Synthesis of (1-Allylcyclohexa-2,5-dienyl)arenes

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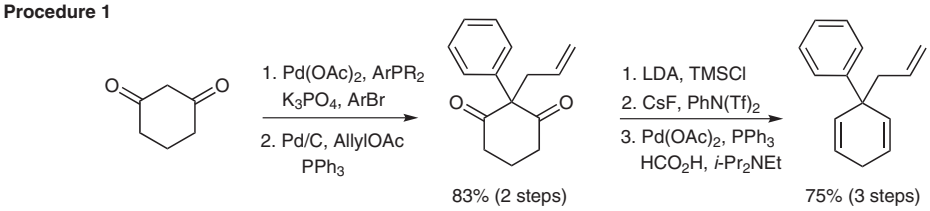
Received 20 October 2009; revised 27 October 2009

PSP No 181

Abstract: (1-Allylcyclohexa-2,5-dienyl)arenes are useful building blocks for the synthesis of natural products including amaryllidaceae, strychnos and morphinan alkaloids. Their synthesis was carried out in a straightforward manner starting from readily available cyclohexane-1,3-dione, through a palladium-mediated arylation–allylation sequence, which was used to install the quaternary center, followed by a transformation of the resulting 1,3-dione into the required diene through generation of a bis-silyl enol ether. After conversion of the latter into the corresponding bis-enol triflate, it was finally hydrogenated using palladium catalysis to give the title compounds.

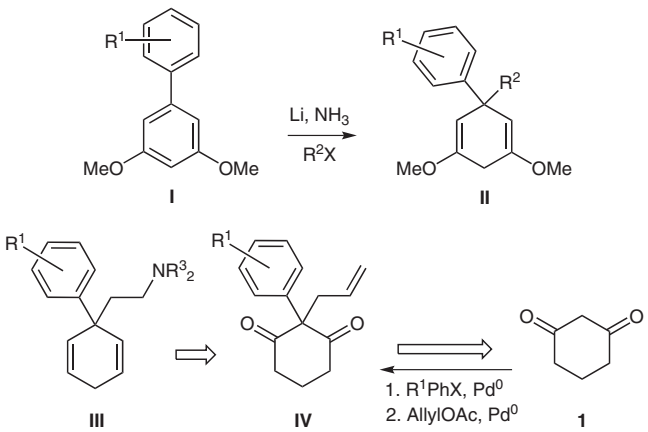
Key words: palladium, allylation, arylation, enols, arenes, cyclohexadienes



Scheme 1

In the course of our studies on desymmetrization processes, we have developed several methodologies based on symmetry-breaking of cyclohexa-1,4-dienes using various asymmetric approaches.[1] The diene precursors **II** were generally accessible using Birch reduction of simple arenes **I** (Scheme 2).[2] More recently, we have developed a new strategy called Birch reductive alkylation desymmetrization (BRAD), in which arylcyclohexadienes such as **III** could be used as simple precursors en route to the synthesis of alkaloids belonging to the Amaryllidaceae, Strychnos and also Morphinan families.[3] Such cyclohexadienes possess a useful quaternary center flanked by an aryl group and an ethylamino chain, which is found in most of the alkaloids mentioned above.[4]

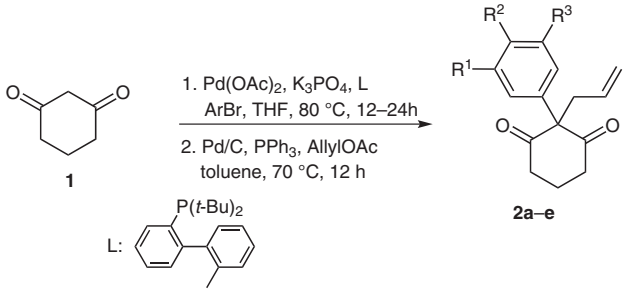
Whereas Birch reductive alkylation provides a rapid route to substituted cyclohexadienes **II**, lithium reduction of arenes to access unsubstituted cyclohexadienes **III** is not so convenient. We thus wanted to develop a short, general and alternative methodology to access to arylcyclohexadienes of type **III**, which would complement the Birch reductive alkylation reported previously. It was envisioned that **III** could be assembled instead, through arylation of cyclohexane-1,3-dione (**1**) followed by C-allylation, starting from readily available starting materials (Scheme 2). The 1,3-diketone function of **IV** would then be converted into the 1,4-diene moiety of **III** through a straightforward three-step sequence involving enol-type chemistry. Few methods are available for the synthesis of 2-aryl-1,3-cyclohexadienones. Amongst those that were reported, photolysis of cyclic 2-diazo-1,3-diketones in aromatic solvents provided low yield of the desired dione.[5] Aromatic nucleophilic substitution has been described by Bonjoch et al., but this approach is restricted to activated arenes such as nitrobenzenes.[6] Radical substitution also allows access to 2-aryl-1,3-diketones, but the scope is also rather limited.[7] Finally, hypervalent iodine-mediated arene-substitution by 1,3-diketones, developed by Kita et al. led to the desired product, but with somewhat modest efficiency.[8] A more general route to these symmetrical diones was envisioned that exploited the strategy devised



Scheme 2 General accesses to 1-substituted (cyclohexa-2,5-dienyl)arenes

SYNTHESIS 2010, No. 7, pp 1223–1228
Advanced online publication: 11.12.2009
DOI: 10.1055/s-0029-1218604; Art ID: Z22409SS

concomitantly by Hartwig[9] and Buchwald,[10] based on palladium-mediated arylation of ketones. Such arylations of 1,3-cyclohexadienone were therefore investigated using $Pd(OAc)_2$ as a catalyst and an electron-rich phosphine as a ligand.[11] This approach was previously tested with simple alkyl arenes and has not yet been extended to more electron-rich arenes possessing methoxy or methylenedioxy groups, which are ubiquitous aryl substituents in natural products.[4] Our preliminary studies showed that Buchwald–Hartwig conditions efficiently provided the required 2-aryl-1,3-cyclohexadiones **2a–e** (Scheme 3). The alternative Ullmann-type procedure,[12] which uses less costly CuI and L-proline, also afforded the expected arylcyclohexadienones but led to contrasting result depending on the nature of the starting arene (see below). The generality of the approach was illustrated with a range of substituted arenes (Table 1). However, all our efforts to apply this procedure to arenes having an *ortho* substituent unfortunately failed, probably for steric reasons. We also noticed that whereas crude yields, estimated through ^1H NMR, were generally high, loss of material occurred upon purification of these intermediates by silica gel chromatography. Therefore, because the easily enolizable crude diketones[13] were sufficiently pure, they were finally used directly in the subsequent allylation step without further purification. Several conditions were thus tested to introduce the allyl group α to both carbonyl groups. Allylation of the 2-aryl-1,3-dione under Fuji's conditions[14] (DBU, THF, allylX) led to a mixture of O- and C-alkylation depending on the nature of the additive salt (LiBr, NaBr or KI), the solvent (THF, MeCN or toluene) and the electrophile. We observed little regioselectivity in tetrahydrofuran or acetonitrile, either in the presence or absence of added salts. In contrast, higher selectivities were obtained in apolar solvents such as toluene. Overall, the base-catalyzed allylation was not found to be suitable for our purpose because it led to mixtures that required lengthy purifications.



Scheme 3 Arylation–allylation of cyclohexa-1,3-dienone (**1**)

More satisfying results were observed using palladium-catalyzed allylation. Various palladium catalysts were tested with 2-phenyl-1,3-diketone in the presence of allyl acetate. Whereas $[Pd(allyl)Cl_2]_2$ and dppe ligand led to allylated product **2a** in only 17% yield, more satisfying yields of the C-alkylation products were obtained under heterogeneous conditions, for example, Pd/C and triphenylphosphine in toluene (Scheme 3).[15] The choice of the solvent proved crucial because O- and C-alkylation products were obtained in a 2:1 mixture of water and 1,2-dimethoxyethane (DME). Overall yields over the two steps are summarized in Table 1.

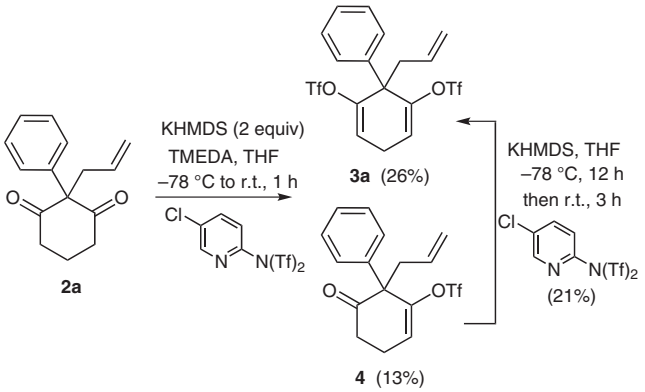
Allylated products **2a–e** were then converted into the corresponding 1,4-dienes. A two-step sequence was envisioned that involved the transformation of the dione into a bis-vinyl triflate, using a method developed by Willis,[16] followed by conversion into the expected 1,4-diene through palladium-mediated hydrogenation.

Table 1 Arylation–Allylation of Cyclohexane-1,3-dione (**1**)

Entry	R^1	R^2	R^3	Product	Yield (%)[a]
1	H	H	H	**2a**	83
2	Me	H	Me	**2b**	96
3	H	OMe	H	**2c**	71
4	OMe	OMe	H	**2d**	82
5	H	OCH_2O		**2e**	81
6	H	H	H	**2a**	80[b]
7	H	OMe	H	**2c**	67[b]

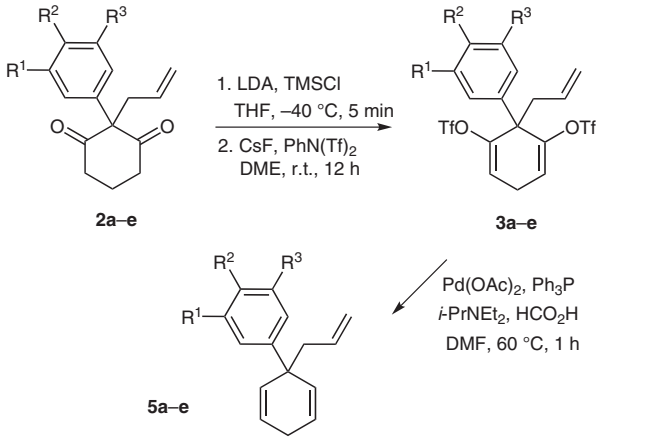
[a] Isolated overall yield over two steps.
[b] The arylation step was carried out using CuI (5 mol%), L-proline (10 mol%), ArI, K_2CO_3, DMSO, 90 °C, 48 h.

In contrast to related examples from the literature, the formation of the bis-vinyl triflate through the formation of the corresponding bis-lithium or potassium enolate and reaction with Comins reagent[17] [3-Cl-PyrN$(Tf)_2$] proved difficult. For instance, the reaction of **2a** with potassium hexamethyldisilazide (KHMDS) in a *N*,*N*,*N*′,*N*′-tetramethylethylenediamine–tetrahydrofuran (TMEDA–THF) mixture at –78 °C, followed by addition of the bis-triflic amide reagent, led to the monotriflate **4** in low yield (13%), along with the expected bis-triflate **3a** (26%) and considerable amounts (42%) of starting material (Scheme 4). Similarly, treatment of **4** under the same conditions led to **3a** in only 21% yield.



Scheme 4 Attempted synthesis of bis-enol triflate **3a** from **2a**

A more satisfying answer to this problem was found, by preparing the bis-enol triflates from the corresponding silyl enol ethers.[18] Accordingly, when diketones **2a–e** were treated with two equivalents of lithium diisopropylamide (LDA), and the resulting lithium enolate was quenched with trimethylsilyl chloride (TMSCl), the desired bis-silyl enol ethers were obtained in high yield (Scheme 5). These moisture-sensitive intermediates were then directly converted, without further purification, into the expected bis-vinyltriflates **3a–e** using $PhN(Tf)_2$ in the presence of CsF.[18] Palladium-catalyzed conversion of the triflate into the corresponding olefin[19] was finally carried out using formic acid as a hydrogen source, which led to formation of the desired trienes **5a–e** in good to excellent overall yields over the three steps (Table 2).



Scheme 5 Three-step access to (1-allylcyclohexa-2,5-dienyl)arenes **5a–e** from 2-allyl-2-arylcyclohexa-1,3-diones **2a–e**

Table 2 Three-Step Access to (1-Allylcyclohexa-2,5-dienyl)arenes **5a–e** from 2-Allyl-2-arylcyclohexa-1,3-diones **2a–e**

Entry	Dione	R^1	R^2	R^3	Diene	Yield (%)[a]
1	**2a**	H	H	H	**5a**	75
2	**2b**	Me	H	Me	**5b**	70
3	**2c**	H	OMe	H	**5c**	87
4	**2d**	OMe	OMe	H	**5d**	34
5	**2e**	H	OCH_2O		**5e**	75

[a] Isolated overall yield over three steps.

In summary, dienes **5a–e** were prepared in five steps from readily available cyclohexane-1,3-dione (**1**) in good overall yield (Scheme 1). The whole sequence requires a single purification (chromatography over silica gel) of one of the intermediates (diketones **2a–e**) and is based on simple and reproducible steps that can be easily extended to gram-scale syntheses. It is also worth noting that three of the steps rely on catalytic processes. These dienes are valuable intermediates for organic synthesis; for instance, they can be further elaborated through transformation of the allyl group into an aldehyde using Lemieux–Johnson oxidation (OsO_4, $NaIO_4$).[20] Such aldehydes can then be converted through reductive amination into chiral amines that can be used in a diastereoselective protonation–hydroamination tandem process, which is a key step in the synthesis of crinine-type alkaloids.[3a]

All reactions were carried out in dry glassware under a nitrogen atmosphere with anhydrous solvents under anhydrous conditions. Yields refer to chromatographically and spectroscopically (^1H and ^{13}C NMR) homogeneous materials, unless otherwise stated. Commercial reagents were used without further purification, unless otherwise stated. THF was distilled from sodium and benzophenone. CH_2Cl_2, DME and DMF were distilled from CaH_2. Toluene was distilled from sodium. Petroleum ether (PE) had a boiling range 40–60 °C. Phosphate buffer (pH 7) was prepared by mixing KH_2PO_4 (34 g, 0.25 mol) and NaOH (5.8 g, 0.15 mol) in H_2O (500 mL).

^1H NMR and ^{13}C NMR were recorded on Brüker AC-250 FT (^1H: 250 MHz, ^{13}C: 62.5 MHz) and Brüker Avance-300 FT (^1H: 300 MHz, ^{13}C: 75.4 MHz) NMR spectrometers. Mass spectra were recorded on a Nermag R10-10C. High-resolution mass spectra were recorded on a Brüker 4.7T BioApex II FT-ICR mass spectrometer. Melting points were determined by using a Stuart Scientific apparatus (SMP3) and are not corrected.

Pd-Catalyzed Arylation–Allylation of Cyclohexane-1,3-dione (1); General Procedure

Preparation of 2-Allyl-2-arylcyclohexane-1,3-diones 2a–e

Into a dry flask equipped with a screw-cap (or a three-necked round-bottom flask for larger quantities), was placed $Pd(OAc)_2$ (2–5 mol%), 2-di-*tert*-butylphosphino-2′-methylbiphenyl (4–11 mol%), cyclohexane-1,3-dione (**1**; 1.2 equiv), and K_3PO_4 (2.3 equiv) under an N_2 atmosphere. The flask was flushed several times with N_2 then THF (0.3 M) and aryl bromide (1 equiv) were added. The reaction mixture was stirred at 80 °C until TLC indicated complete consumption of the starting material. MeOH (5 mL/mmol) was added and the reaction mixture was stirred for 15 min, filtered and concentrated in vacuo. The crude mixture was used without further purification in the next step.

Pd/C (5 mol%), Ph_3P (20 mol%) followed by allyl acetate (1 equiv) were added to a suspension of the preceding crude diketone in toluene (0.1 M, 1 equiv). The reaction mixture was stirred at 70 °C overnight, then filtered and concentrated in vacuo. Purification by flash chromatography (silica gel; PE–EtOAc) yielded the desired diketones.

2-Allyl-2-(3,5-dimethylphenyl)cyclohexane-1,3-dione (2b)

Synthesized according to the general procedure described above from cyclohexane-1,3-dione (**1**; 246 mg, 2.2 mmol, 1.1 equiv), $Pd(OAc)_2$ (18 mg, 0.08 mmol, 4 mol%), 2-di-*tert*-butylphosphino-2′-methylbiphenyl (48 mg, 0.16 mmol, 8 mol%), K_3PO_4 (976 mg, 4.6 mmol, 2.3 equiv) and 1-bromo-3,5-dimethylbenzene (0.28 mL, 2 mmol, 1 equiv) in THF (6 mL) for the first step. Pd/C 10% (106 mg, 0.1 mmol, 5 mol%), Ph_3P (105 mg, 0.4 mmol, 20 mol%), and allyl acetate (0.24 mL, 2 mmol, 1 equiv) in toluene (14 mL) were used for the second step. Purification by flash chromatography (silica gel; PE–EtOAc, 9:1) afforded diketone **2b**.

Yield: 494 mg (96%); pale-yellow oil.

IR (neat, NaCl): 2919, 1728, 1696, 1597, 1048 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.91 (s, 1 H), 6.61 (s, 2 H), 5.71–5.55 (m, 1 H), 5.01–4.91 (m, 2 H), 2.81–2.46 (m, 6 H), 2.27 (s, 6 H), 1.95–1.84 (m, 1 H), 1.77–1.63 (m, 1 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 207.4, 139.0, 137.4, 134.5, 129.5, 124.2, 118.1, 75.4, 39.34, 39.29, 21.4, 17.3.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{20}O_2$: 256.14633; found: 256.1469.

2-Allyl-2-(4-methoxyphenyl)cyclohexane-1,3-dione (2c)

Synthesized according to the general procedure from cyclohexane-1,3-dione (**1**; 246 mg, 2.2 mmol, 1.1 equiv), $Pd(OAc)_2$ (18 mg, 0.08 mmol, 4 mol%), 2-di-*tert*-butylphosphino-2′-methylbiphenyl (48 mg, 0.16 mmol, 8 mol%), K_3PO_4 (976 mg, 4.6 mmol, 2.3 equiv) and 1-bromo-4-methoxybenzene (0.25 mL, 2 mmol, 1 equiv) in THF (6 mL) for the first step. Pd/C 10% (106 mg, 0.1 mmol, 5 mol%), Ph_3P (105 mg, 0.4 mmol, 20 mol%), and allyl acetate (0.24 mL, 2 mmol, 1 equiv) in toluene (14 mL) were used for the second step. Purification by flash chromatography (silica gel; PE–EtOAc, 7:3) afforded diketone **2c**.

Yield: 366 mg (71%); colorless oil.

IR (neat, NaCl): 2959, 1723, 1699, 1513 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.95–6.83 (m, 4 H), 5.71–5.57 (m, 1 H), 4.97–4.88 (m, 2 H), 3.78 (s, 3 H), 2.78–2.45 (m, 4 H), 1.92–1.83 (m, 2 H), 1.77–1.65 (m, 2 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 207.3, 159.1, 134.4, 129.3, 127.8, 118.2, 114.7, 74.6, 55.2, 39.2, 39.1, 17.2.

HRMS (EI): *m*/*z* $[M]^{+\cdot}$ calcd for $C_{13}H_{13}O_3$: 258.12559; found: 258.1259.

2-Allyl-2-(3,4-dimethoxyphenyl)cyclohexane-1,3-dione (2d)

Synthesized according to the general procedure described above from cyclohexane-1,3-dione (**1**; 135 mg, 1.2 mmol, 1.2 equiv), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 5 mol%), 2-di-*tert*-butylphosphino-2′-methylbiphenyl (35 mg, 0.11 mmol, 11 mol%), K_3PO_4 (488 mg, 2.3 mmol, 2.3 equiv) and 4-bromoveratrole (0.14 mL, 1 mmol, 1 equiv) in THF (3 mL) for the first step. Pd/C (53 mg, 0.05 mmol, 5 mol%), Ph_3P (52 mg, 0.2 mmol, 20 mol%), and allyl acetate (0.12 mL, 1 mmol, 1 equiv) in toluene (7 mL) were used for the second step. Purification by flash chromatography (silica gel; PE–EtOAc, 6:4) afforded diketone **2d**.

Yield: 237 mg (82%); colorless oil.

IR (neat, NaCl): 1696, 1516, 1208, 1144, 1024 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.80 (d, *J* = 8.2 Hz, 1 H), 6.56–6.51 (m, 2 H), 5.72–5.57 (m, 1 H), 5.00–4.90 (m, 2 H), 3.85 (s, 3 H), 3.83 (s, 3 H), 2.80–2.70 (m, 4 H), 2.54–2.48 (m, 2 H), 1.94–1.84 (m, 1 H), 1.80–1.63 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 207.3, 149.5, 148.7, 134.4, 129.5, 119.1, 118.2, 74.8, 56.0, 55.9, 39.23, 39.17, 17.2.

MS (EI): *m*/*z* = 288 (43) $[M]^+$, 247 (100) $[M - CH_2\text{-}CH{=}CH_2]^+$, 177 (51).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{20}O_4Na$: 311.1253; found: 311.1255.

2-Allyl-2-(benzo[*d*][1,3]dioxol-6-yl)cyclohexane-1,3-dione (2e)

Synthesized according to the general procedure described above from cyclohexane-1,3-dione (**1**; 246 mg, 2.2 mmol, 1.2 equiv), $Pd(OAc)_2$ (9 mg, 0.04 mmol, 2 mol%), 2-di-*tert*-butylphosphino-2′-methylbiphenyl (24 mg, 0.08 mmol, 4 mol%), K_3PO_4 (976 mg, 4.6 mmol, 2.3 equiv), 4-bromo-1,2-(methylenedioxy)benzene (0.24 mL, 2 mmol, 1 equiv) and THF (6 mL) for the first step. Pd/C 10% (106 mg, 0.1 mmol, 5 mol%), Ph_3P (105 mg, 0.4 mmol, 20 mol%), allyl acetate (0.24 mL, 2 mmol, 1 equiv) and toluene (14 mL) were used for the second step. Purification by flash chromatography (silica gel; PE–EtOAc, 8:2) afforded diketone **2e**.

Yield: 442 mg (81%); yellow solid; mp 73–75 °C.

IR (neat, NaCl): 2985, 1727, 1695, 1494 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.72 (d, *J* = 8.3 Hz, 1 H), 6.50–6.40 (m, 2 H), 5.93 (s, 2 H), 5.67–5.53 (m, 1 H), 4.95–4.86 (m, 2 H), 2.77–2.43 (m, 6 H), 1.92–1.81 (m, 1 H), 1.76–1.63 (m, 1 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 207.0, 148.5, 147.2, 134.2, 130.9, 120.1, 118.2, 108.8, 107.0, 101.4, 74.7, 39.10, 39.06, 17.1.

HRMS (EI): *m*/*z* $[M]^{+\cdot}$ calcd for $C_{16}H_{16}O_4$: 272.10486; found: 272.1063.

Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.80; H, 5.96.

2-Allyl-2-phenylcyclohexane-1,3-dione (2a)

PhI (0.13 mL, 0.5 mmol, 1 equiv) was added to a solution of CuI (9.5 mg, 0.025 mmol, 5 mol%), L-proline (11.5 mg, 0.05 mmol, 10 mol%), K_2CO_3 (276 mg, 2 mmol, 4 equiv) and diketone **1** (168 mg, 1.5 mmol, 3 equiv) in DMSO (2 mL). The reaction mixture was then stirred at 90 °C for 48 h. The cooled solution was poured into aq HCl (1M, 15 mL) and the organic layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (25 mL) and dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of the crude residue by flash chromatography (silica gel; PE–EtOAc, 2:8) afforded the arylated diketone (92 mg, 98% yield) as a colorless oil.

Pd/C (27 mg, 0.025 mmol, 5 mol%), Ph_3P (26 mg, 0.1 mmol, 20 mol%), and allyl acetate (60 μL, 0.5 mmol, 1 equiv) were added to a suspension of the above diketone (0.5 mmol, 1 equiv) in toluene (3 mL). The reaction mixture was stirred at 70 °C overnight, filtered and concentrated in vacuo. Purification by flash chromatography (silica gel; PE–EtOAc, 8:2) afforded diketone **2a**.

Yield: 92 mg (80%); clear oil.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.24 (m, 3 H), 7.03–6.99 (m, 2 H), 5.73–5.59 (m, 1 H), 4.99–4.89 (m, 2 H), 2.78–2.48 (m, 6 H), 1.96–1.82 (m, 1 H), 1.80–1.65 (m, 1 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 207.1, 137.4, 134.3, 129.3, 127.8, 126.6, 118.2, 75.4, 39.21, 39.15, 17.27.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_{16}O_2$: 228.11503; found: 228.1159.

2-Allyl-2-phenylcyclohexa-3,6-diene-1,3-diyl Bis(trifluoromethanesulfonate) (3a) and 6-Allyl-5-oxo-6-phenylcyclohex-1-enyl Trifluoromethanesulfonate (4)

Into a three-necked round-bottom flask was placed a solution of diketone **2a** (114 mg, 0.5 mmol, 1 equiv), Comins' reagent (432 mg, 1.1 mmol, 2.2 equiv) and TMEDA (0.15 mL, 1 mmol, 2 equiv) in THF (5 mL). KHMDS (0.5 M in toluene, 2.1 mL, 1 mmol, 2 equiv) was then added dropwise, over 30 min at –78 °C. The reaction mixture was stirred at –78 °C for 1 h and then allowed to warm slowly to r.t. over 5 h. Hexane (20 mL) was added and the organic layer was washed with H_2O (5 mL), aq NaOH (10%, 5 mL) and brine (5 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography (silica gel; pentane–EtOAc, 9:1) gave bis-triflate **3a**, mono-triflate **4** and starting material **2a** (48 mg).

3a

Yield: 64 mg (26%); yellow oil.

IR (neat, NaCl): 2971, 1711, 1598, 1416, 1211 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.34 (m, 5 H), 5.97 (t, *J* = 3.6 Hz, 2 H), 5.87–5.73 (m, 1 H), 5.30–5.22 (m, 2 H), 3.18 (dt, *J* = 22.9, 3.7 Hz, 2 H), 2.93 (d, *J* = 7.3 Hz, 2 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 147.3, 137.1, 131.3, 128.7, 128.6, 127.7, 120.2, 118.0, 113.0, 51.2, 35.2, 24.6.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{14}O_6F_6NaS_2$: 512.0028; found: 512.0027.

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Yield: 23 mg (13%); yellow oil.

IR (neat, NaCl): 1726, 1416, 1209, 1140, 975 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.42–7.29 (m, 5 H), 6.36–6.32 (m, 1 H), 5.74–5.58 (m, 1 H), 5.22–5.11 (m, 2 H), 3.53 (dd, *J* = 13.4, 6.7 Hz, 1 H), 2.68–2.35 (m, 5 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 204.8, 147.6, 137.6, 132.2, 129.0, 128.1, 126.8, 119.9, 118.1, 117.5, 61.3, 37.3, 35.0, 20.3.

Preparation of (1-Allylcyclohexa-2,5-dienyl)arenes 5a–e from 2-Allyl-2-arylcyclohexane-1,3-dione 2a–e; General Procedure

In a three-necked round-bottom flask, a solution of diketone **2a–e** (1 equiv) in THF (0.13 M) was added dropwise at –40 °C to a mixture of LDA (0.67 M in THF, 3.5 equiv) and TMSCl (5.5 equiv). After complete addition and further stirring for 5 min, NH_4Cl (10 mL/mmol) was added followed by pentane (10 mL/mmol). The two layers were separated and the aqueous layer was extracted with Et_2O (15 mL/mmol) . The combined organic extracts were washed with brine (5 mL/mmol), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was used in the next step without further purification.

In a flask equipped with a screw-cap, $PhN(Tf)_2$ (5 equiv) and CsF (8 equiv) were sequentially added to a solution of the preceding bis-silylenol ether in DME (1.65 M) and the tube was sealed. The reaction mixture was stirred at r.t. for 18 h, then the flask was carefully opened and Et_2O (2.5 mL/mmol) and a pH 7 buffer solution (2.5 mL/mmol) were then added sequentially. The two layers were separated and the aqueous phase was extracted with Et_2O (10 mL/mmol). The combined organic layers were washed with brine (2.5 mL/mmol), dried over $MgSO_4$, filtered and the solvents concentrated in vacuo. The crude mixture was used without any purification in the next step.

HCO_2H (8 equiv) was added to a solution of the preceding bis-triflate (1 equiv), DIPEA (6 equiv), $Pd(OAc)_2$ (10 mol%) and Ph_3P (20 mol%) in DMF (0.12 M) and the reaction mixture was stirred at 60 °C for 1 h. EtOAc (10 mL/mmol) was added and the reaction mixture was washed with H_2O (5 mL/mmol) and brine (5 mL/mmol), dried over $MgSO_4$, filtered and the solvents concentrated in vacuo. Purification by flash chromatography (silica gel) yielded the desired dienes **5a–e**.

(1-Allylcyclohexa-2,5-dienyl)benzene (5a)

Synthesized according to the general procedure described above from diketone **2a** (792 mg, 3.47 mmol, 1 equiv), LDA (18 mL, 12.16 mmol, 3.5 equiv), TMSCl (2.4 mL, 19.11 mmol, 5.5 equiv) and THF (20 mL) for the first step. $PhN(Tf)_2$ (6.2 g, 17.4 mmol, 5 equiv), CsF (4.22 g, 27.8 mmol, 8 equiv) and DME (12 mL) were used for the second step. HCO_2H (1.05 mL, 27.79 mmol, 8 equiv), DIPEA (3.63 mL, 20.84 mmol, 6 equiv), $Pd(OAc)_2$ (78 mg, 0.35 mmol, 10 mol%), Ph_3P (182 mg, 0.69 mmol, 20 mol%) and DMF (20 mL) were used for the third step. Purification by flash chromatography (silica gel; pentane) gave triene **5a**.

Yield: 507 mg (75% overall yield); yellow oil.

IR (neat, NaCl): 3023, 2923, 1638, 1598 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.19 (m, 5 H), 5.91–5.68 (m, 5 H), 5.12–5.03 (m, 2 H), 2.72–2.68 (m, 2 H), 2.67–2.62 (m, 2 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 147.5, 135.3, 132.5, 128.3, 126.6, 126.0, 123.5, 116.9, 44.8, 43.7, 26.1.

MS (EI): *m*/*z* = 155 (100) $[M - C_3H_5]^+$.

1-(1-Allylcyclohexa-2,5-dienyl)-3,5-dimethylbenzene (5b)

Synthesized according to the general procedure described above from diketone **2b** (494 mg, 1.93 mmol, 1 equiv), LDA (9.8 mL, 6.56 mmol, 3.5 equiv), TMSCl (1.3 mL, 10.62 mmol, 5.5 equiv) and THF (10 mL) for the first step. $PhN(Tf)_2$ (3.45 g, 9.65 mmol, 5 equiv), CsF (2.35 g, 15.44 mmol, 8 equiv) and DME (8 mL) were used for the second step. HCO_2H (0.58 mL, 15.44 mmol, 8 equiv), DIPEA (2 mL, 11.58 mmol, 6 equiv), $Pd(OAc)_2$ (43 mg, 0.19 mmol, 10 mol%), Ph_3P (101 mg, 0.39 mmol, 20 mol%) and DMF (18 mL) were used for the third step. Purification by flash chromatography (silica gel; PE–EtOAc, 99:1) gave triene **5b**.

Yield: 302 mg (70% overall yield); colorless oil.

IR (neat, NaCl): 3022, 2916, 1602, 1439 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.99 (s, 2 H), 6.85 (s, 1 H), 5.89–5.64 (m, 5 H), 5.10–5.00 (m, 2 H), 2.71–2.56 (m, 2 H), 2.60 (td, *J* = 7.0, 1.3 Hz, 2 H), 2.32 (s, 6 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 147.5, 137.7, 135.4, 132.6, 132.6, 127.7, 124.4, 124.4, 123.3, 116.7, 44.9, 43.5, 26.0, 21.5.

HRMS (EI): *m*/*z* $[M]^{+\cdot}$ calcd for $C_{17}H_{20}$: 224.1565; found: 224.1556.

1-(1-Allylcyclohexa-2,5-dienyl)-4-methoxybenzene (5c)

Synthesized according to the general procedure described above from diketone **2c** (360 mg, 1.40 mmol, 1 equiv), LDA (7.3 mL, 4.90 mmol, 3.5 equiv), TMSCl (1.0 mL, 7.67 mmol, 5.5 equiv) and THF (10 mL) for the first step. $PhN(Tf)_2$ (2.5 g, 7.00 mmol, 5 equiv), CsF (1.7 g, 11.2 mmol, 8 equiv) and DME (6 mL) were used for the second step. HCO_2H (0.42 mL, 11.20 mmol, 8 equiv), DIPEA (1.46 mL, 8.40 mmol, 6 equiv), $Pd(OAc)_2$ (31 mg, 0.14 mmol, 10 mol%), Ph_3P (73 mg, 0.28 mmol, 20 mol%) and DMF (13 mL) were used for the third step. Purification by flash chromatography (silica gel; PE–EtOAc, 96:4) gave triene **5c**.

Yield: 286 mg (87% overall yield); yellow oil.

IR (neat, NaCl): 3018, 2932, 1608, 1464, 1440, 1248, 1180, 1038, 912, 828 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 7.31–7.24 (m, 2 H), 6.90–6.84 (2 H), 5.88–5.62 (m, 5 H), 5.11–5.02 (m, 2 H), 3.80 (s, 3 H), 2.69–2.65 (m, 2 H), 2.59 (d, *J* = 7.0 Hz, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 159.8, 141.9, 137.4, 134.8, 134.8, 129.7, 125.3, 116.3, 57.3, 46.9, 28.1.

HRMS (EI): *m*/*z* $[M - C_3H_5]^+$ calcd for $C_{13}H_{13}O$: 185.09664; found: 185.0963.

4-(1-Allylcyclohexa-2,5-dienyl)-1,2-dimethoxybenzene (5d)

Synthesized according to the general procedure described above from diketone **2d** (0.3 g, 1.04 mmol, 1 equiv), LDA (1.6 mL, 1.04 mmol, 3.5 equiv), TMSCl (0.72 mL, 5.72 mmol, 5.5 equiv) and THF (8 mL) for the first step. $PhN(Tf)_2$ (1.86 g, 5.21 mmol, 5 equiv), CsF (1.27 g, 8.33 mmol, 8 equiv) and DME (3.6 mL) were used for the second step. HCO_2H (0.31 mL, 8.32 mmol, 8 equiv), DIPEA (1.1 mL, 6.24 mmol, 6 equiv), $Pd(OAc)_2$ (23 mg, 0.1 mmol, 10 mol%), Ph_3P (54 mg, 0.21 mmol, 20 mol%) and DMF (10 mL) were used for the third step. Purification by flash chromatography (silica gel; PE–EtOAc, 95:5) gave triene **5d**.

Yield: 90 mg (34% overall yield); colorless viscous oil.

IR (neat, NaCl): 3015, 2933, 2834, 1603, 1255, 1145 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.93–6.81 (m, 3 H), 5.88–5.64 (m, 5 H), 5.09–5.00 (m, 2 H), 3.87 (s, 3 H), 3.86 (s, 3 H), 2.69–2.66 (m, 2 H), 2.59 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 148.7, 147.2, 140.3, 135.2, 132.6, 123.3, 118.4, 116.8, 110.9, 110.5, 55.8, 44.9, 43.3, 26.0.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{20}O_2$: 256.14633; found: 256.1469.

5-(1-Allylcyclohexa-2,5-dienyl)benzo[*d*][1,3]dioxole (5e)

Synthesized according to the general procedure described above from diketone **2e** (346 mg, 1.27 mmol, 1 equiv), LDA (7 mL, 4.41 mmol, 3.5 equiv), TMSCl (0.9 mL, 7 mmol, 5.5 equiv) and THF (10 mL) for the first step. $PhN(Tf)_2$ (2.27g, 6.35 mmol, 5 equiv), CsF (1.54g, 10.16 mmol, 8 equiv) and DME (4.4 mL) were used for the second step. HCO_2H (0.38 mL, 10.16 mmol, 8 equiv), DIPEA (1.33 mL, 7.62 mmol, 6 equiv), $Pd(OAc)_2$ (28 mg, 0.13 mmol, 10 mol%), Ph_3P (67 mg, 0.25 mmol, 20 mol%) and DMF (12 mL) were used for the third step. Purification by flash chromatography (silica gel; pentane) gave triene **5e**,

Yield: 229 mg (75% overall yield); yellow viscous oil.

IR (neat, NaCl): 2881, 1483, 1235, 1039 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.89–6.74 (m, 3 H), 5.93 (s, 2 H), 5.88–5.60 (m, 5 H), 5.10–5.00 (m, 2 H), 2.66 (m, 2 H), 2.56 (td, *J* = 7.0, 1.3 Hz, 2 H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 147.6, 145.6, 141.7, 135.1, 132.4, 123.3, 119.4, 116.9, 107.9, 107.7, 100.9, 44.9, 43.4, 26.0.

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{16}H_{16}O_2$: 240.11503; found: 240.1153.

Acknowledgment

We gratefully acknowledge the CNRS and MNERT for financial support.

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