General Procedure for Photolysis of the Cyclobutabenzofuranones. A magnetically stirred solution of the cyclobutanone 1 (500 mg, 2.48 mmol) in dry methanol (260 mL) was degassed by bubbling a continuous stream of nitrogen through the solution for 15 min. This solution was irradiated through a Pyrex filter with a Hanovia 450-W mercury lamp at rt for 20 h (monitored by the absence of IR absorption at 1780 cm^{-1}). The oily residue obtained after removal of methanol under reduced pressure was subjected to preparative TLC with 2% ethyl acetate in petroleum ether. Extraction of the band furnished the acetals **10a,b** as an inseparable mixture in a combined yield of 56%; ot 110–15 °C (0.5 mmHg). The proportion of the isomeric mixture (1.5:1) was arrived at from the ratio of the integrals for the methoxy protons in the ^1H NMR, δ 3.42 (s, 3H) for the β-isomer **10a** and δ 3.15 (s, 3H) for the α-isomer **10b**. This was further supported from GLC analysis which showed this to be a mixture of two compounds in a proportion of 1.5:1 t_R 1.69 min (major) and 2.07 min (minor) at 180 °C. Because of the isomeric nature, elemental analysis was done on the mixture.

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.55; H, 7.60.

For obtaining ^1H NMR spectrum of the pure isomers, this mixture was again subjected to preparative TLC and eluted with 2% ethyl acetate in petroleum ether. Thin portions from the top and bottom areas of the band were sliced off and extracted.

The major, less polar, isomer assigned the β-methoxy structure, **10a** showed ^1H NMR ($CDCl_3$) δ 1.38 (s, 3H), 1.64 (s, 3H), 2.02 (q, A of ABX, J_{AB} = 12 Hz, 1H), 2.32 (s, 3H), 2.52 (q, B of ABX, J_{BA} = 12 Hz, 1H), 3.42 (s, 3H), 4.94 (t, X of ABX, $J_{AX} = J_{BX}$ = 4 Hz, 1H), 6.66 (br s, 1H), 6.78 (m, 1H), 7.04 (d, J = 4 Hz, 1H).

The minor, more polar α-epimer **10b** showed ^1H NMR ($CDCl_3$) δ 1.38 (s, 3H), 1.58 (s, 3H), 2.25 (m, 2H), 2.29 (s, 3H), 3.15 (s, 3H), 5.06 (d, J = 4 Hz, 1H), 6.60 (br s, 1H), 6.74 (m, 1H), 7.00 (d, J = 8 Hz, 1H).

Irradiation of cyclobutanone **2** (250 mg, 1.33 mmol) furnished the acetals **11a,b** (140 mg, 48%); ot 70–74 °C (0.05 mmHg). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.59; H, 7.18. GLC analysis showed this to be a mixture of two components in a ratio of 1.5:1, t_R 1.32 min (major) and 1.53 min (minor). Pure isomers were obtained for spectral use as before. **11a** (major): ^1H NMR (CCl_4) δ 1.36 (s, 3H), 1.56 (s, 3H), 1.97 (q, A of ABX, J_{AB} = 12 Hz, 1H), 2.39 (q, B of ABX, J_{BA} = 12 Hz, 1H), 3.33 (s, 3H), 4.81 (t, X of ABX, $J_{AX} = J_{BX}$ = 5 Hz, 1H), 6.91 (m, 4H).

11b (minor): ^1H NMR (CCl_4) δ 1.36 (s, 3H), 1.5 (s, 3H), 2.1 (m, 2H), 3.06 (s, 3H), 4.86 (d, J = 4 Hz, 1H), 6.9 (m, 4H).

Irradiation of **3** (250 mg, 1.33 mmol) furnished the acetals **12a,b** (145 mg, 50%) in a 1.5:1 proportion as determined from the ratio of the integrals for the methoxy protons in ^1H NMR; ot 68–70 °C (0.5 mmHg).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.25; H, 7.57. These were separated by preparative TLC, using 2% ethyl acetate in petroleum ether for elution.

Isomer 12a (major): ^1H NMR ($CDCl_3$) δ 1.48 (s, 3H), 2.04 (q, A of ABX, J_{AB} = 12 Hz, 1H), 2.28 (s, 3H), 2.42 (q, B of ABX, J_{BA} = 12 Hz, 1H), 3.44 (s, 3H), 5.04 (t, X of ABX, $J_{AX} = J_{BX}$ = 4 Hz, 1H), 5.88 (s, 1H), 6.68 (m, 1H), 6.80 (br s, 1H), 7.04 (d, J = 8 Hz, 1H).

Isomer 12b (minor): ^1H NMR (CCl_4) δ 1.43 (s, 3H), 2.19 (m, 2H), 2.30 (s, 3H), 3.10 (s, 3H), 5.03 (d, J = 5 Hz, 1H), 5.73 (s, 1H), 6.49 (br s, 1H), 6.66 (m, 1H), 6.89 (d, J = 6 Hz, 1H).

In one experiment during preliminary preparative TLC a more polar component was isolated. This was identified as the γ-lactone **14**, produced in 12% yield, ot 100–104 °C (0.1 mmHg): IR 1780 cm^{-1}; ^1H NMR (CCl_4) δ 1.49 (s, 3H), 2.33 (s, 3H), 2.72 (br d, J = 1 Hz, 2H), 5.97 (s, 1H), 6.66 (br s, 1H), 6.79 (m, 1H), 7.00 (d, J = 8 Hz, 1H).

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.56; H, 5.94.

Irradiation of **4** (150 gm, 0.66 mmol) afforded the acetals **13a,b** (102 mg, 58%) in 1.5:1 as determined from ^1H NMR, ot 86–96 °C (0.05 mmHg).

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.55; H, 7.67. These were separated by preparative TLC.

Isomer 13a (major): ^1H NMR ($CDCl_3$) δ 1.40 (s, 3H), 2.00 (q, A of ABX, J_{AB} = 12 Hz, 1H), 2.29 (s, 3H), 2.51 (q, B of ABX, J_{BA} = 12 Hz, 1H), 2.68 (m, 2H), 4.96 (t, X of ABX, $J_{AX} = J_{BX}$ = 4 Hz, 1H), 3.42 (s, 3H), 5.16 (br s, 1H), 5.28 (m, 1H), 6.12 (m, 1H), 6.68 (br s, 1H), 6.76 (br s, 1H), 7.00 (d, J = 8 Hz, 1H).

Isomer 13b (minor): ^1H NMR ($CDCl_3$) δ 1.40 (s, 3H), 2.24 (m, 2H), 2.28 (s, 3H), 2.68 (br d, J = 4 Hz, 2H), 3.12 (s, 3H), 5.06 (d, J = 4 Hz, 1H), 5.12 (m, 1H), 5.26 (m, 1H), 6.12 (m, 1H), 6.60 (br s, 1H), 6.72 (br d, J = 8 Hz, 1H), 6.96 (d, J = 8 Hz, 1H).

Irradiation of **1** (300 mg, 1.5 mmol) in THF (260 mL, containing water 20 mL) was carried out as in the case of methanol, for 6 h. Removal of solvent followed by preparative TLC (2% ethyl acetate in petroleum ether, multiple elution) of the resulting oily residue afforded the epimeric mixture of hemiacetals **15a,b** as a crystalline solid (160 mg, 50%). This melted at 118–120 °C. No attempt was made to separate the individual isomers.

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.69; H, 7.22.

15a,b: ^1H NMR ($CDCl_3$) δ 1.38, 1.41 (2s, 3H, in 1:3 proportion) 1.6, 1.66 (2s, 3H in 1:3 proportion), 1.8–2.7 (m, 2H), 2.33 (s, 3H), 3.96 (br, 1H), 5.36 (m, 1H), 6.66 (br s, 1H), 6.73 (br d, J = 8 Hz, 1H), 7.06 (dd, J = 2, 8 Hz, 1H).

Irradiation of **1** (100 mg, 0.5 mmol) in petroleum ether (110 mL) for 5 h furnished a crude product which was subjected to preparative TLC. Elution with 1% ethyl acetate in petroleum ether afforded **16** as a colorless liquid (30 mg, 37%): ^1H NMR (CCl_4) δ 2.12 (s, 3H), 2.33 (s, 3H), 2.46 (s, 3H), 7.09 (m, 3H).

Irradiation of **4** (200 mg, 0.88 mmol) in cyclohexane (260 mL) for 2 h followed by preparative TLC of the crude product yielded **17** as an oil (80 mg, 50%): ^1H NMR (CCl_4) δ 2.13 (s, 3H), 2.43 (s, 3H), 3.43 (br d, J = 6 Hz, 2H), 4.97 (m, 1H), 5.19 (m, 1H), 5.95 (m, 1H), 7.04 (m, 3H).

Due to their volatile nature, analytical data for **16** and **17** could not be obtained. However, homogeneity was evident from ^1H NMR, additionally supported by TLC in different solvent systems.

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Condensation of Arylacetonitriles with Glyoxylic Acid. Facile Synthesis of Arylmaleic Acid Derivatives

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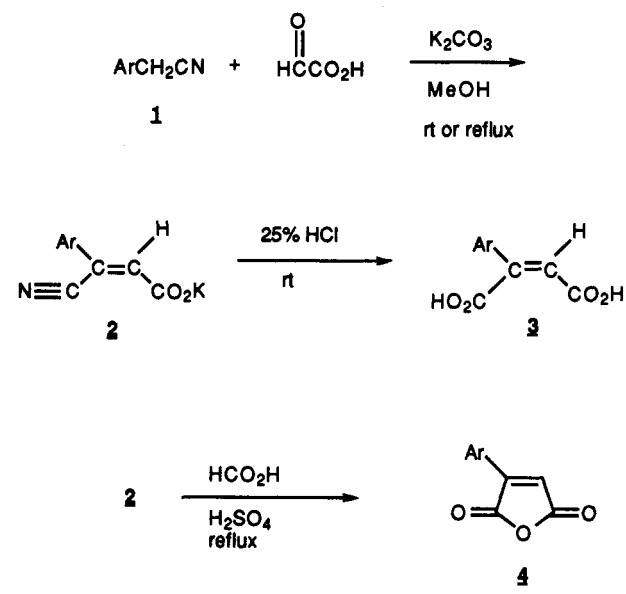
During a synthetic program aimed at the preparation of certain CNS agents, we required an efficient route to arylmaleic acid derivatives for use as intermediates in the large-scale preparation of arylmaleimides and arylmaleic anhydrides. Of the numerous literature procedures for the preparation of these compounds,[1-6] the most general and direct method appeared to be the Meerwein arylation of maleimides[1] or dialkylmaleates.[2] In our hands, this method was used in the initial phases of our program to prepare several arylmaleimides. However, since we were ultimately interested in the preparation of kilogram quantities of materials, we found that several factors precluded scale-up of this reaction. In particular, the maleimides used in these reactions were quite expensive and the arylations were always accompanied by a substantial amount of aryl coupling to form biphenyls.

Another method that we explored for the preparation of these arylmaleic acid derivatives involved Wittig reaction of aroyl cyanides with (carbalkoxymethylene)-triphenylphosphoranes.[4] In our hands, reaction of commercially available benzoyl cyanide with (carbethoxymethylene)triphenylphosphorane using the literature procedure[4] gave ethyl 3-cyano-3-phenylpropenoate as a 2.5:1 mixture of *Z*:*E* isomers. This ratio could be improved to ca. 10:1 *Z*:*E* by treatment of the mixture with thiophenol in refluxing toluene. The desired *Z*-cyano ester could be cyclized in hot formic acid to phenylmaleimide.[7] Despite its overall efficiency, this method was abandoned due to the lack of availability of the desired aroyl cyanides.

We had felt that condensations of readily available arylacetonitriles with glyoxylic acid might provide an easy alternate route to 3-aryl-3-cyanopropenoates. Glyoxylic acid has been shown to condense readily with ketones under acidic[11] or basic conditions[12] to provide acylacrylic acids or hydroxyacetic acids, respectively, but the reactions of arylacetonitriles with glyoxylic acid have not been reported. Initially, these condensations were studied using an aqueous sodium hydroxide–methanol reaction medium. Under these conditions, at room temperature, the corresponding sodium (*Z*)-3-aryl-3-cyanopropenoates were isolated in good yield. Actually, more consistent results were

Scheme I



obtained by treatment of the arylacetonitriles 1 with 1.5–2.0 equiv of glyoxylic acid hydrate in methanol using potassium carbonate as the base. Use of these conditions smoothly provided the potassium (*Z*)-3-aryl-3-cyanopropenoates 2 (Scheme I). Data for these reactions are reported in Table I.

In general, arylacetonitriles containing electron-withdrawing groups (entries b–d) reacted readily at room temperature while phenylacetonitrile and nitriles with electron-donating groups reacted best at reflux. In all cases, the products 2 precipitated from the reaction mixtures and could be freed from inorganic impurities by suspension in cold water.

It is interesting to note that all of the condensations examined resulted in the formation of a single geometric isomer as evidenced by NMR. Also, the CN stretch in the IR spectra of these products showed a shift from ca. 2250–2260 cm^{-1} of the arylacetonitriles to ca. 2220 cm^{-1} which suggested a conjugated nitrile. These products were shown to be the desired *Z* isomers by their cyclization in hot formic acid to the known arylmaleic anhydrides 4 in good yield (Table II).

In an effort to prepare the corresponding (*Z*)-arylcyanopropenoic acids, several compounds 2 were stirred at room temperature with 25% aqueous HCl which resulted in the isolation of the corresponding arylmaleic acids 3 (Table III). The structures of these acids were confirmed by NMR and by their conversion to the anhydrides 4 with acetic anhydride.

Our work has demonstrated that arylacetonitriles and glyoxylic acid condense under mild conditions, providing intermediates that can easily be converted to various useful arylmaleic acid derivatives. The ease of the reaction sequence as well as the high availability of the starting arylacetonitriles makes our route an attractive alternative to published procedures for the large-scale synthesis of these derivatives.

Experimental Section

Arylacetonitriles and glyoxylic acid were obtained commercially from Aldrich Chemical Co. and were used without prior purification. NMR spectra were recorded on a Nicolet NT-300 or a General Electric QE-300 spectrometer. Infrared spectra

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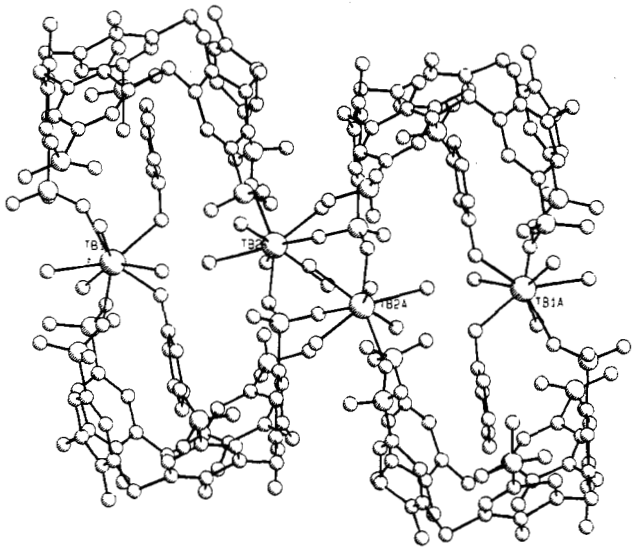

Figure 6. X-ray crystal structure of the supercomplex $Na_8[Tb_4(py\text{-}N\text{-}O)_4(H_2O)_{18}(p\text{-sulfonatocalix[5]arene})_4]\cdot 2H_2O$ showing the two types of bridging Tb(III) ion.

structural details are clear and warrant discussion. As with all the compounds reported, the formulation of **7** is supported by analytical data. Fascinatingly, each host molecule in complex **7** consists of four *p*-sulfonatocalix[5]arene ligands along with four bridging Tb(III) ions which link the structure together, all related in pairs by a crystallographic inversion center, Figure 6. Of the two crystallographically independent, eight-coordinate Tb(III) ions, one of them, Tb(1), situated on the outside of the "supercomplex", bridges between two independent *p*-sulfonatocalix[5]arene 5- anions in a similar way to that observed for both **5** and **6** but is ligated by two py-*N*-O moieties, each of which occupies one of the molecular cavities of the calixarenes, resulting in simultaneous first- and second-sphere coordination of Tb(1) by both calixarene ligands. The other pair of Tb(III) ions, Tb(2) and its symmetry equivalent, are situated at the center of the tetrameric array and engage in a unique triply bridging coordination mode with each metal ion simultaneously binding *via* the sulfonate oxygen atoms to three calixarene ligands. Interestingly, Tb(2) is not coordinated to any py-*N*-O ligands, once again highlighting the dominance of crystal packing forces in the determination of molecular stoichiometry. In general, the bilayer packing arrangement is similar to that observed for complexes **4**−**6**, with an interlayer separation of 15.2 Å and hydrophobic and hydrophilic regions of 6.7 and 8.5 Å, respectively. The relatively narrow hydrophilic layer presumably results from the presence of two bridging metal ions per calixarene pair. A similar effect has been noted for the Mn(II) bridged *p*-sulfonatocalix[4]arene dimer $Na_4[\{Mn(H_2O)_4(p\text{-sulfonatocalix[4]arene})\}_2]\cdot 5H_2O$.[23]

$Na_2[Yb(py\text{-}N\text{-}O)(H_2O)_6$(calix[5]arene-*p*-sulfonato)]$\cdot 13H_2O$. In contrast to the structures of **5**−**7** the product resulting from the interaction of $YbCl_3\cdot H_2O$ with **1b** in the presence of py-*N*-O, $Na_2[Yb(py\text{-}N\text{-}O)(H_2O)_6$(calix[5]arene-p-sulfonato)]$\cdot 13H_2O$ (**8**), involves the first-sphere coordination of the eight coordinate Yb(III) ion to a single calixarene ligand, again *via* one of the sulfonato oxygen atoms, Figure 7. The calixarene is thus capped by a "$Yb(H_2O)_6$(py-*N*-O)" moiety instead of a bridging coordination mode of the metal ion between two calixarene units as in **5** and **6**, (Yb−OH_2 2.341(3) Å av, Yb−ONC_5H_5 2.275(4) Å, Yb−O_{calix} 2.313(3) Å). Bond distances to the Yb(III) ion are shorter than the Ln−O distances

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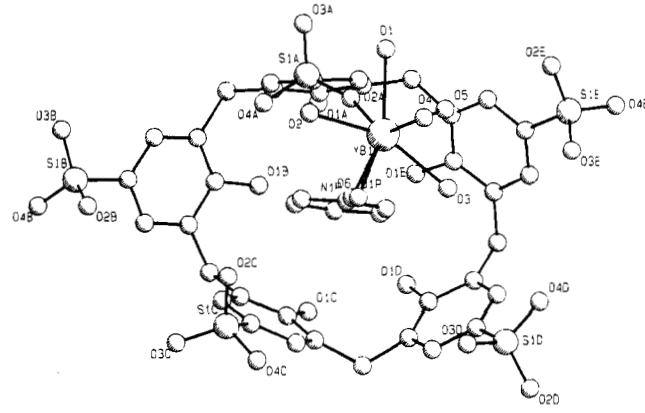

Figure 7. X-ray crystal structure of the $[Yb(H_2O)_6$(py-*N*-O)(*p*-sulfonatocalix[5]arene)$]^{2-}$ ion in **8** showing the second sphere coodination of the pyridine *N*-oxide ring by the calixarene.

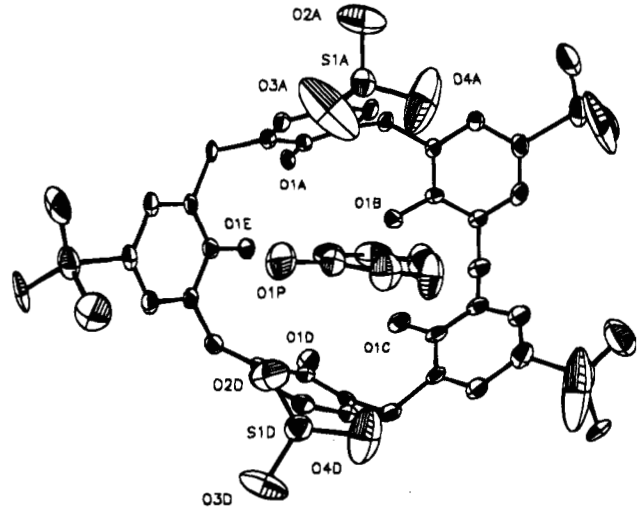

Figure 8. Structure of the 1:1 inclusion complex Na_5[calix[5]-arenesulfonato]·py-*N*-O·$8.5H_2O$ **3**.

observed for **5** and **6** consistent with the smaller ionic radius of Yb(III).[22] It is likely that the smaller ionic radius of Yb(III) relative to that of Eu(III) and Gd(III) means that it is not sufficiently large to span the hydrophilic layer of the structure. If this is the case it indicates the high degree of stability possessed by the claylike layered structures adopted by complexes of calix[5]arene sulfonate in the solid state, suggesting that this is the dominant factor in the crystal packing and indeed the determination of the composition of the metal ion coordination spheres. This implies that complexes **4**−**8** are labile in solution, with their stoichiometry and composition becoming fixed upon crystallization. The fact that the packing arrangements are so similar across the series La−Yb is a tribute to the principles of self-assembly in that, even presented with a wide range of metal ions, the same basic crystal packing arrangement is sufficiently robust to accommodate these varying requirements.

Na_5[*p*-sulfonatocalix[5]arene]·py-N-O·$8.5H_2O$. In contrast to the formation of $Na_2[Zn(H_2O)_4(py\text{-}N\text{-}O)_2]$[calix[4]arene-*p*-sulfonato]·$8.5H_2O$, reaction of **2** with $Zn(NO_3)_2$ and py-*N*-O,[18] results in the separate deposition of crystals of zinc nitrate and the py-*N*-O/*p*-sulfonatocalix[5]arene 1:1 inclusion complex Na_5-[calix[5]arenesulfonato]·py-*N*-O·$8.5H_2O$ (**3**), Figure 8. While the conformation of the calixarene and geometry of the host−guest interaction is similar to that found for the other py-*N*-O inclusion complexes **4**−**8**, there is a particularly short contact between the py-*N*-O guest oxygen atom and one of the sulfonate groups, O(1P)−O(2D), of only 2.56(1) Å, suggesting a strong