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Dehydrogenative Formation of Resorcinol Derivatives Using Pd/C–Ethylene Catalytic System

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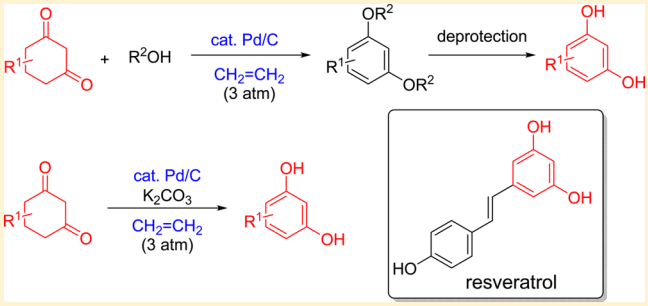
Supporting Information

ABSTRACT: The conversion of substituted 1,3-cyclohexanediones to the alkyl ethers of resorcinol using a Pd/C–ethylene system is reported. In these reactions, ethylene works as a hydrogen acceptor. The efficient synthesis of resveratrol was achieved using this protocol as a key step. In addition, the direct formation of substituted resorcinols was carried out by adding K_2CO_3 into the reaction media.



INTRODUCTION

Resorcinol is one of the most fundamental and important industrial chemicals.[1] The resorcinol moiety is also a common motif in many natural products and pharmaceuticals, as shown in Figure 1.

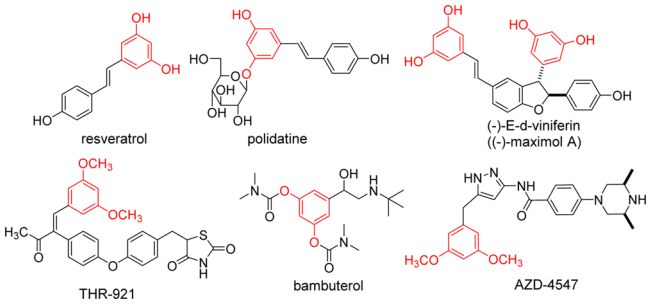


Figure 1. Resorcinol moiety found in natural products and pharmaceuticals.

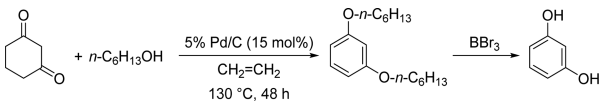
A classical method for manufacturing resorcinol is a sulfonate fusion process that uses 1,3-benzenesulfonic acid disodium salt as an intermediate, starting from benzene. However, this method is limited by the formation of organic substances containing Na_2SO_3 and Na_2SO_4, which are produced as byproducts. An alternative method is a modified Hock method utilizing 1,3-diisopropylbenzene as a starting material. However, this method also suffers from a serious drawback, as the two hydroperoxide groups in the molecules cause the occurrence of simultaneous secondary side reactions to give rise to a greater number of byproducts than just cumene hydroperoxide. In addition, the rate of reaction is considerably low. Therefore, a practical and efficient method for the synthesis of resorcinol derivatives is strongly desired.

In 2000, we reported the reactions of cyclohex-2-en-1-ol (2-cyclohexenol) and cyclohex-2-en-1-one (2-cyclohexenone) with a catalytic amount of $Pd(OAc)_2$ under an ethylene atmosphere, which afforded phenol in 68% and >99% yields, respectively.[2,3] Both reactions include a dehydrogenation process, as confirmed by the quantitative formation of ethane. Since our initial report on the dehydrogenation of cyclohex-2-en-1-one by a palladium catalyst to produce phenol, the palladium-catalyzed transformation of cyclohexanone and cyclohex-2-en-1-one to phenol (especially via aerobic oxidation) has been widely investigated. For example, Stahl and co-workers reported the oxidative dehydrogenation of cyclohexanones using $Pd(DMSO)_2(TFA)_2$ and $Pd(TFA)_2$/2-dimethylaminopyridine ($2\text{-}Me_2NPy$) catalytic systems to produce cyclohex-2-en-1-one and phenol,[4−7] respectively. Lemaire et al. and we have also reported a Pd-catalyzed reaction for the synthesis of aryl ethers.[8,9]

Herein, we present a Pd/C–ethylene catalytic system for the conversion of substituted 1,3-cyclohexanediones to their corresponding resorcinols (Scheme 1).

RESULTS AND DISCUSSION

We first examined the reaction of 1,3-cyclohexanedione with 1-hexanol in the presence of 5% Pd/C (15 mol %) under an ethylene atmosphere (3 atm) at 130 °C for 48 h. The reaction took place readily to produce 1,3-dihexylresorcinol in 82% yield. The dihexyl ether of resorcinol was then converted into resorcinol by adding BBr_3 (in CH_2Cl_2, 0 °C, 12 h, 80% yield) or $AlCl_3$/NaI (in CH_3OH, 60 °C, 24 h, 89% yield) (eq 1).



(1)

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Scheme 1. Pd Catalyzed Synthesis of Phenol and Resorcinol

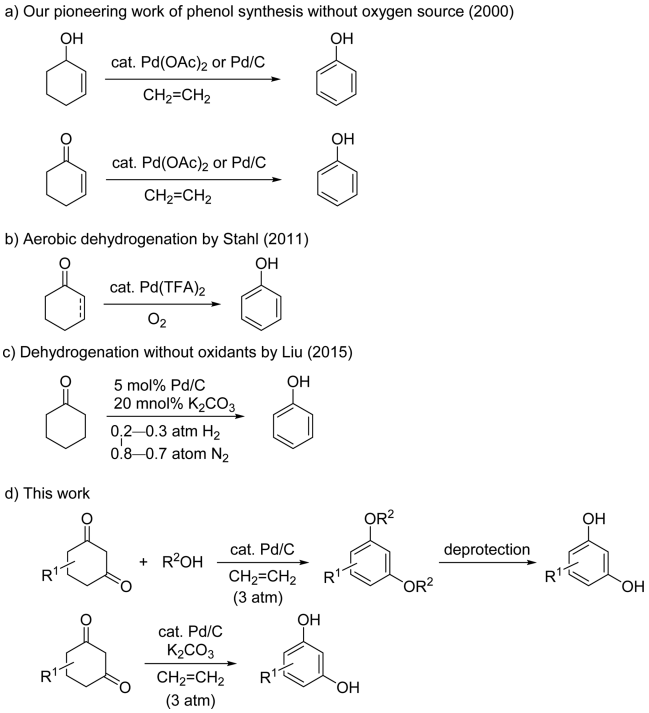
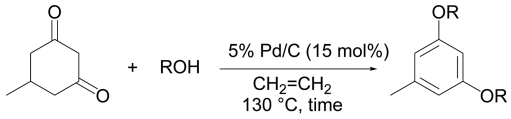


Table 1. Reaction of 5-Methyl-1,3-cyclohexanedione with Alcohol in the Presence of 5% Pd/C (15 mol %) under an Ethylene Atmosphere



entry[a]	ROH[c]	time (h)		yield (%)[b] 1 atm[d]	3 atm[e]
1	CH_3OH	18	**2a**	25	86
2	C_2H_5OH	18	**2b**	21	80
3	n-C_3H_7OH	18	**2c**	48	85
4	n-C_4H_9OH	12	**2d**	65	86
5	n-$CgH_{11}OH$	12	**2c**	44	85
6	n-$C_eH_{13}OH$	12	**2f**	22	88

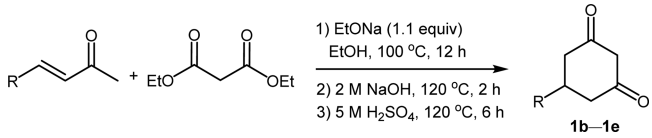
[a]All reactions were carried out in the presence of 5% Pd/C (15 mol %) at 130 °C using an autoclave. [b]Isolated yield. [c]120 equiv of alcohol was used. [d]Initial pressure (1 atm = 15 psi). [e]Initial pressure (3 atm = 44 psi).

Subsequently, we examined the reaction of 5-methyl-1,3-cyclohexanedione with a variety of alcohols. The results obtained are summarized in Table 1.

It is clear that 1 atm of ethylene is not always sufficient to give the corresponding ethers of resorcinols in high yields. High yields of products were achieved in the reaction under 3 atm of ethylene. All ethers obtained were easily converted to the corresponding 5-substituted resorcinols using BBr_3. Therefore, we successfully demonstrated the practical synthesis of 5-substituted resorcinols from 1,3-cyclohexanediones. From the viewpoint of alkyl aryl ether preparation, this method is comparable to palladium-catalyzed C−O bond formation (Buchwald−Hartwig coupling), although the concept and mechanism are completely different.[10,11]

We prepared different 5-substituted 1,3-cyclohexanediones starting from the condensation of aldehyde with acetone to give 4-substituted but-3-en-2-one derivatives[12] (**3**, **4**), followed by condensation with diethylmalonate in an ethanolic solution of sodium ethoxide to give compounds (**1b**−**1e**) as shown in Table 2.

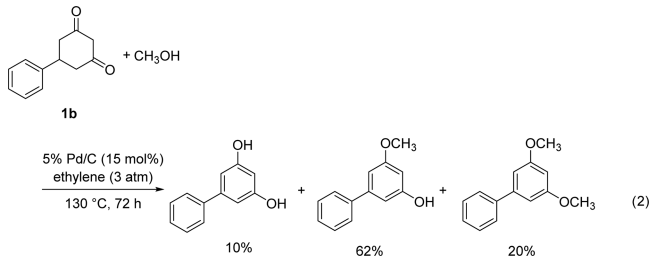
Table 2. Preparation of 5-Substituted 1,3-Cyclohexanedione Derivatives



entry	R	product	yield (%)[a]
1	C_6H_5	**1b**	78
2	4-$CH_3C_6H_4$	**1c**	80
3	4-$CH_3OC_6H_4$	**1d**	77
4	$CH(CH_3)_2$	**1e**	79

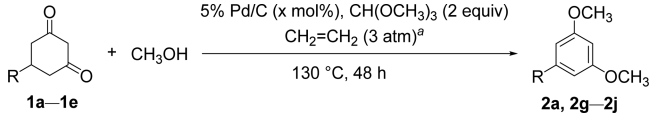
[a]Isolated yield after recrystallization.

Next, we focused on the reaction of various 5-substituted 1,3-cyclohexanediones with methanol, as there are many important compounds that are known to incorporate methyl ethers of resorcinol as a structural component (see, Figure 1). Based on our preliminary findings, the reaction afforded a mixture of resorcinol, monomethylresorcinol, and dimethylresorcinol in 10%, 62%, and 20% yields, respectively (eq 2).



After several attempts, we overcame this problem by adding trimethyl orthoformate into the reaction mixture. The reaction of substituted 1,3-cyclohexanediones with methanol in the presence of 5% Pd/C and $CH(OCH_3)_3$ under an ethylene atmosphere (3 atm) proceeded smoothly to afford substituted dimethoxy ethers of resorcinols in high yields (Table 3).

Table 3. Oxidation of Monosubstituted 1,3-Cyclohexanedione Derivatives in the Presence of 5% Pd/C (15 mol %) under an Ethylene Atmosphere



entry[a]	R	X	product	yield (%)[c]
1	CH_3	15	**2a**	71
2	C_6H_5	1	**2g**	73
3	4-$CH_3C_6H_4$	1	**2h**	88
4	4-$CH_3OC_6H_4$	1	**2i**	70
5	$(CH_3)_2CH$	15	**2j**	52

[a]Initial pressure. [b]All reactions were carried out in the presence of 5% Pd/C at 130 °C for 48 h using a molar ratio of diketone/CH_3OH/trimethyl orthoformate = 1:120:2 in an autoclave. [c]Isolated yield.

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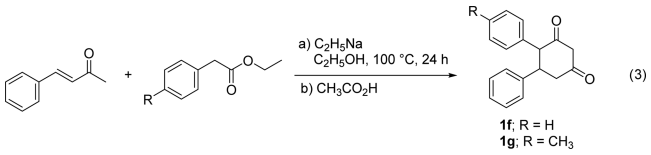
The starting material of multisubstituted 1,3-cyclohexanediones which will be used in the next step were prepared via a condensation reaction between benzalacetone and ethyl phenylacetate derivatives to give compounds (**1f**, **1g**) according to (eq 3).



(3)

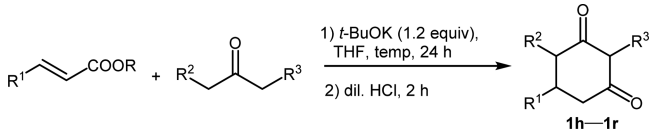
The other starting materials (**1h**−**1r**) were prepared through the reaction of α,β-unsaturated esters and ketones as shown in Table 4.

We then examined the conversion of multisubstituted 1,3-cyclohexanediones to the corresponding dimethoxy ethers of resorcinols with the same method used for monosubstituted 1,3-cyclohexanediones but with a more equimolecular amount of trimethylorthoformate and 5% Pd/C due to more substituents and gave substituted dimethoxy ethers of resorcinols in high yields (Table 5).

With respect to the reaction mechanism, we would like to propose the mechanism shown in Scheme 2. The formation of the dialkyl ethers of resorcinol begins via the reaction of 5-methyl-1,3-cyclohexandione with alcohol through a nucleophilic addition reaction to give the hemiacetal **A**, followed by losing alcohol to give the ketoenol **B**. This intermediate then undergoes acetalization and dehydration to give the dialkoxy-1,3-cyclohexanediene derivative **C**, which goes on to react with Pd/C to lose one molecule of hydrogen and, thus, affords the dialkyl ether resorcinol as well as the $Pd(H_2)/C$ species. The catalyst then undergoes a hydrogen transfer to ethylene to regenerate the free Pd/C species and ethane.

We applied this method to the synthesis of resveratrol, a known antioxidant. As shown in Scheme 3, we synthesized resveratrol in five steps with a 62% total yield. The first and the most crucial step is the oxidation of 5-methyl-1,3-cyclohexanedione to

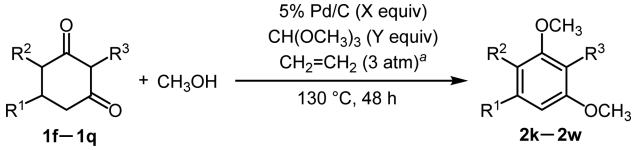
Table 4. Preparation of Multisubstituted 1,3-Cyclohexanedione Derivatives



entry	R	R^1	R^2	R^3	temp (°C)	product	yield (%)[a]
1	$C(CH_3)_3$	CH_3	CH_3	H	30	**1h**	32
2	C_2H_5	C_6H_5	CH_3	H	30	**1i**	55
3	$C(CH_3)_3$	CH_3	C_2H_5	H	30	**1j**	58
4	C_2H_5	C_6H_5	C_2H_5	H	30	**1k**	70
5	$C(CH_3)_3$	CH_3	CH_3	CH_3	25	**1l**	51
6	C_2H_5	C_6H_5	CH_3	CH_3	35	**1m**	70
7	C_2H_5	C_6H_5	C_6H_5	C_6H_5	40	**1n**	71
8	C_2H_5	CH_3	C_6H_5	C_6H_5	35	**1o**	65
9	C_2H_5	CH_3	C_6H_5	CH_3	40	**1p**	64
10	C_2H_5	C_6H_5	C_6H_5	CH_3	40	**1q**	75
11	C_2H_5	4-$CH_3C_6H_4$	CH_3	CH_3	40	**1r**	78

[a]Yield after recrystallization.

Table 5. Oxidation of Substituted 1,3-Cyclohexanediones to the Dimethoxy Ethers of Resorcinols



entry	R^1	R^2	R^3	X	Y	product	yield (%)[b]
1	C_6H_5	C_6H_5	H	0.15	2	**2k**	75
2	C_6H_5	C_6H_5	C_6H_5	0.2	50	**2l**	80
3	C_6H_5	C_6H_5	CH_3	0.2	50	**2m**	69
4	C_6H_5	4-$CH_3C_eH_4$	H	0.2	50	**2n**	78
5	C_6H_5	CH_3	H	0.15	8	**2o**	70
6	C_6H_5	CH_3	CH_3	0.15	4	**2p**	68
7	C_6H_5	C_2H_5	H	0.15	8	**2q**	74
8	4-$CH_3C_6H_4$	CH_3	CH_3	0.15	4	**2r**	77
9	CH_3	C_6H_5	C_6H_5	0.2	50	**2s**	71
10	CH_3	C_6H_5	CH_3	0,15	50	**2t**	75
11	CH_3	CH_3	H	0.15	2	**2u**	68
12	CH_3	CH_3	CH_3	0.2	8	**2v**	75
13	CH_3	C_2H_5	H	0.15	7	**2w**	70

[a]Initial pressure. [b]Isolated yield.

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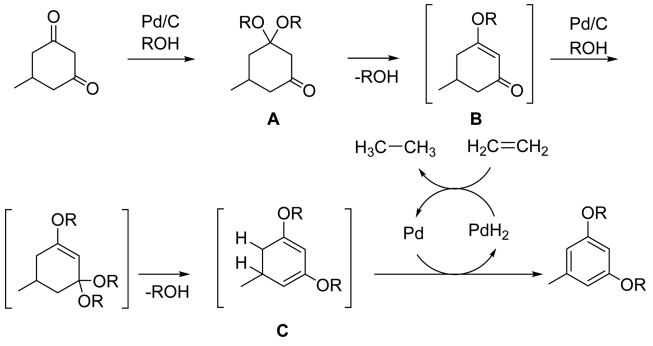
Scheme 2. Proposed Mechanism for the Conversion of 1,3-Cyclohexanediones to the Corresponding Alkyl Ethers of Resorcinol

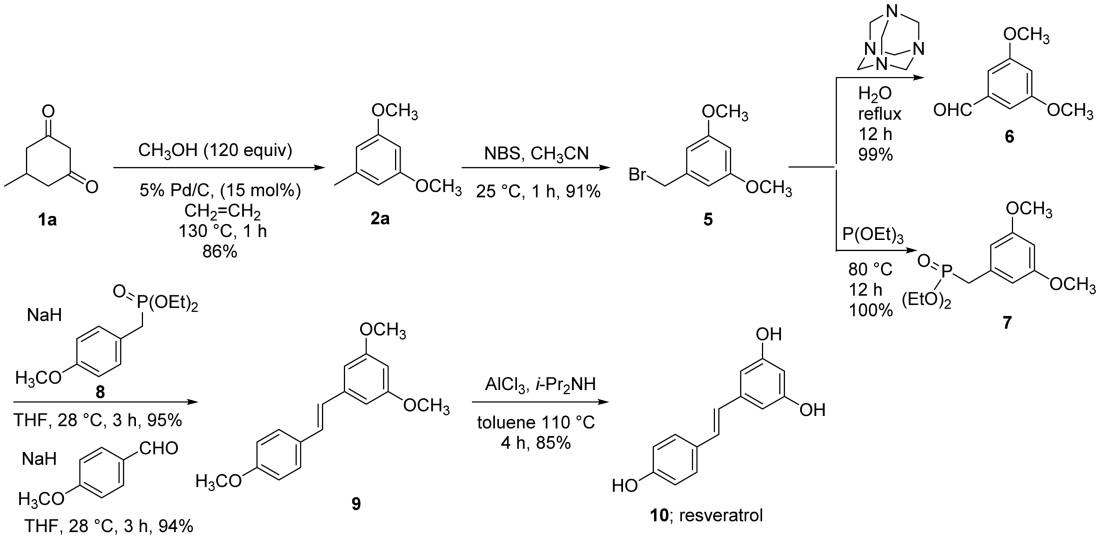


3,5-dimethoxytoluene. In this case, the addition of trimethyl orthoformate is unnecessary. During the Horner–Wadsworth–Emmons reaction, we employed two separate routes: one is the reaction of 3,5-dimethoxybenzaldehyde (**6**) with diethyl 4-methoxybenzylphosphonate (**8**), and the other is the reaction of 4-methoxybenzaldehyde with diethyl 3,5-dimethoxybenzylphosphonate (**7**). In both routes, the reactions proceeded smoothly to give trimethoxy resveratrol (**9**) followed by demethylation giving resveratrol (**10**) in high yield.

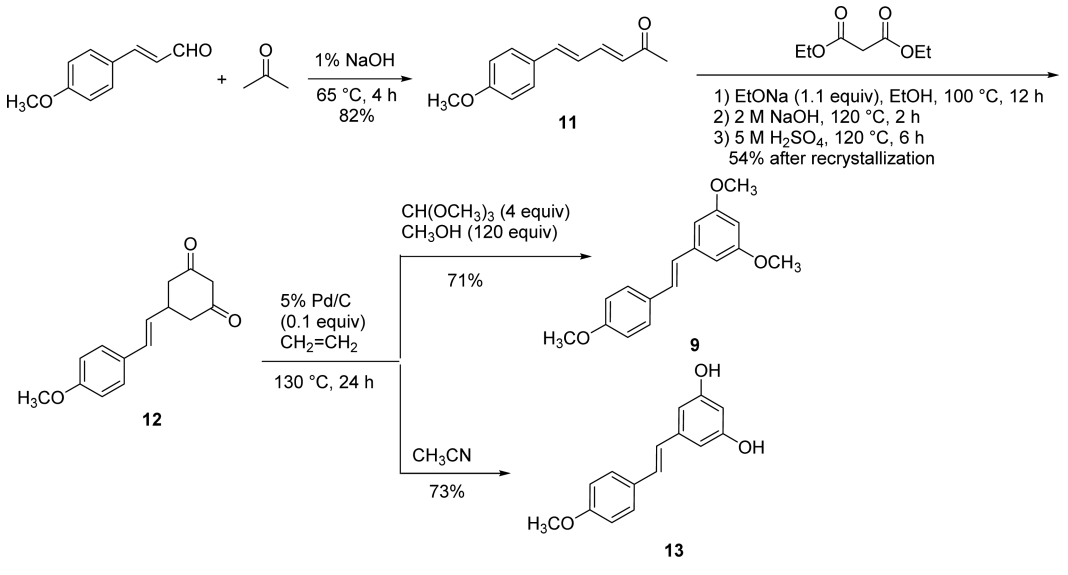
During the synthesis of resveratrol, we performed a couple of experimental modifications for practical reasons. First, the bromination step involving *N*-bromosuccinimide (NBS) was carried out in CH_3CN as opposed to CCl_4 (a typical solvent choice). The second experimental adjustment concerns the final demethylation step; specific to our study, the combination of $AlCl_3$ and *i*-Pr_2NH gave a higher yield of resveratrol compared to the use of BBr_3 or $AlCl_3$/NaI.

Scheme 4 shows an alternative route for synthesis of resveratrol which avoids the limitation of a Wittig-type reaction, i.e. the formation of a stoichiometric amount of phosphine oxide as a coproduct. A Wittig-type reaction provides a powerful tool to form double bonds; however, recently, from the viewpoints of atomic economy, it is recommended to avoid Wittig-type reactions.[13,14]

Scheme 3. Synthesis of Resveratrol



Scheme 4. Improved Synthesis of Resveratrol



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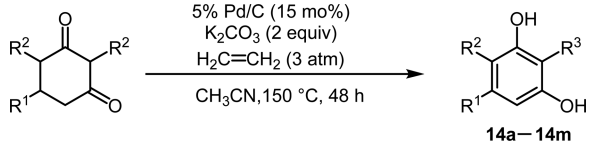
Finally, during our attempts to directly synthesize substituted resorcinols, we found that the addition of a catalytic amount of K_2CO_3 facilitated the formation of substituted resorcinols in good to high yields (Table 6). It is postulated that K_2CO_3 may assist the enolization of 1,3-cyclohexanedione.

Table 6. Direct Oxidation of Substituted 1,3-Cyclohexanediones to Resorcinol Derivatives



entry[a]	R^1	R^2	R^3	product	yield (%)[b]
1	C_6H_5	H	H	**14a**	80
2	C_6H_5	C_6H_5	H	**14b**	75
3	C_6H_5	C_6H_5	C_6H_5	**14c**	76
4	C_6H_5	C_6H_5	CH_3	**14d**	60
5	C_6H_5	4-$CH_3C_6H_4$	H	**14e**	78
6	C_6H_5	CH_3	H	**14f**	70
7	C_6H_5	CH_3	CH_3	**14g**	45
8	C_6H_5	C_2H_5	H	**14h**	71
9	4-$CH_3C_6H_4$	H	H	**14i**	81
10	4-$CH_3C_6H_4$	CH_3	CH_3	**14j**	35
11	4-$CH_3OC_6H_4$	H	H	**14k**	84
12	$(CH_3)_2CH$	H	H	**14l**	70
13	CH_3	C_6H_5	C_6H_5	**14m**	69

[a]All reactions were carried out in the presence of 5% Pd/C (15 mol %) at 130 °C using an autoclave. [b]Isolated yield.

CONCLUSION

In conclusion, we have successfully achieved the conversion of substituted 1,3-cyclohexanediones to resorcinols and their corresponding dialkyl ethers using a Pd/C−ethylene catalytic system. It is important to take note of the crucial role of ethylene as a hydrogen acceptor. The efficient synthesis of resveratrol was also accomplished using this protocol as a key step. The present method provides the following advantages over the related procedure: (1) A variety of ethers of resorcinols having multiple substituents were provided. (2) The addition of trimethyl orthoformate enabled the complete conversion of substituted 1,3-cyclohexanediones to dimethyl ether of resorcinols. (3) Direct formation of resorcinols was achieved by the addition of K_2CO_3.

EXPERIMENTAL SECTION

General. All reactions were carried out in oven-dried glassware under magnetic stirring. All starting materials were obtained from commercial sources or were synthesized using standard procedures. Melting points were measured on a Yanaco MP-500D instrument and were not corrected. ^1H and ^{13}C NMR spectra (400 and 100 MHz, respectively) were recorded on a Bruker Avance III HD 400 spectrometer; TMS (0 ppm) and $CDCl_3$ (77.0 ppm) were used as internal standards, respectively. The following abbreviations are used to describe NMR peak multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. GC mass spectra were measured on a Thermo Auest LCQ DECA Plus instrument with GL Sciences Inc. Inert Cap5 as a column (70−310 °C). GC analyses were performed using a Shimadzu GC-2025 gas chromatograph equipped with GL Science Inert Cap5 (70−310 °C). HRMS was measured using JEOL JMS-T100LP. Preparative column chromatography was performed with Fuji Silysia BW-4:10MH silica gel or YMC_GEL Silica (6 nm I-40−63 μm). Thin layer chromatography (TLC) was carried out on Merck 25 TLC silica gel 60 F_{254} aluminum sheets.

Typical Procedure for the Reaction of 5-Methyl-1,3-cyclohexanedione with Alcohol in the Presence of Pd/C under an Ethylene Atmosphere. To a mixture of 5-methyl-1,3-cyclohexanedione (0.5 g, 3.96 mmol) and 5% Pd/C, the alcohol derivatives (120 equiv) were added. The reaction mixture was capped in an autoclave under 3 atm pressure of ethylene gas. The reaction mixture was heated to 130 °C for several hours. The reaction mixture was cooled to ambient temperature and then filtered through Celite, the solvent was removed *in vacuo*, and the obtained residue was purified by silica-gel column chromatography (hexane/ethyl acetate (10:1)).

*3,5-Dimethoxytoluene (**2a**).*[15] 0.52 g, 86% yield. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.34 (s, 2H), 6.28 (s, 1H), 3.79 (s, 6H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 140.1, 107.1, 97.5, 55.1, 21.8; IR (cm^{-1}) 91737, 1595, 1461, 1426, 1372, 1345, 1320, 1295, 1236, 1204, 1148, 1097, 1044, 962, 936, 920, 828, 685, 633, 607. Anal. calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 71.08; H, 7.99.

*3,5-Diethoxytoluene (**2b**).*[16] 0.57 g, 80% yield. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, J = 2.0 Hz, 2H), 6.27 (t, J = 2.0 Hz, 1H), 3.95−4.00 (m, 4H), 2.27 (s, 3H), 1.38 (t, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 21.8, 63.2, 98.4, 107.6, 140.0, 160.0; IR (cm^{-1}): 1592, 1467, 1390, 1368, 1342, 1318, 1292, 1240, 1153, 1114, 1090, 1059, 996, 981, 817, 733, 684, 586. Anal. calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.29; H, 9.09.

*3,5-Dipropyloxytoluene (**2c**).* 0.7 g, 85% yield. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.32 (d, J = 1.6 Hz, 2H), 6.28 (t, J = 2.2 Hz, 1H), 3.90 (t, J = 6.4 Hz, 4H), 2.28 (s, 3H), 1.77−1.82 (m, 4H), 1.03 (t, J = 7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 140.0, 107.6, 98.5, 69.4, 22.7, 21.8, 10.6; IR (cm^{-1}) 1738, 1372, 1234, 1158, 1096, 1044, 846, 805, 633, 607. Anal. calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.680. Found: C, 74.80; H, 9.92.

*3,5-Dibutyloxytoluene (**2d**).* 0.81 g, 86% yield. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, J = 2.0 Hz, 2H), 6.27 (t, J = 2.0 Hz, 1H), 3.91 (t, J = 6.6 Hz, 4H), 2.28 (s, 3H), 1.70−1.77 (m, 4H), 1.40−1.51 (m, 4H), 0.96 (t, J = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 139.9, 107.5, 98.4, 67.5, 31.4, 21.4, 21.8, 19.3, 13.9; IR (cm^{-1}) 1593, 1463, 1383, 1344, 1319, 1291, 1156, 1069, 988, 827, 734, 684. Anal. calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.14; H, 10.52.

*3,5-Dipentyloxytoluene (**2e**).* 0.89 g, 85% yield. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, J = 2.0 Hz, 2H), 6.27 (t, J = 2.0 Hz, 1H), 3.91 (t, J = 6.6 Hz, 4H), 2.28 (s, 3H), 1.74−1.78 (m, 4H), 1.34−1.38 (m, 8H), 0.92 (t, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 139.9, 107.5, 98.4, 67.8, 29.1, 28.3, 22.5, 21.8, 14.1; IR (cm^{-1}) 1593, 1464, 1383, 1343, 1321, 1291, 1156, 1059, 824, 807, 730, 684. Anal. calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.14; H, 11.02.

*3,5-Dihexyloxytoluene (**2f**).* 1.01 g, 88% yield. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, J = 2.0 Hz, 2H), 6.27 (t, J = 2.0 Hz, 1H), 3.91 (t, J = 6.6 Hz, 4H), 2.28 (s, 3H), 1.75 (q, J = 4.9 Hz, 4H), 1.32−1.46 (m, 12H), 0.90 (t, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 140.0, 107.6, 98.4, 67.9, 31.7, 29.4, 25.8, 22.7, 21.8, 14.1; IR (cm^{-1}) 1738, 1595, 1465, 1372, 1235, 1166, 1044, 845, 633, 606. Anal. calcd for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 78.09; H, 11.40.

Preparation of 4-Substituted But-3-en-2-one Derivatives. The aldehyde (1 equiv) was suspended in a mixture of acetone/water (5 mL/5 mL). A 1% aqueous solution of sodium hydroxide (10 mL) was added slowly to the reaction mixture. The reaction mixture was heated to 65 °C for 4 h. The reaction mixture was cooled to ambient temperature; water (20 mL) and toluene (20 mL) were added. The organic phase was separated, washed with brine, and dried over magnesium sulfate. The solution was then filtered, and the solvent was removed *in vacuo* to give the product.

*4-(4-Methoxyphenyl)-3-buten-2-one (**3**).*[17] 6.14 g, 95% yield. Yellow solid; mp 68−70 °C (lit.[17] 70−72 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.51−7.44 (m, 2H), 7.46 (d, J = 16.0 Hz, 1H), 6.94−6.89 (m, 2H), 6.59 (d, J = 16.0 Hz, 1H), 3.82 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 161.5, 143.2, 129.9, 127.0, 124.9, 114.4, 55.3, 27.3; IR (cm^{-1}) 3034, 2994, 2961, 1720, 1640, 1591, 1508, 817; GCMS: m/z calcd for $C_{11}H_{12}O_2$ 176.08, found 176.1. Anal. calcd

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for $C_{11}H_{12}O_2$: C, 74.96; H, 6.81. Found: C, 74.75; H, 6.64. The spectral data were identical with those previously reported.[17]

*4-(4-Metylphenyl)-3-buten-2-one (**4**).*[18] 6 g, 90% yield. Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.51 (m, 3H), 7.26−7.20 (m, 2H), 6.68 (d, J = 16.0 Hz, 1H), 2.38 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 143.6, 141.1, 131.8, 129.8, 128.4, 126.4, 27.5, 21.6; IR (cm^{-1}) 3034, 2994, 2961, 1720, 1640, 1591, 1508, 817; GCMS: m/z calcd for $C_{11}H_{12}O$ 160.09, found 160.20. Anal. calcd for $C_{11}H_{12}O$: C, 82.45; H, 7.49. Found: C, 82.23; H, 7.60. The spectral data were identical with those previously reported.[18]

Preparation of 5-Substituted 1,3-Cyclohexanedione Derivatives (1b−1e). To a stirred solution of (1.1 equiv) sodium ethoxide (freshly prepared) under argon was added diethylmalonate (1.1 equiv). The reaction mixture was stirred under ambient temperature for 20 min. 4-Substituted but-3-en-2-one (1 equiv) was dissolved in ethanol (20 mL) and added dropwise to the reaction mixture followed by refluxing with constant stirring for 12 h. An aqueous solution of sodium hydroxide (2 M) was added, and the reaction mixture was refluxed for 2 h. Excess ethanol was removed by evaporation followed by quenching with an aqueous solution of hydrochloric acid (5 M) and refluxing for 6 h. Then the mixture was left to cool to ambient temperature, extracted with ethyl acetate, and dried with magnesium sulfate. The solvent was removed, and the title compound was purified by recrystallization.

*5-Phenyl-1,3-cyclohexanedione (**1b**).*[19] 5.02 g, 78% yield. Solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 185−188 °C (lit.[19] 86−187 °C); ^{1}H NMR (400 MHz, CD_3OD) δ 7.20−7.34 (m, 5H), 5.42 (s, 2H), 3.32−3.39 (m, 1H), 2.5−2.7 (m, 4H); IR (cm^{-1}) 3025, 2942, 1681, 1553, 1349, 1185, 831; GCMS: m/z calcd for $C_{12}H_{12}O_2$ 188.08, found 188.2. Anal. calcd for $C_{12}H_{12}O_2$: C, 76.56; H, 6.38. Found: C, 76.41; H, 6.43. The spectral data were identical with those previously reported.[19]

*5-(4-Methylphenyl)-1,3-cyclohexanedione (**1c**).* 5.04 g, 80% yield. Pale buff-colored solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 180−184 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.10−7.17 (m, 4H), 5.42 (s, 2H), 3.32−3.35 (m, 1H), 2.45−2.63 (m, 4H), 2.28 (s, 3H); IR (cm^{-1}) 3025, 2942, 1681, 1553, 1349, 1185, 831; GCMS: m/z calcd for $C_{13}H_{14}O_2$ 202.10, found 202.00 Anal. calcd for $C_{13}H_{14}O_2$: C, 77.18; H, 6.92. Found: C, 76.95; H, 6.99.

*5-(4-Methoxylphenyl)-1,3-cyclohexanedione (**1d**).* 4.77 g, 77% yield. Buff-colored solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 179.5−183.5 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.20−7.26 (d, J = 8.8 Hz, 2H), 6.85−6.88 (d, J = 8.8 Hz, 2H), 5.41 (s, 2H), 3.76 (s, 3H), 3.26−3.33 (m, 1H), 2.47−2.65 (m, 4H); IR (cm^{-1}) 3019, 2956, 1601, 1508, 1292, 1216, 1120, 824; GCMS: m/z calcd for $C_{13}H_{14}O_3$ 218.09, found 218.20. Anal. calcd for $C_{13}H_{14}O_3$: C, 71.53; H, 6.42. Found: C, 71.36; H, 6.46.

*5-Isopropyl-1,3-cyclohexanedione (**1e**).*[20] 5.43 g, 79% yield. Pale yellow solid after column chromatography (hexane/ethyl acetate (1:2)); mp 57−62 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.09 (s, 1H, OH), 5.48 (s, 1H, enol), 3.39 (t, 2H keto form), 2.40 (m, 2H), 1.89−1.92 (m, 1H), 1.58−1.63 (m, 1H), 0.94 (d, J = 8.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.2, 192.4, 57.7, 36.2, 31.2, 19.3; IR (cm^{-1}) 2961, 1562, 1365, 1330, 1299, 1149, 833; GCMS: m/z calcd for $C_9H_{14}O_2$ 154.00, found 154.20. Anal. calcd for $C_9H_{14}O_2$: C, 70.08; H, 9.09. Found: C, 69.94; H, 9.07. The spectral data were identical with those previously reported.[20]

General Procedure for Oxidation of 5-Substituted 1,3-Cyclohexanedione. To a mixture of 1,3-cyclohexanedione derivatives (0.5 g, 1 equiv) and 5% Pd/C methanol (120 equiv) was added followed by trimethyl orthoformate (2 equiv). The reaction mixture was capped in an autoclave under 3 atm of pressure of ethylene gas. The reaction mixture was heated to 130 °C for 48 h. The reaction mixture was cooled to ambient temperature and then filtered through Celite, the solvent was removed *in vacuo*, and the obtained residue was purified by silica-gel column chromatography (hexane/ethyl acetate (10:1)).

*3,5-Dimethoxy-1,1′-biphenyl (**2g**).*[15] 0.42 g, 73% yield. Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.7 Hz, 2H), 7.44 (t, J = 7.5 Hz, 2H), 7.36 (t, J = 7.3 Hz, 2H), 6.73 (d, J = 2.4 Hz, 2H), 6.47 (t, J = 2.2 Hz, 1H), 3.86 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 143.5, 141.2, 128.7, 127.5, 127.2, 105.5, 99.3, 55.4; IR (cm^{-1}) 2998, 2933, 1591, 1574, 1415, 1335, 1151, 1064, 830; GCMS: m/z calcd for $C_{14}H_{14}O_2$ 214.10, found 214.19. Anal. calcd for $C_{14}H_{14}O_2$: C, 78.47; H, 6.53. Found: C, 78.50; H, 6.83. The spectral data were identical with those previously reported.[15]

*3,5-Dimethoxy-4′-methyl-1,1′-biphenyl (**2h**)..*[21,22] 0.39 g, 70% yield. White solid; mp 57−59 °C (lit.[22] 57−59 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.7 Hz, 2H), 7.23 (d, J = 7.6 Hz, 2H), 6.71 (d, J = 2.4 Hz, 2H), 6.45 (t, J = 2.2 Hz, 1H), 3.83 (s, 6H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 143.8, 138.7, 137.7, 129.7, 127.3, 105.6, 99.4, 55.7, 21.4; IR (cm^{-1}) 3018, 2956, 1588, 1453, 1422, 1346, 1204, 1149, 807; GCMS: m/z calcd for $C_{15}H_{16}O_2$ 228.12, found 228.10. Anal. calcd for $C_{15}H_{16}O_2$: C, 78.91; H, 7.01. Found: C, 78.91; H, 7.20. The spectral data were identical with those previously reported.[21,22]

*3,4′,5-Trimethoxy-1,1′-biphenyl (**2i**)..*[23,24] 0.39 g, 70% yield. White solid; mp 59−62 °C (lit.[24] 58−59 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 6.64 Hz, 2H), 6.95 (d, J = 6.68 Hz, 2H), 6.72 (d, J = 2.2 Hz, 2H), 6.46 (t, J = 2.2 Hz, 1H), 3.87 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 159.3, 143.1, 133.7, 128.2, 114.1, 105.1, 98.7, 55.4; IR (cm^{-1}) 3020, 2994, 1588, 1455, 1422, 1204, 1149, 810; GCMS: m/z calcd for $C_{15}H_{16}O_3$ 244.11, found 244.23. Anal. calcd for $C_{15}H_{16}O_3$: C, 73.74; H, 6.55. Found: C, 73.91; H, 6.74. The spectral data were identical with those previously reported.[23,24]

*1,3-Dimethoxy-5-isopropylbenzene (**2j**).* 0.31 g, 52% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (d, J = 2.4 Hz, 2H), 6.21 (t, J = 2.2 Hz, 1H), 3.69 (s, 6H), 2.721−2.79 (m, 1H, CH), 1.15 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ160.6, 150.5, 103.8, 96.4, 54.8, 33.4, 22.6; IR (cm^{-1}) 2996, 2957, 1593, 1459, 1426, 1201, 1148, 1044, 830; GCMS: m/z calcd for $C_{11}H_{16}O_2$ 180.12, found 180.39. Anal. calcd for $C_{11}H_{16}O_2$: C, 73.28; H, 8.88. Found: C, 73.02; H, 9.01.

Preparation of 4,5-Disubstituted 1,3-Cyclohexanedione Derivatives (1f, 1g). To a stirred solution of freshly prepared sodium ethoxide (1 equiv) under argon was added ethyl phenyl acetate derivatives (1 equiv). The reaction mixture was stirred under ambient temperature for 20 min. Benzalacetone (1 equiv) was dissolved in ethanol (30 mL) and added dropwise to the reaction mixture followed by refluxing with constant stirring for 12 h. Water was then added, and the thick brown precipitate was filtered. The filtrate was concentrated, acetic acid was added to give a yellow gum, which was ether extracted, and the ether solution was dried and concentrated *in vacuo*.

*4,5-Diphenyl-1,3-cyclohexanedione (**1f**).*[25] 3.43 g, 38% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 159−163 °C (lit.[25] 160−161 °C); ^{1}H NMR (400 MHz, CD_3OD) δ 7.00−7.17 (m, 6H), 6.80−6.83 (dd, J = 2 Hz, 3.6 Hz, 2H), 6.71−7.74 (m, 2H), 5.7 (s, 1H, enol), 3.79−3.94 (m, 2H), 3.49−3.59 (m, 2H), 2.82−2.93 (m, 1H), 2.56−2.63 (dd, J = 4.8 Hz, 4.8 Hz, 1H) ppm; IR (cm^{-1}) 3029, 2359, 1941, 1591, 1490, 1416, 1320, 1213, 1185, 1074, 998, 851; GCMS: m/z calcd for $C_{18}H_{16}O_2$ 264.32, found 264.10. Anal. calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.50; H, 6.11.

*4-(4-Methylphenyl)-5-phenyl-1,3-cyclohexanedione (**1g**).* 3.33 g, 35% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 191−194 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.06−7.19 (m, 4H), 6.81−7.97 (m, 5H), 5.42 (s, 2H), 3.76−3.89 (m, 2H), 3.46−3.52 (m, 1H), 2.81−2.90 (m, 2H), 2.55−2.61 (dd, J = 4.8 Hz, 4.8 Hz, 1H); IR (cm^{-1}) 2904, 2358, 1698, 1607, 1557, 1453, 1339, 1239, 1209, 1075, 961, 831; GCMS: m/z calcd for $C_{19}H_{18}O_2$ 278.35, found 278.90. Anal. calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 81.73; H, 6.44.

Preparation of Multisubstituted 1,3-Cyclohexanedione Derivatives (1h−1r). To a solution of ketone (1.2 equiv) in THF (50 mL) was added *t*-BuOK (1.2 equiv) at room temperature, and then the mixture was stirred at 0 °C for 20 min. To this mixture the unsaturated ester (1 equiv) was added dropwise at 0 °C. The reaction mixture was stirred for 24 h. The reaction mixture was quenched with dil. HCl and was stirred for 2 h followed by extraction from ethyl acetate. Then, the organic layer was separated, and the organic solvent was evaporated *in vacuo* to give the dione.

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*4,5-Dimethyl-1,3-cyclohexanedione (**1h**).*[26] 1.57 g, 32% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 95−98 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 5.29 (s, 1H, enol), 3.50−3.55 (m, 2H), 2.43−2.49 (dd, J = 4.8 Hz, 4.8 Hz, 1H), 2.13−2.22 (m, 2H), 2.01−2.09 (m, 1H), 1.83−1.94 (m, 1H), 1.17−1.19 (d, J = 6.8 Hz, 3H), 1.07−1.09 (d, J = 6.8 Hz, 3H); IR (cm^{-1}) 2981, 2932, 2891, 1868, 1588, 1514, 1462, 1359, 1310, 1221, 1189, 1154, 1082, 952, 845; GCMS: m/z calcd for $C_8H_{12}O_2$ 140.18. Found 140.20. Anal. calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.28; H, 8.71.

*4-Methyl-5-phenyl-1,3-cyclohexanedione (**1i**).* 3.15 g, 55% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 145−148 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.20−7.34 (m, 5H), 5.35 (s, 1H, enol), 3.53−3.59 (m, 1H), 2.92−3.00 (m, 1H), 2.58−2.78 (m, 2H), 2.44−2.54 (m, 2H), 0.88−0.99 (d, J = 7.6 Hz, 3H); IR (cm^{-1}) 2875, 1888, 1600, 1495, 1454, 1372, 1325, 1225, 1176, 1051, 970, 849; GCMS: m/z calcd for $C_{13}H_{14}O_2$ 202.25, found 202.10. Anal. calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.20; H, 6.98.

*4-Ethyl-5-methyl-1,3-cyclohexanedione (**1j**).* 3.14 g, 58% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 129−130 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 2.38−3.2.45 (m, 3H), 2.19−2.27 (q, J = 7.3 Hz, 2H), 2.10−2.16 (m, 3H), 1.04−1.06 (d, J = 6 Hz, 3H), 0.88−0,99 (t, J = 7.6 Hz, 2H); IR (cm^{-1}) 2991, 2821, 1761, 1587, 1456, 1398, 1232, 1204, 1119, 1007, 976, 843; GCMS: m/z calcd for $C_9H_{14}O_2$ 154.21, found 154.20. Anal. calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.95; H, 9.14.

*4-Ethyl-5-phenyl-1,3-cyclohexanedione (**1k**).* 4.29 g, 70% yield. White solid after isolation by silica-gel column chromatography (hexane/ethyl acetate (1:2)); mp 127−131 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.20−7.37 (m, 5H), 2.65−2.73 (m, 3H), 2.55−2.62 (dd, J = 4.8 Hz, 4.8 Hz, 3H), 2.26−2.33 (q, J = 7.3 Hz, 2H), 0.91−0,96 (t, J = 7.4 Hz, 2H); IR (cm^{-1}) 2965, 2878, 1584, 1506, 1369, 1326, 1302, 1221, 1172, 987, 848, 759; GCMS: m/z calcd for $C_{14}H_{16}O_2$ 216.28, found 216.23. Anal. calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.47; H, 7.45.

*2,4,5-Trimethyl-1,3-cyclohexanedione (**1l**).* 2.76 g, 51% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 142−146 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 2.50−2.58 (m, 2H), 2.16−2.28 (m, 1H), 1.97−2.06 (m, 1H), 1.79−1.89 (m, 1H), 1.63 (br s, 3H), 1.17−1.19 (d, J = 6.8 Hz, 3H), 1.07−1.09 (d, J = 6.4 Hz, 3H); IR (cm^{-1}) 2975, 2948, 1740, 1709, 1591, 1458, 1238, 1163, 932, 898; GCMS: m/z calcd for $C_9H_{14}O_2$ 154.00, found 154.20. Anal. calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.95; H, 8.95.

*2,4-Dimethyl-5-phenyl-1,3-cyclohexanedione (**1m**).* 4.29 g, 70% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 208−210 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.20−7.34 (m, 5H), 3.52−3.58 (m, 2H), 2.95−3.04 (m, 1H), 2.64−2.72 (m, 1H), 2.53−2.61 (dd, J = 4 Hz, 4.4 Hz, 1H), 1.71 (br s, 3H), 0.88−0.99 (d, J = 7.2 Hz, 3H); IR (cm^{-1}) 2990, 2931, 2602, 1705, 1631, 1563, 1497, 1369, 1234, 1369, 1234, 1211, 1098, 1017, 973, 896; GCMS: m/z calcd for $C_{14}H_{16}O_2$ 216.28, found 216.10. Anal. calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.51; H, 7.45.

*2,4,5-Triphenyl-1,3-cyclohexanedione (**1n**).* 6.85 g, 71% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 215−219 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.09−7.37 (m, 15H), 4.04−4.16 (m, 2H), 3.60−3.68 (m, 1H), 2.99−3.08 (m, 1H), 2.76−2.83 (dd, J = 4.8 Hz, 4.8 Hz, 1H); IR (cm^{-1}) 3025, 2901, 1690, 1574, 1493, 1377, 1302, 1268, 1073, 1029, 951, 907; GCMS: m/z calcd for $C_{24}H_{20}O_2$ 340.15, found 340.21. Anal. calcd for $C_{24}H_{20}O_2$: C, 84.68; H, 5.92. Found: C, 84.44; H, 5.98.

*2,4-Diphenyl-5-methyl-1,3-cyclohexanedione (**1o**).* 7.91 g, 65% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 153−157 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.17−7.28 (m, 10H), 3.40−3.49 (m, 2H), 2.61−2.72 (m, 2H), 2.40−2.52 (m, 1H), 0.98−1.65 (d, J = 4.8 Hz, 1H); IR (cm^{-1}) 3032, 2964, 2944, 1604, 1557, 1495, 1385, 1322, 1269, 1172, 1015, 959, 898; GCMS: m/z calcd for $C_{19}H_{18}O_2$ 278.13, found 278.10. Anal. calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 81.74; H, 6.52.

*2,5-Dimethyl-4-phenyl-1,3-cyclohexanedione (**1p**).* 6.05 g, 64% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 136−139 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.13−7.35 (m, 5H), 3.25−3.36 (m, 1H), 2.47−2.59 (m, 2H), 2.26−2.36 (m, 2H), 1.72 (br s, 3H), 0.91−0.95 (d, J = 4.8 Hz, 3H); IR (cm^{-1}) 2922, 2868, 2639, 1680, 1603, 1551, 1454, 1319, 1253, 1079, 1061, 909, 822; GCMS: m/z calcd for $C_{14}H_{16}O_2$ 216.28, found 216.20. Anal. calcd for $C_{14}H_{16}O_2$: C, 77.97; H, 7.56. Found: C, 77.44; H, 7.23.

*4,5-Diphenyl-2-methyl-1,3-cyclohexanedione (**1q**).* 5.92 g, 75% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 166−169 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.00−7.21 (m, 10H), 3.88−3.92 (d, J = 9.6 Hz, 1H), 3.44−3.51 (m, 1H), 2.83−2.92 (dd, J = 10 Hz, 9.6 Hz, 1H), 2.63−2.70 (dd, J = 4.4 Hz, 4.8 Hz, 1H), 1.77 (br s, 3H); IR (cm^{-1}) 3028, 2951, 2901, 1683, 1573, 1460, 1403, 1293, 1223, 1172, 1021, 1172, 1021, 974, 863; GCMS: m/z calcd for $C_{19}H_{18}O_2$ 278.13, found 278.20. Anal. calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 81.83; H, 6.27.

*2,4-Dimethyl-5-(4-methylphenyl)-1,3-cyclohexanedione (**1r**).* 4.72 g, 78% yield. White solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 186−190 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.09−7.15 (m, 5H), 3.44−3.50 (m, 1H), 2.91−3.01 (m, 1H), 2.57−2.67 (m, 1H), 2.46−2.53 (m, 1H), 2.30 (s, 3H), 1.69 (br s, 3H), 0.84−0.88 (d, J = 7.2 Hz, 3H); IR (cm^{-1}) 2969, 2926, 2868, 1597, 1558, 1426, 1360, 1262, 1019, 999, 878; GCMS: m/z calcd for $C_{15}H_{18}O_2$ 230.13, found 230.20. Anal. calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 77.93; H, 7.89.

Oxidation of Multisubstituted 1,3-Cyclohexanedione Derivatives. To a mixture of 1,3-cyclohexanedione derivatives (0.5 g, 1 equiv), 5% Pd/C and methanol (120 equiv) was added followed by trimethyl orthoformate. The reaction mixture was capped in an autoclave under 3 atm of pressure of ethylene gas. The reaction mixture was heated to 130 °C for 48 h. The reaction mixture was cooled to ambient temperature and then filtered through Celite; the solvent was removed *in vacuo*, and the residue was purified by silica-gel column chromatography (hexane/ethyl acetate (10:1)).

*3′,5′-Dimethoxy-o-terphenyl (**2k**).* 0.41 g, 75% yield. Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04−7.21 (m, 10H), 6.57 (s, 2H), 3.86 (s, 3H), 3.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 158.1, 143.4, 141.6, 136.7, 131.6, 131.2, 129.7, 127.5, 127.3, 126.3, 126.1, 106.5, 97.9, 55.8, 55.4; IR (cm^{-1}) 3006, 2941, 2837, 1461, 1343, 1203, 1064, 1039; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{20}H_{19}O_2$ 291.1385, found 291.1386.

*1,5-Dimethoxy-2,3,5-triphenylbenzene (**2l**).* 0.43 g, 80% yield. White solid; mp 146−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10−7.52 (m, 15H), 6.83 (s, 1H), 3.78 (s, 3H), 2.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.6, 156.3, 142.3, 141.5, 136.9, 134.1, 131.4, 130.8, 129.8, 127.8, 127.7, 127.6, 127.5, 127.1, 126.5, 126.2, 123.7, 108.9, 60.2, 56.1; IR (cm^{-1}) 3100, 2910, 1454, 1385, 1234, 1094, 1015; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{26}H_{23}O_2$ 367.1698, found 367.1717.

*3′,5′-Dimethoxy-4′-methyl-o-terphenyl (**2m**).* 0.37 g, 69% yield. Buff-colored solid; mp 135−139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06−7.21 (m, 10H), 6.72 (s, 1H), 3.86 (s, 3H), 3.28 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 156.8, 141.7, 140.1, 137.1, 131.4, 192.8, 127.6, 127.4, 126.3, 126.1, 118.9, 108.1, 60.1, 55.7, 9.1; IR (cm^{-1}) 3010, 2925, 2890, 1439, 1389, 1332, 1260, 1189, 1116, 1028; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{21}H_{21}O_2$ 305.1542, found 305.1559.

*3′,5′-Dimethoxy-4-methyl-o-terphenyl (**2n**).* 0.42 g, 78% yield. Buff-colored solid; mp 155−158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06−7.17 (m, 5H), 6.93−6.99 (m, 4H), 6.56 (s, 2H), 3.85 (s, 3H), 3.74 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 158.2, 143.4, 141.9, 135.6, 133.7, 131.5, 129.8, 128.2, 127.6, 126.3, 122.7, 106.6, 97.9, 55.9, 55.5, 21.3; IR (cm^{-1}) 3020, 2959, 2837, 1584, 1477, 1461, 1343, 1236, 1158, 1107; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{21}H_{21}O_2$ 305.1542, found 305.1529.

*3,5-Dimethoxy-2-methy-1,1′-biphenyl (**2o**).* 0.39 g, 70% yield. Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.40 (m, 5H), 6.47 (d, J = 2.4 Hz, 1H), 6.41 (d, J = 2.4 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 158.1,

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143.5, 142.1, 129.2, 128.3, 128.1, 126.5, 116.7, 105.6, 97.4, 55.6, 55.4, 12.7; IR (cm^{-1}) 3010, 2995, 2835, 1455, 1412, 1329, 1204, 1143, 1055, 1042; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{15}H_{17}O_2$ 229.1229, found 229.1230.

*2-Ethyl-3,5-dimethoxy-1,1′-biphenyl (**2p**).* 0.41 g, 74% yield. Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29−7.41 (m, 5H), 6.48 (d, J = 2.4 Hz, 1H), 6.35 (d, J = 2.4 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 2.48 (q, J = 7.6 Hz, 2H), 1.01 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 157.8, 143.3, 142.2, 129.1, 127.9, 126.8, 123.27, 105.5, 97.7, 55.5, 55.3, 19.9, 14.9; IR (cm^{-1}) 3004, 2958, 2870, 1462, 1414, 1351, 1203, 1144, 1053, 1041; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{16}H_{19}O_2$ 243.1385, found 243.1370..

*3,5-Dimethoxy-2,4,4′-dimethy-1,1′-biphenyl (**2q**).* 0.43 g, 77% yield. Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (s diffuse, 4H), 6.55 (s, 1H), 3.78 (s, 3H), 3.73 (s, 3H), 2.39 (s, 3H), 2.20 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 156.1, 140.6, 139.3, 136.4, 129.2, 128.8, 120.8, 118.3, 108.1, 59.9, 55.6, 21.2, 13.2, 9.1; IR (cm^{-1}) 3040, 2934, 2863, 1577, 1480, 1445, 1388, 1277, 1232, 1117, 1019; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{17}H_{21}O_2$ 257.1542, found 257.1529.

*3,5-Dimethoxy-2,4-dimethy-1,1′-biphenyl (**2r**).* 0.38 g, 68% yield. Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31−7.43 (m, 5H), 6.56 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 2.21 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 155.1, 141.1, 139.6, 128.2, 126.9, 125.7, 119.6, 117.4, 106.8, 58.8, 54.5, 12.1, 8.05; IR (cm^{-1}) 3002, 2961, 1566, 1463, 1392, 1257, 1114, 1007; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{16}H_{19}O_2$ 243.1385, found 243.1374.

*4′-Methyl-2′,6′-dimethoxy-m-terphenyl (**2s**).* 0.38 g, 71% yield. Pale yellow solid; mp 145−147 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28−7.47 (m, 10H), 6.70 (s, 1H), 3.76 (s, 3H), 2.98 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 156.1, 137.8, 137.3, 134.2, 130.9, 130.8, 130.6, 130.2, 128.8, 128.7, 128.5, 128.1, 127.7, 126.7, 126.6, 122.1, 108.4, 60.3, 55.8, 21.1; IR (cm^{-1}) 3063, 2935, 2848, 1529, 1461, 1388, 1246, 1192, 1097; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{21}H_{21}O_2$ 305.1542, found 305.1558.

*2,4-Dimethoxy-3,6-dimethy-1,1′-biphenyl (**2t**).* 0.42 g, 75% yield. Buff-colored solid; mp 90−93 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21−7.41 (m, 5H), 6.56 (s, 1H), 3.81 (s, 3H), 3.30 (s, 3H), 2.16 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 156.7, 137.9, 134.7, 130.3, 128.2, 127.9, 126.5, 116.8, 107.7, 60.2, 55.6, 20.7, 8.9; IR (cm^{-1}) 3055, 2936, 1572, 1441, 1395, 1271, 1224, 1133, 1101; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{16}H_{19}O_2$ 243.1385, found 243.1382.

*1,5-Dimethoxy-2,3-dimethylbenzene (**2u**).* 0.4 g, 68% yield. Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.32 (d, J = 2.8 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 2.23 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 158.1, 138.1, 117.2, 106.3, 95.9, 55.5, 55.2, 20.4, 10.9; IR (cm^{-1}) 3095, 2937, 2835, 1591, 1493, 1416, 1314, 1200, 1148, 1111, 1059; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{10}H_{15}O_2$ 167.1072, found 167.1063.

*1,5-Dimethoxy-2,3,5-trimethylbenzene (**2v**).* 0.43 g, 75% yield. Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.48 (s, 1H), 3.79 (s, 3H), 3.67 (s, 3H), 2.25 (s, 3H), 2.13 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 156.1, 135.1, 121.4, 116.6, 108.1, 60.1, 55.7, 20.3, 11.8, 8.9; IR (cm^{-1}) 3012, 2935, 1584, 1463, 1316, 1224, 1121, 1086; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{11}H_{17}O_2$ 181.1229, found 181.1223.

*2-Ethyl-1,5-dimethoxy-3-methylbenzene (**2w**).* 0.4 g, 70% yield. Pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.29 (s, 2H), 3.72 (s, 6H), 2.54 (q, J = 7.3 Hz, 2H), 2.25 (s, 3H), 0.98 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 135.3, 116.9, 103.6, 54.6, 28.6, 20.9, 15.1, 12.9; IR (cm^{-1}) 2961, 2923, 1588, 1456, 1412, 1257, 1009, 863; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{11}H_{17}O_2$ 181.1229, found 181.1223.

Bromination of 3,5-Dimethoxytoluene. To a solution of 3,5-dimethoxytoluene (0.76 g, 5.0 mmol) in acetonitrile (10 mL) freshly crystallized *N*-bromosuccinimide (0.93 g, 5.25 mmol) was added. The mixture was stirred at 25 °C for 1 h under an argon atmosphere, then after completing the reaction, the mixture was quenched with a saturated aqueous sodium thiosulfate solution (30 mL), then extracted by diethyl ether three times, and washed was brine solution. The combined organic layer was dried over anhydrous sodium sulfate and then filtered, followed by evaporation *in vacuo* to give a white solid of 3,5-dimethoxybenzyl bromide (**5**) which was used without further purification (1.05 g, 91%).

*3,5-Dimethoxybenzyl Bromide (**5**).* Mp 70−73 °C; ^1H NMR (400 MHz, $CDCl_3$) 3.79 (s, 6H), 4.42 (s, 2H), 6.39 (s, 1H), 6.53 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 139.8, 107.0, 100.6, 55.4, 33.7; IR (cm^{-1}) 3002, 2965, 2935, 2836, 1614, 1590, 1474, 1455, 1429, 1325, 1205, 1153, 1115, 1068, 1056, 939, 864, 852, 821, 697, 645, 600; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_9H_{12}BrO_2$ 231.0021, found 230.9993.

Oxidation Reaction of 3,5-Dimethoxybenzyl Bromide.[27] To a mixture of 3,5-dimethoxybenzyl bromide (4.36 g, 18.9 mmol) and hexamethylenetetramine (2.65 g, 18.9 mmol) water (40 mL) was added. The reaction mixture was refluxed for 12 h at 120 °C under an argon atmosphere. After completion of the reaction the reaction mixture was quenched with a 1 M aqueous solution of hydrochloric acid (10 mL) and then extracted three times with ethyl acetate. The combined organic layers were washed with a saturated aqueous solution of sodium chloride, and the organic layer was dried over anhydrous sodium sulfate. The organic solution was filtered and then concentrated *in vacuo* to give a white solid of 3,5-dimethoxy benzaldehyde (**6**) which was used in the next step without further purification (3.10 g, 99%).

*3,5-Dimethoxybenzaldehyde (**6**).* Mp 47−50 °C (lit.[27] 47−50 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 6H), 6.70 (s, 1H), 7.05 (s, 2H), 9.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.9, 161.2, 138.4, 107.1, 55.6; IR (cm^{-1}) 1693, 1590, 1467, 1429, 1396, 1384, 1344, 1297, 1205, 1190, 1157, 1064, 1049, 949, 925, 872, 821, 729, 683; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_9H_{11}O_3$ 167.0708, found 167.0734.

Preparation of Diethyl 3,5-Dimethoxybenzylphosphonate (7).[28] A mixture of 3,5-dimethoxybenzyl bromide (5.0 g, 21.0 mmol) and triethyl phosphite (3.8 g, 23.0 mmol) was refluxed at 80 °C for 12 h under an argon atmosphere. After completion of the reaction, the reaction mixture was distilled under vacuum to give diethyl 3,5-dimethoxybenzylphosphonate (**7**) as a yellow oil (6.05 g, 100%).

*3,5-Dimethoxybenzylphosphonate (**7**).* ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J = 7.0 Hz, 6H), 3.09 (d, J = 21.6 Hz, 2H), 3.78 (s, 6H), 4.01−4.05 (m, 4H), 6.36 (s, 1H), 6.46 (dd, J = 2.4, 2.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 133.7, 107.9, 99.18, 62.3, 62.2, 55.4, 34.7, 33.9, 16.5; IR (cm^{-1}) 1593, 1517, 1461, 1429, 1389, 1346, 1324, 1297, 1246, 1204, 1149, 1097, 1047, 1021, 952, 844, 780, 731, 692, 611, 578; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{13}H_{22}O_5P$ 289.1205, found 289.1220.

Preparation of Diethyl 4-Methoxybenzylphosphonate (8). A mixture of 4-methoxybenzyl bromide (17.0 g, 85.0 mmol) and triethyl phosphite (16.3 mL, 93.0 mmol) was heated at 80 °C for 5 h under an argon atmosphere. After completion of the reaction, the reaction mixture was distilled under vacuum to give a yellow oil of diethyl 4-methoxybenzylphosphonate (21.9 g, 100%).

*Diethyl 4-Methoxybenzylphosphonate(**8**).* ^1H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, J = 7.0 Hz, 6H), 3.09 (d, J = 21.2 Hz, 2H), 3.79 (s, 3H), 3.79−4.03 (m, 4H), 6.85 (d, J = 8.8 Hz, 2H), 7.21 (dd, J = 8.8, 2.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 130.7, 129.3, 123.4, 113.9, 62.0, 55.1, 33.4, 32.0, 16.3; IR (cm^{-1}) 1611, 1584, 1511, 1442, 1391, 1299, 1245, 1178, 1163, 1097, 1021, 956, 849, 782, 566; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{12}H_{20}O_4P$ 259.1099, found 259.1122.

Preparation of Trimethoxy Resveratrol (9) from 3,5-Dimethoxybenzaldehyde. Sodium hydride (0.65 g, 27.0 mmol) was added to a solution of diethyl-4-methoxybenzylphosphonate (4.65 g, 18.0 mmol) in anhydrous THF (13 mL) at 0 °C under an argon atmosphere, and then the mixture was stirred at room temperature for 10 min. To this mixture was slowly added dropwise a solution of 3,5-dimethoxy benzaldehyde (2.99 g, 18.0 mmol) in anhydrous THF (30 mL) followed by continued stirring at room temperature for 3 h. After completion the reaction mixture was quenched with ice water (30 mL) and then extracted three times with ethyl acetate, and then

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the combined organic layer was dried over anhydrous sodium sulfate and filtered. Then, the organic solvent was evaporated to give a white solid of trimethoxy resveratrol (**9**) (4.61 g, 95%) after isolation by silica-gel column chromatography (hexane/ethyl acetate (10:1)).

*Trimethoxy Resveratrol (**9**).* Mp 54−57 °C (lit.[28] 54−55 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 9H), 6.70 (t, J = 2.2 Hz, 1H), 6.65 (d, J = 2.4 Hz, 2H), 6.89−6.93 (m, 3H), 7.04 (d, J = 16.4 Hz, 1H), 7.45 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 159.4, 139.7, 129.9, 128.7, 127.8, 126.6, 114.2, 104.4, 99.6, 55.3; IR (cm^{-1}) 1736, 1587, 1509, 1457, 1425, 1344, 1325, 1314, 1300, 1277, 1246, 1207, 1192, 1175, 1150, 1110, 1063, 1029, 987, 953, 941, 927, 857, 838, 829, 820, 771, 719, 681, 637, 596, 572; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{17}H_{19}O_3$ 271.1334, found 271.1316. The spectral data were identical with those previously reported.[28]

Preparation of Trimethoxy Resveratrol (9) from 4-Methoxybenzaldehyde. Sodium hydride (0.65 g, 27.0 mmol) was added to a solution of diethyl-3,5-dimethoxybenzylphosphonate (5.18 g, 18.0 mmol) in anhydrous THF (13 mL) at 0 °C under an argon atmosphere, and then the mixture was stirred at room temperature for 10 min. To this mixture was slowly added dropwise a solution of 4-methoxy benzaldehyde (2.45 g, 18.0 mmol) in anhydrous THF (30 mL) followed by continued stirring at room temperature for 3 h. After completion the reaction mixture was quenched with ice water (30 mL) and extracted three times with ethyl acetate. Then, the combined organic layer was dried over anhydrous sodium sulfate and filtered, and the organic solvent was evaporated to give a white solid of trimethoxy resveratrol (**9**) after isolation by silica-gel column chromatography (hexane/ethyl acetate (10:1)) (4.57 g, 94%).

Preparation of Resveratrol (10).[28] In a two-necked flask, diisoropyl amine (4.65 g, 46.0 mmol) was added to aluminum chloride (6.13 g, 46.0 mmol) at room temperature, which was stirred vigorously at 110 °C for 30 min under argon atmosphere, and then a solution of trimethoxy resveratrol **6** (2.07 g, 7.66 mmol) in toluene was added dropwise at 110 °C. The reaction mixture was stirred vigorously at 110 °C for 4 h. After completion of the reaction, it was allowed to cool to 80 °C followed by quenching with chilled water (10 mL) and stirring at 45 °C for 30 min. The precipitated residue was filtered and washed with water. The wet residue was stirred with 4.5 M aqueous sodium hydroxide (5 mL) for 30 min and then washed with toluene. The aqueous layer was adjusted to pH 2 by adding 1 M hydrochloric acid (25 mL) and extracted with toluene. The organic layer was then dried over anhydrous sodium sulfate, filtered, and concentrated to give a white solid of resveratrol (**10**) after recrystallization from *i*-PrOH (1.48 g, 85%).

*Resveratrol (**10**).* Mp 253−255 °C (lit.[28] 251−252 °C); ^{1}H NMR (400 MHz, acetone-d_6) δ 6.26 (t, J = 2.2 Hz, 1H), 6.54 (d, J = 2.4 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 16.4 Hz, 1H) 7.02 (d, J = 16.4 Hz, 1H), 7.42 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 159.5, 158.2, 141.2, 130.3, 129.3, 128.7, 126.9, 116.4, 105.7, 102.5; IR (cm^{-1}) 3203, 1604, 1583, 1511, 1461, 1441, 1381, 1323, 1264, 1247, 1215, 1174, 1145, 1105, 1009, 986, 964, 829, 804, 674, 623, 602; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{14}H_{13}O_3$ 229.0865, found 229.0893.

Alternative Route for Preparation of Resveratrol. *6-(4-Methoxyphenyl)-3,5-hexadiene-2-one (**11**).* 4-Methoxycinnamaldehyde (5 g, 30.8 mmol) was suspended in a mixture of acetone/water (5 mL/5 mL). A 1% aqueous solution of sodium hydroxide (10 mL) was added slowly to the reaction mixture. The reaction mixture was heated to 65 °C for 4 h. The reaction mixture was cooled to ambient temperature. Water (20 mL) and chloroform (20 mL) were added. The organic phase was separated, washed with brine, and dried over magnesium sulfate, and the solution was filtered. The solvent was then removed *in vacuo* to give **11** (6.08 g, 82% yield). Yellow solid; mp 107−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.30 (d, J = 8.8 Hz, 2H), 7.11−7.19 (m, 1H), 6.74−6.80 (m, 3H), 6.59−6.66 (m, 1H), 6.06−610 (d, J = 15.6 Hz, 1H), 3.69 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 159.8, 142.9, 142.1, 140.1, 128.3, 127.7, 123.4, 113.2, 54.3, 26.2; IR (cm^{-1}) 2998, 2933, 1591, 1574, 1415, 1335, 1151, 1064, 830; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{13}H_{15}O_2$ 203.1072, found 203.1060.

*5-(4-Methoxystyryl)-1,3-cyclohexanedione (**12**).* To a stirred solution of freshly prepared sodium ethoxide (0.4 g, 14.8 mmol) under argon was added diethylmalonate (2.4 g, 14.8 mmol). The reaction mixture was stirred under ambient temperature for 20 min. 6-(4-Methoxyphenyl)-3,5-hexadiene-2-one (3 g, 14.8 mmol) was dissolved in ethanol (30 mL) and added dropwise to the reaction mixture which was then refluxed with constant stirring for 12 h. An aqueous solution of sodium hydroxide (2 M) was added, and the reaction mixture was refluxed for 2 h. Excess ethanol was removed by evaporation, followed by quenching with an aqueous solution of hydrochloric acid (5 M) and refluxing for 6 h. Then, the mixture was allowed to cool to ambient temperature, extracted with ethyl acetate, and dried with magnesium sulfate. The solvent was removed, and the title compound was purified by recrystallization to give **12** (2.89 g, 80% yield). Buff-colored solid after recrystallization from a mixture of hexane/ethyl acetate (5:1); mp 182−185 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.27−7.31 (d, J = 8.4 Hz, 2H), 6.80−6.85 (d, J = 8.8 Hz, 2H), 6.39−6.45 (d, J = 15.6 Hz, 1H), 6.04−6.13 (dd, J = 7.2 Hz, 7.2 Hz, 1H), 5.35 (s, 1H, enol), 3.76 (s, 3H), 2.86−2.98 (m, 1H), 2.44−2.55 (m, 3H), 2.34−2.43 (m, 2H). IR (cm^{-1}) 2995, 2954, 2835, 2360, 2338, 1887, 1506, 1370, 1275, 1215, 1182, 1119, 962, 842, 762; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{15}H_{17}O_3$ 245.1178, found 245.1165.

*4-Methoxyresveratrol (**13**).*[29] A mixture of 5-(4-methoxystyryl)-1,3-cyclohexanedione (0.5 g, 2.1 mmol) and 5% Pd/C (15 mol %) in acetonitrile (20 mL) was capped in an autoclave under 3 atm of pressure of ethylene gas. The reaction mixture was heated to 130 °C for 48 h. The reaction mixture was cooled to ambient temperature and filtered through Celite, and the solvent was removed *in vacuo* to give **13** (0.4 g, 81% yield). White solid by silica-gel column chromatography (hexane/ethyl acetate (1:1)); mp 158−163 °C (lit.[29] 158−160 °C); ^{1}H NMR (400 MHz, acetone-d_6) δ 8.2 (s, 2H), 7.51 (d, J = 8.8 Hz, 2H), 7.07 (d, J = 16.8 Hz, 1H), 6.90−6.97 (m, 3H), 6.58 (d, J = 2 Hz, 2H), 6.3 (t, J = 2 Hz, 1H), 3.8 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 161.2, 160.4, 141.6, 131.8, 129.6, 129.4, 128.3, 115.7, 106.6, 103.6, 56.4; IR (cm^{-1}) 2998, 2933, 1591, 1574, 1415, 1335, 1151, 1064, 830; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{15}H_{15}O_3$ 243.1021, found 243.1007. The spectral data were identical with those previously reported.[29]

*3,4′,5′-Trimethoxyresveratrol (**9**).*[28] To a mixture of 5-(4-methoxystyryl)-1,3-cyclohexanedione (0.5 g, 2.1 mmol) and 5% Pd/C (15 mol %), methanol (9.8 mL, 245 mmol) was added followed by trimethyl orthoformate (0.9 g, 8.2 mmol). The reaction mixture was capped in an autoclave under 3 atm of pressure of ethylene gas. The reaction mixture was heated to 130 °C for 48 h. The reaction mixture was cooled to ambient temperature and filtered through Celite, and the solvent was removed *in vacuo*, giving a white solid which, after purification by silica-gel column chromatography (hexane/ethyl acetate (1:1)), was **9** (0.45 g, 83% yield).

Oxidation of Multisubstituted 1,3-Cyclohexanedione Derivatives (Resorcinol Formation). To a mixture of 1,3-cyclohexanedione derivatives (0.5 g, 1 equiv), 5% Pd/C (15 mol %) and potassium carbonate (2 equiv) in (20 mL) acetonitrile. The reaction mixture was capped in an autoclave under 3 atm of pressure of ethylene gas. The reaction mixture was heated to 150 °C for 48 h. The reaction mixture was cooled to ambient temperature and filtered through Celite, and the solvent was removed *in vacuo*. The residue was purified by silica-gel column chromatography.

*3,5-Dihydroxy-1,1′-biphenyl (**14a**).*[31] 0.39 g, 80% yield. White solid after isolation by silica-gel column chromatography (hexane/ethyl acetate (1:1)); mp 155−158 °C (lit.[30] 155−156 °C); ^{1}H NMR (400 MHz, acetone-d_6) δ 8.45 (s, 2H, OH), 7.62 (d, J = 7.2 Hz, 2H), 7.42 (t, J = 7.2 Hz, 2H), 7.32 (t, J = 7.4 Hz, 1H), 6.71 (d, J = 2 Hz, 2H), 6.48 (t, J = 2 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d_6) δ 158.9, 143.4, 141.2, 128.8, 127.4, 126.7, 105.7, 101.8; IR (cm^{-1}) 3326, 3054, 2991, 1608, 1480, 1352, 1255, 1153, 1001; HRMS [DART+] m/z: $[M + H]^+$ calcd for $C_{12}H_{11}O_2$ 187.0759, found 187.0751.

*3′,5′-Dihydroxy-o-terphenyl (**14b**).* 0.37 g, 75% yield. Buff-colored solid after isolation by silica-gel column chromatography (hexane/ethyl acetate (2:1)); mp 95−100 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.34 (s, 1H, OH), 7.83 (s, 1H, OH), 7.04−7.35 (m, 10H), 6.53

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(d, J = 2.4 Hz, 1H), 6.43 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d_6,) δ 157.2, 155.6, 143.4, 142.1, 137.2, 131.7, 129.6, 127.6, 127.4, 125.9, 119.9, 109.1, 101.9; IR (cm^{-1}) 3361, 3001, 2980, 1616, 1455, 1435, 1337, 1262, 1155, 1072, 1005; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{18}H_{15}O_2$ 263.1072, found 263.1071.

*1,3-Dihydroxy-2,4,5-triphenylbenzene (**14c**).* 0.37 g, 76% yield. Pale yellow solid after isolation by silica-gel column chromatography (hexane/ethyl acetate (1:1)); mp 210−213 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.11 (s, 1H, OH), 7.10−7.55 (m, 15H), 6.68 (s, 1H), 6.52 (s, 1H, OH). ^{13}C NMR (100 MHz, acetone-d_6) δ 154.2, 152.1, 141.9, 141.8, 136.9, 134.1, 131.9, 131.2, 129.6, 128.2, 127.9, 127.6, 127.1, 126.4, 126.2, 120.1, 115.9, 109.2; IR (cm^{-1}) 3520, 3436, 3055, 2995, 1558, 1449, 1408, 1315, 1164, 1040; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{24}H_{19}O_2$ 339.1385, found 339.1404.

*3′,5′-Dihydroxy-4′-methyl-o-terphenyl (**14d**).* 0.29 g, 60% yield. Yellow oil after isolation by silica-gel column chromatography (hexane/ethyl acetate (2:1)); ^{1}H NMR (400 MHz, acetone-d_6) δ 8.32 (s, 1H, OH), 6.95−7.28 (m, 10H), 6.62 (s, 1H), 6.52 (s, 1H, OH), 2.19 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 155.1, 152.9, 142.1, 139.6, 136.9, 131.7, 128.1, 127.4, 126.5, 125.9, 119.4, 110, 108.7, 8.2; IR (cm^{-1}) 3498, 3055, 1598, 1478, 1406, 1307, 1244, 1067; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{19}H_{17}O_2$ 277.1229, found 277.1242.

*3′,5′-Dihydroxy-4-methyl-o-terphenyl (**14e**).* 0.39 g, 78% yield. Buff-colored solid after isolation by silica-gel column chromatography (hexane/ethyl acetate (1:1)); mp 165−168 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.34 (br s, 1H, OH), 7.73 (br s, 1H, OH), 6.94−7.16 (m, 9H), 6.53 (d, J = 2.4 Hz, 1H), 6.43 (d, J = 2.4 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 157.1, 155.6, 143.4, 142.2, 135.1, 134.1, 131.5, 129.6, 128.2, 127.4, 126.1, 119.4, 108.9, 101.6, 20.2; IR (cm^{-1}) 3344, 3019, 2920, 1601, 1454, 1433, 1337, 1272, 1151, 1006; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{19}H_{17}O_2$ 277.1229, found 277.1220.

*3,5-Dihydroxy-2-methy-1,1′-biphenyl (**14f**).* (0.35 g, 70%). Pale yellow oil after isolation by silica-gel column chromatography (hexane/ethyl acetate (1:1)); ^{1}H NMR (400 MHz, acetone-d_6) δ 8.19 (br s, 2H, OH), 7.27−7.45 (m, 5H), 6.43 (d, J = 2.4 Hz, 1H), 6.26 (d, J = 2.4 Hz, 1H), 1.99 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 156.7, 155.9, 144.1, 142.8, 129.3, 128.3, 126.9, 113.1, 108.4, 101.7, 12.3; IR (cm^{-1}) 3260, 2965, 1520, 1422, 1403, 1252, 1130, 1009; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{13}H_{12}O_2$ 201.0916, found 201.0903.

*3,5-Dihydroxy-2,4-dimethy-1,1′-biphenyl (**14g**).* 0.22 g, 45% yield. Yellow oil after isolation by silica-gel column chromatography (hexane/ethyl acetate (1:1)); ^{1}H NMR (400 MHz, acetone-d_6) δ7.97 (br s, 1H, OH), 7.08−7.48 (m, 5H), 6.36 (s, 1H), 2.16 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 156.1, 155.1, 144.2, 141.9, 130.8, 129.6, 128.2, 114.4, 111.6, 109.9, 14.3, 9.9; IR (cm^{-1}) 3391, 3004, 2924, 1592, 1455, 1411, 1302, 1230, 1149, 1090, 1025; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{14}H_{15}O_2$ 215.1072, found 215.1084.

*2-Ethyl-3,5-dihydroxy-1,1′-biphenyl (**14h**).* 0.35 g, 71% yield. Buff-colored solid after isolation by silica-gel column chromatography (benzene:ethyl acetate (5:1)); mp 80−83 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.99 (s, 2H, OH), 7.25−7.42 (m, 5H), 6.43 (d, J = 2.4 Hz, 1H), 6.21 (d, J = 2.4 Hz, 1H), 2.46 (q, J = 7.3 Hz, 2H), 1.00 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 156.2, 155.4, 143.7, 142.6, 128.8, 127.9, 126.6, 119.6, 108.2, 101.9, 19.8, 14.3; IR (cm^{-1}) 3232, 2969, 2872, 1588, 1455, 1344, 1245, 1025; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{14}H_{15}O_2$ 215.1072, found 215.1084.

*3,5-Dihydroxy-4′-methyl-1,1′-biphenyl (**14i**).*[31] 0.4 g, 81% yield. Buff-colored solid after isolation by silica-gel column chromatography (hexane/ethyl acetate (2:1)); mp 150−155 °C (lit.[31] 152−155 °C); ^{1}H NMR (400 MHz, acetone-d_6) δ 8.35 (s, 2H, OH), 7.45 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 7.2 Hz, 2H), 6.43 (d, J = 2 Hz, 2H), 6.39 (t, J = 2.2 Hz, 1H), 2.32(s, 3H). ^{13}C NMR (100 MHz, acetone-d_6,) δ 160.4, 144.9, 139.9, 138.6, 131.1, 128.2, 107.1, 103.1, 21.9; IR (cm^{-1}) 3289, 2915, 1595, 1490, 1351, 1260, 1151, 1036, 998; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{13}H_{13}O_2$ 201.0916, found 201.0913.

*3,5-Dihydroxy-2,4,4′-trimethy-1,1′-biphenyl (**14j**).* 0.17 g, 35% yield. Pale yellow oil after isolation by silica-gel column chromatography (hexane/ethyl acetate (10:1)); ^{1}H NMR (400 MHz, acetone-d_6) δ 9.0 (br s, 1H, OH), 8.11 (br s, 1H, OH), 7.15−7.37 (m, 4H), 6.37 (s, 1H), 2.37 (s, 3H), 2.31 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 154.6, 150.9, 141.6, 139.9, 139.1, 136.1, 129.2, 128.9, 128.6, 127.4, 112.1, 107.6, 20.2, 17.24, 12.7; IR (cm^{-1}) 3300, 3044, 2976, 1511, 1465, 1370, 1303, 1210, 1134, 1088, 1008; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{15}H_{16}O_2$ 229.1229, found 229.1244.

*3,5-Dihydroxy-4′-methoxy-1,1′-biphenyl (**14k**).* 0.41 g, 84% yield. White solid after isolation by silica-gel column chromatography (hexane/ethyl acetate (1:1)); mp 146−149 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.21 (s, 2H, OH), 7.52 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 8.4 Hz, 2H), 6.57 (d, J = 2 Hz, 2H), 6.32 (t, J = 2.2 Hz, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 159.4, 158.9, 142.6, 133.6, 127.7, 114.1, 105.1, 101.1, 54.6; IR (cm^{-1}) 3361, 2995, 2836, 1539, 1495, 1345, 1243, 1243, 1153, 1000; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{13}H_{13}O_3$ 217.0865, found 217.0863.

*1,3-Dihydroxy-5-isopropylbenzene (**14l**).* 0.3 g, 70% yield. Yellow oil after isolation by silica-gel column chromatography (hexane/ethyl acetate (1:1)); ^{1}H NMR (400 MHz, acetone-d_6) δ 8.14 (s, 2H, OH), 6.23 (d, J = 2.4 Hz, 2H), 6.18 (t, J = 2.2 Hz, 1H), 2.68−2.76 (m, 1H, CH), 1.16 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, acetone-$d6$) δ 158.3, 151.2, 104.9, 100.2, 33.9, 23.3; IR (cm^{-1}) 3285, 2959, 2870, 1595, 1456, 1336, 1298, 1146, 990; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_9H_{13}O_2$ 153.0916, found 153.0912.

*4′-Methyl-2′,6′-dihydroxy-m-terphenyl (**14m**).* 0.34 g, 69% yield. Orange solid after isolation by silica-gel column chromatography (hexane/ethyl acetate (1:1)); mp 117−120 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.82 (s, 1H, OH), 7.25−7.45 (m, 10H), 6.50 (s, 1H), 6.25 (s, 1H, OH), 1.99 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 154.1, 151.7, 137.8, 136.8, 134.4, 131.2, 130.9, 128.4, 127.9, 126.9, 126.6, 121.1, 114.2, 109.9, 19.9; IR (cm^{-1}) 3498, 3436, 3056, 1582, 1475, 1258, 1181, 1056; HRMS [DART+] m/z: [M + H]$^+$ calcd for $C_{19}H_{17}O_2$ 277.1229, found 277.1243

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b03037.

Copies of all ^{1}H and ^{13}C spectra (PDF)

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Notes

The authors declare no competing financial interest.

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