 20.6, 13.4 (d), 13.0, 12.8; HRMS (ESI) exact mass calculated for $[\text{M} + \text{H}]^+$ ($\text{C}_{19}\text{H}_{25}\text{O}_6$) requires m/z 349.1651, found m/z 349.1646.

Methyl (*E*)-4-(2,5-dimethoxy-3,4,6-trimethylphenyl)-2-methylbut-2-enoate (**8b**): clear oil, 61% yield. IR (film) 2916, 2849, 1719, 1649, 1458, 1402, 1300, 1259, 1244, 1206, 1132, 1080, 1059, 997, 802, 743 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.69 (td, $J = 7.0, 1.0$ Hz, 1H), 3.69 (s, 3H), 3.64 (s, 3H), 3.63 (s, 3H), 3.53 (d, $J = 6.9$ Hz, 2H), 2.19 (s, 6H), 2.17 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 168.7, 153.3, 152.9, 141.3, 129.3, 129.1, 128.3, 127.9, 127.5, 61.0, 60.3, 51.8, 27.1, 12.9, 12.8, 12.7, 12.5; HRMS (ESI) exact mass calculated for $[\text{M} + \text{H}]^+$ ($\text{C}_{17}\text{H}_{25}\text{O}_4$) requires m/z 293.1753, found m/z 295.1750.

Methyl (*E*)-2-methyl-4-(2,3,4,5-tetramethoxy-6-methylphenyl)but-2-enoate (**8c**): clear oil, 58% yield. IR (film) 2918, 2849, 1719, 1649, 1458, 1400, 1300, 1259, 1244, 1206, 1132, 1080, 1059, 999, 802, 741 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.64 (t, $J = 6.9$ Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.70 (s, 3H), 3.48 (d, $J = 7.0$ Hz, 2H), 2.13 (s, 2H), 2.00 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 168.7, 148.1, 147.9, 145.8, 144.9, 140.8, 127.5, 126.5, 125.6, 61.3, 61.2, 61.1, 60.9, 51.9, 29.8, 12.7, 12.0; HRMS (ESI) exact mass calculated for $[\text{M} + \text{H}]^+$ ($\text{C}_{17}\text{H}_{25}\text{O}_6$) requires m/z 325.1651, found m/z 325.1547.

(*E*)-2-(4-methoxy-3-methyl-4-oxobut-2-en-1-yl)-3-methylnaphthalene-1,4-diyl diacetate (**8d**): clear oil, 64% yield. IR (film) 2981, 2907, 1736, 1699, 1597, 1446, 1371, 1300, 1234, 1157, 1097, 1043, 937, 846, 785 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.73–7.71 (m, 1H), 7.69–7.67 (m, 1H), 7.51–7.47 (m, 2H), 6.67 (td, $J = 6.8, 1.4$ Hz, 1H), 3.69 (s, 3H), 3.58 (b, 2H), 2.49 (s, 3H), 2.47 (s, 3H), 2.24 (s, 3H), 2.02 (d, $J = 1.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 169.4, 168.3 ($2 \times \text{C}=\text{OCH}_3$), 142.9, 142.8, 138.9, 128.6, 128.1, 126.9, 126.8, 126.7, 126.5, 126.3, 121.6, 121.4, 51.9, 27.8, 20.8, 20.7, 13.4, 12.9; HRMS (ESI) exact mass calculated for $[\text{M} + \text{H}]^+$ ($\text{C}_{21}\text{H}_{23}\text{O}_6$) requires m/z 371.1495, found m/z 371.1489.

Methyl (*E*)-4-(1,4-dimethoxy-3-methylnaphthalen-2-yl)-2-methylbut-2-enoate (**8e**): clear oil, 64% yield. IR (film) 2982, 2939, 1736, 1699, 1597, 1447, 1371, 1300, 1234, 1098, 1043, 937, 847, 785 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.07–8.03 (m, 2H), 7.50–7.46 (m, 2H), 6.74 (t, $J = 6.8$ Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.73 (d, $J = 6.9$ Hz, 2H), 3.70 (s, 3H), 2.36 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 168.6, 150.4, 150.3, 140.7, 128.4, 128.1, 128.0, 127.3, 126.5, 125.9, 125.7, 122.4, 122.3, 62.4, 61.6, 51.9, 27.7, 12.9, 12.8; HRMS (ESI) exact mass calculated for $[\text{M} + \text{H}]^+$ ($\text{C}_{19}\text{H}_{23}\text{O}_4$) requires m/z 315.1596, found m/z 315.1592.

3.7. General Procedure for the Reduction of Cross Metathesis Products

To a stirred solution of ester **6c** (325.1 mg, 6.0 mmol) in anhydrous diethyl ether (10 mL) was added dropwise a suspension of LiAlH₄ in dry THF at 0 °C. The reaction was allowed to warm to room temperature until completion as indicated by TLC (4 h). The reaction mixture was quenched at 0 °C by addition of water (2 mL) and aq sodium hydroxide (20%, 1 mL). The workup was continued by the further addition of water (10 mL) and aq sodium hydroxide (20%, 10 mL). The mixture was stirred for 30 min, after which the mineral solid precipitate was filtrated and washed with diethyl ether (40 mL). The residue was purified by column chromatography with silica gel as the stationary phase (5–10% ethyl acetate/*n*-hexane) to yield alcohol **4** (266.6 mg, 90% yield) as a clear and colorless viscous oil.

(*E*)-4-(2,5-dimethoxy-3,4,6-trimethylcyclohexa-1,5-dienyl)-2-methylbut-2-en-1-ol (**2b**): clear oil, 92%. IR (film) 3435, 2954, 2927, 2870, 1724, 1641, 1456, 1400, 1375, 1248, 1148, 1082, 1006, 804, 765 cm⁻¹; ¹H NMR Spectrum (500 MHz, CDCl₃): 5.36 (t, *J* = 6 Hz, 1H), 4.00 (s, 1H), 3.65 (s, 3H), 3.64 (s, 3H), 3.41 (d, *J* = 6 Hz, 2H), 2.19 (s, 3H), 2.18 (s, 6H); ¹³C NMR Spectrum (125 MHz, CDCl₃): 153.29, 152.92, 134.92, 130.93, 128.79, 128.21, 127.79, 125.22, 69.10, 61.01, 60.30, 26.08, 14.10, 12.98, 12.89, 12.43; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₆H₂₅O₃) requires *m/z* 265.1804, found *m/z* 265.1802.

(*E*)-2-methyl-4-(2,3,4,5-tetramethoxy-6-methylphenyl)but-2-en-1-ol (**2c**): clear oil, 90% yield. IR (film) 3414, 2931, 2860, 1463, 1406, 1350, 1257, 1193, 1103, 1050, 1005, 970, 871 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.34 (t, *J* 6.7 Hz, 1H), 4.00 (s, 2H), 3.90 (s, 3H), 3.90 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.37 (d, *J* = 6.7 Hz, 2H); 2.14 (s, 2H), 1.83 (d, *J* = 1.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 148.0, 147.8, 145.3, 144.8, 134.8, 128.4, 125.2, 124.6, 69.0, 61.3, 61.2 (b, 2CH₃O), 60.7, 25.6, 14.0, 11.9; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₆H₂₅O₅) requires *m/z* 297.1702, found *m/z* 297.1701.

Our above IR and NMR data for prepared alcohol (**2c**) were comparable with the IR and NMR data of alcohol **6** in Reference [25]: IR (CHCl₃) 3432, 2935, 2862, 1466, 1407, 1351, 1219, 1105, 1067, 1039, 1013 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.26 (1H, m), 3.93 (2H, s), 3.83 (3H, s), 3.82 (3H, s), 3.72 (3H, s), 3.70 (3H, s), 3.29 (2H, dd, *J* = 6.8, 0.8 Hz), 2.07 (3H, s), 1.76 (3H, s), ¹³C NMR (100 MHz, CDCl₃) δ 147.93, 147.72, 145.19, 144.75, 134.68, 128.29, 125.23, 124.52, 68.83, 61.02, 60.99, 60.63, 25.51, 13.81, 11.76.

(*E*)-4-(1,4-dimethoxy-3-methylnaphthalen-2-yl)-2-methylbut-2-en-1-ol (**2e**): clear oil, 91%. IR 3397, 1659, 1597, 1454, 1379, 1366, 1263, 1159, 1066, 1037, 1007, 899, 758, 739 cm⁻¹; ¹H NMR Spectrum (500 MHz, CDCl₃): 8.05 (m, 2H), 7.59–7.36 (m, 2H), 5.54–5.31 (m, 1H), 4.02 (d, *J* = 5.1 Hz, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.61 (dd, *J* = 6.6, 2 Hz), 2.38 (s, 3H), 1.89 (d, *J* = 0.9 Hz, 3H); ¹³C NMR Spectrum (125 MHz, CDCl₃): 150.42, 150.10, 135.55, 130.21, 127.83, 127.45, 126.82, 125.73, 125.56, 124.61, 122.47, 122.36, 68.98, 62.35, 61.52, 26.22, 14.19, 12.69; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₁₈H₂₃O₃) requires *m/z* 287.1647, found *m/z* 287.1645.

Our above NMR data for prepared ancol (**2e**) were comparable with the NMR data of compound **21** in Reference [30]: ¹H NMR (400 MHz, CDCl₃) δ 8.07–8.02 (m, 2H), 7.48–7.44 (m, 2H), 5.43–5.41 (m, 1H), 4.02 (s, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.61 (d, *J* = 6.5, 2H), 2.38 (s, 3H), 1.90 (d, *J* = 1.0, 3H)

3.8. Bromination of **2b**

Alcohol **2b** (5 mmol) was dissolved in 20 mL of anhydrous tetrahydrofuran and PBr₃ (2.5 mmol) was slowly added to the reaction at –5 °C for 15 min under an N₂ atmosphere. After 2 h, the reaction mixture was poured into cold saturated sodium bicarbonate solution and then extracted with ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated under vacuum. The crude bromide **9** was used for the next reaction without purification.

3.9. General Procedure for the Sulfinatation

Bromide (**9**) (4 mmol) and sodium benzene sulphinat were dissolved in 25 mL dimethyl formamide. The reaction mixture was stirred at room temperature for 12 h under an N₂ atmosphere. The mixture was then poured into ice-cold water, acidified to pH ~4 with 2N HCl and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated under

vacuum. The residue was purified by column chromatography with silica gel as the stationary phase (0%–10% ethyl acetate/*n*-hexane) to yield the titular sulfonyl compound (**10**).

(*E*)-1,4-dimethoxy-2,3,5-trimethyl-6-(3-methyl-4-(phenylsulfonyl)but-2-enyl)benzene (**10**): white solid, 90% yield, mp = 186–187 °C. IR 3065, 2938, 2847, 1587, 1447, 1400, 1350, 1302, 1292, 1248, 1165, 1132, 1082, 1055, 1009, 955, 901, 768, 743 cm⁻¹; ¹H NMR Spectrum (500 MHz, CDCl₃): 7.83–7.75 (m, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 4.97 (t, *J* = 6.4 Hz, 1H), 3.71 (s, 2H), 3.61 (s, 3H), 3.54 (s, 3H), 3.27 (d, *J* = 6.6 Hz, 1H), 2.17 (s, 3H), 2.15 (s, 3H), 2.01 (s, 3H), 1.95 (s, 3H); ¹³C NMR Spectrum (125 MHz, CDCl₃): 138.49, 138.46, 136.71, 135.36, 135.12, 133.50, 129.00, 128.54, 128.19, 127.85, 127.57, 123.44, 66.23, 60.93, 60.29, 26.78, 17.16, 12.96, 12.87, 12.37; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₂₂H₂₉O₄S) requires *m/z* 389.1787, found *m/z* 389.1784.

3.10. General Procedure for the Solanesylation:

Sulfonyl (**10**) (0.50 mmol) and solanesol bromide (0.75 mmol) were dissolved in 10 mL of anhydrous tetrahydrofuran. Solution of potassium *tert*-butoxide (0.75 mmol) in 5 mL anhydrous tetrahydrofuran was added dropwise to the above solution containing sulfonyl and solanesol bromide at –25 °C. After 2 h, the reaction was allowed to reach room temperature and the stirring was continued for 12 h under an N₂ atmosphere. After completion, the mixture was poured into ice-water, acidified to pH ~4 with 2N HCl, and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄, and concentrated under vacuum. The residue was purified by column chromatography with silica gel as the stationary phase (0%–5% ethyl acetate/*n*-hexane) to yield the titular compound.

1-((2*E*,6*E*,10*E*,14*E*,18*E*,22*E*,26*E*,30*E*,34*E*)-3,7,11,15,19,23,27,31,35,39-decamethyl-4-(phenylsulfonyl)tetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-2,5-dimethoxy-3,4,6-trimethylbenzene (**11**): clear oil, 43%. IR (film) 3296, 3233, 2914, 2849, 1728, 1468, 1418, 1290, 1217, 1194, 1177, 1101, 1047, 991, 943, 719 cm⁻¹; ¹H NMR Spectrum (500 MHz, CDCl₃): 7.77 (m, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 5.13–5.10 (m, 7H), 5.05 (t, *J* = 6.6 Hz, 1H), 4.97 (t, *J* = 5.9 Hz, 1H), 4.87 (t, *J* = 6.8 Hz, 1H), 3.60 (s, 3H), 3.48 (m, 4H), 3.30 (dd, *J* = 15.7, 6.9 Hz, 1H), 3.17 (dd, *J* = 15.4, 5.3 Hz, 1H), 2.86–2.77 (m, 1H), 2.68–2.56 (m, 1H), 2.16 (s, 3H), 2.14 (s, 3H), 2.10–2.04 (m, 16H), 2.02–1.92 (m, 19H), 1.84 (s, 3H), 1.68 (s, 3H), 1.64–1.50 (s, 32H), 1.26 (s, 6H); ¹³C NMR Spectrum (125 MHz, CDCl₃): 153.16, 152.68, 135.53, 135.09, 131.41, 130.04, 128.93, 128.86, 128.86, 128.13, 127.68, 126.97, 124.63, 124.50, 124.36, 123.96, 118.84, 74.07, 60.89, 60.26, 39.91, 29.89, 26.77, 26.59, 25.87, 17.84, 16.50, 16.22, 12.93, 12.87, 12.31; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₂₇H₃₇O₄S) requires *m/z* 457.2413, found *m/z* 457.2413.

3.11. General Procedure for the De-Sulfinatation

To a solution of **11** (0.1 mmol) in 5 mL anhydrous tetrahydrofuran was added ethanol (0.005 mol). Sodium (1.5 mmol) pieces were slowly added to the reaction mixture under vigorous stirring at room temperature for 12 h under an N₂ atmosphere. The reaction was then poured into ice-water and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄, and evaporated under vacuum. The residue was purified by column chromatography with silica gel as the stationary phase (0%–2% ethyl acetate/*n*-hexane) to yield the titular compound.

1-((2*E*,6*E*,10*E*,14*E*,18*E*,22*E*,26*E*,30*E*,34*E*)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl)-2,5-dimethoxy-3,4,6-trimethylbenzene (**12**): clear oil, 41%. IR (film) 3103, 2989, 2936, 2626, 1587, 1510, 1450, 1400, 1300, 1246, 1169, 1130, 1246, 1169, 1130, 1082, 1053, 1002, 903, 822, 741 cm⁻¹; ¹H NMR Spectrum (500 MHz, CDCl₃): 5.28–5.00 (m, 10H), 3.64 (s, 6H), 3.36 (d, *J* = 6.3 Hz, 2H), 2.69 (m, 3H), 2.18 (s, 12H), 2.08 (m, 22H), 2.06 (m, 24H), 1.78 (s, 3H), 1.68 (s, 6H), 2.63–1.56 (m, 38H); ¹³C NMR Spectrum (125 MHz, CDCl₃): 153.25, 152.90, 135.27, 135.22, 135.13, 135.08, 131.84, 128.43, 128.07, 127.94, 124.62, 124.46, 124.33, 123.46, 123.36, 61.06, 60.29, 40.38, 39.94, 39.89, 27.21, 26.97, 26.92, 26.82, 26.37, 25.88, 16.50, 16.21, 12.96, 12.89, 12.34, 12.21; HRMS (ESI) exact mass calculated for [M + H]⁺ (C₂₁H₃₃O₂) requires *m/z* 317.2481, found *m/z* 317.2478.

4. Conclusions

In conclusion, we devised an alternative synthesis route of benzylallyl ester intermediates for the preparation of coenzyme Q₁₀ and its derivatives. The key features of this strategy were the use of catalytic formation of allylarenes and cross-metathesis reactions to selectively prepare *E*-benzylallyl esters. The resultant esters were reduced to benzylallylic alcohols on the pathway toward coenzyme Q₁₀ and derivatives. One alcohol was utilized to synthesize a coenzyme Q₁₀ derivative.

Supplementary Materials: The following Supplementary material including NMR and IR spectra of new synthetic compounds are available online.

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References

1. Garrido-Maraver, J.; Cordero, M.D.; Oropesa-Ávila, M.; Fernández Vega, A.; de la Mata, M.; Delgado Pavón, A.; de Miguel, M.; Carmen Pérez Calero, C.P.; Paz, M.V.; David Cotán, D.; et al. Coenzyme Q₁₀ therapy. *Mol. Syndr.* **2014**, *5*, 187–197. [[CrossRef](#)] [[PubMed](#)]
2. Sumien, N.; Heinrich, K.R.; SHetty, R.A.; Sohal, R.S.; Forster, M.J. Prolonged intake of coenzyme Q₁₀ impairs cognitive functions in mice. *J. Nutr.* **2009**, *139*, 1926. [[CrossRef](#)] [[PubMed](#)]
3. Singal, P.K.; Khaper, N.; Palace, V.; Kumar, D. On the role of coenzyme Q₁₀ in cardiovascular diseases. *Cardiovasc. Res.* **1999**, *43*, 250–251. [[CrossRef](#)]
4. Bentinger, M.; Tekle, M.; Dallner, G. Coenzyme Q₁₀ biosynthesis and functions. *Biochem. Biophys. Res. Commun.* **2010**, *396*, 74–79. [[CrossRef](#)] [[PubMed](#)]
5. Kawamukai, M. Biosynthesis and bioproduction of coenzyme Q₁₀ by yeasts and other organisms. *Biotechnol. Appl. Biochem.* **2009**, *53*, 217–226. [[CrossRef](#)] [[PubMed](#)]
6. Lipschutz, B.H.; Butler, T.; Lower, A.; Servesko, J. Enhancing regiocontrol in carboaluminations of terminal alkynes. Application to the one-pot synthesis of coenzyme Q₁₀. *Org. Lett.* **2007**, *9*, 3737–3740. [[CrossRef](#)] [[PubMed](#)]
7. Lipschutz, B.H.; Lower, A.; Berl, V.; Schein, K.; Wetterich, F. An improved synthesis of the “miracle nutrient” coenzyme Q₁₀. *Org. Lett.* **2005**, *7*, 4095–4097. [[CrossRef](#)]
8. Lipschutz, B.H.; Mollard, P.; Pfeiffer, S.S.; Chrisman, W. A short, highly efficient synthesis of coenzyme Q₁₀. *J. Am. Chem. Soc.* **2002**, *124*, 14282–14283. [[CrossRef](#)]
9. Negishi, E.-I.; Liou, S.-Y.; Xu, C.; Huo, S. A novel, highly selective, and general methodology for the synthesis of 1,5-diene-containing oligoisoprenoids of all possible geometrical combinations exemplified by an iterative and convergent synthesis of coenzyme Q₁₀. *Org. Lett.* **2002**, *4*, 261–264. [[CrossRef](#)] [[PubMed](#)]
10. Yanagisawa, A.; Nomura, N.; Noritake, Y.; Yamamoto, H. Highly S_N2'-, (*E*)-, and antiselective alkylation of allylic phosphates. facile synthesis of coenzyme Q₁₀. *Synthesis* **1991**, 1130–1136. [[CrossRef](#)]
11. Luo, M.; Yang, X.; Hu, J.; Ruan, X.; Mu, F.; Fu, Y. The Synthesis of Coenzyme Q₁₀. *Curr. Org. Chem.* **2017**, *21*, 489–502. [[CrossRef](#)]
12. Duveau, D.Y.; Arce, P.M.; Schoenfeld, R.A.; Raghav, N.; Cortopassi, G.A.; Hecht, S.M. Synthesis and characterization of mitoQ and idebenone analogues as mediators of oxygen consumption in mitochondria. *Bioorg. Med. Chem.* **2010**, *18*, 6429–6441. [[CrossRef](#)] [[PubMed](#)]
13. Chatterjee, A.K.; Choi, T.-L.; Sanders, D.P.; Grubbs, R.H. A general model for selectivity in olefin cross metathesis. *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370. [[CrossRef](#)] [[PubMed](#)]
14. Blackwell, H.E.; O'Leary, D.J.; Chatterjee, A.K.; Washenfelder, R.A.; Bussmann, D.A.; Grubbs, R.H. New approaches to olefin cross-metathesis. *J. Am. Chem. Soc.* **2000**, *122*, 58–71. [[CrossRef](#)]

15. Bilel, H.; Hamdi, N.; Zagrouba, F.; Fischmeister, C.; Bruneau, C. Eugenol as a renewable feedstock for the production of polyfunctional alkenes via olefin cross-metathesis. *Rcs Adv.* **2012**, *2*, 9584–9589. [[CrossRef](#)]
16. Moise, J.; Arseniyadis, S.; Cossy, J. Cross-metathesis between α -methylene- γ -butyrolactone and olefins: A dramatic additive effect. *Org. Lett.* **2007**, *9*, 1695–1698. [[CrossRef](#)]
17. Li, J.; Grubbs, R.H.; Stoltz, B.M. Palladium-catalyzed aerobic intramolecular aminoacetoxylation of alkenes enabled by catalytic nitrate. *Org. Lett.* **2016**, *18*, 5449–5451. [[CrossRef](#)]
18. Gajare, A.S.; Jensen, R.S.; Toyota, K.; Yoshifuji, M.; Ozawa, F. Low-coordinated diphosphinidene-cyclobutene ligands: A new entry for stille cross-coupling of aryl bromides. *Synlett* **2005**, 0144–0148. [[CrossRef](#)]
19. Lee, B.C.; Paik, J.-Y.; Chi, D.Y.; Lee, K.-H.; Choe, E.S. Potential and practical adrenomedullary PET radiopharmaceuticals as an alternative to m-iodobenzylguanidine: m-(ω -[18 F]fluoroalkyl)benzylguanidines. *Bioconjugate Chem.* **2004**, *15*, 104–111. [[CrossRef](#)]
20. Tamura, K.; Kato, Y.; Ishikawa, A.; Kato, Y.; Himori, M.; Yoshida, M.; Takashima, Y.; Suzuki, T.; Kawabe, Y.; Cynshi, O.; et al. Design and synthesis of 4,6-di-tert-butyl-2,3-dihydro-5-benzofuranols as a novel series of antiatherogenic antioxidants. *J. Med. Chem.* **2003**, *46*, 3083–3093. [[CrossRef](#)]
21. Green, I.R.; Nefdt, S.; Hugo, V.I.; Snijman, P.W. Claisen and fries rearrangement studies of some naphthalene derivatives. *Synth. Commun.* **1994**, *24*, 3189–3196. [[CrossRef](#)]
22. Hasegawa, T.; Yoshida, K.; Hachiya, K.; Miyazaki, M.; Tsuruta, H.; Nambu, F.; Ohuchida, S.; Kawamura, M. Synthesis of a novel class of water-soluble and bioavailable antioxidants: 5-Hydroxycoumaran derivatives possessing imidazole group. *Synlett* **1997**, *1997*, 511–512. [[CrossRef](#)]
23. Kraus, G.A.; Liras, S.; Man, T.O.; Molina, M.T. Synthesis of 4,11-dideoxydaunomycinone by a Claisen/Diels-Alder sequence. *J. Org. Chem.* **1989**, *54*, 3137–3139. [[CrossRef](#)]
24. Naruta, Y.; Nagai, N.; Arita, Y.; Maruyama, K. Copper-catalyzed double cyclization reaction of azidoquinones: One-step synthesis of dihydropyrroloindoloquinones and related quinolinoquinones. *J. Org. Chem.* **1987**, *52*, 3956–3967. [[CrossRef](#)]
25. Ravada, S.R.; Emani, L.R.; Garaga, M.R.; Meka, B.; Golakoti, T. Synthesis of coenzyme Q₁₀. *Am. J. Infect Dis.* **2009**, *5*, 83–89. [[CrossRef](#)]
26. Perrin, D.D.; Armarego, W.L.F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: Oxford, UK, 1988.
27. Still, W.C.; Kahn, M.; Mitra, A.J.J. Rapid chromatographic technique for preparative separations with moderate resolution. *Org. Chem.* **1978**, *43*, 2923. [[CrossRef](#)]
28. Gilbert, J.C.; Pinto, M. Development of novel phenolic antioxidants, synthesis, structure determination, and analysis of spiro [2,3-dihydro-6-hydroxy-4,6,7-trimethyl-benzofuran-2,1'-cyclopropane]. *J. Org. Chem.* **1992**, *57*, 5271–5276. [[CrossRef](#)]
29. Syper, L.; Kloc, K.; Mzochowski, J. Synthesis of ubiquinone and menaquinone analogues by oxidative demethylation of alkenylhydroquinone ethers with argentic oxide or ceric ammonium nitrat. *Tetrahedron* **1980**, *36*, 123–129. [[CrossRef](#)]
30. Fujii, S.; Shimizu, A.; Takeda, N.; Oguchi, K.; Katsurai, T.; Shirakawa, H.; Komai, M.; Kagechika, T. Systematic synthesis and anti-inflammatory activity of α -carboxylated menaquinone derivatives—investigations on identified and putative vitamin K2 metabolites. *Bioorg. Med. Chem.* **2015**, *23*, 2344–2352. [[CrossRef](#)]

Sample Availability: Samples of all compounds are available in mg amounts from the authors.



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