

On the scope and limitations of the Heck reaction of upper rim tetraiodocalix[4]arenes

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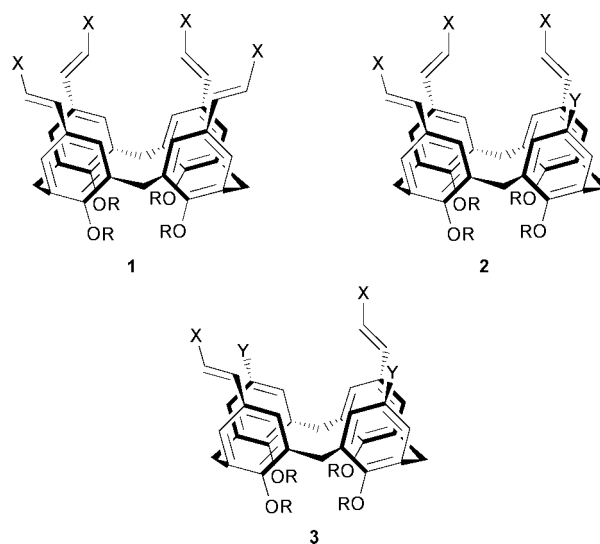
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Upper rim substituted tetraiodocalix[4]arenes are coupled to a variety of olefins using the palladium catalysed Heck reaction. Tetraolefinic upper rim substituted calix[4]arenes are obtained in good yields. All of the olefins are coupled with exceptionally high stereoselectivity to produce the all-(*E*) isomers. The optimisation of reaction conditions as well as the scope and limitation of the reaction with respect to a variety of olefins are discussed.

Calixarenes are well defined macrocyclic molecules of the phenolic metacyclophane type first synthesised by Zinke.¹ Due to their facile large scale preparation, distinctive concave molecular architecture, tunable size, and excellent capability of derivatisation they have emerged as one of the prime building blocks for supramolecular chemistry.^{2–4} Simple cavitand type calix[*n*]arenes as well as box-shaped derivatives are able to complex complementary neutral organic guest molecules.^{4,5}

In an ongoing research project we are aiming at the synthesis of dynamic combinatorial libraries. The concept of dynamic libraries was recently introduced by Lehn and by Sanders and shown to be viable.^{6–11} Whereas conventional or “static” combinatorial chemistry is based on extensive libraries of prefabricated molecules, dynamic combinatorial chemistry implements the reversible connection of sets of basic components to give access to virtual combinatorial libraries whose constituents comprise at least in theory all possible combinations that may potentially be generated. In contrast to the Lehn and Sanders approach, in which difunctional building blocks are assembled to a library of macrocyclic receptors^{7–10} in the presence of suitable guest molecules, we opted for the use of prefabricated macrocyclic building blocks with well defined architecture and recognition properties, namely, the calix[4]arenes. For the successful generation of a dynamic combinatorial library we required calix[4]arene derivatives that are able to undergo a variety of reversible transformations, leading to reversible bond formation in the presence of potential guest molecules, suitable reagents and additional building blocks. Furthermore, our ultimate aim is to bind neutral organic molecules, in particular, environmental toxins, which suggests that elaboration of the calix[4]arene at the upper rim would result in more suitably shaped receptors. With these requirements in mind we considered calix[4]arene derivatives of types **1–3** with a tetra-, tri- or di-olefinic substitution pattern as ideal synthetic targets. The double bond functionality offers exceptional versatility for further reversible functionalisations such as by olefin metathesis, conjugate addition or transesterification (for X = COOR). Moreover, the double bonds are predisposed to undergo a variety of non-reversible transformations such as cycloadditions or oxidations potentially leading to a multitude of interesting novel calix[4]arene based synthetic receptors. In this contribution we report on the synthesis of compounds of type **1** using palladium catalysed Heck chemistry and on the scope and limitations of this chemistry.



Results and discussion

Synthesis of Heck products and optimisation of reaction conditions

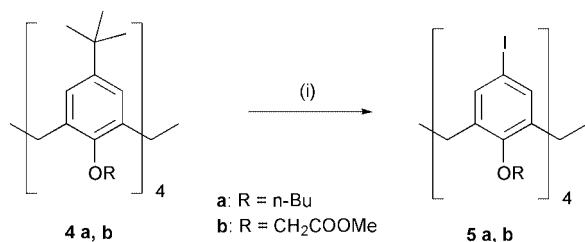
In order to synthesise compounds of type **1** we considered the palladium catalysed Heck reactions of calix[4]arene tetraiodides **5a,b** with suitable olefins as the most promising and most direct approach. Palladium catalysed functionalisations of calix[4]arenes have been reported in the literature. Ungaro and co-workers have reported the application of the Suzuki–Miyura coupling methodology in the synthesis of calix[4]arenylvinylenes and calix[4]arenylphenylene oligomers.^{12,13} Suzuki couplings have been frequently used in the synthesis of deep cavity calix[4]arenes.^{14–16} The groups of Georghiou,¹⁷ Csok¹⁸ and Gonzalez¹⁹ have reported attempted Pd couplings on lower rim derivatised calix[4]arene triflates. To our knowledge no Heck functionalisations of calix[*n*]arenes have been reported.

As starting materials we chose the tetraiodides **5a,b** with O(*n*-Bu) and OCH₂COOMe substituents on the lower rim in the cone conformation. These compounds should display both sufficient solubility and conformational stability under the rather harsh Heck conditions employed. Compounds **5a,b** were obtained in excellent yields from **4a,b** using Ag(OOCCF₃) and

Table 1 Optimisation of Heck conditions using acrylate esters **8a–c** and **5a**

Substrates	Conditions ^a	Time/h	Temperature/°C	Ratio 6a : 7 ^b	Yield (%)
5a + 8a	2.5% Pd(OAc) ₂ -PPh ₃	72	70	60 : 40	3
5a + 8a	3% Pd(OAc) ₂ -dppp	72	70	—	0
5a + 8a	5% Pd(OAc) ₂ -PPh ₃	72	70	80 : 20	15
5a + 8b	5% Pd(OAc) ₂ -PPh ₃	72	70	70 : 30	25
5a + 8c	5% Pd(OAc) ₂ -PPh ₃	72	70	65 : 35	20
5a + 8a	10% Pd(OAc) ₂ -dppp	72	70	98 : 2	10
5a + 8a	10% Pd(OAc) ₂ - <i>o</i> -phen	72	100	—	0
5a + 8a	2.5% Pd(OAc) ₂ -dppp	48	100	>98 : 2	15
5a + 8a	10% Pd(PPh ₃) ₄	48	100	>98 : 2	45
5a + 8a	10% Pd(OAc) ₂ -dppe	48	100	>98 : 2	50
5a + 8a	10% Pd(OAc) ₂ -PPh ₃	48	100	>98 : 2	80
5a + 8a	10% Pd(OAc) ₂ -dppp	48	100	>98 : 2	70

^a All reactions were performed in DMF with 1 equivalent NEt₃ and twofold mol% of co-ligand. ^b Ratio determined by ¹H NMR spectroscopy at 270 MHz.

**Scheme 1** Reagents and conditions: (i) I₂, AgOOCF₃, CHCl₃, reflux.

iodine (Scheme 1) following the established protocol of Ungaro and co-workers.²⁰ The spectroscopic data clearly indicate that the tetraiodides are in the cone conformation. It is noteworthy that tetraiodides **5a,b** decompose upon standing, even in the absence of light, within 2 weeks.

For the Heck reaction^{21,22} we chose initial conditions using 5 mol% Pd(OAc)₂, 10 mol% PPh₃, NEt₃, and methyl acrylate **8a** in DMF as solvent at 70 °C. After 5 days of reaction we observed the formation of 2 products, which we could not separate using column chromatography (Table 1). Nevertheless, we cautiously identify the reaction products as tetraolefinic calix[4]arene **6a** and triolefinic substituted calix[4]arene **7a** (Scheme 2). This assignment results from the ¹H NMR data and more convincingly from the liquid secondary ion mass spectroscopy (LSIMS) mass spectral data of the mixture showing the expected molecular ions at 1026 and 1068.

Changing the Pd catalyst to Pd(PPh₃)₄ or Pd(OAc)₂-dppp [dppp = 1,3-bis(diphenylphosphino)propane] and increasing the catalyst loading to 10% did not result in a significant change in the reaction. Change of the co-ligand to dppp or *o*-phenanthroline (*o*-phen) did result in minor changes in the outcome of the reaction or in no reaction at all in the latter case (Table 1). The use of alternative electron deficient olefins, ethyl and *tert*-butyl acrylate **8b,c**, resulted in the production of an increased amount of the trisubstituted derivative **7b,c** as judged by the ¹H NMR and mass spectra of the mixtures isolated after

reaction at 70 °C. We attribute this observation to the increased steric demand of the Et and ^tBu groups, in comparison to the Me group. Although these results seem to be disappointing, it has to be kept in mind that even a defined mixture of two distinct macrocycles could be beneficial in the dynamic combinatorial library approach.

To bring the reaction to completion and obtain the tetraolefinic calix[4]derivative **6a** we increased the reaction temperature to 100 °C using the initial combination of reagents. After 48 h reaction time the crude tetraolefinic calix[4]arene **6a** could be obtained in very good yields and reasonable purity (Scheme 3, Table 1). Optimisation of the co-ligand and the palladium source used revealed that 10 mol% Pd(OAc)₂ and 20 mol% dppp were the best combination of reagents (Table 1). The amount of catalyst required seems to be rather high at first, however, it should be noted that four Heck reactions are performed thus reducing the real amount of catalyst to 2.5 mol% per coupling reaction. Furthermore, it is worth noting that our conditions deviate substantially from the recommended conditions for Heck couplings. Our reaction temperature is unusually high, indeed approaching the decomposition temperature of DMF. Secondly, chelating phosphine ligands such as dppp have been found on most occasions to be inferior to monodentate phosphine ligands such as PPh₃ and P(*o*-tolyl)₃. This finding emphasises the fact that for each individual substrate in a Heck coupling the reaction conditions with respect to the co-ligand have to be optimised.

Heck reaction of the lower rim OCH₂COOMe substituted calix[4]arene **5b** did not result in the production of the desired tetraolefinic product. We attribute this to the fact that the four reactive iodines at the upper rim in **5b** are closer in space to one another in comparison to those of derivative **5a**, resulting in increased steric crowding at the upper rim reactive side. Variation of the olefinic reaction partner did show that the conditions are very compatible with other acrylic acid esters (R = Me, Et, ^tBu) and the crude yields of **6b,c** were generally good (Table 2). It should be mentioned that the low final

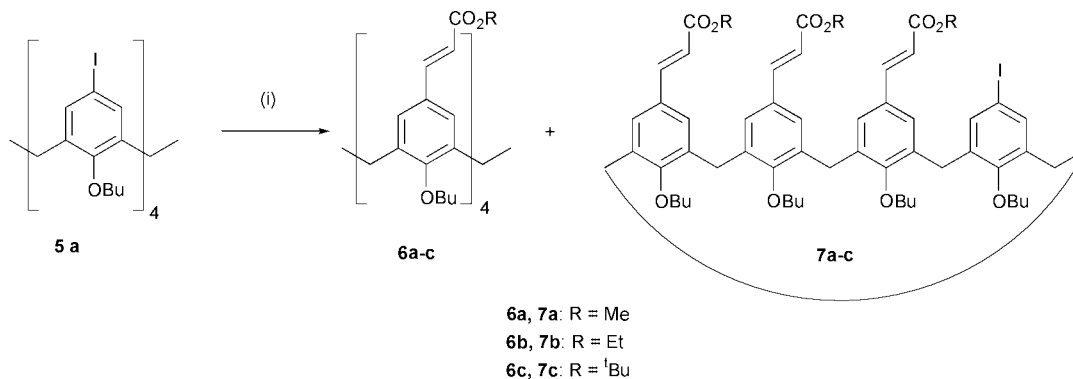
**Scheme 2** Reagents and conditions: (i) see Table 1.

Table 2 Heck reaction of acrylate esters **8a–c** with tetraiodides **5a,b**

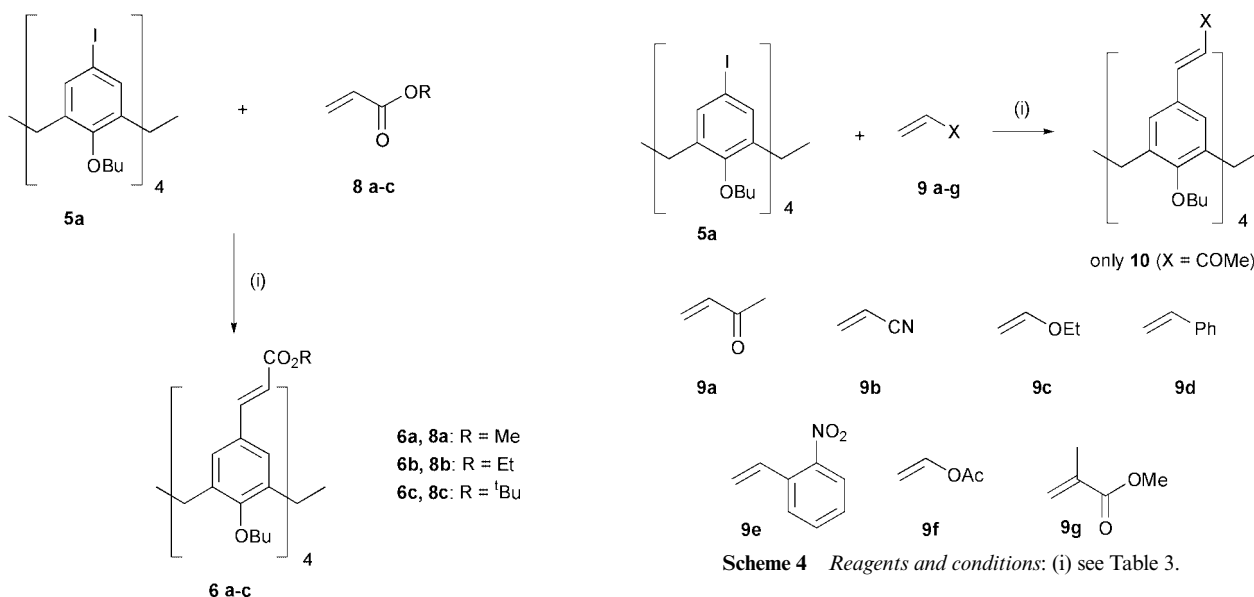
Substrates	Product	Conditions ^a	Time/h	Crude yield ^b (%)	Isolated yield ^c (%)
5a + 8a	6a	10% Pd(OAc) ₂ -dppp	48	88	82
5a + 8a	6a	10% Pd(OAc) ₂ -PPh ₃	72	45	23
5a + 8b	6b	10% Pd(OAc) ₂ -dppp	100	10	Mixture
5a + 8b	6b	10% Pd(OAc) ₂ -PPh ₃	48	60	50
5b + 8a	None	10% Pd(OAc) ₂ -PPh ₃	72	—	—
5a + 8c	6c	10% Pd(OAc) ₂ -dppp	72	60	55

^a All reactions were performed in DMF with 1 equivalent NEt₃ and twofold mol% of co-ligand. ^b Determined by ¹H NMR spectroscopy at 270 MHz. ^c Yield producing material showing correct elemental analysis.

Table 3 Heck reactions using olefins **9a–h** with tetraiodide **5a**

Substrates	Conditions ^a	Time/h	Product ^b	Yield (%)
5a + 9a	10% Pd(OAc) ₂ -dppp	48	10	82 %
5a + 9b	10% Pd(OAc) ₂ -dppp	100	Mixture	41 ^c
5a + 9b	10% Pd(OAc) ₂ - <i>o</i> -phen	72	Mixture	—
5a + 9c	10% Pd(OAc) ₂ -dppp	72	None	—
5a + 9d	10% Pd(OAc) ₂ -dppp	72	None	—
5a + 9e	10% Pd(OAc) ₂ -dppp	72	None	—
5a + 9f	10% Pd(OAc) ₂ -dppp	72	None	—
5a + 9g	10% Pd(OAc) ₂ -dppp	100	None	—
5a + 9h	10% Pd(OAc) ₂ -dppp	48	11	82

^a All reactions were performed in DMF with 1 equivalent NEt₃ and twofold mol% of co-ligand. ^b Determined by ¹H NMR spectroscopy at 270 MHz and TLC. ^c As judged ¹H NMR spectroscopy by integrating starting material *versus* total product, data not given in Experimental due to lack of assignment.



isolated yields stated in Table 2 refer to material that is pure by elemental analysis, a technique whose reliability has been frequently questioned in calixarene chemistry.^{23,24} The crude yields, however, representing spectroscopically pure material are very good (Table 2). All reactions proceed completely stereoselectively to produce the all-(*E*) tetraolefinic calix[4]arenes as a single stereoisomer. All products are additionally found exclusively in the cone conformation. It has to be stressed that this highly chemo- and stereoselective outcome of the reaction is remarkable indeed, bearing in mind that a total of 120 isomeric products are possible in this reaction.²⁵

Next we investigated the coupling to a variety of other olefins. The Heck coupling is also successful with methyl vinyl ketone **9a** to give the tetravinyl ketone **10a** in very good yield again as a single all-(*E*) stereoisomer (Scheme 4). The reaction of tetraiodide **5a** with acrylonitrile **9b** gave an undefined mixture of products showing signals in the ¹H

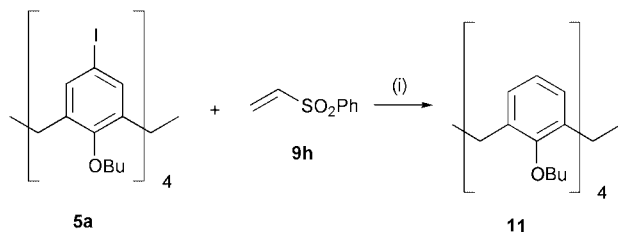
NMR for both (*Z*) and (*E*) unsaturated nitriles as judged by the ³J_{H_C-CH} coupling constant in the ¹H NMR spectra. The use of *o*-phenanthroline, a ligand shown to be beneficial in Heck reactions with **9b**,²⁶ did not improve the outcome of the reaction. Heck reactions with ethyl vinyl ether **9c** and styrene derivatives **9d,e** resulted in decomposition and polymerisation; coupling with vinyl acetate **9f** and methyl methacrylate **9g** were completely unsuccessful, whereas Heck reaction with phenyl vinyl sulfone **9h** resulted in complete and clean deiodination of the starting material to give calix[4]arene **11** in quantitative yield (Scheme 5). This finding might be attributed to contamination by traces of water of the reagents, in particular, the solvent. Interestingly, identical conditions and reagents were used in all the other reactions without any traces of deiodinated material being recovered.

Spectroscopic data

The structures can be directly deduced from their NMR spectra. All compounds are found to adopt the cone conformation

Table 4 Characteristic spectroscopic data of tetraolefins **6a–c**, **10** and tetraiodides **5a,b**

Compound	<i>m/z</i> (LSIMS)	δ (^1H) CH_2Ar^a	$\Delta\delta$ (CH_2Ar^a)	$^2J_{\text{ArCHHAr}}^b$	$^3J_{\text{HC-CH}}^b$
5a	1152	4.21, 3.16	1.05	13.3	—
5b	1243	4.72, 3.14	1.58	13.3	—
6a	984	4.41, 3.16	1.25	13.5	16.2
6b	1040	4.41, 3.16	1.25	13.5	16.2
6c	1152	4.41, 3.16	1.25	13.5	16.2
10	920	4.41, 3.16	1.25	13.5	16.2

^a In ppm. ^b In Hz.**Scheme 5** Reagents and conditions: (i) see Table 3.

exhibiting perfectly symmetric spectra as expected for a C_4 symmetric molecule. In all of the tetraolefinic substituted derivatives the stereochemical relationship across the double bond is an (*E*) geometry as indicated by their large $^3J_{\text{HC-CH}}$ coupling constants between 16.1 to 17.6 Hz (Table 4). It is worth noting that these coupling constants are unusually large. The two pairs of doublets observed for the “axial” and “equatorial” methylene hydrogens as well as the corresponding ^{13}C signal for the methylene bridge carbon reinforce the finding that all of the molecules synthesised adopt the cone conformation (Table 4). As pointed out by Gutsche the difference in chemical shifts between the axial and equatorial methylene bridge hydrogens gives an indication of the symmetry of the cone conformation.²⁷ The $\Delta\delta$ values in compounds **6a–c** and **10** are found to be fairly constantly at 1.25 ppm and are a good indication of the increased steric crowding in these derivatives, resulting in a more planar and parallel orientation of the aromatic rings^{27,28} as indicated by the $\Delta\delta$ parameter. The increase in size of the ester substituents (Me to ^tBu) does not seem to affect the overall geometry of the compounds.

The ^{13}C carbon signals of the olefins are in the expected region as unambiguously shown in a ^1H - ^{13}C -HMQC experiment on derivative **6a**. Further assignment of all the ^{13}C signals is based on an ^1H - ^{13}C -HMQC HMBC experiment in conjunction with the HMQC experiment. The mass spectra of the compounds show the expected molecular ions (see Table 4).

Conclusion

In conclusion, we have synthesised the first tetraolefinic upper rim calix[4]arene derivatives and applied the Heck reaction to the synthesis of functionalised calix[4]arenes. Formally these compounds are cyclic oligomers of coumaric acid. The Heck reaction has been optimised with respect to the Pd source, temperature and co-ligands and is successful for a variety of electron deficient olefins such as esters and ketones. All of the reactions proceed in good yield and give stereoselectively the all-(*E*) tetraolefinic calix[4]arenes. All of the compounds synthesised are useful intermediates in organic synthesis and supramolecular chemistry and are currently being investigated as building blocks for the generation of dynamic combinatorial libraries.

Experimental

^1H and ^{13}C NMR spectra were recorded on a JEOL GSX 270MHz and a Bruker Avance 500 MHz spectrometer. δ values

are quoted relative to tetramethylsilane (δ_{H} 0.00 ppm) or chloroform (δ_{H} 7.23 ppm) for ^1H NMR and relative to chloroform (δ_{C} 77.0 ppm) for ^{13}C NMR. Coupling constants J are in Hz. Microanalyses were carried out using a Leeman CE 440 automatic elemental analyser. Infrared spectra were determined on a Perkin Elmer 200 spectrometer. The mass spectra were recorded at the EPSRC National Centre for Mass Spectrometry in Swansea. Thin layer chromatography (TLC) was carried out on commercially available pre-coated plates (Merck Kieselgel 60 F₂₅₄ silica) using 1 : 3 ethyl acetate–hexane as the solvent system. Flash column chromatography at a pressure of 1 bar was carried out on Merck Kieselgel 60 (230–400 mesh) silica. All chemicals/reagents were purchased from the Aldrich Chemical Company. Solvents were dried using the usual procedures and reagents used without further purification unless stated otherwise. Calix[4]arenes **4a,b** were prepared according to the literature procedures.^{29,30}

5,11,17,23-Tetraiodo-25,26,27,28-tetrabutoxycalix[4]arene (**5a**)

Silver trifluoroacetate (0.37 g, 1.62 mmol) was added to a stirred solution of 25,26,27,28-tetrabutoxycalix[4]arene **4a** (0.2 g, 0.3 mmol) in CHCl_3 (20 ml). After 3 h of vigorous refluxing the mixture was cooled to 50 °C and iodine (0.417 g, 4.15 mmol) was added. The mixture was stirred at 50 °C for 24 h. After cooling, the AgI was filtered off and the violet filtrate collected and bleached with 50 ml sodium metabisulfite (20% w/w). The organic extract was dried (Na_2SO_4) and evaporated under reduced pressure. The residue was recrystallised from methanol to give the calix[4]arene **5a** (0.146 g, 41%) as off-white cubes, mp 195–198 °C; $\nu_{\text{max}}(\text{Nujol})/\text{cm}^{-1}$ 1100 (C–O); $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 6.93 (8H, s, Ar–H), 4.21 (4H, d, J 13.3, $\text{CH}_A\text{H}_B\text{Ar}$), 3.78 (8H, t, J 7.4, CH_2O), 3.16 (4H, d, J 13.3, $\text{CH}_A\text{H}_B\text{Ar}$), 1.75 (8H, m, $\text{CH}_2\text{CH}_2\text{O}$), 1.40–1.25 (8H, m, CH_2CH_3), 1.00 (12H, t, J 6.0, CH_3CH_2); $\delta_{\text{C}}(\text{CDCl}_3)$ 156.2, 137.1, 137.3, 137.6, 75.5, 32.9, 31.2, 20.4, 14.0; m/z (LSIMS) 1152 (Found: C, 44.7; H, 4.55. $\text{C}_{44}\text{H}_{52}\text{I}_4\text{O}_4$ requires C, 45.85; H, 4.55%).

5,11,17,23-Tetraiodo-25,26,27,28-tetrakis(methoxycarbonylmethoxy)calix[4]arene (**5b**)

Silver trifluoroacetate (3.08 g, 14 mmol) was added to a stirred solution of 25,26,27,28-tetrakis(methoxycarbonylmethoxy)calix[4]arene **4b** (2.0 g, 2.8 mmol) in CHCl_3 (20 ml). After 3 h of vigorous refluxing the mixture was cooled to 50 °C and iodine (3.5 g, 14 mmol) was added. The mixture was stirred at 50 °C for 24 h. After cooling, the AgI was filtered off and the violet filtrate collected and bleached with 50 ml sodium metabisulfite (20% w/w). The organic extract was dried (Na_2SO_4) and evaporated under reduced pressure. The residue was recrystallised from methanol to give the calix[4]arene **5b** (2 g, 60%) as off-white cubes, combusts before reaching mp; $\nu_{\text{max}}(\text{Nujol})/\text{cm}^{-1}$ 1758 (C=O), 1180 (C–O); $\delta_{\text{H}}(270 \text{ MHz}; \text{CDCl}_3)$ 7.03 (8H, s, Ar–H), 4.72 (4H, d, J 13.3, $\text{CH}_A\text{H}_B\text{Ar}$), 4.65 (8H, s, CH_2O), 3.68 (12H, s, CH_3O), 3.14 (4H, d, J 13.3, $\text{CH}_A\text{H}_B\text{Ar}$); $\delta_{\text{C}}(\text{CDCl}_3)$ 169.1, 162.9, 137.1, 137.2, 136.8, 75.5, 53.4, m/z (LSIMS) 1243 (Found: C, 38.50; H, 3.22. $\text{C}_{40}\text{H}_{36}\text{I}_4\text{O}_{12}$ requires C, 39.50; H, 2.98%).

Heck coupling at 70 °C using methyl acrylate and calix[4]arene 5a

Triethylamine (0.8 ml, 0.53 g, 5.22 mmol) and methyl acrylate **8a** (0.69 ml, 0.6 g, 6.96 mmol) were added to a stirred solution of 5,11,17,23-tetraiodo-25,26,27,28-tetrabutoxycalixarene **5a** (0.9 g, 0.79 mmol) in DMF (20 ml). After 10 minutes of vigorous stirring at 25 °C palladium acetate (0.02 g, 0.087 mmol) and 1,3-bis(diphenylphosphino)propane (0.036 g, 0.087 mmol) were added and the mixture heated to 70 °C and stirred for 48 h. After addition of 50 ml dichloromethane the mixture was washed with acid (3 × 20 ml, 3 M HCl). The organic extract was dried (Na₂SO₄) and evaporated under reduced pressure. The oily brown residue was partially separated using column chromatography (4 : 1 hexane–ethyl acetate) to give a mixture of **7** (89%) and the (*E,E,E*)-tricoupled equivalent (11%) as off-white cubes. Signals observed for **7** (for **6a** see Experimental section below): δ_{H} (270 MHz; CDCl₃) 7.4 (2H, d, *J* 16.2 Ar-CH=), 7.35 (1H, d, *J* 16.2, Ar-CH=), 6.94 (2H, s, Ar-H), 6.87 (2H, s, Ar-H), 6.78 (2H, s, Ar-H), 6.74 (2H, s, Ar-H), 6.15 (2H, d, *J* 16.5, CH-C=O), 6.06 (1H, d, *J* 16.5, CH-C=O), 4.44 (2H, d, *J* 13.5, CH_AH_BAr), 4.38 (2H, d, *J* 13.5, CH_AH_BAr), 3.9 (8H, t, *J* 7.4, CH₂O), 3.75 (12H, s, CH₃O), 3.16 (2H, d, *J* 13.4, CH_AH_BAr), 3.09 (2H, d, *J* 13.4, CH_AH_BAr), 1.85 (8H, m, CH₂CH₂O), 1.42 (8H, m, CH₂CH₃), 1.00 (12H, t, *J* 8.3, CH₃CH₂); *m/z* (LSIMS) 1026.4 and 984.3.

Heck coupling at 70 °C using ethyl acrylate (8b) and calix[4]arene 5a

Triethylamine (0.7 ml, 0.47 g, 4.68 mmol) and ethyl acrylate **8b** (0.67 ml, 0.62 g, 6.24 mmol) were added to a stirred solution of 5,11,17,23-tetraiodo-25,26,27,28-tetrabutoxycalixarene **5a** (0.9 g, 0.79 mmol) in DMF (20 ml). After 10 minutes of vigorous stirring at 25 °C palladium acetate (0.018 g, 0.078 mmol) and 1,3-bis(diphenylphosphino)propane (0.032 g, 0.078 mmol) were added and the mixture heated to 70 °C and stirred for 48 h. After addition of 50 ml dichloromethane the mixture was washed with acid (3 × 20 ml, 3 M HCl). The organic extract was dried (Na₂SO₄) and evaporated under reduced pressure. The oily brown residue was partially separated using column chromatography (4 : 1 hexane–ethyl acetate) to give a mixture of calix[4]arene **6b** (15%) and the (*E,E,E*)-tricoupled equivalent (85%) as off-white cubes. Signals observed for **7b** (for the signals of **6b** see Experimental section below): δ_{H} (270 MHz) 7.47 (2H, d, *J* 16.5, Ar-CH=), 7.39 (1H, d, *J* 16.2, Ar-CH=), 6.98 (2H, s, Ar-H), 6.93 (2H, s, Ar-H), 6.75 (2H, s, Ar-H), 6.70 (2H, s, Ar-H), 6.18 (2H, d, *J* 16.2, CH-C=O), 6.06 (1H, d, *J* 16.5, CH-C=O), 4.44 (2H, d, *J* 13.1, CH_AH_BAr), 4.38 (2H, d, *J* 13.5, CH_AH_BAr), 4.19 (6H, m, OCH₂CH₃), 3.90 (8H, m, CH₂O), 3.19 (2H, d, *J* 13.5, CH_AH_BAr), 3.09 (2H, d, *J* 13.1, CH_AH_BAr), 1.85 (17H, m, CH₂CH₂O and OCH₂CH₃), 1.42 (8H, m, CH₂CH₃), 1.00 (12H, t, *J* 8.3, CH₃CH₂); *m/z* (LSIMS) 1040.2 and 1068.4.

5,11,17,23-Tetrakis[(*E*)-2-(methoxycarbonyl)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (6a)

Triethylamine (0.8 ml, 0.53 g, 5.22 mmol) and methyl acrylate **8a** (0.69 ml, 0.6 g, 6.96 mmol) were added to a stirred solution of 5,11,17,23-tetraiodo-25,26,27,28-tetrabutoxycalixarene **5a** (0.9 g, 0.79 mmol) in DMF (20 ml). After 10 minutes of vigorous stirring at 25 °C palladium acetate (0.02 g, 0.087 mmol) and 1,3-bis(diphenylphosphino)propane (0.036 g, 0.087 mmol) were added and the mixture heated to 90 °C and stirred for 24 h. After addition of 50 ml dichloromethane the mixture was washed with acid (3 × 10 ml, 3 M HCl). The organic extract was dried (Na₂SO₄) and evaporated under reduced pressure. The residue was further dried in a desiccator (SiO₂) under reduced pressure for 12 h and recrystallised from methanol to give the calix[4]arene **6a** (0.70 g, 82%) as off-white cubes, mp 238–240 °C; ν_{max} (Nujol)/cm⁻¹ 1732 (C=O), 1620 (C=C); δ_{H} (270 MHz;

CDCl₃) 7.32 (4H, d, *J* 16.2, Ar-CH=), 6.79 (8H, s, Ar-H), 6.07 (4H, d, *J* 16.2, CH-C=O), 4.41 (4H, d, *J* 13.5, CH_AH_BAr), 3.9 (8H, t, *J* 7.4, CH₂O), 3.75 (12H, s, CH₃O), 3.16 (4H, d, *J* 13.5, CH_AH_BAr), 1.85 (8H, m, CH₂CH₂O), 1.42 (8H, m, CH₂CH₃), 1.00 (12H, t, *J* 8.3, CH₃CH₂); δ_{C} (CDCl₃) 168.1, 144.9, 135.8, 129.5, 129.3, 129.0, 116.2, 75.5, 53.4, 33.9, 32.2, 19.3, 14.0; *m/z* (LSIMS) 984 (Found: C, 73.87; H, 7.09. C₆₀H₇₂O₁₂ requires C, 73.15; H, 7.37%).

5,11,17,23-Tetrakis[(*E*)-2-(ethoxycarbonyl)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (6b)

Triethylamine (0.7 ml, 0.47 g, 4.68 mmol) and ethyl acrylate **8b** (0.67 ml, 0.62 g, 6.24 mmol) were added to a stirred solution of 5,11,17,23-tetraiodo-25,26,27,28-tetrabutoxycalixarene **5a** (0.9 g, 0.79 mmol) in DMF (20 ml). After 10 minutes of vigorous stirring at 25 °C palladium acetate (0.018 g, 0.078 mmol) and 1,3-bis(diphenylphosphino)propane (0.032 g, 0.078 mmol) were added and the mixture was heated to 90 °C and stirred for 48 h. After addition of 50 ml dichloromethane the mixture was washed with acid (3 × 20 ml, 3 M HCl). The organic extract was dried (Na₂SO₄) and evaporated under reduced pressure. The residue was further dried in a desiccator (SiO₂) under reduced pressure for 12 h and recrystallised from methanol to give the calix[4]arene **6b** (0.41 g, 50%) as off-white cubes, mp 168–171 °C; ν_{max} (Nujol)/cm⁻¹ 1732 (C=O), 1620 (C=C); δ_{H} (270 MHz; CDCl₃) 7.28 (4H, d, *J* 16.2, Ar-CH=), 6.79 (8H, s, Ar-H), 6.07 (4H, d, *J* 16.2, CH-C=O), 4.41 (4H, d, *J* 13.5, CH_AH_BAr), 4.19 (8H, q, *J* 6.3, OCH₂CH₃), 3.9 (8H, t, *J* 7.1, CH₂O), 3.16 (4H, d, *J* 13.5, CH_AH_BAr), 1.90 (8H, m, CH₂CH₂O), 1.50–1.19 (20H, m, CH₂CH₃ and OCH₂CH₃), 1.00 (12H, t, *J* 8.3, CH₃CH₂); δ_{C} (CDCl₃) 167.0, 144.9, 135.4, 129.4, 128.9, 128.8, 117.2, 75.5, 60.5, 33.9, 32.2, 19.3, 14.0, 13.9; *m/z* (LSIMS) 1040 (Found: C, 73.5; H, 7.74. C₆₄H₈₀O₁₂ requires C, 73.82; H, 7.74%).

5,11,17,23-Tetrakis[(*E*)-2-(*tert*-butoxycarbonyl)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (6c)

Triethylamine (0.8 ml, 0.53 g, 5.22 mmol) and *tert*-butyl acrylate **8c** (1.2 ml, 0.89 g, 6.96 mmol) were added to a stirred solution of 5,11,17,23-tetraiodo-25,26,27,28-tetrabutoxycalixarene **5a** (0.9 g, 0.79 mmol) in DMF (20 ml). After 10 minutes of vigorous stirring at 25 °C palladium acetate (0.02 g, 0.087 mmol) and 1,3-bis(diphenylphosphino)propane (0.036 g, 0.087 mmol) were added and the mixture was heated to 90 °C and stirred for 48 h. After addition of 50 ml dichloromethane the mixture was washed with acid (3 × 20 ml, 3 M HCl). The organic extract was dried (Na₂SO₄) and evaporated under reduced pressure. The residue was further dried in a desiccator (SiO₂) under reduced pressure for 12 h and recrystallised from methanol to give the calix[4]arene **6c** (0.61 g, 55%) as off-white cubes, mp 151–154 °C; ν_{max} (Nujol)/cm⁻¹ 1732 (C=O), 1620 (C=C); δ_{H} (270 MHz; CDCl₃) 7.30 (4H, d, *J* 16.2, Ar-CH=), 6.82 (8H, s, Ar-H), 6.03 (4H, d, *J* 16.2, CH-C=O), 4.41 (4H, d, *J* 13.5, CH_AH_BAr), 3.9 (8H, t, *J* 7.4, CH₂O), 3.16 (4H, d, *J* 13.5, CH_AH_BAr), 1.90 (8H, m, CH₂CH₂O), 1.59–1.20 (44H, m, CH₂CH₃ and (CH₃)₃C), 1.00 (12H, t, *J* 8.3, CH₃CH₂); δ_{C} (CDCl₃) 164.1, 143.9, 135.8, 132.5, 129.3, 129.0, 118.2, 79.6, 75.5, 33.9, 32.2, 28.4, 19.3, 14.0; *m/z* (LSIMS) 1152 (Found: C, 74.0; H, 8.71. C₇₂H₉₆O₁₂ requires C, 74.97; H, 8.39%).

5,11,17,23-Tetrakis[(*E*)-3-oxobut-1-enyl]-25,26,27,28-tetrabutoxycalix[4]arene (10)

Triethylamine (0.8 ml, 0.53 g, 5.22 mmol) and methyl vinyl ketone **9a** (0.59 ml, 0.5 g, 6.88 mmol) were added to a stirred solution of 5,11,17,23-tetraiodo-25,26,27,28-tetrabutoxycalixarene **5a** (1.0 g, 0.89 mmol) in DMF (20 ml). After 10 minutes of vigorous stirring at 25 °C palladium acetate (0.02 g, 0.087 mmol) and 1,3-bis(diphenylphosphino)propane (0.036 g, 0.087 mmol) were added and the mixture was heated to 90 °C and stirred for 24 h. After addition of 50 ml dichloromethane the

mixture was washed with acid (3 × 20 ml, 3 M HCl). The organic extract was dried (Na₂SO₄) and evaporated under reduced pressure. The residue was further dried in a desiccator (SiO₂) under reduced pressure for 12 h and recrystallised from methanol to give the calix[4]arene **10** (0.4 g, 82%) as off-white cubes, mp 195–197 °C; ν_{\max} (Nujol)/cm⁻¹ 1720 (C=O), 1620 (C=C); δ_{H} (270 MHz; CDCl₃) 7.20 (4H, d, *J* 16.2, Ar-CH=), 6.79 (8H, s, Ar-H), 6.28 (4H, d, *J* 16.2, CH-C=O), 4.41 (4H, d, *J* 13.5, CH_AH_BAr), 4.05 (12H, s, CH₃CO), 3.79 (8H, t, *J* 7.4, CH₂O), 3.16 (4H, d, *J* 13.5, CH_AH_BAr), 1.85 (8H, m, CH₂CH₂O), 1.39 (8H, m, CH₂CH₃), 1.00 (12H, t, *J* 8.3, CH₃CH₂); δ_{C} (CDCl₃) 158.1, 144.7, 136.1, 129.1, 128.9, 128.8, 75.5, 33.9, 32.2, 27.3, 19.3, 14.8; *m/z* (EI) 920 (Found: C, 78.94; H, 7.81. C₆₀H₇₂O₈ requires C, 78.23; H, 7.88%).

25,26,27,28-Tetrabutoxycalix[4]arene (11)

Triethylamine (0.8 ml, 0.53 g, 5.22 mmol) and phenyl vinyl sulfone **9g** (1.16 g, 6.88 mmol) were added to a stirred solution of 5,11,17,23-tetraiodo-25,26,27,28-tetrabutoxycalixarene **5a** (1.0 g, 0.89 mmol) in DMF (20 ml). After 10 minutes of vigorous stirring at 25 °C palladium acetate (0.02 g, 0.087 mmol) and 1,3-bis(diphenylphosphino)propane (0.036 g, 0.087 mmol) were added and the mixture was heated to 90 °C and stirred for 24 h. After addition of 50 ml dichloromethane the mixture was washed with acid (3 × 20 ml, 3 M HCl). The organic extract was dried (Na₂SO₄) and evaporated under reduced pressure. The residue was further dried in a desiccator (SiO₂) under reduced pressure for 12 h and recrystallised from methanol to give the calix[4]arene **11** (0.4 g, 82%) as off-white cubes, mp 241 °C; ν_{\max} (Nujol)/cm⁻¹; δ_{H} (300 MHz; CDCl₃) 6.63 (12H, m, Ar-H), 4.46 (4H, d, *J* 13.5, CH_AH_BAr), 3.90 (8H, t, *J* 7.5 CH₂O), 3.15 (4H, d, *J* 13.5, CH_AH_BAr), 1.90 (8H, m, CH₂CH₂O), 1.53–1.40 (8H, m, CH₂CH₃), 1.01 (12H, t, *J* 8.3, CH₃CH₂); *m/z* (LSIMS) 649 (Found: C, 84.22; H, 8.36. C₄₄H₅₆O₄ requires C, 84.4; H, 8.64%).

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