Heterocalixarenes. 1. Calix[2]uracil[2]arene: Synthesis, X-ray Structure, Conformational Analysis, and Binding Character

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1,3-Bis[(1-uracilyl)methyl)]benzene derivatives **3**, formed by selective N-1 alkylation of 1,3-bis(trimethylsilyloxy)pyrimidine with 1,3-bis(bromomethyl)benzene derivatives **2**, on cyclization with the same or different derivative of **2**, provide calix[2]uracil[2]arenes **4**. Their conformations, investigated through X-ray, variable temperature ^{1}H NMR, and molecular modeling MM2 calculations, are found to depend on the nature of substituent(s) on the position 2 of 1,3-phenylene rings. **4a** exists in equilibrium between various conformations, and **4b**, **4d**−**4i** adopt an inward flattened partial cone conformation. In **4j**, the equilibrium is restricted to two conformations at −60 °C, but the **4j**·ethanol complex (2:1), in the solid state, has a cone conformation with ethanol being a H-bond donor through H of OH and CH_2 and an acceptor through O of OH. **4d**, **4j**, and **4k** exhibit significant preferences toward alkaline earth metal ions over alkali metal ions though overall bindings are poor.

Calixarenes[1] constitute π-electron-rich cavities that are responsible for their binding with aromatic,[2] ammonium,[3] and metal ion[4] guests through $\pi-\pi$ and $\pi-$cation interactions. Heterocalixarenes,[5−10] constituted by replacement of arylene unit(s) of calixarenes with heterocyclic moieties, depending on the electron-deficient[6] or rich[5] nature of a heterocyclic unit(s), encompass numerous new opportunities for $\pi-\pi$ interactions with electron-rich and electron-deficient π systems. The protonizable H and heteroatom of the heterocyclic constituent could also induce H-bonding interactions with anionic and acidic H substrates. Thus, pyrrole[5,7] and pyridinium cation[6a] based calix[4]arenes exhibit binding character toward halide ions and alcohols, etc., and carboxylate ions, respectively. A COOH-functionalized appendage at a methylene bridge in calix[4]pyrrole shows unique self-assembling properties.[7] The heterocalixarenes possessing cyclic urea[8−10] based heterocycles such as benzimidazol-2-one, 1,3,5-triazinone, and ethylene/propylene urea along with phenolic units also show unique conformational and inclusion properties, unprecedented in homocyclic calixarenes.

Despite the significance of uracil and its derivatives toward complexation with H^+ and other biological cations in RNA strands[11] and in other catalytic functions,[12] the uracil-based synthetic cyclic receptors have scarcely been studied.[13] In addition, inbuilt subheterocyclic urea oxygen, present in the macrocycles, is known to be directed toward the cavity, sterically less hindered, and better binding than ether or ester oxygens.[14] We have now developed a facile two-step synthesis of uracil-based heterocalix[4]arenes possessing two uracil and two similarly or differently substituted 1,3-phenylene units.[15] X-ray crystal structure, ^{1}H NMR, and molecular modeling studies show that these calix[2]uracil[2]arenes (**4**), depending on the nature of the substituents on 2-position of 1,3-phenylene rings, attain an inward flattened partial cone, a cone, or other flexible structures.

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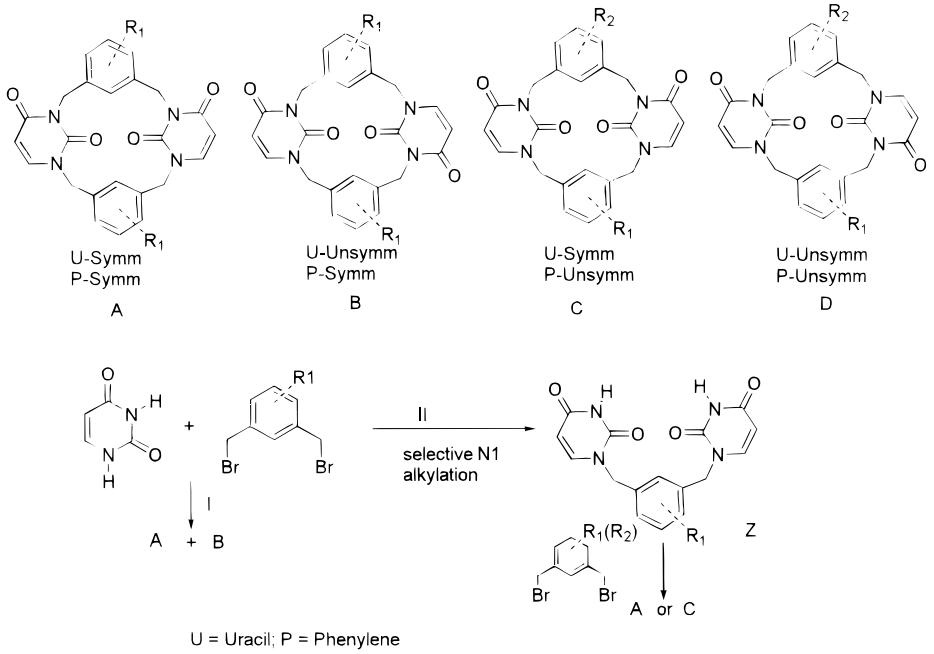
Scheme 1. Projection of Synthetic Approaches for the Target Calix[2]uracil[2]arenes



U = Uracil; P = Phenylene

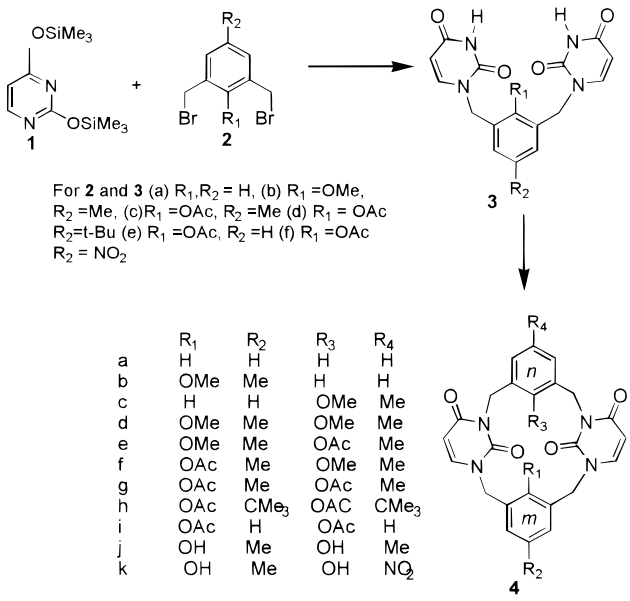
Synthesis

The uracil-based calix[4]arene models, possessing two uracil and two 1,3-phenylene units, due to nonequivalence of uracil N1 and N3 positions and possibility of similar and different substitution pattern in 1,3-phenylene units, are composed of the four structures A−D (Scheme 1). Their synthesis through single-step 2:2 stoichiometric alkylation (Scheme 1, path I) of uracil with a 1,3-bis(bromomethyl)benzene derivative would provide a product mixture of two structural isomers A and B. Using a mixture of two 1,3-bis(bromomethyl)benzene derivatives, all the possible four structures could be formed. However, the alkylation (path I) of uracil with **2a** under phase-transfer catalytic conditions (K_2CO_3−CH_3CN−tetrabutylammonium hydrogensulfate) or in a DMF−NaH mixture gave a multiple-component reaction mixture, which could not be separated even by repeated column chromatography.

An alternate two-step approach (path II, Scheme 1), requiring selective N1 alkylation of uracil followed by subsequent cyclization of the intermediate product (Z) with the same or a different 1,3-bis(bromomethyl)benzene derivative, would provide calix[2]uracil[2]arene derivatives A or C selectively (Scheme 1). Thus, 1,3-bis(trimethylsilyloxy)pyrimidine (**1**) on refluxing with **2a** in 1,2-dichloroethane by using I_2 as catalyst[16] provides **3a** (60%), mp 268 °C, M^+ *m/z* 326. The cycloalkylation of **3a** with **2a** under phase-transfer catalytic conditions (K_2CO_3−CH_3CN−tetrabutylammonium hydrogensulfate) provides **4a**, a heterocalix[4]arene of type A (24%), mp 287−90 °C, M^+ *m/z* 428. The latter approach though involves two steps and provides only one calix[2]uracil[2]arene in good yield. So, for procuring **4a**−**4k** only the two-step approach has been used.

1,3-Bis(bromomethyl)benzene derivatives **2b**−**e** react with **1** to give acyclic products **3b**−**e** which on subsequent cyclization with the same dibromoalkyl derivatives **2b**−**e** provide type A (U-symm, P-Symm) calix[2]uracil[2]arenes **4d**, **4g**−**i** in 20−30% yields (Scheme 2). The cycloalkylations of **3a** with **2b**, **3b** with **2a**, **3b** with **2c**, and **3c** with **2b** provide respective type C (U-symm, P-unsymm) calix[2]uracil[2]arene derivatives **4c**, **4b**, **4e**, and **4f**. To evaluate the complexation of dihydroxycalix[2]uracil[2]-arenes with alkali and alkaline earth metal using UV spectrophotometric techniques, we have synthesized the calix[2]uracil[2]arene **4k**, having a chromogenic NO_2 group. The cycloalkylation of **3c** with **2f** forms a nonseparable product mixture which on hydrolysis (HCl:EtOH) provides pure calix[2]uracil[2]arene **4k** (10%).

Scheme 2. Synthesis of Calix[2]uracil[2]arenes 4a−k



	R_1	R_2	R_3	R_4
a	H	H	H	H
b	OMe	Me	H	H
c	H	H	OMe	Me
d	OMe	Me	OMe	Me
e	OMe	Me	OAc	Me
f	OAc	Me	OMe	Me
g	OAc	Me	OAc	Me
h	OAc	CMe_3	OAC	CMe_3
i	OAc	H	OAc	H
j	OH	Me	OH	Me
k	OH	Me	OH	NO_2

Conformational Analysis

The ^1H NMR and off-resonance ^{13}C NMR spectra of compounds **3** exhibit NCH_2 as a singlet and a triplet, respectively. In the ^1H NMR spectra of calix[2]uracil[2]-

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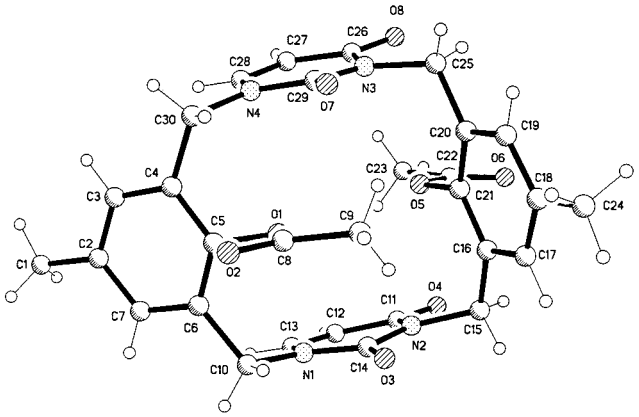
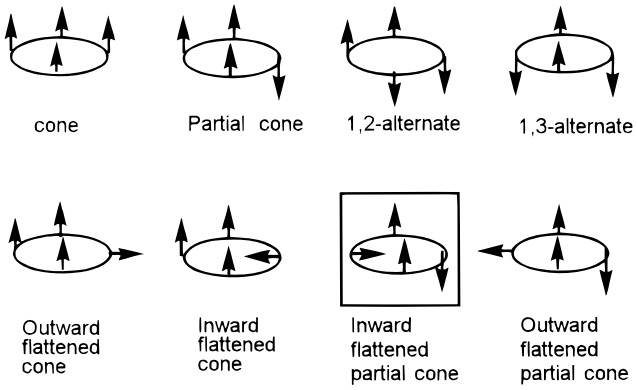


Figure 1. Diagram showing the numbering system of **4g**.

Scheme 3. Iconographic Representations of Conformations



arene **4**, N1−CH_2 (4H) and N3−CH_2 (4H) units appear as combinations of (i) two singlets (**4a**) or (ii) sharp singlet−broad signal (**4j**, **4k**) or (iii) one singlet−one AB quartet (**4c**) or (iv) two AB quartets (**4b**, **4d**−**i**), depending on the presence/absence and nature of the substituents on the position 2 of the two 1,3-phenylene units. Evidently, heterocalix[4]arenes **4**, depending on the substituents on 1,3-phenylene rings, exhibit various conformations. The four distinct conformations of calix[4]arenes—cone, partial cone, 1,3-alternate, and 1,2-alternate—have been recognized (first row, Scheme 3). The flattening of one of the rings either inward or outward the cavity can lead to four additional conformations[9] (second row, Scheme 3). The structures of calix[2]uracil[2]arenes (**4**) have been assigned by ^{1}H NMR in solution, single-crystal X-ray crystallography in two cases, and by force field energy minimization studies.

A. X-ray Structural Studies. Single-crystal X-ray structural studies show that **4g** adopts an inward flattened partial cone conformation (Figure 1). The torsion angles χ and ϕ around C10, C15, C25, and C30 ArCH bonds are 104.4(5)°, −62.0(6)°; 117.1(5)°, 126.8(5)°; −131.4(5)°, −116.4(5)°; and 66.1(5)°, −106.7(5)°, respectively. Both the phenylene rings are planar whereas the uracil rings are almost planar with a maximum deviation of 0.06 Å of C14 and C29 carbons. The four methylene carbons lie almost in a plane (± 0.06 Å), and two uracil rings make interplanar angles of 95.6(1)° and 83.1(1)° with the plane of methylene carbons. The phenylene ring (C2−C3−C4−C5−C6−C7) placed between N-1 positions of uracil units forms a dihedral angle of 141.9(1)°, and a phenylene ring (C16−C17−C18−C19−C20−C21) placed between N-3 positions of uracil units has a dihedral angle of 105.3(1)° with the plane of methylene carbons. The larger dihedral angle of the phenylene ring linked between N-1 positions of uracil units places the corresponding acetyl-substitued O1 directed inward to the cavity of calix[2]uracil[2]arene **4g** to form an inward flattened partial cone conformation (Scheme 3). The interplanar angles between oppositely placed phenylene and uracil rings are 36.7(2)° and 12.6(2)°. Therefore, both the uracil rings are parallel to each other about the cone axis with their respective carbonyl units at C-2 pointing in the same direction, but the phenylene rings are not parallel, again due to above-mentioned flattening. Also, the *O*-acetyl unit of the 1,3-phenylene ring (m) (Scheme 2) faces the π-cloud of the other phenylene ring placed between N-3 positions of the uracils. The 3.362(1) Å distance between $OCOCH_3$ and phenylene ring shows the presence of $CH_3-\pi$ interactions which might be responsible for stabilization of inward flattened conformation. Both the acetyl groups are planar and rotated with respect to the phenylene rings through angles of 86.6(2)° and 79.1(2)°, respectively.

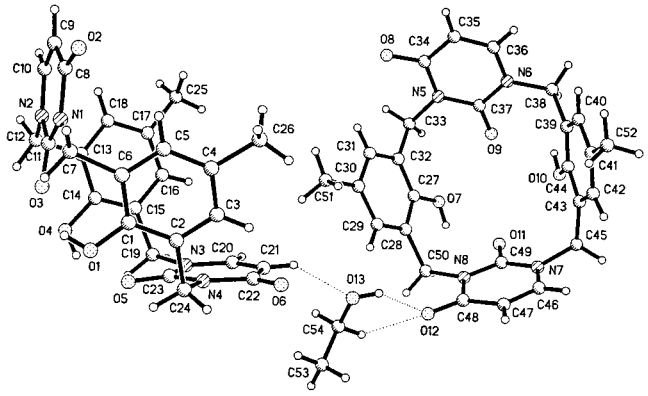


Figure 2. Diagram showing the numbering system of the 2:1 complex of **4j**·ethanol.

The X-ray crystal structure of 2:1 complex of **4j**·ethanol shows the presence of two crystallographically independent types of molecules (X and Y) in the unit cell. The environment around the two types of molecules is different; therefore, they show slight variation in their bond lengths and bond angles. There are eight calix[2]uracil[2]arene and four ethanol molecules per unit cell thus giving a 2:1 stoichiometric calix:ethanol complex. Ethanol is H-bonded to **4j** (Figure 2) and acts as a H-bond donor through alcoholic oxygen O13H and methylene H at C54, giving two intramolecular contacts (O13−H13A···O12, O13···O12 2.87(4) Å, ∠O13−H13A···O12 137(5)°; C54−H54A···O12, C54···O12 2.19(3) Å, ∠C54−H54A···O12 129(3)°) to one of calix[2]uracil[2]arene molecule (Y) while it behaves as a H-bond acceptor due to the presence of an intermolecular H-bond (C21−H21A···O13(i), C21..O13 3.02(4) Å, ∠C21−H21A···O13 147(2)° where $i = x - 1, y - 1, z$) to the second calix[2]uracil[2]arene molecule (X).

The small-sized alcohols such as methanol, ethanol, propanol, etc., which lack large hydrocarbon surfaces necessary for efficient hydrophobic interactions, show only weak OH-induced H-bondings with the receptors.[17] So in these cases, only oxygen of alcohol is involved in binding with acidic protons of the host. Here, in case of the **4j**:ethanol complex, ethanol shows an unusual binding, where in addition to OH of ethanol, the adjacent CH proton also undergoes H-bonding with the C4═O of the

uracil units. As a result, ethanol shows a unique three-center H-bonding with the uracil units of heterocalix **4j**.

In the **4j**·ethanol complex, both heterocalixarene units have a cone conformation characterized by a continual change of sign (+,−) of the torsion angles about the $ArCH_2$ bonds.[18] As the two independent molecules have different environments so their torsion angles also vary. These torsion angles about C7, C12, C19, C24 are 85(2), −100(2); 94(2), −73(2); 80(2), −98(2); and 90(2), −75(2) and about C33, C38, C45, C50 are 77(2), −97(2); 104(2), −85(2); 74(2), −83(2); and 96(2), 88(2) for X and Y units, respectively. The interplanar angles between two phenylene and two uracil rings are 46(2)°, 97(1)° and 50(1)°, 101(2)°, respectively, for molecules X and Y. Thus, uracil rings are almost perpendicular, but phenylene rings are nearly parallel in both molecules X and Y. The interplanar angles found between the best plane fitted to the connecting methylene C-atoms and the uracil rings of two molecules are 47(1)°, 50(1)° and 47(2)°, 54(2)°, between this plane and phenylene rings lying between N-1 positions of the uracil units are 116(1)°, 113(3)° whereas between this plane and phenylene rings placed between N-3 positions of uracil are 67(1)°, 63(1)°, respectively, for molecules X and Y. Thus, in both the molecules, the phenylene rings placed between N-1 positions of uracils are more flattened inward as in comparison to the one placed between N-3 positions of uracils. Both molecules show intramolecular H-bonding involving hydroxy groups and the corresponding carbonyl oxygens at the positions C-2 of the uracil rings which stabilize the cone conformation [O1−H1A···O3, with O1..O3 2.64(2) Å, ∠O1−H1A···O3 121(1)°; O4−H4A···O5, O4···O5 2.77(2) Å, ∠O4−H4A···O5, 116(1)°; O7−H7A···O11, O7···O11 2.60(2) Å, ∠O7−H7a···O11 120(1)°; O10−H10A···O9, O10···O9 2.63(1) Å, ∠O10···H10A···O9 115(1) Å]

The average O···O distance in molecules X and Y are 2.821(2) Å and 2.793(2) Å, respectively, with lengthening of 0.2 Å with respect to those observed in the normal calix[4]arenes.[18] Crystal packing (Figure 3) shows extensive $\pi-\pi$ interactions between the various rings. The molecules are packed in alternate layers of centrosymmetrically related pairs of molecules X and Y along [010] plane. The uracil ring (N1−C8−C9−C10−N2−C11) of molecule X is showing intramolecular $\pi-\pi$ interaction with the phenylene ring (C39 to C44) placed between N-1 positions of molecule Y (distance between the centers of these two rings being 4.162(2) Å). This may be considered as a donor−acceptor $\pi-\pi$ interaction, uracil being an electron-deficient ring. At the same time the other phenylene ring (C27 to C32) and H-bonded uracil ring (N7−C46−C47−C48−N8−C49) of molecule Y are showing $\pi-\pi$ interaction with their symmetry-related counterparts having a center-to-center distance of 3.881(2) Å and 4.390(3) Å, respectively.

B. ^{1}H NMR and Force Field Energy Minimization Studies. In the ^{1}H NMR spectrum of **4g** in $CDCl_3$, eight methylene protons appear as two 4H AB quartets at δ 3.80, 5.46 (J = 14 Hz) and 4.20, 5.79 (J = 14 Hz). The correlation between AB quartets have been established by decoupling experiments. The ^{13}C NMR spectrum exhibits the expected two signals for NCH_2 carbons at δ 42.30 and 46.86. Its ^{1}H NMR spectrum shows two singlets each due to $COCH_3$ (δ 1.50 and 2.01) and Ar−CH_3 (δ 2.33 and 2.41) protons. In consonance with X-ray structure, the signal at δ 1.50 could be due to $COCH_3$ on the 1,3-phenylene (m) which faces the π-cloud of phenylene ring *n* (Scheme 2) and is shifted upfield to the other $COCH_3$ signals (δ 2.01) due to π ring currents.

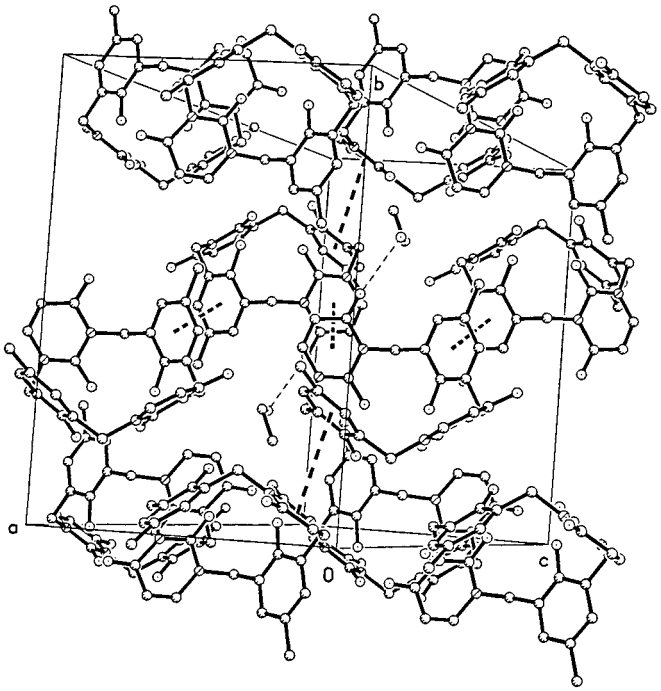


Figure 3. Packing diagram of **4j**·ethanol showing H-bonding and $\pi-\pi$ interaction.

Like **4g**, other U-symm, P-symm calix[2]uracil[2]arenes **4d**, **4h**, and **4i** in their ^{1}H NMR spectra exhibit two AB quartets due to N1−CH_2 and N3−CH_2 protons, and one of the methoxy (in case of **4d**) or acetoxy (in case of **4h** and **4i**) singlets is shifted upfield by 0.5−1.00 ppm. Therefore, replacement of the acetoxy groups with less bulky methoxy units in **4d** or the replacement of methyl units of the phenylene ring with H in **4i** or *tert*-butyl in **4h** does not affect the conformation of these calix[4]arenes.

The force field energy minimization[19] studies on these calix[2]uracil[2]arenes show them to attain either cone or the partial cone nonconvertible conformations and more appropriately to be designated as configurations. The cone configurations are in general more stable than the partial cone ones. In case of partial cone configurations the phenylene ring placed between N1 positions of uracils undergoes inward flattening in the cavity to provide an inward flattened partial cone configuration (Figures 4 and 5) as shown by the X-ray crystal structure of **4g** and ^{1}H NMR studies. The cone configuration as deduced by energy minimization studies does not envisage any ^{1}H NMR upfield shift of the signal for the substituent at 2-position of one of the phenylene rings. Therefore, a combination of ^{1}H NMR and energy mini-

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(19) The energy minimization studies have been performed by Using PCMODEL, provided by Serena Software.

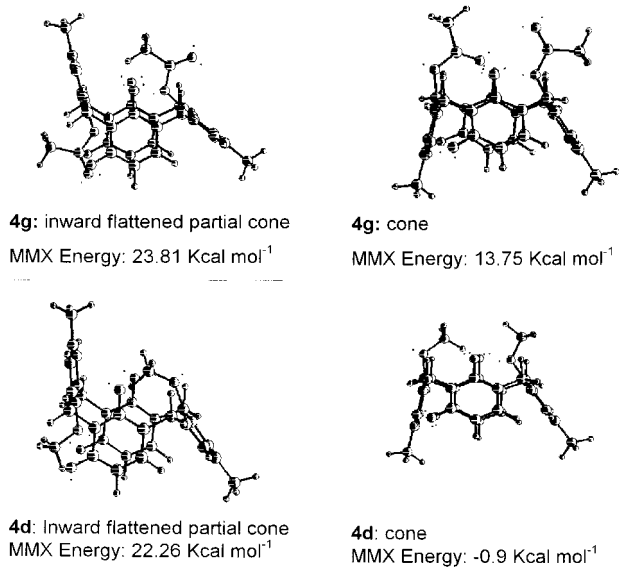

Figure 4. Energy-minimized structures of **4g** and **4d**.

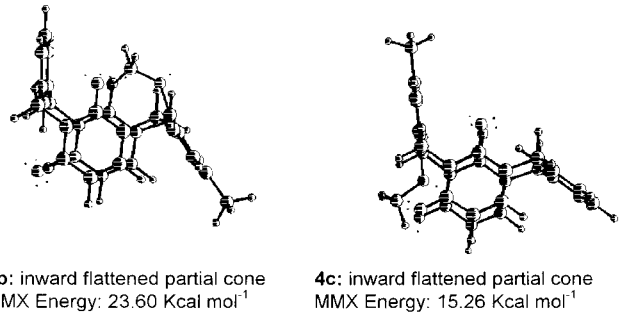

Figure 5. Energy-minimized structures of **4b** and **4c**.

mization studies can assist in assignment of configurations to these calixarenes, which is in consonance with X-ray crystal structure. The energy minimization studies of the compounds **4d** (Figure 4), **4h** and **4i**, corroborate either cone configuration or inward flattened partial cone configuration, in parallel with **4g**. The upfield shift of the methyl or acetyl substituents present at the 2-position of phenylene ring can be explained only by inward flattened partial cone configurations.

The U-symm, P-unsymm type calix[2]uracil[2]arenes **4b**, **4e**, and **4f** in their ^{1}H NMR spectra exhibit two AB quartets due to N1−CH_2 and N3−CH_2 protons. In case of **4b** and **4e**, it is the signal for the methoxy group that is shifted upfield, whereas in **4f**, the acetoxy group signal is shifted upfield. In the ^{1}H NMR spectrum of **4c** in $CDCl_3$, four methylene protons appear as one sharp singlet at δ 4.01, four methylene protons appear as one AB quartet at δ 4.49, 5.12 (J = 14 Hz), and the methoxy signal appears as singlet at δ 3.67 (normal position). It may be concluded that, in these calix[2]uracil[2]arenes **4b**, **4d**−**i**, the susbtituent present at the 2-position of 1,3-phenylene ring placed between N-1 of the two uracils is shifted upfield in their ^{1}H NMR spectra. These observations lead to a conformation with the phenylene ring placed between N-1 of uracils flattened inward and both phenylene rings in anti configuration, i.e., flattened inward partial conelike conformation as found in case of **4g** (X-ray).

The ^{1}H NMR spectra of **4g**, **4d**−**i** show only one conformation which remains unaffected by solvents

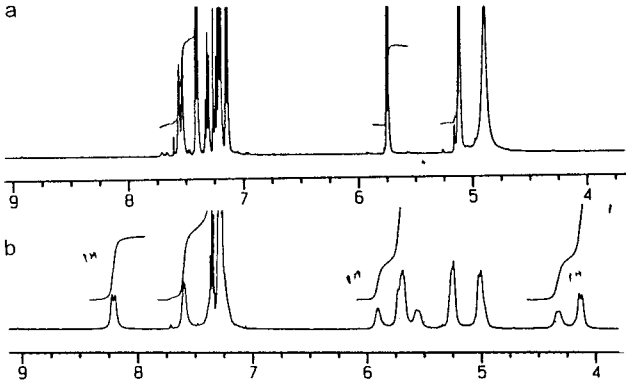

Figure 6. ^{1}H NMR spectra of **4a** at (a) 27 °C and (b) −60 °C in $CDCl_3$ at 500 MHz.

($CDCl_3$, DMSO-d_6, or TFA) unlike the conventional p-*tert*-butylcalix[4]arene.[18] The latter due to the presence of intramolecular H-bonding forms a stable cone conformation, but its tetra-*O*-methyl and *O*-ethyl derivatives,[20] depending on the polarity of the solvent, exist as different conformational isomers, and the increase in bulk in case of tetra-*O*-propyl derivative restricts this free interconversion between different conformers. However, in these calix[2]uracil[2]arenes, even the presence of two methoxy groups along with less bulky uracil oxo units, restricts the conformational interconversion. The X-ray crystal structure of **4j**, elaborated subsequently, shows that in case of calix[2]uracil[2]arene, due to shorter N−C distances in comparison with C−C distances, the distance between two phenylene units is decreased to 6.0−6.2 Å units in comparison to > 7 Å units in case of conventional calix[4]arenes. These smaller cavities of calix[2]uraci[2]-arenes in comparison with conventional calix[4]arenes could also be responsible for inhibition of conformational interconversions and thereby stabilization of one of the conformers.

The ^{1}H NMR of **4a** in $CDCl_3$ at 27 °C exhibits both NCH_2 signals as broad singlets at δ 4.96 and 5.16 (Figure 6a) which on lowering the temperatures to 0 °C or −25 °C undergo further broadening. Its ^{1}H NMR spectrum at −60 °C shows two pairs of distorted AB quartets (Figure 6b) (3:2), but the signals are not well defined. Therefore, **4a**, which lacks any substituent on 1,3-phenylene rings, even at −60 °C, undergoes interconversion between two conformers. In the case of calix[2]-uracil[2]arene **4c**, the presence of two NCH_2 signals as one singlet and one AB quartet shows that in the solution phase **4c** also has a semiflexible conformation.

Due to presence of circular hydrogen bonding, the conventional calix[4]arenes derived from the para-substituted phenol and formaldehyde exist in a cone conformation, whereas the conformations of O-alkylated calix[4]arenes depend on the nature and number of the alkoxy groups. So, we envisaged that such hydrogen bonding could be invoked in a calix[2]uracil[2]arene constituted by the phenylene rings having hydroxy groups at 2-position. The acid-catalyzed (HCl:EtOH) hydrolysis of **4g** provides **4j** (90%), which crystallizes from

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Table 1. Extraction (%) and Transport Profile (mol/24 H × 10^{-8}) of Calix[2]uracil[2]arenes 4d and 4j

	Li^+	Na^+	K^+	Tl^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}	Pb^{2+}	Ag^+
extraction										
4d	0.01	0.02	0.01	0.03	0.00	0.26	0.23	–	0.22	0.01
4j	0.01	0.01	0.01	0.02	0.01	0.00	0.00	–	0.06	0.01
transport rates										
4d	9	23	17	98	9	341	266	22	–	38

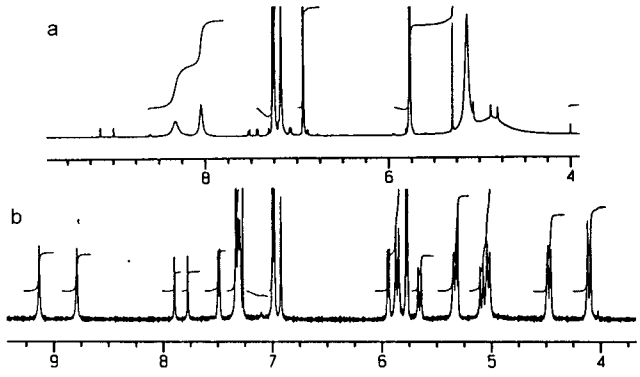

Figure 7. ^{1}H NMR spectra of **4j** at (a) 27 °C and (b) −60 °C in $CDCl_3$ at 500 MHz.

ethanol as a 2:1 **4j**·ethanol complex. Calix[2]uracil[2]arene **4j** on crystallization from methanol and ethylene glycol provides 2:1 **4j**·methanol/ethylene glycol complexes but in case of higher alcohols **4j**·alcohol complexes are not formed.

The X-ray crystal structure of **4j** shows its cone conformation in solid state, but in its ^{1}H NMR spectrum (27 °C) recorded on a 200 Mz instrument, the appearance of one of the 4H (NCH_2) signals at δ 4.85 as a broad singlet indicates that the molecule exists as a mixture of a number of conformers which undergo fast interconversion to provide the average signals. However, on recording the spectrum on a 500 MHz instrument at 25 °C, in addition to broad signals for both N-1 and N-3 CH_2 at δ 4.85 (4H) and δ 5.12 (4H), a number of small signals (<10% intensity) appear (Figure 7a). On recording the spectrum at 0 °C, further broadening of these signals occurs and two OH broad singlets at δ 8.00 and 8.25 also appear as one broad singlet. At −25 °C, a number of broad signals appear in the region δ 4.00−6.00, which undergo further splitting at −45 °C. Further lowering of the temperature to −60 °C provides a well-defined ^{1}H NMR spectrum, which shows four sets of AB quartets. The U-5H and U6-H appear as two sets of doublets at δ 5.80 and 5.95 (2:1) and at δ 7.35 and 7.50 (2:1), respectively (Figure 7). Similarly, two OH groups appear in two sets of singlets (δ 7.80, 7.92) and (δ 8.82, 9.16) in a 1:2 ratio. Therefore, **4j** at −60 °C (Figure 7b) exists as a mixture of two conformers which undergoes quite slow interconversion at least on an NMR time scale.

The binding capacities of **4j** with methanol, ethanol, and ethylene glycol could be observed from differential scanning calorimetry. The uncomplexed **4j**, obtained by crystallization of the **4j**·methanol complex from *tert*-butyl alcohol, exhibits only a small endothermic peak at 216−258 °C along with an endothermic melting peak at 295 °C. The **4j**·methanol/ethanol/ethylene glycol complexes exhibit these as common peaks along with following additional peaks. The **4j**·ethanol complex shows one exothermic and one endothermic peak at 65−102 °C (6.74 kJ mol^{-1}) and 178−209 °C (2.99 kJ mol^{-1}), respectively. **4j**·methanol and **4j**·ethylene glycol complexes exhibit only one additional endothermic peak at 176−213 °C and 50−141 °C, respectively. In thermogravimetric analysis, **4j**·ethanol/**4j**·methanol complexes show a respective loss of ethanol and methanol between 178 and 250 °C which is in consonance with DSC results. However, in case of the **4j**·ethylene glycol complex, no loss of ethylene glycol in the 50−141 °C range could be observed, and finally ethylene gycol is lost above 200 °C, i.e, at its boiling point. Therefore, ethylene gylcol forms a weaker complex which is cleaved below 140 °C whereas methanol and ethanol complexes are cleaved at a much higher temperature range of 178−210 °C.

In conclusion, calix[2]uracil[2]arenes **4** with (i) both phenylene rings *n* and *m* para-disubstituted or (ii) phenylene ring *n* para-disubstituted and *m* unsubstituted, have a very unique inward flattened partial conelike conformation. The analogue of category i, possessing phenolic rings *n* and *m*, because of H-bonding, constitute a conelike conformation which undergoes fast interconversions between various conformers in solution phase. In **4**, with ring *n* being unsubstituted and ring *m* being para-disubstituted and both phenylene rings *n* and *m* being unsubstituted, the calix[4]arenes have a flexible conformation. Since the uracil moieties in all these heterocalix[4]arenes are placed similarly, their conformations depend on the substitution pattern of phenylene rings and their placement at N1, N1 or N3, N3 positions of uracil.

Recognition Behavior

Calix[2]uracil[2]arenes (**4d**−**i**) constituted by the phenylene rings having substituents other than hydroxy group at the 2-position have similar inward flattened partial cone conformations, and out of these, the representative case of calix[2]uracil[2]arene **4d** was selected for study of extraction and transporation of metal picrates. Calixarenes **4d** show both extraction and transportation (Table 1), preference for Ca^{2+}, Sr^{2+}, Ba^{2+}, and Pb^{2+} picrates over Li^+, Na^+, K^+, Tl^+, Ag^+, and Mg^{2+} picrates.

The calix[2]uracil[2]arene **4k**, having the chromogenic nitrophenol unit as one of the binding sites, on addition of alkali metal (Li^+, Na^+, K^+) and Tl^+ acetate shows only a marginal change in absorbance, but on the addition of alkaline earth metal (Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}) acetates, the absorbances are significantly increased (Figure 8), though the λ_{max} value remains unchanged. The titration of **4k** against metal acetates shows the formation of 1:1, **4k**·metal acetate complexes with nearly 80−100 times the preference for alkaline earth metal cations over alkali metal cations (Table 2).

The calix[2]uracil[2]arene **4j** undergoes fast equilibration between the various conformers (as seen by variable temperature NMR), and its ^{1}H NMR spectrum exhibits two signals (δ 8.31, 7.97) due to OH protons, and NCH_2 protons appear as one broad (δ 4.80) and one sharp singlet (δ 5.14). The addition of malonitrile to a solution

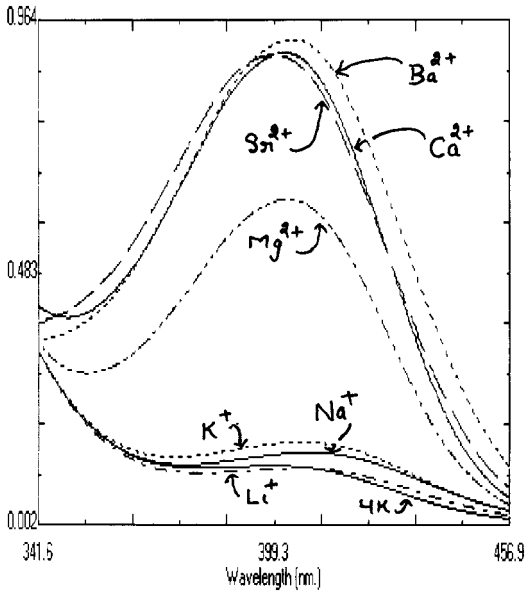

Figure 8. Spectra of **4k** and **4k** + metal acetates.

Table 2. Stability Constants of Calixarene 4k with Metal Acetates

no.	additive	stability constant (mol^{-1} L)
1	lithium acetate	0
2	sodium acetate	1.59×10^2
3	potassium acetate	2.81×10^2
4	magnesium acetate	6.18×10^3
5	calcium acetate	1.62×10^4
6	strontium acetate	1.61×10^4
7	barium acetate	1.78×10^4

of **4j** in $CDCl_3$ shifts the OH protons upfield from δ 8.31 to 7.97. The ^{1}H NMR spectrum of **4j**·malonitrile (1:40) exhibits only one singlet at δ 7.97, and one NCH_2 singlet at δ 4.80 becomes sharp and a second NCH_2 at δ 5.14 becomes broad, in comparison with that observed in **4j**. So, malonitrile binds weakly with **4j** (K = 6.5 + 0.5 mol^{-1}). A similar effect is observed with acetonitrile, but addition of nitromethane does not effect the ^{1}H NMR spectrum of **4j**.

Experimental Section

For general experimental details, see ref 21.

1,3-Bis(bromomethyl)-2-acetoxy-5-(*tert*-butyl)benzene (2d). To a mixture of *p*-*tert*-butylphenol (28.0 g, 0.185 mol) and K_2CO_3 (30.0 g, 0.217 mol) in 300 mL of water stirred under N_2 at 70 °C was added 37% aqueous formaldehyde solution (60 mL, 0.74 mol), and it was stirred at 65−70 °C for 5 h. The CO_2 was bubbled through the reaction mixture until the yellow solution turned very cloudy. The mixture was extracted with ethyl acetate, and the organic layer was dried over Na_2SO_4 (anhydrous). The solvents were removed under vaccum, and the residue was added to the cooled solution of 37% HBr in acetic acid (60 mL) and stirred for 30 min at room temperature and then heated to 50 °C for another 30 min. Acetic anhydride (120 mL) was added to the reaction mixture very carefully, and the reaction mixture was heated on water-bath for 1 h. The solvent was removed under vaccum, and the residue was dissolved in ether solvent and washed with aqueous $NaHCO_3$ solution. The organic layer was separated and dried (Na_2SO_4). The solvent was evaporated, and the residue was sublimed under vaccum to get **2e** (55%): mp 61 °C; MS *m*/*z* 376, 378, 380 (1:2:1, M^+); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.33 (9H, s, 3 × CH_3), 2.44 (3H, s, $COCH_3$), 4.35 (4H, s, 2 × CH_2), 7.37 (2 H, s, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 20.60 (+ve, CH_3), 27.98 (+ve, CH_3), 28.61 (absent, C), 30.70 (−ve, CH_2), 126.10 (absent, ArC), 128.15 (+ve, ArCH), 130.09 (absent, ArC), 149.64 (absent, ArC), 168.48 (absent, C=O); IR ν_{max}/cm^{-1} (KBr): 1710 (C=O).

1,3-Bis(bromomethyl)-2-acetoxy-5-nitrobenzene (2f). A mixture of 2,6-bis(bromomethyl)-4-nitrophenol[22] (3.23 g, 0.01 mol) and acetic anhydride (10 mL) containing a catalytic amount of H_2SO_4 was heated on water bath for 30 min, and the solvent was removed under vaccum. The residue was dissolved in 25 mL of ether solvent and washed with aqueous sodium bicarbonate. The organic layer was dried (Na_2SO_4) and evaporated under vaccum and used without further purification (80%): mp 81 °C (hexane + ether); MS *m*/*z* 365, 367, 369 (1:2:1, M^+); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.50 (3H, s, CH_3), 4.41 (4H, s, 2 x CH_2), 8.32 (2 H, s, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 20.58 (+ve, CH_3), 25.79 (−ve, CH_2), 126.19 (+ve, ArCH), 133.05 (absent, ArC), 145.42 (absent, ArC), 151.94 (absent, ArC), 167.46 (absent, C=O); IR ν_{max}/cm^{-1} (KBr): 1700 (C=O).

Synthesis of 1,3-Bis(1-uracilylmethyl)aryl Derivatives 3(a−e). General Procedure. A solution of 2,4-bis(trimethylsilyloxy)pyrimidine **1** (1.96 g, 0.01 mol), **2a**[23] (1.32 g, 0.005 mol), and I_2 (20 mg) in 1,2-dichloroethane (20 mL) was heated to reflux, and the progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was cooled to 5 °C, and methanol (15 mL) was added. After couple of minutes the separated solid was filtered and recrystallized from methanol to get pure **3a**. Similarly, reactions of dihalides **2b**,[24] **2c**,[25] **2d** and **2e**[26] with **1** gave compounds **3b**, **3c**, **3d**, and **3e**, respectively.

1,3-Bis(1-uracilylmethyl)benzene (3a): 60%, 48 h; mp 268 °C (AcOH + H_2O); MS *m*/*z* 326 (M^+); ^{1}H NMR (200 MHz, $CDCl_3$ + TFA): δ 5.18 (4H, s, 2 × NCH_2), 6.21 (2 H, d, J = 7.8 Hz, C5-H), 7.23−7.43 (4H, m, ArH), 7.52 (2H, d, J = 7.8 Hz, C6-H); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$ + DMSO-d_6): δ 49.68 (−ve, NCH_2), 101.28 (+ve, C5-H), 126.49 (+ve, ArCH), 128.42 (+ve, ArCH), 135.82 (absent, C), 140.05 (+ve, ArCH), 143.60 (+ve, C6−H), 150.34 (absent, C), 163.18 (absent, C); IR ν_{max}/cm^{-1} (KBr): 3200 (NH), 1700 (C=O), 1658 (C=O). Anal. Calcd for $C_{16}H_{14}O_4N_4$: C 58.90, H 4.29, N 17.18. Found: C 58.55, H 4.02, N 17.57.

1,3-Bis(1-uracilylmethyl)-2-methoxy-5-methylbenzene (3b): 90%, 36 h; mp 263 °C (MeOH); MS *m*/*z* 370 (M^+); ^{1}H NMR (200 MHz, $CDCl_3$ + DMSO-d_6): δ 2.28 (3H, s, CH_3), 3.82 (3H, s, OCH_3), 4.92 (4H, s, 2 × NCH_2), 5.61 (2 H, dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, C5-H), 6.99 (2H, s, ArH), 7.29 (2H, d, J = 7.8 Hz, C6-H), 7.58 (1H, s, NH), 11.08 (1H, s, NH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$ + DMSO-d_6): δ 19.25 (+ve, CH_3), 44.36 (−ve, NCH_2), 59.90 (+ve, OCH_3), 101.06 (+ve, C5-H), 127.53 (+ve, ArCH), 127.95 (absent, C), 132.49 (absent, C), 144.02 (+ve, C6−H), 149.60 (absent, C), 152.11 (absent, C), 162.69 (absent, C); IR ν_{max}/cm^{-1} (KBr): 3205 (NH), 1710 (C=O), 1695 (C=O), 1675 (C=O), 1644(C=O). Anal. Calcd for $C_{18}H_{18}O_5N_4$: C 58.38, H 4.86, N 15.14. Found: C 58.37, H 4.85, N 15.58.

1,3-Bis(1-uracilylmethyl)-2-acetoxy-5-methylbenzene (3c): 70%, 48 h; mp 272 °C (AcOH); MS *m*/*z* 398 (M^+); ^{1}H NMR (200 MHz, $CDCl_3$ + TFA): δ 2.38 (3H, s, CH_3), 2.44 (3H, s, OAc), 4.90 (4H, s, 2 × NCH_2), 6.11 (2 H, d, J = 7.9 Hz, C5-H), 7.20 (2H, s, ArH), 7.46 (2H, d, J = 7.9 Hz, C6-H), 10.83 (2H, s, 2 × NH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$ + TFA): δ 20.39 (+ve, CH_3), 37.98 (+ve, OAc), 47.19 (−ve, NCH_2), 103.20 (+ve, C5-H), 127.60 (absent, C), 131.63 (+ve,

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ArCH), 139.62 (absent, C), 144.96 (+ve, C6-H), 146.78 (absent, C), 152.42 (absent, C), 162.27 (absent, C), 173.47 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1758 (C═O), 1713 (C═O), 1676 (C═O). Anal. Calcd for $C_{19}H_{18}O_6N_4$: C 57.29, H 4.52, N 14.07. Found: C 57.39, H 4.39, N 13.86.

2,6-Bis(1-uracilylmethyl)-1-acetoxy-4-(*tert*-butyl)benzene (3d): 70%, 48 h; mp 271−273 °C (AcOH); MS *m*/*z* 440 (M^+); ^{1}H NMR (200 MHz, $CDCl_3$ + DMSO-d_6): δ 1.30 (9H, s, 3 × CH_3), 2.36 (3H, s, OAc), 4.78 (4H, s, 2 × NCH_2), 5.56 (2 H, dd, J_1 = 8.0 Hz, J_2 = 2.0, C5-H), 7.18 (2H, d, J = 8.0 Hz, C6-H), 7.32 (2H, s, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$ + DMSO-d_6): δ 25.90 (+ve, CH_3), 36.09 (+ve, OAc), 39.37 (absent, C), 50.66 (−ve, NCH_2), 106.66 (+ve, C5-H), 132.07 (absent, C), 134.02 (absent, C), 150.09 (+ve, C6-H), 153.95 (absent, C), 156.10 (absent, C), 168.61 (absent, C), 174.32 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1753 (C═O), 1716 (C═O), 1672 (C═O). Anal. Calcd for $C_{22}H_{24}O_6N_4$: C 60.00, H 5.45, N 12.72. Found: C 60.35, H 5.11, N 12.86.

2,6-Bis(1-uracilylmethyl)-1-acetoxybenzene (3e): 70%, 48 h; mp 258−62 °C (MeOH); MS *m*/*z* 384 (M^+); ^{1}H NMR ($CDCl_3$ + TFA): δ 2.46 (3H, s, OAc), 4.95 (4H, s, 2 × NCH_2), 6.08 (2 H, d, J = 8.0 Hz, C5-H), 7.26−7.45 (5H, s, ArH, C6-H), ^{13}C NMR (normal/DEPT-135) ($CDCl_3$ + TFA): δ 20.59 (+ve, OAc), 47.06 (−ve, NCH_2), 103.21 (+ve, C5-H), 128.10 (+ve, ArCH), 128.42 (absent, ArC), 130.97 (+ve, ArCH), 146.24 (+ve, ArCH), 152.05 (absent, ArC), 166.97 (absent, C═O), 166.62 (absent, C═O), 171.79 (absent, C═O); IR ν_{max}/cm^{-1} (KBr): 1770 (C═O), 1700 (C═O), 1670 (C═O). Anal. Calcd for $C_{18}H_{16}O_6N_4$: C 56.25, H 4.16, N 14.58. Found: C 56.45, H 4.01, N 14.36.

Synthesis of Calix[2]uracil[2]arenes (4a−i). A suspension of **3a** (3.26 g, 0.01 mol) in acetonitrile (1000 mL) containing dibromide **2a** (3.168 g, 0.012 mol), K_2CO_3 (10 g), and TBA−HSO_4 (20 mg) was heated to reflux, and the progress of the reaction was monitored by TLC. After completion of reaction, K_2CO_3 was filtered off and washed with acetonitrile. The filtrate and washings were combined, the solvent was distilled off, and the residue was column chromatographed on silica gel (60−120 mesh) using ethyl acetate:chloroform (20:80) as eluent to isolate product **4a**. Similar reactions of **3a** with **2b** and **3b** with **2a**, **2b**, and **2c** gave calix[4]arenes **4c**, **4b**, **4d**, and **4e**. The reactions of **3c** with **2b** and **2c**, **3d** with **2d**, and **3e** with **2e** gave calix[4]arenes **4f**, **4g**, **4h**, and **4i**, respectively.

4a: 24%, 30 h; mp 287−290 °C ($CHCl_3$); MS *m*/*z* 428 (M^+); ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.97 (4H, s, 2 × NCH_2), 5.16 (4H, s, 2 × NCH_2), 6.16 (2 H, d, J = 8.0 Hz, C5-H), 7.21−7.46 (10H, m, ArH and C6-H); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 45.51 (−ve, NCH_2), 53.95 (−ve, NCH_2), 102.13 (+ve, C5-H), 126.94 (+ve, ArCH), 128.65 (+ve, ArCH), 129.10 (+ve, ArCH), 129.84 (+ve, ArCH), 129.98 (absent, C), 135.39 (absent,C), 136.00 (absent,C), 144.83 (+ve, C6-H), 152.08 (absent, C), 166.36 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1700 (C═O), 1660 (C═O), 1652 (C═O). Anal. Calcd for $C_{24}H_{20}O_4N_4$: C 67.29, H 4.67, N 13.48. Found: C 67.02, H 4.37, N 13.86.

4b: 20%, 24 h; mp 297 °C decomp ($CHCl_3$ + MeOH); MS *m*/*z* 472 (M^+); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.31 (3H, s, CH_3), 2.95 (3H, s, OCH_3), 3.91, 5.50 (4H, AB quartet, J = 15 Hz, 2 × NCH_2), 4.75, 5.82 (4H, AB quartet, J = 15 Hz, 2 × NCH_2), 5.59 (2 H, d, J = 7.8 Hz, C5-H), 6.65 (s, 1H, ArH), 6.73 (2H, d, J = 7.8 Hz, C6-H), 7.06 (2H, s, ArH), 7.27 (3H, s, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 20.59 (+ve, CH_3), 43.75 (−ve, NCH_2), 47.62 (−ve, NCH_2), 61.27 (+ve, OCH_3), 101.40 (+ve, C5-H), 122.37 (+ve, ArCH), 127.19 (+ve, ArCH), 127.66 (+ve, ArCH), 130.78 (absent, C), 132.42 (+ve, ArCH), 134.26 (absent, C), 137.34 (absent, C), 140.46 (+ve, C6-H), 151.42 (absent, C), 155.71 (absent, C), 162.65 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1707 (C═O), 1660 (C═O), 1652 (C═O). Anal. Calcd for $C_{26}H_{24}O_5N_4$: C 66.10, H 5.08, N 11.86. Found: C 65.87, H 4.88, N 11.56.

4c: 15%, 30 h; mp 276 °C ($CHCl_3$); MS *m*/*z* 472(M^+); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.33 (3H, s, CH_3), 3.67 (3H, s, OCH_3), 4.01 (4H, s, 2 × NCH_2), 4.49, 5.76 (4H, AB quartet, J = 14 Hz, 2 × NCH_2), 5.58 (2 H, d, J = 8.0 Hz, C5-H), 6.92 (2H, d, J = 8.0 Hz, C6-H), 7.21−7.40 (6H, m, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 20.66 (+ve, CH_3), 42.15 (−ve, NCH_2), 51.16 (−ve, NCH_2), 62.37 (+ve, OCH_3), 102.32 (+ve, C5-H), 123.99 (+ve, ArCH), 127.58 (+ve, ArCH), 128.91 (+ve, ArCH), 129.51 (absent, C), 132.62 (absent, ArC), 137.55 (absent, C), 141.37 (+ve, C6-H), 151.55 (absent, C), 155.48 (absent, C), 162.40 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1710 (C═O), 1670 (C═O). Anal. Calcd for $C_{26}H_{24}O_5N_4$: C 66.10, H 5.08, N 11.86. Found: C 66.40, H 485, N 11.92.

4d: 18%, 24 h; mp > 340 °C ($CHCl_3$ + MeOH); FAB MS *m*/*z* 517 (M^+ + 1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.32 (3H, s, CH_3), 2.33 (3H, s, CH_3), 2.86 (3H, s, OCH_3), 3.65 (3H, s, OCH_3), 3.74, 5.74 (4H, AB quartet, J = 14 Hz, NCH_2), 4.20, 5.87 (4H, AB quartet, J = 14 Hz, NCH_2), 5.50 (2 H, d, J = 7.8 Hz, C5-H), 6.62 (2H, d, J = 7.8 Hz, C6-H), 7.01 (2H, s, ArH), 7.26 (2H, s, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 15.69 (+ve, CH_3), 29.80 (−ve, NCH_2), 41.78 (−ve, NCH_2), 47.04 (−ve, NCH_2), 61.21 (+ve, OCH_3), 61.83 (+ve, OCH_3), 101.62 (+ve, C5-H), 129.75 (absent, C), 130.90 (absent, C), 131.47 (absent, C), 132.46 (+ve, ArCH), 133.81 (absent, C), 134.13 (+ve, ArCH), 139.48 (+ve, C6-H), 150.98 (absent, C), 156.46 (absent, C), 162.37 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1710 (C═O), 1700 (C═O), 1657 (C═O). Anal. Calcd for $C_{28}H_{28}O_6N_4$: C 65.12, H 5.43, N 10.85. Found: C 64.81, H 5.09, N 11.16.

4e: 27%, 24 h; mp > 340 °C decomp ($CHCl_3$ + MeOH); FAB MS *m*/*z* 545 (M^+ + 1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.15 (3H, s, OAc), 2.32 (3H, s, CH_3), 2.37 (3H, s, CH_3), 2.91 (3H, s, OCH_3), 3.78, 5.75 (4H, AB quartet, J = 14 Hz, 2 × NCH_2), 4.22, 5.68 (4H, AB quartet, J = 14 Hz, 2 × NCH_2), 5.56 (2 H, d, J = 7.8 Hz, C5-H), 6.76 (2H, d, J = 7.8 Hz, C6-H), 7.04 (2H, s, ArH), 7.36 (2H, s, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 20.57 (+ve, 2 × CH_3), 21.99 (+ve, OAc), 41.79 (−ve, NCH_2), 47.07 (−ve, NCH_2), 61.12 (+ve, OCH_3), 101.97 (+ve, C5-H), 129.24 (absent, C), 130.50 (absent, C), 132.64 (+ve, ArCH), 133.88 (absent, C), 134.10 (absent, C), 134.19 (+ve, ArCH), 140.53 (+ve, C6-H), 146.20 (absent, C), 150.86 (absent, C), 156.35 (absent, C), 162.34 (absent, C), 170.37 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1750 (C═O), 1712 (C═O), 1675 (C═O), 1592 (C═C). Anal. Calcd for $C_{29}H_{28}O_7N_4$: C 63.97, H 5.15, N 10.29. Found: C 64.35, H 4.87, N 10.25.

4f: 20%, 24 h; mp > 340 °C decomp ($CHCl_3$ + MeOH); FAB MS *m*/*z* 545 (M^+ + 1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.47 (3H, s, OAc), 2.29 (3H, s, CH_3), 2.40 (3H, s, CH_3), 3.54 (3H, s, OCH_3), 3.76, 5.43 (4H, AB quartet, J = 14 Hz, 2 × NCH_2), 4.21, 5.97 (4H, AB quartet, J = 14 Hz, 2 × NCH_2), 5.58 (2 H, d, J = 7.8 Hz, C5-H), 6.74 (2H, d, J = 7.8 Hz, C6-H), 7.16 (2H, s, ArH), 7.20 (2H, s, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 20.37 (+ve, CH_3), 20.64 (+ve, CH_3), 42.17 (−ve, NCH_2), 46.77 (−ve, NCH_2), 62.53 (+ve, OCH_3), 102.00 (+ve, C5-H), 130.05 (absent, C), 132.37 (+ve, ArCH), 132.94 (absent, C), 133.40 (+ve, ArCH), 136.49 (absent, C), 139.91 (+ve, C6-H), 150.50 (absent, C), 162.45 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1740 (C═O), 1707 (C═O), 1662 (C═O). Anal. Calcd for $C_{29}H_{28}O_7N_4$: C 63.97, H 5.15, N 10.29. Found: C 64.42, H 4.87, N 10.12.

4g: 28%, 20 h; mp > 340 °C decomp ($CHCl_3$ + MeOH); FAB MS *m*/*z* 573 (M^+ + 1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.50 (3H, s, OAc), 2.01 (3H, s, OAc), 2.33 (3H, s, CH_3), 2.41 (3H, s, CH_3), 3.80, 5.46 (4H, AB quartet, J = 15 Hz, 2 × NCH_2), 4.20, 5.79 (4H, AB quartet, J = 15 Hz, 2 × NCH_2), 5.63 (2 H, d, J = 8.0 Hz, C5-H), 6.87 (2H, d, J = 7.8 Hz, C6-H), 7.18 (2H, s, ArH), 7.26 (2H, s, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 20.40 (+ve, CH_3), 20.44 (+ve, CH_3), 20.64 (+ve, OAc), 21.67 (+ve, OAc), 42.30 (−ve, NCH_2), 46.86 (−ve, NCH_2), 101.60 (+ve, C5-H), 130.55 (absent, C), 130.68 (absent, C), 132.45 (+ve, ArCH), 133.39 (+ve, ArCH), 135.48 (absent, C), 136.73 (absent, C), 140.71 (+ve, C6-H), 146.01 (absent, C), 150.27 (absent, C), 156.35 (absent, C), 162.33 (absent, C), 169.50 (absent, C), 170.04 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1753 (C═O), 1710 (C═O), 1660 (C═O), 1672 (C═O). Anal. Calcd for $C_{30}H_{28}O_8N_4$: C 62.94, H 4.89, N 9.79. Found: C 62.65, H 4.61, N 10.06.

4h: 18%, 20 h; mp > 340 °C (decomp) ($CHCl_3$); FAB MS *m*/*z* 657 (M^+ + 1); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.34 (9H, s, 3 × CH_3), 1.37 (9H, s, 3 × CH_3), 1.39 (3H, s, OAc), 1.97 (3H, s, OAc), 3.85, 5.57 (4H, AB quartet, J = 14.4 Hz, 2 × NCH_2), 4.25, 5.82 (4H, AB quartet, J = 14.4 Hz, 2 × NCH_2), 5.66 (2

H, d, J = 8.0 Hz, C5-H), 6.84 (2H, d, J = 7.8 Hz, C6-H), 7.33 (2H, s, ArH), 7.42 (2H, s, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 21.18 (+ve, OAc), 21.66 (+ve, OAc), 31.36 (+ve, CH_3), 34.34 (absent, C), 34.61 (absent, C), 42.71 (−ve, NCH_2), 47.22 (−ve, NCH_2), 101.52 (+ve, C5-H), 128.68 (+ve, ArCH), 129.26 (+ve, ArCH), 130.20 (absent, C), 140.84 (+ve, C6-H), 145.65 (absent, C), 146.61 (absent, C), 148.40 (absent, C), 150.24 (absent, C), 162.46 (absent, C), 169.31 (absent, C), 170.99 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1753 (C═O), 1710 (C═O), 1660 (C═O), 1672 (C═O). Anal. Calcd for $C_{36}H_{40}O_8N_4$: C 65.85, H 6.09, N 8.54. Found: C 65.63, H 5.87, N 8.37.

4i: 16%, 36 h; mp > 340 °C (decomp) ($CHCl_3$); MS m/z 544 (M^+); ^{1}H NMR ($CDCl_3$): δ 1.46 (3H, s, OAc), 2.01 (3H, s, OAc), 3.87, 5.49 (4H, AB quartet, J = 14.4 Hz, 2 × NCH_2), 4.26, 5.83 (4H, AB quartet, J = 14.4 Hz, 2 × NCH_2), 5.62 (2 H, d, J = 8.0 Hz, C5-H), 6.85 (2H, d, J = 7.8 Hz, C6-H), 7.20−7.49 (6H, m, ArH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 20.19 (+ve, OAc), 21.68 (+ve, OAc), 34.34 (absent, C), 43.21 (−ve, NCH_2), 446.91 (−ve, NCH_2), 101.70 (+ve, C5-H), 125.93 (+ve, ArCH), 126.76 (+ve, ArCH), 131.14 (absent, C), 131.96 (+ve, ArCH), 132.73 (+ve, ArCH), 139.75 (+ve, C6-H), 148.23 (absent, C), 149.32 (absent, C), 150.28 (absent, C), 162.31 (absent, C), 169.29 (absent, C), 170.80 (absent, C); IR ν_{max}/cm^{-1} (Kbr). Anal. Calcd for $C_{28}H_{24}O_8N_4$: C 61.76, H 4.41, N 10.29. Found: C 61.92, H 4.13, N 10.12.

4j. A suspension of **4g** (0.57 g, 0.001 mol) in HCl−ethanol (1:1) (300 mL) was refluxed, and the progress of hydrolysis was monitored by TLC. After the completion of hydrolysis, the reaction mixture was concentrated under vaccum, and the separated solid was filtered and recrystallized from ethanol−chloroform to get **4j**·ethanol (2:1) complex (80%) (20 h), mp 279 °C ($CHCl_3$ + MeOH). The crystalline product upon heating at approximately 200 °C, due to a loss of trapped solvent, became an amorphous powder: MS m/z 488 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.16 (3H, s, CH_3), 2.22 (3H, s, CH_3), 5.12 (4H, bs, 2 × NCH_2), 5.29 (4H, s, 2 × NCH_2), 5.74 (2 H, d, J = 7.8 Hz, C5-H), 6.90 (2H, s, ArH), 7.17 (2H, d, J = 7.8 Hz, C6-H), 7.22 (2H, s, ArH), 7.97 (1H, bs, OH), 8.34 (1H, bs, OH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 20.36 (+ve, CH_3), 40.53 (−ve, NCH_2), 50.27 (−ve, NCH_2), 101.17 (+ve, C5-H), 123.39 (absent, C), 123.91 (absent, C), 128.84 (absent, C), 130.14 (absent, C), 131.92 (+ve, ArCH), 133.08 (+ve, ArCH), 142.14 (+ve, C6-H), 151.40 (absent, C), 152.78 (absent, C), 162.56 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1753 (C═ O), 1710 (C═O), 1660 (C═O), 1672 (C═O). Anal. Calcd for $C_{26}H_{24}O_6N_4{}^1/_2C_2H_5OH$: C 62.92, H 5.62, N 10.48. Found: C 62.45, H 5.31, N 10.36.

4k. The phase transfer catalyzed cyclocondensation of **3c** with **2f**, as described above for synthesis of **4a**−**i**, gave a mixture of products which was refluxed in HCl−ethanol (1:1) for 24 h. After removal of solvent under vaccum, the residue was column chromatographed using chloroform−ethyl acetate (8:2) as eluent to get pure **4k** (12%) (36 h), mp 295 °C ($CHCl_3$ + MeOH); MS m/z 519 (M^+); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.21 (3H, s, CH_3), 4.90 (4H, bs, 2 × NCH_2), 5.19 (4H, s, 2 × NCH_2), 5.79 (2 H, d, J = 7.8 Hz, C5-H), 6.94 (2H, s, ArH), 7.25 (2H, d, J = 7.8 Hz, C6-H), 8.05 (1H, bs, OH), 8.31 (2H, s, ArH), 9.20 (1H, bs, OH); ^{13}C NMR (normal/DEPT-135) (50 MHz, $CDCl_3$): δ 20.24 (+ve, CH_3), 40.45 (−ve, NCH_2), 50.06 (−ve, NCH_2), 103.17 (+ve, C5-H), 123.30 (absent, C), 123.56 (absent, C), 128.75 (absent, C), 130.08 (absent, C), 132.08 (+ve, ArCH), 139.94 (absent, ArC), 142.37(+ve, C6-H), 151.28 (absent, C), 152.80 (absent, C), 159.70 (absent, C), 162.24 (absent, C); IR ν_{max}/cm^{-1} (KBr): 1750 (C═O), 1709 (C═O), 1658 (C═O), 1676 (C═O). Anal. Calcd for $C_{25}H_{21}O_8N_5$: C 57.80, H 4.05, N 13.49. Found: C 58.13, H 4.00, N 13.17.

X-ray Structure Analysis of Calix[2]uracil[2]arenes 4g and 4j·Ethanol (2:1). All intensity data measurements were carried out on a Siemens P4 four circle diffractometer with graphite monochromatic Mo−Kα radiation (λ = 0.71069 Å). All structures were solved and refined using the SHELXTL software[27] package on a Siemens Nixdorf computer. The crystals of **4g** and **4j**·ethanol suitable for X-ray diffraction work were obtained by recrystallization from acetonitrile and ethanol, respectively. The unit cell parameters were determined from a least-squares fit of setting angles of 25 reflections in the range 20 ≤ 2θ ≤ 25°. Three standard reflections were measured every 100 reflections and showed no significant intensity variation during the data collection. The data were corrected for Lorentz and polarization effects. No absorption corrections were applied. The structures were solved by direct methods. Full matrix least squares refinement was employed with anisotropic thermal parameters for the non hydrogen atoms. The hydrogen atoms placed at calculated positions were refined isotropically with fixed thermal parameters and included in structure factor calculations. Crystal data and parameters for data collection and refinements are summarized in Table 3.

Table 3. Crystal Data Collection and Refinement Parameters for Calix[2]uracil[2] Arenes 4g and 4j·Ethanol (2:1)

	4g	**4j**·ethanol (2:1)
empirical formula	$C_{30}H_{28}N_4O_8$	$C_{54}H_{54}N_8O_{13}$
MW	572.56	1023.05
crystal system	monoclinic	monoclinic
space group	$p2_1/c$	$p2_1/c$
a/Å	9.5660(10)	11.346(3)
b/Å	18.271(2)	17.125(3)
c/Å	15.602(2)	25.281(5)
β/deg	93.750(10)	102.63(2)
V/Å^3	2721.1(5)	4743(2)
Z	4	4
crystal size/mm	0.3 × 0.3 × 0.2	0.4 × 0.3 × 0.3
μ(Mo Kα)/cm^{-1}	1.03	1.03
θ_{max}/deg	2.13 to 20°	1.45 to 20.00°
no. of measured reflections	2629	4404
no. of unique reflections	2433	4105
R_{int}	0.0267	0.0976
no. observations [$I > 3\sigma(I)$]	2211	3140
no. of variables	379	416
residuals: R	R1 = 0.0494 wR2 = 0.1147	R1 = 0.0979 wR2 = 0.2262
max and min residual electron density/e Å^{-3}	0.203 and −0.204	0.362 and −0.255
goodness of fit (GOOF)	1.056	1.015

Extraction Measurements.[28] For the extraction experiments, metal picrate solutions (0.01 mol dm^{-3}) were prepared in deionized, distilled water. The solutions of macrocycles (0.01 mol dm^{-3}) were prepared in chloroform (A.R. grade).

An aqueous solution (2 cm^3) of metal picrate (0.01 mol dm^{-3}) and a chloroform solution (2 cm^3) of the macrocycle (0.01 mol dm^{-3}) were shaken in a cylindrical tube closed with a septum for 5 min and kept at 27 ± 1 °C for 3−4 h. An aliquot of the chloroform layer (1 cm^{-3}) was withdrawn with a syringe and diluted with acetonitrile to 10 cm^{-3}. The UV absorption was measured against $CHCl_3$−CH_3CN (1:9) solution at 374 nm. Extraction of metal picrate has been calculated as the percentage of metal picrate extracted in the chloroform layer, and the values reported here are the mean of three independent measurements which were within ±2% error (Table 1).

Transport Measurements.[29] The transport experiments were carried out at constant temperature (27 ± 1 °C) in a cylinderical glass cell consisting of outer and inner jackets by using (i) metal picrate (0.01 mol dm^{-3}) in water (3 cm^3) in the inner phase; (ii) water (10 cm^3) in the outer phase; (iii) ligand (10 mmol dm^{-3}) in the chloroform layer (15 cm^3) with stirring (150 ± 5 rpm) at 27 ± 1 °C. After stirring for 6 h, the picrates transported in the aqueous receiving phase were determined from the UV absorptions at 355 nm. Each value is a mean of three experiments which are consistent ±10% (Table 1). Before

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the transport rates were determined, blank experiments were performed in the absence of the carrier macrocycle in the chloroform layer to check the leakage of metal picrates. The only significant leakage was observed in the case of Pb^{2+}, and so, transport of Pb^{2+} was not determined.

Spectrophotometric Determination of Stability Constants.[30] The complexation (1:1) of metal cation M by a ligand L in solution can be represented by the equilibrium

$$M + L \rightleftharpoons ML$$

which is controlled by the stability constant

$$K_S = [ML]/[M][L]$$

expressing the degree of stability of the complex in given solvent and temperature conditions.

The absorption spectra were recorded on a UV−visible spectrophotometer at 25 ± 1 °C. The stock solutions of calix[2]uracil[2]arene **2j** (10^{-3} M) and metal acetates (10^{-2} M) were prepared in a methanol:deionized water (95:5) mixture. The titrations were carried out by addition of known volumes of metal acetate stock solutions to 1 mL of calix[2]uracil[2]arene **2j** stock solutions in 10 mL measuring flasks and diluted up to the mark with a methanol:deionized water (95:5) mixture and recording the absorption spectra of these solutions. On plotting the absorption against the metal acetate concentrations, we observed a monotonic dependence, thus indicating a constant 1:1 stoichiometry of complexation. The limiting value of complexation was determined by recording absorption of **2j** in the presence of 2 equiv of NaOH. The stability constants were calculated according to the method described in the literature.[30]

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Supporting Information Available: Crystal data for **4g** and **4j**·ethanol. This material is available free of charge via the Internet at http://pubs.acx.org.

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