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SYNTHESIS OF DECAHYDROXYCALIX [10]ARENE DERIVATIVES

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ABSTRACT

The present synthesis relates to a novel method for preparing 2,8,14,20,26,32,38,44,50,56-deca(4-nitro)phenyl-,11,17, 23, 29, 35, 41, 47, 53, 59-deca -tertbutyl- 61, 62, 63, 64, 65, 66, 67, 68, 69, 70-decahydroxycalix[10]arene(VI);2,8,14,20,26, 32,38,44,50,56-deca(3-nintro)phenyl- 5,11,17,23,29,35, 41,47,53,59-decatertbutyl-61,62,63, 64,65,66,67,68,69,70-decahydroxycalix[10]arene(VII),2, 8,14, 20,26, 32, 38,44,50,56-deca(2-nintro)phenyl-5,11,17,23,29, 35,41,47,53,59-deca-tertbutyl-61,62,63,64,65,66,67,68,69,70-Decahydroxy calix[10] arene(VIII),2,8,14,20,26,32,38,44,50,56-deca(4-cyano)phenyl-5,11,17, 23,29,35,41,47,53, 59-deca-tertbutyl-61,62,63,64,65,66,67,68,69,70 -decahydroxycalix [10] arene (IX) in presence of base.

KEYWORDS: Calix[10]arenes, Macrocycles, Cancer immunotherapy.

INTRODUCTION

Calixarenes are currently enjoying considerable interest in the field of supermolecular chemistry because their derivatives can form inclusion complexes with cations or with neutral molecules.[1,2] They have been widely used as building blocks for the synthesis of ionophores either of the polydentate type or macrobicyclic as the calixcrowns, which show efficiency and selectivity according to the calixarene ring size and conformation.[3] For this purpose calixarenes are readily converted into a wide variety of derivatives at the lower rim by alkylation of the phenolic groups such as polydentate ester,[4] carboxylate,[5] ether,[6] amide,[7] and keto[8] groups. Calixarene was used as scaffold to assemble a construct bearing four Tn-antigen unit, at upper rim and immune adjuvant P3CS, at the lower rim. The construct showed a cluster effect in the production of Tn specific IgG antibodies in mice when compared to an analogous monovalent construct. This reveals perspectives for potential

application in cancer immunotherapy.[9] Calixarenes have also been used in the recovery of Cesium and Uranium ion selective electrodes and field-effect transistors. Other applications such as phase transfer agents, hydrolysis catalysts and separation of organic molecules have also been reported.[10-11]

EXPERIMENTAL SECTION

Synthesis of 2,8,14,20,26,32,38,44,50,56-deca (4-nitro)phenyl- 5,11, 17,23,29,35,41,47,53, 59-deca-tertbutyl-61,62,63,64,65, 66,67, 68, 69,70- decahydroxycalix[10] arene (VI).

Mixture of 4-tertbutyl phenol (I) (5 mmol) and 4-nitrobenzaldehyde (II) (5mmol) was dissolved in 15ml 1,4-dimethylbenzene and then 0.5ml of 5N K_2CO_3 were added. The mixture was heated in heating mantle with stirring using reflux condenser at about 120 ^{0}C for 3 hrs. The reaction mixture was allowed to cool to room temperature. The reaction mixture was washed with methanol. The residue obtained was treated with dimethyl sulphoxide (DMSO) and filtered. The dimethyl sulphoxide from filtrate was recovered by vacuum distillation.The residue obtained was washed with water and dried in oven at 110^{0}C . It gave buff coloured solid of 2,8,14,20,26,32,38,44,50,56-deca(4-nintro)phenyl-5,11,17,23,29,35,41, 47,53,59-deca-tertbutyl-61,62,63,64,65,66,67,68,69,70-decahydroxycalix[10] arene (VI), (yield:32.1%), (m .p.>400^{0}C).

Spectral data of the compound (VI)

IR (KBr) : 840 (v- Ar);1072 (v-C-O str.);1501 (v-C-H deforming, -C$(CH_3)_3$);1609 (v-Ar-H str);2964 (v-C-H str., -CH3);3435 (v-Ar-OH str.).

^{1}H-NMR (DMSO-d6) : 1.029 - 1.066 (s, 90H, (CH3)3);5.838 and 5.968 (s,10H,(Ph)3 C-H);6.338 – 8.189 (m, 60H, Ar-H);9.37 (s, 10H, Ar-OH).

^{13}C-NMR (DMSO-d6) : 31.92 **(-C**(CH3)3);34.21 (-C(CH3)3);72.72 and 73.30(C-H);123.32, 124.34, 127.66, 129.20,138.22 and 146.64,(Ar-**C**);154.69 and 155.28 (Ar-(**C**)-OH).**UV (DMSO)** : λmax 265.6(0.743) , Mass(M^+) m/z = 2830,

Synthesis of 2,8,14,20,26,32,38,44,50,56,- deca (3- nitro)phenyl-5,11,17,23,29,35,41,47,53, 59-deca-tertbutyl- 61,62,63,64,65, 66, 67, 68, 69,70- decahydroxycalix [10] arene (VII).

Mixture of 4-tertbutylphenol (I) (5 mmol) and 3-nitrobenzaldehyde (III) (5 mmol) was dissolved in 15ml 1,4-dimethylbenzene and then 0.5ml of 5NK_2CO_3 were added. The mixture was heated in heating mantle with stirring using reflux condenser at about 120 ^{0}C for 4 hrs. The reaction mixture was allowed to cool to room temperature. The reaction mixture was washed with methanol. The residue obtained was treated with dimethyl sulphoxide (DMSO)

and filtered. The dimethyl sulphoxide from filtrate was recovered by vacuum distillation.The residue obtained was washed with water and dried in oven at 110^0C. It gave buff coloured solid of 2,8,14, 20,26, 32,38,44,50,56-deca (3-nintro) phenyl- 5,11,17,23, 29, 35, 41,47,53,59-decatertbutyl-61,62,63,64,65,66,67,68,69,70- decahydroxycalix [10] arene(VII), (yield:25.6%), (m .p.>400^0C).

Spectral data of the compound (VII)

IR (KBr) : 828, (v- Ar);1071 (v-C-O str.);1499 (v-C-H deforming, -C(CH3)3;1615 (v-Ar-H str);2962 (v-C-H str., CH3-);3435 (v-Ar-OH str.);1H-**NMR (DMSO-d6)** : 1.036 and 1.070 (s, 90H, -(CH_3)3),5.697 and 5.958 (s, 10H, (C-H));6.392 – 8.316 (m, 60H, Ar-H);9.376 (s, 10H, Ar-O**H**);**13C-NMR (DMSO-d6)** : 31.89 (-C(CH3)3) ; 33.87 (-C(**C**H3)3);73.11 (**C**-H);116.93, 121.80, 122.47, 122.76, 129.34,134.90, 138.58 (Ar-**C**);149.12 (Ar-(C)-OH). 2830, **UV (DMSO)** : λmax 261.2(0.491) 237.2(0.478) , **Mass**(M^+) m/z 2830,

Synthesis of 2,8,14,20,26,32,38,44,50,56,- deca (2- nitro) phenyl- 5,11,17,23,29,35,41,47, 53,59-deca-tertbutyl-61, 62, 63,64,65, 66, 67, 68, 69,70- decahydroxycalix [10] arene (VIII).

Mixture a 4-tertbutyl phenol (I) (5 mmol) and 2-nitrobenzaldehyde (IV) (5 mmol) was dissolved in 15ml 1,4-dimethylbenzene and then 0.5ml of 5N K_2CO_3 were added. The mixture was heated in heating mantle with stirring using reflux condenser at about 120 0C for 5 hrs. The reaction mixture was allowed to cool to room temperature. The reaction mixture was washed with methanol. The residue obtained was treated with dimethyl sulphoxide (DMSO) and filtered. The dimethyl sulphoxide from filtrate was recovered by vacuum distillation.The residue obtained was washed with water and dried in oven at 110^0C. It gave buff coloured solid of 2,8,14,20,26,32,38,44,50,56-deca(2-nintro)phenyl-5,11,17,23,29, 35,41,47,53,59-deca-tertbutyl- 61,62,63,64,65,66,67,68,69, 70- decahydroxycalix [10] arene (VIII), (yield:22.8%), (m .p.>400^0C).

Spectral data of the compound (VIII)

IR (KBr) : 789 (v- Ar);1072 (v-C-O str.);1499 (v-C-H deforming, -C(CH3)3);
1633 (v-Ar-H str);2962 (v-C-H str., CH3-);3450 (v-Ar-OH str.).
Mass(M^+) m/z=2830.

Synthesis of 2,8,14,20,26,32,38,44,50,56-deca (4-cyano) phenyl-5,11,17,23,29,35,41,47,53, 59-deca-tertbutyl-61,62,63,64,65,66,67, 68, 69,70- decahydroxycalix [10] arene (IX).

Mixture of 4-tertbutyl phenol (I) (5 mmol) and 4-cyanobenzaldehyde (V) (5 mmol) was dissolved in 15ml 1,4-dimethylbenzene and then 0.5ml of 5NK2CO3 were added. The mixture was heated in heating mantle with stirring using reflux condenser at about 1200C for 3 hrs. The reaction mixture was washed with methanol. The residue obtained was treated with dimethyl sulphoxide (DMSO) and filtered. The dimethyl sulphoxide from filtrate was recovered by vacuum distillation.The residue obtained was washed with water and dried in oven at 110^0C white solid of 2,8,14,20,26,32,38,44,50,56-deca(4-cyano)phenyl-5,11,17, 23,29,35,41,47, 53,59-deca-tertbutyl-61,62, 63,64,65,66,67,68,69,70-decahydroxycalix [10] arene (IX), (yield:35.2%), (m .p.>400^0C).

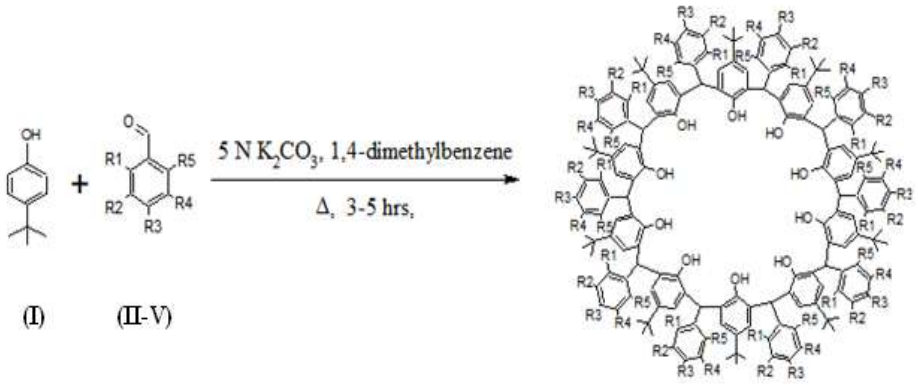
Spectral data of the compound (IX).

IR (KBr) : 865 (tetrasubstituted);1072 (v-C-O str.);1497 (v-C-H deforming, -C(CH3)3);1611 (v-Ar-H str);2230 (v-CN);2963(v-C-H str., CH3-);3434 (v-Ar-OH str.);**1H-NMR (DMSO-d6)** : 1.028 and 1.063 (s, 90H, -C(CH3)3);5.761 and 5.894 (s,10H, (C-H));6.306 – 7.766 (m, 60H, Ar-H);9.315 (s,10H,Ar-OH);

13C-NMR (DMSO-d6) : 31.92 and 33.86 (-**C**(CH3)3); 73.77 (**C**-H);

119.65, 122.58, 124.14, 127.89, 129.39,132.12, 138.16, 152.27 (Ar-**C**);155.30 (Ar-(**C**)-OH).

Mass(M^+) m/z = 2630,**UV (DMSO)** : λmax 241.6(2.811), 280.6(0.979).



	R1	R2	R3	R4	R5
II,VI	H	H	NO_2	H	H
III,VII	H	NO_2	H	H	H
IV,VIII	NO_2	H	H	H	H
V,IX	H	H	CN	H	H

RESULTS AND DISCUSSION

The literature survey on 4-alkyl calix[10] arene synthesis revealed that aromatic aldehydes have not been employed. This is probably due to the use of strong bases like KOH, NaOH etc. which may bring about Cannizzaro's reaction rather than the formation of calixarenes. A Process of preparing 4-tertbutyl calix[10] arene derivatives with phenyl substituents on methylene bridges (Scheme) afforded V-VII.

CONCLUSION

In conclusion we have developed a short synthesis of a 4-tert-butyllcalix[10]arenes having substituted phenyl functionalities on all the methylene bridges of the calixarene.

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