Preparation and properties of some crown ethers incorporating stable carbocations

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Reaction of 1,3-xylyl-18-C5 [**12** (n = 3)] and 1,3-xylyl-21-C6 [**12** (n = 4)] with diazomethane yields mixtures of crown ethers incorporating cycloheptatrienes, and these have been converted to crown ethers incorporating tropylium ions **5** (n = 3 and 4) by hydride abstraction with triphenylcarbenium tetrafluoroborate. These compounds have $pK_{R^+} \approx 3.8$. Crown ethers containing the 1,8-dioxyxanthone residue, **22** (n = 3–5), have been prepared by alkylation of 1,8-dihydroxyxanthone with polyethylene glycol dibromides. These have been converted into the corresponding xanthydrols, **16** (n = 3–5). The conjugate acids of the ketones have $-2.14 < pK_a < -1.94$. The alcohols exist in equilibrium with the bridged 9-xanthylium cations and have $0.78 < pK_{R^+} < 1.08$. For 1,8-diethoxyxanthone and 1,8-diethoxyxanthydrol, the corresponding values are $pK_a = -1.93$ and $pK_{R^+} = 1.38$. The possibility that crown ethers incorporating relatively stable carbocationic centres may catalyse amide hydrolyses is briefly discussed.

Interest continues in crowns and cryptands with binding properties which may be easily switched in response to solution pH, redox condition, or even photochemical excitation.[1] Many such show enhanced efficiencies in mediating transport of selected guests across liquid membranes;[2] others not only bind selectively, but transform particular organic compounds with reaction-rate enhancement, inhibition by competitively bound species and true catalytic turnover.[3]

The range of functional groups which have been incorporated into macrocyclic arrays to provide pH responsive centres is large, but alcohols are not usually thought of in this sense. However, those arising formally from hydrolysis of a relatively stable carbocationic centre would exist at low pH as that carbocation **1**, and at higher pH as the related alcohol, **2** (Fig. 1), with the operational pH range depending on both the nature of the cationic centre and its mode of incorporation into a macrocyclic array. Compounds of this type have been described. Vögtle and Itter[4] have prepared crown ethers containing bridged diphenyl- and triphenyl-methanols; Okazaki *et al.* have described a sulfur containing crown incorporating a tropylium ion[5] and most recently, Kimura *et al.*[6] have described a malachite green with a crown linked to one of the phenyl groups, and demonstrated anomalous photochromism and photoinduced switching of cation binding. Carbocation stabilities and structural types vary widely and the possibilities of combining carbocation and crown ether or cryptand chemistry are far from exhausted.

Carbocations may react with neutral molecules other than water. Amides, for example, can be *N*-alkylated under appropriate conditions, and this reaction might place the amide residue close to or within a macrocyclic ether, **3**. Amines and ammonia are also alkylated by carbocations, and in acid, the resulting amines, **4**, may decompose to regenerate the cation and ammonium ion.[7] The relationship between the **3** and **4** is hydrolysis of the amide residue, and enhanced reactivity of the amide residue in the complexes may follow from binding of metal cations to these intermediate covalently bound forms, as suggested by recent observations of catalyses of methanolyses of intra-crown phenolic esters by alkali and alkaline earth cations.[8]

With these considerations in mind, we have embarked on a study of crown ethers and cryptands incorporating precursors

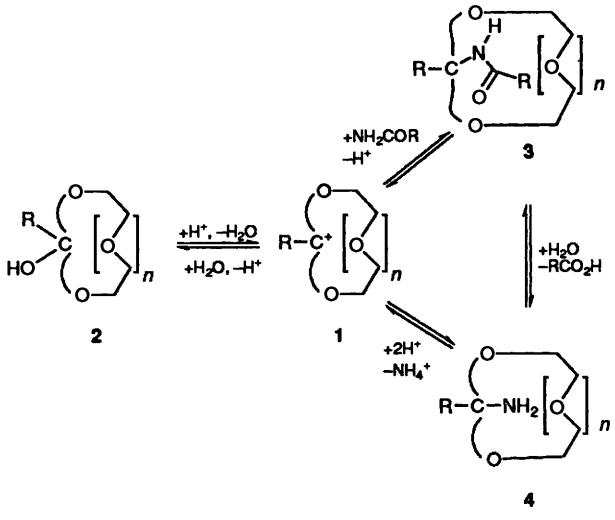


Fig. 1 Possible cationic crown ether catalyses of amide hydrolyses

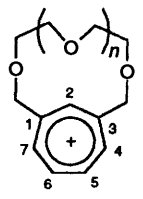
of relatively stable carbocations, and describe here the preparation and some properties of the tropylium containing crowns, **5** (n = 3 and 4), and 9-xanthylium containing crowns, **6** (n = 3–5). Alkylations of amines and amides by both tropylium[9] and 9-xanthylium[10] have been described. Indeed, xanthydrol itself is a classical reagent for crystalline derivatives of amides, with *N*-9-xanthylamides prepared by heating with primary or secondary amides in acetic acid solution.[11]

Carbocation stabilities in aqueous media are measured by K_{R^+}, the equilibrium constant for hydrolyses of the cation, as shown in eqn. (1) for a secondary ion.

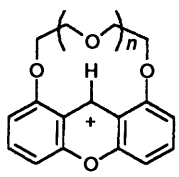
$$>\overset{+}{C}\text{–H} + H_2O \underset{}{\overset{K_{R^+}}{\rightleftharpoons}} >\text{CH–OH} + H^+;$$

$$K_{R^+} = \frac{[>\text{CHOH}][H^+]}{[>\text{C–H}^+]} \quad (1)$$

The fully aromatic tropylium ion has $pK_{R^+} = 4.74$,[12] and alkyl substitution increases pK_{R^+} by about 0.5 units per alkyl group,[13] so that, in the absence of a large effect from a bridging



5 (n = 3 and 4)

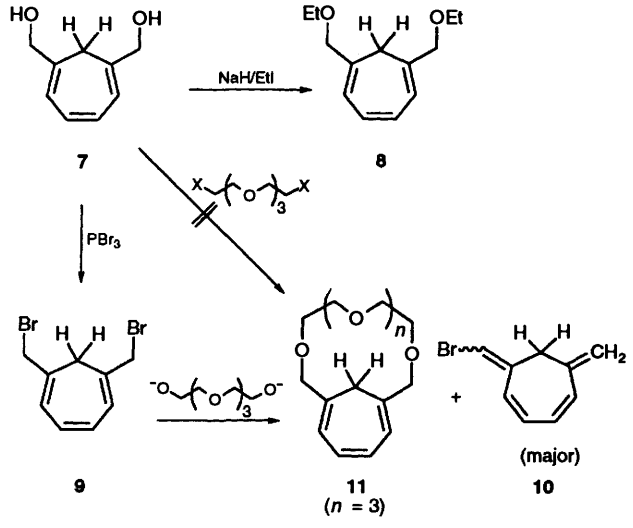


6 (n = 3,4, and 5)

polyether chain, cations **5** (n = 3 and 4) were expected to be stable in very dilute aqueous acid. 9-Xanthylium has a pK_{R^+} = −0.17,[14] and requires much stronger acid (*ca.* 5% sulfuric) for generation of a high equilbrium concentration of the cation from the alcohol. However, in crown ethers **6** (n = 3–5), the oxygens at the 1- and 8-positions which provide the attachment of the macrocyclic polyether would also stabilize the cations and perhaps permit them to survive in more moderately acidic conditions, approaching those in which amidases usually function. Xanthydrols are also known to suffer adiabatic photodehydroxylation[15] in aqueous solution, and this suggests the possibility that xanthenols derived from **6** (n = 3–5) might be photoactivated in their catalysis of amide hydrolyses in neutral solution.

Preparation and characterization of 5 (n = 3 and 4)

Since cycloheptatrienes are readily converted to tropylium ions by hydride transfer to a less stable carbocation such as triphenylcarbenium,[16] the poly(oxyethylene) bridged cycloheptatrienes were attractive stable precursors of the cations. Initial efforts to prepare these (see Scheme 1) centred on use of



Scheme 1 Conversions of 1,6-hydroxymethylcycloheptatriene

1,6-bis(hydroxymethyl)cycloheptatriene, **7**, available from cycloheptatriene[17] in a five-step sequence, as the cycloheptatriene component. Alkylations with ethyl iodide were successful yielding the corresponding diethyl ether, **8**, but a crown ether product could not be isolated from reactions with tetragol dibromide or ditosylate. Conversion of **7** to the dibromide, **9**, and reaction with the bis(alkoxide) of tetragol yielded the reactive tetraene, **10**, a product of 1,6-elimination of HBr from **9**, and small amounts (< 5%) of the crown ether **11**. This showed a ^{1}H NMR spectrum with only two signals in the alkene region and a singlet at δ 2.55 from the endocyclic methylene, consistent with its symmetry, as was the 4 H singlet at δ 4.15, from the oxymethylenes attached directly to the cycloheptatriene. Signals of the protons of the bridging tetraethylene glycol chain were not resolved, appearing as a 16 H signal centred at δ 3.7.

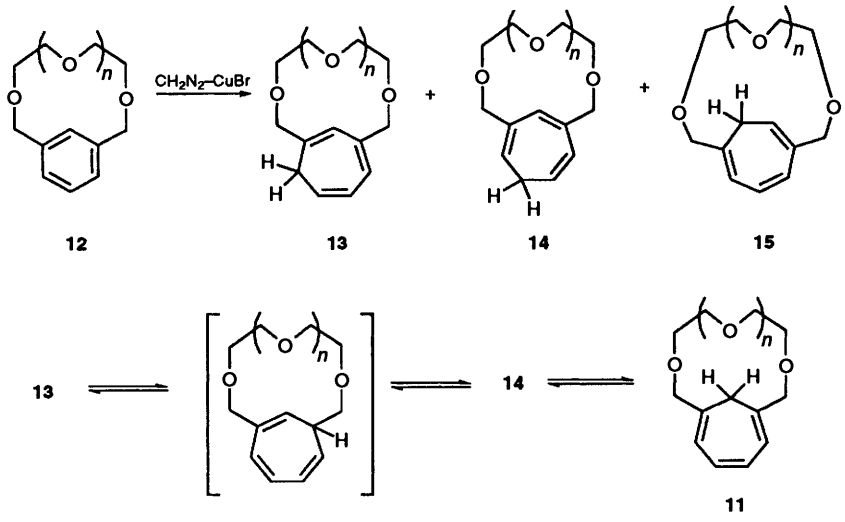
An alternative approach (Scheme 2), by ring expansion of readily available bridged *meta*-xylenes,[18] **12**, afforded a shorter and more practicable route to bridged cycloheptatrienes. Reaction of **12** (n = 3) with diazomethane, to low conversions, yielded a 2:2:1 mixture of three isomeric ring expansion products, separable only by preparative HPLC. The minor component had a distinctive ^{1}H NMR spectrum in that none of the four signals in the alkene region were singlets and was assigned the 1,5-bridged cycloheptatriene structure, **15** (n = 3). ^{1}H NMR spectra of both major components showed 1 H singlets in their alkene region, and we associate these with hydrogen attached at the ring site between the oxymethyl substituents. Other alkene signals were a well resolved doublet, quartet and triplet, consistent with either structures **13** (n = 3) or **14** (n = 3), and assignments were resolved by splitting patterns of the 7-methylene signals which was a 2 H doublet in the case of **13** (n = 3), and a triplet in the case of **14** (n = 3).

Confirmation that these two compounds were indeed double-bond position isomers was provided by their thermal equilibration by sequential 1,5-hydrogen shifts[19] as shown in Scheme 2, to yield a 1:2:6 mixture of **13** (n = 3), **14** (n = 3) and **11** (n = 3), which cannot be formed by the ring expansion, but which was readily identified by its simple ^{1}H NMR spectrum and comparison with material prepared by the alkylation sequence of Scheme 1. The ratio of isomers is in qualitative agreement with the results of empirical force field calculations which gave steric energies of 105.3, 105.2 and 101.1 kJ mol^{-1}, respectively, for the isomers. The equilibration might also yield the isomer with a tertiary 7-cycloheptatrienyl hydrogen, but this was not formed in detectable amounts.

The ambient temperature ^{1}H NMR spectra of **13** (n = 3), **14** (n = 3) and **11** (n = 3) give no suggestion of a substantial barrier to tub-to-tub ring inversion of the bridged cycloheptatrienes, and indeed, precedent[20] and molecular modelling suggests that the bridging tetraethylene glycol chain will not hinder the process. At lower temperatures, however, 500 MHz spectra of the isomers in freon solution showed changes consistent with this slowing of this process. Most obviously, signals from cycloheptatriene methylenes, a singlet at δ 2.81 from **11**, a triplet at δ 2.48 from **14**, and a doublet at δ 2.55 from **13**, broadened, vanishing into the base line at −115 °C. Lowest accessible temperatures were only a few degrees below this, and 'static' spectra were not obtained. However, if the chemical shift differences between non-equivalent methylene protons are of the order of those found by Anet[21] in cycloheptatriene itself (1.2 ppm), the observed line broadening allows estimation[22] of rates of *ca.* 10^4 s^{-1} at −80 °C for the process which exchanges methylene hydrogen sites, close to those found for cycloheptatriene itself, and confirming that the polyethylene glycol bridge does not inhibit the ring inversion process.

Similar diazomethane treatment of **12** (n = 4) yielded the corresponding ring expanded isomers, again requiring separation by preparative HPLC. The ratio of isomers was now 2:5:3, and isomers were readily identified from their ^{1}H NMR spectra as described above. Thermal rearrangement of either **13** (n = 4) or **14** (n = 4) produced a 1:3 mixture of **14** (n = 4) and the symmetrical isomer **11** (n = 4). Again, this equilibrium distribution is in reasonable qualitative agreement with the results of the molecular modelling studies which gave steric energies for **13** (n = 4) or **14** (n = 4) and **11** (n = 4) of 90.1, 86.0 and 85.5 kJ mol^{-1}, respectively.

For conversion to the cationic crowns, the bridged cycloheptatrienes were dissolved in either deuteriated acetonitrile, or deuteriated dichloromethane in a NMR tube, and aliquots of



Scheme 2 Ring expansion of 1,3-xylyl-18C5 and 1,3-xylyl-21C6 and thermal rearrangement of bridged cycloheptatrienes

triphenylcarbenium tetrafluoroborate solution added, with changes monitored by ^{1}H NMR spectroscopy. Reactions were quantitative, with persistence of the deep orange colour of excess triphenylcarbenium serving as a convenient indicator for the equivalence point.

Isomers **13** (n = 3), **14** (n = 3) or **11** (n = 3) reacted to yield material with identical spectra. The conversions of **13** (n = 3) and **14** (n = 3) were rapid, occurring within the time required to transfer the tube to the NMR probe; those of **11** (n = 3) were a little slower, and the course of reaction could be followed by sequential monitoring. These solutions were indefinitely stable in the absence of atmospheric moisture. In all cases, signals for the trityl cation were replaced by those of triphenylmethane, with its methine hydrogen giving a characteristic singlet at δ 5.52. Alkene signals from the cycloheptatriene were replaced by a 1 H singlet at δ 9.71, and a 4 H multiplet centred at δ 8.9, chemical shift changes which are consistent with formation of the symmetrically 1,3-disubstituted tropylium ion, **5** (n = 3).[23] Signals associated with methylenes attached to the cycloheptatrienes, which appear between δ 4.1 and 4.2 in all isomers, were replaced by a sharp 4 H singlet at δ 5.15, and the signals from the protons of the tetraethylene glycol chain were now resolved into four distinct 4 H signals lying between δ 3.5 and 4.0, forming two clear A_2B_2 patterns.

Similar treatment of the homologous bridged cycloheptatrienes **13** (n = 4), **14** (n = 4) or **11** (n = 4) yielded corresponding spectra, also consistent with tropylium ion formation. Signals from the protons of the pentaethylene glycol chain of **5** (n = 4) now appeared as two 4 H multiplets at δ 3.9 and 3.75, with a 12 H multiplet centred at δ 3.6.

That these changes are associated with tropylium ion formation is supported further by regeneration of the cycloheptatrienes on reaction with ethanolic sodium borohydride. Reaction of **5** (n = 3) yielded **13** (n = 3), **14** (n = 3), and **11** (n = 3) in 8:3:9 ratio, with reaction at the intra-annular site between the bridge attachments thus showing a small preference in this kinetically controlled addition. This preference is not, however, shown in reduction of the homologous cation **5** (n = 4) which yields **13** (n = 4), **4** (n = 4) and **11** (n = 4) in 2:1:1 ratio.

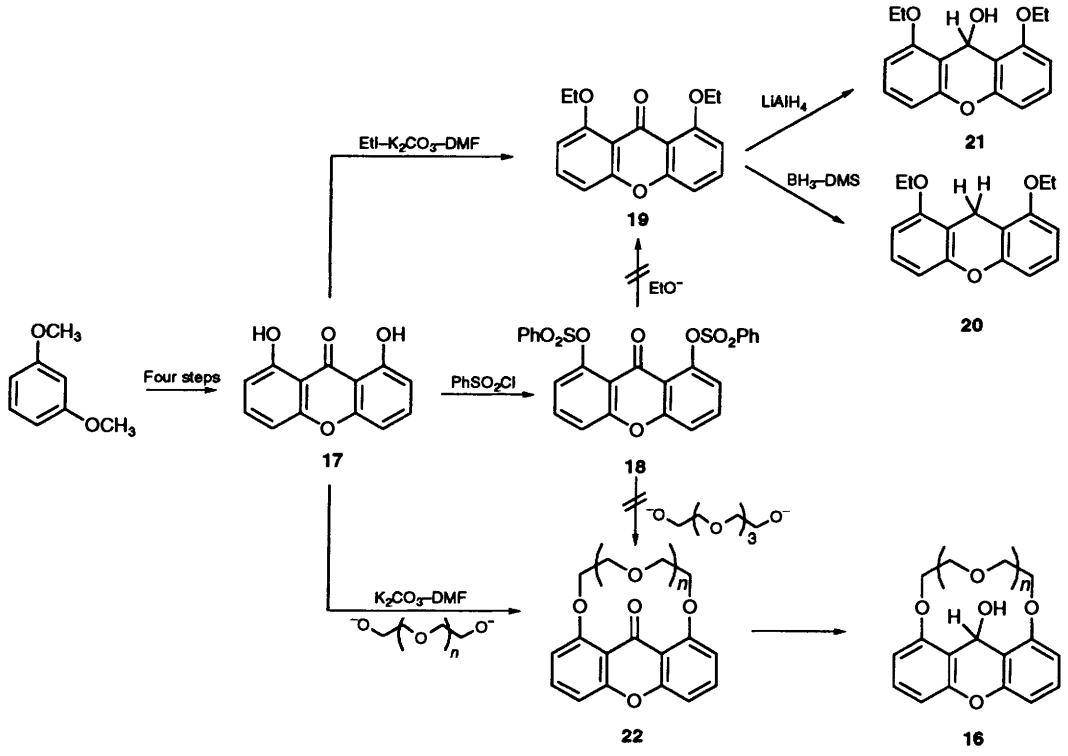
UV spectra obtained by addition of aliquots of the acetonitrile cation solutions to buffered 50:50 vol:vol aqueous acetonitrile, provided an approximate pK_{R^+} measurement of the cations. Absorptions are those of the bridged tropylium or cycloheptatrienols superimposed on that of triphenylmethane and perhaps also a trace of triphenylmethanol. Neither of the latter have significant absorption above 240 nm and are not sensitive to pH changes in the region of interest. When solutions have pH $\leqslant$ 3.5, the spectra are not pH dependent, and show distinct shoulders at 257 (log ε = 4.18) and at 301 nm (3.88), and a significant tailing absorption out to 330 nm. In solutions with pH $\geqslant$ 4.0, the long wavelength shoulder and tail are absent, and the spectra develop a distinct maximum at 259 nm (log ε = 4.15). These pH dependent changes are reversible, although solutions with high pH decompose slowly, irreversibly developing longer wavelength absorptions. We associate the reversible changes with interconversion of cation with pK_{R^+} = 3.8 ± 0.2 and its hydrolyses products. The decomposition products formed irreversibly at high pH, have not been characterized, and at present we can only speculate on the possibility of disproportionation of cations and cycloheptatrienols to cycloheptatrienones and cycloheptatrienes,[24] or of polymerization *via* heptafulvene formation.[25]

Preparation and characterization of 6 (n = 3–5)

The xanthydrols, **16**, are the obvious neutral precursors of these cations, but xanthenes could also yield the cations by a hydride abstraction reaction. Either were to be available by the synthetic scheme adopted (Scheme 3).

1,8-Dihydroxyxanthone, **17**, provided the xanthyl component of the crown ethers, and of related model compounds carrying 1,8-diethoxy groups. Baeyer[26] prepared **17** by aluminium bromide induced cyclization and demethylation of 2,2',6,6'-tetramethoxybenzophenone and we found that, provided the aluminium bromide was of high quality, we could not improve on the original method. 2,2',6,6'-Tetramethoxybenzophenone was itself obtained conveniently from 1,3-dimethoxybenzene by metalation[27] and reaction with ethyl formate to yield 2,2',6,6'-tetramethoxydiphenylmethanol which was oxidized in high yield by chromic acid in acetone. Others have commented[28] on the strong hydrogen intramolecular bonding in 1,8-dihydroxyxanthone revealed by low frequency OH and >C=O stretching bands in its IR spectrum. In its ^{1}H NMR spectrum, hydroxy hydrogens give a signal at δ 11.9 and exchange with added D_2O was only complete after several hours.

Reactions of the bis(benzene sulfonate) of 1,8-dihydroxyxanthone, **18**, with ethoxide or polyetheneglycol alkoxides were attempted, in the hope of displacing the sulfonate leaving groups by an addition–elimination sequence of the kind observed by Gokel *et al.*[29] in his preparation of anthraquinone-containing crowns. However, no substitution products were



Scheme 3 Preparation of 1,8-diethoxyxanthydrol, 1,8-diethoxyxanthone, and crown ethers containing xanthone and xanthydrol residues

observed, and under forcing conditions, 1,8-dihydroxyxanthone was reformed, presumably by attack of alkoxide at sulfur rather than at the 1- or 8-carbons of the xanthone.

Alkylation of 1,8-dihydroxyxanthone with ethyl iodide in the presence of potassium carbonate in dimethylformamide (DMF) proceeded smoothly to give 1,8-diethoxyxanthone, **19**. Interestingly, this compound seemed more polar than its phenolic precursor, showing lower R_f values on silica, and being extremely difficult to free from water. Both IR and ^{1}H NMR spectroscopy of recrystallized material showed the presence of hydroxy hydrogens and elemental analysis gave a poor agreement with values calculated for its molecular formula, but reasonable agreement with the composition of a hemi-hydrate.

The reduction of xanthone itself by borane is reported to yield xanthene[30] and reaction of the 1,8-diethoxyxanthone, **19**, with borane–dimethylsulfide in refluxing tetrahydrofuran (THF), yielded the corresponding hydrocarbon 1,8-diethoxyxanthene, **20**. With lithium aluminium hydride in THF (but not with potassium borohydride in methanol) ketone **19** was reduced to 1,8-diethoxyxanthydrol, **21**. IR spectroscopy confirmed loss of the carbonyl group, and presence of the hydroxy group. In the ^{1}H NMR spectrum, the alcohol hydroxy hydrogen, exchangeable with D_2O, appeared as a doublet, $J = 3.9$ Hz, at δ 2.8, and the alcohol methine hydrogen as a doublet also, at δ 6.4. Signals from the ethoxy group methylenes and methyl showed additional splittings consistent with their being diastereotopic hydrogens, confirming the conversion of the ketone to a prochiral centre at the 9-position of the xanthyl residue.

Incorporation of phenolic residues into macrocyclic ethers has usually involved the alkylation of phenoxides by polyethylene glycol ditosylates. In our hands, the dibromides, conveniently prepared from the glycols with phosphorus tribromide in ether, were as effective in cyclizations with phenoxides. Thus, the xanthone containing crown ethers **22** (n = 3–5) were prepared in 44, 58 and 44% recrystallized yield, respectively, by reaction of 1,8-dihydroxyxanthone with the appropriate polyethyleneglycol dibromide in DMF in the presence of potassium carbonate. Replacement of potassium carbonate by caesium carbonate caused no dramatic difference in rates of consumption of 1,8-dihydroxyxanthone or yield of cyclized material.[31]

Reductions of the crown ketones were less straightforward than those of 1,8-diethoxyxanthone. The smallest of the crowns, **22** (n = 3), was reduced by methanolic potassium borohydride, and yielded the corresponding xanthydrol, **16** (n = 3), with little difficulty. Reduction of the larger ring ketones, **22** (n = 4) and **22** (n = 5), however, again required use of lithium aluminium hydride in THF, and careful control of reaction time and temperature. Their reactions were clearly slower than those of 1,8-diethoxyxanthone and the resulting xanthydrols were not indefinitely stable to the reaction conditions, especially at higher temperatures, being slowly converted to secondary reduction products identified as the xanthenes.

The low field regions of ^{1}H NMR spectra bridged xanthydrols, **16** (n = 3–5), differ little from that of 1,8-diethoxyxanthydrol **21**, showing signals from the aromatics of the xanthyl residue as a triplet and two doublets at δ 7.31, 6.75 and 6.86, respectively, and from the alcohol methine at δ 6.3. Solutions in chloroform are colourless, but become deep red on addition of trifluoroacetic acid (TFA), and show downfield shifts in all signals of the spectrum; *e.g.*, the triplet and doublets of the xanthyl are shifted to δ 8.41, 7.6 and 7.21, respectively. Most notably, the signal of the alcohol methine shifts downfield by over 4 ppm to δ 10.6, a shift comparable to that accompanying ionization of simpler diphenylmethanols,[32] and indicating substantial development of positive charge at this centre. Notable also in the spectrum of **21** in TFA is the simplification of the signals of the ethyl groups to a simple triplet and quartet, consistent with destruction of the prochiral centre at the 9-position (Fig. 2). We believe that these solutions, which are indefinitely stable, contain the cations.

The acid–base behaviour of both the alcohols, **16** (n = 3–5) and the ketones, **22** (n = 3–5) in aqueous media were examined, and we report here measurements of the equilibria for form-

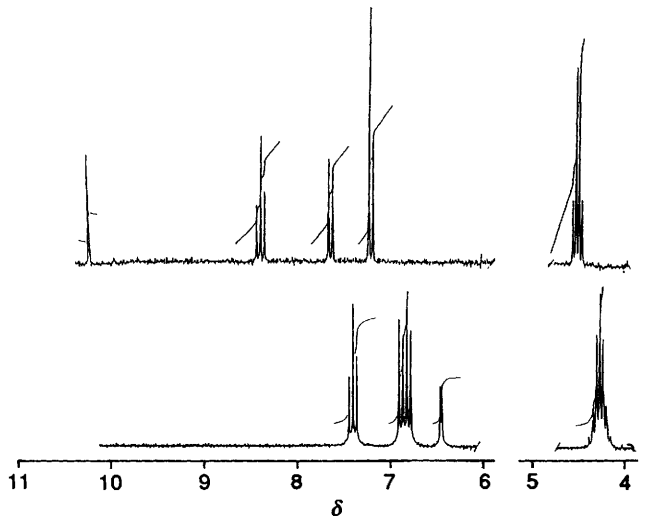


Fig. 2 Low field region of the ^{1}H-NMR spectra of 1,8-diethoxyxanthydrol in deuteriochloroform solution, with (above) and without (below) added trifluoroacetic acid

Table 1 Basicity data for ionization of xanthones (**19** and **22**) and xanthydrols (**16** and **21**) in aqueous sulfuric acid solutions at 25 °C

Compound	pK_a[b]	pK_{R^+}[b]
Xanthone[a]	−4.81	
19	−1.93	
22 (n = 3)	−1.94	
22 (n = 4)	−1.99	
22 (n = 5)	−2.12	
Xanthydrol[a]		−0.17
21		1.38
16 (n = 3)		0.78
16 (n = 4)		1.08
16 (n = 5)		0.99

[a] Data from Arnett and Bushwick, see ref. 11. [b] Mean values of two separate determinations; estimated uncertainties ≤ ±0.05 units.

ation of the cations from the xanthydrols [eqn. (1)] and of the basicity of the ketones [eqn. (2)].

$$>C{=}OH^+ \overset{K_a}{\rightleftharpoons} >C{=}O + H^+;$$

$$K_a = \frac{[>C{=}O][H^+]}{[>C{=}OH^+]} \quad (2)$$

1,8-Diethoxyxanthone and the crown ketones show indistinguishable UV spectra with λ_{max} = 240 (log ε = 4.26), 304 (3.90) and 338 nm (3.57). Solutions in 80% sulfuric acid are yellow and show bands at 272 (log ε = 4.56), 319 (3.77), 368 (4.05) and 438 nm (3.63). The solutions appear to be stable, and the ketones were recovered unchanged on dilution and extraction, and we associate the spectroscopic changes with reversible protonation on carbonyl oxygen.[33] Spectrophotometric measurements on a series of solutions in sulfuric mixtures of known strengths from 80 to 5% sulfuric acid yielded acidity constants (based on the H_0 scale) of the conjugate acids of the ketones which are presented in Table 1.

1,8-Diethoxyxanthydrol and the crown xanthydrols also show indistinguishable spectra with λ_{max} = 224 (log ε = 4.38) and 274 nm (3.86). Solutions in 80% sulfuric acid are red, showing bands at 226 (log ε = 4.48), 282 (4.45), 358 (4.21), 448 (3.88) and 516 nm (3.52), and we associate the red colour with formation of the 9-xanthylium cations.[34] Immediate dilution and extraction recovers the xanthydrols in good yield. These acid solutions are not indefinitely stable, with the red colour being discharged over a period of several hours at 25 °C. The

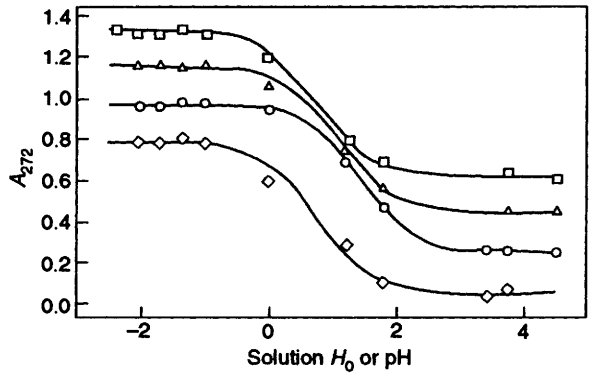
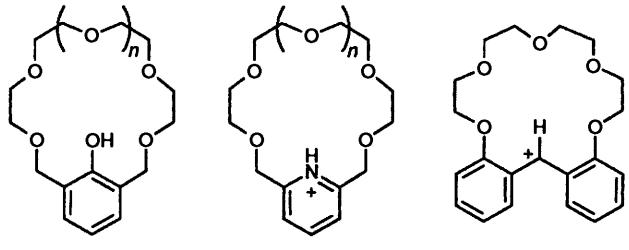


Fig. 3 Spectrometric titration of **16** (n = 3), ◇, **16** (n = 4), △, **16** (n = 5), □, and **21**, ○. For clarity, data sets have been offset on the absorbance axis.

nature of this decay is still under investigation; it may involve a disproportionation of cation and alcohol, a process known to occur in acid treatment of xanthydrol itself,[35] but it does not interfere significantly with measurements of the equilibria for ionization. The variation of absorbance at 282 nm of freshly made solutions in acids of varying strength as measured by H_0 or pH are shown in Fig. 3, together with the best fit curves to the data. A more appropriate measure of acid strength[36] for carbocation formation is the H_R scale, but in practice, H_0 and H_R scales diverge only at acid strengths well above those at which these xanthydrols ionize. The results of the measurements are presented also in Table 1.

As expected, introduction of the alkoxy substituents at 1- and 8-positions of the xanthyl residue stabilizes the cationic forms. 1,8-Diethoxyxanthone is 2.88 pK units more basic than xanthone itself, but the replacement of ethyl groups by the macrocyclic ether link has little further effect on carbonyl basicity, with a weak trend only to higher basicity in the larger ring sizes. The pattern resembles that found in 2-hydroxy-1,3-xylyl crown ethers, **23**.[37] For the 15-crown-4, 18-crown-4 and 21-crown-6, the pK_a of intra-annular phenol are 10.8, 10.6 and 10.5, while the model 2,6-dimethylphenol has pK_a = 10.7. Where more substantial ring size effects have been observed in, *e.g.*, the 2,6-pyridocrowns, **24**, where the



23 **24** **25**

pK_a of the pyridiniums are 4.88, 4.95 and 4.16 for the 15-, 18- and 21-membered rings and the model 2,6-bismethoxymethylpyridine has pK_a = 3.36, enhancement of basicity is linked to the ability of the protonated pyridiniums to encapsulate a water molecule.[38]

With the xanthydrols, ethoxy groups at 1- and 8-positions stabilize the xanthylium cation by 1.55 pK_{R^+} units, but introduction of the macrocyclic array in **16** (n = 3) destabilizes the cation by 0.6 pK units. The pattern is thus reversed from that observed in the 18-membered ring containing diphenylmethyl cation, **25**, which has pK_{R^+} = −8.25, while the model 2,2′-dimethoxydiphenylmethyl cation has pK_{R^+} = −8.85.[4] There is no obvious trend in pK_{R^+} associated with increasing the macrocycle ring size in this series.

Experimental

^{1}H NMR spectra were recorded on a Varian Gemini-200 (200 MHz) spectrometer and ^{13}C NMR spectra on a Brüker AC-300 (75 MHz) spectrometer. All chemical shifts are quoted downfield from tetramethylsilane (δ). Signal splittings are reported as: singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m); *J*-values are in Hz. IR spectra were recorded on a Perkin-Elmer 1710 Infrared Fourier Transform Spectrometer or an ATI Mattson Genesis Series FTIR and were run as films evaporated from dichloromethane. UV spectra were recorded on a Shimadzu UV-260 UV–Visible Recording Spectrophotometer or on a Hewlett Packard 8452A Diode Array Spectrophotometer. Mass spectra were recorded on a Kratos MS25 or a Fisons VG Trio 2000. Modes of ionization are indicated as follows: electron impact (EI), chemical ionization (CI) and fast atom bombardment (FAB). Melting points were recorded on a Kofler heated stage microscope and are uncorrected. All temperatures are quoted in °C. TLC was carried out on Polygram Sil G/UV$_{254}$ 0.25 mm silica gel plates or Polygram ALOX N/UV$_{254}$ 0.2 mm aluminium oxide plates with solvent systems as indicated. Analytical HPLC was carried out using the following systems: Waters 510 HPLC pump, Waters 'Z' module with 4 m ODS Nova-Pak 100 × 8 mm column, Perkin-Elmer LC480 Diode Array System. Preparative HPLC was carried out using Gilson 306 and 303 pumps with 25 cm^3 heads, Gilson Monometric Module with Monometric Adaptor, Gilson 811B Dynamic Mixer with 1.5 cm^3 filter unit, Gilson 115 UV Detector at 273 nm, Rainin Dynamax 60A C18 column ODS 21.4 mm ID × 250 mm with a guard column. Elemental analyses were carried out at the micro-analytical laboratories at the University of Manchester under the direction of Mr M. Hart.

3,6,9,12,15-Pentaoxabicyclo[15.4.1]docosa-17,19,21-triene [(11) (*n* = 3)]

A solution of the potassium salt of tetraethylene glycol was prepared by heating the glycol (1.005 g, 5.2 mmol) with a suspension of potassium *tert*-butoxide (1.163 g, 10.4 mmol) in toluene (10 cm^3) under a nitrogen atmosphere for 1 h. This alkoxide solution (1.8 cm^3) was then added by syringe to a stirred solution of 1,6-bis(bromomethyl)cyclohepta-1,3,5-triene[39] (**9**) (0.104 g, 0.37 mmol) in toluene and the mixture refluxed under nitrogen for 3 h before cooling and filtration to remove precipitated potassium bromide. The filtrate was applied directly to a column of neutral alumina. Elution with tetrahydrofuran yielded two compounds. The less polar, **10**, (0.062 g, 84%) had δ_H(CDCl$_3$) 6.52 (1 H, d), 6.34 (1 H, d), 6.15 (2 H, m), 6.15 (1 H, s), 6.02 (1 H, dd, *J* 8 and 12) and 5.85 (1 H, dd, *J* 8 and 12) 3.29 (2 H, s); the more polar, **11** (*n* = 3) (0.009 g, 8%) showed ν_{max}(CHCl$_3$)/cm^{-1} 2254, 1522, 1440, 1384, 1257 and 1217; δ_H(CDCl$_3$) 6.5 (2 H, t, *J* 4, cht†), 6.15 (2 H, dd, *J* 4, cht), 4.15 (4 H, s, chtCH_2), 3.8–3.55 (16 H, m, OCH_2CH_2O) and 2.55 (2 H, s, cht); *m*/*z* (CI/NH$_3$) 328 (M + 18, 73%) and 311 (M + 1, 100) (Found: M, 328.2122. $C_{17}H_{30}NO_5$ (*M* + NH$_4$) requires 328.2124).

1,6-Bis(ethoxymethyl)cyclohepta-1,3,5-triene (8)

1,6-Bis(hydroxymethyl)cyclohepta-1,3,5-triene[20] (**7**) (0.1 g, 0.66 mmol) was dissolved in dry diethyl ether (5 cm^3) and added to a suspension of oil-free sodium hydride (0.062 g, 2.6 mmol) in diethyl ether (2 cm^3). An excess of ethyl iodide (0.4 g, 2.6 mmol) was then added and the mixture stirred overnight. Excess sodium hydride was destroyed by cautious addition of methanol (1 cm^3) and then water (2 cm^3) before the layers separated and the aqueous one was washed with more diethyl ether (2 cm^3). The combined organic phase was dried (magnesium sulfate) and removal of solvent under reduced pressure gave a brown oil. The crude material was bulb-to-bulb distilled (130 °C/18 mmHg) to give a colourless, odourless oil (0.1 g, 72%); ν_{max}(CHCl$_3$)/cm^{-1} 3432, 2925, 1678, 1453, 1376, 1197, 1103 and 744; δ_H(CDCl$_3$) 6.55 (2 H, dd, 3-, 4-H), 6.15 (2 H, t, 2-, 5-H), 4.0 (4 H, s, CH$_2$), 3.48 (4 H, q, OCH_2CH$_3$), 2.4 (2 H, s, 7-H) and 1.2 (6 H, t, OCH$_2$CH_3); *m*/*z* (EI) 208 (M$^+$, 5%), 193 (20), 162 (70), 148 (80) and 91 (100); *m*/*z* (CI, NH$_3$) 226 (M + 18, 20%), 179 (40) and 165 (100).

3,6,9,12,15-Pentaoxabicyclo[15.3.1]henicosa-1(21),17,19-triene [1,3-xylyl-18-C5, 12 (*n* = 3)] and 3,6,9,12,15,18-hexaoxabicyclo[18.3.1]tetracosa-1(24),20,22-triene [1,3-xylyl-21-C6, 12 (*n* = 4)]

These were prepared from 1,3-bisbromomethylbenzene and either tetra- or penta-ethylene glycol by the method of Reinhoudt and Gray.[18]

3,6,9,12,15-Pentaoxabicyclo[15.4.1]docosatriene {-1(22),17,19- [13 (*n* = 3)]} and {-1(22),17,20- [14 (*n* = 3)]} and 3,6,9,12,15-pentaoxabicyclo[15.3.2]docosa-1(21),17,19-triene [15 (*n* = 3)]

A distilled solution of *ca.* 3 g of diazomethane in 70 cm^3 of dichloromethane was prepared from Diazald (*N*-methyl-*N*-nitrosotoluene-*p*-sulfonamide) (18.7 g, 0.087 mol) using apparatus without ground glass joints and dried (potassium hydroxide pellets). This solution was added from a dropping funnel over 20 min to a refluxing mixture of the crown ether **12** (*n* = 3) (0.5 g, 1.69 mmol) and copper(I) bromide (100 mg, 0.7 mmol) in dichloromethane (20 cm^3) which had been refluxing for 1 h. The resulting solution was refluxed for a further 30 min and allowed to cool before the solvent was removed and diethyl ether (10 cm^3) added. A precipitate of polyethylene was filtered off and the resulting pale green solution was concentrated under reduced pressure to afford an oil (0.61 g). Isomeric products were separated by HPLC with elution time in the range 25–30 min (flow rate 15 cm^3 min^{-1}, 52% methanol, 48% water, UV detector, 10 mm cell at 273 nm, reverse phase). The isomers, **13** (*n* = 3), **14** (*n* = 3) and **15** (*n* = 3), in order of increasing retention time, were formed in the approximate ratio 1:2:1. The mixture of cycloheptatrienyl isomers gave ν_{max}(CHCl$_3$)/cm^{-1} 2917m, 2850m, 1450m, 1352m and 1106s; λ_{max}(log ε_{max})(EtOH)/nm 206 (3.3) and 267 (3) (Found: M, 328.2140. $C_{17}H_{30}NO_5$ requires *M*, 328.2124); *m*/*z* (CI/NH$_3$) 328 (M + 18, 10%), 311 (M + 1, 15), 195 (5), 133 (10), 118 (100), 104 (20) and 91 (10). The isomers were distinguished after separation by their ^{1}H NMR spectra; **13** (*n* = 3) δ_H(CDCl$_3$) 6.48 (1 H, d, *J* 5, cht), 6.3 (1 H, s, cht), 6.15 (1 H, dt, *J* 5, cht), 5.45 (1 H, t, *J* 5, cht), 4.17 (2 H, s, chtCH$_2$), 4.08 (2 H, s, chtCH$_2$), 3.65 (16 H, m, OCH$_2$CH$_2$O) and 2.25 (2 H, d, *J* 5, cht); **14** (*n* = 3) δ_H(CDCl$_3$) 6.85 (1 H, s, cht), 6.1 (1 H, d, *J* 7, cht), 5.5 (1 H, dt, *J* 5, cht), 5.3 (1 H, t, *J* cht), 4.3 (2 H, s, chtCH$_2$), 4.15 (2 H, s, chtCH$_2$), 3.7 (16 H, m, OCH$_2$CH$_2$O) and 2.25 (2 H, t, *J* 6, cht); **15** (*n* = 3) δ_H(CDCl$_3$) 6.55 (1 H, t, *J* 5, cht) 6.1 (2 H, d, *J* 5, cht), 5.5 (1 H, t, *J* 7, cht), 4.15 (2 H, s, chtCH$_2$), 4.14 (2 H, s, chtCH$_2$), 3.7 (16 H, m, OCH$_2$CH$_2$O) and 2.4 (2 H, d, *J* 9, cht).

Thermal equilibration of bridged cycloheptatrienes

A mixture of the isomers **13** and **14** (*n* = 3), (0.005 g, 0.016 mmol), was dissolved in deuteriated benzene (0.5 cm^3) and placed under nitrogen in a NMR tube. The sealed NMR tube was placed in refluxing xylene (bp 151 °C). The NMR spectrum

† cht = cycloheptatriene.

was recorded every 24 h until no further changes in the spectra were observed (72 h). Signals attributable to isomers **13** and **14** ($n = 3$) decreased in intensity and were matched by a corresponding increase in signals due to the symmetrical isomer **11** ($n = 3$), which were also identified by HPLC comparison with material prepared by an alternative route (see above). Integration of the signals from cycloheptatrienyl methylenes and HPLC gave the ratio of **11** ($n = 3$):**14** ($n = 3$):**13** ($n = 3$) as 6:2:1.

3,6,9,12,15,18-Hexaoxabicyclo[18.4.1]pentacosatrienes {-1(25),20,22- [13 ($n = 4$)] and -1(25),20,23- [14 ($n = 4$)]} and 3,6,9,12,15,18-hexaoxabicyclo[18.3.2]pentacosa-1(24),20,22-triene [15 ($n = 4$)]

Addition of a dichloromethane solution of diazomethane to a refluxing mixture of the crown ether **12** ($n = 4$) (0.5 g, 1.69 mmol) and copper(I) bromide (100 mg, 0.7 mmol), as described above, yielded a crude product (oil 600 mg) which by NMR spectroscopy showed a 40% conversion to substituted cycloheptatrienes. The mixture of cycloheptatrienyl isomers gave $\nu_{max}(CHCl_3)/cm^{-1}$ 2917m, 2850m, 1450m, 1352m and 1106s; λ_{max}(EtOH)/nm 206 and 267 (Found: M, 372.2375. $C_{19}H_{34}NO_6$ requires *M*, 372.2386); *m/z* (EI) 355 (M^+, 0.6%), 239 (3), 195 (6) and 118 (100); *m/z* (CI/NH_3) 372 (M + 18, 100%), 328 (20) and 256 (30). Isomers were separated by HPLC with elution times in the range 28–35 min (flow rate 15 $cm^3\ min^{-1}$, 52% methanol, 48% water, UV detector, 10 mm cell at 273 nm, reverse phase). The isomers **13** ($n = 4$), **14** ($n = 4$) and **15** ($n = 4$), eluted in order of increasing retention time, were formed in the ratio 20:53:27. The separated isomers were distinguished by their NMR spectra; isomer **13** ($n = 4$) $\delta_H(CDCl_3)$ 6.48 (1 H, d, *J* 5, cht), 6.3 (1 H, s, cht), 6.15 (1 H, dt, *J* 5, cht), 5.45 (1 H, t, *J* 5, cht), 4.17 (2 H, s, chtCH_2), 4.08 (2 H, s, chtCH_2), 3.65 (20 H, m, OCH_2CH_2O) and 2.25 (2 H, d, *J* 5, cht); isomer **14** ($n = 4$) $\delta_H(CDCl_3)$ 6.85 (1 H, s, cht), 6.1 (1 H, d, *J* 7, cht), 5.5 (1 H, dt, *J* 5, cht), 5.3 (1 H, t, *J* 5, cht), 4.3 (2 H, s, chtCH_2), 4.15 (2 H, s, chtCH_2), 3.7 (20 H, m, OCH_2CH_2O) and 2.25 (2 H, t, *J* 6, cht); isomer **15** ($n = 4$) $\delta_H(CDCl_3)$ 6.55 (1 H, t, *J* 5, cht) 6.1 (2 H, d, *J* 5, cht), 5.5 (1 H, t, *J* 7, cht), 4.15 (2 H, s, chtCH_2), 4.14 (2 H, s, chtCH_2), 3.7 (20 H, m, OCH_2CH_2O) and 2.4 (2 H, d, *J* 9, cht).

Thermal rearrangement of isomers 13 ($n = 4$) and 14 ($n = 4$)

A mixture of the isomers **13** ($n = 4$) and **14** ($n = 4$) (0.005 g, 0.014 mmol) was heated at 150 °C in a sealed NMR tube as described above. Signals attributable to isomers **13** ($n = 4$) and **14** ($n = 4$) decreased in intensity with those of **13** ($n = 4$) disappearing completely after 72 h, and were matched by a corresponding increase in new signals; $\delta_H(CDCl_3)$ 6.5 (2 H, t, *J* 4 cht), 6.15 (2 H, dd, *J* 4, cht), 4.15 (4 H, s, chtCH_2), 3.8–3.55 (20 H, m, OCH_2CH_2O) and 2.55 (2 H, s, cht). These are assigned to the symmetrical isomer **11** ($n = 4$). Integration of cycloheptatrienyl methylene signals and HPLC analysis gave the ratio **14** ($n = 4$):**11** ($n = 4$) as 1:3.

Generation of carbocations 5 ($n = 3$ and 4)

Triphenylcarbenium tetrafluoroborate (0.17 g) was warmed to 40 °C and evacuated to constant weight. Deuteriated acetonitrile (5 cm^3) was added under nitrogen to give a deep orange solution of known concentration. Aliquots of this solution were added to deuterioacetonitrile solutions of the precursors (*ca.* 0.025 g) in an NMR tube using a microsyringe, and ^1H NMR spectra were obtained after each addition. The procedure was repeated until all the hydrocarbon had been converted to carbocation (by NMR), or the yellow colour of excess triphenylcarbenium ion persisted. The solutions then showed signals of the cations superimposed on those of triphenylmethane.

Reaction of **11** ($n = 3$), **14** ($n = 3$) and **13** ($n = 3$) gave **5** ($n = 3$) with $\delta_H(CD_3CN)$ 9.7 (1 H, s, 2-H), 9.0–8.85 (4 H, m, 4-, 5-, 6-, 7-H), 5.15 (4 H, s, $C_7H_7{}^+CH_2$), 4–3.85 (8 H, m, $C_7H_7{}^+CH_2OCH_2CH_2$) and 3.8–3.65 (8 H, m, OCH_2CH_2O).

Reaction of **11** ($n = 4$), **14** ($n = 4$) gave **5** ($n = 4$) with $\delta_H(CD_3CN)$ 9.3 (1 H, s, 2-H), 8.95 (4 H, m, 4-, 5-, 6-, 7-H), 5.2 (4 H, s, $C_7H_7{}^+CH_2$), 3.9 (4 H, m, $C_7H_7{}^+CH_2OCH_2$), 3.75 (4 H, m, $C_7H_7{}^+CH_2OCH_2CH_2$) and 3.7–3.5 (12 H, m, OCH_2CH_2O).

1,8-Dihydroxyxanthone (17)

2,2',6,6'-Tetramethoxybenzophenone[40] (2.95 g, 9.8×10^{-3} mol) was dissolved in benzene (100 cm^3) in a dry round-bottomed flask fitted for stirring and distillation. A solution of freshly prepared aluminium bromide[41] in carbon disulfide (18 cm^3 of prepared solution, 5.7×10^{-2} mol of $AlBr_3$) was added and the temperature raised to 46 °C to allow the carbon disulfide to distil off. The temperature was then maintained at 74 °C for 15 min before being raised to 80 °C to distil off most of the benzene. After cooling, ice (60 g), dichloromethane (50 cm^3) and 60% aqueous hydrogen bromide (90 cm^3) were added and the mixture distilled to remove the dichloromethane, the remainder of the benzene and the water. The mixture was cooled and the crude brown product filtered off. Sublimation (1–3 mmHg/150–180 °C) yielded yellow crystals (1.73 g, 78%); mp 192–194 °C (lit.,[29] 187 °C); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2929, 1654, 1628, 1604, 1487, 1285 and 1218; δ_H(200 MHz; $CDCl_3$) 6.6–6.8 (2 H, d, *J* 10), 6.8–7.0 (2 H, d, *J* 10), 7.6–7.8 (2 H, t, *J* 10) and 11.8 (2 H, s); *m/z* (EI) 229 (20%), 228 (100) and 200 (25); *m/z* (CI/NH_3) 229 (100%) and 228 (100).

1,8-Bis(benzenesulfonyloxy)xanthone (18)

Benzenesulfonyl chloride (0.1 g, 3 drops) was added to a solution of 1,8-dihydroxyxanthone (0.1 g, 4.4×10^{-4} mol) in a mixture of pyridine (2 cm^3) and triethylamine (2 cm^3). The mixture was refluxed for 5 min, cooled in ice, and water (0.5 cm^3) was added. After standing at room temperature for 5 min, the mixture was diluted with water and extracted with dichloromethane. The combined organic extracts were washed with dilute (1 mol dm^{-3}) hydrochloric, dried (Na_2SO_4) and evaporated. Recrystallization of the residue from toluene afforded yellow crystals of **12** (0.15 g, 67%); mp 174–176 °C (Found: C, 59.2; H, 2.9; S, 12.3. $C_{25}H_{16}O_8S_2$ requires C, 59.06; H, 3.15; S, 12.6%); ν_{max}/cm^{-1} 1671, 1467, 1348, 1003, 822 and 758; δ_H(200 MHz; $CDCl_3$) 7.1–7.3 (2 H, d, *J* 10), 7.3–7.5 (2 H, d, *J* 10), 7.5–7.8 (10 H, m) and 8.0–8.2 (2 H, d, *J* 10); *m/z* (EI) 509 (100%), 508 (45), 444 (45), 368 (35), 302 (20) and 77 (15); *m/z* (CI/NH_3) 526 (100%), 508 (35) and 369 (35).

1,8-Diethoxyxanthone (19)

1,8-Dihydroxyxanthone (1.0 g, 4.4×10^{-3} mol) was dissolved in dimethylformamide (200 cm^3) and potassium carbonate (2.0 g) was added. Iodoethane (1.4 cm^3, 0.0176 mol) was added and the mixture refluxed for 2 h. The mixture was cooled, water (80 cm^3) was added and the resulting precipitate extracted with chloroform (3×50 cm^3). The combined chloroform extracts were dried (Na_2SO_4) and evaporated to yield the crude product. Recrystallization from ethanol afforded yellow crystals (0.87 g, 70%); mp 156–160 °C (Found: C, 70.1; H, 5.8. $C_{17}H_{16}O_4$ requires C, 71.83; H, 5.63%); ν_{max}/cm^{-1} 2978, 2953, 2885, 1674, 1595, 1570, 1483, 1456, 1262, 1113, 1092 and 1070; λ_{max} see text; δ_H(200 MHz; $CDCl_3$) 1.55–1.65 (6 H, t, *J* 7.5), 4.15–4.3 (4 H, q, *J* 7.5), 6.7–6.8 (2 H, d, *J* 10), 6.9–7.0 (2 H, d, *J* 10) and 7.45–7.6 (2 H, t, *J* 10); δ_C(75 MHz; $CDCl_3$) 14.67, 65.02,

106.82, 109.10, 114.02, 133.83, 157.09, 159.88 and 175.92; *m/z* (EI) 286 (3%), 285 (10), 284 (30), 269 (50), 255 (100), 241 (40) and 237 (39); *m/z* (CI/NH_3) 287 (3%), 286 (15), 285 (100), 271 (5), 257 (5), 255 (5) and 241 (3).

1,8-Diethoxyxanthydrol (21)

To a solution of 1,8-diethoxyxanthone (0.10 g, 3.5×10^{-4} mol) in dry diethyl ether (50 cm^3) was added lithium aluminium hydride (0.03 g). The mixture was stirred for 15 min after which time saturated aqueous sodium sulfate was added until all the excess lithium aluminium hydride had been transformed into a white solid. The resulting mixture was filtered and evaporated to yield the crude product. Recrystallization from acetone afforded white crystals (0.04 g, 40%); mp 123–125 °C (Found: C, 71.1; H, 6.3. $C_{17}H_{18}O_4$ requires C, 71.33; H, 6.29%); ν_{max}/cm^{-1} 2979, 2929, 1740, 1711, 1624, 1605, 1583, 1459, 1271, 1236, 1084 and 1066; λ_{max} see text; δ_H(200 MHz; $CDCl_3$) 1.55–1.65 (6 H, t, *J* 7.5), 4.15–4.3 (4 H, q, *J* 7.5), 6.7–6.8 (2 H, d, *J* 10), 6.9–7.0 (2 H, d, *J* 10) and 7.45–7.6 (2 H, t, *J* 10); δ_C(75 MHz; $CDCl_3$) 15.13, 55.13, 64.74, 105.99, 108.25, 112.36, 129.81, 152.42 and 158.281; *m/z* (EI) 301 (5%), 300 (30), 286 (78), 285 (28), 270 (18), 269 (100), 241 (22) and 213 (20); *m/z* (CI/NH_3) 302 (5%), 301 (8), 286 (30), 272 (22), 271 (42) and 269 (100).

1,8-Diethoxyxanthene (20)

1,8-Diethoxyxanthone (0.1 g, 3.5×10^{-4} mol) was dissolved in THF. Borane:methyl sulfide complex (5.0×10^{-4} mol) was added by syringe and the mixture refluxed for 2 h. Methanol (4 cm^3) was then added and the mixture evaporated to dryness. The solid residue was recrystallized from acetone to yield white crystals (0.042 g, 44%); mp 127–129 °C: ν_{max}/cm^{-1} 2993, 2929, 1726, 1626, 1581, 1456, 1269, 1239, 1080 and 1066; δ_H(200 MHz; $CDCl_3$) 1.60 (6 H, t, *J* 7.5), 3.95 (2 H, s), 4.30 (4 H, q, *J* 7.5), 6.75 (2 H, d, *J* 10), 6.84 (2 H, d, *J* 10) and 7.31 (2 H, t, *J* 10); δ_C(75 MHz; $CDCl_3$) 14.94, 17.94, 105.04, 108.55, 109.51, 122.2, 152.02 and 157.16; *m/z* (EI) 217 (8%), 270 (100), 241 (70), 225 (60), 213 (72), 197 (35) and 184 (15); *m/z* (CI/NH_3) 271 (100%), 241 (20), 225 (25) and 213 (15).

1,11-Dibromo-3,6,9-trioxaundecane

Tetraethylene glycol (10 g, 0.052 mol) was dissolved in dry diethyl ether (100 cm^3) in a dry two-necked round-bottomed flask fitted with a septum cap and reflux condenser, under nitrogen and with stirring, and the resulting solution was cooled in ice. Phosphorous tribromide (10 cm^3, 0.055 mol) was added *via* a syringe and the mixture refluxed overnight. After cooling the mixture was poured into ice (75 g) and the layers separated. The organic extracts were shaken with saturated sodium hydrogen carbonate, separated, dried ($MgSO_4$) and evaporated to yield a yellow liquid (7.78 g, 47%); ν_{max}/cm^{-1} 2870, 1460, 1531, 1278, 1114, 1042 and 1022; δ_H(200 MHz; $CDCl_3$) 3.3–3.45 (t, 4 H, *J* 7.5), 3.5–3.65 (s, 8 H) and 3.65–3.8 (t, 4 H, *J* 7.5); δ_C(75 MHz; $CDCl_3$) 31.12, 71.18, 71.30 and 71.84; *m/z* (CI/NH_3) 341 (4%), 340 (54), 338 (100) and 336 (52).

1,14-Dibromo-3,6,9,12-tetraoxatetradecane

This tetraoxatetradecane was prepared from pentaethylene glycol (10 g, 0.042 mol) and phosphorous tribromide (8 cm^3, 0.044 mol) following the method outlined above. The dibromide was isolated as a light yellow liquid (6.18 g, 41%); ν_{max}/cm^{-1} 2871, 1462, 1423, 1531, 1278, 1251 and 1117; δ_H(200 MHz; $CDCl_3$) 3.3–3.45 (t, 4 H, *J* 7.5), 3.5–3.65 (s, 12 H) and 3.65–3.8 (t, 4 H, *J* 7.5); δ_C(75 MHz; $CDCl_3$) 31.06, 71.20, 71.25, 71.32 and 71.85; *m/z* (EI) 368 (2%), 367 (8), 365 (15), 363 (10), 109 (98), 107 (100), 153 (37) and 151 (40); *m/z* (CI/NH_3) 386 (2%), 385 (5), 384 (54), 382 (100) and 380 (52).

1,17-Dibromo-3,6,9,12,15-pentaoxaheptadecane

This pentaoxaheptadecane was prepared from hexaethylene glycol (5 g, 0.018 mol) and phosphorous tribromide (3.8 cm^3, 0.02 mol) as described above to yield a yellow liquid (3.17 g, 43%); ν_{max}/cm^{-1} 2871, 1461, 1423, 1531, 1278, 1250, 1115 and 1041; δ_H(200 MHz; $CDCl_3$) 3.3–3.45 (t, 4 H, *J* 7.5), 3.5–3.65 (s, 16 H) and 3.65–3.8 (t, 4 H, *J* 7.5); δ_C(75 MHz; $CDCl_3$) 31.06, 71.20, 71.25, 71.32 and 71.86; *m/z* (EI) 426 (1%), 412 (2), 411 (10), 409 (25), 407 (11), 153 (26), 151 (27), 109 (95) and 107 (100); *m/z* (CI/NH_3) 430 (1%), 429 (5), 428 (45), 426 (100) and 424 (55).

1,8-(3,6,9-Trioxaundecane-1,11-diyldioxy)xanthone [22 (*n* = 3)]

1,8-Dihydroxyxanthone (1.0 g, 4.4×10^{-3} mol) was dissolved in DMF (340 cm^3) in a dry two-necked round-bottomed flask fitted with a septum cap and reflux condenser, under nitrogen and with stirring and potassium carbonate (2.0 g) was added. 1,11-Dibromo-3,6,9-trioxaundecane (2.8 g, 8.8×10^{-3} mol) was added *via* a syringe and the mixture refluxed overnight. Most of the DMF was distilled off and the contents of the flask allowed to cool. The resulting mixture was diluted with water (60 cm^3), extracted with chloroform (3×50 cm^3) and the chloroform extracts evaporated. The residue was dissolved in toluene (100 cm^3) and half the solvent removed by distillation in order to azeotrope off any water. The remaining solution was filtered hot through celite and its volume reduced by evaporating under reduced pressure. On cooling, the toluene solution yielded off-white crystals (0.74 g, 44%); mp 187–189 °C (Found: C, 65.0; H, 6.0. $C_{21}H_{22}O_7$ requires C, 65.29; H, 5.70%); λ_{max} see text; ν_{max}/cm^{-1} 2957, 2928, 2871, 1662, 1615, 1600, 1474, 1451, 1279, 1277, 1110, 1086 and 1074; δ_H(200 MHz; $CDCl_3$) 3.75–3.95 (4 H, m), 3.95–4.15 (8 H, m), 4.15–4.4 (4 H, m), 6.65–6.7 (2 H, d, *J* 7.5), 6.9–7.1 (2 H, d, *J* 7.5) and 7.4–7.6 (2 H, t, *J* 7.5); δ_C(75 MHz; $CDCl_3$) 69.91, 69.52, 69.97, 70.81, 106.48, 109.49, 114.35, 133.77, 157.03, 159.23 and 175.53; *m/z* (CI/NH_3) 404 (3%), 389 (4), 388 (20), 387 (100), 72 (15) and 58 (35).

1,8-(3,6,9,12-Tetraoxatetradecane-1,14-diyldioxy)-xanthone [22 (*n* = 4)]

The general method described above was used. 1,8-Dihydroxyxanthone (1.0 g, 4.4×10^{-3} mol), potassium carbonate (2.0 g) and 1,14-dibromo-3,6,9,12-tetraoxatetradecane (2.4 g, 6.6×10^{-3} mol) gave an off-white solid (1.09 g, 58%); 143–145 °C (Found: C, 63.9; H, 6.25. $C_{23}H_{26}O_8$ requires C, 64.19; H, 6.05%); λ_{max} see text; ν_{max}/cm^{-1} 2955, 2929, 2872, 1661, 1615, 1597, 1471, 1447, 1281, 1115, 1087 and 1077; δ_H(200 MHz; $CDCl_3$) 3.7–3.95 (8 H, m), 3.95–4.05 (4 H, m), 4.05–4.2 (4 H, m), 4.2–4.4 (4 H, m), 6.7–6.85 (2 H, d, *J* 7.5), 6.95–7.05 (2 H, d, *J* 7.5) and 7.45–7.6 (2 H, t, *J* 7.5); δ_C(75 MHz; $CDCl_3$) 69.33, 69.80, 71.06, 71.64, 106.86, 109.59, 114.12, 133.88, 157.04, 159.42 and 175.41; *m/z* (CI/NH_3) 450 (3%), 449 (8), 448 (40), 432 (25), 431 (100), 387 (10) and 58 (55).

1,8-(3,6,9,12,15-Pentaoxaheptadecane-1,17-diyldioxy)-xanthone [22 (*n* = 5)]

The general method described above was used, with the modification that residue after chloroform extraction and evaporation was dissolved in THF rather than toluene. 1,8-Dihydroxyxanthone (1.0 g, 4.4×10^{-3} mol), potassium carbonate (2.0 g) and 1,17-dibromo-3,6,9,12,15-pentaoxapentadecane (2.0 g,

4.9 × 10^{-3} mol) gave an off-white crystalline product (0.91 g, 44%); mp 113–115 °C (Found: C, 62.7; H, 6.3. $C_{25}H_{30}O_9$ requires C, 63.29; H, 6.33%); λ_{max} see text; ν_{max}/cm^{-1} 2955, 2929, 2871, 1663, 1614, 1598, 1472, 1280, 1263, 1105 and 1089; δ_H(200 MHz; $CDCl_3$) 3.55–3.9 (12 H, m), 3.9–4.15 (8 H, m), 4.15–4.35 (4 H, m), 6.65–6.8 (2 H, d, *J* 7.5), 6.9–7.05 (2 H, d, *J* 7.5) and 7.45–7.6 (2 H, t, *J* 7.5); δ_C(75 MHz; $CDCl_3$) 69.43, 70.32, 70.49, 71.16, 71.69, 106.79, 108.63, 114.04, 133.87, 156.99, 159.44 and 175.25; *m/z* (EI) 477 (2%), 476 (5), 475 (14), 474 (6), 387 (35), 369 (55), 341 (42), 325 (52), 254 (33) and 45 (100); *m/z* (CI/NH_3) 494 (3%), 493 (8), 492 (27), 475 (100), 255 (10), 254 (12), 224 (10), 212 (10) and 168 (14).

1,8-(3,6,9-Trioxaundecane-1,11-diyldioxy)xanthydrol [16 (*n* = 3)]

To a solution of 1,8-(3,6,9-trioxaundecane-1,11-diyldioxy)-xanthone **22** (*n* = 3), (0.1 g, 2.59 × 10^{-4} mol) in methanol (8 cm^3) was added potassium borohydride (0.2 g, 3.7 × 10^{-3} mol). The reaction mixture was stirred for 15 min after which time the methanol was evaporated off. Dichloromethane (5 cm^3) was added to the residue and the resulting solution was filtered and evaporated to yield the crude product. Recrystallization from toluene yielded yellow crystals (0.058 g, 58%); mp 175–177 °C (Found: C, 64.9; H, 6.1. $C_{21}H_{24}O_7$ requires C, 64.95; H, 6.19%); λ_{max} see text; ν_{max}/cm^{-1} 3472, 2872, 1622, 1604 and 1582; δ_H(200 MHz; CD_2Cl_2) 3.5–3.85 (10 H, m), 3.85–3.95 (3 H, t, *J* 4), 4.1–4.4 (3 H, t, *J* 4), 6.35 (1 H, s), 6.7–6.85 (2 H, d, *J* 7.5), 6.85–6.9 (2 H, d, *J* 7.5) and 7.25–7.35 (2 H, t, *J* 7.5); δ_C(75 MHz; CD_2Cl_2) 68.67, 69.53, 70.57, 70.95, 106.52, 109.71, 113.51, 129.51, 152.42 and 158.12; *m/z* (EI) 372 (74%), 212 (100), 196 (66), 139 (65) and 84 (58); *m/z* (CI/NH_3) 406 (1%), 391 (18), 390 (70), 388 (65), 372 (25) and 371 (100); *m/z* (FAB) 371 (70%), 149 (75), 136 (70), 123 (60) and 109 (100).

1,8-(3,6,9,12-Tetraoxatetradecane-1,14-diyldioxy)-xanthydrol [16 (*n* = 4)]

To a stirred solution of the xanthone (0.10 g, 2.4 × 10^{-4} mol) in dry THF (100 cm^3) was added lithium aluminium hydride (0.02 g). The mixture was stirred at room temperature for 10 min, after which saturated sodium sulfate solution was added dropwise to destroy excess $LiAlH_4$ and yield a granular white solid. The THF solution was then filtered through a short column of alumina and evaporated to yield crude product which was recrystallized from toluene (0.051 g, 51%). Mp 138–140 °C (Found: C, 64.5; H, 6.6. $C_{23}H_{28}O_8$ requires C, 63.89; H, 6.48%); λ_{max} see text; ν_{max}/cm^{-1} 3435, 2918, 1620, 1458, 1273, 1236 and 1089; δ_H(200 MHz; CD_2Cl_2) 3.5–4.4 (20 H, m), 6.30 (1 H, s), 6.6–6.7 (2 H, d, *J* 7.5), 6.75 (2 H, d, *J* 7.5) and 7.25 (2 H, t, *J* 7.5); δ_C(75 MHz; CD_2Cl_2) 68.46, 69.93, 71.06, 71.10, 105.74, 109.45, 113.38, 129.3, 152.38 and 158.15; *m/z* (EI) 415 (100%), 239 (22), 213 (35) and 212 (28); *m/z* (CI/NH_3) 434 (70%), 417 (30), 239 (65), 223 (62) and 212 (100).

1,8-(3,6,9,12,15-Pentaoxaheptadecane-1,17-diyldioxy)-xanthydrol [16 (*n* = 5)]

Reduction of the xanthone (0.10 g, 2.11 × 10^{-4} mol) with $LiAlH_4$ in THF as described above, but with stirring for no more than 5 min before the aqueous sodium sulfate quench, yielded the xanthydrol (0.054 g, 55%) after recrystallization from methanol. Mp 90–92 °C (Found: C, 63.8; H, 7.0. $C_{25}H_{32}O_9$ requires C, 63.03; H, 6.72%); λ_{max} see text; ν_{max}/cm^{-1}, 2871, 1621, 1582, 1347, 1274, 1238 and 1089; δ_H(200 MHz; CD_2Cl_2) 3.5–3.85 (4 H, m), 3.85–4.1 (4 H, m), 4.1–4.4 (4 H, m), 6.40 (1 H, s), 6.55–6.7 (2 H, d, *J* 7.5), 6.75 (2 H, d, *J* 7.5) and 7.25 (2 H, t, *J* 7.5); δ_C(75 MHz; CD_2Cl_2) 68.86, 70.13, 70.99, 71.03, 71.13, 71.26, 106.26, 109.62, 113.48, 129.42, 152.62 and 158.12; *m/z* (EI) 475 (25%), 460 (30) and 459 (100); *m/z* (CI/NH_3) 480 (10%), 479 (25), 478 (100), 460 (30) and 459 (95).

pK_a Measurements and pK_{R^+} measurements

For the tropylium ions, buffer solutions were made up using mixtures of 0.02 mol dm^{-3} sodium hydroxide solution and aqueous dichloroacetic acid ranging from 0.04 to 0.02 mol dm^{-3}. Solutions were then diluted with an equal volume of acetonitrile and pH values were measured using a pH meter fitted with a glass electrode. Aliquots of cation solution prepared as described above (10 μl of 0.016 mol dm^{-3} in cation) (1 μl = 1 mm^3) were added to buffer solution (3 cm^3) in an UV cell and spectra determined. Spectra in 0.01 mol dm^{-3} hydrochloric acid and 0.01 mol dm^{-3} sodium hydroxide provided details of the cation and alcohol and a change of absorbance at 300 nm between the extremes was used to estimate an approximate pK_{R^+} value.

For the xanthones and xanthydrols, sulfuric acid solutions of known strength from pH 5.5 to H_0 −7.4 were prepared according to Rochester.[42] Sulfuric acid solution of known strength (3 cm^3) was placed in a stoppered cell in the spectrometer and a base line spectrum recorded. An aliquot (20 μl) of a stock solution (*ca.* 5.0 × 10^{-3} mol dm^{-3}) of the ketone or alcohol under examination in acetonitrile was added, the cell was stoppered, shaken quickly, and the spectrum re-recorded as rapidly as possible. The procedure was then repeated with a range of sulfuric acid solutions and the complete experiment duplicated for each compound. Absorbances at 282 nm for the cations or 272 nm for the ketones were then plotted against pH or H_0 and p*K* values for the compounds extracted by non-linear least squares regression[43] to a calculated absorbance given by

$$A_{tot} = (A_+^{-X} + A_-^{-pK})/(10^{-pK} + 10^{-X})$$

where A_{tot} = absorbance for all species present at equilibrium, A_+ and A_- = absorbance of species in all-acid or all-base form, X = pH or H_0 of the solution and pK = pK_a or pK_{R^+} to be determined. In all cases, the values obtained from the separate experiments for each compound agreed to within 0.05 pK units and values given in the text are mean values of the two separate determinations.

Monitoring the decay of cation solutions from 1,8-diethoxy-xanthydrol, by repeat scanning of a single solution yielded spectra showing isosbestic points at 262, 290, 331, 365 and 399 nm, but solutions became turbid after less than one half-life. Initial rates, determined at 50 °C in acid at the pK_{R^+} were: $-dA/dt = -0.075$ h^{-1} (for $A_0 = 0.865$) and $-dA/dt = -0.037$ h^{-1} (for $A_0 = 0.430$).

Empirical force field calculations

The molecular modelling package was Macromodel 4.0,[44] running on a Silicon Graphics 4D 240 GTX work station. The MM2 force field of Allinger *et al.*[45] was used for all calculations with no modification of parameters.

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