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1 About the Author



Oliver Sutcliffe graduated from the University of Liverpool with a BSc (Hons) in Chemical Sciences (1996) and subsequently obtained a PhD in Synthetic Organic Chemistry working on “*New Extended Dipolar Systems*” under Drs Richard C. Storr and Thomas L. Gilchrist from the same institution. In 1999, he joined Professor Martin R. Bryce’s group at the University of Durham as a postdoctoral fellow investigating the application of enantiopure ferrocene ligands in asymmetric synthesis, before moving to industry and working as a medicinal chemist on the design, development and optimisation of drug molecules for a broad-range of biological targets, including cancer. He moved to the University of Strathclyde in 2006, obtained an MSc in Pharmaceutical Analysis and after a period at the European Directorate for the Quality of Medicines and Healthcare (EDQM) in

13 Strasbourg was appointed as a lecturer in the Strathclyde Institute of Pharmacy and Biomedical Sciences (SIPBS). In
14 January 2012, Dr Sutcliffe joined the staff at Manchester Metropolitan University as both a Senior Lecturer in
15 Pharmaceutical and Analytical Chemistry and Co-Director of the Manchester Centre for the Study of Legal Highs
16 (MCSLH). Dr Sutcliffe’s research interests include the isolation, identification and analysis of “*new psychoactive*
17 *substances*” (formally known as “*legal highs*”) such as mephedrone and its derivatives, and the development of
18 simple, rapid and selective presumptive tests and devices which can be applied by “*non-specialists*” for the detection
19 of illicit substances in the field. He is the co-inventor of 10 international patents and co-author of 33 peer-reviewed
20 research articles.

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33 **Key term 1:** Cucurbit[*n*]uril

34 Cucurbit[*n*]urils are supramolecular structures made of glycoluril monomers linked by methylene bridges. The
35 oxygen atoms are located along the peripheral edge of the macrocycle and are tilted inwards, forming a partly
36 enclosed hydrophobic cavity that has been shown to bind to a range of organic molecules and inorganic ions. The
37 name is derived from the resemblance of this molecule with a pumpkin of the family of *Cucurbitaceae*.

38
39 **Key term 2:** Hemicucurbit[*n*]uril

40 Hemicucurbit[*n*]urils are supramolecular structures made of *N*-substituted ethyleneureas monomers linked by
41 methylene bridges. These macrocycles resemble a cucurbit[*n*]uril bisected along its equator where the ethyleneurea
42 subunits adopt an alternating “zigzag” conformation. Unlike cucurbit[*n*]urils, hemicucurbit[*n*]urils have a limited
43 ability to form inclusion complexes with organic compounds and do not to bind to inorganic ions.

44
45 **Key term 3:** Bambus[*n*]uril

46 Bambus[*n*]urils are supramolecular structures made of 2,4-disubstituted glycoluril monomers linked by methylene
47 bridges. These macrocycles combines the features of both cucurbit[*n*]urils and hemicucurbit[*n*]urils to give a
48 hyperbolic three-dimensional structure where the glycouril subunits adopt an alternating “zigzag” conformation and
49 allow the formation of inclusion complexes. The name is derived from the resemblance of this molecule with the
50 bamboo plant stem of the family of *Bambusoidea*.

51
52 **Key term 4:** Microwave Synthesis

53 Microwave synthesis is a rapidly expanding field in both organic and inorganic chemistries where microwave energy
54 is focussed directly (and efficiently) into the reactive components of a mixture, rather than being transferred from
55 the bulk solvent by convection/conduction (as occurs in conventionally heated reactions). This technique has been
56 applied to a wide-range of chemical processes, using both solution- and solid-phase reagents, and is able to greatly
57 enhance the rate and overall yield of many reactions leading to products, which in general, require minimal work-up
58 and purification.

59

Classical and microwave-assisted synthesis of cucurbit[*n*]urils, hemicucurbit[*n*]urils and bambus[*n*]urils

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Abstract

This chapter gives a concise overview of the synthetic and supramolecular chemistry of cucurbit[*n*]uril (CB[*n*]) family of macrocycles and expands it to hemicucurbit[*n*]urils (HemCB[*n*]) and bambus[*n*]urils (BU[*n*]). The application of microwave-assisted synthesis to access these macrocycles is reviewed. Several extensive papers describing the synthesis, physical and recognition properties and applications of CB[*n*]s have been published and the reader is directed to these key sources throughout this chapter.

1. Introduction

The toroidal cucurbit[*n*]uril (CB[*n*]; *n* = 5, 6, 7, 8 or 10) (**1**) family of macrocycles represent a unique class of compounds that display a variety of host–guest interactions [1 – 7]. Their symmetrical, oxygen-lined portals give access to a hydrophobic cavity that has been shown to bind organic or inorganic compounds, gases and alkali earth metal salts with binding constants of up to 10^{15}M^{-1} . Hemicucurbit[*n*]urils (**2**) and bambus[*n*]urils (**3**) can be viewed as structurally-related to cucurbit[*n*]urils where the former are bisected along their equators and adopt a “zigzag” conformation [1], whilst the latter combines the structural features of both cucurbit[*n*]urils and hemicucurbit[*n*]urils to give a hyperbolic three-dimensional arrangement [8] (Figure 1). Cucurbit[*n*]urils have been extensively reviewed in terms of their synthesis, properties and potential applications in both chemical and pharmaceutical sciences and the author directs the reader to the recent series of articles published in the Israel Journal of Chemistry for more in-depth information regarding selected aspects of CB[*n*] chemistry [7]. This chapter seeks to provide a concise overview of these macrocycles, their synthesis and applications and how the field has expanded to the structurally-related hemicucurbit[*n*]uril and bambus[*n*]uril families.

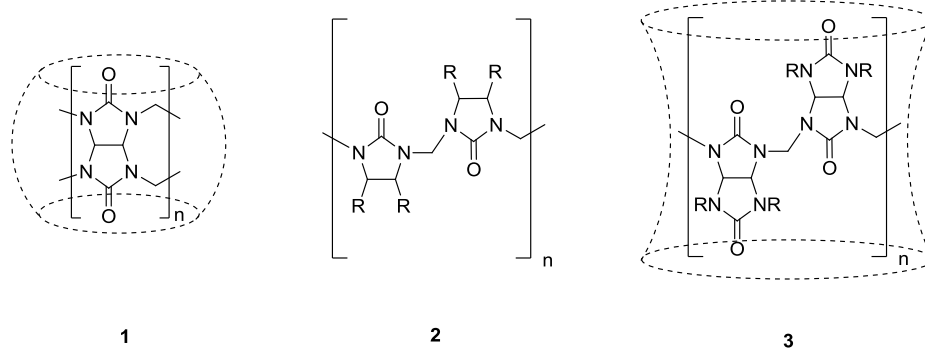
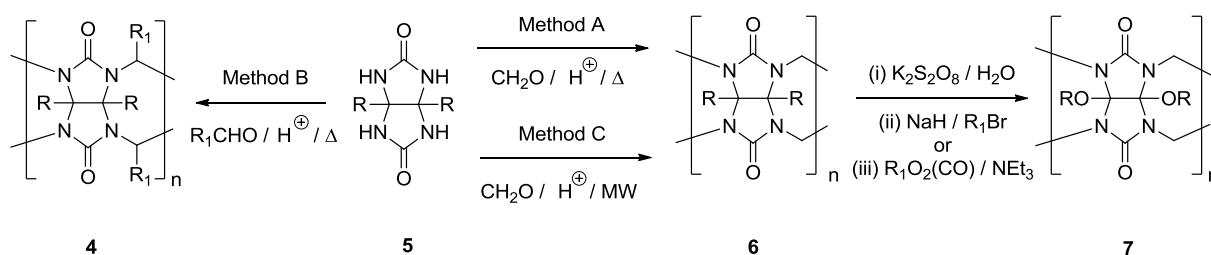


Figure 1. Structures of cucurbit[*n*]uril (**1**), hemicucurbit[*n*]uril (**2**) and bambus[*n*]uril (**3**)

2. Synthesis of cucurbit[*n*]urils, hemicucurbit[*n*]urils and bambus[*n*]urils

The large-scale production of CB[*n*]s for commercial and industrial applications, particularly drug delivery, requires reliable methods of synthesis that are effective in terms of both the ready availability of cheap starting materials and energy consumption. Cucurbit[*n*]urils (**6**) are typically made through the condensation of glycoluril (**5**, R = H) and formaldehyde (or paraformaldehyde) in hot concentrated mineral acids (Scheme 1, Method A) [1 – 7, 9]. By changing the type of acid used, the molarity of the acid and/or the concentration of glycoluril, the distribution of the CB[*n*] products can be adjusted. For instance, synthesis in concentrated sulfuric acid typically produces samples containing 88% CB[6] with approximately 12% CB[5] and inconsequential amounts of CB[7] and CB[8] [9]. Alternatively, the use of 5M hydrochloric acid produces mixtures containing up to 35% CB[7] through the use of very high concentrations of glycoluril (*circa.* 1700 mg mL⁻¹) and concentrated hydrochloric acid solutions produce mixtures containing up to 8% CB[8] [9].



102

103

Scheme 1. Synthesis of cucurbit[*n*]urils (*n* = 5, 6, 7, 8 or 10) and functionalised cucurbit[*n*]urils (*n* = 5, 6 or 7). Method A (*n* = 5 – 10 [R = H]; *n* = 5 or 6 [R = Me or cyclohexyl-]); Method B (*n* = 5 – 10, R = R₁ = H); Method C (*n* = 5 – 10, R = H, see Scheme 6 for conditions).

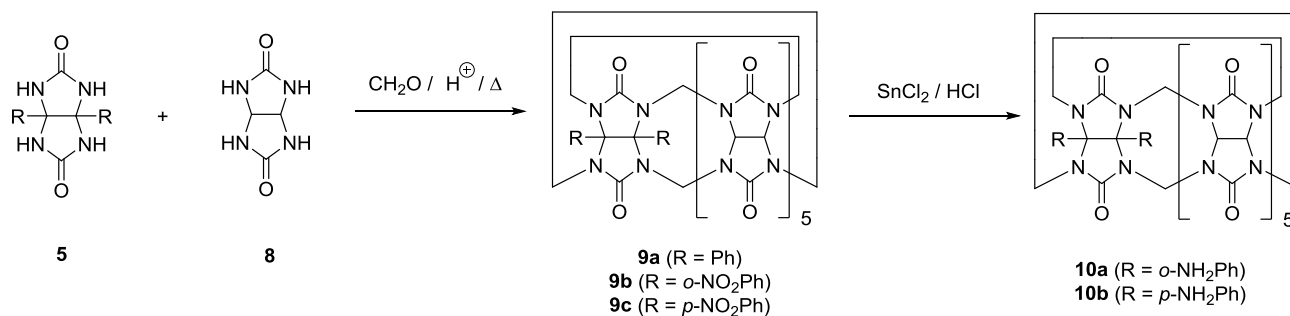
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Efforts to further extend the supramolecular chemistry and improve the solubility of CB[*n*] in common solvents led to the development of efficient synthetic methods to prepare functionalized CB[*n*] derivatives. Principally three routes were envisaged: (i) condensation of glycoluril (**5**, R = H) with substituted aldehydes to introduce substituents at the methylene bridgehead (**4**, Scheme 1, Method B); (ii) acid-catalysed condensation of substituted glycolurils (**5**, R = alkyl, aryl etc.) with formaldehyde (Scheme 1, Method A) and finally (iii) direct functionalization of cucurbit[*n*]uril itself (for example: **6** → **7**) (Scheme 1). The first route was unsuccessful and the second has met with little success with only Me₁₀CB[5] (**6**, *n* = 5, R = Me), Me₁₀CB[6] (**6**, *n* = 6, R = Me) and the cyclohexano-derivatives (**6**, *n* = 5 or 6, R = cyclohexano-) reported *via* this route [1]. CB[*n*] (*n* = 6 or 7) analogues utilising *bis*(phthalylhydrazide) and substituted glycoluril(*bis*-cyclic ether) as the building blocks have also been reported and show significant improvements in solubility in organic and aqueous media depending on the substituents present and have a similar binding capacity to CB[6] [1].

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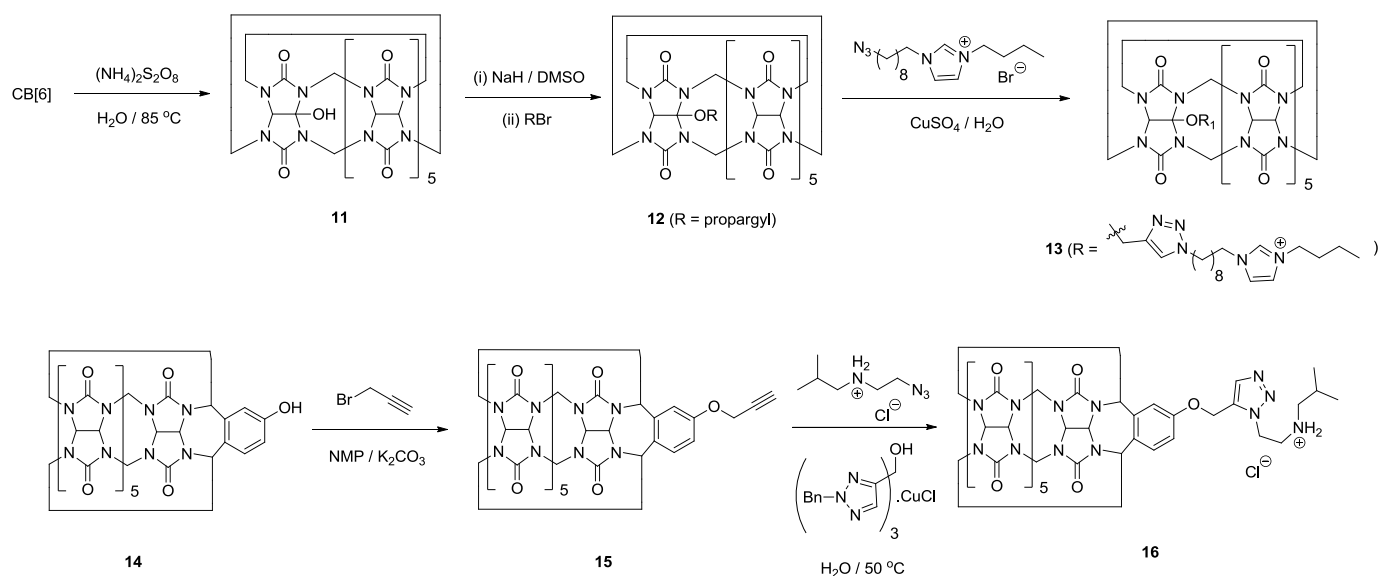
Partially substituted CB[*n*] derivative, Ph₂CB[6] (**9a**, R = Ph) was first prepared by Nakamura *et al.* by sulphuric acid-catalysed mixed condensation of formaldehyde with diphenylglycoluril (**5**, R = Ph) and glycoluril in a 1:5 ratio [1, 3] with Kim *et al.* patenting the synthesis, *via* di(*o*-nitro)phenylCB[6] (**9b**, R = *o*-NO₂Ph) and di(*p*-nitro)phenylCB[6] (**9c**, R = *p*-NO₂Ph-), of di(*o*-amino)phenylCB[6] (**10a**, R = *o*-NH₂Ph) and di(*p*-amino)phenylCB[6] (**10b**, R = *p*-NH₂Ph-) shortly thereafter [3] (Scheme 2). Other partially substituted derivatives, namely Me₄CB[6] and (Me₂CyP)_{*n*}CB[6] (cyclopentano, CyP), have been reported [1, 3].

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Scheme 2. Synthesis of functionalised cucurbit[*n*]urils.

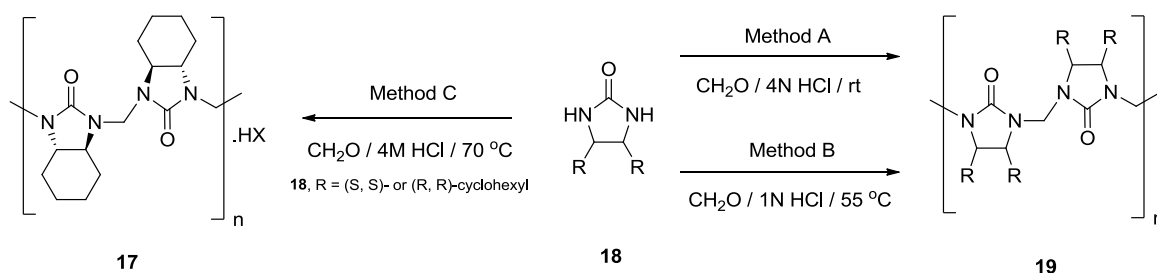
A major step in the field was accomplished by the Kim *et al.* direct perhydroxylation of CB[*n*] using aqueous K₂S₂O₈ as an oxidant to provide the multi-functionalised derivative, (HO)_{2*n*}CB[*n*](**7**, *n* = 5, 6 or 7, R = H), in low to moderate yield (5 – 45% yield) (Scheme 1). Subsequent functionalization with either an alkyl bromide or anhydride yielded the corresponding alkoxy (**7**, R = R₁) or acyloxy- (**7**, R = COR₁) products which have exploited in numerous biological applications [3, 10]. Scherman *et al.* refined the persulfate oxidation of CB[6] facilitating isolation of (HO)₁CB[6] (**11**) in 12% yield (Scheme 3). Concomitant transformation into the propargyloxyCB[6] (**12**) facilitates Huisgen azide–acetylene click reaction to generate the self-complexing CB[6] derivative (**13**) [11]. Isaacs *et al.* who recently reported the gram scale synthesis of a number of monofunctionalized CB[6] derivatives by the reaction with substituted phthalaldehydes, have built on this work and published the preparation of phenol-substituted CB[6] (**14**), its transformation into propargyloxy compound (**15**). Cycloaddition of (**15**) in the presence of *tris*(triazolyl)methanol–Cu(I) (Pericás’ catalyst) [12] to give stimuli-responsive triazole (**16**) (Scheme 3) [13].



Scheme 3. Functionalization of cucurbit[*n*]urils using Huisgen azide-acetylene click reaction

147 Miyahara and Buschmann have independently reported that acid-catalysed condensation reactions using equimolar
 148 amounts of ethyleneureas (**18**, R = H) with formaldehyde in 4N hydrochloric acid (at room temperature) provides
 149 access to hemicucurbit[*n*]urils (Scheme 4, Method A, *n* = 6) in 94% yield [1, 14, 15]. Hemicucurbit[*n*]urils are cyclic
 150 and structurally-related to cucurbit[*n*]urils where the former are bisected along their equators as demonstrated by
 151 their X-ray structures which feature an alternate (or “zigzag”) arrangement of the six ethylene urea units and a
 152 chloride ion (which is believed to act as a templating agent during the cyclocondensation process) present within the
 153 cavity. The larger macrocycle, HmCB[12], can be obtained in excellent yield and purity by heating an equimolar
 154 mixture of (**18**, R = H) and 37% formaldehyde in 1N HCl at 55 °C for three hours (Scheme 4, Method B, *n* = 12, 93%
 155 yield) and subsequent purification by recrystallization with chloroform [14]. The X-ray crystal structure of **18** (R = H)
 156 has been determined and indicates cyclic structural architecture exhibiting an analogous “zigzag” conformation as
 157 the hexamer with several chloroform molecules in its crystal lattice. In contrast to CB[*n*]s, hemicucurbit[*n*]urils are
 158 soluble in non-polar solvents and exhibit significantly different behaviour in terms of their ability to selectively
 159 complex to small molecules (e.g. formamide, CHCl₃ and propargyl alcohol), anions (e.g. Cl⁻, SCN⁻, Br⁻ and I⁻) and
 160 cations (Co²⁺, Ni²⁺ and UO₂²⁺) but not alkali or alkaline earth metals, Ag⁺ or NH₄⁺ ions [1, 3, 5, 14, 15].

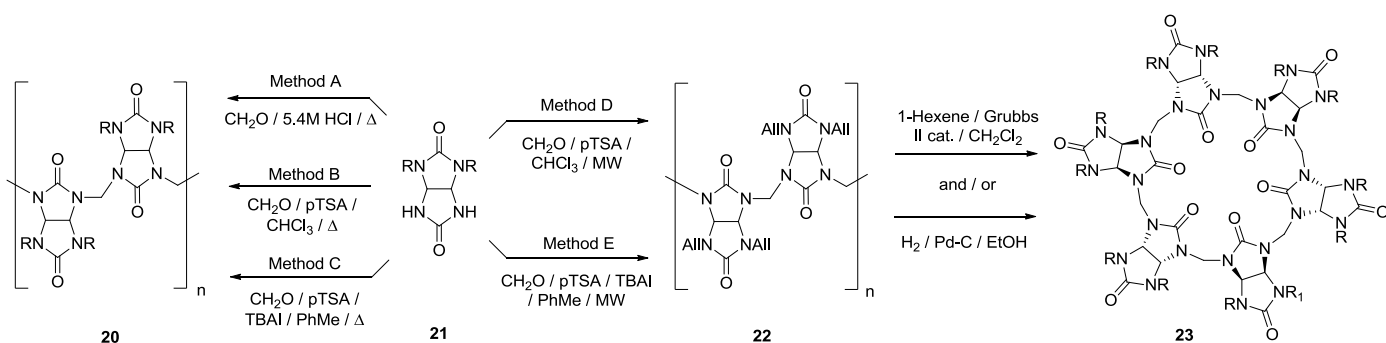
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Scheme 4. Synthesis of hemicucurbit[*n*]urils and chiral hemicucurbit[*n*]urils

Recently Aav *et al.* have disclosed the chiral (*R, R*)-cyclohexylhemicucurbit[6]uril and (*S, S*)-cyclohexylhemicucurbit[6]urils (**17**), prepared (as their corresponding hydrochloride and hydrobromide salts) from equimolar amounts of the enantiopure perhydrobenzimidazolines (**18**, R = (*S, S*)- or (*R, R*)-cyclohexyl) and paraformaldehyde in 4M hydrochloric (or hydrobromic) acid at 70 °C in 75 – 85% yield after flash chromatography (Scheme 4, Method C). The enantiopure cyclohexylhemicucurbit[6]urils formed 1:1 complexes with Cl⁻, Br⁻, carboxylic and thiolacetic acids and amines. Diastereomeric complexes with (*R*)- and (*S*)-*O*-methylmandelic acid in organic media were also prepared [16].

Bambus[*n*]urils (BU[*n*]s), which combined the structural features of both cucurbit[*n*]urils and hemicucurbit[*n*]urils, were first disclosed by Sindelar *et al.* in 2010 and subsequently patented in 2011 [8, 17]. The cyclic hexamer, Me₁₂BU[6] (**20**, R = Me, as the HCl salt) was prepared as a white powder, in 30% yield, by heating 2,4-dimethylglycoluril (**21**, R = Me) and paraformaldehyde in 5.4M HCl for 24h (Scheme 5, Method A). The structure of BU[6] was confirmed by X-ray analysis of microcrystals (formed by slow evaporation of BU[6] in EtOH-CHCl₃-tetrabutylammonium chloride) and indicated a cyclic structure exhibiting a hyperbolic conformation (**3**, Figure 1) with the chloride anion situated within the 6.4 Å cavity and the tetrabutylammonium cation located outside the macrocycle.



Scheme 5. Synthesis of bambus[*n*]urils (*n* = 4, 6, 12). Method A (reflux, 24h); Method B (reflux, 24h); Method C (reflux, 22h); Method D (200W, 75 °C, 72h); Method E (200W, 110 °C, 4h)

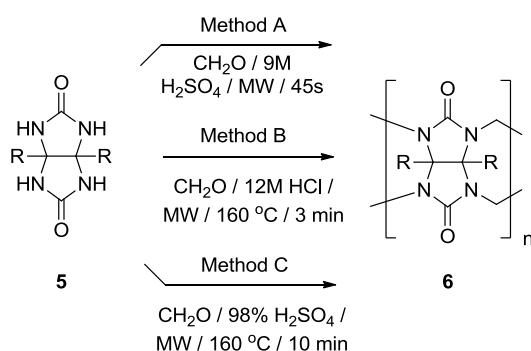
Subsequent to this report a number of bambus[*n*]urils were synthesised, from their prerequisite 2,4-disubstituted-glycoluril (**20**, R = Pr, Bn) derivatives [18], using either: (i) an equimolar mixture of paraformaldehyde and *p*-toluenesulfonic acid (pTSA) in refluxing chloroform (Scheme 5, Method B) or (ii) an equimolar mixture of paraformaldehyde, *p*-toluenesulfonic acid and tetrabutylammonium iodide (TBAI) in refluxing toluene (Scheme 5, Method C). Anion-free bambus[*n*]urils were originally prepared by sequential displacement of the chloride anion within the cavity with a suitable solvent (e.g. MeCN), however, more robust methods involving displacement of the chloride anion with an iodide ion and the concomitant removal *via* oxidation (with hydrogen peroxide in the absence of light; 92% yield) or photocatalytically (using flash photolysis and titanium dioxide; 84% yield) have been recently reported [19].

Bambus[*n*]urils exhibit solubility in both organic and aqueous media and are primarily capable of forming stable complexes with various anions (e.g. Cl^- , Br^- , I^- , BF_4^- , NO_3^- and CN^-) with significant selectivity [8, 17 – 19]. A number of theoretical studies of the affinity of BU[6] with various cations (e.g. H^+ , Cs^+) and anions (e.g. F^- , CN^-) using quantum mechanical density functional theory [20, 21] have also been reported.

The application of microwave-mediated synthetic chemistry has grown in significance over the last two decades and it is now routinely used in the chemical and pharmaceutical industries for parallel and combinatorial synthesis. Since microwave energy (operating at a frequency of 2.45 GHz) can be focussed directly into the reactive components [22, 23], rather than being transferred from the bulk solvent by convection/conduction (as occurs in regular hotplate/oil bath reactions), microwave irradiation is able to greatly enhance the rate and overall yield of many reactions [22]. It is common for microwave-assisted processes to be significantly faster than 'conventional' methods; taking minutes

209 instead of days and/or seconds instead of hours [22, 23]. Microwave-mediated processes are, therefore, more
210 economic in terms of overall energy efficiency, but also because fewer side-products are (in general) formed during
211 these processes leading to simple work-up and purification of the desired targets [22, 23].

212
213 The application of microwave-assisted synthesis for the production of cucurbit[*n*]urils (Scheme 1, Method C) was first
214 patented by Kim *et al.* using an equimolar mixture of (**5**, R = H) and paraformaldehyde in 9M sulphuric acid.
215 Microwave irradiation for 45s gave a mixture of CB[5] (15%), CB[6] (45%), CB[7] (20%) and CB[8] (15%) respectively
216 [24]. Sutcliffe and Wheate reinvestigated and optimised the application of microwave-assisted synthesis in the
217 production of CB[*n*]s and by varying the reaction time (1 – 10 mins), temperature (100 – 200 °C) and the type of acid
218 used to promote the cyclocondensation reaction. The study indicated that after irradiation (160 °C) a mixture of
219 CB[*n*]s was produced using either 12M hydrochloric (Scheme 6, Method B) or 98% sulfuric acids (Scheme 6, Method
220 C) [25]. Hydrochloric acid, after 10 minutes, was found to produce a mixture of CB[5] (23%), CB[6] (58%), CB[7] (13%)
221 and CB[8] (6%) which approximated the distribution reported by Kim (Scheme 6, Method A), whilst sulfuric acid, after
222 3 minutes, produced mostly CB[6] (*circa.* 90%) with small amounts of CB[5] and CB[7].



226 **Scheme 6.** Microwave-assisted synthesis of cucurbit[*n*]urils (*n* = 5, 6, 7, 8 or 10).

227
228 The type of the acid used was a critical factor as phosphoric, formic, acetic and trifluoroacetic (TFA) acids failed to
229 produce any of the desired CB[*n*]s and nitric acid was unsuitable due to a violent off-gassing that occurred during
230 dissolution of the starting materials. Mixtures of strong and weak acids (e.g. H₂SO₄:TFA in ratios between 20:80 and
231 80:20) produce CB[*n*] less efficiently and with CB[6] as the prominent macrocycle. Scale-up of the reaction by 2-4x
232 was shown to be viable with the distribution of the CB[*n*]s produced remaining unchanged.

233

234 Though the application of microwave-assisted synthesis has not, to date, been applied to the preparation of
235 hemicucurbit[*n*]urils, Sutcliffe and Wheate's method for cucurbit[*n*]urils has been successfully applied to the
236 synthesis of novel bambus[*n*]urils by Heck *et al.* (Scheme 5, Methods D and E) [26]. Irradiation of an equimolar
237 mixture of 2,4-allylglycoluril (**21**, R = Allyl), paraformaldehyde and catalytic *p*-toluenesulfonic acid in chloroform (75
238 °C, 72h, Scheme 5, Method D) afforded allyl₈BU[4] (**23**, *n* = 4, 85% yield) and irradiation of an equimolar mixture of
239 paraformaldehyde, *p*-TSA and TBAI in toluene (110 °C, 4h, Scheme 5, Method E) gave the hexamer, allyl₁₂BU[6] (**23**, *n*
240 = 6, R = R₁ = allyl), in 60% yield – which was vastly superior to the classical route (*circa.* 20% yield). Subsequent
241 manipulation of allyl₈BU[4] (**23**, *n* = 4, R = R₁ = allyl) was achieved through cross-metathesis with Hovyeda-Grubbs
242 catalyst (90% yield) and concomitant hydrogenation with Pd-C (100% yield) providing access to three further
243 examples of this emerging class of macrocycles: propen₈BU[4] (**23**, *n* = 4, R = R₁ = CH=CH-CH₃); allyl₇HepBU[4] (**23**, *n* =
244 4, R = allyl, R₁ = CH₂-CH=CH-(CH₂)₃CH₃) and Pr₈BU[4] (**23**, *n* = 4, R = R₁ = propyl).

246 3. Applications

247 The high binding affinity and selectivity of cucurbit[*n*]urils has attracted significant attention, as such, CB[*n*]s have
248 demonstrated enormous potential in a range of applications, including microelectronics and nanomachine
249 components, chromatography and waste remediation, drug delivery, biosensors, and self-assembly and reaction
250 catalysis [1 – 7]. The construction of self-assembling molecular machines, which can switch between two different
251 states *via* a chemical, photochemical or electrochemical stimulus, is currently of interest and the CB[*n*] family is
252 ideally suited for such applications due to their recognition properties. A detailed discussion of these applications is
253 outside the scope of this chapter, so we recommend the extensive reviews by Lagona *et al.* [1], Kim [3] and Isaacs [4].
254 Functionalised cucurbit[*n*]urils have also used for a number biomimetic applications as artificial biological structures
255 and processes in living cells such as: selective ion channels, vesicles for targeted drug delivery and even gene
256 transfection [1, 3, 5, 7]. Hemicucurbit[*n*]urils have limited applications but have been utilised as supramolecular
257 catalysts in the esterification of 4-methoxy-4-oxobut-2-enoic, acrylic and benzoic acids using methanol [27] and
258 patented as potential cosmetic agents [28]. In contrast to the cucurbit[*n*]uril and hemicucurbit[*n*]uril families, the
259 detailed recognition properties and practical applications of bambus[*n*]urils remain to be explored.

261 4. Future Perspective

262 Many of the early concerns with the cucurbit[*n*]uril family, such as poor solubility, have been circumvented, either by
263 the use of salts or by chemical modification of the macrocycle itself. Since the turn of the century, the scientific
264 literature has expanded greatly, aided by the commercial availability of many of the CB[*n*]s and new synthetic
265 procedures for the functionalization of these materials, which has widened their use greatly. The utility of CB[*n*]s in
266 an assortment of chemical (microelectronics, chromatography, waste remediation and self-assembly or reaction

267 catalysts) and pharmaceutical (nanomachines, drug delivery and biosensors) applications have been consistently
268 demonstrated *in vitro* and in a few *in vivo* examples. Their progress from “*bench to bedside*”, however, is reliant on
269 the future development of functionalized CB[*n*]s and reproducibility of structurally consistent CB[*n*]s and their host–
270 guest complexes. Cucurbit[*n*]urils have already been revealed to prevent the degradation of some drugs and diminish
271 their toxicity. The development of new CB[*n*]s with suitable functional groups (e.g. amine and carboxylic acids) will
272 allow the growth of targeted drug-delivery vehicles through the attachment of biologically relevant substrates,
273 antibodies, peptides or aptamers to the CB[*n*]s. To date, few biologically useful functionalized CB[*n*]s have been
274 reported and the application of novel and efficient synthetic methodologies (for example: microwave-assisted
275 organic synthesis [MAOI]) may provide instrumental in the expansion of the CB[*n*]s family.

276 A requirement of pharmaceutical drug approval is to demonstrate the ability to produce new drugs (or, in this case,
277 CB[*n*]-based drug-delivery systems) in a single form both robustly and reproducibly. It is well documented that CB[*n*]s
278 produce a range of different crystal polymorphs (i.e. the ability of a solid material to exist in more than one
279 crystalline form) based on CB[*n*]-drug interactions and the crystal’s hydration state [25]. As such, the crystallization
280 processes of CB[*n*]s and their host–guest complexes needs to be scrutinized in great detail, in order to determine the
281 number of different polymorphs which may form, the physicochemical processes that drive their crystallization and
282 solid-state packing, as well as methods to produce CB[*n*]-drug formulations suitable for clinical use (e.g., oral, liquid
283 or solid dosage forms). Though the application of hemicucurbit[*n*]urils and bambus[*n*]urils has, to-date, not been
284 exploited as much as their cucurbit[*n*]uril cousins their potential in biological, pharmaceutical and chemical science,
285 especially in light of new derivatives being reported in the literature, is far from exhausted.

287 **Executive Summary**

- 288 • Cucurbit[*n*]urils (CB[*n*]s) are macrocycles made from the acid-catalyzed condensation reaction of glycoluril
289 and formaldehyde.
- 290 • Hemicucurbit[*n*]urils (HemCB[*n*]s) are macrocycles made from the acid-catalyzed condensation reaction of
291 ethyleneureas and formaldehyde.
- 292 • Bambus[*n*]urils (BU[*n*]s) are macrocycles made from the acid-catalyzed condensation reaction of 2,4-
293 disubstituted glycoluril subunits and formaldehyde.
- 294 • CB[*n*]s have applications in many chemical, pharmaceutical and biomimetic fields, however, the application
295 hemCB[*n*]s and BU[*n*]s have, to-date, not been exploited to their full potential.
- 296 • Microwave synthesis can applied as an efficient and low cost method on the industrial scale for the
297 production of CB[*n*]s and BU[*n*]s for a variety of applications.

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