Synthesis of Acerogenin C and (+)-Acerogenin A, Two Macrocyclic Diarylheptanoid Constituents of *Acer nikoense*

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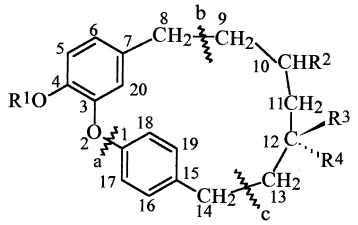
The macrocyclic ketone acerogenin C (**3**) and the corresponding alcohol (+)-accerogenin A (**1**), diarylheptanoid constituents of the maple *Acer nikoense* were synthesized. The key steps were the selective reduction of the double bond of an α,β-unsaturated ketone (**10**) and macrocyclization of an iodophenol (**13**) by a modified Ullmann diarylether synthesis.

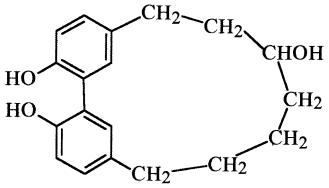
Introduction

Studies continued by now over two decades by Kubo, Nagai, and their associates on the elucidation of the constituents of *Acer nikoense* MAXIM (Aceraceae), a maple indigenous in Japan, led to the isolation of several macrocyclic diarylheptanoids, namely the acerogenins A (**1**), B (**2**), C (**3**), D (**4**), and E (**6**) and seven of their glycosides, the acerosides.[1]

Scheme 1



1 $R^1 = H, R^2 = R^3 = H, R^4 = OH$ (acerogenin A)
2 $R^1 = H, R^2 = OH, R^3,R^4 = H$ (acerogenin B)
3 $R^1 = H, R^2 = H, R^3,R^4 = O$ (acerogenin C)
4 $R^1 = H, R^2 = OH, R^3,R^4 = O$ (acerogenin D)
5 $R^1 = Me, R^2 = H, R^3,R^4 = O$



6 Acerogenin E

The relatively simple structure of the acerogenins and the fact that at the time of starting our work no synthesis of a natural macrocyclic diarylheptanoid with a diarylether linkage had been reported, prompted us to synthesise these compounds. In the meantime we have completed the syntheses of three other macrocyclic diarylheptanoids of more complex structure (garugamblin-1[2], garugamblin-2[3], and garuganin III[4]). Attempts at the synthesis of acerogenins were reported in a separate paper.[5] Now we report the syntheses of acerogenin C (**3**) and (+)-acerogenin A (**1**).

Two basic strategies can be envisaged for the synthesis of acerogenins A to C: (i) Linking the two aryl rings first, preferably between C-1 and O-2 (bond a) followed by elaboration of the aliphatic chain and ring closure to form the C-8−C-9 bond (b) in the case of acerogenin B or the C-13−C-14 bond (c) with acerogenin A and C. (ii) Preparation of a suitably substituted 1,7-diarylheptane derivative and formation of the diarylether bond at a late stage of the synthesis. Failure of strategy (i)[5] prompted us to turn to strategy (ii). This approach, combined with the use of a recently introduced reagent [$Cu^IH \cdot Ph_3P$ hexamer)][6] for the selective reduction of α,β-unsaturated ketones to saturated ketones enabled finally the synthesis of acerogenin C (**3**) and (+)-acerogenin A (**1**).

Results and Discussion

First the hydroxyester **7** was prepared in three steps from 3-benzyloxy-4-methoxybenzaldehyde and 4-triphenylphosphoniobutanoic acid.[5] The hydroxyl group of **7** was blocked by tetrahydropyranylation and the product **8** reacted with diethyl methylphosphonate to give the ketophosphonate **9.** Condensation of the latter with 4-iodobenzaldehyde[7] gave the protected enone **10**, or using acidic workup, the hydroxyenone **11**. Reduction of the latter with either diisobutylaluminium hydride or $LiAlH_4$ at low temperature gave only the corresponding allylic alcohol (**14**). Treatment, however, of **10** with Cu(I)H.Ph_3P hexamer[6] in benzene saturated with water provided the desired heptanone **12**. Removal of the tetrahydropyranyl group from **12** gave our key intermediate the diarylheptanone **13**.

Macrocyclization was carried out by a modification of the classical Ullmann reaction, as recommended by Boger

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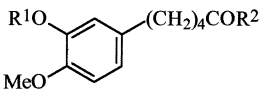
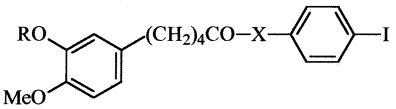
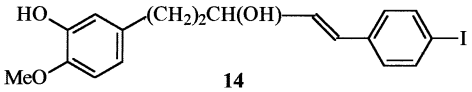
Scheme 2



7 R^1 = H, R^2 = OMe
8 R^1 = THP, R^2 = OMe
9 R^1 = THP, R^2 = $CH_2PO(OEt)_2$



10 R = THP, X = (*E*)-CH=CH-
11 R = H, X = (*E*)-CH=CH-
12 R = THP, X = -CH_2CH_2-
13 R = H, X = -CH_2CH_2-



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et al.[8] i.e. using $CuBr \cdot Me_2S$ complex as catalyst. This gave finally the cyclized product **5** in low yield. M.p. and ^{1}H-NMR spectrum of **5** was in complete agreement with data for acerogenin C methyl ether.[1b]

Methyl ether **5** was demethylated by heating with pyridine hydrochloride at 210°C to give the phenol **3,** that proved to be identical (m.p., ^{1}H NMR) with acerogenin C.[1d]

Reduction of acerogenin C (**3**) with $NaBH_4$ led to racemic acerogenin A (**1**) of m.p. 186−188°C (ref.[1b] for (+)-**1** 151−152°C). M.p. of (+)-**1** indicated that it formed a racemic phase. Note that the m.p. of acerogenin B (**2**), a racemic compound is very similar (179°C).[1c]

It was already observed by Nagai et al.[1b] that in the ^{13}C-NMR spectrum of acerogenin A (**1**) unsubstituted carbons of the *para* disubstituted benzene ring gave rise to four signals. Now we observed the same phenomenon for the corresponding proton signals too. Inspection of a model indicated clearly that rotation of this benzene ring is severely hindered. Although the ground state conformation of acerogenin C (**3**) is also chiral, no such signal splitting was observed, probably owing to the flexibility of the seven carbon chain.

We have been informed that Dr. Jieping Zhu and his coworkers (Gif-sur-Yvette, France) have also accomplished very recently a total synthesis of acerogenin C.

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Experimental Section

General: NMR: Bruker DRX 500 (500.15 and 125.77 MHz for ^{1}H and ^{13}C NMR, respectively). Signal assignments of **1** were based on COSY and HMQC spectra. M.p.s were not corrected, evaporations were carried out in vacuum, for chromatography silica gel 60 (Merck) was used.

Methyl 5-[4-Methoxy-3-(tetrahydropyran-2-yloxy)phenyl]pentanoate (**8**): Hydroxyester 7[5] (4.4 g, 17.6 mmol), pyridinium *p*-toluenesulphonate (80 mg) and 3,4-dihydropyran (4.4 ml) were left standing for 48 h. After neutralization with triethylamine the solution was evaporated and the residue purified by chromatography (eluent hexane-Me_2CO 3:1) to give the ether **8** as an oil (3.9 g, 66%). − ^{1}H NMR ($CDCl_3$): δ = 1.60 (mc, 4 H, 3,4-CH_2), 1.8−2.2 (m, 6 H, 3′′,4′′,5′′-CH_2), 2.30 (t, *J* = 7.3 Hz, 2 H, 5-CH_2), 2.55 (t, *J* = 7.3 Hz, 2 H, 2-CH_2), 3.55 (m, 1 H) and 4.00 (m, 1 H, 6′′-CH_2), 3.66 (s, 3 H, CO_2CH_3), 3.83 (s, 3 H, OCH_3), 5.55 (m, 1 H, 2′′-H), 6.6−6.75 (m, 2 H, 5′,6′-H), 6.94 (br. s, 1 H, 2′-H). − $C_{18}H_{26}O_5$ (322.4): calc. C 67.06, H 8.13; found C 67.23, H 7.98.

Diethyl 6-[4-Methoxy-3-(tetrahydropyran-2-yloxy)phenyl]-2-oxohexylphosphonate (**9**): a) To a solution of methyl diethylphosphonate (2.6 ml, 17.4 mmol) in dry THF first BuLi (10.6 ml of a 1.6 M solution in hexane, 17 mmol) was added at −70°C, followed by a solution of ester **8** (2.9 g, 8.7 mmol) in THF (10 ml). The mixture was allowed to warm up to room temperature, evaporated, the residue dissolved in CH_2Cl_2 and the solution washed with aq. $NaHCO_3$ solution. Evaporation gave the phosphonate **9** (3.6 g, 94%) as a viscous oil. − ^{1}H NMR ($CDCl_3$): δ = 1.33 (t, *J* = 7.1 Hz, 6 H, CMe), 1.59 (m, 4 H, 4,5-CH_2), 1.5−1.9 (m, 6 H, 3′′,4′′,5′′-CH_2), 2.52 (t, *J* = 6.7 Hz, 2 H, 3-CH_2), 2.65 (t, *J* = 6.7 Hz, 2 H, 6-CH_2), 3.05 (d, *J* = 22.7 Hz, 2 H, PCH_2), 3.50 (m, 1 H) and 4.00 (m, 1 H, 6"-CH_2), 3.85 (s, 3 H, OCH_3), 4.13 (mc, 4 H, C*H*$_2$Me), 5.63 (m, 1 H, 2"-H), 6.63 (dd, *J* = 8.1 and 1.5 Hz, 1 H, 6′-H), 6.75−6.80 (m, 2 H, 2′,5′-H). − $C_{22}H_{35}O_7P$ (442.3): calcd. C 59.72, H 7.97; found C 59.57, H 7.78.

b) Diethyl 6-(3-hydroxy-4-methoxyphenyl)-2-oxohexylphosphonate[5] (6.1 g, 17 mmol), was converted to the tetrahydropyranyl ether **9** as described for **8**.

(E)-1-(4-Iodophenyl)-7-[4-methoxy-3-(tetrahydropyran-2-yloxy)phenyl]hept-1-en-3-one (**10**): To a solution of phosphonate **9** (4.5 g, 8.7 mmol) and 4-iodobenzaldehyde (2.0 g, 8.6 mmol) in MeOH (90 ml) 1 M NaOMe (8.7 ml) was added. After 30 min the solution was evaporated, the residue treated with water and taken up in CH_2Cl_2. Evaporation, chromatography (eluent hexane/Me_2CO, 3:1) and trituration with diethyl ether gave enone **10** (2.0 g, 44%) as colorless crystals of m.p. 74−75°C. − ^{1}H NMR ($CDCl_3$): δ = 1.6−1.8 (m, 6 H, 3′′′,4′′′,5′′′-CH_2), 1.7 (mc, 4 H, 5,6-CH_2), 2.59 (t, *J* = 7.2 Hz, 2 H,) and 2.68 (t, *J* = 6.7 Hz, 2 H, 4,7-CH_2), 3.61 (m, 1 H) and 4.04 (m, 1 H, 6′′′-CH_2), 3.85 (s, 3 H, Me), 5.40 (m, 1 H, 2′′′-H), 6.73 (d, *J* = 16.0 Hz, 1 H, 2-H), 6.79−6.83 (m, 2 H, 5′′,6′′-H), 7.27−7.29 (m, 3 H, 3′,5′, 2′′-H), 7.45 (d, *J* = 16.0 Hz, 1 H, 1-H), 7.75 (d, *J* = 7.8 Hz, 2-H, 2′,6′-H). − $C_{25}H_{29}IO_4$ (520.4): calcd. C 57.70, H 5.62; found C 57.84, H 5.70.

7-[4-Methoxy-3-(tetrahydropyran-2-yloxy)phenyl]-1-(4-iodophenyl)heptan-3-one (**11**): A solution of heptenone **10** (2.0 g, 3.85 mmol) in benzene (40 ml) to which water (1.0 ml) was added was boiled in a stream of argon for 15 min. The mixture was cooled to r.t., $[Cu^IH \cdot Ph_3P]_6$ (2.3 g, 1.17 molar equivalents) added and stirring continued for 24 h. The mixture was filtered through a layer of Cellite and evaporated (1.6 g, 80%). A small sample was purified for analysis and spectroscopy. Viscous oil. − ^{1}H NMR ($CDCl_3$): δ = 1.57 (mc, 4 H, 5,6-CH_2), 1.5−1.9 (m, 6 H, 3′′′,4′′′,5′′′-CH_2), 2.37 (t, *J* = 7.2 Hz, 2 H), and 2.50 (t, *J* = 7.3 Hz, 2 H, 4,7-CH_2), 2.67 (t, *J* = 7.3 Hz, 2 H,) and 2.81 (t, *J* = 7.4 Hz, 2 H, 1,2-CH_2), 3.53 (m, 1 H) and 4.00 (m, 1 H, 6′′′-CH_2), 3.86 (s, 3 H, OMe), 4.95 (m, 1 H, 2′′′-H), 6.61 (dd, *J* = 8.1, 2.1 Hz, 1 H, 6′′-H), 6.73 (d, *J* = 2.1 Hz, 1 H, 2′′-H), 6.75 (d, *J* = 8.1 Hz, 1 H, 5"-H), 6.92 (d, *J* = 8.2 Hz, 2 H, 2′,6′-H), and 7.5 (d, *J* = 8.2 Hz, 2 H, 3′,5′-H). − $C_{25}H_{31}IO_4$ (522.4): calcd. C 57.48, H 5.98; found C 57.25, H 5.64.

7-(3-Hydroxy-4-methoxyphenyl]-1-(4-iodophenyl)heptan-3-one (**13**): Unpurified heptan-one **12** (2.0 g) (containing Ph_3P arising

from the reducing agent) was boiled for 40 min in a mixture of MeOH (100 ml) and 10% HCl (10 ml). After 16 h the solution was decanted from the deposited crystals of Ph_3P, evaporated and the residue chromatographed (eluent hexane/Me_2CO, 3:1) to give the iodophenol **13** (1.0 g, 59% calculated on **9**) as colourless crystals of m.p. 176−178°C. − ^{1}H NMR ($CDCl_3$): δ = 1.56 (mc, 4 H, 5,6-CH_2), 2.37 (t, *J* = 7.2 Hz, 2 H) and 2.50 (t, *J* = 7.3 Hz, 2 H, 4,7-CH_2), 2.69 (t, *J* = 7.3 Hz, 2 H) and 2.81 (t, *J* = 7.3 Hz, 2 H, 1,2-CH_2), 3.86 (s, 3 H, OMe), 6.62 (dd, *J* = 8.1, 2.1 Hz, 1 H, 6"-H), 6.74 (d, *J* = 2.1 Hz, 1 H, 2′′-H), 6.76 (d, *J* = 8.1 Hz, 1 H, 5′′-H), 6.93 (d, *J* = 8.3 Hz, 2 H, 2′,6′-H), and 7.59 (d, *J* = 8.3 Hz, 2 H, 3′,5′-H). − $C_{20}H_{23}IO_3$ (438.3): calcd. C 54.81, H 5.29; found C 54.60, H 5.35.).

4-Methoxy-2-oxatricyclo[13.2.2.1^{3,7}]eicosa-3,5,7(20),15,17,18-hexaen-12-one, Acerogenin C Methyl Ether (**5**): To a solution of iodophenol **13** (500 mg, 1.14 mmol) in dry benzene (10 ml) KO*t*Bu (180 mg, 1.6 mmol) was added and the solution evaporated to dryness. $Me_2S \cdot CuBr$ (2.35 g, 11.4 mmol) was added and dry pyridine (250 ml) filtered through a column of powdered molecular sieve. The mixture was stirred under argon for 8 h in a bath of 130°C, the solvent evaporated, the residue treated with 10% HCl and extracted with CH_2Cl_2. Chromatography (eluent hexane/acetone, 3:1) gave methyl ether **5** (56 mg, 16%) as colourless needles of m.p. 122−124°C (ref.[1b] m.p. 124°C). − ^{1}H NMR ($CDCl_3$): δ = 1.11 (q, *J* = 7.4 Hz, 2 H, 9-CH_2) and 1.37 (mc, 2 H, 10-CH_2), 1.90 (t, *J* = 8.1 Hz, 2 H, 11-CH_2), 2.44 (t, *J* = 5.6 Hz, 2 H, 8-CH_2), 2.60 (t, *J* = 6.6 Hz, 2 H, 13-CH_2), 2.98 (t, *J* = 6.3 Hz, 2 H, 14-CH_2), 3.94 (s, 3 H, OMe), 5.64 (d, *J* = 1.6 Hz, 1 H, 20-H), 6.64 (dd, *J* = 8.1, 1.6 Hz, 1 H, 6-H), 6.81 (d, *J* = 8.1 Hz, 1 H, 7-H), 7.02 (d, *J* = 8.4 Hz, 2 H), and 7.17 (d, *J* = 8.4 Hz, 2 H, 17,18- and 16,19-H); (ref.[1b] ^{1}H NMR ($CDCl_3$): δ = 1.09, 1.37, 1.90, 2.44, 2.61, 2.96, 3.93, 5.65, 6.63, 6.82, 7.01, 7.20). − ^{13}C NMR ($CDCl_3$): δ = 20.4 (C-10), 27.5 (C-9), 31.3 (C-8), 32.3 (C-14), 44.6 (C-13), 46.3 (C-11), 56.3 (Me), 112.4 (C-5), 117 4 (C-20), 122.0 (C-6), 123.7 (C-17,18), 130.6 (C-16,19), 133.7 (C-7), 137.1 (C-15), 146.8 (C-4), 150.9 (C-3), 156.9 (C-1), 212.1 (CO) (ref.[1c] 20.5, 27.6, 31.5, 32.3, 44.6, 46.2, 56.4, 112.7, 117.7, 122.2, 123.9, 130.8, 133.9, 137.3, 147.1, 151.2, 157.4, 212.0). − $C_{20}H_{22}O_3$ (310.4): calcd. C 77.39, H 7.14; found C 77.52, H 7.23.

12-Oxo-2-oxatricyclo[13.2.2.1^{3,7}]eicosa-3,5,7(20),15,17,18-hexaen-4-ol, Acerogenin C (**3**): A mixture of methoxyketone **5** (50 mg) and pyridine·HCl (200 mg) was heated under argon at 210°C for 3 h. After adding water (4 ml) the raw product was extracted with CH_2Cl_2 and purified by TLC (eluent benzene/EtOAc, 20:1) to give **3** (28 mg, 59%), as colourless crystals of m.p. 114−116°C, (ref.[1d] m.p. 116°C). − ^{1}H NMR ($CDCl_3$): δ = 1.05 (q, *J* = 7.4 Hz, 2 H, 9-CH_2), and 1.37 (mc, 2 H, 10-CH_2), 1.90 (t, *J* = 8.1 Hz, 2 H, 11-CH_2), 2.45 (t, *J* = 5.6 Hz, 2 H, 8-CH_2), 2.61 (t, *J* = 6.6, Hz 2 H, 13-CH_2), 3.00 (t, *J* = 6.3 Hz, 2 H, 14-CH_2), 5.64 (d, *J* = 1.6 Hz, 1 H, 20-H), 6.62 (dd, *J* = 8.2, 1.8 Hz, 1 H, 6-H), 6.85 (d, *J* = 8.2 Hz, 1 H, 7-H), 7.00 (d, *J* = 8.3 Hz, 2 H), and 7.18 (d, *J* = 8.3 Hz, 2 H, 17,18- and 16,19-H); (ref.[1d] ^{1}H NMR ($CDCl_3$): δ = 1.09, 1.37, 1.90, 2.44, 2.61, 2.96, 5.55, 5.64, 6.63, 6.85, 6.99, 7.19.). − ^{13}C NMR ($CDCl_3$): δ = 20.4 (C-10), 27.4 (C-9), 31.5 (C-8), 32.2 (C-14), 44.5 (C-13), 46.3 (C-11), 115.5 (C-5), 117 0 (C-20), 122.8 (C-6), 123.5 (C-17,18), 130.7 (C-16,19), 133.0 (C-7), 137.6 (C-15), 143.0 (C-4), 149.1 (C-3), 156.8 (C-1), 212.8 (CO). − $C_{19}H_{20}O_3$ (296.4): calcd. C 77.00, H 6.80; found C 69.85, H 6.88.

rac-2-Oxatricyclo[13.2.2.1^{3,7}]eicosa-3,5,7(20),15,17,18-hexaen-4,12-diol, Acerogenin A (**1**): A solution of acerogenin C (**3**) (13 mg, 0.044 mmol) in EtOH (4 ml) was treated under argon with $NaBH_4$ (5 mg) for 1 h. Acidification with AcOH, evaporation, and TLC (eluent benzene/EtOAc, 8:1) gave the alcohol **1** [(+)-acerogenin A] (10 mg, 71%), m.p. 186−188°C; (ref.[1b] for (+)-**1** 151−152°C). − ^{1}H NMR ($CDCl_3$): δ = 0.838 (m, 1 H) and 1.036 (m, 1 H, 10-CH_2), 0.949 (m, 1 H) and 1.095 (m, 1 H, 11-CH_2), 1.26 (m, 1 H) and 1.62 (m, 1 H, 9-CH_2), 1.62 (m, 1 H) and 1.88 (dq, *J* 14.1, 4.4 Hz, 1 H, 13-CH_2), 2.46 (m, 2 H, 8-CH_2), 2.69 (dt, *J* 12.8, 4.1 Hz, 1 H), and 2.99 (dt, *J* = 13.2, 3.9 Hz, 1 H, 14-CH_2), 3.35 (q, *J* = 5.5 Hz, 1 H, 12-H), 5.63 (br. s, 1 H, 20-H), 6.60 (d, *J* = 8.2 Hz, 1 H, 6-H), 6.83 (d, *J* = 8.1 Hz, 1 H, 5-H), 6.94 (dd, *J* = 8.8, 3.1 Hz, 1 H) and 7.21 (dd, *J* = 8.2, 2.5 Hz, 1 H, 16,19- or 17,18-H), 7.16 (dd, *J* = 8.8, 3.1 Hz, 1 H) and 7.29 (dd, *J* = 8.2, 2.5 Hz, 1 H, 16,19- or 17,18-H); [(ref.[1d] (in C_5D_5N at 100 MHz): 0.68−1.12, 1.12−1.48, 1.48−1.84, 1.84−2.24, 2.24−2.52, 2.52−2.99, 3.24−3.56, 5.84, 6.64, 6.93, 7.06−7.22]. − ^{13}C NMR ($CDCl_3$): δ = 24.9 (C-10), 27.9 (C-9), 31.7 (C-8), 32.5 (C-14), 39.5 (C-11), 40.5 (C-13), 71.1 (C-12), 115.1 (C-5), 115.3 (C-20), 122.5 (C-6), 123.1 and 124.1 (C-17,18), 130.1 and 131.6 (C-16,19), 133.9 (C-7), 139.6 (C-15), 142.9 (C-4), 149.0 (C-3), 155.7 (C-1), [ref.[1c] (in C_5D_5N at 25 MHz) δ = 25.3, 28.5, 32.0, 32.7, 39.7, 40.9, 69.8, 116.7, 117.1, 122.5, 123.0, 124.2, 130.2, 131.8, 132.8, 139.7, 145.1, 150.7, 156.6]. − $C_{19}H_{22}O_3$ (298.4): calcd. C 76.48, H 7.43; found C 76.58, H 7.50.

(E)-7-(3-Hydroxy-4-methoxyphenyl)-1-(4-iodophenyl)hept-1-en-3-one (**13**): This compound was prepared as **10**, except that the crude product was hydrolyzed with a 5% citric acid solution. Colourless crystals, m.p. 98−100°C. − ^{1}H NMR ($CDCl_3$): δ = 1.6−1.8 (m, 4 H, 5,6-CH_2), 2.56 (t, *J* = 7.2 Hz, 2 H) and 2.65 (t, *J* = 6.7 Hz, 2 H, 4,7-CH_2), 3.83 (s, 3 H, Me), 6.71 (d, *J* = 16.1 Hz, 1 H, 2-H), 6.78 (dd, *J* = 8.1, 1.5 Hz, 1 H, 6′′-H), 6.81 (d, 8.1 Hz, 1 H, 5′′-H), 6.96 (d, *J* = 1.5 Hz, 1 H, 2′′-H), 7.26 (d, *J* = 8.3 Hz, 2 H, 3′,5′-H), 7.44 (d, *J* = 16.1 Hz, 1 H, 1-H), 7.75 (d, *J* = 8.3 Hz, 2 H, 2′,6′-H). − $C_{20}H_{21}IO_3$ (436.3): calcd. C 55.06, H, 4.85; found C 54.91, H, 4.66.

(E)-7-(3-Hydroxy-4-methoxyphenyl)-1-(4-iodophenyl)hept-1-en-3-ol (**14**): To a solution of **11** (120 mg, 0.23 mmol) in dry THF (5 ml) *i*Bu_2AlH (0.46 mmol, 0.65 ml of a 0.7 M solution in toluene) was added at −70°C. After 1 h the reaction mixture was quenched with MeOH and then with 5% HCl. Evaporation, extraction with CH_2Cl_2 and chromatography of the crude product (eluent benzene/EtOAc, 20:1) gave the alcohol **14** (100 mg, 83%) as a resin. Reduction of **11** with $LiAlH_4$ at r.t. produced the same compound. − ^{1}H NMR ($CDCl_3$): δ = 1.5−1.65 (m, 4 H, 5,6-CH_2), 2.15 (m, 2 H, 4-CH_2), 2.51 (t, *J* = 6.7 Hz, 2 H, 7-CH_2), 3.69 (m, 1 H, 3-H), 3.85 (s, 3 H, OMe), 6.19 (dd, *J* = 15.9, 6.6 Hz, 1 H, 2-H), 6.55 (d, *J* = 15.9 Hz, 1 H, 1-H), 6.62 (dd, *J* = 8.1, 1.6 Hz, 1 H, 6′′-H), 6.73 (d, *J* = 8.1 Hz, 1 H, 5′′-H), 6.74 (d, *J* = 1.6 Hz, 1 H, 2′′-H), 7.12 (d, *J* = 8.3 Hz, 2 H, 3′,5′-H), 7.65 (d, *J* = 8.3, 2 H, 2′,6′-H). − $C_{20}H_{23}IO_3$ (438.3): calcd. C 54.81, H 5.29; found C 54.90, H 5.09.

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