A Protocol for the Direct Conversion of Aldehydes into Arenes – Proof of Principle

Maud Gayral, John. M. Brown*

Chemistry Research Laboratory, Mansfield Rd., Oxford OX1 3TA, UK
Fax +44(1865)285002; E-mail: john.brown@chem.ox.ac.uk

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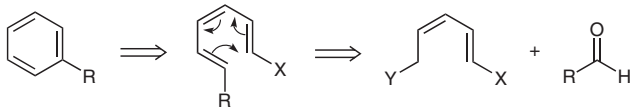
Abstract: A functional C5-phosphonate reagent serves as the direct precursor of a phenyl group, the remaining carbon atom arising from an aldehyde.

Key words: Horner–Emmons, *E*,*Z*,*E*-trienes, cyclohexadienes, Pd coupling, semihydrogenation

There has been a revival of interest in the direct synthesis of aromatic compounds from acyclic precursors. In addition to the application of Bergman cyclisation,[1] annulation,[2] and alkyne trimerisation routes,[3] alkene metathesis has emerged as a useful method.[4] In parallel, recent advances in organocatalytic asymmetric synthesis have provided new methods for preparation of aldehydes with α- or β-stereogenic centres that supplement existing ones.[5] This has stimulated our efforts to develop a direct conversion of aldehydes into arenes in which the carbonyl carbon becomes the *ipso*-carbon of the arene. We report the development of an approach demonstrating proof of principle, shown in outline in Scheme 1. The aldehyde is reacted with the terminal carbon of a U-shaped pentadienyl anion carrying a leaving group at the opposing terminus, so that triene cyclisation may afford the arene in a single step. Since the Horner–Emmons reaction may avoid compromising adjacent stereocentres, this provides a likely precursor.[6] The desired triene should possess an *E*,*Z*,*E*-configuration, since disrotatory thermal cyclisation is far faster here than with the *Z*,*Z*,*E*- or *Z*,*Z*,*Z*-stereoisomers.[7]



Scheme 1 Proposed arene retrosynthesis

The precursor triene was prepared by a published route.[8] (*E*)-5-Chloro-pent-4-en-2-yn-1-ol (**1**, Figure 1) is readily available by Sonogashira cross-coupling between (*E*)-dichloroethylene and propargyl alcohol [($PdCl_2(PPh_3)_2$, cuprous iodide, piperidine, toluene, r.t.] in 88% yield. This compound was kept in the freezer in order to prevent its decomposition to a black solid.

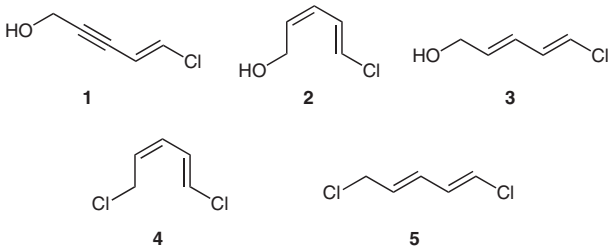


Figure 1

After some trials to find a satisfactory method for selective semihydrogenation of the alkyne, hydrogenation was carried out in anhydrous degassed MeOH in the presence of 3 mol% Rh catalyst under hydrogen pressure (1.4 atm). As Schrock and Osborn reported in the original work,[9] the nature of the ligand can influence reactivity and selectivity. Thus, our optimum catalyst proved to be [Rh^+(dppb)NBD]OTf^- (full conversion and excellent stereo- and chemoselectivity). The *Z*-isomer **2** formed was unstable, however, and tended to isomerise on silica gel or on standing. Hence the corresponding *E*-isomer was prepared by Sonigashira coupling as before, followed by reduction with $LiAlH_4$ in Et_2O at 0 °C giving (2*E*,4*E*)-5-chloropenta-2,4-dien-1-ol (**3**) in quantitative yield.[10] On attempted mesylation of either *E*,*E* or *Z*,*E* allylic alcohols, the only isolated product was the corresponding chloride **4** (64%) or **5** (61%), most probably formed by direct S_N2 displacement of the mesyloxy group by chloride ion.

Exploratory chemistry was carried out with the *E*,*E*-isomer **5**. This was converted into the corresponding triphenylphosphonium chloride **6**. Under various conditions, and with different aromatic aldehydes (4-NO_2, 4-OMe, 3,4-OBn), the desired terminal *E*-isomer of triene was never formed in better than 70:30 ratio with the corresponding *Z*-isomer. This encouraged the synthesis of phosphonate **7**, from which a 9:1 ratio of *E*/*Z* isomers of the terminal double bond in product **8** was readily obtained under standard Horner–Emmons conditions with 4-$MeOC_6H_4CHO$. The pure *E*,*E*-isomer was obtained by flash chromatography. With this result in hand, the same sequence was tested for *E*,*Z*-diene **4**, with equally favourable results. The phosphonate ester **9**, prepared in 57% yield, reacted under the same conditions, and again gave a 9:1 preference for the *E*,*Z*,*E*-isomer of product **10**, separable from its stereoisomer by flash chromatography (Scheme 2).

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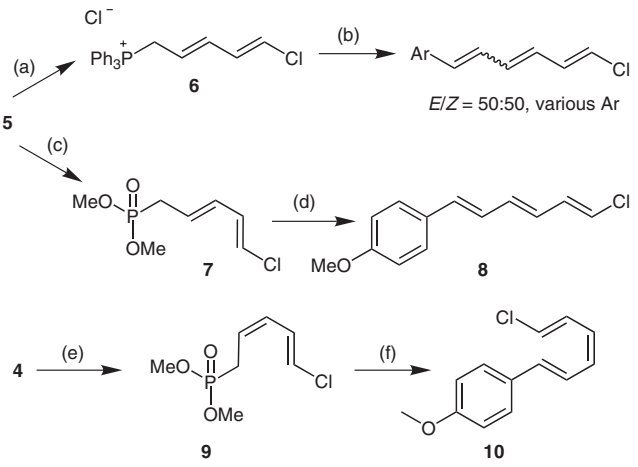


Scheme 2 Triene preparations: (a) PPh_3, MeCN, 50 °C, 16 h, 79%; (b) ArCHO, Wittig under various conditions; (c) $P(OMe)_3$, NaI, neat, r.t., 16 h, 46%; (d) *p*-$MeOC_6H_4CHO$, $LiN(SiMe_3)_2$, THF, r.t., 3 h, 50%; (e) as (c), 57%; (f) *p*-$MeOC_6H_4CHO$, $NaN(SiMe_3)_2$, THF, r.t., 3 h, 48%.

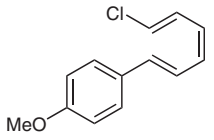
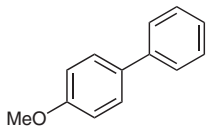
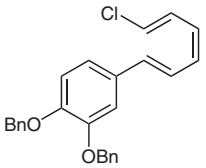
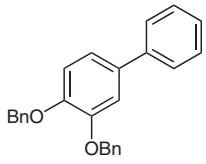
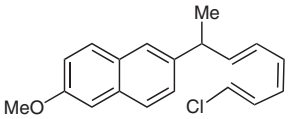
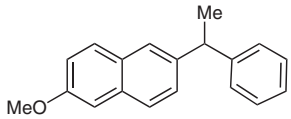
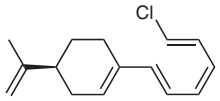
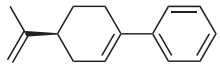
At this stage the relative reactivity of **8** and **10** towards cyclisation was evaluated. On injection of the *E*,*Z*,*E*-isomer **10** into a GC-MS inlet (15 m ZBS column, 0.25 mm ID, 80–280 °C, 20 °C/min) the aromatised product **11** of *m/z* = 184.07 (calcd 184.09) was observed. Only the parent ion of the *E*,*E*,*E*-isomer **8** was observed in a parallel experiment, hence cyclisation did not occur. An isolable quantity of the product **11** (60:40 with reactant) was, however, obtained by passage of **8** through an empty 2 m preparative GC column, (20 mg per pass, EtOAc solution), with the oven held at 300 °C. Likewise the *E*,*Z*,*E*-isomer **10** was converted into the same mixture, but with an oven temperature of 200 °C.

These early results encouraged preparative-scale experiments. Several further *E*,*Z*,*E*-trienes **12**–**14** were prepared and purified as before by the Horner–Emmons route. In the case of **13**, and also the *3E*,3*Z*)-mixture of the 4-NO_2 analogue of **8**,[11] cyclisation–aromatisation was successfully demonstrated by GC-MS as described above. After exploratory experiments, a standard technique was then adopted.

The reactant was heated in pyridine, or preferably pyridine-d_5 to aid monitoring by ^{1}H NMR, for up to 12 hours at 120 °C. At that stage cyclisation is complete, the aromatic product being accompanied by a small amount of the unreactive *E*,*E*,*E*-isomer of the parent triene, arising by 3*Z*,3*E*-isomerisation. The results of these experiments are recorded in Table 1.

The desired aromatic products were separated by preparative TLC and fully characterised. A good example of monitoring the course of reaction by ^{1}H NMR is afforded by reactant **13**. The $CHCH_3$ doublets of reactant and product are at δ = 1.41 and 1.55 ppm, respectively. After 12 hours at 120 °C, only the 1.55 ppm signal remains. The initial spectrum shows the diene protons in the region 5.9–6.8 ppm, and a trace of H_2O in the C_5D_5N solvent at 5.4 ppm. Over time the diene peaks diminish and then disappear whilst the water peak increases and shifts downfield from 5.4 to 6.8 ppm as pyridinium chloride is formed. The aromatisation reaction of **10** also occurs in toluene in the presence of pyridine (1 equiv) at 100 °C over 12 hours, product **11** being isolated in 71% yield. In the absence of pyridine, only double-bond isomerisation of **10** to **8** is observed.

Table 1 Cyclisation–Aromatisation in Pyridine[a]

Reactant[b]	Product (isolated yield, %)
 **10**	 **11** (60)
 **12**	 **15** (71)
 **13**	 **16** (68)
 **14**	 **17** (54)

[a] Reaction conditions: 110 °C, 4–12 h.
[b] Prepared in 23–65% yield as described for **8**.

These simple experiments demonstrate the potential of a simple method for extending the synthetic utility of aldehydes. It is potentially applicable to enantiomerically pure aldehydes, to labelled aldehydes (^{11}C, ^{13}C) and to more highly substituted arenes by simple structural modification of the C_5 entity. Future work will follow these directions.

(2*Z*,4*E*)-5-Chloropenta-2,4-dien-1-ol (2)

(*E*)-5-Chloro-pent-4-en-2-yn-1-ol (**1**, 150 mg, 1.29 mmol) and $[Rh^+(dppb)NBD]OTf^-$ (20 mg, 3% mmol) were dissolved in anhyd and degassed MeOH (5 mL). The orange solution was put under H_2 pressure in a closed vessel (1.4 atm) and the reduction was monitored by computer. After 8 h stirring, the solvent was removed in vacuo leading to a brown oil (170 mg, ca. 100% conversion). As the obtained diene **2** is subject to isomerisation, the crude product was used without any further purification in the next step; C_5H_7ClO (118.6). IR (neat): 3608, 3020, 1522, 1430, 757, 652 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.73 (1 H, ddd, $J_{2,1}$ = 13.0 Hz, $J_{2,3}$ = 11.3 Hz, $J_{2,4}$ = 1.1 Hz, H-2), 6.25 (1 H, d, H-1), 6.02 (1 H, ddt, $J_{3,4}$ = 11.1 Hz, $J_{3,5}$ = 1.0 Hz, H-3), 5.63 (1 H, m, H-4), 4.27 (2 H, dd, $J_{4,5}$ = 6.8 H, H-5), 2.12 (1 H, br s, OH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 130.6 (C-4), 128.6 (C-2), 126.7 (C-3), 122.9 (C-1), 58.6 (C-5). MS (TOF FI$^+$): *m/z* calcd for for [M$^+$]: 118.0185; found: 118.0184. The *E*,*E*-isomer has been prepared previously;[9] we used $LiAlH_4$ in reduction of alkyne **1**, 99% yield.

(1*E*,3*Z*)-1,5-Dichloropenta-1,3-diene (4)

To a solution of allylic alcohol **2** (0.41 g, 3.44 mmol) in anhyd CH_2Cl_2 (10 mL) was added dropwise Et_3N (0.96 mL, 6.88 mmol) at 0 °C under an argon atmosphere. After 15 min, mesyl chloride (0.40 mL, 5.16 mmol) was added dropwise at 0 °C to the brown solution. The dark red solution was allowed to warm to r.t. and stirred for 3 h. The dark red solution was then hydrolysed with a sat. aq NH_4Cl solution (5 mL), the layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 × 15 mL). The organic layer was washed with brine, dried over $MgSO_4$, and the solvent removed in vacuo to lead to a brown oil. The crude product was purified by chromatography on silica gel (EtOAc–pentane, 1:9) to yield allylic chloride **4** as a pale yellow oil (0.30 g, 64%). IR (neat): 3065, 2928, 1648, 1586, 734, 651 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.74 (1 H, ddd, $J_{1,2}$ = 12.9 Hz, $J_{2,3}$ = 11.5 Hz, $J_{2,4}$ = 1.2 Hz, H-2), 6.35 (1 H, d, H-1), 6.10 (1 H, ddt, $J_{3,4}$ = 11.3 Hz, $J_{3,5}$ = 0.8 Hz, H-3), 5.66 (1 H, m, H-4), 4.16 (2 H, dd, $J_{4,5}$ = 8.1 Hz, H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 128.4 (C-3), 127.7 (C-2), 126.5 (C-4), 124.7 (C-1), 38.9 (C-5). MS (TOF FI+): *m/z* calcd for [M+]: 135.9847, found: 135.9848.

(1*E*,3*E*)-1,5-Dichloropenta-1,3-diene (5)

As **4**, colourless oil (0.34 g, 72%). IR (neat): 3066, 2928, 1648, 1585, 974, 777 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.46 (1 H, dd, $J_{1,2}$ = 13.1 Hz, $J_{2,3}$ = 10.9 Hz, H-2), 6.28 (1 H, dd, $J_{1,3}$ = 0.5 Hz, H-1), 6.26 (1 H, ddt, $J_{3,4}$ = 14.9 Hz, $J_{3,5}$ = 0.8 Hz, H-3), 5.83 (1 H, dt, $J_{4,5}$ = 7.2 Hz, H-4), 4.09 (2 H, dd, H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 132.1 (C-2), 129.9 (C-3), 129.1 (C-4), 122.8 (C-1), 44.5 (C-5). MS (TOF FI+): *m/z* calcd for [M+]: 135.9847; found: 135.9848.

(2*E*,4*E*)-5-Chloropenta-2,4-dienyl)triphenylphosphonium Chloride (6)

From PPh_3 and halide **5** in MeCN, r.t., 79%; mp 112–114 °C. IR (KBr): 3066, 2979, 1661, 1587, 982, 743 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.83–7.78 (6 H, m, H-8), 7.75–7.71 (3 H, m, H-9), 7.65–7.60 (6 H, m, H-7), 6.52 (1 H, m, H-3), 6.24 (1 H, dd, $J_{1,2}$ = 13.1 Hz, $J_{2,3}$ = 10.9 Hz, H-2), 6.14 (1 H, dd, $J_{1,3}$ = 2.4 Hz, H-1), 5.43 (1 H, dt, $J_{3,4}$ = 13.6 Hz, $J_{4,5}$ = 7.1 Hz, H-4), 4.99 (2 H, dd, J_{PH} = 15.8 Hz, H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.2 (d, J_{PC} = 13.5 Hz, C-3), 134.9 (d, J_{PC} = 2.4 Hz, C-9), 133.9 (d, J_{PC} = 9.6 Hz, C-7), 132.0 (d, J_{PC} = 4.7 Hz, C-2), 130.2 (d, J_{PC} = 12.8 Hz, C-8), 123.5 (d, J_{PC} = 5.6 Hz, C-1), 118.0 (d, J_{PC} = 86.3 Hz, C-6), 117.9 (d, J_{PC} = 11.2 Hz, C-4), 27.6 (d, J_{PC} = 50.3 Hz, C-5). ^{31}P NMR (161 MHz, $CDCl_3$): δ = 21.5. MS (ESI+): *m/z* calcd for [M+]: 363.1064; found: 363.1067. Wittig reactions reported here were carried out using the modified method of Niwa et al.[12] with $(Me_3Si)_2NNa$ in THF.

Dimethyl (2*E*,4*E*)-5-Chloropenta-2,4-dienylphosphonate (7)

A solution of allylic chloride **5** (0.34 g, 2.48 mmol) in $(Me_3O)_3P$ (2.93 mL, 24.8 mmol) was treated with NaI (0.45 g, 2.97 mmol) and stirred vigorously at 40 °C overnight. The cooled dark yellow solution was quenched with H_2O (5 mL) and extracted with EtOAc (3 × 15 mL). The organic layer was washed with brine, dried over $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified by chromatography on silica gel (EtOAc) to yield phosphonate **7** as a pale yellow oil (0.43 g, 82%). IR (neat): 2956, 2853, 1584, 1462, 978, 733 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.35 (1 H, ddd, $J_{1,2}$ = 13.2 Hz, $J_{2,3}$ = 11.8 Hz, $J_{2,4}$ = 0.6 Hz, H-2), 6.10 (1 H, dd, $J_{1,3}$ = 2.7, H-1), 6.06 (1 H, m, H-3), 5.57 (1 H, m, $J_{3,4}$ = 15.2 Hz, $J_{4,5}$ = 7.6 Hz, H-4), 3.67 (3 H, s, OMe), 3.65 (3 H, s, OMe), 2.56 (2 H, ddd, $^2J_{PH}$ = 22.4 Hz, $J_{3,5}$ = 0.9 Hz, H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 132.6 (d, J_{PC} = 4.8 Hz, C-2), 130.8 (d, J_{PC} = 14.4 Hz, C-3), 122.8 (d, J_{PC} = 12.8 Hz, C-4), 120.7 (d, J_{PC} = 5.6 Hz, C-1), 52.6 (OMe), 52.5 (OMe), 30.0 (d, J_{PC} = 140.6 Hz, C-5). ^{31}P NMR (161 MHz, $CDCl_3$): δ = 28.5. MS (TOF FI+): *m/z* calcd for [M + Na+]: 233.0110; found: 233.0105.

Dimethyl (2*Z*,4*E*)-5-Chloropenta-2,4-dienylphosphonate (9)

Compound **9** was prepared likewise from **4** in 82% yield. IR (neat): 2956, 1576, 1464, 735, 651 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.65 (1 H, ddd, $J_{1,2}$ = 12.9 Hz, $J_{2,3}$ = 11.5 Hz, $J_{2,4}$ = 1.2 Hz, H-2), 6.28 (1 H, dd, $J_{1,3}$ = 2.0 Hz, H-1), 6.11 (1 H, m, H-3), 5.46 (1 H, m, H-4), 3.74 (3 H, s, OMe), 3.72 (3 H, s, OMe), 2.71 (2 H, ddd, $^2J_{PH}$ = 23.0 Hz, $J_{4,5}$ = 8.2 Hz, $J_{3,5}$ = 1.4 Hz, H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 128.4 (d, J_{PC} = 14.4 Hz, C-3), 128.1 (d, J_{PC} = 4.8 Hz, C-2), 123.5 (d, J_{PC} = 3.9 Hz, C-1), 120.0 (d, J_{PC} = 12.0 Hz, C-4), 52.8 (OMe), 52.7 (OMe), 25.5 (d, J_{PC} = 140.7 Hz, C-5). ^{31}P NMR (161 MHz, $CDCl_3$): δ = 28.6. MS (TOF MS FI+): *m/z* calcd for [M + Na+]: 233.0110; found: 233.0105.

Typical Procedure for the HWE Reaction

The base was synthesised in situ: A solution of *n*-BuLi (1.6 M in hexanes, 1.1 equiv) was added to a solution of HMDS (1.1 equiv) in anhyd THF (2 mL) at 0 °C. After 15 min a solution of phosphonate **7** (1 equiv) in anhyd THF (3 mL) was added slowly to the pale yellow solution. After 30 min 4-methoxybenzaldehyde (1.2 equiv) in anhyd THF (2 mL) was added slowly at 0 °C and allowed to warm to r.t. After 16 h, the dark orange solution was quenched with H_2O (5 mL) and extracted with Et_2O (3 × 15 mL). After washing with brine and drying over $MgSO_4$, the solvent was removed in vacuo. The crude product was purified by chromatography on silica gel (EtOAc–pentane, 1:n).

1-[(1*E*,3*E*,5*E*)-6-Chlorohexa-1,3,5-trienyl]-4-methoxybenzene (8)

Pale brown solid (51%). Mp 99–101 °C (lit.[13] 100–102 °C).

1-[(1*E*,3*Z*,5*E*)-6-Chlorohexa-1,3,5-trienyl]-4-methoxybenzene (10)

Yellow solid (25 mg, 48%), mp 79–80 °C. IR (neat): 3100, 2810, 1600, 1513, 1465, 1254, 1180, 1034, 737, 650 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39 (2 H, d, $J_{8,9}$ = 8.7 Hz, H-8), 7.05 (1 H, ddd, $J_{5,6}$ = 14.4 Hz, $J_{4,5}$ = 11.4 Hz, $J_{3,5}$ = 0.8 Hz, H-5), 7.03 (1 H, m, H-2), 6.88 (2 H, d, H-9), 6.57 (1 H, d, H-6), 6.25 (1 H, d, $J_{1,2}$ = 13.0 Hz, H-1), 6.16 (1 H, dt, $J_{3,4}$ = 10.7 Hz, H-4), 5.94 (1 H, ddd, $J_{2,3}$ = 12.3 Hz, H-3), 3.83 (3 H, s, OMe). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.5 (C-10), 134.1 (C-6), 130.7 (C-4), 129.8 (C-7), 129.5 (C-2), 127.9 (C-8), 123.9 (C-3), 121.4 (C-5), 121.3 (C-1), 114.1 (C-9), 55.3 (OMe). MS (TOF CI+): *m/z* calcd for [M+]: 220.0655; found: 220.0652.

{4-[(1*E*,3*Z*,5*E*)-6-Chlorohexa-1,3,5-trienyl]-1,2-phenylene} Bis(oxy)bis(methylene)dibenzene (12)

Chromatography on silica gel (EtOAc–pentane, 1:6), pale yellow solid (25%); mp 98–100 °C. IR (KBr): 3134, 1510, 1382, 1135, 1090, 735, 650 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.32 (10 H, m, $OCH_2C_6H_5$), 7.07 (1 H, m, H-2), 7.01 (1 H, ddd, $J_{5,6}$ = 15.4 Hz, $J_{4,5}$ = 11.9 Hz, $J_{3,5}$ = 0.8 Hz, H-5), 6.96–6.87 (3 H, m, H-8, H-11, and H-12), 6.50 (1 H, d, H-6), 6.26 (1 H, d, $J_{1,2}$ = 12.9 Hz, H-1), 6.14 (1 H, dt, $J_{3,4}$ = 11.1 Hz, H-4), 5.94 (1 H, dt, H-3), 5.20 (4 H, d, J_{gem} = 2.5 Hz, OCH_2Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.1 (C-9), 149.0 (C-10), 137.2 (C-14), 137.0 (C-14′), 134.0 (C-6), 130.7 (C-4), 130.5 (C-5), 129.4 (C-7), 128.6 and 126.5 (C-15 and C-15′), 127.9 and 127.8 (C-17 and C-17′), 127.3 and 127.2 (C-16 and C-16′), 124.2 (C-3), 121.9 (C-1), 121.5 (C-8), 120.7 (C-12), 114.7 (C-11), 112.7 (C-2), 71.5 and 71.2 (C-13 and C-13′). MS (TOF ESI+): *m/z* calcd for [M + Na+]: 425.1284; found: 425.1279.

2-[(3*E*,5*Z*,7*E*)-8-Chloroocta-3,5,7-trien-2-yl]-6-methoxy Naphthalene (13)

Chromatography on silica gel (EtOAc–pentane, 5:95), pale yellow solid (65%); mp 71–73 °C. IR (KBr): 3054, 1654, 1422, 1265, 1029, 929, 740 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.70 (1 H, d, $J_{11,12}$ = 8.3 Hz, H-11), 7.69 (1 H, m, H-16), 7.59 (1 H, m, H-9), 7.34

(1 H, dd, $J_{16,17}$ = 8.2 Hz, $J_{17,9}$ = 1.8 Hz, H-17), 7.16–7.11 (2 H, m, H-12 and H-14), 6.90 (1 H, tt, $J_{5,6}$ = 13.1 Hz, $J_{6,7}$ = 1.3 Hz, H-6), 6.49 (1 H, m, H-2), 6.21 (1 H, d, $J_{1,2}$ = 12.9 Hz, H-1), 6.06–5.99 (2 H, m, H-3 and H-5), 5.86 (1 H, m, H-4), 3.93 (3 H, s, H-19), 3.70 (1 H, dq, $J_{7,18}$ = 6.8 Hz, H-7), 1.49 (3 H, d, H-18). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9 (C-13), 141.8 (C-8), 140.3 (C-15), 134.6 (C-6), 130.7 (C-4), 130.5 (C-5), 129.4 (C-10), 129.1 (C-11), 127.0 (C-17), 126.6 (C-9), 125.0, 123.7 and 123.5 (C-1, C-2, and C-3), 121.3 (C-16), 118.8 (C-12), 105.7 (C-14), 55.3 (C-19), 42.6 (C-7), 14.2 (C-18). MS (TOF ESI$^+$): *m/z* calcd for [M + Na$^+$]: 321.1022; found: 321.1017.

(*S*)-1-[(1*E*,3*Z*,5*E*)-6-Chlorohexa-1,3,5-trienyl]-4-(prop-1-en-2-yl)cyclohex-1-ene (14)

Chromatography on silica gel (pentane), yellow oil (23%). IR (KBr): 3054, 2987, 1422, 909, 737 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 (1 H, ddd, $J_{2,4}$ = 1.0 Hz, $J_{2,3}$ = 11.7 Hz, $J_{1,2}$ = 13.9 Hz, H-2), 6.50 (1 H, dd, $J_{4,5}$ = 11.4 Hz, $J_{5,6}$ = 15.2 Hz, H-5), 6.30 (1 H, d, H-1), 6.22 (1 H, d, H-6), 6.07 (1 H, td, $J_{3,4}$ = 11.5 Hz, H-4), 5.91–5.86 (2 H, m, H-3 and H-8), 4.76–4.73 (2 H, m, H-14), 2.42–2.31 (2 H, m, H-12), 2.28–2.17 (4 H, m, H-9 and H-11), 1.77 (3 H, s, H-15), 1.53 (1 H, m, H-10). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.5 (C-13), 137.9 (C-6), 137.9 (C-7), 135.6 (C-8), 131.2 (C-4), 131.0 (C-2), 129.5 (C-5), 123.6 (C-3), 120.2 (C-1), 108.9 (C-14), 41.0 (C-10), 31.6 (C-9), 29.7 (C-12), 27.3 (C-11), 20.8 (C-15). MS (TOF MS FI$^+$): *m/z* calcd for [M$^+$]: 234.1175; found: 234.1177.

General Procedure for Cyclisation–Aromatisation in Pyridine

Triene (20 mg) was dissolved in pyridine-d_5 (1 mL) and the resulting pale brown solution heated at 120 °C. The reaction was monitored by ^{1}H NMR and after 12 h, the brown solution was quenched with an aq HCl solution (1 M, 1 mL) and extracted with EtOAc (3 × 5 mL). The organic layer was washed with brine, dried over $MgSO_4$, and the solvent removed in vacuo. Preparative plate chromatography yielded the biphenyl.

4-Methoxybiphenyl (11)

Preparative plate chromatography (EtOAc–pentane, 1:9); yield 10 mg, 60%; mp 90–91 °C (lit.[14] 90–91 °C).

3,4-Bis(benzyloxy)biphenyl (15)

Preparative plate chromatography (EtOAc–pentane, 1:4), yellow solid (71%). IR (KBr): 3134, 1514, 1378, 1133, 1090 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.47 (6 H, m, H-1, H-5, H-15 and H-15′), 7.42–7.37 (6 H, m, H-2, H-4, H-16, and H-16′), 7.34–7.31 (3 H, m, H-3, H-17, and H-17′), 7.21 (1 H, d, $J_{8,12}$ = 2.1 Hz, H-8), 7.13 (1 H, dd, $J_{11,12}$ = 8.2 Hz, H-12), 7.01 (1 H, d, H-11), 5.24 (2 H, s, H-13), 5.22 (2 H, s, H-13′). ^{13}C NMR (100 MHz, C_5D_5N): 142.8 (C-7), 139.8 and 139.7 (C-9 and C-10), 136.7 (C-6), 130.9 (C-14 and C-14′), 130.5 (C-2, C-4, 2 C-16, and 2 C-16′), 129.9 (C-17 and C-17′), 129.8 (C-1 and C-5), 129.7 and 129.6 (C-15 and C-15′), 128.8 (C-3), 116.1 (C-12), 107.3 (C-11), 100.0 (C-8), 73.1 and 72.9 (C-13 and C-13′). MS (TOF ESI$^+$): *m/z* calcd for [M + Na$^+$]: 389.1517; found: 389.1512.

2-Methoxy-6-(1-phenylethyl)naphthalene (16)

Preparative plate chromatography (EtOAc–pentane, 5:95), white solid (68%). IR (KBr): 3049, 1652, 1423, 1244, 1029, 742 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.64 (3 H, m, H-9, H-11, and H-16), 7.32–7.26 (5 H, m, H-1 to H-5), 7.20 (1 H, m, H-17), 7.15–7.10 (2 H, m, H-12 and H-14), 4.30 (1 H, q, $J_{7,18}$ = 7.5 Hz, H-7), 3.92 (3 H, s, H-19), 1.73 (3 H, d, H-18). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4 (C-13), 146.5 (C-6), 141.5 (C-8), 134.1 (C-15), 129.2 (C-10), 129.0 (C-11), 128.4 (C-2 and C-4), 127.8 (C-1 and C-5), 127.3 (C-16), 126.8 (C-17), 126.1 (C-9), 125.2 (C-3), 118.7 (C-12), 105.6 (C-14), 55.3 (C-19), 44.6 (C-7), 21.9 (C-18). MS (TOF CI$^+$): *m/z* calcd for [M$^+$]: 262.1358; found: 262.0696.

(*S*)-[4-(Prop-1-en-2-yl)cyclohex-1-enyl]benzene (17)

Preparative plate chromatography (EtOAc–pentane, 5:95), pale yellow oil (54%). IR (KBr): 3054, 1625, 1422, 896 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (2 H, m, H-2 and H-4), 7.34–7.30 (2 H, m, H-1 and H-5), 7.23 (1 H, tt, $J_{1,3\text{ and }3,5}$ = 1.4 Hz, $J_{2,3\text{ and }3,4}$ = 7.1 Hz, H-3), 6.15 (1 H, m, H-8), 4.78–4.77 (2 H, m, H-14), 2.55–2.49 (2 H, m, H-12), 2.40–1.96 (4 H, m, H-9 and H-11), 1.80 (3 H, s, H-15), 1.64 (1 H, m, H-10). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.8 (C-13), 142.2 (C-6), 136.3 (C-7), 128.2 (C-2 and C-4), 126.6 (C-8), 124.9 (C-1 and C-5), 124.1 (C-3), 108.7 (C-14), 40.8 (C-10), 31.3 (C-9), 28.0 (C-12), 27.9 (C-11), 20.9 (C-15). MS (TOF CI$^+$): *m/z* calcd for [M$^+$]: 198.1409; found: 198.1404.

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