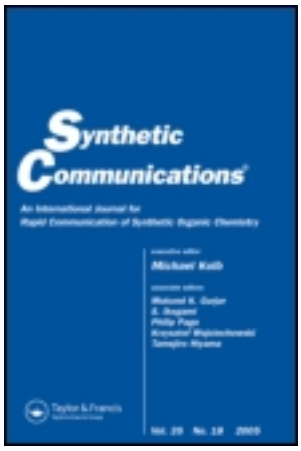

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Synthesis of New Biosynthetically Important Diarylheptanoids and Their Oxa- and Fluoro-Analogues by Three Different Strategies

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ABSTRACT

Wittig, aldol and Wittig-Horner reactions have been used to synthesize new diarylheptanoids, which are putative intermediates in phenylphenalenone biosynthesis in plants. The Wittig-Horner approach was most suitable and gave significantly higher yields in comparison with other methods.

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Key Words: Diarylheptanoids; Aldol reaction; Wittig reaction; Wittig-Horner reaction.

1. INTRODUCTION

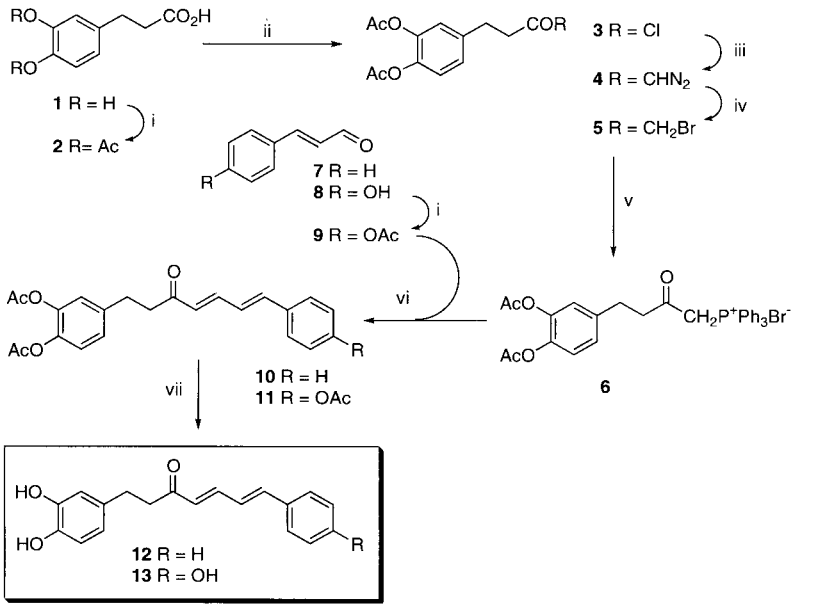
Diarylheptanoids represent a group of natural products occurring in various monocot and dicot plant species.[1,2] The Zingiberaceae plant family is an especially rich source of diarylheptanoids. Curcumin, the most well-known diarylheptanoid, is a major spice and pigment principle of *Curcuma longa* (Zingiberaceae) and other *Curcuma* species. In bioassays it exhibits strong antioxidant and chemopreventive activities.[3,4] Diarylheptanoids of the Zingiberaceae structurally related to curcumin are also referred to as curcuminoids. Compounds of that type are considered intermediates in the biosynthesis of cyclic phenolic natural products, the phenylphenalenones, which represent characteristic constituents of the Haemodoraceae and Musaceae plant families. Involvement of diarylheptanoids in phenylphenalenone biosynthesis has been confirmed by feeding experiments using a labelled precursor of that type.[5] More detailed studies to establish the occurrence of and exact biosynthetic pathway to phenylphenalenones require synthesis of diarylheptanoids as analytical standards and putative intermediates.

As putative intermediates of phenylphenalenone biosynthesis, diarylhepta-4,6-dien-3-ones are of special interest. In the original synthesis of diarylheptadienones, the Wittig reaction was used as the central step.[6,7] Since then many approaches to related diaryl dienones and other diarylheptanoids have been elaborated[8,9] mainly based on the aldol condensation[10–12] and the Wittig-Horner reaction.[13,14] We herein describe the synthesis of new (*E*,*E*)-diarylhepta-4,6-dien-3-ones, which were prepared *via* three different approaches: Wittig reaction following the procedure of Sakakibara et al.,[6] aldol condensation, and Wittig-Horner reaction.

2. RESULTS AND DISCUSSION

2.1. Wittig Approach

The procedure described for the synthesis of 4,6-heptadien-3-ones[6,7] was found rather laborious and, in the case of phenolic compounds, gave low yields. It starts from a phenylpropionic acid e.g., hydrocaffeic acid (**1**), which after protection was treated subsequently with thionyl chloride, diazomethane, HBr, and triphenylphosphine. In the final step,

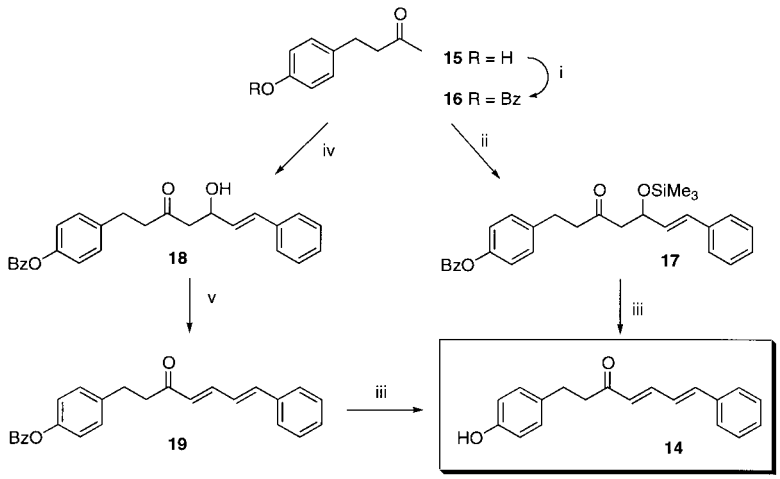


Scheme 1. *Reagents and conditions*: i: Ac_2O, Py, r.t., 8 h, 87 % for **2** and 75 % for **9**; ii: $(COCl)_2$, benzene, reflux, 45 min; iii: 1) CH_2N_2, benzene, 8°C, 30 min, 2) r.t., 2 h; iv: HBr (48%), benzene, 5°C, 30 min, 48% based on **2**; v: $P(C_6H_5)_3$, benzene, r.t., 48 h, 80%; vi: 1) K_2CO_3, H_2O, 80°C, 10 min, 2) **7** or **9**, benzene, reflux, 48 h, 48% for **10** and 46% for **11** based on **6**; vii: MeONa, MeOH, r.t., 10 min, 82% for **12** and 76% for **13**.

the phosphonium salt **6** was reacted with aldehyde **7** and **9**, respectively (Sch. 1).[15] Two low-yield steps, the bromination (48%) and the Wittig reaction (48% for **10** and 45% for **11**) diminished total yield of compounds **12** and **13** to only 13% and 11% respectively.

2.2. Aldol Condensation

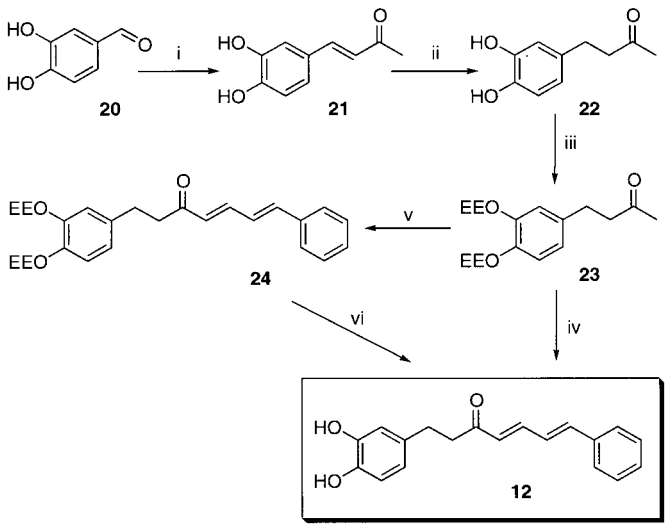
As a result of the low total yields of the diarylheptanoids obtained by the Wittig approach, further strategies were pursued. The synthesis of dienone **14** was started from the commercially available ketone **15**. The phenolic hydroxyl group was protected as the benzoate ester because this protection group does not interfere with preparation of a ketone enolate with LDA and is furthermore advantageous by the ease of removal by treatment with mild base.[16] The protected ketone **16** was treated with



Scheme 2. *Reagents and conditions*: i: BzCl, Py, DMAP, DCM, r.t., 12 h, 90%; ii: 1) LDA, THF, −78°C, 2) cinnamic aldehyde, 3) TMSCl, THF, r.t., 1 h, 40%; iii: K_2CO_3, MeOH, r.t., 2 h, 49% from **17**, 65% from **19**; iv: 1) LDA, THF, −78°C, 2) cinnamic aldehyde, 63%; v: TsOH(cat), C_6H_6, reflux, 10 min, 99%.

LDA at low temperature and the resulting enolate was reacted with cinnamic aldehyde (Sch. 2). Reports had shown that the addition of TMSCl to the reaction mixture drastically improved yields of dienones.[17,18] However, in our case, analysis of the reaction mixture showed a very slow formation of dienone from the TMS-ether **17**. Finally, the reaction was quenched and **17** was isolated in 40% yield after chromatography. Treatment of TMS-ether **17** with K_2CO_3 in methanol effected hydrolysis of protection group and subsequent dehydration to give **14**. Unfortunately, the reaction was accompanied by formation of the retroaldol product, which reduced the yield of the desired diarylheptanoid **14** to 49%. The aldol reaction was repeated without adding TMSCl, and the intermediate product **18** was dehydrated with TsOH, which resulted in a greater yield. The overall yield of **14** from three steps (addition, dehydration and hydrolysis) was substantially better (40%) than in the first procedure (19% for two steps).

The starting material for the synthesis of dienone **12** was prepared in a two-step procedure from 3,4-dihydroxybenzaldehyde **20** (Sch. 3). Knoevenagel condensation with piperidinium acetate as a catalyst[18,19] gave ketone **21** and avoided the need for protection of the hydroxy groups. There are no reports on chemoselective hydrogenation of



Scheme 3. *Reagents and conditions*: i: Me_2CO, MeCN, AcOH, $C_5H_{10}NH$, reflux, 4 h, 48%; ii: HCO_2NH_4, Pd/C, Me_2CO, MeOH, r.t., 1 h, 90%; iii: $EtOCH{=}CH_2$, Et_2O, r.t., 24 h, 95%; iv: 1) LDA, THF, −78°C, 2) cinnamic aldehyde, 3) TsOH(cat), MeOH, r.t., 5 min, 4) TsOH, THF, C_6H_6, r.t., 48 h, 38%; v: 1) LDA, THF, −78°C, 2) cinnamic aldehyde, TMSCl, 3) DBU, THF, reflux, 3 h, 44 %; vi: TsOH(cat), MeOH, r.t., 5 min, 96%.

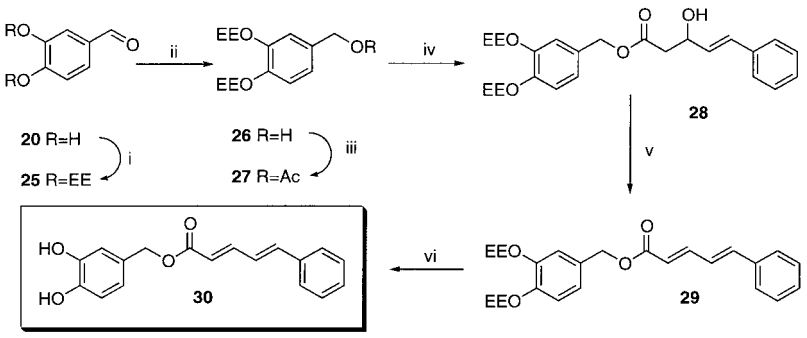
double bond in the unprotected ketone **21**. Transfer hydrogenation of **21** with ammonium formate was performed in order to simplify the procedure and to avoid the use of hydrogen gas. The problem of excessive reduction resulting in the saturated alcohol, which heavily diminished the yield of the desired ketone,[20,21] was avoided by adding acetone to reaction mixture.[22,23] The ketone **22** was obtained in 90% yield.

Subsequent steps required the selection of a protecting group for the catechol moiety. It is known[5] that the final compound **12** is rather unstable and would not withstand the harsh conditions used for deprotection of typical protection groups in catechols.[16] On the other hand, the protection group had to be stable during the aldol reaction and purification. The ethoxyethyl group (*EE*) was chosen, because this protection group fulfills the above requirements, gives good yields, and does not hinder the reaction site. The drawback is the introduction of two chiral centers into the molecule, which generates two diastereomers that complicate the interpretation of NMR spectra to some extent.

Thus, ketone **22** was protected as *EE* ether **23**, and the latter was used in the aldol reaction. However, we obtained very modest yields (38–44%)

of compound **12** in the elimination step under both basic (DBU) and acidic (TsOH) conditions. Again, the major concurrent reaction was the retroaldol process.

Oxa-analogues of diarylheptanoids (e.g., 2-hydroxy-5-phenylpentanoic acid benzyl ester) are accessible by enantioselective aldol addition using benzyl acetate derived silyl ketene acetal.[24] In our case enantioselectivity was not necessary because dehydration resulted in the subsequent loss of stereochemistry. Accordingly, the oxa-analogue of diarylheptanoid **12** was synthesized by means of an aldol-type condensation of cinnamic aldehyde with protected acetic acid 3,4-dihydroxybenzyl ester. The procedure started with 3,4-dioxybenzaldehyde **20**, which was protected as the *EE*-ether **25**[25] and reduced with $NaBH_4$. The obtained alcohol **26** was acetylated to give acetate **27**. These steps gave almost quantitative yields and did not require additional purification. The reaction of cinnamic aldehyde **7** with the anion of ester **27** led to hydroxy ester **28** in a good yield (81%). The dehydration step was carried out in the presence of acetic anhydride and DBU and the dienonate **29** was isolated in 74% yield. The ^{1}H NMR spectrum revealed a minor admixture of *cis*-isomer of compound **29**. The deprotected dienoate **30** (Sch. 4) was extremely labile under acidic and basic conditions due to its benzylic nature and in order to obtain compound **30** in high yields, compound **29** was treated with TsOH and the reaction quenched with pyridine to ensure neutral conditions during the work up.



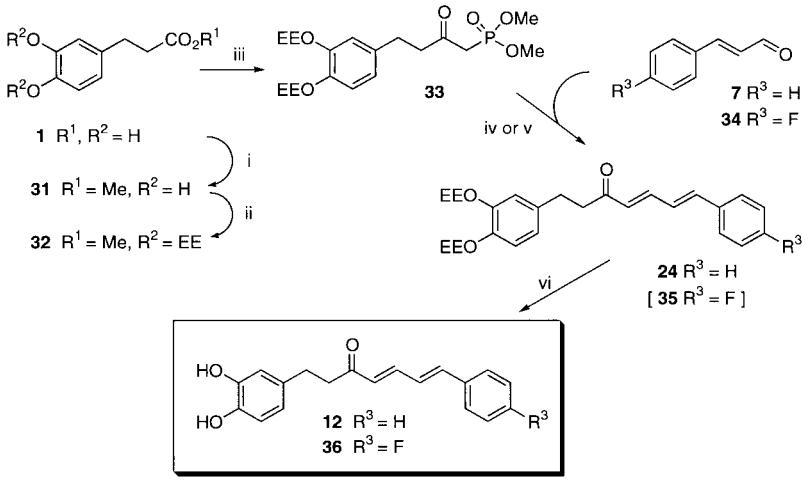
Scheme 4. *Reagents and conditions*: i: $EtOCH{=}CH_2$, Et_2O, r.t., 3d, 91%; ii: $NaBH_4$, CH_2Cl_2–MeOH, −5°C, 0.5 h, 99%; iii: Ac_2O, Py, CH_2Cl_2, r.t., 1 h, 99%; iv: 1) LDA, THF, −78°C, 2) cinnamic aldehyde, 0.5 h, 81%; v: Ac_2O, DBU, C_6H_6, 90°C, 2.5 h, 74%; vi: TsOH(cat), MeOH, r.t., 5 min, 99%.

2.3. Wittig-Horner Approach

Having such low yields, we reconsidered our approach and decided to use the Wittig-Horner reaction. The starting material for the synthesis, ester **32**, was prepared from hydrocaffeic acid (**1**) in 92% yield. As expected, the transformation of ester **32** into phosphonate **33** after purification gave the product in 87% yield (11% of starting material was recovered). Phosphonate **33** was used under conditions of the Wittig-Horner reaction proposed in the synthesis of shogaol[26] (Sch. 5).

However, the use of NaH as a base resulted in moderate yields of the product, which were compatible with yields of the aldol reaction. Conditions[13,27,28,29] employing LiCl and an organic base were also unsatisfactory, as the dienone was contaminated with low-molecular weight byproducts. When the latter reaction was performed with only DBU as a base, the desired compound **24** was isolated in 71% yield. Deprotection was accomplished without complication to give dienone **12** in 96%. The overall yield in the latter procedure over five steps, using DBU in the condensation, was 54%.

It was desirable to synthesise a fluorine containing analogue of **12** and **13** for use in biosynthesis studies. In order to minimise the stereoelectronic



Scheme 5. *Reagents and conditions*: i: AcCl, MeOH, r.t., 12 h, 99%; ii: $EtOCH{=}CH_2$, Et_2O, r.t., 24 h, 92%; iii: 1) $MeP(O)(OMe)_2$, THF, −78°C, 2) MeLi 3) **32**, 1 h, 87%; iv: 1) NaH, THF, 0°C, 2) **7**, reflux, 3 h, 43%; v: DBU, **7** or **34**, THF, reflux, 4 h, 71% for **24** and 44% for **36**; vi: TsOH(cat), MeOH, r.t., 5 min, 96% for **12**.

pertubation caused by the introduction of fluorine, the 4″-hydroxyl group of **13** was substituted for fluorine. As the Wittig-Horner approach to synthesize gave better yields compared with the Wittig synthesis and aldol reaction, this method was chosen for the synthesis of the fluoro-analogue of **13**. The starting material, 3-(4-fluorophenyl)-2-propenal (**34**), was prepared from *p*-fluorobenzaldehyde and acetaldehyde by aldol condensation.[30] The product was purified *via* preparative TLC. Condensation of the aldehyde **34** with phosphonate **33** and deprotection in a one-pot process without isolation of the ethoxyethyl derivative **35** gave the fluorodiarylheptanoid (**36**) as the free catechol.

3. CONCLUSIONS

The synthesis of diarylheptanoids and analogues has been achieved by three different strategies. The improved Wittig-Horner approach proved the most suitable scheme for synthesis of (*E*,*E*)-diaryl-4,6-hepta-dien-3-ones. A total yield of 54% in five steps was obtained compared with 40% (from **22**) in the aldol and approximately 12% in the Wittig approach. Owing to the high overall yield, the proposed Wittig-Horner approach is also suitable for syntheses of diarylhepta-4,6-dien-3-ones and further diarylheptanoids in labelled form. Compound **12** and new diaryl-heptanoids **13** and **14** have been suggested as biosynthetic intermediates of phenylphenalenone biosynthesis, which after *o*-hydroxylation of the phenolic ring (compound **14**) and oxidation to *o*-quinones may represent substrates for intramolecular Diels-Alder reaction.

4. EXPERIMENTAL SECTION

4.1. General Methods

Melting points were measured in a Büchi B-540 apparatus and are uncorrected. Infrared spectra were recorded on a FTIR, Bruker EQUINOX 55 spectrometer and only characteristic absorptions are reported. NMR spectra were recorded on a Bruker DRX 500 spectrometer at 500.13 MHz (^{1}H) and 125.75 MHz (^{13}C), respectively, using standard Bruker software. TMS was used as internal standard. ^{1}H NMR, ^{1}H–^{1}H COSY, HMBC, and HMQC experiments were recorded in a 2.5 mm inverse detection microprobe head. Broadband decoupled ^{13}C and DEPT spectra were run using a 2.5 mm broadband microprobe head. Chemical shifts are reported in δ values and coupling

constants are in Hz. MS and HRMS data were obtained with a Micromass MasSpec mass spectrometer (70 eV). The ratio m/z and relative intensities (%) are indicated for the significant peaks. Column chromatography was performed on Merck silica gel 60 (0.04–0.2 mm). Solvents were dried and freshly distilled according to common practice. All reactions were carried out under positive nitrogen pressure. Reactions were monitored by TLC on precoated silica gel 60 F-254 plates (Merck), and visualization of the compounds was accomplished by UV light and/or spraying with $FeCl_3$ solution.

4.2. Wittig Synthesis

4.2.1. (*E*)-Acetoxycinnamaldehyde (**9**)

Compound **9** was synthesized from *p*-cumaraldehyde (**8**) by standard acetylation procedure using acetic anhydride in pyridine. ^{1}H NMR (acetone-d_6): δ 2.28 (3H, s, AcO), 6.75 (1H, dd, $J = 16.4$, 7.6 Hz, H-2), 7.24 (2H, d, $J = 8.8$ Hz, H-3′ and H-5′), 7.68 (1H, d, $J = 16.4$ Hz, H-3), 7.76 (2H, d, $J = 8.8$ Hz, H-2′ and H-6′), 9.71 (1H, d, $J = 7.6$ Hz, H-1); EIMS: m/z 190 (M^+, 26), 148 (100), 131 (29), 120 (50).

4.2.2. (4*E*,6*E*)-1-(3,4-Diacetoxyphenyl)-7-(4-Acetoxyphenyl)-Hepta-4,6-dien-3-one (**11**)

The Wittig reaction of the phosphonium bromide **6** with aldehyde **7** and **9**, respectively, was performed using the procedure of Bazan et al.[7] Phosphoniumbromide **6** (0.112 g, 0.185 mmol) was dissolved in hot water (1.5 mL), and 0.5 mL of an aqueous solution of K_2CO_3 (0.027 g, 0.2 mmol) were added dropwise with stirring. The precipitated phoshonium ylide was separated, dissolved in benzene, dried by azeotropic evaporation, and redissolved in dry benzene. Acetoxy-*trans*-cinnamaldehyde (**9**) (0.034 g, 0.19 mmol) was added, and the mixture was refluxed for 48 h. The red solution was evaporated, and after chromatography on a silica gel column with hexane-acetone 6:1 as eluent, gave 0.037 g (46%) compound **11**, M.p. 127–129°C. IR (KBr): (ν_{max} cm^{-1}) 2982, 1782, 1764, 1681, 1593, 1505, 1371, 1218, 1006, 886, 839; ^{1}H NMR ($CDCl_3$): δ 2.27 (3H, s, AcO), 2.28 (3H, s, AcO), 2.30 (3H, s, AcO), 2.92 (2H, t, $J = 7.0$ Hz, H-2), 2.97 (2H, t, $J = 7.0$ Hz, H-1), 6.26 (1H, d, $J = 15.4$ Hz, H-4), 6.81 (1H, d, $J = 15.4$, 10.8 Hz, H-6), 6.92

(1H, d, $J = 15.4$ Hz, H-7), 7.05 (1H, d, $J = 1.5$ Hz, H-2′), 7.09 (m, H-5′, H-6′, H-3″ and H-5″), 7.30 (1H, dd, $J = 15.4$, 10.8 Hz, H-5), 7.47 (2H, d, $J = 8.5$ Hz, H-2″ and H-6″); ^{13}C NMR ($CDCl_3$): δ 20.6 (CH_3CO), 20.6 (CH_3CO), 21.1 (CH_3CO), 29.4 (C-1), 41.9 (C-2), 122.0 (C-3″ and C-5″), 123.3 (C-2′ and C-5′), 126.6 and 126.8 (C-6 and C-6′), 128.3 (C-2″ and C-6″), 129.5 (C-4), 140.2 (C-1′), 134.9 (C-1″), 140.3 (C-4′), 140.4 (C-7), 141.9 (C-3′), 142.7 (C-5), 151.3 (C-4″), 168.3 (CH_3CO), 168.4 (CH_3CO), 169.2 (CH_3CO),198.8 (C-3); EIMS: m/z 436 (M^+, 31), 393 (69), 352 (54), 310 (39), 187 (60), 173 (100). HRMS: Calcd. for $C_{25}H_{24}O_7$: 436.1522, Found: 436.1518.

4.2.3. (4*E*,6*E*)-1-(3,4-Dihydroxyphenyl)-7-Phenylhepta-4,6-dien-3-one (**12**)

Compound **12** was prepared from dihydrocaffeic acid (**1**) as described by Bazan et al.[7] For analytical data, see 4.3.12. The intermediate phosphonium bromide **6** was also used for the preparation of (*4E*,*6E*)-1-(3,4-hydroxyphenyl)-7-(4-hydroxyphenyl)-hepta-4,6-dien-3-one (**13**).

4.2.4. (4*E*,6*E*)-1-(3,4-Dihydroxyphenyl)-7-(4-Hydroxyphenyl)-Hepta-4,6-dien-3-one (**13**)

For deprotection, 120 µL of 1 M solution of NaOMe in abs. MeOH were added dropwise within 5 min to a stirred solution of compound **11** (0.037 g, 0.085 mmol) in abs. MeOH (1 mL). The mixture turned deep red and was stirred for another 5 min. Water (1 mL) was added and after 5 min the alkaline mixture was acidified to pH 5.5 by the dropwise addition of 0.5 M HCl. The solution was extracted with $CHCl_3$ and purified by preparative TLC ($CHCl_3$:MeOH 19:1). ^{1}H NMR (acetone-d_6): δ 2.76 (2H, t, $J = 7.9$ Hz, H-1), 2.86 (2H, t, $J = 7.9$ Hz, H-2), 6.25 (1H, d, $J = 15.5$ Hz, H-4), 6.57 (1H, dd, $J = 8.0$, 2.1 Hz, H-6′), 6.72 (1H, d, $J = 8.0$ Hz, H-5′), 6.73 (1H, d, $J = 2.1$ Hz, H-2′), 6.86 (2H, d, $J = 8.8$ Hz, H-3″ and H-5″), 6.89 (1H, dd, $J = 15.5$, 10.5 Hz, H-6), 7.01 (1H, d, $J = 15.5$ Hz, H-7), 7.38 (1H, dd, $J = 15.5$, 10.5 Hz, H-5), 7.44 (2H, d, $J = 8.8$ Hz, H-2″ and H-6″); ^{13}C NMR (acetone-d_6): δ 30.3 (C-1), 42.8 (C-2), 115.9 (C-5′), 116.3 (C-2′), 116.6 (C-3″ and C-5″), 120.4 (C-6′), 125.0 (C-6), 129.0 (C-1″), 129.3 (C-4), 129.8 (C-2″ and C-6″), 134.2 (C-1′), 142.2 (C-7), 143.7 (C-4′), 144.1 (C-5), 145.8 (C-3′), 159.5 (C-4″), 199.4 (C-3); EIMS: m/z 310 (M^+, 92), 173 (100). HRMS: Calcd. for $C_{25}H_{24}O_7$: 310.1207, Found: 310.1205.

4.3. Aldol Condensation

4.3.1. 4-(4-Benzoyloxyphenyl)-Butan-2-one (**16**)

A solution of ketone **15** (0.98 g, 6 mmol), benzoyl chloride (0.77 mL, 6.6 mmol), pyridine (1.06 mL, 13.2 mmol) and DMAP (0.09 g, 0.7 mmol) in CH_2Cl_2 (30 mL) was stirred at room temperature. After 4 h the solution was diluted with CH_2Cl_2, washed with water, brine, dried over Na_2SO_4 and evaporated to yield the product (2.0 g). The crude product was crystallized from EtOAc-hexane to give the protected ketone **16** (1.46 g, 90%), M.p. 72.3–72.7°C. IR (KBr): (ν_{max} cm^{-1}) 2945, 2918, 1729, 1702, 1600, 1272, 1057, 883; ^{1}H NMR ($CDCl_3$): δ 2.14 (3H, s, H-1), 2.76 (2H, t, $J = 7.6$ Hz, H-3), 2.90 (2H, t, $J = 7.6$ Hz, H-4), 7.11 (2H, d, $J = 8.2$ Hz, H-3′ and H-5′), 7.22 (2H, d, $J = 8.2$ Hz, H-2′ and H-6′), 7.49 (2H, m, H-3″ and H-5″), 7.61 (1H, t, $J = 7.5$ Hz, H-4″), 8.18 (2H, d, $J = 7.9$ Hz, H-2″ and H-6″); ^{13}C NMR ($CDCl_3$): δ 29.1 (C-4), 30.1 (C-1), 45.1 (C-3), 121.7 (C-3′ and C-5′), 128.5 (C-3″ and C-5″), 129.3 (C-2′ and C-6′), 129.5 (C-1′), 130.1 (C-2″ and C-6″), 133.5 (C-4″), 138.6 (C-1″), 149.2 (C-4′), 165.3 (COO), 207.7 (C-2); EIMS: m/z 268 (M^+, 19), HRMS: Calcd. for $C_{17}H_{16}O_3$: 268.1099, Found: 268.1099.

4.3.2. (6*E*)-1-(4-Benzoyloxyphenyl)-7-Phenyl-5-trimethylsilyloxy-hept-6-en-3-one (**17**)

To a stirred solution of LDA (1.6 mmol) in THF (5 mL) at −78°C was added a solution of ketone **16** (0.295 g, 1.1 mmol) in THF (5 mL) via syringe. After 15 min, cinnamic aldehyde (0.138 mL, 1.05 mmol) in THF (5 mL) was added. The mixture was stirred for 30 min at the indicated temperature and TMSCl (0.265 mL, 2 mmol) was added in one portion. The cooling bath was removed and the solution was allowed to warm to ambient temperature. After 4 h, saturated $NaHCO_3$ was added and the mixture was extracted with EtOAc. The organic phase was washed with brine, dried, and evaporated. The obtained residue was separated on a silica gel column with CH_2Cl_2:hexane as eluent to yield TMS-ether **17** as a pale yellow oil (0.188 g, 40%). IR (neat): (ν_{max} cm^{-1}) 3027, 2953, 1736, 1714, 1600, 1264, 1058, 841; ^{1}H NMR ($CDCl_3$): δ 0.12 (9H, s, CH_3Si), 2.54 (1H, dd, $J = 4.8$, 15.1 Hz, H-4a), 2.80 (3H, m, H-4b and H-2), 2.92 (2H, t, $J = 7.7$ Hz, H-1), 4.81 (1H, m, H-5), 6.17 (1H, dd, $J = 6.4$, 15.7 Hz, H-6), 6.55 (1H, d, $J = 15.7$ Hz, H-7), 7.11 (2H, d, $J = 8.5$ Hz, H-3′ and H-5′), 7.23 (2H, d, $J = 8.5$ Hz, H-2′ and H-6′), 7.25 (1H, tt, $J = 7.7$, 1.3 Hz, H-4″), 7.31 (2H, dd, $J = 7.7$, 7.7 Hz, H-3″

and H-5″), 7.36 (2H, d, $J = 7.7$ Hz, H-2″ and H-6″), 7.51 (2H, dd, $J = 7.7$, 8.1 Hz, H-3‴and H-5‴), 7.62 (1H, tt, $J = 7.4$, 1.3 Hz, H-4‴), 8.18 (2H, d, $J = 8.1$ Hz, H-2‴ and H-6‴); ^{13}C NMR ($CDCl_3$): δ 0.2 (CH_3Si), 28.8 (C-1), 46.1 (C-2), 51.1 (C-4), 70.2 (C-5), 121.6 (C-3′ and C-5′), 126.5 (C-2″ and C-6″), 127.6 (C-4″), 128.5 (C-3‴ and C-5‴), 128.6 (C-3″ and C-5″), 129.3 (C-2′ and C-6′), 129.6 (C-1′), 129.7 (C-7), 130.1 (C-2‴ and C-6‴), 131.7 (C-6), 133.5 (C-4‴), 136.6 (C-1″), 138.7 (C-1‴), 149.2 (C-4′), 165.3 (COO), 207.8 (C-3); EIMS: m/z 472 (M^+, 30), 447 (10), 382 (10), 367 (15), 325 (15), 261 (20), 247 (20), 205 (80). HRMS: Calcd. for $C_{29}H_{32}O_4Si$: 472.2070, Found: 472.2074.

4.3.3. (6*E*)-1-(4-Benzoyloxyphenyl)-5-Hydroxy-7-phenylhept-6-en-3-one (**18**)

To a stirred solution of LDA (1.57 mmol) in THF (5 mL) at −78°C was added a solution of ketone **16** (0.35 g, 1.32 mmol) in THF (5 mL) *via* a syringe. After 15 min, cinnamic aldehyde (0.17 mL, 1.31 mmol) in THF (5 mL) was added. The mixture was stirred for 20 min at the indicated temperature and the reaction was quenched with saturated NH_4Cl. The solution was allowed to warm to ambient temperature and then extracted with EtOAc. The organic phase was washed with brine, dried, and evaporated. The obtained residue was purified on a silica gel column with EtOAc:hexane as eluent to give 0.33 g (63%) of ketol **18**, M.p. (hexane-ether) 74.2–75.0°C. IR (KBr): (ν_{max} cm^{-1}) 3446, 3035, 2933, 1736, 1690, 1288, 1061, 960; ^{1}H NMR (acetone-d_6): δ 2.70 (2H, dd, $J = 15.6$, 4.8 Hz, H-4a), 2.76 (2H, dd, $J = 15.6$, 8.1 Hz, H-4b), 2.91 (4H, s, H-1 and H-2), 4.77 (1H, m, H-5), 6.34 (1H, dd, $J = 15.9$, 5.7 Hz, H-6), 6.65 (1H, dd, $J = 15.9$, 1.3 Hz, H-7), 7.17 (2H, d, $J = 8.6$ Hz, H-3′ and H-5′), 7.23 (1H, tt, $J = 7.3$, 1.3 Hz, H-4″), 7.31 (2H, dd, $J = 7.3$, 7.7 Hz, H-3″ and H-5″), 7.32 (2H, d, $J = 8.6$ Hz, H-2′ and H-6′), 7.41 (2H, d, $J = 7.7$ Hz, H-2″ and H-6″), 7.59 (2H, dd, $J = 7.5$, 8.1 Hz, H-3‴ and H-5‴), 7.72 (1H, tt, $J = 7.5$, 1.3 Hz, H-4‴), 8.17 (2H, d, $J = 8.1$ Hz, H-2‴ and H-6‴); ^{13}C NMR (acetone-d_6): δ 29.5 (C-1), 45.5 (C-2), 50.9 (C-4), 69.2 (C-5), 122.5 (C-3′ and C-5′), 127.2 (C-2″ and C-6″), 128.2 (C-4″), 129.4 (C-3″ and C-5″), 129.6 (C-3‴ and C-5‴), 129.8 (C-7), 130.2 (C-2′ and C-6′), 130.6 (C-1′), 130.7 (C-2‴ and C-6‴), 133.4 (C-6), 134.6 (C-4‴), 138.0 (C-1″), 140.2 (C-1‴), 150.3 (C-4′), 165.6 (COO), 208.6 (C-3); EIMS: m/z 400 (M^+, 14), 382 (28), 268 (52), 331 (56), 105 (100). HRMS: Calcd. for $C_{26}H_{24}O_4$: 400.1675, Found: 400.1674.

4.3.4. (4*E*,6*E*)-1-(4-Benzoyloxyphenyl)-7-Phenylhepta-4,6-dien-3-one (**19**)

To a solution of ketol **18** (0.29 g, 0.73 mmol) in benzene (10 mL) was added a catalytical amount of TsOH and activated molecular sieves 4 Å. The resulting solution was heated under reflux for 10 min, cooled and diluted with ether. The solution was washed with water, brine, dried, and evaporated to give compound **19**, M.p. (toluene) 92.7–94.7°C. The diene **19** was used in the next step without purification. IR (KBr): (ν_{max} cm^{-1}) 3068, 3035, 2933, 1737, 1730, 1680, 1664, 1264, 1059; ^{1}H NMR ($CDCl_3$): δ 2.93 (2H, t, $J = 7.3$ Hz, H-2), 2.99 (2H, t, $J = 7.3$ Hz, H-1), 6.28 (1H, d, $J = 15.3$ Hz, H-4), 6.86 (1H, dd, $J = 10.5$, 15.6 Hz, H-6), 6.93 (1H, d, $J = 15.6$ Hz, H-7), 7.12 (2H, d, $J = 8.3$ Hz, H-3′ and H-5′), 7.26 (2H, d, $J = 8.3$ Hz H-2′, and H-6′), 7.34 (4H, m, H-5, H-3″, H-4″, and H-5″), 7.46 (2H, $J = 8.1$ Hz, H-2″ and H-6″), 7.49 (2H, dd, $J = 8.1$, 7.5 Hz, H-3‴ and H-5‴), 7.61 (1H, t, $J = 7.5$ Hz, H-4‴), 8.19 (2H, d, $J = 8.1$ Hz, H-2‴ and H-6‴); ^{13}C NMR ($CDCl_3$): δ 29.6 (C-1), 42.3 (C-2), 121.7 (C-3′ and C-5′), 126.7 (C-6), 127.3 (C-2″ and C-6″), 128.6 (C-2′ and C-6′), 128.8 (C-3‴ and C-5‴), 129.2 (C-4″), 129.3 (C-1′), 129.4 (C-3″ and C-5″), 130.2 (C-2‴ and C-6‴), 133.5 (C-4‴), 136.0 (C-1″), 138.9 (C-1‴), 141.5 (C-7), 142.8 (C-5), 149.3 (C-4′), 165.3 (COO), 199.1 (C-3); EIMS: m/z 382 (M^+, 70), 291 (6), 287 (10), 105 (100); HRMS: Calcd. for $C_{26}H_{22}O_3$: 382.1569, Found: 382.1568.

4.3.5. (4*E*,6*E*)-1-(4-Hydroxyphenyl)-7-Phenylhepta-4,6-dien-3-one (**14**) From **17**

To a solution of TMS-ether **17** (0.163 g, 0.35 mmol) in MeOH (5 mL) was added anhydrous K_2CO_3 (0.097 g, 0.7 mmol) and the solution was stirred at room temperature for 3 h. The reaction was quenched with 0.1 N HCl by adjusting to pH 8. The methanol was evaporated, and the residue extracted with EtOAc, washed with brine, dried, and evaporated. The obtained oil was separated on a silica gel column with CH_2Cl_2 as eluent to yield ketone **14** (0.048 g, 49%). For analytical data, see 4.3.6.

4.3.6. (4*E*,6*E*)-1-(4-Hydroxyphenyl)-7-Phenylhepta-4,6-dien-3-one (**14**) From **19**

To a solution of diene **19** (0.24 g, 0.63 mmol) in MeOH (12 mL) was added anhydrous K_2CO_3 (0.02 g, 0.15 mmol). The solution was stirred at

room temperature for 0.5 h and reaction was quenched with 0.1 N HCl by adjusting to pH 8. Water was added, and the mixture was extracted with EtOAc. The organic phase was washed with brine, dried, and evaporated. The obtained oil was purified as above to yield ketone **14** (0.11 g, 65%), M.p. (hexane-ether) 129.3–130.0°C. IR (neat): (ν_{max} cm^{-1}) 3359, 3027, 1664, 1645, 1614, 1223; ^{1}H NMR ($CDCl_3$): δ 2.82 (2H, t, $J=7.6$, H-2), 2.83 (2H, t, $J=7.6$, H-1), 6.19 (1H, d, $J=15.4$ Hz, H-4), 6.67 (2H, d, $J=8.3$ Hz, H-3′ and H-5′), 6.84 (1H, d, $J=15.4$ Hz, H-7), 7.00 (2H, d, $J=8.5$ Hz, H-2′ and H-6′), 6.77 (1H, dd, $J=15.4$, 10.5, H-6), 7.23 (1H, dd, $J=15.4$, 10.5 Hz, H-5), 7.26 (1H, m, H-3″, H-4″ and H-5″), 7.37 (2H, d, $J=8.5$ Hz, H-2″ and H-6″); ^{13}C NMR ($CDCl_3$): δ 30.3 (C-1), 42.9 (C-2), 115.2 (C-3′ and C-5′), 126.5 (C-6), 127.0 (C-2″ and C-6″), 128.5 (C-3″ and C-5″), 128.9 (C-4″), 129.2 (C-2′ and C-6′), 129.2 (C-4), 133.3 (C-1′), 135.6 (C-1″), 141.3 (C-7), 142.8 (C-5), 154.0 (C-4′), 199.7 (C-3); EIMS: m/z 278 (M^+, 100), 184 (30), 171 (50), 157 (90), 128 (70); HRMS: Calcd. for $C_{19}H_{18}O_2$: 278.1307, Found: 278.1307.

4.3.7. (3*E*)-4-(3,4-Dihydroxyphenyl)-But-3-en-2-one (**21**)

3,4-Dihydroxybenzaldehyde **20** (1.38 g, 10 mmol) and acetone (5 mL, 66 mmol) were dissolved in degassed acetonitrile (30 mL). Subsequently, piperidine (0.247 mL, 2.5 mmol), acetic acid (0.143 mL, 2.5 mmol) and molecular sieves 4Å (0.3 g) were added to the solution, and the resulting purple mixture was refluxed for 4 h. The solution was cooled and solvent was evaporated. The residue obtained was dissolved in a small amount of acetone and absorbed on silica gel, and acetone was evaporated. The resultant material was purified on a silica gel column with $CHCl_3$:EtOAc 95:5 as eluent to yield the yellow ketone **21** (0.95 g, 53%) which was identical to the described compound,[31] M.p. 177.3–178.0°C (lit. 175–177°C, water). ^{1}H NMR (acetone-d_6): δ 2.28 (3H, s, H-1), 6.54 (1H, d, $J=16.3$ Hz, H-3), 6.88 (1H, d, $J=8.1$ Hz, H-5′), 7.06 (1H, dd, $J=1.7$, 8.1 Hz, H-6′), 7.17 (1H, d, $J=1.7$ Hz, H-2′), 7.48 (1H, d, $J=16.3$ Hz, H-4); ^{13}C NMR (acetone-d_6): δ 27.3 (C-1), 115.2 (C-5′), 116.4 (C-2′), 122.7 (C-6′), 125.3 (C-3), 127.9 (C-1′), 144.2 (C-4), 146.4 (C-3′), 148.8 (C-4′), 197.8 (C-2); EIMS: m/z 178 (M^+, 84), 163 (100).

4.3.8. 4-(3,4-Dihydroxyphenyl)-Butan-2-one (**22**)

To a solution of ketone **21** (1.16 g, 6.5 mmol) and ammonium formate (0.82 g, 13 mmol) in methanol (20 mL) was carefully added 10%

palladium on charcoal (0.67 g) and the resulted mixture was stirred for 10 min at room temperature. To this was added acetone (2.5 mL, 33 mmol) and the solution was stirred for another 50 min after which the catalyst was filtered off and washed with $CHCl_3$, and the combined filtrates were evaporated. The obtained oil was purified on a silica gel column with $CHCl_3$:EtOAc 80:20 as eluent to yield the colorless ketone **22** (1.06 g, 90%), in all respects identical to the described compound[32] M.p. 85.5–85.8°C (lit. 85–86°C, ether). ^{1}H NMR (acetone-d_6): δ 2.08 (3H, s, H-1), 2.69 (4H, m, H-3 and H-4), 6.52 (1H, dd, $J = 1.9$, 8.1 Hz, H-6′), 6.69 (1H, d, $J = 1.9$ Hz, H-2′), 6.72 (1H, d, $J = 8.1$ Hz, H-5′); ^{13}C NMR (acetone-d_6): δ 29.8 (C-1), 29.7 (C-4), 46.6 (C-3), 116.0 and 116.2 (C-2′ and C-5′), 120.2 (C-6′), 133.9 (C-1′), 143.9 (C-4′), 145.7 (C-3′), 207.8 (C-2); EIMS: m/z 180 (M^+, 80), 137 (50), 123 (100); HRMS: Calcd. for $C_{10}H_{12}O_3$: 180.0786, Found: 180.0787.

4.3.9. 4-[3,4-*bis*-(1-Ethoxyethoxy)-Phenyl]-Butan-2-one (**23**)

Pyridinium *p*-toluenesulfonate (0.18 g, 10 mol%) was added to a solution of ketone **22** (1.29 g, 7.15 mmol) in ethyl ether (25 mL) and vinyl ethyl ether (15 mL). The resulting solution was stirred for 24 h at room temperature. When the reaction was complete, the solution was diluted with hexane, separated from the catalyst by decanting, washed with water, brine, dried over Na_2SO_4, and evaporated to give ketone **23** as oil (2.20 g). The product was sufficiently pure for using in the next step. A small amount was purified for an analytical purposes on a silica gel column with CH_2Cl_2 as eluent to give a slightly yellow oil in 95% yield. IR (neat): (ν_{max} cm^{-1}) 2982, 2936, 1715, 1600, 1263, 1107, 947; ^{1}H NMR (acetone-d_6): δ 1.13 (6H, m, CH_3CH$_2$), 1.41 (6H, m, CH_3CH), 2.08 (3H, s, H-1), 2.75 (4H, m, H-3 and H-4), 3.55 (2H, m, CH$_3$CH_2), 3.79 (2H, m, CH$_3$CH_2), 5.32 (1H, q, $J = 5.3$ Hz, CH$_3$CH), 5.37 (1H, dq, $J = 5.3$, 2.1 Hz, CH$_3$CH), 6.79 (1H, dd, $J = 2.1$, 8.2 Hz, H-6′), 6.96 (1H, d, $J = 2.1$ Hz, H-2′), 6.97 (1H, d, $J = 8.2$ Hz, H-5′); ^{13}C NMR (acetone-d_6): δ 15.55/15.56 (*C*H$_3$CH$_2$), 20.86/20.89/20.90/20.93 (*C*H$_3$-CH), 29.76 (C-4), 29.83 (C-1), 45.33 (C-3), 62.34/62.38/62.42/62.47 (CH$_3$*C*H$_2$), 101.56/101.64/101.68/101.75 (CH$_3$-*C*H), 120.42/120.46 and 120.52/120.58 (C-2′ and C-5′), 123.06/123.10 (C-6′), 136.93/136.98 (C-1′), 146.92/146.99 (C-4′), 148.78/148.85 (C-3′), 207.24 (C-2); EIMS: m/z 324 (M^+, 10), 252 (65), 180 (90), 123 (70); HRMS: Calcd. for $C_{18}H_{28}O_5$: 324.1937, Found: 324.1935.

4.3.10. (4*E*,6*E*)-1-[3,4-*bis*-(1-Ethoxyethoxy)-Phenyl]-7-Phenylhepta-4,6-dien-3-one (**24**)

To a stirred solution of LDA (1.12 mmol) in THF (5 mL) at −78°C was added a solution of ketone **23** (0.246 g, 0.76 mmol) in THF (5 mL). After 15 min, cinnamic aldehyde (0.092 mL, 0.7 mmol) in THF (5 mL) was added. The almost colorless mixture was stirred for 30 min at the indicated temperature and TMSCl (0.12 mL, 0.95 mmol) was added in one portion. The cooling bath was removed and solution was allowed to warm to ambient temperature. After 30 min DBU (0.12 mL, 0.8 mmol) was added and the mixture was refluxed for 3 h. The mixture was cooled and the reaction quenched with saturated NH_4Cl and diluted with EtOAc. The organic phase was washed with water and brine, dried and evaporated. The obtained oil was purified on a silica gel column with EtOAc:hexane 1:9 as eluent to give ketone **24** as yellow oil (0.147 g, 44%). IR (neat): (ν_{max} cm^{-1}) 2977, 2932, 1683, 1660, 1619, 1265, 942; ^1H NMR ($CDCl_3$): δ 1.20 (6H, m, CH_3CH_2), 1.48 (6H, m, CH_3CH), 2.89 (4H, m, H-1 and H-2), 3.57 (2H, m, CH_3CH_2), 3.84 (2H, m, CH_3CH_2), 5.30 (1H, q, $J = 5.1$ Hz, CH_3CH), 5.34 (1H, q, $J = 5.1$ Hz, CH_3CH), 6.27 (1H, d, $J = 15.5$ Hz, H-4), 6.80 (1H, dd, $J = 1.3$, 8.2 Hz, H-6′), 6.85 (1H, dd, $J = 15.5$, 10.5 Hz, H-6), 6.92 (1H, d, $J = 15.5$ Hz, H-7), 6.94 (1H, d, $J = 1.3$ Hz, H-2′), 6.99 (1H, d, $J = 8.2$ Hz, H-5′), 7.31 (2H, m, H-4″ and H-5), 7.35 (2H, dd, $J = 7.8$, 7.2 Hz, H-3″ and H-5″), 7.45 (2H, d, $J = 7.8$ Hz, H-2″ and H-6″); ^{13}C NMR ($CDCl_3$): δ 15.23, 15.27 (CH_3CH_2), 20.45/20.49/20.50/20.56 (CH_3-CH), 29.72 (C-1), 42.32 (C-2), 61.96/62.01/62.19/62.24 (CH_3CH_2), 101.06/101.13/101.13/101.20 (CH_3-CH), 119.84/119.90 and 119.98/120.05 (C-2′ and C-5′), 122.56/122.63 (C-6′), 126.66 (C-6), 127.24 (C-2″ and C-6″), 128.45 (C-3″ and C-5″), 129.21 (C-4″), 129.56 (C-4), 135.99/136.03 (C-1′), 136.11 (C-1″), 141.41 (C-7), 142.69 (C-5), 146.03/146.06 (C-4′), 147.78/147.82 (C-3′), 199.32 (C-3); EIMS: m/z 438 (M^+, 10), 366 (25), 321 (20), 294 (100), 157 (50); HRMS: Calcd. for $C_{27}H_{34}O_5$: 438.2406, Found: 438.2405.

4.3.11. (4*E*,6*E*)-1-(3,4-Dihydroxyphenyl)-7-Phenylhepta-4,6-dien-3-one (**12**) From **23**

To a stirred solution of LDA (1.78 mmol) in THF (5 mL) at −78°C was added a solution of ketone **23** (0.45 g, 1.36 mmol) in THF (5 mL) *via* a syringe. The reaction mixture was stirred for 15 min and a solution of cinnamic aldehyde (0.182 mL, 1.38 mmol) in THF (5 mL) was added. The mixture was stirred for 30 min at the indicated temperature, after which

the cooling bath was removed and the solution allowed to warm to ambient temperature and stirred for an additional 1 h. The reaction mixture was cooled again to $-30^{\circ}C$, quenched with saturated NH_4Cl and extracted with EtOAc. The organic phase was washed with brine, dried, and evaporated. The obtained oil was dissolved in methanol (5 mL) and a few crystals of TsOH were added. After 5 min the solvent was evaporated without heating and the resulting dark orange oil was dissolved in a 1:1 mixture of benzene:THF (8 mL). TsOH (0.026 g, 0.14 mmol) was added and the mixture was stirred for 48 h at room temperature. The solvent was evaporated and the residue was separated on a silica gel column with EtOAc:hexane 3:7 as eluent to give ketone **12** as yellow oil (0.15 g, 38%). For analytical data, see 4.3.12.

4.3.12. (4*E*,6*E*)-1-(3,4-Dihydroxyphenyl)-7-Phenylhepta-4,6-dien-3-one (**12**) From **24**

To a solution of ketone **24** (0.308 g, 0.7 mmol) in methanol (5 mL), TsOH (0.010 g, 0.05 mmol) was added. After 5 min the solvent was evaporated without heating and the resulting dark orange oil was purified on a silica gel column with EtOAc:hexane 3:7 as eluent to give ketone **12** (0.197 g, 96%). IR (neat): (ν_{max} cm^{-1}) 3357, 3028, 1642, 1610, 1281, 997; ^1H NMR ($CDCl_3$): δ 2.88 (2H, t, $J = 7.2$ Hz, H-1), 2.90 (2H, t, $J = 7.2$ Hz, H-2), 6.28 (1H, d, $J = 15.3$ Hz, H-4), 6.65 (1H, dd, $J = 2.0$, 8.2 Hz, H-6′), 6.76 (1H, d, $J = 2.0$ Hz, H-2′), 6.79 (1H, d, $J = 8.2$ Hz, H-5′), 6.87 (1H, dd, $J = 10.3$, 15.3 Hz, H-6), 6.95 (1H, d, $J = 15.3$ Hz, H-7), 7.35 (4H, m, H-5, H-3″, H-4″ and H-5″), 7.47 (2H, d, $J = 7.2$ Hz, H-2″ and H-6″); ^{13}C NMR ($CDCl_3$): δ 29.7 (C-1), 42.5 (C-2), 115.2 and 115.4 d (C-2′ and C-5′), 120.4 (C-6′), 127.7 (C-6), 127.3 (C-2″ and C-6″), 128.9 (C-3″ and C-5″), 129.2 (C-4″), 129.5 (C-4), 133.9 (C-1′), 136.0 (C-1″), 141.5 (C-7), 142.2 (C-4′), 142.9 (C-5), 143.9 (C-3′), 199.9 (C-3); EIMS: m/z 294 (M^+, 100), 223 (15), 184 (30), 171 (50), 157 (100), 128 (70); HRMS: Calcd. for $C_{19}H_{18}O_3$: 294.1256, Found: 294.1255.

4.3.13. 3,4-Di-(1-Ethoxyethoxy)-Benzaldehyde (**25**)

Pyridinium *p*-toluenesulfonate (0.75 g, 10 mol%) was added to the solution of aldehyde **20** (4.14 g, 30 mmol) in diethyl ether (30 mL) and vinyl ethyl ether (37 mL). The resulting solution was stirred for 3 d at room temperature. When protection was complete, the solution was diluted with hexane, separated from the catalyst by decanting, washed

with water, brine, dried over Na_2SO_4, and evaporated (8.46 g). The product was further purified on a silica gel column with EtOAc:hexane 1:9 as eluent to give aldehyde **25** (7.67 g, 91%). IR (neat): (ν_{max} cm^{-1}) 2978, 2934, 2897, 1695, 1596, 1582, 1512, 1435, 1382, 1344, 1271, 1230; ^{1}H NMR (acetone-d_6): δ 1.17 (6H, m, CH_3CH$_2$), 1.50 (6H, m, CH_3CH), 3.58 (2H, m, CH$_3$CH_2), 3.80 (2H, m, CH$_3$CH_2), 5.45 (1H, dq, $J = 1.9$, 5.4 Hz, CH$_3$CH), 5.59 (1H, q, $J = 5.4$ Hz, CH$_3$CH), 7.27 (1H, d, $J = 8.5$ Hz, H-5), 7.56 (1H, m, H-6), 7.60 (1H, d, $J = 2.0$ Hz, H-2), 9.82 (1H, s, CHO); ^{13}C NMR (acetone-d_6): δ 15.50/15.52 (*C*H$_3$CH$_2$), 20.54/20.55/20.66/20.70 (*C*H$_3$CH), 63.08/63.10/63.26/63.28 (CH$_3$*C*H$_2$), 101.84/101.87/102.44/102.45 (CH$_3$*C*H), 118.39/118.47 (C-5), 119.60/119.81 (C-2), 127.73/127.77 (C-6), 132.43/132.46 (C-1), 148.85/148.90 (C-3), 154.99/155.00 (C-4), 192.73 (CHO). HRMS: Calcd. for $C_{15}H_{22}O_5$: 282.1467, Found: 282.1473.

4.3.14. [3,4-*bis*-(1-Ethoxyethoxy)-Phenyl]-Methanol (**26**)

Sodium borohydride (0.20 g, 5.26 mmol) was added portionwise to a solution of aldehyde **25** (5.03 g, 17 mmol) in a mixture of CH_2Cl_2–MeOH (50 mL, 1:1) at -5°C over 5 min. The resulting solution was stirred for 0.5 h and then the reaction was quenched with solid NH_4Cl followed by addition of water. The organic phase was separated, washed with brine, dried, and evaporated to give alcohol **26** as pale yellow oil (5.10 g). The product was used without purification. IR (neat): (ν_{max} cm^{-1}) 3453, 2982, 2936, 2891, 1500, 1267, 1034; ^{1}H NMR (acetone-d_6): δ 1.14 (6H, m, CH_3CH$_2$), 1.43 (6H, m, CH_3CH), 3.56 (2H, m, CH$_3$CH_2), 3.80 (2H, m, CH$_3$CH_2), 4.54 (2H, brs, CH_2OH), 5.36 (1H, q, $J = 5.2$ Hz, CH$_3$CH), 5.39 (1H, q, $J = 5.2$ Hz, CH$_3$CH), 6.93 (1H, m, H-6), 7.03 (1H, d, $J = 8.1$ Hz, H-5), 7.11 (1H, d, $J = 2.1$ Hz, H-2); ^{13}C NMR (acetone-d_6): δ 15.58 (*C*H$_3$CH$_2$), 20.90/20.93/20.93/20.97 (*C*H$_3$CH), 62.47/62.49/62.49/62.54 (CH$_3$*C*H$_2$), 64.33 (CH$_2$OH), 101.67/101.75/101.78/101.85 (CH$_3$*C*H), 118.79/118.97 (C-2), 120.28/120.40 (C-5), 121.57/121.61 (C-6), 138.16/138.21 (C-1), 147.71/147.78 (C-4), 148.86/148.93 (C-3). HRMS: Calcd. for $C_{15}H_{24}O_5$: 284.1624, Found: 284.1622.

4.3.15. Acetic acid 3,4-*bis*-(1-Ethoxyethoxy)-Benzyl ester (**27**)

To a solution of alcohol **26** (5.10 g, 17 mmol) and pyridine (1.91 mL, 23.8 mmol) in CH_2Cl_2 (30 mL) at room temperature was added acetic anhydride (1.93 mL, 20.4 mmol). The resulted solution was stirred for

1 h and then saturated $NaHCO_3$ was added. The organic phase was separated, washed with brine, dried, and evaporated to give acetate **27** as a pale yellow oil (5.90 g). The product was used without purification. IR (neat): (ν_{max} cm^{-1}) 2982, 2945, 2891, 1738, 1509, 1038; ^{1}H NMR (acetone-d_6): δ 1.14 (6H, m, CH_3CH$_2$), 1.44 (6H, m, CH_3CH), 2.03 (3H, s, OAc), 3.57 (2H, m, CH$_3$CH_2), 3.80 (2H, m, CH$_3$CH_2), 5.00 (2H, s, CH_2OAc), 5.39 (2H, m, CH$_3$CH), 6.98 (1H, m, H-6), 7.08 (1H, d, $J = 8.4$ Hz, H-5), 7.14 (1H, d, $J = 1.9$ Hz, H-2); ^{13}C NMR (acetone-d_6): δ 15.54 (*C*H$_3$CH$_2$), 20.80/20.83/20.83/20.86 (*C*H$_3$CH and *C*H$_3$CO), 62.37/62.40/62.43/62.46 (CH$_3$*C*H$_2$), 66.16 (*C*H$_2$OAc), 101.61/101.68/101.69/101.76 (CH$_3$*C*H), 119.99/120.09 (C-2′), 120.59/120.70 (C-5′), 123.50/123.54 (C-6′), 131.83/131.88 (C-1′), 148.69/148.75/148.78/148.83 (C-3′ and C-4′), 170.82 (CO); HRMS: Calcd. for $C_{17}H_{26}O_6$: 326.1732, Found: 284.1729.

4.3.16. (4*E*)-3-Hydroxy-5-phenylpent-4-enoic acid 3,4-*bis*-(1-Ethoxyethoxy)-Benzyl ester (**28**)

To a stirred solution of LDA (3.6 mmol) in THF (10 mL) at −78°C was added a solution of acetate **27** (1.02 g, 3 mmol) in THF (7 mL) *via* a syringe. After 15 min cinnamic aldehyde (0.4 mL, 3 mmol) in THF (5 mL) was added. The mixture was stirred for 20 min at the indicated temperature and the reaction was quenched with saturated NH_4Cl. The solution was allowed to warm to ambient temperature and extracted with EtOAc. The organic phase was washed with brine, dried, and evaporated. The obtained residue was purified on a silica gel column with EtOAc:hexane 1:2 as eluent to give 1.15 g (81%) of hydroxy ester **28.** IR (neat): (ν_{max} cm^{-1}) 3471, 2982, 2932, 2895, 1734, 1505, 1267; ^{1}H NMR (C_6D_6): δ 1.08 (6H, m, CH_3CH$_2$), 1.42 (6H, m, CH_3CH), 2.43 (1H, dd, $J = 15.4$, 4.2 Hz, H-2a), 2.56 (1H, ddd, $J = 15.4$, 8.3, 2.0 Hz, H-2b), 3.40 (2H, m, CH$_3$CH_2), 3.74 (2H, m, CH$_3$CH_2), 4.69 (1H, m, H-3), 4.99 (1H, d, $J = 12.2$ Hz, CH_2OCO), 5.05 (1H, dd, $J = 12.2$, 4.9 Hz, CH_2OCO), 5.25 (1H, q, $J = 5.2$ Hz, CH$_3$CH), 5.30 (1H, q, $J = 5.2$ Hz, CH$_3$CH), 6.12 (1H, dd, $J = 16.1$, 5.7 Hz, H-4), 6.59 (1H, d, $J = 16.1$ Hz, H-5), 6.89 (1H, brd, $J = 8.3$ Hz, H-6″), 7.02 (1H, m, H-5″), 7.05 (1H, t, $J = 7.5$ Hz, H-4′), 7.12 (2H, dd, $J = 8.5$, 7.5 Hz, H-3′ and H-5′), 7.21 (2H, d, $J = 8.5$ Hz, H-2′ and H-6′), 7.23 (1H, s, H-2″); ^{13}C NMR (C_6D_6): δ 15.40/15.43 (*C*H$_3$CH$_2$), 20.54/20.58/20.59/20.62 (*C*H$_3$CH), 42.13/42.15 (C-2), 61.78/61.80/61.92/61.92/61.94/61.95/61.96/61.96 (CH$_3$*C*H$_2$), 66.25/66.28 (*C*H$_2$OCO), 69.07 (C-3), 101.13/101.22/101.24/

101.24/101.26/101.33/101.35/101.38 (CH_3CH), 119.72/119.75/119.78/119.80 (C-5″), 120.27/120.33/120.43/120.51 (C-2″), 123.23/123.25/123.30/123.32 (C-6″), 126.91 (C-2′ and C-6′), 127.82 (C-4′), 128.80 (C-3′ and C-5′), 130.52/130.54 (C-5), 130.90/130.92/130.93/130.95 (C-1″), 131.04/131.07 (C-4), 137.18 (C-1′), 148.47/148.51/148.58/148.62 (C-3″), 148.61/148.67/148.70/148.77 (C-4″), 171.67/171.69 (C-1). HRMS: Calcd. for $C_{26}H_{34}O_7$: 458.2305, Found: 458.2300.

4.3.17. (2*E*,4*E*)-5-Phenylpenta-2,4-dienoic acid 3,4-*bis*-(1-Ethoxyethoxy)-Benzyl ester (**29**)

To a solution of the hydroxy ester **28** (1.02 g, 2.17 mmol) and DBU (0.79 mL, 5.2 mmol) in benzene (20 mL) was added acetic anhydride (0.24 mL, 2.6 mmol). The solution was heated under reflux for 2.5 h, cooled and evaporated. The residue was filtered through a short silica gel column to give 0.73 g (74%) of compound **29**. IR (neat): (ν_{max} cm^{-1}) 2979, 2933, 2891, 1715, 1626, 1501, 1129; ^1H NMR (C_6D_6): δ 1.09 (6H, m, CH_3CH_2), 1.43 (6H, m, CH_3CH), 3.40 (2H, m, CH_3CH_2), 3.76 (2H, m, CH_3CH_2), 5.19 (2H, s, CH_2OCO), 5.26 (1H, q, $J = 5.2$ Hz, CH_3CH), 5.31 (1H, q, $J = 5.2$ Hz, CH_3CH), 6.01 (1H, d, $J = 15.4$ Hz, H-2), 6.41 (1H, d, $J = 15.4$ Hz, H-5), 6.53 (1H, dd, $J = 15.4$, 11.0 Hz, H-4), 6.98 (1H, dd, $J = 8.2$, 1.8 Hz, H-6″), 7.07 (6H, m, H-2′- H-6′ and H-5″), 7.31 (1H, m, H-2″), 7.56 (1H, dd, $J = 15.4$, 11.0 Hz, H-3); ^{13}C NMR (C_6D_6): δ 15.40/15.44 (CH_3CH_2), 20.62/20.65/20.66/20.70 (CH_3CH), 61.96/61.98/61.99/62.00 (CH_3CH_2), 66.12 (CH_2OCO), 101.28/101.30/101.39/101.42 (CH_3CH), 119.80/119.87 (C-5″), 120.46/120.53 (C-2″), 121.50 (C-2), 123.39/123.41 (C-6″), 126.43 (C-4), 127.52 (C-2′ and C-6′), 128.88 (C-3′ and C-5′), 129.07 (C-4′), 131.45/131.47 (C-1″), 136.42 (C-1′), 140.64 (C-5), 145.22 (C-3), 148.57/148.61 and 148.67/148.70 (C-3″ and C-4″), 166.54 (C-1); HRMS: Calcd. for $C_{26}H_{32}O_6$: 440.2199, Found: 440.2205.

4.3.18. (2*E*,4*E*)-5-Phenylpenta-2,4-dienoic acid 3,4-dihydroxybenzyl ester (**30**)

To a solution of the dienoate **29** (0.083 g, 0.18 mmol) in methanol (1 mL) was added TsOH (10 mg, 0.005 mmol). After 5 min pyridine (0.1 mL) and water were added. The organic phase was extracted with EtOAc, washed with brine, dried, and evaporated to give compound **30** (0.057 g, quant), M.p. 108.8–110.6°C (aq. MeOH). IR (KBr): (ν_{max} cm^{-1})

3497, 3381, 2956, 2928, 2854, 1681, 1620, 1519, 1288, 1001; ^{1}H NMR (acetone-d_6): δ 5.06 (2H, s, CH_2), 6.09 (1H, d, $J = 15.3$ Hz, H-2), 6.78 (1H, dd, $J = 8.0$, 2.0 Hz, H-6″), 6.83 (1H, d, $J = 8.0$ Hz, H-5″), 6.93 (1H, d, $J = 2.0$ Hz, H-2″), 7.10 (2H, m, H-4 and H-5), 7.34 (1H, tt, $J = 7.3$, 1.5 Hz, H-4′), 7.39 (2H, ddd, $J = 8.5$, 7.3, 1.5 Hz, H-3′ and H-5′), 7.47 (1H, ddd, $J = 15.3$, 9.1, 1.2 Hz, H-3), 7.58 (2H, dd, $J = 8.5$, 1.5 Hz, H-2′ and H-6′); ^{13}C NMR (acetone-d_6): δ 66.6 (*C*H$_2$), 116.0 (C-5″), 116.7 (C-2″), 121.2 (C-6″), 122.1 (C-2), 127.2 (C-4), 128.0 (C-2′ and C-6′), 129.0 (C-1″), 129.6 (C-3′ and C-5′), 129.8, (C-4′), 137.1 (C-1′), 141.3 (C-5), 145.6 (C-3), 145.9 (C-3″), 146.1 (C-4″), 167.0 (C-1). HRMS: Calcd. for $C_{18}H_{16}O_4$: 296.1049, Found: 296.1049.

4.4. Wittig-Horner Synthesis

4.4.1. 3-(3,4-Dihydroxyphenyl)-Propionic acid methyl ester (**31**)

To a solution of hydrocaffeic acid (**1**) (1.80 g, 10 mmol) in methanol (30 mL) was added acetyl chloride (0.079 g, 1 mmol) and the resulting solution was stirred at room temperature. After 12 h no starting material was detected and the solvent was evaporated and the obtained oil was dried thoroughly under vacuum. ^{1}H NMR ($CDCl_3$): δ 2.54 (2H, t, $J = 7.7$ Hz, H-2), 2.78 (2H, t, $J = 7.7$ Hz, H-3), 3.62 (3H, s, OMe), 6.56 (1H, dd, $J = 2.2$, 8.2 Hz, H-6′), 6.65 (1H, d, $J = 2.2$ Hz, H-2′), 6.71 (1H, d, $J = 8.2$ Hz, H-5′); ^{13}C NMR ($CDCl_3$): δ 30.3 (C-3), 35.9 (C-2), 51.8 (OCH_3), 115.4 (C-2′), 115.4 (C-5′), 120.6 (C-6′), 133.4 (C-1′), 142.0 (C-4′), 143.6 (C-3′), 173.9 (*C*$OOCH_3$).

4.4.2. 3-[3,4-*bis*-(1-Ethoxyethoxy)-Phenyl]-Propionic acid methyl ester (**32**)

The dried ester **31** was dissolved in a mixture of diethyl ether (15 mL) and ethyl vinyl ether (14.4 mL). Pyridinium *p*-toluenesulfonate (0.251 g, 10 mol%) was added to the solution and the resulting mixture was stirred for 24 h at room temperature. When protection had been completed, the solution was diluted with hexane, separated from the catalyst by decanting, washed with water and brine, dried over Na_2SO_4, and evaporated to yield an oily product (3.5 g). The product was purified on silica gel column with CH_2Cl_2 as eluent, giving a slightly yellow oil in 92% yield. IR (neat): (ν_{max} cm^{-1}) 2982, 2936, 1738, 1600, 1505, 1263, 947;

^{1}H NMR (acetone-d_6): δ 1.14 (6H, m, CH_3CH$_2$), 1.43 (6H, m, CH_3CH), 2.59 (2H, t, $J = 7.6$ Hz, H-2), 2.84 (2H, t, $J = 7.6$ Hz, H-3), 3.56 (2H, m, CH$_3$CH_2), 3.61 (3H, s, OCH$_3$), 3.81 (2H, m, CH$_3$CH_2), 5.34 (1H, q, $J = 5.3$ Hz, CH$_3$CH), 5.39 (1H, dq, $J = 5.3$, 2.1 Hz, CH$_3$CH), 6.81 (1H, dd, $J = 2.1$, 8.2 Hz, H-6′), 6.70 (1H, d, $J = 2.0$ Hz, H-2′), 6.70 (1H, d, $J = 8.2$ Hz, H-5′); ^{13}C NMR (acetone-d_6) δ 15.55/15.56 (CH_3CH$_2$), 20.86/20.89/20.90/20.93 (CH_3-CH), 30.94 (C-3), 36.17 (C-2), 51.56 (OCH_3), 62.37/62.40/62.47/62.52 (CH$_3$CH_2), 101.61/101.69/101.69/101.76 (CH$_3$-CH), 120.44/120.46 and 120.53/120.58 (C-2′ and C-5′), 123.10/123.14 (C-6′), 136.28/136.33 (C-1′), 147.15/147.23 (C-4′), 148.82/148.88 (C-3′), 173.35 (C-1); EIMS: m/z 324 (M^+, 10), 252 (65), 180 (90), 123 (70); EIMS: m/z 340 (M^+, 10), 268 (30), 196 (95), 123 (45); HRMS: Calcd. for $C_{18}H_{28}O_6$: 340.1886, Found: 340.1885.

4.4.3. 4-[3,4-*bis*-(1-Ethoxyethoxy)-Phenyl]-2-Ketobutylphosphonic acid dimethyl ester (**33**)

To a stirred solution of dimethyl methylphosphonate (2.03 mL, 19 mmol) in THF (30 mL) at −78°C was added a 1.6 N solution of MeLi in ether (11.6 mL, 18.6 mmol) *via* a syringe. The resulting solution was stirred for 1 h at the indicated temperature and ester **32** (2.36 g, 6.5 mmol) in THF (15 mL) was added dropwise at −78°C. After this addition the cooling bath was removed and the reaction was allowed to warm slowly to room temperature. The reaction was stirred at room temperature for 3 h, quenched with saturated NH_4Cl, and extracted with EtOAc. The organic phase was washed with brine, dried, and evaporated to give an oily material (2.9 g). The product was separated *via* a silica gel column with $CHCl_3$ as eluent to give the starting material (0.23 g, 11%) followed by phosphonate **33** as pale yellow oil (2.45 g, 87%). IR (neat): (ν_{max} cm^{-1}) 2981, 1718, 1600, 1507, 1260, 1034, 948; ^{1}H NMR (acetone-d_6): δ 1.14 (6H, m, CH_3CH$_2$), 1.42 (6H, m, CH_3CH), 2.79 (2H, t, $J = 7.4$ Hz, H-4), 2.96 (2H, t, $J = 7.4$ Hz, H-3), 3.18 (2H, d, $^2J_{H\text{-}P} = 22.5$ Hz, H-1), 3.55 (2H, m, CH$_3$CH_2), 3.69 (3H, s, OCH$_3$), 3.71 (3H, s, OCH$_3$), 3.80 (2H, m, CH$_3$CH_2), 5.33 (1H, q, $J = 5.4$ Hz, CH$_3$CH), 5.39 (1H, dq, $J = 1.4$, 5.4 Hz, CH$_3$CH), 6.81 (1H, dd, $J = 1.9$, 8.0 Hz, H-6′), 6.98 (1H, d, $J = 1.9$ Hz, H-2′), 6.99 (1H, d, $J = 8.0$ Hz, H-5′); ^{13}C NMR (acetone-d_6): δ 15.57/15.59 (CH_3CH$_2$), 20.88/20.92/20.96/20.99 (CH_3CH), 29.48 (C-4), 41.58 (d, $^1J_{C\text{-}P} = 126.5$ Hz, C-1), 45.89/45.90 (C-3), 53.04 (OCH$_3$), 53.09 (OCH$_3$), 62.42/62.45/62.55/62.59 (CH$_3$CH_2), 101.66/101.73/101.76/101.83 (CH$_3$CH), 120.46/120.52 and 120.56/120.64 (C-2′ and C-5′), 123.15/123.19 (C-6′), 136.62/136.73

(C-1′), 147.01/147.08 (C-4′), 148.88/148.94 (C-3′), 201.64 (d, $^2J_{C\text{-}P} = 6.0$ Hz, C-2); EIMS: *m/z* 432 (M^+, 10), 360 (5), 315 (20), 288 (100), 178 (65); HRMS: Calcd. for $C_{20}H_{33}O_8P$: 432.1913, Found: 432.1921.

4.4.4. (4*E*,6*E*)-1-[3,4-*bis*-(1-Ethoxyethoxy)-Phenyl]-7-Phenylhepta-4,6-dien-3-one (**24**), Using NaH as Base

To a stirred suspension of NaH (0.019 g of 60% dispersion in mineral oil, 0.48 mmol) in THF (5 mL) at 0°C was added a solution of phosphonate **33** (0.210 g, 0.49 mmol) in THF (5 mL) *via* a syringe. When the evolution of gas had ceased, the red solution was cooled to −30°C and a solution of cinnamic aldehyde (0.06 mL, 0.46 mmol) in THF (3 mL) was added. The cooling bath was removed, and the solution was warmed and then refluxed for 2 h until the red color had faded to yellow. The reaction mixture was cooled, quenched with saturated NH_4Cl, and extracted with EtOAc. The organic phase was washed with water and brine, dried, and evaporated. The obtained oil was purified on a silica gel column with EtOAc:hexane 1:9 as eluent to give ketone **24** (0.093 g, 43%). For analytical data, see 4.3.10.

4.4.5. (4*E*,6*E*)-1-[3,4-*bis*-(1-Ethoxyethoxy)-Phenyl]-7-Phenylhepta-4,6-dien-3-one (**24**), Using DBU as Base

To a stirred solution of phosphonate **33** (0.271 g, 0.62 mmol) in THF (6 mL) were added DBU (0.096 g, 0.63 mmol) and cinnamic aldehyde (0.082 g, 0.62 mmol). The resulting solution was refluxed for 4 h and cooled. The solution was poured in water and the resulting mixture was extracted with EtOAc. The organic phase was washed with water and brine, dried and evaporated. The obtained oil was purified using the method described above (4.4.4.) to yield ketone **24** (0.193 g, 71%). For analytical data, see 4.3.10.

4.4.6. (4*E*,6*E*)-1-(3,4-Dihydroxyphenyl)-7-Phenylhepta-4,6-dien-3-one (**12**)

For procedure and analytical data, see 4.3.12.

4.4.7. 3-(4-Fluorophenyl)-2-Propenal (**34**)

To a solution of acetaldehyde (1.01 g, 8.95 mM) in ethanol (10 mL) at 0°C was added 3 M NaOH (4.88 mL, 12.21 mM) and stirring maintained for 20 min.[30] *p*-Fluorobenzaldehyde (0.394 g, 8.14 mM) in ethanol (5 mL) was added dropwise and the reaction allowed to warm to room temperature and stirred for 90 min. The mixture was poured into water and adjusted to pH 7.0 by the addition of 1 M HCl. The mixture was extracted with EtOAc, the organic extract washed with brine, dried over Na_2SO_4 and the solvent evaporated. Purification by preparative TLC (*n*-hexane:EtOAc 6:1) gave **34** (0.745 g, 61%) as a yellow oil. IR (KBr): (ν_{max} cm^{-1}) 3067, 3031, 2181, 1683, 1621, 1497, 1450, 1419, 1305, 1279, 978, 942, 761. ^{1}H NMR (MeOH-d_4): δ 6.65 (1H, dd, $J = 16.3$, 7.5 Hz, H-2), 7.13 (2H, dd, $J_{H\text{-}3',H\text{-}5'-H\text{-}2',H\text{-}6'} = 8.5$ Hz, $J_{H\text{-}3',H\text{-}5'-F\text{-}4'} = 9.0$ Hz, H-3′, H-5′), 7.45 (1H, d, $J = 16.3$ Hz, H-3), 7.57 (2H, dd, $J_{H\text{-}2',H\text{-}6'-H\text{-}3',H\text{-}5'} = 8.5$ Hz, $J_{H\text{-}2',H\text{-}6'-F\text{-}4'} = 5.2$ Hz, H-2′,H-6′), 9.69 (1H, d, $J = 7.5$ Hz, H-1); ^{13}C NMR (MeOH-d_4): δ 116.4 (d, $^2J_{C\text{-}F} = 22$ Hz, C-3′,5′), 128.3 and 128.4 (C-2 and C-1′), 130.5 (d, $^3J_{C\text{-}F} = 9$ Hz, C-2′,6′), 151.3 (C-3), 164.5 (d, $^1J_{C\text{-}F} = 253$ Hz, C-4′), 193.4 (C-1); EIMS: m/z 150 (M^+, 100).

4.4.7. (4*E*,6*E*)-1-(3,4-Dihydroxyphenyl)-7-(4-Fluorophenyl)-4,6-Heptadien-3-one (**36**)

A solution of freshly prepared aldehyde **34** (0.082 g, 0.55 mM), phosphonate **33** (0.235 g, 0.57 mM) and DBU (0.093 g, 0.61 mM) in THF (10 mL) was heated under reflux for 4 h. The reaction mixture was poured into water and extracted with EtOAc. The organic extract was washed with brine and dried over Na_2SO_4. The *EE* derivative **35** was not isolated and removal of the solvent immediately resulted in **36** as an yellow oil. Purification by preparative TLC (*n*-hexane:EtOAc 6:1) gave **36** (0.075 g, 44%). IR (KBr): (ν_{max} cm^{-1}) 3434, 2952, 1701, 1618, 1541, 1363, 1283, 1158, 1305, 1113, 995. ^{1}H NMR (MeOH-d_4): 2.77 (2H, t, $J = 7.4$ Hz, H-1), 2.88 (2H, t, $J = 7.4$ Hz, H-2), 6.31 (1H, d, $J = 15.4$ Hz, H-4), 6.52 (1H, dd, $J = 8.2$, 2.1 Hz, H-6′), 6.66 (1H, d, $J = 2.1$ Hz, H-2′), 6.67 (1H, d, $J = 8.2$ Hz, H-5′), 6.92 (1H, dd, $J = 15.6$, 10.6 Hz, H-6), 7.00 (1H, d, $J = 15.6$ Hz, H-7), 7.08 (2H, dd, $J_{H\text{-}3'',H\text{-}5''-H\text{-}2'',H\text{-}6''} = 8.6$ Hz, $J_{H\text{-}3'',H\text{-}5''-F\text{-}4''} = 9.0$ Hz, H-3″,H-5″), 7.36 (1H, dd, $J = 15.4$, 10.6 Hz, H-5), 7.55 (2H, dd, $J_{H\text{-}2'',H\text{-}6''-H\text{-}3'',H\text{-}5''} = 8.6$ Hz, $J_{H\text{-}2'',H\text{-}6''-F\text{-}4''} = 5.4$ Hz, H-2″,H-6″); ^{13}C NMR (MeOH-d_4): δ 31.0 (C-1), 43.3 (C-2), 116.4 and 116.5 (C-2′ and C-5′), 116.7 (d, $^2J_{C\text{-}F} = 22$ Hz,

C-3″, C-5″), 120.6 (C-6′), 127.8 and 127.9 (C-6 and C-1″), 130.4 (d, $^{3}J_{C\text{-}F} = 8$ Hz, C-2″, C-6″), 130.5 (C-4), 134.1 (C-1′), 141.6 (C-7), 144.5 (C-4′), 144.9 (C-5), 146.2 (C-3′), 164.5 (d, $^{1}J_{C\text{-}F} = 247$ Hz, C-4″), 202.8 (C-3); EIMS: *m/z* 312 (M^{+}, 98), 175 (100); HRMS: Calcd. for $C_{19}H_{17}O_3F$: 312.1162, Found: 312.1156.

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