

Synthesis of Calixfuran Macrocycles and Evidence for Gas-phase Ammonium Ion Complexation

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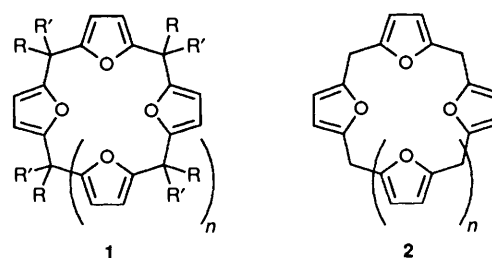
Furan and 2-hydroxymethylfuran reacted under Lewis acidic conditions to yield oligomeric furylmethane compounds **5** and **6**. Difurylmethane **5** was also obtained *via* the reaction of 2-furyllithium with bromochloromethane or reaction with 2-furaldehyde, followed by *in situ* reduction of the resulting lithium alkoxide with sodium boranuide-trifluoroacetic acid mixture. The trimeric furan compound **6a** could also be prepared from furyllithium by a similar route. Oligomers **5** and **6** were utilised for a subsequent Lewis acid-catalysed cyclisation to afford calixfurans, *i.e.* cyclic tetramer **2a**, and small quantities of the cyclic pentamer **2b**, hexamer **2c** and octamer **2e**. Traces of cyclic heptamer **2d** could also be detected under certain conditions. Chemical ionisation mass spectrometry using ammonia gas demonstrates that the calixfurans and their acyclic precursors are capable of chelating hydrogen and ammonium ions in the gas phase.

Since the pioneering work of Ruzicka¹ involving the studies of large-ring hydrocarbons, ketones and lactones, macrocyclic chemistry has become an area of intense research. Macrocyclic compounds have diverse physical and chemical properties which have prompted investigations ranging from the development of new synthetic methodologies for the synthesis of stereochemically complex macrolide antibiotics;² the study of molecular complexation of neutral guests by cyclodextrins,³ polycyclophanes⁴ and calixarenes;⁵ and to the development of ion recognition and binding selectivity in crown ethers, cryptands⁶ and lately calixarenes.⁷ The chemical and biological importance of macrocyclic compounds based on polyethers is derived from their selectivity in the complexing of various metal cations.⁸

Calixarenes⁷ derived from phenol derivatives have become important materials for a wide range of synthetic applications, from molecular scaffolds for building artificial enzymes to their use in studying basic molecular interactions.^{7,9} However, the chemistry of the related furan-containing macrocycles or calixfurans has received little attention.¹⁰ The reason for this is partly due to the problem of ready accessibility of such compounds, and to date only structures typified by the cyclic compounds of the type **1**, **2a**, **3** and **4** have been reported.¹¹⁻¹⁴

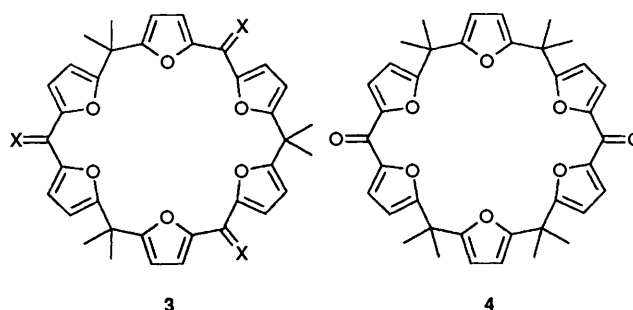
The simplest of all these calixfuran compounds, *i.e.* compound **2a**, has been reported by several groups, but yields vary from 0.5–1.0%.¹² The lack of efficient access to such compounds, coupled with the fact that the furan rings in structures of type **1** can be reduced¹³ or ring opened¹⁵ to yield efficient ionophoric compounds attracted our attention. The main problem with the preparation of unsubstituted macrocycles of type **2** is probably in large part due to their chemical reactivity. It has been reported that the addition of metal salts such as lithium perchlorate to the reaction mixture when preparing macrocycles of type **1** leads to increased yields of macrocycles of type **1**, suggesting that a template effect may be operating.¹⁶ However, the acidity of the reaction mixtures used for the preparation of the macrocycles has also been proposed as an alternative explanation for the observed increased yields of the macrocycles **1**.^{11c,17} Other studies, involving the extraction of alkali metal and ammonium cations from an aqueous to an organic phase, have suggested that the oxygen atoms of the furan rings act as efficient electron donors when the furan rings are reduced.^{11c,13}

We have recently reported¹⁸ an efficient synthesis of calix[4]furan **2a** and the first reported syntheses (albeit in low



1
a; $n = 1$, $R = R' = \text{Me}$
b; $n = 2$, $R = R' = \text{Me}$
c; $n = 3$, $R = R' = \text{Me}$
d; $n = 1$, $R = \text{H}$, $R' = \text{alkyl}$
e; $n = 1$, $R = R' = \text{alkyl}$

2
a; $n = 1$
b; $n = 2$
c; $n = 3$
d; $n = 4$
e; $n = 5$



3
a; $X = \text{O}$
b; $X = \text{H}_2$

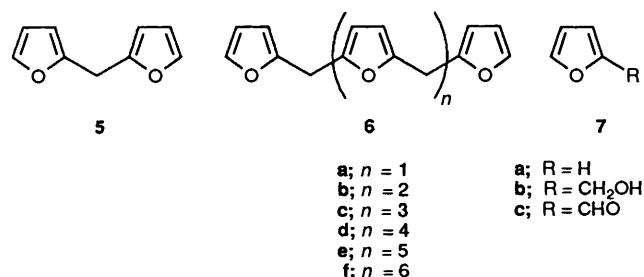
yields) of the related larger ring oligomers, *i.e.* calixfurans **2b**, **2c** and **2e**. In this paper we report on the full details of our endeavours and report evidence for the first existence of calixfuran **2d** in trace quantities in certain reaction mixtures. We also report our unsuccessful attempts to increase the yields of the calixfurans *via* template assistance and contrast these results with mass spectrometric studies using chemical ionisation (CI) methods on both the furan-based linear compounds and the furan-based macrocyclic compounds.

The starting point for the preparation of calixfurans **2** involved the cyclisation of non-cyclic oligomers **5** and **6**, since these materials should act as intermediates for cyclisation to their cyclic counterparts **2**, and were obtainable in reasonable yields from readily available starting materials. This approach

Table 1

Entry	Reactants (molar ratio)	Catalyst	Solvent	Temp. (T/°C)	Yields (%) ^a						
					5	6a	6b	6c	6d	6e	6f
1	7b (4)	BF ₃ ·Et ₂ O (1)	CH ₂ Cl ₂	0–room temp.	~ 5% yield of a mixture + 1.3% 2a						
2	7a (2), 7b (1)	BF ₃ ·Et ₂ O (cat.)	CH ₂ Cl ₂	–78–room temp.	16	11	1	2	~ 1	~ 1	0
3	7a (2), 7b (1)	BF ₃ ·Et ₂ O (cat.)	none	0–room temp.	16	11	1	2	~ 1	~ 1	0
4	7a (10), 7b (1)	BF ₃ ·Et ₂ O (cat.)	CH ₂ Cl ₂	0–room temp.	28	20	4	2	0	0	0
5	7a (2), 7b (1)	conc. HCl (cat.)	CH ₂ Cl ₂	0–room temp.	0.4	0.5	0.6	0.6	< 0.1	0	0

^a All yields are unoptimised and after purification.

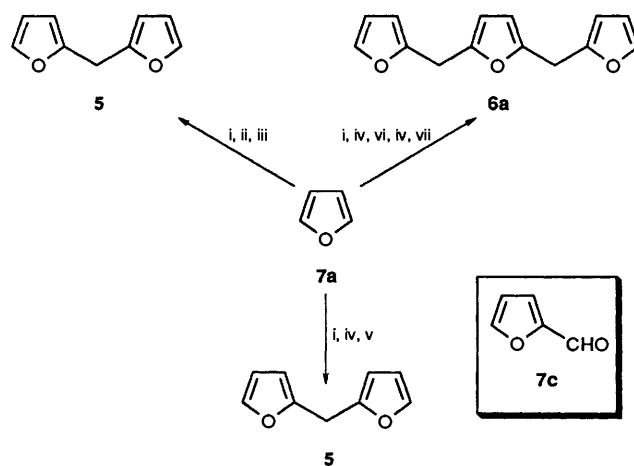


allowed us to test whether it was possible to template cyclisation reactions of oligomeric furan-containing compounds, using the furan oxygens to chelate either metal ions or ammonium salts.

For the preparation of the compounds **5** and **6**, literature procedures were employed initially, *i.e.* using the self-condensation of hydroxymethylfuran **7b**, or furan **7a** with formaldehyde in the presence of a protic acid.^{12d,19} These procedures tend to form large quantities of resinous material and various alkoxyethyl ether derivatives. In order to minimise the production of these kinds of by-products, we examined the condensation of furan **7a** with hydroxymethylfuran **7b** under protic acidic conditions.¹⁸ However, these reactions also led to poor overall conversions into the oligomers **5** and **6**, and caused considerable charring of the reaction mixture and production of resinous material. It was therefore important to develop improved reaction conditions for the preparation of the linear oligomers **5** and **6** that would result in improved overall conversions and simultaneously reduce charring and resinification. It was also of interest to see if some element of selectivity could be introduced in terms of which of the linear oligomers **5** and **6** were produced as the major products by changing the reaction conditions. To this end, Lewis acid-catalysed, non-protic conditions were initially examined with the expectation that they would be more compatible with the reactive furan moiety, *i.e.* by avoiding either hydrolysis or alcoholysis of the furan rings. The reaction conditions examined which gave highest yields of linear oligomers **5** and **6** from a series of reactions involving different Lewis acids, solvents and temperatures are outlined in Table 1.

Since these furan-based linear compounds **5** and **6** seemed to be unstable under acidic conditions, alternative synthetic routes were also attempted. These involved the reaction of 2-furyllithium with bromochloromethane in the presence of a copper(I) salt and reaction of furyllithium with 2-furaldehyde followed by *in situ* reduction of the resulting alcohol to afford difurylmethane **5** (Scheme 1). Trimer **6a** was also prepared by a very similar route, *i.e.* by the reaction of furyllithium with 2-furaldehyde, followed by redepotiation of one of the furan rings with *tert*-butyllithium and a second reaction with 2-furaldehyde. The resulting bis-alkoxide was then reduced *in situ* using sodium boranuide (borohydride) under acidic conditions to afford trimer **6a**.

The highest yield (64%) of difurylmethane **5** was obtained under basic reaction conditions, *i.e.* from the reaction of 2-furyllithium and 2-furaldehyde **7c**, followed by *in situ* sodium boranuide and trifluoroacetic acid (TFA)-mediated reduction



Scheme 1 Reagents and conditions: i, Bu^tLi, THF, –78 °C, 1 h; ii, CuI, –78→0 °C, 2.5 h; iii, ClCH₂Br, –78 °C→reflux, 2 h (14%); iv, **7c**, –78 °C, 1 h; v, NaBH₄, TFA, 0 °C, 1 h (64%); vi, Bu^tLi, –78 °C→room temp.; vii, NaBH₄, TFA, 0 °C, 2 h (22%).

of the intermediate difurylmethanol (Scheme 1). This procedure was an adaptation of a successful method used for the preparation of diarylmethanes (from the respective diarylmethanols)^{20,21} and was particularly efficient due to the elimination of unwanted side products. However, the low yield obtained for compound **6a** under these conditions (22%) was due to the insolubility of the intermediate difurylmethyl lithium alkoxide (Scheme 1). Even when the reaction mixture was diluted (tenfold) the insolubility of the intermediate still made the reaction inconvenient to use for a large-scale synthesis of trimer **6a** and would therefore be even more inconvenient to use for the other linear compounds **6b–f**.

Overall, the most convenient method for preparing precursors **5** and **6a** on large scales was using the boron trifluoride–diethyl ether, dichloromethane, furan and hydroxymethylfuran conditions (entry 4, Table 1) with a large excess of furan and using a catalytic amount of the Lewis acid. The large excess of furan in this reaction is presumably essential for chain termination of the polymerised hydroxymethylfuran, preventing the build-up of long-chain resins. Under these conditions there was minimal charring of the reaction mixture and very little resinous material produced. The added benefit of the Lewis acid-catalysed reaction conditions in general was that sufficient quantities of the other oligomers **6b–6e** could also be isolated, allowing separate cyclisation reactions to be carried out. Overall yields in these reactions were not spectacular (54% maximum), but taking into account the sensitivity of the products and the convenience of the reaction they were acceptable.

Having obtained a series of the different oligomers **5** and **6**, we examined cyclisation of these compounds to the calixfurans **2** under conditions that minimised decomposition of the furan derivatives. We therefore examined a range of different acidic

Table 2^a

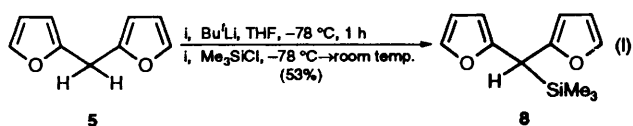
Entry	Reactants (molar ratio)	Catalyst	Solvent	Yields (%)						
				6b	6c	6d	2a	2b	2c	2e
1	5 (1), 37% CH ₂ O (4)	conc. HCl	EtOH	15	0	24	0	0	0	0
2	5 (2), H ₂ C(OMe) ₂ (2)	BF ₃ ·Et ₂ O (4)	CH ₂ Cl ₂	<1	0	<1	6	0	<1	0 ^b
3	6a (1), H ₂ C(OMe) ₂ (1)	BF ₃ ·Et ₂ O (2)	CH ₂ Cl ₂	0	0	trace ^c	0	0	0	0
4	6a (2), H ₂ C(OMe) ₂ (9)	BF ₃ ·Et ₂ O (6)	CH ₂ Cl ₂	0	0	1.3	0	0	0.4	0
5	6b (1), H ₂ C(OMe) ₂ (1)	HCl (g) (sat.)	C ₆ H ₆	0	0	0	0	0	0	0 ^d
6	6b (1), H ₂ C(OMe) ₂ (1)	BF ₃ ·Et ₂ O (2)	CH ₂ Cl ₂	10	0	0	34	0	0	2
7	6c (1), H ₂ C(OMe) ₂ (141)	HCl (g) (sat.)	C ₆ H ₆	0	0	0	0	0	0	0 ^d
8	6c (1), H ₂ C(OMe) ₂ (1)	BF ₃ ·Et ₂ O (2)	CH ₂ Cl ₂	0	3	0	0	3–5	0	0
9	6d (1), H ₂ C(OMe) ₂ (1)	BF ₃ ·Et ₂ O (2)	CH ₂ Cl ₂	0	0	~100	0	0	0	0
10	6d (1), H ₂ C(OMe) ₂ (24)	BF ₃ ·Et ₂ O (10)	CH ₂ Cl ₂	0	0	0	0	0	1	0

^a All experiments conducted at between 0 °C and room temp. ^b Small quantities of a mixture of compounds of **6b**, **6d** and **2c** were isolated as an inseparable mixture. ^c The linear hexamer **6d** was observed by TLC and NMR (present in small quantities) after the first few hours of reaction. However, no cyclic hexamer **2c** was isolated and complete decomposition of all materials occurred after 4 days. ^d Complete decomposition of starting material occurred.

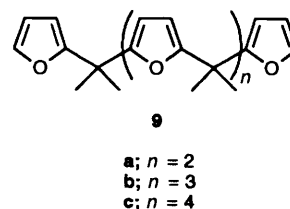
reaction conditions, both protic and Lewis acid-catalysed, for the cyclisation of the oligomers with either formaldehyde or a suitable formaldehyde derivative. The results of this search for suitable cyclisation reaction conditions are summarised in Table 2.

As can be seen from the results it was not possible to cyclise difurylmethane **5** to the calix[4]furan **2a** under protic conditions with formaldehyde (entry 1, Table 2). However, when dimethoxymethane was used (entry 2, Table 2), in the presence of excess of boron trifluoride–diethyl ether in dichloromethane, the calix[4]furan **2a** was obtained in 6% yield together with a trace of calix[6]furan **2c**. An improved preparation of calix[4]furan **2a** was achieved when cyclisation of the linear tetramer **6b** was attempted (entry 6, Table 2). In fact, ¹H NMR analysis of the crude reaction mixture showed that the reaction was essentially quantitative. However, all the yields quoted in Table 2 are after silica gel chromatography, which caused considerable product decomposition and which was not significantly reduced by using alumina. It is interesting to note that the worst reaction conditions tried involved treatment of the linear compounds with dry hydrogen chloride gas in benzene solution.¹³ These conditions have been used to cyclise alkylated polyfurylmethyl chains; however, the much more reactive and unsubstituted compounds **6b** and **6c** rapidly decompose under these reaction conditions (entries 5 and 7, Table 2). The calix[5]furan **2b** could only be obtained by cyclisation of the linear pentamer **6c**, again using the milder conditions (entry 8, Table 2), and calix[8]furan **2e** was obtained in highest yield (2%), by *in situ* dimerisation of the linear tetramer **6b**, followed by cyclisation (entry 6, Table 2).

As an alternative to the Lewis acid-catalysed cyclisation reactions reported in Table 2, we also examined whether it was possible to deprotonate the linear oligomers **5** and **6** on each of the terminal furan rings in the 2-position selectively. This type of procedure has been employed successfully for cyclisation of substituted furylmethane derivatives to compounds **3** and **4**.¹⁴ However, not surprisingly, we were unable to deprotonate compound **5** on the furan ring *via* lithiation with *tert*-butyllithium because of clean deprotonation at the more reactive furylmethane moiety affording the trimethylsilylated derivative **8** after quenching with chlorotrimethylsilane [eqn. (1)].



It is intriguing to note that the linear tetramer **6b** cyclised reasonably readily (Table 2); however, when the chain length was increased, *i.e.* to the linear pentamer, hexamer, heptamer and octamer (**6c**, **6d**, **6e** and **6f** respectively), the yield of cyclised products dropped dramatically to the point where cyclisation was virtually non-existent (*i.e.* for conversion of **6d** into **2c**). These results strongly suggest that cyclisation of the precursor to compound **2a** is possible or even likely on conformational grounds, but, as the chain length becomes longer, cyclisation becomes less likely probably due to increased flexibility of the chain. This interesting result contrasts markedly with results reported¹³ for the more substituted counterparts of the calixfurans. For example, oligomers **9** have been readily cyclised; the efficiency of the reactions seems to increase with increasing chain length, and the reaction occurs under reaction conditions which destroy the unsubstituted oligomers **6b–6d**.^{*} This may be explained by the increased stability of oligomers **9** to hydrolysis or alcoholysis and the existence of the *geminal* dimethyl groups which may be assisting cyclisation.²²



For the preparation calix[7]furan **2d**, we attempted to cyclise the linear heptamer **6e** under the standard conditions of dimethoxymethane and boron trifluoride–diethyl ether. Unfortunately, this reaction failed to provide any of the required products and the starting material was completely decomposed. By contrast, reaction of the linear trimer **6a** and the linear tetramer **6b** resulted only in the production of the cyclic tetramer **2a**, together with some decomposition of the starting materials. However, reaction of difurylmethane **5** and the linear trimer **6a** with dimethoxymethane and boron trifluoride–diethyl ether yielded a mixture of products, including calixfurans **2a**, **2b** and **2c**, together with a mixture of the linear oligomers. Examination of the crude reaction mixture by ¹H NMR spectroscopy and MS revealed the presence of trace quantities of the cyclic heptamer **2d**, the identity of which was

^{*} The linear pentamer and hexamer (**9b** and **9c** respectively) were cyclised in 45 and 52% yield respectively, using acetone and HCl, in benzene. However, the linear tetramer **9a** was cyclised in only 13–36% yield with a range of different carbonyl compounds.¹³

confirmed by the following diagnostic data: (1) new signals were observed at δ 3.91 and 5.95, integrating to a ratio of 1:1, with no corresponding terminal furan hydrogens (*i.e.* in the 5-position), indicating the formation of a new calixfuran; (2) new signals in the +ve ion CI spectrum of the mixture at m/z 578 ($M^+ + NH_4$) and 561 ($M^+ + H$) revealed the mass of the new calixfuran and hence its ring size; (3) accurate mass measurement revealed the constitution of the ($M^+ + NH_4$) ion. The fact that this material was produced in only trace amounts and that its mobility on silica gel was identical with that of the linear oligomers meant that it was not possible to isolate it in a pure form. However, its identity was confirmed by accurate mass measurement of an ion which corresponded to the calix[7]-furan + NH_4^+ .

The problem of low yields for the cyclisations, coupled with the fact that addition of metal salts has been claimed to increase the yields of calixfurans of the type **1**,^{11c,16,17} suggested that addition of a metal or ammonium salt template to assist these cyclisation processes would be necessary for optimisation of the cyclisation, by making conformations that could cyclise more easily accessible. To this end we tried adding a series of likely templates to the reaction mixtures of the linear polyethers **6b–d**, in the presence of boron trifluoride–diethyl ether and dimethoxymethane. In particular, we added lithium perchlorate, lithium chloride, ammonium chloride, benzylammonium chloride, and *sec*-butylammonium chloride to the attempted cyclisation reactions of tetramer **6b**, pentamer **6c** and hexamer **6d**. Unfortunately, in all cases we failed to get any discernible evidence for templating the cyclisations. In fact, the reactions with lithium ions present were virtually the same as their non-lithium-containing counterparts, and the reactions involving ammonium salts produced virtually no cyclisation at all. Failure to template the cyclisations is probably due to the fact that, unlike their non-aromatic polyether counterparts, the furan-derived polyether substrates are weak ligands for cations under the reaction conditions we have used. The unsuccessful attempts to template cyclisation of the linear furan oligomers contrasts markedly with evidence obtained from studying the CI mass spectra of both the linear furan oligomers **5** and **6** and the calixfurans **2**. In the gas phase and in the presence of excess of ammonia gas, these linear and cyclic furan-based compounds show properties which indicate that complexation of both proton and ammonium ions does indeed take place. The results from the CI-induced mass spectral analyses for the linear furan derivatives and calixfurans are shown in Table 3.

Closer examination of the results shown in Table 3 revealed that ($M + H^+$) and ($M + NH_4^+$) ions are observed for virtually all the different furan oligomers **5** and **6**, and calixfurans **2**. Furthermore, the ($M + NH_4^+$) ions generally occurred with a higher intensity than the corresponding ($M + H^+$) ions, suggesting that formation of ammonium complexes is preferred over formation of the corresponding protonated complexes for compounds **6b–f** and **2a–e**. Similar results have been observed from the CI mass spectrometric analysis of different diols, which are able to bind ammonium ions with preference over protons.²³ However, the most important conclusion to be drawn from the mass spectrometric analysis of the furan oligomers and macrocycles is that these materials are able to complex ammonium ions (and protons) in the gas phase.

The fact that complexation of ammonium ions by oligomers **6** and calixfurans **2** is a favourable process in the gas phase, but not in solution, is perhaps not surprising in the light of work²⁴ that demonstrates the phenomenon of the reversal of proton affinities of molecules in the gas phase *versus* solution. For example, it is well known that in the gas phase, toluene is a stronger acid than water and *tert*-butoxide is a weaker base than methoxide. Hence, the calixfurans **2** and their open-chain analogues **5** and **6** show both proton- and ammonium-binding

Table 3

Entry	Compound	Relative intensities (%)	
		($M + H^+$)	($M + NH_4^+$)
1	5	35	0
2	6a	100	68
3	6b	43	100
4	6c	7	57
5	6d	5	100
6	6e	0	3
7	6f	4	71
8	2a	20	23
9	2b	21	75
10	2c	0	36
11	2d	2	10
12	2e	17	91

abilities in the gas phase, but not in solution. Therefore, it is understandable that extrapolating gas-phase complexation to solution chemistry, in terms of developing a model for template-assisted construction of the macrocycles, has to date been unsuccessful.

In conclusion, we have been able to isolate cyclic calix-[4]furan **2a** in 34% yield by cyclisation of the linear tetramer **6b**. Cyclisation of the homologous linear pentamer and hexamer **6c** and **6d** respectively has also been achieved, providing calixfurans **2b** and **2c** for the first time, though in low yields. The calix[8]furan **2e** has also been prepared for the first time, from dimerisation of the linear tetramer **6b**. Trace amounts of calix[7]furan **2d** have also been detected. The optimal yield (64%) for compound **5** has also been obtained *via* a one-pot reaction. The fact that compounds **2b–e** have been prepared and isolated (with the exception of cyclic heptamer **2d**) at all shows that they are relatively stable. Mass spectrometric analysis by CI techniques in the presence of ammonia gas has shown that these furan-based compounds **2** and **6** are able to complex proton and ammonium ions in the gas phase. Studies to try to predict what the actual structure of the gas-phase complexes are and to study their stability in the gas phase are underway. Also, further work to develop milder methods for the preparation of these calixfurans in higher yields is being carried out.

Experimental

Dichloromethane was distilled over calcium hydride. Light petroleum refers to the fraction boiling in the range 40–60 °C. Anhydrous furan, boron trifluoride–diethyl ether, dimethoxymethane, and 2,2-dimethoxypropane were purchased from Aldrich or Janssen and used directly; hydroxymethylfuran was distilled prior to use and stored over activated molecular sieves (4 Å).

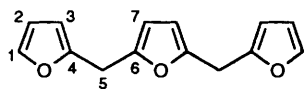
TLC was performed on Merck plastic or aluminium sheets coated with silica gel 60 F₂₅₄ (Art. 5735); the chromatograms were initially examined under UV light and then developed either with iodine vapour or an ethanolic anisaldehyde (1.0%) solution containing sulfuric acid (9%) used as a spray and visualised by heating with a heat gun. Column chromatography was achieved under medium pressure or under gravity, using Merck Kieselgel H (Type 60) or Prolabo neutral alumina (50–160 μ m).

All anhydrous, low-temperature reactions were carried out in glassware which was dried prior to use by storage in a glass oven maintained at 140 °C and cooled under a stream of argon. All organic extractions were dried with anhydrous magnesium sulfate or anhydrous sodium sulfate. Evaporations were carried

out using a Buchi rotary evaporator or Buchi cold-finger rotary evaporator, followed by evaporation under high vacuum (typically at approximately 2 mmHg). Kugelrohr distillations were carried out using a Buchi GKR-51 Kugelrohr apparatus. M.p.s were determined using an Electrothermal melting point apparatus and are uncorrected. ^1H NMR spectra were recorded at 200 or 300 MHz on a Bruker AC200 or AC300 NMR spectrometer. ^{13}C NMR spectra were recorded at 75 MHz on a Bruker AC300. Both ^1H and ^{13}C spectra were recorded using CDCl_3 as solvent and CHCl_3 as internal standard respectively. J -Values are given in Hz. IR spectra were recorded on a Perkin-Elmer 783 equipped with a PE600 data station or a Perkin-Elmer 598 and UV spectra were recorded on a Perkin-Elmer λ 15 spectrometer. Electron impact (EI) (70 eV) and chemical ionisation (CI) spectra were recorded with a VG 7070EQ spectrometer using ammonia gas and an ion-source temperature of 150 °C. Fast-atom bombardment (FAB) spectra were recorded on a Kratos MS50 spectrometer, using a *m*-nitrobenzyl alcohol matrix, and accurate mass determinations were carried out on a Kratos Concept IS spectrometer. Microanalyses were performed using a Carlo-Erba 1106 elemental analyser.

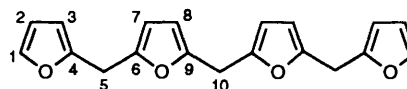
Preparation of Linear Oligomers 5 and 6.—**Method A.** To a stirred, cooled (0 °C) mixture of furan **7a** (68.00 g, 1.00 mol), 2-(hydroxymethyl)furan **7b** (9.80 g, 0.10 mol), and dichloromethane (200 cm^3) was added (dropwise) boron trifluoride-diethyl ether (1.00 cm^3 , 0.008 mol). The reaction mixture was stirred at 0 °C for 2 h, followed by 4 h at room temperature. The resulting dark green mixture was diluted with dichloromethane (50 cm^3), washed with 5% aq. sodium hydrogen carbonate (3 \times 50 cm^3), dried, and evaporated to give a dark green oil, which was distilled (Kugelrohr) to give **compound 5** as a light yellow liquid (4.20 g, 28%); b.p. 95–100 °C (30 mmHg); λ_{max} (hexane)/nm 219.6 ($\log_{10} \epsilon$ 4.17); ν_{max} (neat)/ cm^{-1} *inter alia* 3125m, 2920s and 1600m; δ_{H} (200 MHz) 4.01 (2 H, s, CH_2), 6.10 (2 H, dd, J 3.1 and 0.8, 2 \times OCHCH) 6.32 (2 H, dd, J 3.1 and 1.9, 2 \times OCHCH) and 7.35 (2 H, dd, J 1.8 and 0.7, 2 \times OCHCH); δ_{C} 27.4 (CH₂), 106.4 (2 \times OCHCHCH), 110.4 (2 \times OCHCHCH), 141.6 (2 \times OCHCHCH) and 151.5 (CCH₂C); m/z (+ve CI) *inter alia* 149 (M^+ + H) and 30 (CH_2O , base peak) (Found: C, 73.0; H, 5.4. C₉H₈O₂ requires C, 73.0; H, 5.4%).

The residue (4.67 g) was purified by silica gel chromatography [hexane, followed by toluene–hexane (1:9), then (1:4), and lastly toluene as eluent] to give three fractions. The first fraction (a light yellow liquid) was identified as **compound 6a** (2.30 g, 20%); b.p. 95–100 °C (1–2 mmHg); λ_{max} (hexane)/nm 223.7 ($\log_{10} \epsilon$ 4.32); ν_{max} (neat)/ cm^{-1} *inter alia* 3120, 2920m and 1600m; δ_{H} (200 MHz) 3.98 (4 H, s, 2 \times CH₂), 6.01 (2 H, s, 2 \times 7-H), 6.08 (2 H, d, J 3.1, 2 \times 3-H), 6.32 (2 H, dd, J 3.1 and 1.8, 2 \times 2-H) and 7.34 (2 H, m, 2 \times 1-H); δ_{C} 27.3 (2 \times C-5), 106.3, 107.2 and 109.9 (each 2 \times C-2, -3 and -7), 141.4 (2 \times C-1) and 150.4 and 151.6 (each 2 \times C-4 and -6); m/z (+ve CI) *inter alia* 246 (M^+ + NH₄), 229 (M^+ + H, base peak) and 228 (M^+) (Found: C, 73.5; H, 5.0%. C₁₄H₁₂O₃ requires C, 73.7; H, 5.3%).

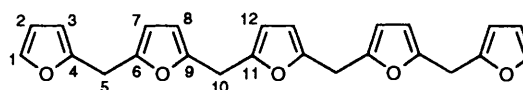
**6a**

The second fraction afforded **compound 6b** as a cream solid (0.670 g), which was recrystallised from hexane to give light cream crystals (0.43 g, 4%); m.p. 76–78 °C (lit.,^{12d} 77–78 °C); λ_{max} (hexane)/nm 224 ($\log_{10} \epsilon$ 4.54) nm; ν_{max} (KBr disc)/ cm^{-1} *inter alia* 3125, 2925 and 1600; δ_{H} (300 MHz) 3.93 (2 H, s, 10-H₂),

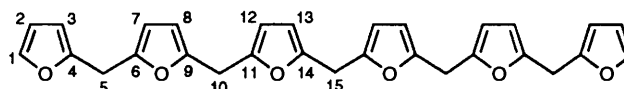
3.97 (4 H, s, 2 \times 5-H), 5.99 (4 H, m, 1 \times 7- and 8-H), 6.08 (2 H, d, J 3.1, 2 \times 3-H), 6.31 (2 H, dd, J 2.9 and 2.0, 2 \times 2-H) and 7.34 (2 H, d, J 1.0, 2 \times 1-H); δ_{C} 28.1 (2 \times C-5), 28.2 (C-10), 107.0, 107.8, 107.9 and 111.0 (each 2 \times C-2, -3, -7 and -8), 142.1 (2 \times C-1) and 151.1, 151.3 and 152.3 (each 2 \times C-4, -6 and -9); m/z (+ve CI) *inter alia* 326 (M^+ + NH₄, base peak) and 309 (M^+ + H) (Found: C, 73.7; H, 5.2. Calc. for C₁₉H₁₆O₄: C, 74.0; H, 5.3%).

**6b**

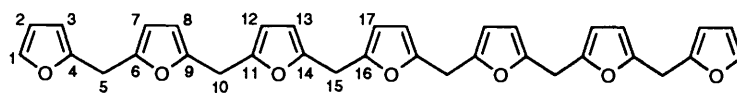
The third fraction was a cream solid (0.240 g), which was recrystallised from light petroleum–ethyl acetate to give **compound 6c** as light cream crystals (0.180 g, 2%); m.p. 98–100 °C (lit.,^{19c} 99–101 °C); λ_{max} (hexane)/nm 226.1 ($\log_{10} \epsilon$ 4.62); ν_{max} (KBr disc)/ cm^{-1} *inter alia* 3125, 2940 and 1610m; δ_{H} (200 MHz) 3.92 (4 H, s, 2 \times 10-H₂), 3.96 (4 H, s, 2 \times 5-H), 5.98 (6 H, m, 2 \times 7-, 8- and 12-H), 6.07 (2 H, dd, J 3.2 and 0.8, 2 \times 3-H), 6.30 (2 H, dd, J 3.1 and 1.9, 2 \times 2-H) and 7.33 (2 H, m, 2 \times 1-H); δ_{C} 27.5 (2 \times C-5), 27.6 (2 \times C-10), 106.4, 107.2, 107.3 and 110.4 (2 \times C-2, -3, -7, -8 and -12), 141.5 (2 \times C-1) and 150.4, 150.5, 150.6 and 151.7 (2 \times C-4, -6, -9 and -11); m/z (+ve, EI) *inter alia* 388 (M^+) and 308 (M^+ – C₅H₄O, base peak) (Found: C, 74.3; H, 5.2. Calc. for C₂₄H₂₀O₅: C, 74.2; H, 5.2%).

**6c**

Method B. The previous experiment was repeated but with a 1:2 ratio of hydroxymethylfuran to furan, *i.e.* furan **7a** (25.0 cm^3 , 340 mmol), hydroxymethylfuran **7b** (15.0 cm^3 , 170 mmol), dichloromethane (10 cm^3) and boron trifluoride–diethyl ether (0.50 cm^3 , 4.07 mmol) at room temperature for 15 h. Unchanged furan was removed by evaporation and the resulting oil was extracted with diethyl ether and worked up as in the previous experiment. Distillation (as above) gave **compound 5** (4.00 g, 16%) which was identical with that previously prepared. Purification of the residue (as above) by silica gel chromatography gave **compounds 6a** (2.13 g, 11%), **6b** (0.25 g, 1%), **6c** (0.32 g, 2%), **6d** (0.10 g, 0.6%) and **6e** (0.08 g, 0.5%). However, from these reaction conditions, small amounts of the linear oligomers **6d** and **6e** were also obtained as 4th and 5th fractions respectively.

**6d**

Compound 6d had m.p. 128–130 °C (lit.,^{12d} 100 °C); λ_{max} (MeCN)/nm ($\log_{10} \epsilon$ 4.60); ν_{max} (KBr disc)/ cm^{-1} *inter alia* 3120, 2920 and 1610; δ_{H} (200 MHz) 3.92 (6 H, s, 2 \times 10-H₂ and 15-H₂), 3.96 (4 H, s, 2 \times 5-H), 5.97 and 5.98 (each 4 H, s, 2 \times 7-, 8-, 12- and 13-H), 6.07 (2 H, d, J 3.1, 2 \times 3-H), 6.30 (2 H, dd, J 3.0 and 1.9, 2 \times 2-H) and 7.33 (2 H, m, 2 \times 1-H); δ_{C} 27.5 (2 \times C-5), 27.6 (2 \times C-10 and C-15), 106.5, 107.2, 107.3 and 110.4 (2 \times C-2, -3, -7, -8, -12 and -13), 141.5 (2 \times C-1) and 150.5, 150.6, 150.7 and 151.8 (2 \times C-4, -6, -9, -11 and -14); m/z (+ve CI) *inter alia* 486 (M^+ + NH₄, base peak), 469 (M^+ + H) and 468 (M^+) (Found: C, 74.2; H, 5.2. C₂₉H₂₄O₆ requires C, 74.4; H, 5.2%).



6e

Compound **6e** had m.p. 140–142 °C; ν_{\max} (KBr disc)/ cm^{-1} *inter alia* 3120, 2920 and 1610; δ_{H} (300 MHz) 3.92 (8 H, s, 2 × 10- and 15-H), 3.96 (4 H, s, 2 × 5-H), 5.97 and 5.98 (6 H and 4 H respectively, each s, 2 × 7-, 8-, 12-, 13- and 17-H), 6.07 (2 H, d, J 2.9, 2 × 3-H), 6.30 (2 H, t, J 2.9, 2 × 2-H) and 7.33 (2 H, s, 2 × 1-H); m/z (+ve FAB) *inter alia* 549 (M^+ + H), 548 (M^+) and 286 ($\text{C}_{16}\text{H}_{14}\text{O}_5^+$, base peak) (Found: C, 74.4; H, 5.0. $\text{C}_{34}\text{H}_{28}\text{O}_7$ requires C, 74.4; H, 5.1%).

Method C. To a stirred mixture of 2,2'-difurylmethane **5** (0.64 g, 4.30 mmol), 37% aq. formaldehyde (1.35 cm^3 , 16.70 mmol) and absolute ethanol (8 cm^3) was added conc. hydrochloric acid (1.50 cm^3). The resulting mixture was stirred at room temperature for 2 days, diluted with water, and extracted with chloroform (4 × 20 cm^3). The combined extracts were shaken with 5% aq. sodium hydrogen carbonate (2 × 50 cm^3), dried, filtered and evaporated to yield a purple residue (0.810 g). This material was purified by silica gel column chromatography (light petroleum, then 1% dichloromethane–light petroleum as the eluent) to give two fractions. The first fraction was identified as compound **6b** (0.100 g, 15%) and the second fraction as compound **6d** (0.160 g, 24%), both compounds identical (NMR, TLC) with the samples prepared in the preceding experiments.

Method D. To a stirred solution of furan **7a** (0.90 cm^3 , 12.40 mmol) in tetrahydrofuran (THF) (20 cm^3) was added dropwise *tert*-butyllithium (8.00 cm^3 , 13.60 mmol) at -78°C under argon. After being stirred for 1 h the resulting yellow solution was transferred *via* a cannula into a mixture of copper(I) iodide (1.181 g, 6.20 mmol) and THF (50 cm^3) at -78°C . The resulting mixture was then warmed to 0 °C, maintained at 0 °C for 2.5 h, cooled to -78°C , and treated with bromochloromethane (0.80 cm^3 , 12.50 mmol) dropwise. The reaction mixture was stirred at -78°C for 2 h, warmed to room temperature overnight, and lastly refluxed for 2 h. The resulting dark brown solution was quenched with saturated aq. ammonium chloride (100 cm^3), extracted with dichloromethane (4 × 50 cm^3), and the combined extracts were dried, filtered and concentrated to yield a dark yellow liquid (0.445 g). Purification by silica gel chromatography (hexane as eluent) gave compound **5** as a light yellow liquid (0.127 g, 14%). This compound was identical (NMR, TLC) with the sample prepared in the preceding experiments.

Method E. To a stirred solution of furan **7a** (0.80 cm^3 , 11.01 mmol) in THF (20 cm^3) was added dropwise *tert*-butyllithium (8.00 cm^3 , 13.60 mmol) at -78°C under argon. After being stirred for 1 h at -78°C , the mixture was treated with 2-furaldehyde **7c** (0.92 cm^3 , 11.10 mmol) added dropwise into the yellow solution. The resulting solution was then stirred at -78°C for 1 h, warmed to 0 °C, and treated with sodium boranuide (4.17 g, 110.24 mmol), followed by dropwise addition of TFA (15.0 cm^3). After being stirred for 1 h at 0 °C, the orange coloured solution was neutralised with 26% aq. sodium hydroxide (50 cm^3), extracted with dichloromethane (2 × 50 cm^3), and the extracts were dried, filtered, and concentrated to yield a brown liquid (1.644 g). Purification by silica gel chromatography (hexane as eluent) gave compound **5** as a liquid (1.04 g, 64%). This compound was identical (NMR, TLC) with the sample prepared in the preceding experiments.

Method F. To a stirred solution of furan **7a** (0.80 cm^3 , 11.01 mmol) in THF (20 cm^3) was added dropwise *tert*-butyllithium (8.00 cm^3 , 13.60 mmol) at -78°C under argon. After the mixture had been stirred for 1 h at -78°C , 2-furaldehyde **7c**

(0.92 cm^3 , 11.10 mmol) was added dropwise into the resulting yellow solution. After stirring of this mixture for 1 h at -78°C , further *tert*-butyllithium (8.00 cm^3 , 13.60 mmol) was added dropwise. After the reaction mixture had warmed to room temperature, the resulting brown solid was diluted with dry, redistilled THF (100 cm^3), further 2-furaldehyde **7c** (0.92 cm^3 , 11.10 mmol) was added dropwise at -78°C , and the reaction mixture was warmed to room temperature. After 2 h, sodium boranuide (4.17 g, 110.24 mmol) was added at 0 °C, followed by dropwise addition of TFA (15.0 cm^3). After being stirred for a further 2 h at 0 °C, the reaction mixture was neutralised with 26% aq. sodium hydroxide (50 cm^3), extracted with dichloromethane (3 × 50 cm^3), and the extracts were dried, filtered and concentrated to yield a dark oil (1.44 g). Purification by silica gel chromatography (hexane as eluent) gave compound **6a** as a yellow oil (0.54 g, 22%). This compound was identical (NMR, TLC) with the sample prepared in the preceding experiments.

Lithiation of Difurylmethane 5.—To a stirred solution of difurylmethane **5** (0.474 g, 5.05 mmol) in THF (30 cm^3) was added dropwise *tert*-butyllithium (3.30 cm^3 , 5.61 mmol) at -78°C under argon. After the mixture had been stirred for 1 h at -78°C , chlorotrimethylsilane (0.71 cm^3 , 5.60 mmol) was added dropwise to the resulting brown solid to give a yellow solution. After being stirred at room temperature for 1 h, the reaction mixture was quenched with saturated aq. ammonium chloride (100 cm^3), extracted with dichloromethane (3 × 50 cm^3), and the extracts were dried, filtered and concentrated to yield a dark brown oil (1.307 g). Purification by silica gel chromatography (hexane as eluent) gave a fraction which was identified as compound **8** (0.592 g, 53%); λ_{\max} (hexane)/nm 225.9 ($\log_{10} \epsilon$ 4.03) and 266.2 ($\log_{10} \epsilon$ 3.57); ν_{\max} (thin film)/ cm^{-1} *inter alia* 3116, 2957, 2899, 1639 and 1586; δ_{H} (300 MHz) 0.05 (9 H, s, Me_3Si), 3.75 (1 H, s, CHSi), 6.00 (2 H, dd, J 3.1 and 0.5, 2 × OCHCH), 6.29 (2 H, dd, J 3.1 and 1.9, 2 × OCHCH) and 7.30 (2 H, d, J 1.7, 2 × OCH); δ_{C} -2.3 (MeSi), 32.0 (CHSi), 104.8 (2 × OCHCH), 110.3 (2 × OCHCH), 140.5 (2 × OCH) and 154.2 (2 × CCHSi); m/z (+ve FAB) *inter alia* 221 (M^+ + H) and 139 ($\text{C}_9\text{H}_{15}\text{O}^+$, base peak) (Found: C, 65.3; H, 7.3; Si, 12.6. $\text{C}_{12}\text{H}_{16}\text{O}_2\text{Si}$ requires C, 65.4; H, 7.3; Si, 12.8%).

Preparation of Octamethylcalix[4]furan 1a.—To a stirred, cooled (-78°C) mixture of furan **7a** (1.00 cm^3 , 13.76 mmol), 2,2-dimethoxypropane (3.40 cm^3 , 27.78 mmol) and dichloromethane (50 cm^3) was added boron trifluoride–diethyl ether (3.40 cm^3 , 27.63 mmol) dropwise. The resulting orange reaction mixture was left to warm to room temperature, when the colour changed to dark brown. The reaction mixture was stirred at room temperature overnight, diluted with dichloromethane (100 cm^3), washed with 5% aq. sodium hydrogen carbonate (2 × 50 cm^3), dried, filtered and evaporated to yield a brown semi-solid. Ethanol (50 cm^3) was added to yield a light cream solid (0.146 g), which was recrystallised from chloroform–light petroleum to give compound **1a** as light cream needles (0.101 g, 7%); m.p. 241–244 °C (lit., $^{11\text{c}}$ 240–243 °C); ν_{\max} (KBr disc)/ cm^{-1} *inter alia* 3115, 2980, 2940, 2865 and 1600; δ_{H} (300 MHz) 1.45 (24 H, s, 8 × Me) and 5.87 (8 H, s, furan-H); δ_{C} 25.5 (8 × Me), 36.6 (4 × Me_2C), 103.1 (8 × OCHCH) and 158.5 (8 × OCHCH); m/z (+ve CI) *inter alia* 432 (M^+) and 417 (M^+ – CH_3 , base peak) (Found: C, 77.5; H, 7.5. Calc. for $\text{C}_{28}\text{H}_{32}\text{O}_4$: C, 77.8; H, 7.4%).

Preparation of Calix[4]furan 2a.—To a stirred, cooled (0 °C) mixture of 2-(hydroxymethyl)furan **7b** (0.90 cm³, 10.4 mmol) in dichloromethane (40 cm³) was added boron trifluoride–diethyl ether (0.30 cm³, 2.5 mmol) under argon. After being stirred for 1 h at 0 °C, the reaction mixture was stirred at room temperature for 3 h. The dark green solution was diluted with dichloromethane (100 cm³), washed with 5% aq. sodium hydrogen carbonate (2 × 50 cm³), dried, filtered and evaporated give a dark green semi-solid (0.54 g). Purification by silica gel chromatography (toluene as eluent) gave a cream solid (0.06 g) which consisted of a mixture of furan linear oligomers (by NMR spectroscopy and TLC). Further elution gave calix[4]furan **2a** as light cream solid (0.01 g, 1.3%), m.p. 158–160 °C (lit.,^{12b} 158–159 °C); λ_{\max} (hexane)/nm 222 (log₁₀ ϵ 4.59); ν_{\max} (KBr disc)/cm⁻¹ *inter alia* 3100, 2920s and 1610m; δ_{H} (300 MHz) 3.85 (8 H, s, 4 × CH₂) and 5.96 (8 H, s, 8 × furan-H); δ_{C} 27.6 (4 × CH₂), 106.7 (8 × OCHCH) and 151.0 (8 × OCHCH); *m/z* (+ve FAB) *inter alia* 321 (M⁺ + H), 320 (M⁺) and 149 (C₆H₆O₂⁺, base peak) (Found: C, 74.7; H, 5.2. Calc. for C₂₀H₁₆O₄: C, 75.0; H, 5.0%).

Preparation of Calix[4]furan 2a from 2,2'-Difurylmethane 5.—To a stirred, cooled (0 °C) solution of difurylmethane **5** (0.269 g, 1.82 mmol) and dimethoxymethane (0.20 cm³, 2.26 mmol) in dichloromethane (100 cm³) was added boron trifluoride–diethyl ether (0.50 cm³, 4.07 mmol) dropwise, under argon. After 12 h, the reaction mixture was allowed to warm to room temperature and was stirred for a further 7 days, washed with 5% aq. sodium hydrogen carbonate (2 × 50 cm³), dried, filtered and concentrated to yield a dark solid (0.040 g). This solid was purified by silica gel chromatography (toluene as eluent) to give a cream solid (0.010 g) which was a mixture of linear oligomers **6b**, **6d** and calix[6]furan **2c** (by NMR and TLC). Further elution gave calix[4]furan **2a** as a cream solid (0.020 g, 6%), which was identical with that prepared previously.

Preparation of Calix[6]furan 2c from Linear Trimer 6a.—To a stirred, cooled (0 °C) mixture of trimer **6a** (0.456 g, 2.00 mmol), dimethoxymethane (0.20 cm³, 2.26 mmol), dichloromethane (100 cm³), and activated molecular sieves (4 Å) was added (dropwise) boron trifluoride–diethyl ether (0.10 cm³, 0.81 mmol) under argon. The reaction mixture was allowed to warm to room temperature and further small quantities of dimethoxymethane and boron trifluoride–diethyl ether were added in portions. After 5 days, further boron trifluoride–diethyl ether (0.20 cm³, 1.62 mmol) was added; after 6 days more dimethoxymethane (0.10 cm³, 1.13 mmol) was added; after 19 days, further dimethoxymethane (0.20 cm³, 2.26 mmol) was added, together with boron trifluoride–diethyl ether (0.10 cm³, 0.81 mmol); after 20 days, dimethoxymethane (0.20 cm³, 2.26 mmol) was added; after 21 days, more dimethoxymethane (0.10 cm³, 1.13 mmol) and boron trifluoride–diethyl ether (0.30 cm³, 2.43 mmol) were added. After a further day, the resulting dark solution was washed with 5% aq. sodium hydrogen carbonate (2 × 50 cm³), dried, filtered and evaporated to give a dark viscous liquid (0.039 g), which was purified by neutral alumina chromatography [hexane, then toluene–hexane (1:4), and finally toluene–hexane (1:1) as eluent]. The first eluted fraction was the linear oligomer **6d** (0.006 g, 1.3%), followed by compound **2c** as a cream solid (0.002 g, 0.4%); δ_{H} (300 MHz) 3.90 (12 H, s, 6 × CH₂) and 5.89 (12 H, s, 12 × furan-H); δ_{C} 29.7 (6 × CH₂), 107.1 (12 × OCCH) and 150.4 (12 × OCCH); *m/z* (+ve CI) *inter alia* 498 (M⁺ + NH₄), 391 (M⁺ + NH₄ – C₇H₇O) and 58 (C₃H₆O⁺, base peak) [Found: (M + NH₄)⁺, 498.1924. C₃₀H₂₄O₆·NH₄⁺ requires *m/z* 498.1916].

Preparation of Calix[4]furan 2a and Calix[8]furan 2e from Linear Tetramer 6b.—To a stirred, cooled (0 °C) mixture of

compound **6b** (0.308 g, 1.00 mmol), dimethoxymethane (0.09 cm³, 1.02 mmol) and dichloromethane (100 cm³) was added (dropwise) boron trifluoride–diethyl ether (0.30 cm³, 2.44 mmol) under argon. The resulting dark green solution was stirred for 2 h, warmed to room temperature, and stirred for a further 22 h. The reaction mixture was diluted with dichloromethane (50 cm³), washed with 5% aq. sodium hydrogen carbonate (2 × 50 cm³), dried, filtered and evaporated to give a dark solid (0.246 g). Purification by silica gel chromatography (hexane, followed by toluene as eluent) gave three fractions, the first of which was starting material **6b** (0.030 g, 10% recovery). The second fraction was calix[8]furan **2e**, obtained as a cream solid (0.007 g, 2%); δ_{H} (300 MHz) 3.89 (16 H, s, 8 × CH₂) and 5.94 (16 H, s, 16 × furan-H); *m/z* (+ve CI) *inter alia* 658 (M⁺ + NH₄), 641 (M⁺ + H) and 44 (C₂H₄O⁺, base peak) [Found: (M + NH₄)⁺, 658.2433. C₄₀H₃₂O₈·NH₄⁺ requires *m/z*, 658.2441].

The last fraction, isolated as a light yellow solid (0.110 g, 34%) after treatment with decolourising charcoal, was calix[4]furan **2a**, and was identical with the material previously prepared.

Preparation of Calix[5]furan 2b from Linear Pentamer 6c.—To a stirred, cooled (0 °C) solution of pentamer **6c** (0.388 g, 1.00 mmol) and dimethoxymethane (0.09 cm³, 1.02 mmol) in dichloromethane (70 cm³) was added (dropwise) boron trifluoride–diethyl ether (0.30 cm³, 2.44 mmol) under argon. After 2 h, the reaction mixture was warmed to room temperature, stirred for a further 3 days, washed with 5% aq. sodium hydrogen carbonate (2 × 50 cm³), dried, filtered and evaporated to give a dark semi-solid, which was dissolved in toluene, and the solution was treated with decolourising charcoal, filtered and reevaporated to give a light-yellow viscous oil (0.040 g). This oil was purified by neutral alumina chromatography (hexane followed by toluene as eluent) to give two fractions. The first was the starting material **6c** (0.010 g, 3% recovery). The second fraction gave calix[5]furan **2b** as an oil (0.020 g, 5%); δ_{H} (300 MHz) 3.88 (10 H, s, 5 × CH₂) and 5.94 (10 H, s, 10 × furan-H); δ_{C} 29.6 (5 × CH₂), 106.9 (10 × OCCH) and 150.4 (10 × OCCH); *m/z* (+ve CI) *inter alia* 418 (M⁺ + NH₄), 401 (M⁺ + H), 400 (M⁺) and 44 (C₂H₄O⁺, base peak) (Found: M⁺, 400.1311. C₂₅H₂₀O₅ requires M, 400.1307).

Preparation of Calix[6]furan 2c from Linear Hexamer 6d.—To a stirred, cooled (0 °C) solution of compound **6d** (0.110 g, 0.24 mmol) in toluene (30 cm³) were added dimethoxymethane (0.42 cm³, 4.75 mmol) and boron trifluoride–diethyl ether (0.25 cm³, 2.04 mmol), each in small portions over a period of 6 days. The additions were made in portions of 0.02 cm³ (dimethoxymethane) and 0.05 cm³ (boron trifluoride) at the start of the reaction; 0.1 cm³ of each was added after 1 day; and 0.3 cm³ and 0.1 cm³ (respectively) after a further 2 days. The red-brown solution was washed with 5% aq. sodium hydrogen carbonate (2 × 50 cm³), dried, filtered through a thin layer of silica gel and evaporated to give compound **2c** as a cream solid, (0.001 g, 1%). The spectral data were the same as those of the compound obtained previously.

Preparation of Calix[7]furan 2e from Linear Compounds 5 and 6a.—To a stirred, cooled (0 °C) mixture of difurylmethane **5** (0.300 g, 2.03 mmol), linear trimer **6a** (0.462 g, 2.03 mmol), dimethoxymethane (0.5 cm³, 4.03 mmol) and dichloromethane (200 cm³) under argon was added (dropwise) boron trifluoride–diethyl ether (0.5 cm³, 4.07 mmol). After 3 h, the reaction mixture was warmed to room temperature, stirred for a further 4 days, washed with 5% aq. sodium hydrogen carbonate (2 × 50 cm³), dried and evaporated to give a dark green solid. The solid was dissolved in warm toluene, and the solution was

filtered and evaporated to give a brown-yellow solid (0.117 g). This solid contained a mixture of products, including calixfurans **2a**, **2b** and **2c**, together with a mixture of the linear oligomers (by TLC, ^1H NMR and MS). The presence of trace quantities of the cyclic heptamer **2d** was shown by the following data: δ_{H} (300 MHz) 3.91 (14 H, s, $7 \times \text{CH}_2$) and 5.95 (14 H, s, $14 \times \text{OCCH}$); m/z (+ve CI) *inter alia* 578 ($\text{M}^+ + \text{NH}_4$) and 561 ($\text{M}^+ + \text{H}$) [Found: ($\text{M} + \text{NH}_4^+$), 578.2184. $\text{C}_{35}\text{H}_{28}\text{O}_7 \cdot \text{NH}_4^+$ requires m/z , 578.2179].

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