Ytterbium(III) triflate-catalysed preparation of calix[4]resorcinarenes: Lewis assisted Brønsted acidity

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Calix[4]resorcinarenes **1**–**5** have been prepared in good yields by the ytterbium(III) triflate hydrate-catalysed condensation of equimolar amounts of aldehydes and resorcinol. The lanthanide salt was easily recovered and re-used following the reaction thus providing an atom economic synthesis of resorcinarenes. Evidence is presented that indicates that ytterbium(III) triflate can significantly increase the Brønsted acidity of organic acids.

Introduction

Calix[4]resorcinarenes (resorcinarenes) are versatile host compounds for ions, sugars and organic molecules and exhibit molecular recognition as well as being starting materials for cavitands and other macrocyclic host molecules.[1] They are most often prepared by the mineral acid-catalysed condensation of resorcinol with an aliphatic or aromatic aldehyde.[2,3] The only products in this reaction are the tetrameric resorcinarenes and water. Of the four diastereoisomeric products that could theoretically form, only three have been identified in the reaction of aliphatic[4,5] aldehydes, and two in the reaction of aromatic[3,5] aldehydes with resorcinol. The more desirable and thermodynamically stable product, which possesses a bowl or cup-like shape (crown conformation) with all side chains positioned axially (all-*cis*), can be selectively obtained by increasing the proportion of alcohol in the solvent mixture and increasing the reaction temperature and time.[2,4] This has been attributed to several factors including selective precipitation of the all-*cis* isomer and conversion of the kinetically favoured diastereoisomer to the thermodynamically stable isomer *via* reversible protodealkylative macrocyclic ring opening.[2–4]

Lanthanide(III) triflates are mild and selective catalysts which have been utilised widely in carbon–carbon and carbon–heteroatom bond-forming reactions. Examples include Mukaiyama,[6] Friedel–Crafts,[7] esterification,[8] aromatic nitration[9] and Diels–Alder[10] reactions. In contrast to classical Lewis acids which often are required in stoichiometric quantities, lanthanide(III) triflates readily promote a range of reactions in catalytic quantities and in the presence of coordinating additives or solvents such as THF, DMSO, DMF, MeCN, and most remarkably, water.[6,9,11–13] This is consistent with a high ligand exchange rate,[14] a high coordination number[15] and the hydrolytically stable[16,17] ionic nature of lanthanide(III) triflates in which the triflate counterion is outer sphere. Moreover, the stability and solubility of these catalysts in water means that they can be readily recovered unchanged from the aqueous phase of reaction mixtures on work-up, and subsequently re-used.[8–10,12,13]

In only two examples have classical Lewis acids ($BF_3{\cdot}OEt_2$, $AlCl_3$ and $SnCl_4$) been used in the synthesis of resorcinarenes from resorcinol and aldehydes, albeit only for aromatic aldehyde-derived resorcinarenes.[18,19] Unfortunately, moderate to large quantities (50–200 mol%) of the Lewis acids were required to provide good yields of the products. From an environmental and safety standpoint, the sensitivity of these Lewis acids to water, which results in acidic and metal oxide by-products upon aqueous work-up, is a large drawback and the process is not 'atom economic'.[20] Moreover, in these reactions two diastereoisomers are produced, the relative amounts of which are, in contrast to the mineral acid-catalysed condensation, fixed. For this reason the often more desirable bowl-like (all-*cis*) diastereoisomer can only be obtained in moderate yield.

Herein, we wish to report the use of ytterbium(III) triflate nonahydrate $\{[Yb(H_2O)_9](OTf)_3\}$ as a catalyst in the preparation of resorcinarenes which is superior to previous Brønsted and Lewis acid-catalysed/promoted methods and overcomes the problems encountered with classical Lewis acids. We also describe some of our efforts to better understand the mechanism of lanthanide catalysis which has more general implications in synthetic organic chemistry.

Results and discussion

Synthesis

We have found that 8 mol% commercially available $Yb(OTf)_3$ nonahydrate catalysed the condensation of resorcinol with a range of aldehydes to afford the desired resorcinarenes **1**–**5** in 71–94% yield (Scheme 1). Given the difficulty in handling the highly hygroscopic anhydrous form of this salt, it was particularly pleasing that the hydrate was sufficiently active. These reactions were homogeneous when conducted in absolute EtOH, except for the reaction with benzaldehyde which became heterogeneous as the products precipitated from solution. Upon completion, the reaction mixtures were worked up by pouring into distilled water and the precipitated resorcinarenes collected. The reactions were readily performed on larger scales; indeed, approximately 10 g of resorcinarene **4** was obtained in quantitative yield using our conditions and we do not envisage problems with a further increase in scale. Micro- and spectroscopic analyses indicated that the crude cream coloured products were pure enough to be used without further purification. In fact the ^1H NMR spectra of the crude resorcinarene **4** indicated that it was not significantly less pure than that of the recrystallised material. Evaporation of the filtrate furnished the catalyst which could be re-used for subsequent reactions without a decrease in yield of the products (*vide infra*).

The ^1H and ^{13}C NMR spectra and microanalyses of the crude dried resorcinarenes **1**–**5** revealed that they were of good purity although they remained hydrated unless heated under high vacuum.[5] ^1H NMR spectroscopic analysis of resorcinarenes **2**–**5** showed that each set of aromatic (H_b and H_c) and benzylic hydrogens (H_a) were equivalent, indicating that the desired all-*cis* diastereoisomers had been produced. The ^1H NMR spec-

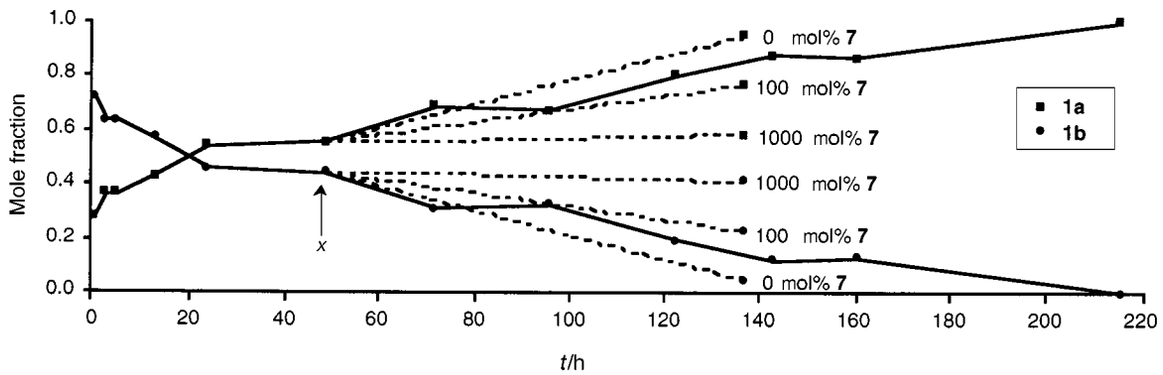
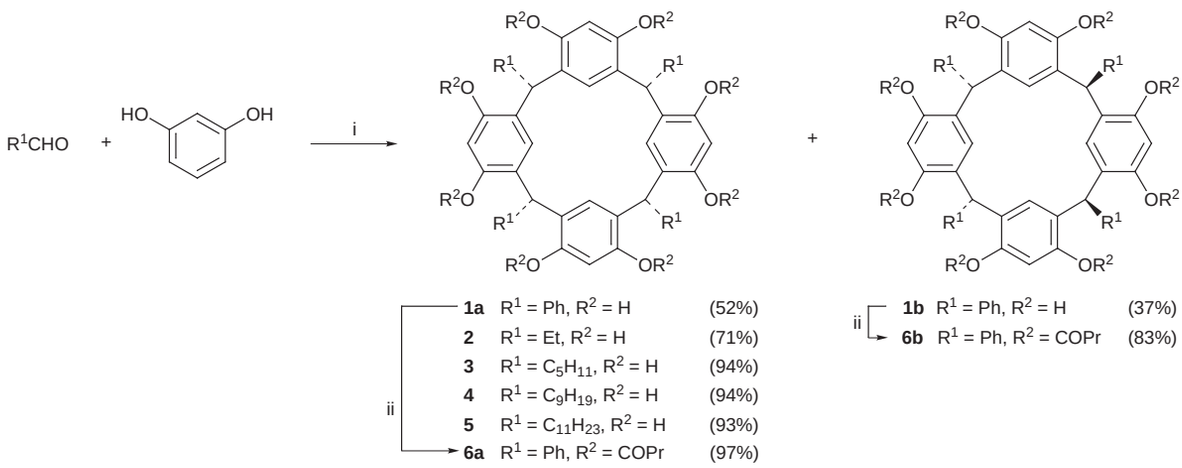
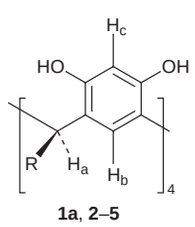


Fig. 1 Ratios of benzaldehyde-derived resorcinarene isomers **1a** and **1b** in the $[Yb(H_2O)_9](OTf)_3$-promoted isomerisation reaction and the effect of a hindered pyridine additive.



Scheme 1 *Reagents and conditions*: i, $[Yb(H_2O)_9](OTf)_3$, EtOH, reflux for 48 h; ii, $(PrCO)_2O$, pyridine, room temp., 45 h.



1a, **2–5**

trum of **2** was identical to that reported for the same product obtained from the hydrochloric acid-catalysed condensation reaction,[5] which has been shown[21] by X-ray crystallography to possess the all-*cis* configuration. Similarly, the ^1H and ^{13}C NMR spectra of resorcinarene **5**, prepared herein, was found to correlate well with data reported for the same resorcinarene prepared by hydrochloric acid-catalysed reaction, which was proposed to have all-*cis* configuration based on spectroscopic evidence,[5,21] and confirmed by X-ray crystallography.[22] From these facts we conclude that resorcinarenes **2**–**5** all possess the desired all-*cis* configuration. It is interesting to note that selective precipitation of the all-*cis* diastereoisomer was not a factor responsible for the diastereoselectivity observed under our reaction conditions.

We have shown previously[8,9] that $Yb(OTf)_3$ can be readily recovered following nitration and acetylation reactions and re-used for the same reactions three or more times without deterioration in catalytic activity. It was therefore expected that $[Yb(H_2O)_9](OTf)_3$ could be recycled in the synthesis of resorcinarenes. Indeed, the catalyst recovered from the syntheses of **3** and **4** was equally active in subsequent condensation reactions, as demonstrated in the multiple preparations of resorcinarenes **3** and **4** (Table 1). The resorcinarenes isolated after each cycle were of good and comparable purity, as judged by ^1H NMR spectroscopy. Although the IR spectrum of the catalyst recovered after three recycles (*i.e.* four uses) in the preparation of resorcinarene **4** was identical to that of authentic $Yb(OTf)_3$ hydrate, the catalyst from the preparation of **3** was slightly contaminated. The contaminant was removed in each cycle by extraction of the catalyst with distilled water and filtration. Thus, $[Yb(H_2O)_9](OTf)_3$ can be recycled without noticeable loss of activity in the preparation of resorcinarenes, as judged by the consistent purity and crude yields obtained.

Table 1 Recycling of $[Yb(H_2O)_9](OTf)_3$ in preparation of resorcinarenes **3** and **4**

Cycle	1	2	3	4
Yield **3** (%)	96	96	96	—
Recycled catalyst (%)	102	96	102[a]	—
Yield **4** (%)	94	91	93	95
Recycled catalyst (%)	96	89	88	93[b]

[a] The IR spectrum revealed that the catalyst was slightly contaminated. [b] The IR spectrum was identical to that of authentic $Yb(OTf)_3$ hydrate.

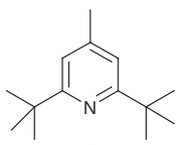
Lewis *vs.* Brønsted acidity

Reaction of benzaldehyde and resorcinol under our standard reaction conditions (48 h) gave, in contrast to that with the aliphatic aldehydes, the kinetically favoured diastereoisomer **1b** in addition to the expected, thermodynamically favoured all-*cis* diastereoisomer **1a** in a 0.7:1.0 ratio, respectively, in a 89% crude yield. The known crystalline octabutyrates **6a** and **6b**[3] (1.0:0.6 mixture, 91% yield) were obtained by acylation of octols **1a** and **1b** with butyric anhydride in the presence of pyridine.

Significantly, the **1a** and **1b** isomer distribution was time dependant (solid lines, Fig. 1) *beyond* completion of the reaction (*ca.* 48 h) indicating that isomerisation, *via* macrocyclic ring opening, had occurred. Indeed, given sufficient time

(216 h) the reaction mixture was found to be composed solely of the all-*cis* isomer **1a**. This is consistent with observations by Högberg[3] and others[5] for Brønsted acid-catalysis *and not consistent with Lewis acid catalysis*.[18,19] Further, it is difficult to envisage direct $Yb(OTf)_3$-promoted opening of the macrocyclic ring, necessary for the observed isomerisation, without formation of the Wheland intermediate *via* arene protonation since this implies the intermediacy of a ytterbium–arene bond.

The hindered base 2,6-di-*tert*-butyl-4-methylpyridine (**7**),



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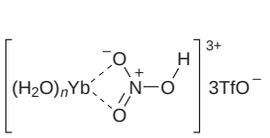
which should differentiate between Brønsted and Lewis acids,[23] was used to probe further the apparent Brønsted acidity of the resorcinarene–$Yb(OTf)_3$ system. In the control experiments it was found that a pre-prepared mixture of the isomers **1a** and **1b** did not isomerise when heated under reflux in EtOH for 166 h, but when a 0.54 : 0.46 mixture (marked with an *x* in Fig. 1) of isomers **1a** and **1b**, respectively, was stirred in EtOH under reflux in the presence of *ca.* 32 mol% $[Yb(H_2O)_9](OTf)_3$ for 88 h a 0.95 : 0.05 mixture resulted (dotted lines, Fig. 1). These conditions and the amounts of reagents were essentially identical to those used in the synthetic reaction. When another portion of the same **1a**/**1b** isomer mixture was stirred under reflux in the presence of *ca.* 32 mol% $[Yb(H_2O)_9](OTf)_3$ and *ca.* 100 mol% hindered pyridine **7** for 88 h it had isomerised to a 0.77 : 0.23 ratio of **1a** and **1b**, respectively. When the reaction was repeated with *ca.* 1000 mol% hindered pyridine **7** a 0.58 : 0.42 mixture of isomers **1a** and **1b**, respectively, was obtained, showing almost complete inhibition of isomerisation. The latter two results clearly demonstrate that hindered pyridine **7** retards the isomerisation of isomer **1b** to **1a**, indicating that the isomerisation process is indeed Brønsted acid promoted. That the resorcinarene mixture used in these reactions isomerised under the standard reaction conditions and had been shown by ^{1}H NMR spectroscopy to be free of resorcinol and benzoic acid indicates that these are not the proton source.

Lewis assisted Brønsted acidity

In recent research conducted in our laboratories we have observed an interesting variation in the role of metal triflates [lanthanide(III), Sc^{III}, Hf^{IV} and Zr^{IV}] in reactions involving acidic reactants. From our investigations into metal triflate-catalysed nitrations with HNO_3[9,24–27] and acetylations with AcOH,[8] it appears that these Lewis acids primarily bind the acidic ligand to form chelates **8** or **9** which are stronger Brønsted acids than nitric or acetic acids, respectively. We speculate that these chelates undergo equilibrium loss of triflic acid, with concomitant replacement of the outer sphere triflate anion with an inner sphere nitrate or acetate anion. The liberated triflic acid, or perhaps the enhanced Brønsted acid intermediates themselves (*viz.* **8** or **9**), are probably responsible for promotion of the respective reactions and not the Lewis acid itself directly. Ultimately these reactions are Brønsted acid-catalysed and the isomer distribution in the electrophilic aromatic nitration was consistent with this. Although Ciufolini *et al.*[28,29] have proposed a related model for the $Yb(fod)_3$–HOAc system in an ene reaction (they do not, however, invoke the loss of the counterion), no-one else to the best of our knowledge has recognised this important Lewis assisted Brønsted acidity[30] of metal triflate–acidic reagent systems. Recently it was reported that benzoic acid greatly enhances the efficiency and reaction rate of $Yb(OTf)_3$ catalysed allylation of aldehydes.[31] The authors suggested that the benzoic acid destroys a ytterbium alkoxide complex that otherwise ties up the catalyst. We believe instead, however, that the benzoic acid becomes bound to the metal centre to form an enhanced Brønsted acid or triflic acid which directly promotes the reaction.



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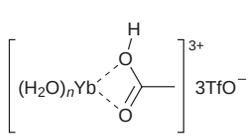

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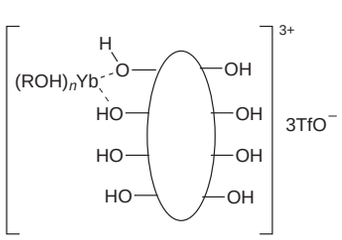


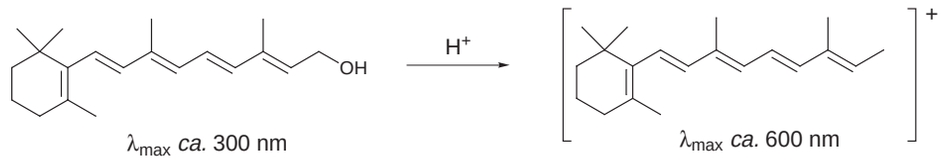
12 R = H or Et
(Further chelation possible)

Recently it has been shown that low levels of Brønsted acidity in zeolites can be detected using retinol (**10**) or its acetate.[32] Elimination of water from protonated retinol results in the formation of a short lived, but highly coloured, blue carbocation **11**. We have used this colour change to probe the Lewis assisted Brønsted acidity of $Yb(OTf)_3$–Brønsted acid systems (Table 2). Although AcOH alone (entry 1) was insufficiently acidic to promote formation of **11**, AcOH in the presence of hydrated or anhydrous $Yb(OTf)_3$ gave rise to an intense but short-lived blue colouration (entry 3). In the control experiment (entry 2) $[Yb(H_2O)_9](OTf)_3$ alone did not promote detectable formation of **11**. Benzoic acid–$[Yb(H_2O)_9](OTf)_3$ mixtures also gave a positive result (entry 4). Tellingly, triflic acid (entry 5) also promoted the colour change. Although resorcinol (entry 6) or resorcinarene **5** (entry 7) alone were not acidic enough to promote the colour change, the latter did in conjunction with $[Yb(H_2O)_9](OTf)_3$ (entry 8). This change, however, was more persistent and of a more green colouration than usual and we suspect that a secondary reaction occurs involving cation **11** and the resorcinarene. Interestingly, $MeNO_2$, which is often used as a solvent in conjunction with metal triflates, produced a positive colour change (entry 9) in the presence of the lanthanide salt and it is therefore possible that reactions conducted with metal triflates in this solvent are Brønsted acid catalysed.

The retinol experiments demonstrate that the interaction of $[Yb(H_2O)_9](OTf)_3$ and resorcinarene **5** result in the formation of a strong Brønsted acid, fully consistent with the observed isomerisation process described above. Thus, in the synthesis of resorcinarenes we propose that the resorcinarene, once formed, becomes (reversibly) bound in a polydentate fashion to $Yb(OTf)_3$ generating a complex (*e.g.* **12**) which liberates triflic acid, or is itself acidic enough to promote protodealkylation and hence isomerisation. Murayama and Aoki[33] recently reported that crystallisation of resorcinarene **2** from aqueous EtOH in the presence of tetraethylammonium perchlorate furnished a resorcinarene head-head dimer encapsulating a tetraethylammonium ion. Most interestingly, no perchlorate anion was associated with the structure, indicating that one of the 16 hydroxy groups of the two resorcinarene units was deprotonated. Furthermore, the solution became increasingly acidic as crystallisation occurred (start pH = 5.0; end pH = 3.7)[34] indicating that perchloric acid must have been formed during the crystallisation; this is analogous to our speculation that triflic acid is liberated under our reaction conditions.

Although the work presented above clearly demonstrates the Brønsted acid nature of the isomerisation of resorcinarenes, and that a resorcinarene–ytterbium complex probably acts as the proton source, it is not clear how the initial resorcinol–

Table 2 Probing the Lewis and Brønsted acidity of $Yb(OTf)_3$–Brønsted acid systems



λ_{max} *ca.* 300 nm — **10**

λ_{max} *ca.* 600 nm — **11**

Entry	Solvent	Solute	Additive	Colour change [a]
1	AcOH	—	—	negative
2	THF	$[Yb(H_2O)_9](OTf)_3$	—	negative
3	THF	$[Yb(H_2O)_n](OTf)_3$ [b]	AcOH	positive
4	THF	$[Yb(H_2O)_9](OTf)_3$	$PhCO_2H$	positive
5	THF	TfOH	—	positive
6	THF	$[Yb(H_2O)_9](OTf)_3$	resorcinol	negative
7	THF	—	**5**	negative
8	THF	$[Yb(H_2O)_9](OTf)_3$	**5**	positive [c]
9	$MeNO_2$	$[Yb(H_2O)_9](OTf)_3$	—	positive

[a] The blue colouration persisted for no more than a few seconds at most. [b] Hydrated ($n = 9$) and anhydrous ($n = 0$) ytterbium(III) triflates were used. [c] An intense green–blue colour persisted for *ca.* 10 s which changed to a persistent green colour.

aldehyde bond formation is initiated. It is probable that the Lewis acidic nature of the lanthanide does indeed activate the aldehyde to attack by resorcinol. However, once quantities of resorcinarenes are present in the reaction mixture it seems likely that the strong Brønsted acid catalysis dominates.

Conclusion

We have presented efficient and selective reaction conditions under which resorcinarenes can be prepared in good to high yield. The lanthanide catalyst was easily recovered and recycled providing an atom economic procedure. Moreover, evidence has been presented that the primary role of the lanthanide catalyst is to enormously accentuate the Brønsted acidity of protonated chelating conjugate bases in the reaction *milieu* (*viz.* AcOH, $MeNO_2$ and resorcinarenes in this work) presumably by binding the respective polydentate conjugate base *via* a Lewis acid–base interaction with concomitant loss of a proton. Essentially this equates to the liberation of free triflic acid. We believe that these observations have significant implications for the mechanism of catalysis by lanthanide(III) triflate salts in the presence of putative proton donors and might affect the choice of solvents used in reactions (*e.g.* $MeNO_2$).

Experimental

Materials and methods

Unless otherwise stated, all chemicals were purchased from Aldrich. All reactions were carried out under a dry argon atmosphere. MeOH, glacial AcOH and absolute EtOH were AnalaR grade solvents from BDH and were used undistilled. MeOH was stored over 3 Å molecular sieves. THF was distilled from potassium metal and Ph_2CO under nitrogen. Benzaldehyde, hexanal, decanal and dodecanal were double distilled under vacuum prior to use. Resorcinol was recrystallised from toluene. Retinol was used as purchased. Ytterbium(III) triflate that had been exposed to the atmosphere was found to be a nonahydrate by thermal gravimetric analysis and was used in these reactions. The anhydrous salt was obtained by heating the nonahydrate under vacuum (0.1 mmHg) for 48 h at 190 °C. Melting points are uncorrected and were determined using a Reichert-Jung Thermo Galen Kofler block. Microanalyses were carried out by the University of Warwick Analytical Service and the University of North London. IR spectra were recorded on a Mattson 5000 FTIR spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker DRX-300, DRX-400 and AM-500 NMR spectrometers. Chemical shifts were measured in ppm relative to internal $CHCl_3$, DMSO or acetone and J values are given in Hz. FAB (*m*-nitrobenzyl alcohol matrix, Cs^+ ion beam) and ESI Mass spectra were recorded at Imperial College using VG AutoSpec and VG platform spectrometers, respectively.

General procedure for preparation of resorcinarenes 1–5

To a solution of resorcinol (233 mg, 2.12 mmol) and the requisite aldehyde (2.12 mmol) in absolute EtOH (3.6 mL) was added $[Yb(H_2O)_9](OTf)_3$ (132 mg, 0.17 mmol). The solution was stirred under reflux for 48 h. The mixture was allowed to cool and was poured into distilled water (20 mL) and the precipitated resorcinarene was washed three times with distilled water (10 mL each), filtered and dried to constant weight *in vacuo*. All spectral data were consistent with those reported in the literature. Refiltration of the filtrate, followed by evaporation *in vacuo*, provided the impure catalyst for the lower molecular weight aldehydes but pure catalyst for the heavier aldehydes. The purity of the catalyst was improved by dissolution of the catalyst in distilled water, followed by filtration and evaporation.

2,8,14,20-Tetraphenylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol 1.[5] The title compound (1.0 : 0.7 mixture of diastereoisomers **1a** and **1b**, 372 mg, 89%) was obtained as a tan coloured solid; δ_C(100 MHz; acetone-d_6) 41.4, 42.1, 120.4, 120.6, 121.0, 124.4, 124.5, 126.9, 127.1, 128.6, 128.9, 129.1, 131.8, 144.3, 145.7, 152.5 and 152.7. When the reaction was conducted for 216 h pure **1a** (387 mg, 92%) was obtained [Found (dried at 100 °C for 24 h at 0.2 mmHg): C, 78.8; H, 5.2. Calc. for $C_{52}H_{40}O_8$: C, 78.8; H 5.1%]; ν_{max}(diffuse reflectance)/cm^{-1} 3500–3000, 1613, 1505 and 1494.

2,8,14,20-Tetraethylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol 2.[5] The title compound (227 mg, 71%) was obtained as a cream coloured solid [Found (dried at 100 °C for 24 h at 0.2 mmHg): C, 71.75; H, 6.6. Calc. for $C_{36}H_{40}O_8$: C, 72.0; H 6.7%]; ν_{max}(diffuse reflectance)/cm^{-1} 3500–3000, 2963, 2934, 2873, 1619 and 1502; δ_C(100 MHz; acetone-d_6) 13.1, 27.1, 36.5, 103.6, 125.1, 125.4 and 152.7.

2,8,14,20-Tetrapentylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol 3.[5] The title compound (576 mg,

94%) was obtained as a cream coloured solid [Found (dried at 100 °C for 24 h at 0.2 mmHg): C, 75.1; H, 8.5. Calc. for $C_{48}H_{64}O_8$: C, 75.0; H 8.4%]; ν_{max}(diffuse reflectance)/cm^{-1} 3500–3000, 2955, 2930, 2861, 1619 and 1500; δ_C(100 MHz; acetone-d_6) 14.4, 23.4, 28.7, 32.7, 34.2, 34.3, 103.6, 125.2, 125.4 and 152.6.

2,8,14,20-Tetranonylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol 4. The title compound (496 mg, 94%) was obtained as a cream coloured solid; mp 312–315 °C (from MeOH) (Found: C, 75.2; H, 9.8. Calc. for $C_{64}H_{96}O_8 \cdot 1.5H_2O$: C, 75.3; H 9.8%); ν_{max}(diffuse reflectance)/cm^{-1} 3500–3000, 2926, 2853, 1616 and 1504; δ_H(400 MHz; $CDCl_3$) 0.88 (12 H, t, *J* 6.60, CH_3), 1.27 (48 H, s, CH_2), 1.38 (8 H, s, CH_2), 2.20 (8 H, distorted m, CH_2CHAr_2), 4.30 (4 H, distorted t, *J* 7.3, H_a), 6.11 (4 H, s, H_c), 7.20 (4 H, s, H_b), 9.30 (4 H, m, ArOH) and 9.61 (4 H, m, ArOH); δ_C(100 MHz; $CDCl_3$) 14.1, 22.7, 28.0, 29.3, 29.57, 29.62, 29.7, 32.0, 33.1, 33.2, 102.8, 123.8, 124.8, 150.3 and 150.5; *m*/*z* (FAB$^+$) 993 (M$^+$, 3%), 865 (3), 137 (60), 123 (100), 69 (53) and 55 (77).

2,8,14,20-Tetraundecylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-4,6,10,12,16,18,22,24-octol 5.[5] The title compound was obtained as a cream coloured solid (545 mg, 93%); mp 295–300 °C (from MeOH) (lit.,[4] 300–301 °C) [Found (dried at 100 °C for 24 h at 0.2 mmHg): C, 78.0; H, 10.2. Calc. for $C_{72}H_{112}O_8$: C, 78.2; H 10.2%].

Recycling of Yb(OTf)$_3$ in the preparation of resorcinarenes 3 and 4

A solution of resorcinol (233 mg, 2.12 mmol) and hexanal or decanal (2.12 mmol) in absolute EtOH (3.6 mL) was stirred under reflux in the presence of [Yb(H$_2$O)$_9$](OTf)$_3$ (132 mg, 0.17 mmol) for 48 h. The reactions were worked up as described above. In the case of resorcinarene **3**, the recovered catalyst was extracted with distilled water (5 mL), filtered and evaporated. The recovered catalysts were then re-used in subsequent runs.

4,6,10,12,16,18,22,24-Octabutyroxy-2,8,14,20-tetraphenylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene 6[3]

A mixture of resorcinarene **1** isomers (362 mg, 0.46 mmol) and butyric anhydride (1230 μL, 7.52 mmol) in pyridine (5 mL) was stirred at room temperature for 45 h. The volatile components were removed by distillation under reduced pressure (*ca.* 0.4 mmHg) giving a brown solid. This was triturated with cold MeOH (6 mL), the solid was ground into a fine powder, triturated with cold MeOH (2 mL) and dried *in vacuo* (568 mg, 91%). The product was found to be a 1.0:0.6 mixture of diastereoisomers **6a** and **6b**, respectively; δ_C(100 MHz; $CDCl_3$) 13.5, 13.7, 18.00, 18.02, 18.2, 35.7, 35.8, 44.4, 44.8, 116.3, 116.6, 117.0, 117.3, 126.39, 126.44, 128.1, 128.5 (br), 128.8, 129.0, 129.7, 130.9, 131.5, 131.9, 132.0, 132.1, 132.8, 139.0, 140.6, 146.6, 146.9, 147.0, 147.2, 170.7, 170.8, 171.1 and 171.2.

4,6,10,12,16,18,22,24-Octabutyroxy-2,8,14,20-tetraphenylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene 6a[3]

A solution of the resorcinarene **1a** (378 mg, 0.48 mmol) and butyric anhydride (1297 μL, 7.93 mmol) in pyridine (5 mL) was stirred at room temperature for 48 h. The volatile components were removed by distillation under reduced pressure (*ca.* 0.3 mmHg) to give a brown solid. This was triturated twice with cold MeOH (4 mL each) to furnish crystalline **6a** (494 mg, 75%); mp 248–250 °C (from EtOH) (lit.,[3] 251–252 °C).

Time dependence of diastereoisomer distribution in the preparation of resorcinarenes 1a and 1b

Solutions of resorcinol (233 mg, 2.12 mmol) and benzaldehyde (216 μL, 2.12 mmol) in absolute EtOH (3.6 mL) were stirred under reflux in the presence of [Yb(H$_2$O)$_9$](OTf)$_3$ (132 mg, 0.17 mmol) for differing amounts of time. The product mixtures were treated as described above in the preparation of **1**. The ratio of diastereoisomers **1b** and **1a** was determined by ^{1}H NMR spectroscopy (300 MHz; DMSO-d_6) of the mixtures by integration of the signal at δ 5.62 (4 × H$_a$ of **1a**) *versus* the two overlapping signals at δ 5.54 (2 × H$_c$ of **1b**) and 5.52 (4 × H$_a$ of **1b**).

Isomerisation of the 1a and 1b mixture with [Yb(H$_2$O)$_9$](OTf)$_3$ in the presence of various amounts of hindered pyridine 7

A solution of the crude resorcinarene mixture obtained from 48.5 h reaction in the above experiment (100 mg, 0.13 mmol) in absolute EtOH (1 mL) was stirred under reflux in the presence of [Yb(H$_2$O)$_9$](OTf)$_3$ (31 mg, 0.04 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (**7**, run 1: 0 mol; run 2: 27 mg, 0.13 mmol; run 3: 271 mg, 1.32 mmol) for 88 h. The product mixtures were poured into distilled water (5 mL) and filtered under vacuum. The filtrates were re-filtered through the collected solids and were dried *in vacuo* for 1 day providing the resorcinarenes **1a** and **1b** (run 1: 87 mg, 0.948:0.052 mixture; run 2: 89 mg, 0.769:0.231 mixture; run 3: 96 mg, 0.584:0.416 mixture).

Detection of Brønsted acidity of Yb(OTf)$_3$–Brønsted acid systems

The colour tests were conducted in 2 mL vials at room temperature. Following addition of the solute (0.01 mmol [Yb(H$_2$O)$_9$](OTf)$_3$ or Yb(OTf)$_3$, or 0.05 mmol TfOH) to THF (200 μL) and the additive (200 μL AcOH, 0.04 mmol resorcinol, 0.01 mmol resorcinarene **5** or 2.6 mmol benzoic acid) was added, a THF solution of retinol (**10**) (0.01 M, 200 μL) was added. Any colour change was formed instantaneously and persisted for no more than a few seconds. When MeNO$_2$ (1 mmol) was tested as an additive a weak and transient blue colour was observed. An intense blue colour was observed when [Yb(H$_2$O)$_9$](OTf)$_3$ was tested in MeNO$_2$ (200 μL).

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