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Graphical Abstract

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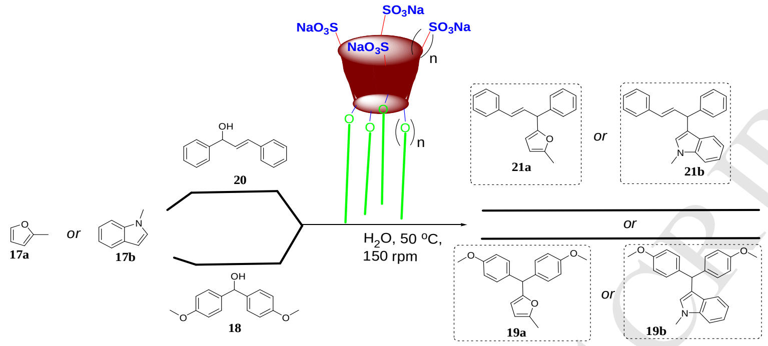

Synthesis and Investigation of Catalytic Affinities of Water-soluble Amphiphilic Calix[n]arene Surfactants in the Coupling Reaction of Some Heteroaromatic Compounds

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ABSTRACT

Six water-soluble calix[n]arene-based Brønsted acid-type catalysts with amphiphilic groups were successfully synthesized by incorporating sulfonic acid moieties. Their structures were characterized using FTIR, ^{1}H-NMR, ^{13}C-NMR, APT-NMR, and elemental analysis techniques. Moreover, their catalytic capabilities were evaluated in the coupling reaction of 2-methylfuran and/or *N*-methylindole with some *sec*-alcohols in aqueous media. The association of their surfactant abilities, and the effects of water amount used and reaction durations on the catalytic activities of these amphiphilic calix[n]arene derivatives were also investigated. Observations indicated that these amphiphilic calix[n]arene catalysts exhibited high catalytic activities in the coupling reactions of 2-methylfuran and *N*-methyl indole with some alcohols in water.

Keywords: Water-soluble calix[n]arene, Brønsted acid type catalyst, alkylation of heteroaromatic compounds, green chemistry.

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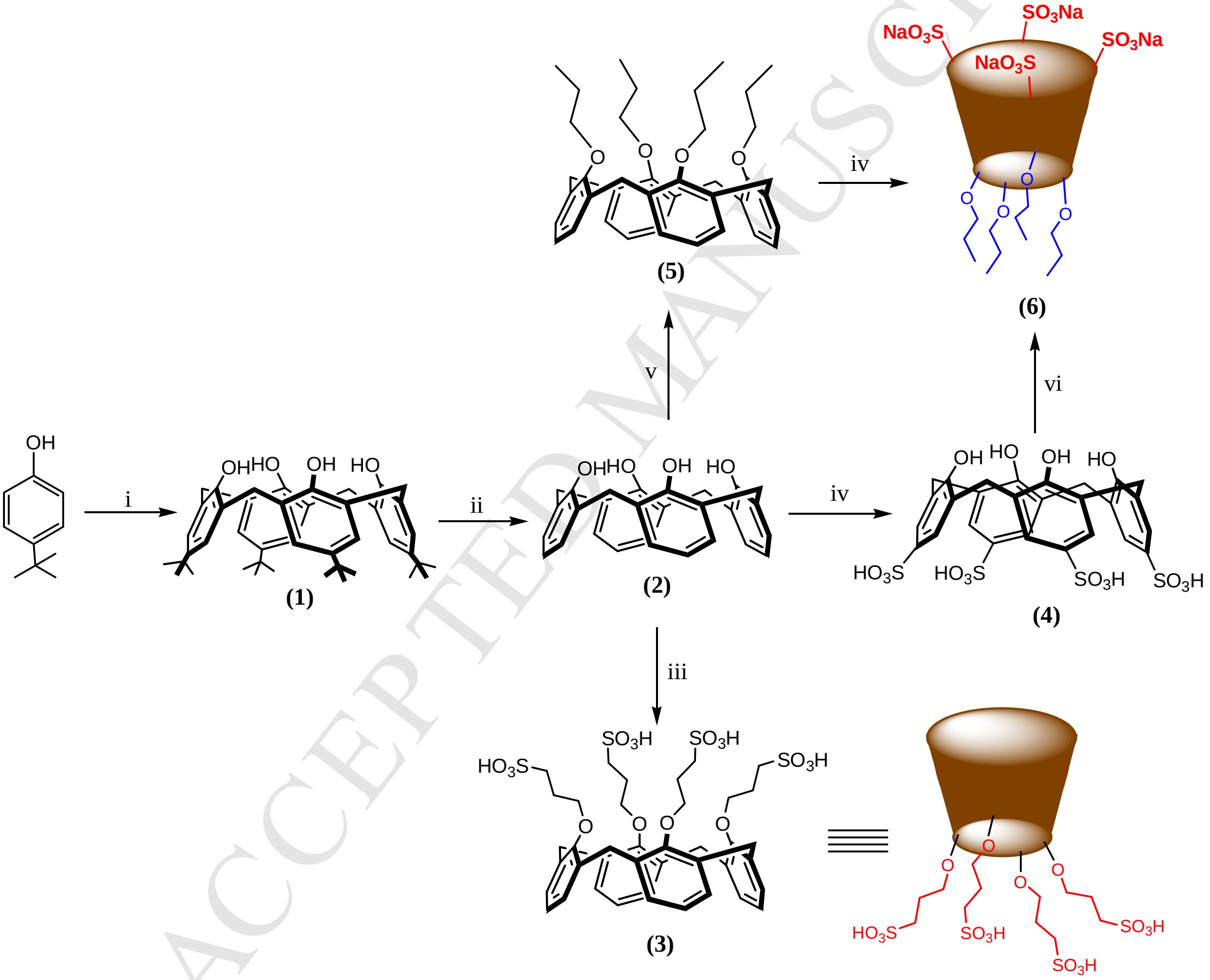
1. Introduction

Reactions involving carbon-carbon bond formation for arenes and heteroarenes represent a substantial approach for the efficient fabrication of diversely functionalized complex compounds such as dyestuffs, perfumes, flavors, agricultural aids, and pharmaceuticals.[1-3] In traditional methods, carbon-carbon bond formation is carried out through the reaction between an electrophile (C-X, X= triflate, halide, mesylate, etc.) with a reactive center of arenes or heteroarenes in the presence of a metallic/organometallic reagent.[4] However, owing to toxicity, a limited number of functional group tolerance, and the poor water-solubility of most metallic/organometallic reagents, developing a reaction for C-C bond construction for arenes/heteroarenes using an alcohol as an electrophile in water is a challenge.[4-6] To perform this kind of reaction, a water-soluble organic-based catalyst with excellent reusability, which catalyzes the coupling reaction by reducing activation energy, is a requirement in terms of environmental toxicology.

Calixarenes, known as the third generation of supramolecules, represent very useful building blocks in that they possess tunable and different cavity sizes and exhibit versatile applications in supramolecular chemistry.[7-10] Because of their easy synthesis, functionalization, and special properties such as having different-sized cavities, including hydrophilic -OH moieties at their lower rim and hydrophobic aromatic subunits along with *tert*-butyl groups, attempts to design and synthesis of new calix[n]arene derivatives have been made.[11-14] It has been reported lately that some of the water-soluble calix[n]arene derivatives acting as surfactant-type Brønsted acid catalysts exhibited substantial catalytic abilities for C-C bond formation.[3a,10,14]

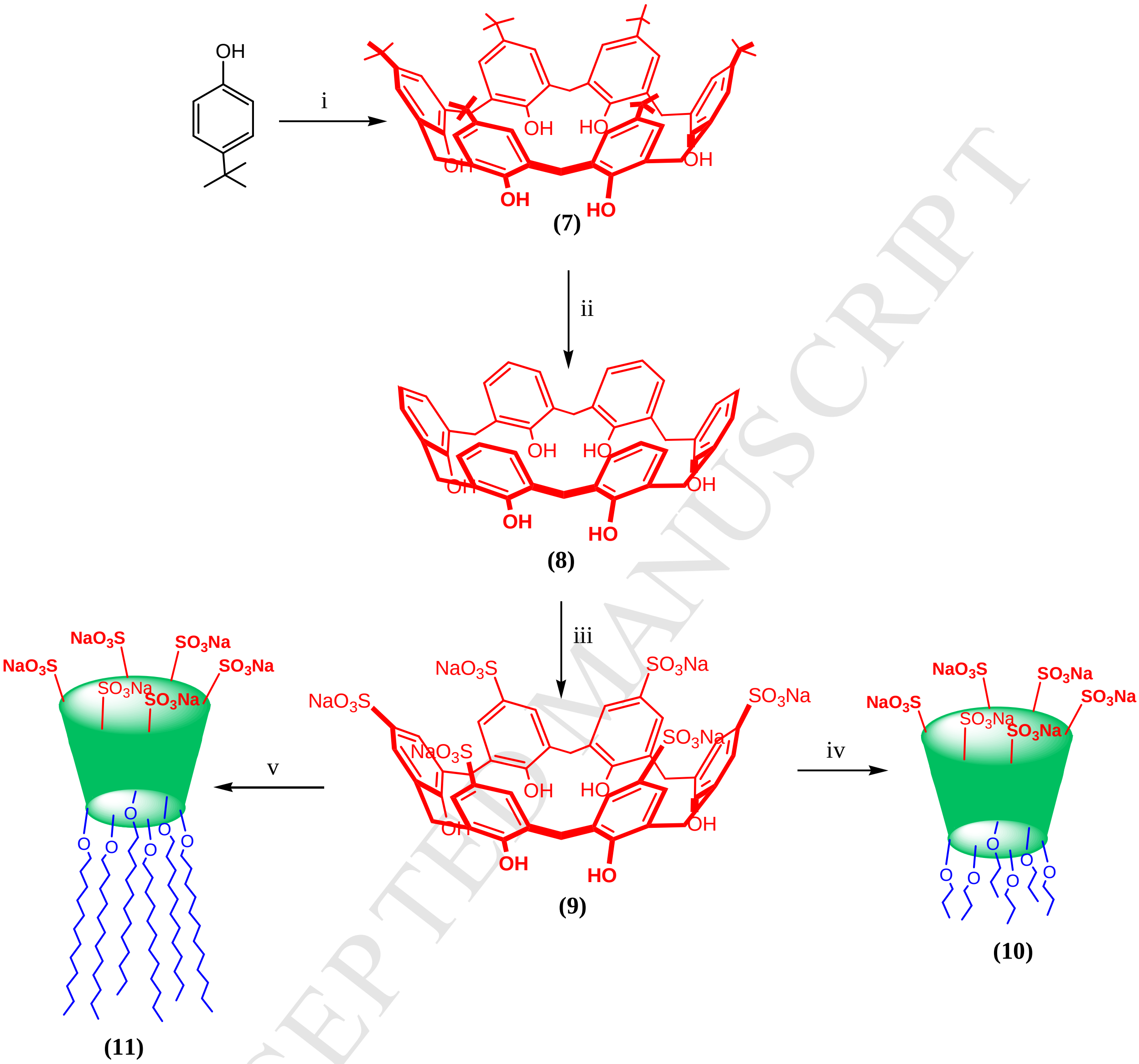
With the goal of translating in aqueous media some organic reactions requiring the usage of a catalyst, in our previous study we have designed *p*-sulfonatocalix[n]arenes (n= 4, 6 and 8) as a catalyst for the alkylation of 2-methylfuran and *N*-methylindole with some alcohols.[3a] We have preliminarily taken a strategy involving the introduction of hydrophobic groups with different straight alkyl chains to Brønsted acid-type calix[n]arene derivatives in order to investigate the effects of amphiphilic groups on the catalytic efficacies of water-soluble calixarenes. Thus, six water-soluble podands, bearing a calix[n]arene backbone with various amphiphilic groups at the lower rim, were successfully synthesized. Furthermore, their catalytic activities were evaluated for the first time in the coupling reaction of 4,4'-dimethoxybenzhydrol and/or (E)-trans-1,3-diphenyl-2-propen-1-ol with 2-methyl furan and/or *N*-methylindole in water without co-solvents.



Scheme 1. Synthesis of Brønsted acid-type calix[4]arene derivatives. Reaction conditions; i) HCHO, NaOH; ii) $AlCl_3$, phenol; iii) 1,3-propanesultone, NaH; iv) H_2SO_4; v) propyliodide, NaH; vi) propylbromide, NaOH.

2. Results and discussion

2.1. Synthesis and characterizations of water-soluble calix[n]arene derivatives



Scheme 2. Synthesis of Brønsted acid-type calix[6]arene derivatives. Reaction conditions; i) HCHO, KOH; ii) $AlCl_3$, phenol; iii) H_2SO_4; iv) propylbromide, NaOH; v); dodecyliodide, NaOH.

With the aim of developing new water-soluble organic-based catalysts, a large number of studies have been published in the last few decades.[3a,14-18] In our previous study, catalytic capabilities of *p*-sulfonatocalix[n]arenes (n=4, 6 or 8) were evaluated in the coupling reactions of some electron-rich arenes with *sec*-alcohols in water.[3a] Inspired by our results,[3a] in this study we investigated the effects of hydrophobic groups of amphiphilic calix[n]arene derivatives. For this purpose, six water-soluble podands, including calix[n]arene backbones bearing different lipophilic subunits, were synthesized and characterized in order to investigate their catalytic efficiencies in the coupling reactions for 4,4'-dimethoxybenzhydrol and/or (E)-trans-1,3-diphenyl-2-propen-1-ol with 2-methyl furan and/or *N*-methylindole in water without co-solvents. Thus, *p*-*tert*-Butylcalix[4]arene (**1**), calix[4]arene (**2**), calix[4]aryloxy-25,26,27,28-tetrakis(propane-3-sulfonic acid) (**3**), calix[4]arene-*p*-sulfonate (**4**), 25,26,27,28-tetrakis(propoxy)calix[4]arene (**5**), 5,11,17,23-tetrasulfonato-25,26,27,28-tetrakis(propoxy)calix[4]arene (**6**), *p*-*tert*-butylcalix[6]arene (**7**), calix[6]arene (**8**), calix[6]arene-*p*-sulfonate (**9**), 5,11,17,23,29,35-hexasulfonato-37,38,39,40,41,42-hexakis(dodecyloxy)calix[6]arene (**11**), *p*-*tert*-butylcalix[8]arene (**12**), calix[8]arene (**13**), calix[8]arene-*p*-sulfonate(**14**), 5,11,17,23,29,35,41,47-octasulfonato-49,50,51,52,53,54,55,56-octakis(dodecyloxy)calix[8]arene (**16**) were synthesized according to literature procedures[15,19-23] (Schemes 1-3). FTIR, ^{1}H-NMR, ^{13}C-NMR spectroscopy and elemental analysis techniques were performed to characterize the structures of the synthesized compounds. However, 5,11,17,23,29,35-hexasulfonato-37,38,39,40,41,42-hexakis(propoxy)calix[6]arene (**10**) and 5,11,17,23,29,35,41,47-octasulfonato-49,50,51,52,53,54,55,56-octakis(propoxy)calix[8]arene (**15**) were synthesized for the first time (Schemes 2 and 3). Typically, an aqueous solution of calix[6]arene-*p*-hexasulfonate (**9**) was treated with propyl bromide and NaOH in DMSO, affording amphiphilic *p*-sulfonatocalix[6]arene **10**, concurrently appended with the hydrophobic propyl chains at the lower rim of *p*-sulfonatocalix[6]arene with a yield of 58% (Scheme 2). An FT-IR spectrum of **10** confirmed the existence of sulfonate groups in which characteristic peaks for the stretching vibrations of S-O, the symmetric and asymmetric vibrations of the SO_2 bands of derivative **10**, appeared at 861, 1050, 1163, and 1111 cm^{-1}, respectively (see Supporting information).

The ^{1}H-NMR spectrum of amphiphilic *p*-sulfonatocalix[6]arene **10** showed that the hydrophobic subunits were successfully attached to the *p*-sulfonatocalix[6]arene, which resonances at 0.88-1.27 (18H), 1.62-2.01 (12H), and 4.25-4.61 (12H) ppm for the protons of the -CH_3, -CH_2, and -OCH_2 groups, respectively (see Supporting information). The APT-^{13}C-NMR spectrum of derivative **10** clearly showed that the peaks at the positive region belonging to the -CH_3 and -CH groups appeared at 9.81 and 124.99-125.77 ppm.

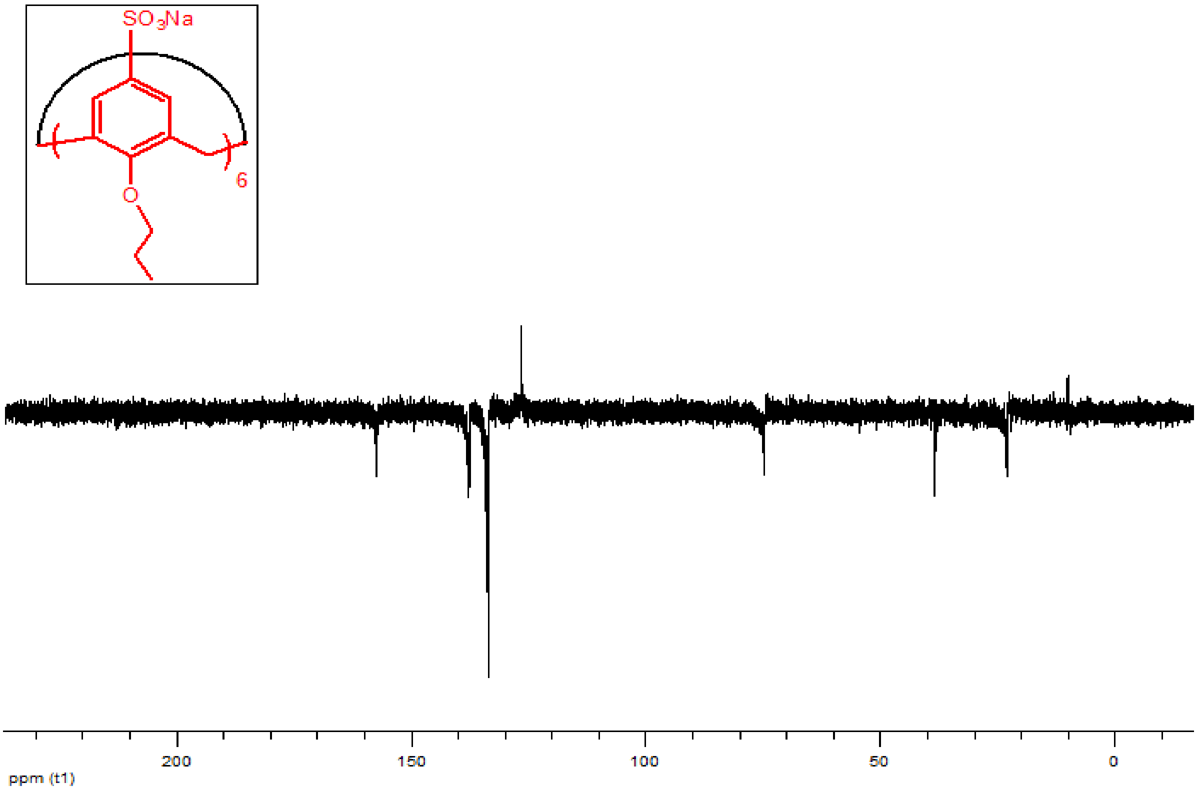
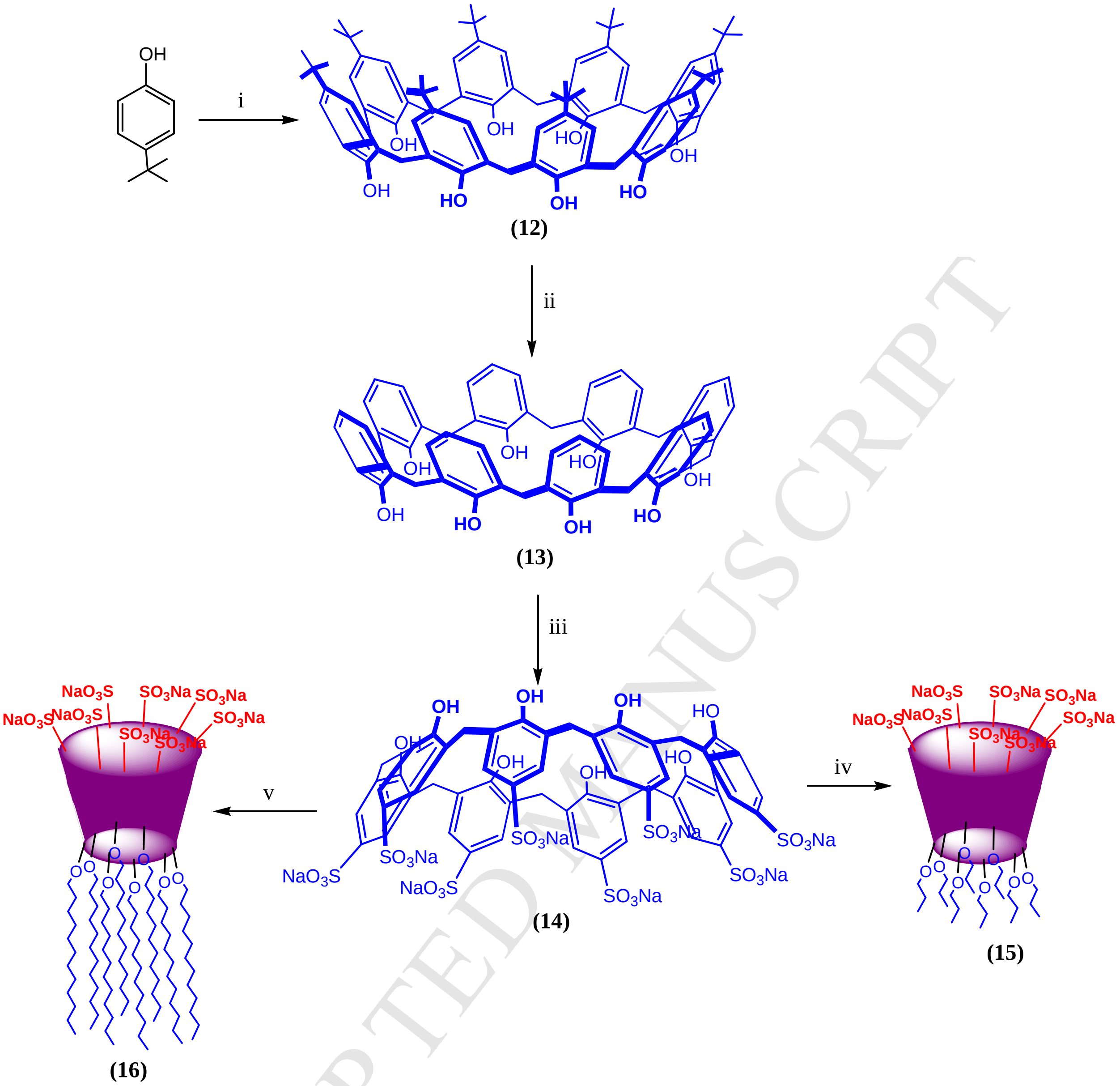


Figure 1. APT-NMR (D_2O) spectrum of amphiphilic hexapropoxyl-*p*-sulfonatocalix[6]arene **10**.



Scheme 3. Synthesis of Brønsted acid-type calix[8]arene derivatives. Reaction conditions; i) paraformaldehyde, NaOH; ii) $AlCl_3$, phenol; iii) H_2SO_4; iv) propylbromide, NaOH; v); dodecyliodide, NaOH.

The substitution of calix[8]arene-*p*-sulfonate (**14**) at the lower rim was conducted with propyl bromide and NaOH in a mixture of H_2O/DMSO to afford 5,11,17,23,29,35,41,47-octasulfonato-49,50,51,52,53,54,55,56-octakis(propoxy)calix[8]arene (**15**) with a yield of 48% (see Scheme 3). The structure of amphiphilic *p*-sulfonatocalix[8]arene **14** was confirmed not only by the appearance of notably characteristic IR peaks at 1175, 1050, and 879 cm^{-1} for the asymmetric and symmetric vibrations of the SO_2 bands, and the stretching vibrations of S-O, respectively on the FT-IR spectrum (see Supporting information), but also by the appearance of the peaks at 0.42-0.87 (24H, $-CH_3$) and the peaks of $-CH_2$, which belong to the propyl moieties on the ^{1}H-NMR spectrum (see Supporting information).

APT-^{13}C-NMR experiment provided valuable information about the type of C atoms for amphiphilic *p*-sulfonatocalix[8]arene **14** (see Fig. 2). On the APT spectrum, the peaks for the $-CH_3$ and -CH groups appeared at 9.89 and 126.26 ppm at the positive region, while the peaks for the $-CH_2$ and quaternary C groups appeared at the negative region.

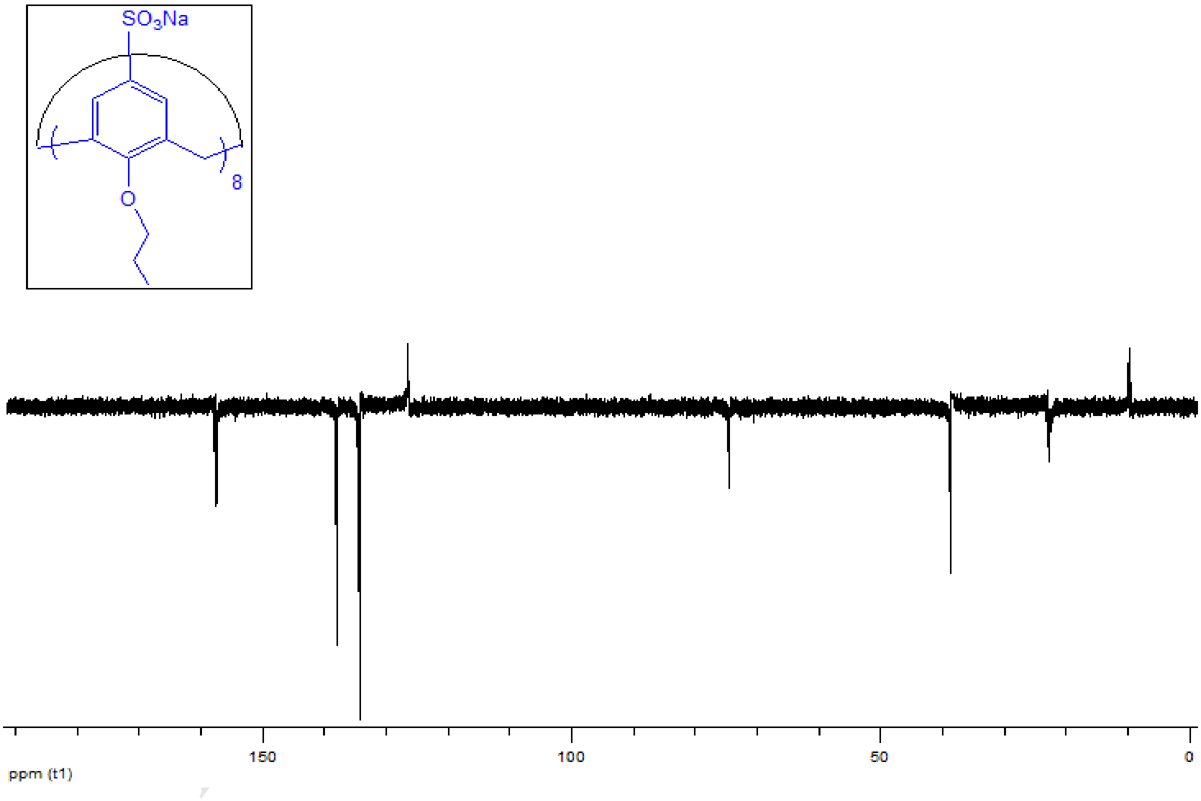
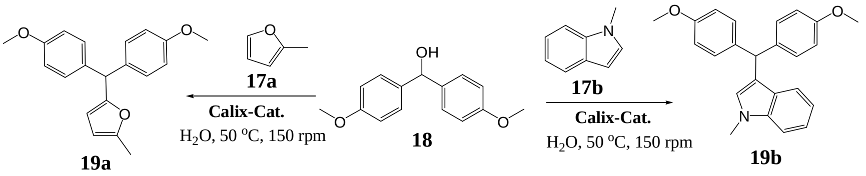


Figure 2. APT-NMR (D_2O) spectrum of amphiphilic octapropoxyl-*p*-sulfonatocalix[8]arene **15**.

2.2. Evaluation of catalytic efficiencies of amphiphilic calix[n]arene derivatives

In our previous study, *p*-sulfonatocalix[n]arenes (n= 4,6 and 8) were used as Brønsted acid type catalysts in the coupling reaction for 4,4'-dimethoxybenzhydrol and/or (*E*)-trans-1,3-diphenyl-2-propen-1-ol with 2-methyl furan and/or *N*-methylindole in water without co-solvents.[3a] It was observed that calix[n]arene sulfonic acids exhibited substantial catalytic activity for the substitution reactions. This study aimed to provide an insight into how hydrophobic groups affected the catalytic properties of water-soluble calixarenes in the coupling reaction for *sec*-alcohols with some heteroaromatic compounds. Thus, we are interested, for the first time, in a study on the catalytic capabilities of six different amphiphilic water-soluble calix[n]arene derivatives in water, which have comprehensive prospects in green synthesis. Considering that C-C bond formation for heteroaromatic compounds has important applications in the fabrication of dyestuffs, perfumes, flavors, agricultural aids, pharmaceuticals, etc.,[3a] the replacement of *sec*-alcohol -OH by aromatic compounds in the coupling reaction of 2-methylfuran or *N*-methylindole at 50 ^{o}C in water was chosen as a substitution reaction system to determine the catalytic efficacies of six amphiphilic calix[n]arene derivatives. From the experimental results presented in Tables 1, 2 and 3, it can be seen that the corresponding products (**19a-b** and **21a-b**) were not synthesized when calixarene based catalyst was not added. However, when Brønsted acid-type calix[n]arene derivatives (**Calix-6**, **Calix-10**, **Calix-11**, **Calix-15**, or **Calix-16**) were employed as catalysts, the corresponding products (**19a-b** and **21a-b**) were isolated in good to excellent yields (see Tables 1-3), whereas the lowest yields of the corresponding products (**19a-b** and **21a-b**) were obtained when Brønsted acid-type calix[n]arene derivative (**Calix-3**) was used as a catalyst. To determine the effects on the reaction by changing the amount of water used and reaction durations, various water amounts and different reaction durations were also performed.

Table 1. The coupling reaction of **17a-b** with **18** in H_2O

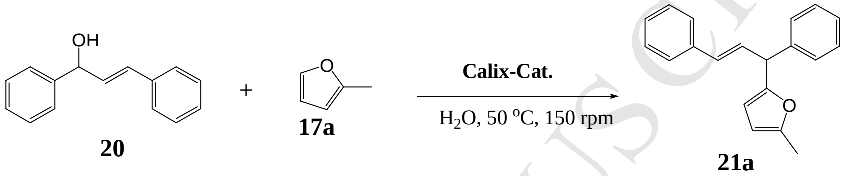


Entry	Catalyst	Catalyst loading	Ar-H	*sec*-Alcohol	Time (h)	H_2O (mL)	Product	Yield (%)[a]
1	**Calix-3**	5 mol%	**17a**	**18**	15	2	**19a**	22
2	**Calix-3**	5 mol%	**17a**	**18**	30	1	**19a**	32
3	**Calix-3**	5 mol%	**17a**	**18**	30	1	**19a**	36
4	**Calix-11**	5 mol%	**17a**	**18**	15	0.5	**19a**	46
5	**Calix-11**	5 mol%	**17a**	**18**	15	1	**19a**	78
6	**Calix-11**	5 mol%	**17a**	**18**	15	2	**19a**	54
7	**Calix-11**	5 mol%	**17a**	**18**	30	1	**19a**	84
8	**Calix-16**	5 mol%	**17a**	**18**	15	0.5	**19a**	33
9	**Calix-16**	5 mol%	**17a**	**18**	15	1	**19a**	100
10	**Calix-16**	5 mol%	**17a**	**18**	15	2	**19a**	42
11	**Calix-4**[b]	5 mol%	**17a**	**18**	15	1	**19a**	50
12	**Calix-9**[b]	5 mol%	**17a**	**18**	15	1	**19a**	62
13	**Calix-14**[b]	5 mol%	**17a**	**18**	15	1	**19a**	97
14	**Calix-3**	5 mol%	**17b**	**18**	24	1	**19b**	71
15	**Calix-3**	5 mol%	**17b**	**18**	24	2	**19b**	74
16	**Calix-6**	5 mol%	**17b**	**18**	24	1	**19b**	88
17	**Calix-6**	5 mol%	**17b**	**18**	24	2	**19b**	100
18	**Calix-10**	5 mol%	**17b**	**18**	24	1	**19b**	88
19	**Calix-10**	5 mol%	**17b**	**18**	24	2	**19b**	66
20	**Calix-11**	5 mol%	**17b**	**18**	24	1	**19b**	85
21	**Calix-11**	5 mol%	**17b**	**18**	24	2	**19b**	77
22	**Calix-15**	5 mol%	**17b**	**18**	24	1	**19b**	89
23	**Calix-15**	5 mol%	**17b**	**18**	24	2	**19b**	87
24	**Calix-16**	5 mol%	**17b**	**18**	24	1	**19b**	85
25	**Calix-16**	5 mol%	**17b**	**18**	24	2	**19b**	77
26	**Calix-4**[b]	5 mol%	**17b**	**18**	24	1	**19b**	63
27	**Calix-9**[b]	5 mol%	**17b**	**18**	24	1	**19b**	63
28	**Calix-14**[b]	5 mol%	**17b**	**18**	24	1	**19b**	28
29	none	-	**17a**	**18**	48	1 or 2	**19a**	0
30	none	-	**17b**	**18**	48	1 or 2	**19b**	0

[a] Reaction conditions: **17a-b** (0.18 mmol), **18** (22 mg, 0.09 mmol); isolated yield.
[b] Reference[3a]

The yields of product **19a** in the presence of catalysts **Calix-11** and **Calix-16** were as high as 84% and 100% in entries 7 and 9, respectively. In addition, the maximum yields of product **19b** in the presence of catalysts **Calix-3**, **Calix-6**, **Calix-10**, **Calix-11**, **Calix-15**, and **Calix-16** were observed as 74, 100, 88, 85, 89 and 85% in entries 15, 17, 18, 20, 22, and 24, respectively (see Table 1).

Table. 2 The coupling reaction of **17a** with **20** in H_2O

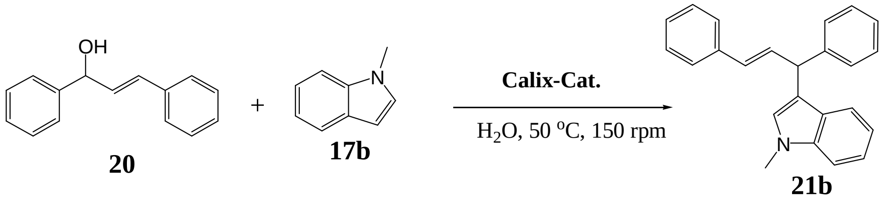


Entry	Catalyst	Catalyst loading	Ar-H	*sec*-Alcohol	Time/h	H_2O/mL	Product	Yield (%)[a]
1	**Calix-6**	5 mol%	**17a**	**20**	61	1	**21a**	77
2	**Calix-6**	5 mol%	**17a**	**20**	61	2	**21a**	95
3	**Calix-6**	5 mol%	**17a**	**20**	86	1	**21a**	100
4	**Calix-10**	5 mol%	**17a**	**20**	61	1	**21a**	54
5	**Calix-10**	5 mol%	**17a**	**20**	61	2	**21a**	87
6	**Calix-10**	5 mol%	**17a**	**20**	86	1	**21a**	100
7	**Calix-11**	5 mol%	**17a**	**20**	61	1	**21a**	45
8	**Calix-11**	5 mol%	**17a**	**20**	61	2	**21a**	87
9	**Calix-11**	5 mol%	**17a**	**20**	86	1	**21a**	57
10	**Calix-15**	5 mol%	**17a**	**20**	61	1	**21a**	46
11	**Calix-15**	5 mol%	**17a**	**20**	86	1	**21a**	58
12	**Calix-16**	5 mol%	**17a**	**20**	61	1	**21a**	45
13	**Calix-16**	5 mol%	**17a**	**20**	61	2	**21a**	87
14	**Calix-16**	5 mol%	**17a**	**20**	86	1	**21a**	57
15	**Calix-4**[b]	5 mol%	**17a**	**20**	61	2	**21a**	81
16	**Calix-9**[b]	5 mol%	**17a**	**20**	61	2	**21a**	86
17	**Calix-14**[b]	5 mol%	**17a**	**20**	61	1	**21a**	42
18	None	-	**17a**	**20**	86	1 or 2	**21a**	0

[a] Reaction conditions: **17a** (0.18 mmol), **20** (19 mg, 0.09 mmol). Isolated yield.
[b] Reference[3a]

The experimental results, which were obtained from the coupling reactions of 2-methylfuran or *N*-methylindole with (*E*)-trans-1,3-diphenyl-2-propen-1-ol in the presence of water-soluble calix[n]arene catalysts, are depicted in Tables 2 and 3. Although **Calix-15** catalyzed this coupling reaction to afford product **21a** with a yield of 58%, this percentage is the lowest percentage yield when compared with the yields achieved by the results of the rest of the catalysts (see Table 2). When **Calix-6**, **Calix-10**, **Calix-11**, or **Calix-16** were used as catalysts, the maximum yields for product **21a** were as high as 100, 100, 87, and 87% in entries 3, 6, 7, and 13, respectively. In addition, the maximum yields of product **21b** in the presence of catalysts **Calix-3**, **Calix-6**, **Calix-10**, **Calix-11**, **Calix-15**, or **Calix-16** were observed as 87, 100, 100, 100, 100, and 100% in entries 2, 6, 9, 12, 16, and 19, respectively (see Table 3). It can be concluded that Brønsted acid-type amphiphilic calix[n]arene derivatives exhibited excellent catalytic activities for coupling reactions of 2-methylfuran or *N*-methylindole in water. Moreover, the results can also be summarized that the catalytic abilities of calixarene-based catalysts were increased when the long alkyl groups such as dodecyl moieties attached to the lower rim of calix[n]arenes. In addition, reaction durations and amount of water also affected the yields of the products.

Table.3 The coupling reaction of **17b** with **20** in Water



Entry	Catalyst	Catalyst loading	Ar-H	*sec*-Alcohol	Time/h	H_2O/mL	Product	Yield (%)[a]
1	**Calix-3**	5 mol%	**17b**	**20**	15	1	**21b**	82
2	**Calix-3**	5 mol%	**17b**	**20**	61	1	**21b**	87
3	**Calix-3**	5 mol%	**17b**	**20**	61	2	**21b**	43
4	**Calix-6**	5 mol%	**17b**	**20**	6	1	**21b**	89
5	**Calix-6**	5 mol%	**17b**	**20**	15	1	**21b**	99
6	**Calix-6**	5 mol%	**17b**	**20**	61	1	**21b**	100
7	**Calix-6**	5 mol%	**17b**	**20**	61	2	**21b**	100
8	**Calix-10**	5 mol%	**17b**	**20**	15	1	**21b**	85
9	**Calix-10**	5 mol%	**17b**	**20**	61	1	**21b**	100
10	**Calix-10**	5 mol%	**17b**	**20**	61	2	**21b**	100
11	**Calix-11**	5 mol%	**17b**	**20**	15	1	**21b**	49
12	**Calix-11**	5 mol%	**17b**	**20**	61	1	**21b**	100
13	**Calix-11**	5 mol%	**17b**	**20**	61	2	**21b**	100
14	**Calix-15**	5 mol%	**17b**	**20**	6	1	**21b**	90
15	**Calix-15**	5 mol%	**17b**	**20**	15	1	**21b**	95
16	**Calix-15**	5 mol%	**17b**	**20**	61	1	**21b**	100
17	**Calix-15**	5 mol%	**17b**	**20**	61	2	**21b**	100
18	**Calix-16**	5 mol%	**17b**	**20**	15	1	**21b**	49
19	**Calix-16**	5 mol%	**17b**	**20**	61	1	**21b**	100
20	**Calix-16**	5 mol%	**17b**	**20**	61	2	**21b**	100
21	**Calix-4**[b]	5 mol%	**17b**	**20**	15	1	**21b**	96
22	**Calix-9**[b]	5 mol%	**17b**	**20**	15	1	**21b**	23
23	**Calix-14**[b]	5 mol%	**17b**	**20**	15	1	**21b**	74
24	None	-	**17b**	**20**	86	1 or 2	**21b**	0

[a] Reaction conditions: **10a-b** (0.18 mmol), **13** (19 mg, 0.09 mmol). Isolated yield.

[b] Reference[3a]

3. Conclusion

In summary, six Brønsted acid-type amphiphilic calix[n]arene derivatives were synthesized and characterized. Moreover, these amphiphilic calix[n]arene derivatives were employed as catalysts in a coupling reaction of 2-methylfuran or *N*-methylindole with two activated *sec*-alcohols in water. The experiments of aromatic substitution catalysis in aqueous media reflected these amphiphilic calix[n]arene catalysts possessed excellent catalytic capabilities. Especially, long alkyl groups attached to the lower rim of calix[n]arenes the catalytic efficacy of calixarene were dramatically increased. Worthy of note is the fact that this effective catalysis system provided by six amphiphilic calix[n]arene catalysts for C-C bond formation reactions in water may open potential prospects in ‘green’ synthesis.

4. Experimental

4.1. General

Melting points of the synthesized compounds was determined using an Ez-Melt apparatus in a sealed capillary. FTIR and NMR spectra were recorded on a Perkin-Elmer 100 spectrometer and a Varian 400 MHz spectrometer, respectively. Elemental analyses were performed at Leco CHNS-932 analyzer.

4.2. Synthesis

p-tert-Butylcalix[4]arene (**1**), calix[4]arene (**2**), calix[4]aryloxy-25,26,27,28-tetrakis(propane-3-sulfonic acid) (**3**), calix[4]arene-*p*-sulfonate (**4**), 25,26,27,28-tetrakis(propoxy)calix[4]arene (**5**), 5,11,17,23-tetrasulfonato-25,26,27,28-tetrakis(propoxy)calix[4]arene (**6**), *p-tert*-butylcalix[6]arene (**7**), calix[6]arene (**8**), calix[6]arene-*p*-sulfonate (**9**), 5,11,17,23,29,35-hexasulfonato-37,38,39,40,41,42-hexakis(dodecyloxy)calix[6]arene (**11**), *p-tert*-butylcalix[8]arene (**12**), calix[8]arene (**13**), calix[8]arene-*p*-sulfonate(**14**), 5,11,17,23,29,35,41,47-octasulfonato-49,50,51,52,53,54,55,56-octakis(dodecyloxy)calix[8]arene (**16**) were synthesized according to the literature procedure.[15,19-23] 5,11,17,23,29,35-Hexasulfonato-37,38,39,40,41,42-hexakis(propoxy)calix[6]arene (**10**) and 5,11,17,23,29,35,41,47-octasulfonato-

49,50,51,52,53,54,55,56-octakis(propoxy)calix[8]arene (**15**) were synthesized for the first time.

*4.2.1. Synthesis of 5,11,17,23-Tetrasulfonato-25,26,27,28-tetrakis(propoxy)calix[4]arene (**6**).*[21]

Method 1; A mixture of 5 (0.2 g, 0.269 mmol) in H_2SO_4 (2.5 mL) was stirred at rt for 10 min. A precipitate was formed by addition of a large amount of Et_2O, filtered and dried. White colored product was obtained in 69% yield.

Method 2; Calix[4]arene-*p*-sulfonate (**4**) (0.2 g, 0.269 mmol) H_2O (1.5 mL) containing NaOH (0.23 g, 5.802 mmol) and propyl bromide (0.3 mL, 3.303 mmol) in DMSO (10 mL) was mixed, and the reaction mixture was heated at 85 ^oC for 30 h. After cooling, the solution was precipitated by addition of acetone, filtered and dried. White powder was synthesized in 99% yield. Melting points >350 ^oC. FTIR (ATR) cm^{-1}: 1639 (V_{H2O}), 1594, 1462 ve 1301 ($V_{C=C}$), 1175 (V_{SO2} asymmetric), 1044 (V_{SO2} symmetric) and 797 ($V_{S\text{-}O}$). ^{1}H-NMR (400 MHz, D_2O): δ 0.87 (t, 12H, *J*= 7.6 Hz, -CH_3), 1.81-1.86 (m, 8H, -CH_2-), 3.25 (d, 4H, *J*= 13.2 Hz, Ar-CH_2-Ar), 3.73 (t, 8H, *J*= 7.2 Hz, O-CH_2-), 4.25 (d, 4H, *J*= 13.2 Hz, Ar-CH_2-Ar), 7.16 (s, 8H, ArH). ^{13}C-NMR (100 MHz, D_2O): δ 10.12, 23.05, 31.80, 76.99, 125.92, 133.76, 137.19, 155.61. Anal. Calcd. For $C_{40}H_{44}O_{16}S_4$ $Na_4{\cdot}4H_2O$ (%): C, 44.03; H, 4.99; S, 11.76. Found (%); C, 44.10; H, 4.88; S, 11.83.

*4.2.2. Synthesis of 5,11,17,23,29,35-hexasulfonato-37,38,39,40,41,42-hexakis(propoxy)calix[6]arene (**10**).* Calix[6]arene-p-hexasulfonate (9) (0.2 g, 0.179 mmol) in H_2O (5 mL) containing NaOH (0.24 g, 5.907 mmol) was mixed a solution of propyl bromide (0.3 mL, 3.043 mmol) in DMSO (20 mL), and the mixture was stirred at 85 ^oC for 30 min. After cooling, a precipitate was formed by addition of acetone, and filtered. The residue was recrystallized from MeOH, and dried. Yield: 58%, m.p. >350 ^oC. FTIR (ATR) cm^{-1}: 1630 (V_{H2O}), 1407 ($V_{C=C}$), 1163, 1111 (V_{SO2} asymmetric), 1050 (V_{SO2} symmetric) and 861 (V_{S-O}). ^{1}H-NMR (400 MHz, D_2O): δ 0.88-1.27 (m, 18H, -CH_3), 1.62-2.01 (m, 12H, -CH_2-), 3.77-3.97 (m, 12H, Ar-CH_2-Ar), 4.25-4.61 (m, 12H, O-CH_2-), 7.69-8.04 (m, 12H, ArH). ^{13}C-NMR (100 MHz, D_2O): δ 9.81, 21.90-22.70, 38.52, 75.53, 124.95-125.77, 128.96-130.15, 135.01-137.69, 156.38. Anal. Calcd. For $C_{60}H_{66}O_{24}S_6Na_6{\cdot}6H_2O$ (%): C, 44.77; H, 4.88; S, 11.95. Found (%); C, 44.71; H, 4.91; S, 12.07.

*4.2.3. Synthesis of 5,11,17,23,29,35,41,47-octasulfonato-49,50,51,52,53,54,55,56-octakis(propoxy)calix[8]arene (**15**).* Calix[8]arene-*p*-sulfonate (**14**) (0.2 g, 0.134 mmol) H_2O (5 mL) containing NaOH (0.24 g, 5.907 mmol) and propyl bromide (0.3 mL, 3.043 mmol) in DMSO (20 mL) was mixed, and the reaction mixture was heated at 85 ^oC for 30 h. After cooling, the solution was precipitated by addition of acetone, and filtered. The residue was recrystallized from MeOH and dried. White powder was synthesized in 48% yield, m.p. >350 ^oC. FTIR (ATR) cm^{-1}: 1413 ($V_{C=C}$), 1175 (V_{SO2} asymmetric), 1050 (V_{SO2} symmetric) and 879 (V_{S-O}). ^{1}H-NMR (400 MHz, D_2O): δ 0.42-0.87 (m, 24H, -CH_3), 1.73 (brs, 16H, -CH_2-), 3.65-3.93 (m, 32H, Ar-CH_2-Ar ve O-CH_2-), 7.09-7.48 (m, 16H, ArH). ^{13}C-NMR (100 MHz, D_2O): δ 9.89, 22.76, 38.55, 74.74, 126.26, 134.17, 137.76, 157.37. Anal. Calcd. For $C_{80}H_{88}O_{32}S_8Na_8{\cdot}8H_2O$ (%): C, 44.77; H, 4.88; S, 11.95. Found (%); C, 44.64; H, 4.85; S, 12.07.

4.3. Typical procedure for nucleophilic substitutions of two *sec*-alcohols in the presence of Brønsted acid-type calix[n]arene catalysts

A previously reported literature procedure was performed.[3a,14,24] Typically, to a solution of catalyst in water (as listed in the tables) were added *sec*-alcohol (**18** or **20**) and a hetero-aromatic compound (**17a-b**). The reaction mixture was stirred vigorously at 50 ^oC for the period of time indicated in the tables. It is worth noting that water soluble catalysts were separaed by centrifugation of the mixture in order to use next reactions. Then, the mixture was treated with $NaHCO_3$ aq. and extracted by Et_2O. The organic phase was washed with H_2O to adjust pH to 7, and dried over anhydrous $MgSO_4$, and evaporated under reduced pressure to obtain the crude product that was purified by column chromatography.

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Figure captions:

Figure 1. APT-^{13}C-NMR (D_2O) spectrum of amphiphilic hexapropoxyl-*p*-sulfonatocalix[6]arene **10**.

Figure 2. APT-^{13}C-NMR (D_2O) spectrum of amphiphilic octapropoxyl-*p*-sulfonatocalix[8]arene **15**.

Scheme 1. Synthesis of Brønsted acid-type calix[4]arene derivatives. Reaction conditions; i) HCHO, NaOH; ii) $AlCl_3$, phenol; iii) 1,3-propanesultone, NaH; iv) H_2SO_4; v) propyliodide, NaH; vi) propylbromide, NaOH.

Scheme 2. Synthesis of Brønsted acid-type calix[6]arene derivatives. Reaction conditions; i) HCHO, KOH; ii) $AlCl_3$, phenol; iii) H_2SO_4; iv) propylbromide, NaOH; v); dodecyliodide, NaOH.

Scheme 3. Synthesis of Brønsted acid-type calix[8]arene derivatives. Reaction conditions; i) paraformaldehyde, NaOH; ii) $AlCl_3$, phenol; iii) H_2SO_4; iv) propylbromide, NaOH; v); dodecyliodide, NaOH.

Figure 1

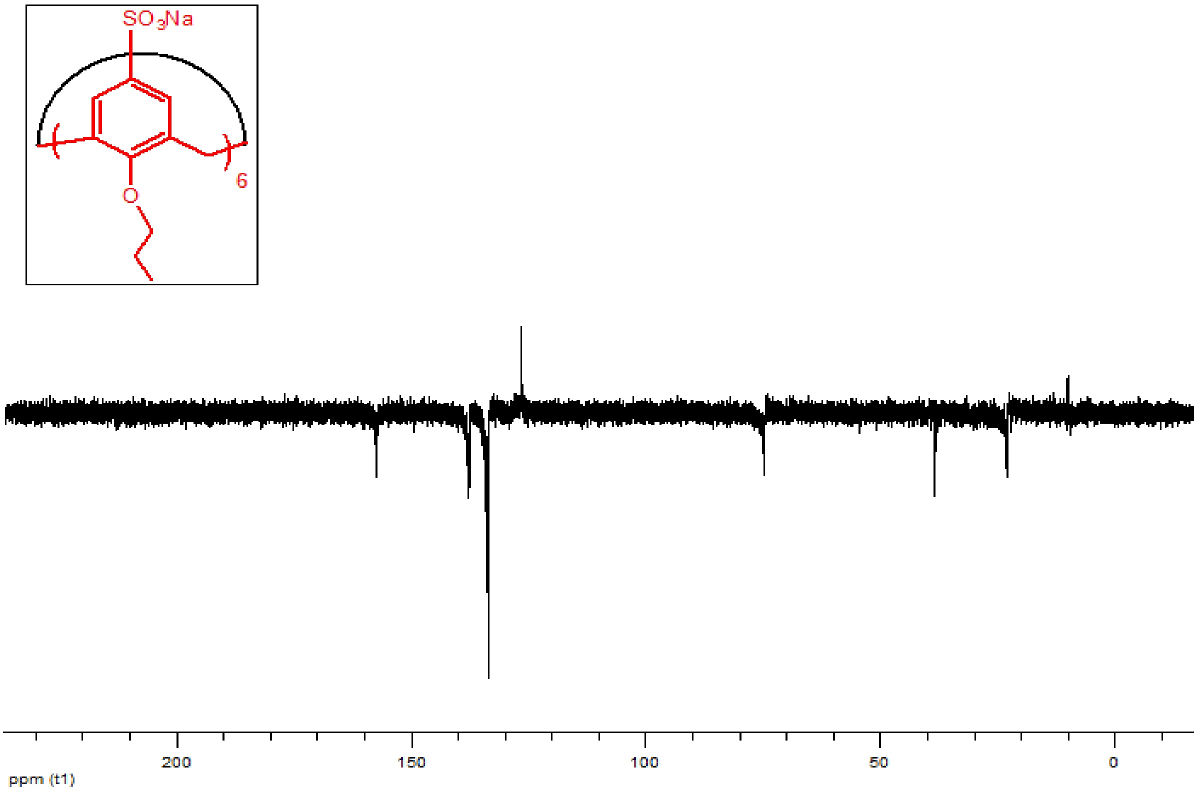
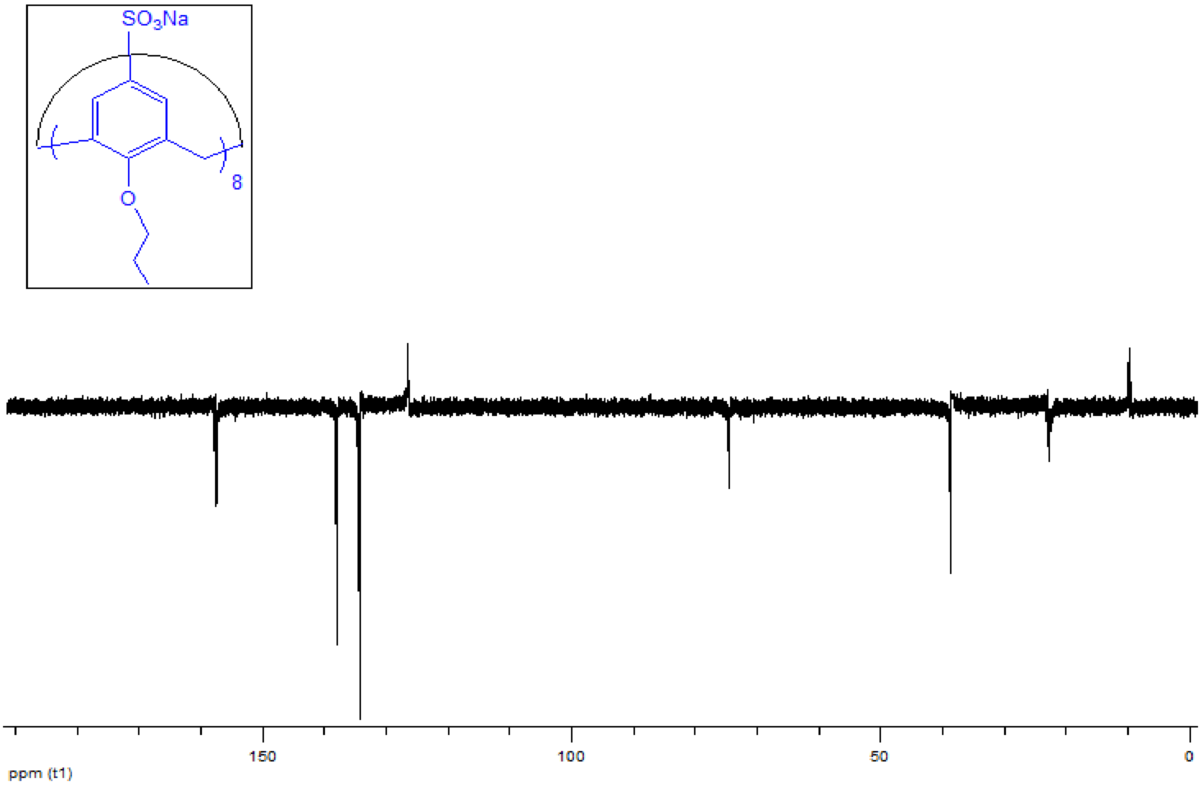
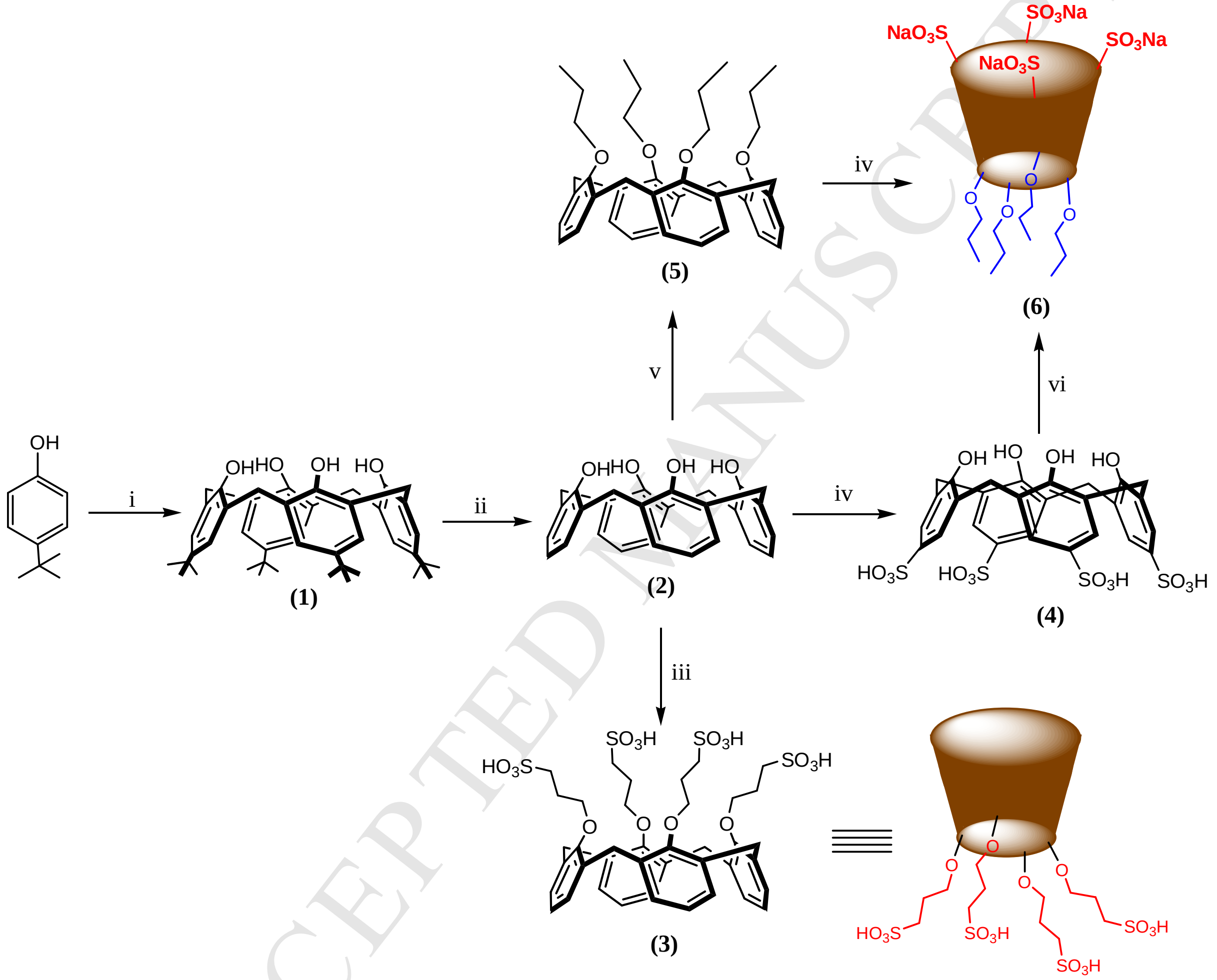


Figure 2



Scheme 1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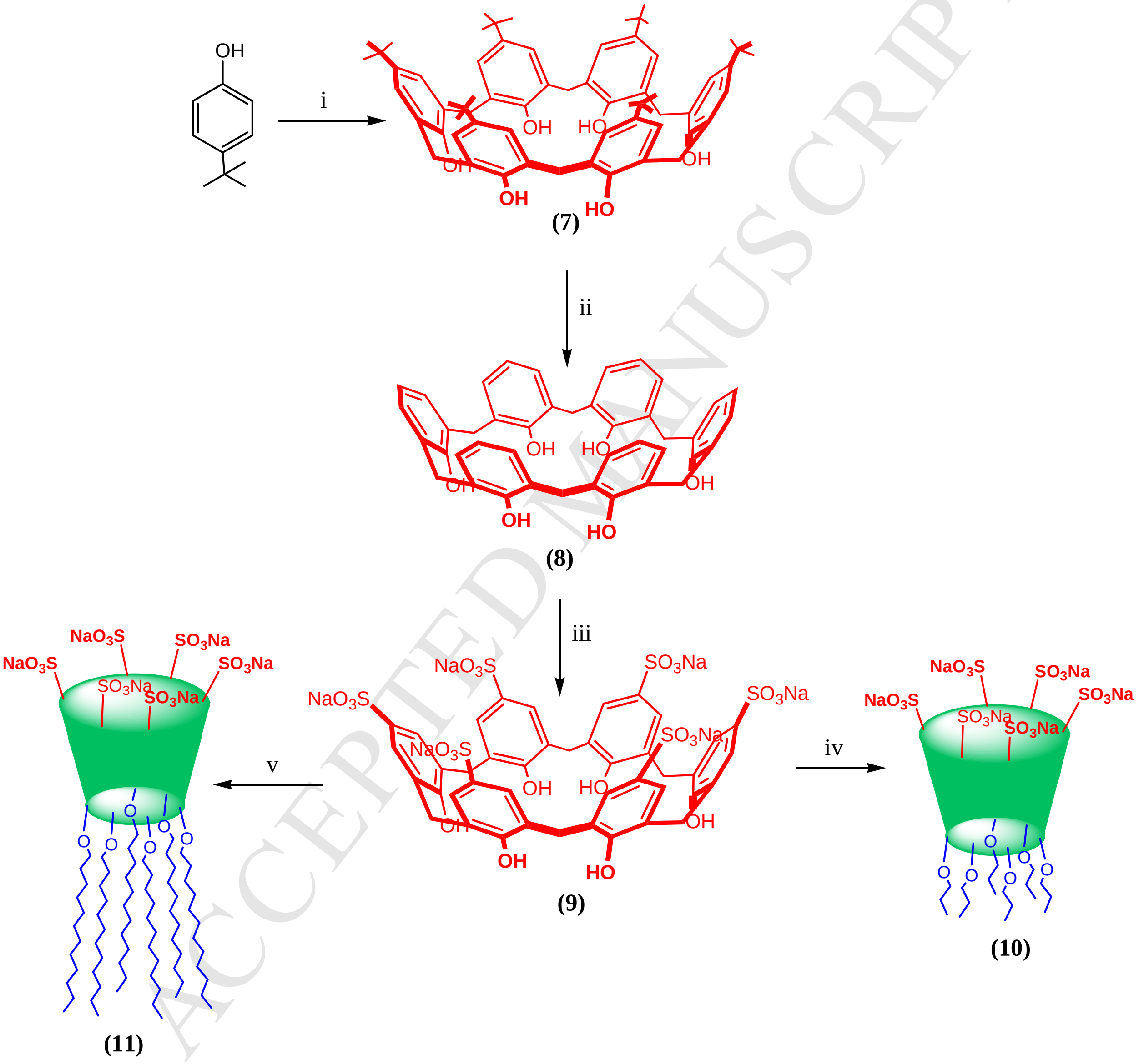
OH HO OH HO
(1)
ii
OH HO OH HO
(2)
iv
OH HO OH HO
HO$_3$S HO$_3$S SO$_3$H SO$_3$H
(4)
v
O O O O
(5)
iv
NaO$_3$S SO$_3$Na NaO$_3$S SO$_3$Na
O O O O
(6)
vi
iii
HO$_3$S SO$_3$H SO$_3$H SO$_3$H
O O O O
(3)
O O O O
HO$_3$S SO$_3$H SO$_3$H SO$_3$H

Scheme 2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HO
OH
OH
OH
HO
(7)
ii
OH
HO
OH
OH
OH
HO
(8)
iii
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SO$_3$Na
NaO$_3$S
SO$_3$Na
NaO$_3$S
SO$_3$Na
OH
HO
OH
OH
OH
HO
(9)
iv
NaO$_3$S
NaO$_3$S
SO$_3$Na
SO$_3$Na
SO$_3$Na
SO$_3$Na
O
(10)
v
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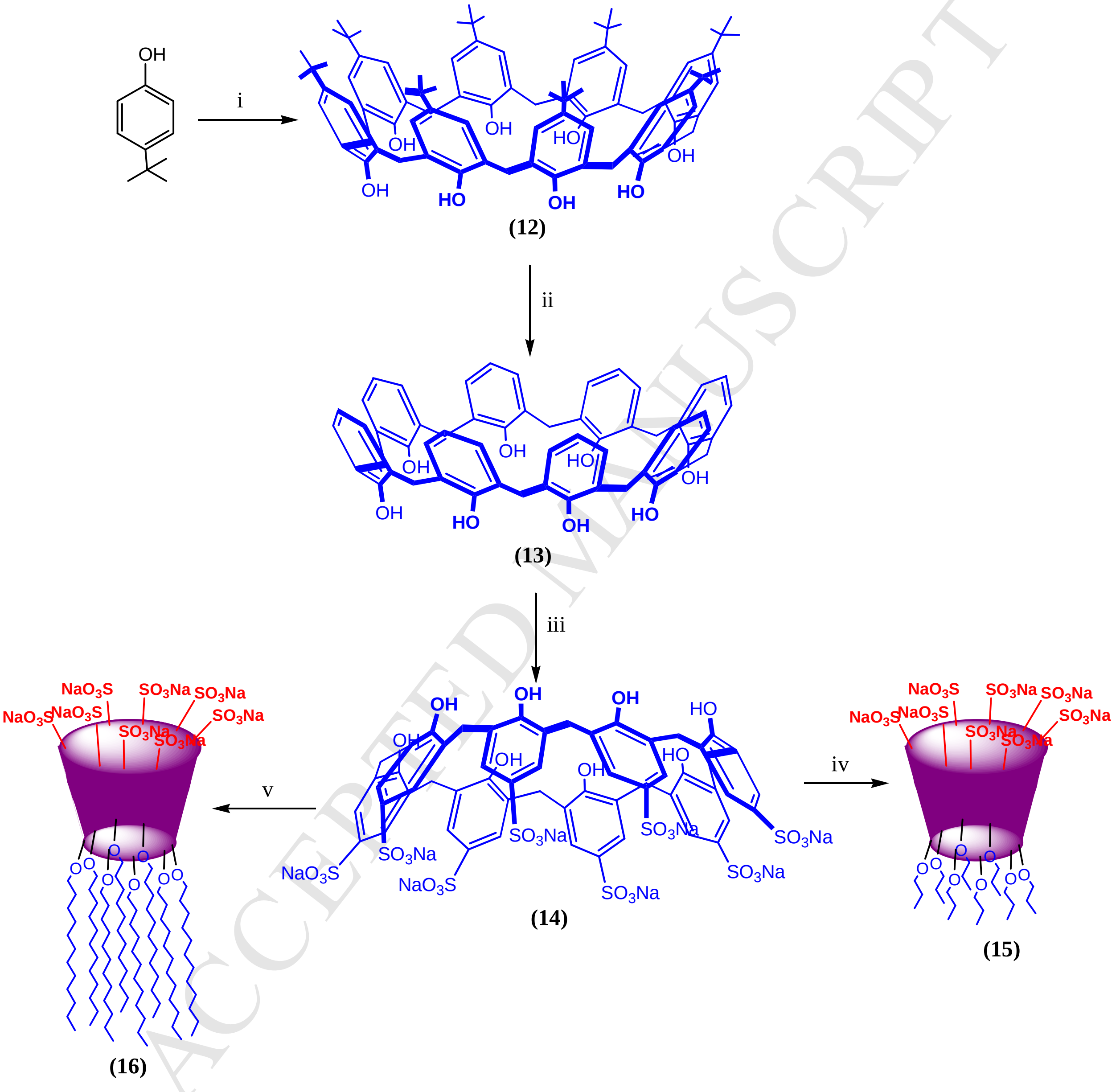
NaO$_3$S
SO$_3$Na
SO$_3$Na
SO$_3$Na
SO$_3$Na
O
(11)

Scheme 3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OH
(12)
ii
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HO
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HO
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HO
OH
(13)
iii
OH
OH
OH
HO
OH
HO
OH
OH
SO$_3$Na
NaO$_3$S
SO$_3$Na
NaO$_3$S
SO$_3$Na
SO$_3$Na
SO$_3$Na
SO$_3$Na
SO$_3$Na
(14)
iv
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SO$_3$Na
SO$_3$Na
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SO$_3$Na
SO$_3$Na
NaO$_3$S
NaO$_3$S
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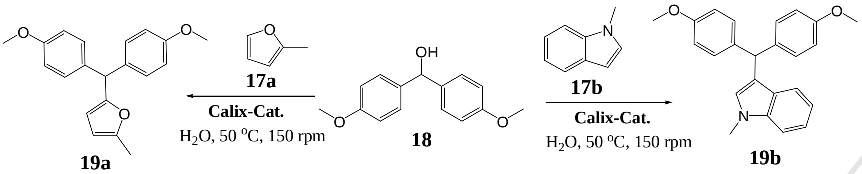
O
(16)

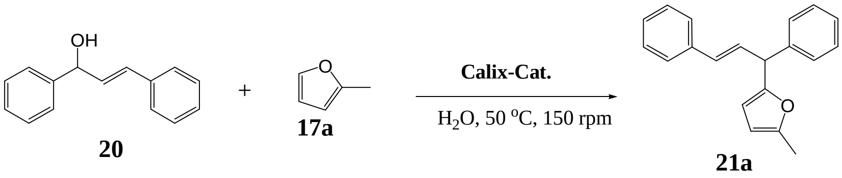
Table 1. The coupling reaction of **17a-b** with **18** in H_2O



Entry	Catalyst	Catalyst loading	Ar-H	*sec*-Alcohol	Time (h)	H_2O (mL)	Product	Yield (%)[a]
1	**Calix-3**	5 mol%	**17a**	**18**	15	2	**19a**	22
2	**Calix-3**	5 mol%	**17a**	**18**	30	1	**19a**	32
3	**Calix-3**	5 mol%	**17a**	**18**	30	1	**19a**	36
4	**Calix-11**	5 mol%	**17a**	**18**	15	0.5	**19a**	46
5	**Calix-11**	5 mol%	**17a**	**18**	15	1	**19a**	78
6	**Calix-11**	5 mol%	**17a**	**18**	15	2	**19a**	54
7	**Calix-11**	5 mol%	**17a**	**18**	30	1	**19a**	84
8	**Calix-16**	5 mol%	**17a**	**18**	15	0.5	**19a**	33
9	**Calix-16**	5 mol%	**17a**	**18**	15	1	**19a**	100
10	**Calix-16**	5 mol%	**17a**	**18**	15	2	**19a**	42
11	**Calix-4**[b]	5 mol%	**17a**	**18**	15	1	**19a**	50
12	**Calix-9**[b]	5 mol%	**17a**	**18**	15	1	**19a**	62
13	**Calix-14**[b]	5 mol%	**17a**	**18**	15	1	**19a**	97
14	**Calix-3**	5 mol%	**17b**	**18**	24	1	**19b**	71
15	**Calix-3**	5 mol%	**17b**	**18**	24	2	**19b**	74
16	**Calix-6**	5 mol%	**17b**	**18**	24	1	**19b**	88
17	**Calix-6**	5 mol%	**17b**	**18**	24	2	**19b**	100
18	**Calix-10**	5 mol%	**17b**	**18**	24	1	**19b**	88
19	**Calix-10**	5 mol%	**17b**	**18**	24	2	**19b**	66
20	**Calix-11**	5 mol%	**17b**	**18**	24	1	**19b**	85
21	**Calix-11**	5 mol%	**17b**	**18**	24	2	**19b**	77
22	**Calix-15**	5 mol%	**17b**	**18**	24	1	**19b**	89
23	**Calix-15**	5 mol%	**17b**	**18**	24	2	**19b**	87
24	**Calix-16**	5 mol%	**17b**	**18**	24	1	**19b**	85
25	**Calix-16**	5 mol%	**17b**	**18**	24	2	**19b**	77
26	**Calix-4**[b]	5 mol%	**17b**	**18**	24	1	**19b**	63
27	**Calix-9**[b]	5 mol%	**17b**	**18**	24	1	**19b**	63
28	**Calix-14**[b]	5 mol%	**17b**	**18**	24	1	**19b**	28
29	none	-	**17a**	**18**	48	1 or 2	**19a**	0
30	none	-	**17b**	**18**	48	1 or 2	**19b**	0

[a] Reaction conditions: **17a-b** (0.18 mmol), **18** (22 mg, 0.09 mmol); isolated yield.
[b] Reference[3a]

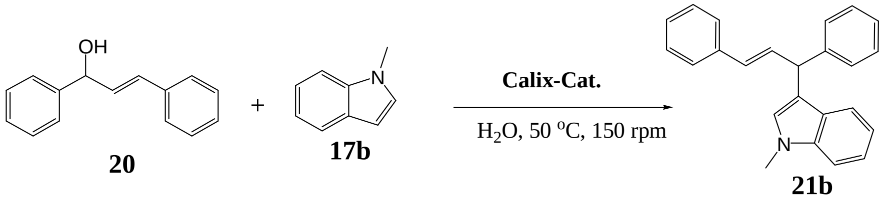
Table. 2 The coupling reaction of **17a** with **20** in H_2O



Entry	Catalyst	Catalyst loading	Ar-H	*sec*-Alcohol	Time/h	H_2O/mL	Product	Yield (%)[a]
1	**Calix-6**	5 mol%	**17a**	**20**	61	1	**21a**	77
2	**Calix-6**	5 mol%	**17a**	**20**	61	2	**21a**	95
3	**Calix-6**	5 mol%	**17a**	**20**	86	1	**21a**	100
4	**Calix-10**	5 mol%	**17a**	**20**	61	1	**21a**	54
5	**Calix-10**	5 mol%	**17a**	**20**	61	2	**21a**	87
6	**Calix-10**	5 mol%	**17a**	**20**	86	1	**21a**	100
7	**Calix-11**	5 mol%	**17a**	**20**	61	1	**21a**	45
8	**Calix-11**	5 mol%	**17a**	**20**	61	2	**21a**	87
9	**Calix-11**	5 mol%	**17a**	**20**	86	1	**21a**	57
10	**Calix-15**	5 mol%	**17a**	**20**	61	1	**21a**	46
11	**Calix-15**	5 mol%	**17a**	**20**	86	1	**21a**	58
12	**Calix-16**	5 mol%	**17a**	**20**	61	1	**21a**	45
13	**Calix-16**	5 mol%	**17a**	**20**	61	2	**21a**	87
14	**Calix-16**	5 mol%	**17a**	**20**	86	1	**21a**	57
15	**Calix-4**[b]	5 mol%	**17a**	**20**	61	2	**21a**	81
16	**Calix-9**[b]	5 mol%	**17a**	**20**	61	2	**21a**	86
17	**Calix-14**[b]	5 mol%	**17a**	**20**	61	1	**21a**	42
18	None	-	**17a**	**20**	86	1 or 2	**21a**	0

[a] Reaction conditions: **17a** (0.18 mmol), **20** (19 mg, 0.09 mmol). Isolated yield.
[b] Reference[3a]

Table.3 The coupling reaction of **17b** with **20** in Water



Entry	Catalyst	Catalyst loading	Ar-H	*sec*-Alcohol	Time/h	H_2O/mL	Product	Yield (%)[a]
1	**Calix-3**	5 mol%	**17b**	**20**	15	1	**21b**	82
2	**Calix-3**	5 mol%	**17b**	**20**	61	1	**21b**	87
3	**Calix-3**	5 mol%	**17b**	**20**	61	2	**21b**	43
4	**Calix-6**	5 mol%	**17b**	**20**	6	1	**21b**	89
5	**Calix-6**	5 mol%	**17b**	**20**	15	1	**21b**	99
6	**Calix-6**	5 mol%	**17b**	**20**	61	1	**21b**	100
7	**Calix-6**	5 mol%	**17b**	**20**	61	2	**21b**	100
8	**Calix-10**	5 mol%	**17b**	**20**	15	1	**21b**	85
9	**Calix-10**	5 mol%	**17b**	**20**	61	1	**21b**	100
10	**Calix-10**	5 mol%	**17b**	**20**	61	2	**21b**	100
11	**Calix-11**	5 mol%	**17b**	**20**	15	1	**21b**	49
12	**Calix-11**	5 mol%	**17b**	**20**	61	1	**21b**	100
13	**Calix-11**	5 mol%	**17b**	**20**	61	2	**21b**	100
14	**Calix-15**	5 mol%	**17b**	**20**	6	1	**21b**	90
15	**Calix-15**	5 mol%	**17b**	**20**	15	1	**21b**	95
16	**Calix-15**	5 mol%	**17b**	**20**	61	1	**21b**	100
17	**Calix-15**	5 mol%	**17b**	**20**	61	2	**21b**	100
18	**Calix-16**	5 mol%	**17b**	**20**	15	1	**21b**	49
19	**Calix-16**	5 mol%	**17b**	**20**	61	1	**21b**	100
20	**Calix-16**	5 mol%	**17b**	**20**	61	2	**21b**	100
21	**Calix-4**[b]	5 mol%	**17b**	**20**	15	1	**21b**	96
22	**Calix-9**[b]	5 mol%	**17b**	**20**	15	1	**21b**	23
23	**Calix-14**[b]	5 mol%	**17b**	**20**	15	1	**21b**	74
24	None	-	**17b**	**20**	86	1 or 2	**21b**	0

[a] Reaction conditions: **10a-b** (0.18 mmol), **13** (19 mg, 0.09 mmol). Isolated yield.
[b] Reference[3a]