Synthesis of 4-Cinnamylidene-2,5-cyclohexadien-1-ones

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Lithium aluminium hydride (LAH) reduction of 4′-hydroxychalcones, followed by dehydration, yielded 4-cinnamylidene-2,5-cyclohexadien-1-ones in 19—42% yields. The LAH reduction of 4′-acetoxychalcones also gave the same products in improved yields.

It has been reported that the oxidations of 2- and 4-alkylphenols with manganese dioxide,[1] lead dioxide,[2] silver oxide,[3] potassium hexacyanoferrate(III),[4] and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone[5] (DDQ) gave 2-alkylidene-3,5-cyclohexadien-1-ones and 4-alkylidene-2,5-cyclohexadien-1-ones. Dehydrochlorination of *p*-(chloromethyl)phenol[6] and the elimination reaction of *p*-(methoxymethyl)phenols also yielded 4-methylene-2,5-cyclohexadien-1-ones, but have a limited value.[7] The lithium aluminium hydride (LAH) reduction of 2′-hydroxychalcones has been reported to give 2-phenyl-2*H*-1-benzopyrans,[8] and 2-cinnamylidene-3,5-cyclohexadien-1-one was postulated as a reaction intermediate. This was proved by obtaining pure 2-cinnamylidene-3,5-cyclohexadien-1-one and by converting the latter to 2-phenyl-2*H*-1-benzopyran[3b] (Fig. 1). We have investigated the synthesis of 4-cinnamylidene-2,5-cyclohexadien-1-ones by dehydration of 1-(*p*-hydroxyphenyl)-3-phenyl-2-propen-1-ols (III), which can be obtained by the LAH reduction of 4′-hydroxychalcones (Ia—i), and found that these reactions indeed yielded the desired compounds (IVc—i) in 19—42% yields (Fig. 1 and Table 1).

4′-Hydroxychalcones (Ia—i) were obtained by the condensation of *p*-hydroxyacetophenones and benzaldehydes with aqueous alkali. The structures of these new chalcones were determined by examining their IR and NMR spectra and by elemental analyses. All chalcones have a *trans*-double bond; this was shown by the large coupling constant (J=15—17 Hz) of the ethylenic hydrogens in their NMR spectra.

When 4′-hydroxy-3′,5′-dimethylchalcone (Ic) was treated with LAH in tetrahydrofuran, followed by the treatment with 1 M sulfuric acid, an orange-red crystalline product was separated by column chromatography on alumina. The NMR spectrum (CCl_4) of this compound indicates the presence of two methyl groups {δ=1.98 (3H, broad singlet) and δ=2.04 (3H, doublet, J=1.0 Hz)}, vinylic protons {δ=6.60 (1H, d, J=11.0 Hz), δ=6.78 (1H, multiplet), and δ=6.98 (1H, d, J=11.0 Hz)}, and seven protons {δ=7.1—7.5 (m)}. The multiplet at δ=6.78 becomes a doublet with a small coupling constant, J=2.5 Hz, when irradiated at the methyl signals. The IR spectrum showed multiple absorptions at 1570, 1592, 1612, and 1625 cm.$^{-1}$ These spectroscopic results are consistent with the structure of 4-cinnamylidene-2,5-cyclohexadien-1-one (IVc). A *cis*-configuration of the ethylenic double bond in the cinnamyl group in IVc is suggested by the coupling constant, J=11.0 Hz, of the ethylenic protons. However, the chalcone has a *trans*-configuration, as already mentioned, and isomerization from *trans* to *cis* is not likely to occur during the reaction. Further study would be neccessary to clarify the matter.

Phenolic products (V, VI, and VII) were separated from the ethyl acetate fraction of the chromatography (Fig. 3). Based on the NMR spectrum, the structure of the product V is 4-*trans*-cinnamyl-2,6-dimethylphenol; this was confirmed by a synthesis. The spectral properties of VI suggest that the structure of this compound

Table 1. Synthesis of 4-*trans*-cinnamylidene-2,5-cyclohexadien-1-ones (IV)

Entry	Chalcone	Reaction conditions				IV (% yield)
		Molar ratio of I: $LiAlH_4$	Solvent	Time (h)	Temp (°C)	
1	Ia[10]	1:3	ether	4.5	0	—
2	Ia	1:2	THF	2.5	20	—
3	Ib[11]	1:2	THF	2.0	20	—
4	Ic[12]	1:2	THF	2.0	20	IVc (27)
5	Ic	1:2	ether	1.0	0	IVc (22)
6	Id	1:2	THF	2.0	20	IVd (33)
7	Ie	1:2	THF	2.0	20	IVe (21)
8	If	1:2	THF	2.0	20	IVf (19)
9	Ig	1:2	THF	1.0	20	IVg (30)
10	Ih	1:2	THF	2.0	20	IVh (26)
11	Ii	1:2	THF	0.5	20	IVi (42)
12	Ij	1:2	THF	1.0	20	IVg (42)
13	IIc	1:2	THF	2.0	20	IVc (46)
14	IId	1:2	THF	2.0	20	IVd (58)
15	IIe	1:2	THF	2.0	20	IVe (28)

is 1-(3,5-dimethyl-4-hydroxyphenyl)-3-phenyl-1-propanone (VI). The structure of VII was determined to be 1-(3,5-dimethyl-4-hydroxyphenyl)-3-phenyl-1-propanol (VII).

The LAH reduction of Ic in ether gave IVc in a slightly decreased yield (22%, entry 5). Five other chalcones (Id—h) gave the corresponding 4-cinnamylidene-2,5-cyclohexadien-1-ones (IVd—h) (entries 6, 7, 8, 9, and 10), but no effort was made to isolate the phenolic products in these cases.

The methyl ether of Obtsusaquinone,[9] which is the first naturally occurring 4-cinnamylidene-2-hydroxy-5-methoxy-2,5-cyclohexadien-1-one, was also synthesized by the reaction of Ii (entry 11) and found to be identical

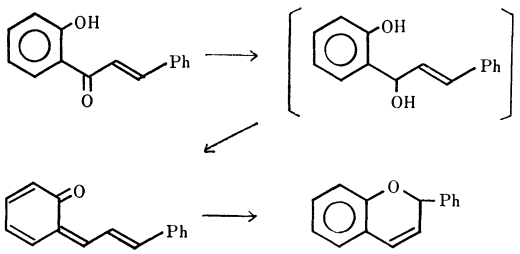
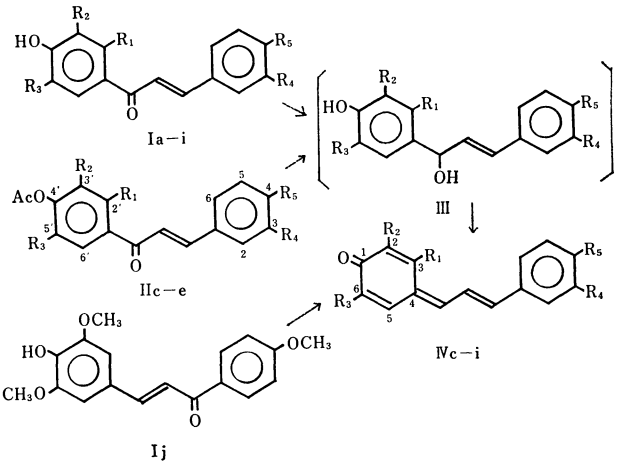


Fig. 1.



Ij

Fig. 2. a: $R_1=R_2=R_3=R_4=R_5=H$, b: $R_1=R_4=R_5=H$, $R_2=R_3=Br$, c: $R_1=R_4=R_5=H$, $R_2=R_3=CH_3$ d: $R_1=R_4=H$, $R_2=R_3=CH_3$, $R_5=OCH_3$, e: $R_1=H$, $R_2=R_3=CH_3$, $R_4=R_5=OCH_3$, f: $R_1=R_4=R_5=H$, $R_2=R_3=OCH_3$, g: $R_1=R_4=H$, $R_2=R_3=R_5=OCH_3$, h: $R_1=H$, $R_2=R_3=R_4=R_5=OCH_3$, i: $R_2=R_4=R_5=H$, $R_1=R_3=OCH_3$.

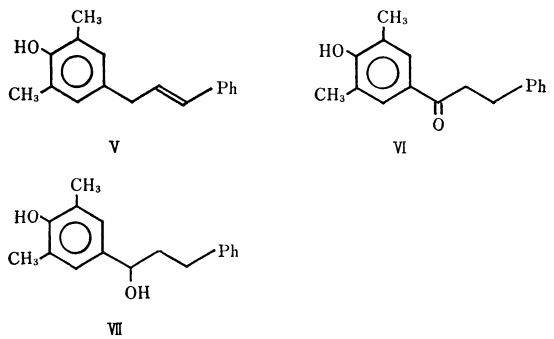


Fig. 3.

with the methyl ether by comparison of their spectral properties (the configuration of the styryl group in IVi could be reversed in Fig. 2).

The LAH reductions of 4'-hydroxychalcone (Ia) and 4'-hydroxy-3',5'-dibromochalcone (Ib) were also carried out, but pure compounds were not isolated due to the decomposition during chromatography. When 4'-acetoxychalcones (IIc—e) were reduced with LAH in tetrahydrofuran, followed by the treatment with 1 M sulfuric acid, IVc, IVd, and IVe were obtained in improved yields (46% (entry 13), 58% (entry 14), and 28% (entry 15)).

It seemed reasonable to assume that a chalcone having a hydroxyl group at the position 4 would also give a 4-cinnamylidene-2,5-cyclohexadien-1-one by the LAH reduction and the dehydration. This proved to be the case. The LAH reduction of 4-hydroxy-3,4',5-trimethoxychalcone (Ij) yielded IVg, identical with that obtained from Ig, but in a better yield (entry 12).

It is thus concluded that the LAH reductions of 4- and 4'-hydroxy-, and 4'-acetoxychalcones can be utilized as a convenient method for the synthesis of 4-cinnamylidene-2,5-cyclohexadien-1-ones.

Experimental

All ^1H NMR spectra were recorded with a Hitachi R 24 NMR spectrometer with TMS as an internal standard. The IR spectra were recoreded with a JASCO IRA-1 IR spectrometer, while the UV spectra were recorded with a Hitachi EPS-3T spectrophotometer. Melting points were determined on a Yanagimoto hot-stage and are uncorrected.

Preparations of Acetophenones. 4-Hydroxy-3,5-dimethoxyacetophenone was synthesized by partial demethylation of 3,4,5-trimethoxyacetophenone with aluminium chloride. 3,4,5-Trimethoxyacetophenone[13] (2.1 g) was dissolved in hot benzene (300 ml) containing anhydrous aluminium chloride (2.66 g) and heated under reflux for 2 h. 2 M hydrochloric acid (100 ml) was added to the solution and the benzene layer was separated. After removal of the benzene, the resulting solid was recrystallized from ether, giving colorless prisms (1.19 g, 61%), mp 119—120 °C (lit,[14] mp 120—121 °C).

4-Hydroxy-3,5-dimethylacetophenone was prepared by the modified Nencki reaction. 2,6-Dimethylphenol (1.22 g) was heated with boron trifluoride–acetic acid complex (5 ml) at 100 °C for 2 h. The reaction mixture was poured into 2 M hydrochloric acid (50 ml) and the precipitates were collected. The crude product was recrystallized from benzene to give colorless plates (623 mg, 38%), mp 150—151 °C(lit,[15] mp 150.5—151.2 °C).

4-Hydroxy-2,5-dimethoxyacetophenone was prepared similarly in 91% yield (mp 128—129 °C (lit,[16] mp 117—118 °C)).

Preparations of 4'-Hydroxy- and 4-Hydroxychalcones (Id—j). A typical preparation of 4'- and 4-hydroxychalcones was as follows. A mixture of an aldehyde (10 mmol) and an acetophenone (10 mmol) in ethanol (20 ml) was treated with 20—40% aqueous potassium hydroxide at an appropriate temperature overnight. The reaction mixture was poured into iced hydrochloric acid (10 ml), and the precipitates were collected and recrystallized.

4'-Hydroxy-3',5'-dimethyl-4-methoxychalcone (Id): Mp 146—147 °C (EtOH), 34% yield; IR ($CHCl_3$) 1656, 1670, and 3440 cm^{-1}. NMR ($CDCl_3$) $\delta=2.30$ (6H, s, $2\times CH_3$), 3.82 (3H, s, OCH_3), 5.7 (1H, broad s, OH), 6.90 (2H, m, $H_{(3)}$ and $H_{(5)}$), 7.41 (1H, d, $J=15.0$ Hz, H_α), 7.57 (2H, m, $H_{(2)}$ and

$H_{(6)}$), 7.73 (1H, d, J=15.0 Hz, H_β), and 7.71 (2H, s, $H_{(2')}$ and $H_{(6')}$). Found: C, 76.02; H, 6.63%. Calcd for $C_{18}H_{18}O_3 \cdot 1/10\ H_2O$: C, 76.08; H, 6.46%.

4'-Hydroxy-3,4-dimethoxy-3',5'-dimethylchalcone (Ie): Mp 184—186 °C (EtOH); 26% yield; IR ($CHCl_3$) 1668, 1675, and 3590 cm.$^{-1}$ NMR ($CDCl_3$) δ=2.33 (6H, s, 2×CH_3), 3.89 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 5.7 (1H, broad s, OH), 6.75—7.3 (3H, m, $H_{(2)}$, $H_{(5)}$, and $H_{(6)}$), 7.36 (1H, d, J=15.0 Hz, H_α), 7.67 (1H, d, J=15.0 Hz, H_β), and 7.67 (2H, s, $H_{(2')}$ and $H_{(6')}$). Found: C, 72.78; H, 6.55%. Calcd for $C_{19}H_{20}O_4$: 73.06; H, 6.45%.

4'-Hydroxy-3',5'-dimethoxychalcone (If): Mp 106—107 °C (aq EtOH); 55% yield; IR ($CHCl_3$) 1650 and 3500 cm^{-1}. NMR ($CDCl_3$) δ=3.98 (6H, s, 2×OCH_3), 6.0 (1H, s, OH), 7.30 (2H, s, $H_{(2')}$. and $H_{(6')}$), 7.48 (1H, d, J=16.0 Hz, H_α), 7.78 (1H, d, J=16.0 Hz, H_β), 7.3—7.7 (5H, m, Ph). Found: C, 71.64; H, 5.74%. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67%.

4'-Hydroxy-3',4,5'-trimethoxychalcone (Ig): Mp 79 °C (EtOH); 29% yield; IR ($CHCl_3$) 1650 and 3530 cm^{-1}. NMR ($CDCl_3$) δ=3.83 (3H, s, OCH_3), 3.95 (6H, s, 2×OCH_3), 6.0 (1H, broad s, OH), 6.95 (2H, m, $H_{(3)}$ and $H_{(5)}$), 7.35 (2H, s, $H_{(2')}$. and $H_{(6')}$), 7.43 (1H, d, J=16.0 Hz, H_α), 7.61 (2H, m, $H_{(2)}$ and $H_{(6)}$), and 7.78 1H, d, J=16.0 Hz, H_β). Found: C, 67.96; H, 5.85%. Calcd for $C_{18}H_{18}O_5 \cdot 1/5H_2O$: C, 68.00; H, 5.83%.

4'-Hydroxy-3,3',4,5'-tetramethoxychalcone (Ih): Mp 90 °C (EtOH); 49% yield; IR ($CHCl_3$) 1650 and 3520 cm^{-1}. NMR ($CDCl_3$) δ=3.90 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 3.95 (6H, s, 2×OCH_3), 6.1 (1H, s, OH), 6.89 (1H, m, $H_{(5)}$), 7.17 (2H, m, $H_{(2)}$ and $H_{(6)}$), 7.30 (2H, s, $H_{(2')}$ and $H_{(6')}$), 7.33 (1H, d, J=17.0 Hz, H_α), and 7.67 (1H, d, J=17.0 Hz, H_β). Found: C, 65.80; H, 5.92%. Calcd for $C_{19}H_{20}O_6 \cdot 1/10H_2O$: C, 65.92; H, 5.88%.

4'-Hydroxy-2',5'-dimethoxychalcone (Ii): Mp 162—163 °C (EtOH); 56% yield; IR ($CHCl_3$) 1630, 1660, and 3530 cm^{-1}. NMR ($CDCl_3$) δ=3.88 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 6.25 (1H, s, $H_{(3')}$), 6.62 (1H, s, $H_{(6')}$), 7.3—7.8 (6H, m, Ph and OH), and 7.69 (2H, s, H_α and H_β). Found: C, 71.23; H, 5.79%. Calcd for $C_{17}H_{16}O_4 \cdot 1/10H_2O$: 71.31; H, 5.71%.

4-Hydroxy-3,4',5-trimethoxychalcone (Ij): Mp 132 °C (EtOH); 28% yield; IR ($CHCl_3$) 1672 and 3540 cm^{-1}. NMR ($CDCl_3$) δ=3.88 (3H, s, OCH_3), 3.94 (6H, s, 2×OCH_3), 5.8 (1H, broad s, OH), 6.87 (2H, s, $H_{(2)}$ and $H_{(6)}$), 6.97 (2H, m, $H_{(3')}$ and $H_{(5')}$), 7.38 (1H, d, J=15 Hz, H_α), 7.70 (1H, d, J=15.0 Hz, H_β), and 8.00 (2H, m, $H_{(2')}$ and $H_{(6')}$). Found: C, 62.85; H, 5.40%. Calcd for $C_{18}H_{18}O_5 \cdot 4/5\ H_2O$: 62.71; H, 5.73%.

Preparation of 4'-Acetoxychalcones (IIc—e). A typical procedure for the preparation of 4'-acetoxychalcone was as follows. A 4'-hydroxychalcone (4 mmol) was treated with a mixture of acetic anhydride (1 ml), acetic acid (1 ml), and pyridine (6 ml) at room temperature overnight. The reaction mixture was poured into iced water and the precipitates were collected.

4'-Acetoxy-3',5'-dimethylchalcone (IIc): Mp 102 °C (EtOH); 92% yield; IR ($CHCl_3$) 1680 (C=O) and 1765 cm^{-1} (OAc). NMR ($CDCl_3$) δ=2.22 (6H, s, 2×CH_3), 2.33 (3H, s, OAc), 7.2—7.8 (5H, m, Ph), 7.43 (1H, d, J=15.0 Hz, H_α), 7.72 (2H, s, $H_{(2')}$ and $H_{(6')}$), and 7.75 (1H, d, J=15.0 Hz, H_β). Found: C, 77.32; H, 6.23%. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16%.

4'-Acetoxy-3',5'-dimethyl-4-methoxychalcone (IId): Mp 125—126 °C (EtOH); 65% yield; IR ($CHCl_3$) 1670 (C=O) and 1765 cm^{-1} (OAc). NMR ($CDCl_3$) δ=2.22 (6H, s, 2×CH_3), 2.35 (3H, s, OAc), 3.84 (3H, s, OCH_3), 6.91 (2H, m, $H_{(3)}$ and $H_{(5)}$), 7.36 (1H, d, J=15.0 Hz, H_α). 7.60 (2H, m, $H_{(2)}$ and $H_{(6)}$), 7.72 (2H, s, $H_{(2')}$ and $H_{(6')}$), and 7.80 (1H, d, J=15.0 Hz, H_β). Found: C, 73.75; H, 6.36%. Calcd for $C_{20}H_{20}O_4$: C, 74.05; H, 6.22%.

4'-Acetoxy-3,4-dimethoxy-3',5'-dimethylchalcone (IIe): Mp 135—136 °C (EtOH); 58% yield; IR ($CHCl_3$) 1680 (C=O) and 1770 cm^{-1} (OAc). NMR ($CDCl_3$) δ=2.23 (6H, s, 2×CH_3), 2.35 (3H, s, OAc), 3.92 (3H, s, OCH_3), 3.94 (3H, s, OCH_3), 6.8—7.3 (3H, m, $H_{(2)}$, $H_{(5)}$ and $H_{(6)}$), 7.30 (1H, d, J=16.0 Hz, H_α), 7.69 (1H, d, J=16.0 Hz, H_β), and 7.69 (2H, s, $H_{(2')}$ and $H_{(6')}$). Found: C, 70.92; H, 6.36%. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26%.

Lithium Aluminium Hydride Reduction of 4- and 4'-Hydroxychalcones (Ia—j) and 4'-Acetoxychalcones (IIc—e). A typical procedure of the LAH reduction of chalcones was as follows. To a stirred THF solution of LAH (2 mmol), a chalcone (1 mmol) was added and stirred for the time shown in the table. The color of the chalcones disappeared within 5—10 min. After the removal of the THF *in vacuo*, 1 M sulfuric acid (20 ml) was added to the residue and the mixture was extracted with chloroform. The chloroform solution was concentrated to a small volume and then passed through an alumina column (5—10 g) by eluting with chloroform. The chloroform was removed and the resulting orange-red colored substance was allowed to crystallize. In the case of Ic, the reaction mixture was extracted with benzene and passed through a silicagel column by eluting with chloroform and ethyl acetate successively. The chloroform fraction was again passed through an alumina column by eluting with benzene to give IVc. The ethyl acetate fraction was further purified by TLC effected with chloroform, yielding V, VI, and VII. The LAH reduction in ether was carried out similarly. Yields were based on the amount of chalcones used.

Ic gave IVc, mp 115—116 °C (cyclohexane); 27% yield THF and 22% yield (ether); IR ($CHCl_3$) 1570, 1592, 1612, and 1625 cm^{-1}; UV (MeOH) λ_{max} (ε) 260 (10800) and 406 nm (4530) (Found: C, 86.34; H, 6.88%. Calcd for $C_{17}H_{16}O$: C, 86.40, H, 6.83%); V: mp 56—57 °C (light petroleum); 1% yield; IR ($CHCl_3$) 3600 cm^{-1} (OH); UV (MeOH) λ_{max} (ε) 258 nm (20300); NMR ($CDCl_3$) δ=2.11 (6H, s, 2×CH_3), 3.25 (2H, m, $-CH_2-$), 4.4 (1H, broad s, OH), 5.85—6.5 (2H, m, $-CH=CH-$), 6.65 (2H, s, aromatic), and 7.15 (5H, m, Ph) (Found: C, 85.71; H, 7.77%. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61%); VI: liquid; 8% yield; IR ($CHCl_3$) 1690 (C=O) and 3580 cm^{-1} (OH); NMR ($CDCl_3$) δ=2.25 (6H, s, 2×CH_3), 2.7—3.4 (4H, m, $-CH_2-CH_2-$), 5.8 (1H, s, OH), 7.21 (5H, s, Ph), and 7.60 (2H, s, aromatic); and VII: liquid; 4% yield; IR ($CHCl_3$) 3400 (OH) and 3580 cm^{-1} (OH); NMR ($CDCl_3$) δ=2.21 (6H, 2×CH_3), 1.6—3.0 (5H, m, $-CH_2-CH_2-$, OH), 4.52 (1H, t, J=6.0 Hz, $-CHOH$), 4.65 (1H, broad s, OH), 6.92 (2H, s, aromatic), and 7.18 (5H, s, Ph). IIc gave IVc in a 46% yield.

2,6-Dimethyl-4-(4-methoxycinnamylidene)-2,5-cyclohexadien-1-one (IVd): Mp 141—142 °C (ethyl acetate); 33% yield; IR ($CHCl_3$) 1560, 1586, 1615, and 1650 cm^{-1}; UV (MeOH) λ_{max} (ε) 273 (15700) and 442 nm (20800); NMR ($CDCl_3$) δ=2.03 (3H, s, CH_3), 2.10 (3H, s, CH_3), 3.79 (3H, s, OCH_3), 6.6—7.6 (9H, m). Found: C, 81.18; H, 6.78%. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81%. IId yielded IVd in a 58% yield.

4-(3,4-Dimethoxycinnamylidene)-2,6-dimethyl-2,5-cyclohexadien-1-one (IVe): Mp 142—143 °C (benzene); 21% yield; IR ($CHCl_3$) 1575, 1595, 1615, and 1650 cm^{-1}; UV (MeOH) λ_{max} (ε) 275 (12700) and 450 nm (41400); NMR ($CDCl_3$) δ=2.05 (3H, s, CH_3), 2.11 (3H, s, CH_3), 3.89 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 6.7—7.5 (7H, m), and 7.55 (1H, m). Found: C, 76.80; H, 6.87%. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80%. IIe gave IVe in a 28% yield

4-Cinnamylidene-2,6-dimethoxy-2,5-cyclohexadien-1-one (IVf): Mp 113—114 °C (benzene); 19% yield; IR ($CHCl_3$) 1570,

1590, 1600, and 1635 cm^{-1}; UV (MeOH) λ_{max} (ε) 275 (shoulder) (4440) and 424 nm (3410) (the ε values could not be accurate as they decreased rapidly); NMR ($CDCl_3$) δ=3.75 (3H, s, OCH_3), 3.82 (3H, s, OCH_3) 6.23 (1H, d, J=2.0 Hz), 6.75 (1H, broad s), 6.74 (1H, d, J=12.7 Hz), 7.07 (1H, d, J=12.7 Hz), and 7.2—7.7 (6H, m). Found: C, 77.12; H, 6.05%. Calcd for $C_{17}H_{16}O_3 \cdot 1/5\ C_6H_6$: C, 76.99; H, 6.11%.

2,6-Dimethoxy-4-(4-methoxycinnamylidene)-2,5-cyclohexadien-1-one (IVg): Mp 142 °C (benzene); 30% yield (from Ig) and 42% yield (from Ij); IR ($CHCl_3$) 1572, 1588, and 1632 cm^{-1}; UV (MeOH) λ_{max} (ε) 245 (10300), 280 (shoulder) (6240), 300 (6240), and 456 nm (41900); NMR ($CDCl_3$) δ=3.77 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 3.96 (3H, s, OCH_3), 6.31 (1H, m), 6.5—7.2 (5H, m), 7.33 (1H, s), and 7.48 (2H, m). Found: C, 73.92; H, 6.15%. Calcd for $C_{18}H_{18}O_4 \cdot 1/4\ C_6H_6$: C, 73.68; H, 6.18%.

2,6-Dimethoxy-4-(3,4-dimethoxycinnamylidene)-2,5-cyclohexadien-1-one (IVh): Mp 149—151 °C (ethyl acetate); 26% yield; IR ($CHCl_3$) 1570, 1590, and 1632 cm^{-1}; UV (MeOH) λ_{max} (ε) 235 (shoulder) (13100), 280 (8450), 300 (shoulder) (5830), and 466 nm (40800); NMR ($CDCl_3$) δ=3.80 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 3.93 (3H, s, OCH_3), 6.32 (1H, d, J=2.0 Hz), 6.6—7.5 (7H, m). Found: C, 69.30; H, 6.18%. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14%.

4-Cinnamylidene-3,6-dimethoxy-2,5-cyclohexadien-1-one (IVi): Mp 165 °C (primarily softening at 130—140 °C, lit,[9] mp 169 °C), 42% yield.

Preparation of 4-trans-Cinnamyl-2,6-dimethylphenol. *trans-Cinnamyl 2,6-Dimethylphenyl Ether*: A mixture of 2,6-dimethylphenol (15 g), *trans*-cinnamyl chloride (15 g), anhydrous potassium carbonate (15 g), and acetone (100 ml) was heated under reflux for 4 days. After the removal of the acetone, water was added to the residue. The mixture was extracted with benzene and the benzene layer was washed with 1 M sodium hydroxide. Evaporation of the benzene gave *trans*-cinnamyl 2,6-dimethylphenyl ether (21.5 g, 91%) as an oil, bp 180 °C (bath temp)/0.03 mmHg. UV (MeOH) λ_{max} (ε) 257 nm (19400); NMR ($CDCl_3$) δ=2.23 (6H, s, 2×CH_3), 4.34 (2H, d, J=4.5 Hz), 6.30 (1H, d t, J=16.0, 4.5 Hz), 6.66 (1H, d, J=16.0 Hz), 6.83 (3H, m, aromatic), and 7.20 (5H, m, Ph). Found: C, 85.72; H, 7.76%. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61%.

4-trans-Cinnamyl-2,6-dimethylphenol: *trans*-Cinnamyl 2,6-dimethylphenyl ether (5.0 g) was heated in *N,N*-dimethylaniline (20 ml) for 2 h at 200 °C under nitrogen atmosphere. The reaction mixture was dissolved into 2 M hydrochloric acid (100 ml) and then extracted with benzene. After the removal of the benzene, the resulting mixture was chromatographed through an alumina column (100 g) by eluting with benzene, giving colorless needles (2.95 g, 59%), mp 56—57 °C (light petroleum) identical with those obtained by the LAH reduction of Ic.

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