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Triazolated calix[4]semitubes: assembling strategies towards long multicalixarene architectures†

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Cone and 1,3-alternate calix[4]arenes bearing pairs of 2-azidoethyl or propargyl groups, and 1,3-alternate calix[4]arenes having four 2-azidoethyl and four propargyl groups or pairs of 2-azidoethyl and silylated propargyl groups were explored as the components for the CuAAC-syntheses of triazolated calix[4]semitubes having three calixarene cores in the structures. Though condition tuning for each of the calixarene combinations was performed, the four-fold CuAACs using the tetrafunctional calixarenes returned the respective tris(calixarenes) in good yields only in the syntheses involving the calixarene tetrakis(alkyne) and hydroxylated bis(azides). The stepwise approach towards the triazolated calix[4]semitubes by using the 2-azidoethylated/propargylated calix[4]arene as the key synthone and de-silylation as the intermediate step was found to be a good alternative, which allowed the preparation of the semitubes with different substituents in the terminal calixarene units and can also be used for further extension of the semi-tubular assemblies.

Introduction

The well-developed approaches for chemical transformations of calixarenes and related macrocycles allow us to treat them as molecular platforms within a chemical 'building kit' for constructing diverse receptor molecules in which the required number of certain functional groups can be introduced and mutually pre-organized in a predictable manner.[1] When several platforms are involved in chemical reactions, more diverse and complicated, and, thus, much more attractive architectures may be created by using such multicalixarene conjugates. To date, many examples have been published on the covalently joining 'classical' calixarene macrocycles,[2] and those of thiacalixarenes,[3] calixpyrroles,[4] calixresorcinarenes,[5] and heteromacrocyclic conjugates from the calixarene family have also been known.[6] Most often, these conjugates comprise only two calixarene macrocycles (or/and related ones), which are connected to each other by one or several linkers. In the latter case, the calixarenes and the linkers form an additional macrocyclic site or cavity, which may possess special or even outstanding receptor abilities. Tris- and even larger multicalixarene assemblies are also known, of which those having a tubular shape are the most attractive,[7] though they are less available. These compounds inherit all the structural benefits from the above biscalixarene assemblies and allow allocation of more than one macrocyclic site/cavity within one molecule and manage their connectivity in the range from pure independent mode where simple binding/recognition of multiple guests is possible, up to tightly bound mode, which is prospective for constructing sophisticated supramolecules, *e.g.* multipositional molecular switchers.

We have recently shown[8] that diverse biscalixarene semitubes may be constructed from the respective bisazide and bisalkyne calixarene precursors using copper(I)-catalyzed azide–alkyne cycloaddition (CuAAC).[9] Each of these assemblies comprises a single binding site formed by two 1,4-disubstituted 1,2,3-triazole groups surrounded by the calixarene cores and targeted to transition cations. Herein we explored the applicability of this synthetic approach for the construction of larger semitubular assemblies having three calix[4]arene cores in their structures and possessing two bistriazole receptor sites separated from each other by the central 1,3-alternate calix[4]arene unit.

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Results and discussion

Alkyne and azide components of calix[4]semitubes

The design of the long triazolated calix[4]semitubes requires azide/alkyne-containing calixarenes of at least two types to be involved in CuAAC. The calixarenes of the first type are the respective bis(azides) or bis(alkynes) which can be used as the terminal units at both sides of a semi-tube, while the calixarenes of the other type are those having two pairs of azide or/and alkyne groups separated from each other by the macrocyclic core. Calix[4]arenes **1**,[10] and **2–4**[8] bearing 2-azidoethyl groups (Fig. 1) were selected as the bisazide terminal units in the triazolated calix[4]semitubes, and the structurally related calixarene dipropargyl ethers **5**,[11] **6**,[12] **7**,[13] and **8**[8] were used as the bisalkyne terminal units. Within each of the series, the bifunctional molecules have free phenolic OH groups or those propylated to fix the calix[4]arene macrocycle in a cone or 1,3-alternate molecular shape. Notably, the bis(azides) or bis(alkynes) of each type have been shown to react with each other to form the respective biscalixarene semitubes,[8] so they were expected to be suitable for building longer semitubes as well.

As for the central macrocycles of the triscalixarene semitubes, calixarene **9**[14] having two pairs of propargyl groups arranged by the two 'sides' of the 1,3-alternate core was selected for the CuAAC reactions with the bis(azides) **1–4**. To study the 'inverted' azide/alkyne-combinations involving dipropargyl ethers **5–8**, the respective tetrakis(azide) **11** was prepared for the first time from the tetrakis(alcohol) **10**[7d] and diphenylphosphoryl azide (DPPA) under the Mitsunobu reaction conditions (Scheme 1).

The attractive idea to prepare the hybrid central core having pairs of propargyl and 2-azidoethyl groups within the same molecule was successfully implemented by alkylating the bis(azide) **2** with propargyl bromide in the presence of Cs_2CO_3. To avoid any self-reactions of the prepared calixarene **12** under the CuAAC conditions, its propargyl groups were de-protonated with lithium bis(trimethylsilyl)amide (LiHMDS) and then silylated with *tert*-butyldimethylsilyl chloride (TBDMSCl) to obtain the protected calixarene **13** in which only the azide groups can participate in the Cu-catalyzed cycloaddition.

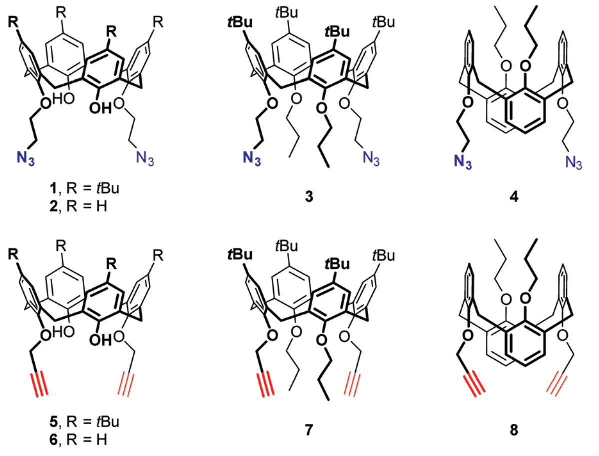
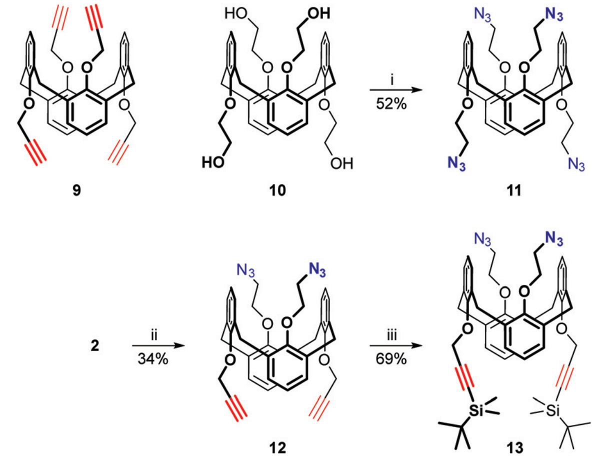


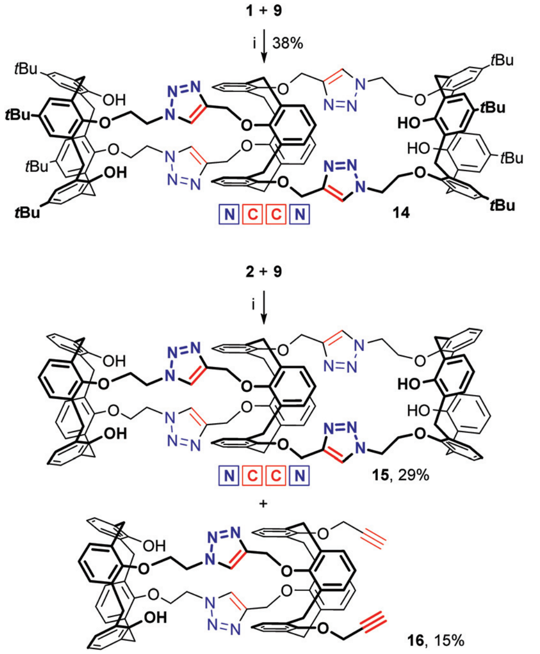
Fig. 1 Calixarenes tested as the terminal units in the calix[4]semitubes.



Scheme 1 Calixarenes used as the central units in the calix[4]semitubes: (i) DPPA, DIAD, Ph_3P, THF, rt; (ii) propargyl bromide, Cs_2CO_3, DMF, rt; (iii) TBDMSCl, LiHMDS, THF, rt.

One-step assembling of triscalixarene semitubes

It has been shown for the preparation of calix[4]semitubes from bis(azides) and bis(alkynes) under CuAAC conditions that the formation of polymeric/oligomeric byproducts during the reaction could not be avoided, so the selection of proper reaction conditions for every bis(azide)/bis(alkyne) combination was crucial for obtaining targeted semitubes in more or less satisfactory yields, which did not exceed 46%.[8] Reasonably, successful preparation of the triscalixarene semitubes using tetrafunctional central cores **9** or **11** requires the same or even more strict tuning of the reaction conditions. Still, the conditions obtained previously for the preparation of a semitube from 1,3-alternate bis(alkyne) **8** and cone bis(azide) **1**[8] were found suitable also for the reaction between the bis(azide) **1** and the tetrakis(alkyne) **9** taken in a 2 : 1 molar ratio (Scheme 2). Indeed, the reaction conducted in the presence of 0.3 equiv. of CuI (per bis(azide)) and triethylamine in toluene at room temperature returned the triscalixarene semitube **14** in 38% yield, which was impressively high considering the formation of four triazole heterocycles in one molecule. The remaining products of the reaction were polymeric/oligomeric compounds as determined from the ^1H NMR spectrum of the reaction mixture after removal of copper salts, in which no other sharp signals except for those from the semitube **14** were observed (Fig. 2a). Deceptively, it may seem that the reaction mixture consisted mainly of the semitube **14**, while the amount of the polymeric/oligomeric product was relatively small. But in fact, the amount of separated polymeric/oligomeric fraction which showed a very broadened ^1H NMR spectrum (Fig. 2c) was nearly equal to that of the pure calix[4]semitube **14** having a sharp NMR pattern (Fig. 2b).



Scheme 2 Syntheses of calix[4]semitubes **14–16**: (i) CuI (0.3 equiv. per bis(azide)), Et_3N, toluene, rt, 48 h; here and below, for a better distinguishability of the quite similar structures, the combination of **C** and **N** symbols in the squares denotes the arrangement of the triazole groups around the central calixarene core, where **C** (carbon) and **N** (nitrogen) mean the acetylene and azide 'parts' of the triazole ring.

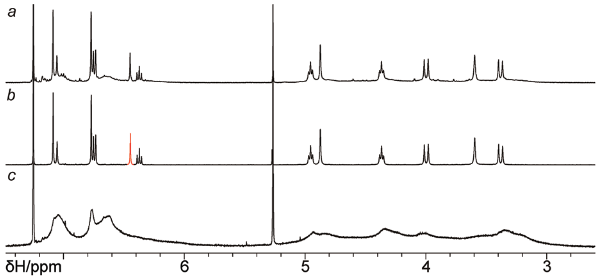


Fig. 2 Parts of the ^1H NMR spectra of (a) the mixture obtained from the reaction between calixarenes **1** and **9** after removal of copper salts, (b) pure triscalixarene semitube **14**, and (c) separated polymeric/oligomeric fraction (scaled up); 400 MHz, $CDCl_3$; the singlet from the triazole protons in the semitube is colored red.

At slow evaporation of a dichloromethane/methanol solution of calix[4]semitube **14** single crystals were collected and subjected to X-ray diffraction analysis.[15] The collected data confirm the triscalixarene molecular structure of compound **14** with the 1,3-alternate central calix[4]arene core linked to two terminal cone calix[4]arene cores by two pairs of triazole groups (Fig. 3). Due to the absence of a second pair of substituents at the narrow rims of the terminal calixarenes, the whole system seems relatively flexible, so the overall shape of the molecule, at least in the crystalline state, is far from a straight tubular one.

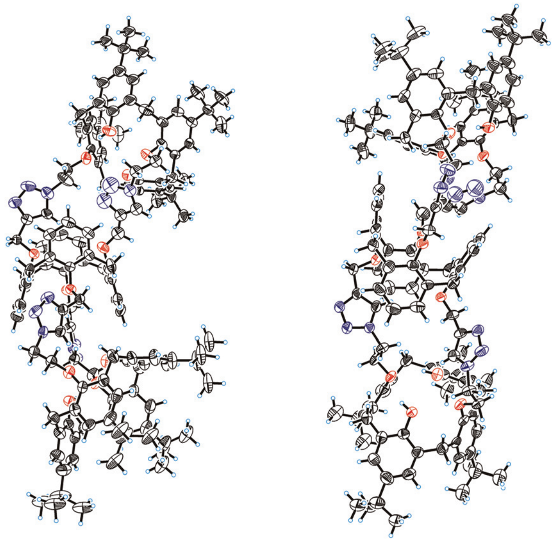
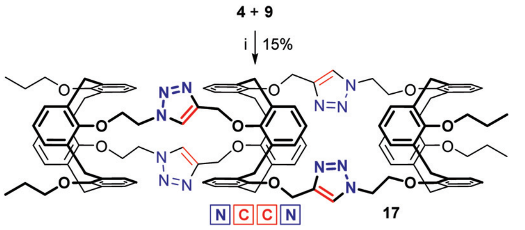


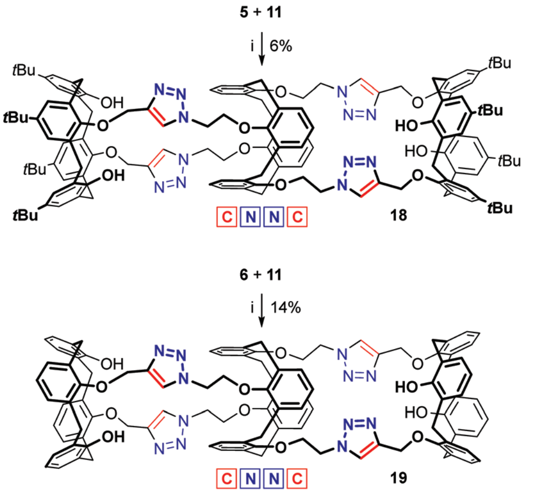
Fig. 3 Molecular structure of the calix[4]semitube **14** in two projections; thermal ellipsoids are drawn at a 50% probability level.

When de-*tert*-butylated bis(azide) **2** was involved in CuAAC with the tetrakis(alkyne) **9** under the conditions used for the preparation of calix[4]semitube **14**, the respective tris(calixarene) **15** was obtained in a good yield of 29% (Scheme 2). But in this case, a part of bis(azide) **2** returned unreacted and a non-polymeric by-product was formed. The latter one was separated and confirmed to be the bis(calixarene) **16** formed at the addition of only one molecule of bis(azide) **2** to the tetrakis(alkyne) **9**. The reasons for the incomplete conversion of the bis(azide) **2** during the reaction are not clear and may be related to its less solubility in toluene at room temperature. Still, the appearance of bis(calixarene) **16** allows one to suggest it to intermediate the stepwise formation of the triscalixarene semitube **15**.

Next, the pair of calixarenes **3** and **9** was studied for the ability to form a semitube. Following our previous observations, the CuAAC between the propylated cone bis(azide) **3** and bis(alkyne) **8** (having the same 1,3-alternate molecular shape as that of the calixarene **9** but only two of four propargyl groups) has given the respective bis(calixarene) separated from a complex mixture with other triazolated huge macrocycles composed of several **3**/**8** calixarene pairs.[8] In the case of calixarenes **3** and **9**, the direct implementation of the previously found reaction conditions (CuI (0.3 equiv. per bis(azide)), Et_3N, toluene/1,2-dichloroethane, 60 °C, 9 h) failed, as the obtained reaction mixture consisted of both starting calixarenes, a polymeric/oligomeric material, and several triazolated multimacrocycles from which the desired semitube could not be separated using column chromatography with different eluents. Several alterations of the reaction conditions were performed (see Table S1 in the ESI†), which included the changing of solvents (toluene, toluene/1,2-dichloroethane, THF, and THF/H_2O) and the catalytic system ($CuI·P(OEt)_3$, CuI, and $CuSO_4·5H_2O$/sodium ascorbate), but none of the conditions



Scheme 3 Synthesis of the calix[4]semitube **17**: (i) CuI (0.3 equiv. per bis(azide)), Et_3N, toluene, 60 °C, 24 h.



Scheme 4 Syntheses of calix[4]semitubes **18** and **19**: (i) CuI (0.3 equiv. per bis(azide)), Et_3N, toluene, 60 °C, 12 h.

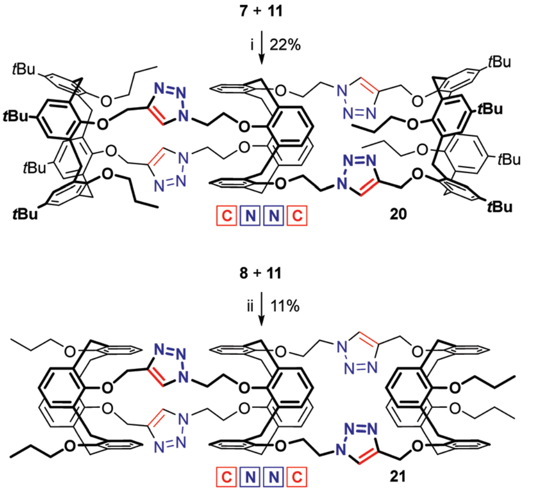
tested gave a satisfactory outcome. In the best run (CuI (0.3 equiv. per bis(azide)), Et_3N, toluene, 75 °C, 24 h) the complete conversion of the starting calixarenes was achieved and the formation of undesired multimacrocycles was suppressed, but the semitube was formed at nearly a trace level among non-separable polymeric products.

When the 1,3-alternate bis(azide) **4** was reacted with the tetrakis(alkyne) **9** (Scheme 3), additional tuning of the reaction conditions was required (see Table S2 in the ESI†). Again, the CuAAC conditions ($CuSO_4·5H_2O$/sodium ascorbate (1.0 equiv. per bis(azide)), THF/H_2O, 60 °C, 24 h), which were found perfect to assemble two 1,3-alternate calixarenes (**4** and **8**) into a biscalixarene semitube, turned non-suitable for the synthesis of the tris(calixarene) **17** from the calixarenes **4** and **9**. The best result was obtained under CuI/Et_3N-catalysis with the catalyst loading decreased back to 0.3 equiv. per bis(azide). After purification by column chromatography the calix[4]semitube **17** was obtained in 15% yield.

The difference in the CuAAC conditions suitable for the formation of bis- and triscalixarene semitubes can be rationalized in terms of the stepwise addition of the calixarenes to each other (see the example of the semitube **15**) and by the formation of an efficient copper-binding site in the intermediate bis(calixarene). This site can entrap the cation and prevent it from migration to the next pair of reacting propargyl groups at the other side of calixarene **9**, or/and prevent the reaction between the cation(s) from the bulk solution and the propargyl groups due to the Coulomb repulsion, or/and can spatially rearrange the propargyl groups in a way they turn more suitable for polymer formation rather than for the desired two-point connection to the second molecule of a bis(azide).

When used as the central core in the triscalixarene semitubes, the tetrakis(azide) **11** enables a more distant arrangement of the pairs of the reacting functional groups than the tetrakis(alkyne) **9** does. Accordingly, this can not only diminish the above repulsive interactions between the two Cu-containing bisazide/bistriazole sites, but also make the azide groups within each site less pre-organized, which can hamper the semitube formation. For the CuAAC reaction between the tetrakis(azide) **11** and bis(alkyne) **5** (Scheme 4), condition tuning (see Table S3 in the ESI†) gave the best outcome in the case when CuI/Et_3N (0.3 equiv. of Cu per bis(azide)) was used under heating. Nevertheless, the yield of the tris(calixarene) **18** was as small as 6%. Analogous synthesis involving de-*tert*-butylated bis(azide) **6** furnished the respective calix[4]semitube **19** in 14% yield. Notably, as in the case of tris(calixarene) **17**, in both the above cases the Cu-catalyst loading was decreased (from 1.0 to 0.3 equiv. per bis(azide)) with respect to the reference reaction between the bis(azide) **4** and bis(alkyne) **5**.[8]

In contrast, the CuAAC between the propylated bis(alkyne) **7** and the tetrakis(azide) **11** (Scheme 5) was successfully conducted under the conditions found previously for the reference reaction between compounds **4** and **7** (1.0 equiv. of CuI and a huge excess of Et_3N at heating),[8] and no improvement was achieved upon varying the catalyst loading (see Table S4†). The tris(calixarene) **20** was obtained in 22% yield which is the highest one among the syntheses involving the tetrakis(azide) **11**. The full-1,3-alternate calix[4]semitube **21** was obtained in 11% yield from calixarenes **8** and **11** using 1.0 equiv. of the



Scheme 5 Syntheses of calix[4]semitubes **20** and **21**: (i) CuI (1.0 equiv. per bis(azide)), Et_3N, toluene, 70 °C, 9 h; and (ii) CuI (1.0 equiv. per bis (azide)), Et_3N, toluene/1,2-dichloroethane, rt, 48 h.

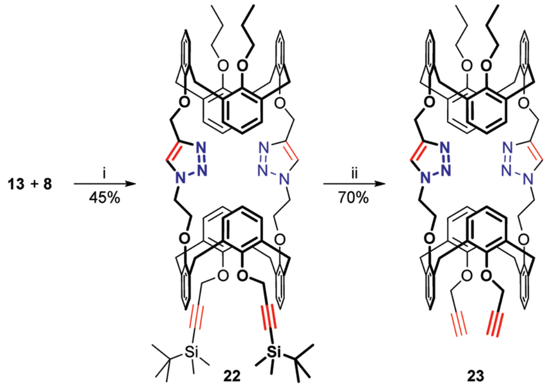
CuI/Et_3N catalyst at room temperature, which were found to be the best conditions (Table S5;† 1,2-dichloroethane was used as the co-solvent due to the lower solubility of the calixarene **8** in neat toluene).

Lower yields of the hydroxylated calix[4]semitubes **18** and **19** in comparison with those of the isomeric semitubes **14** and **15** allow us to propose that two azide groups (which are weak copper-targeted ligands) in calixarenes **1** and **2** are relatively well pre-organized by the reacting Cu-cations during CuAAC to allow their simultaneous connection to the same bisalkyne site of the tetrakis(alkyne) **9**, whereas two propargyl groups in calixarenes **5** and **6** are not held together by the reacting cation(s) near the bisazide site of the calixarene **11**, thus favoring the formation of polymeric/oligomeric products. As for the propylated terminal units of the semitubes (of either a cone or 1,3-alternate shape), the difference in the reactivities of the respective bis(azides) and bis(alkynes) with the central cores **9** or **11** is not easy to rationalize, because too many factors must be taken into account, including shielding the copper cation(s) by the propyl groups (cone isomers) or inverted calixarene aromatics (1,3-alternate isomers), repulsion between the cations bound to bistriazole sites,[9d] and their transfer between pairs of closely located azide[9e] or acetylene groups.[9a]

In general, though triazolated calix[4]semitubes can be obtained by CuAAC using the symmetrical central cores **9** and **11**, only the hydroxylated semitubes (especially the tris(calixarenes) **14** and **15** prepared in good yields) seem to have synthetic perspectives upon further chemical transformations of the OH groups. As for the semitubes constructed from the exhaustively alkylated calixarenes, further development in this direction can be seriously hampered by the need for condition tuning for each combination of the CuAAC counterparts, by the low yields in the syntheses, and by the difficulties in the separation of triazolated by-products from the targeted semitubular assemblies.

Stepwise assembling of triscalixarene semitubes

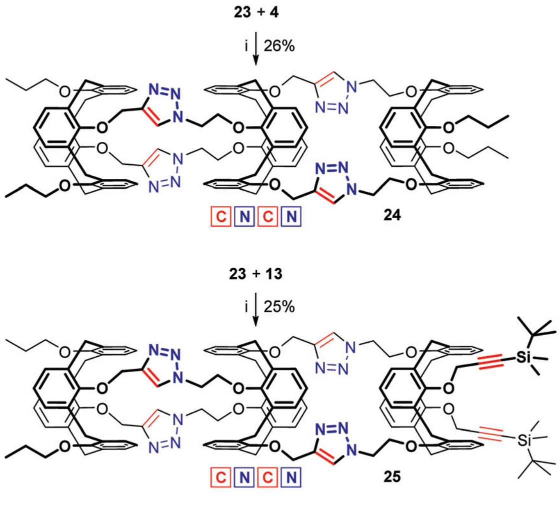
Unlike the tetrafunctional molecules **9** and **11**, the partially protected azide/alkyne-containing calixarene **13** allows a stepwise synthesis of long triazolated calix[4]semitubes when involved in CuAAC with bis(acetylenes) followed by de-protection and further reaction with bis(azides). The obvious advantage of this approach is that two but not four triazole heterocycles are formed during each of the CuAAC steps, which shrinks the range of triazolated by-products and thus improves the yield of the targeted semi-tubular bis(calixarenes). On the other hand, the stepwise syntheses using the calixarene **13** cannot replace the one-step preparation of the C_{2v}-symmetrical calix[4]semitubes **14**, **15**, and **17**–**21**, as only the C_s-symmetrical calix[4]semitubes can be obtained by the stepwise approach.



Scheme 6 Syntheses of calix[4]semitubes **22** and **23**: (i) $CuSO_4 \cdot 5H_2O$ (1.0 equiv. per bis(azide)/bis(alkyne)), sodium ascorbate, THF/H_2O (5 : 1), 60 °C, 24 h; (ii) *n*$Bu_4NF \cdot 3H_2O$, THF/H_2O (100 : 1), 50 °C, 12 h.

The CuAAC between calixarenes **13** and **8** (Scheme 6) was conducted using a copper(II) sulphate/sodium ascorbate catalytic system following the conditions previously found for assembling calixarenes **4** and **8** into a biscalixarene semitube,[8] which were inefficient for the preparation of the tris(calixarenes) **17** and **21** (see above). The yield of the silylated bis(calixarene) **22** reached 45%, so no further tuning of the reaction conditions was required in this case. *tert*-Butyldimethylsilyl protecting groups were removed by treating the compound **22** with tetrabutylammonium fluoride in aqueous THF, and the calix[4]semitube **23** bearing two terminal acetylene groups ready for further CuAAC was obtained.

With no additional tuning of the reaction conditions, the bis(calixarene) **23** was reacted with the bis(azide) **4** for obtaining the triscalixarene semitube **24** in 26% yield (Scheme 7). This compound is the isomer of both the calix[4]semitubes **17** and **21** but has lower symmetry as the two pairs of triazole linkers have different orientations with respect to the central calixarene core. The difference in the molecular symmetry immediately affects the patterns in the NMR spectra of the semitubes, thus allowing clear distinction of these three structures (Fig. 4). In particular, the ^1H NMR spectrum of the less symmetrical calix[4]semitube **24** contains two signals from the



Scheme 7 Syntheses of calix[4]semitubes **24** and **25**: (i) $CuSO_4 \cdot 5H_2O$ (1.0 equiv. per bis(azide)/bis(alkyne)), sodium ascorbate, THF/H_2O (5 : 1), 60 °C, 24 h.

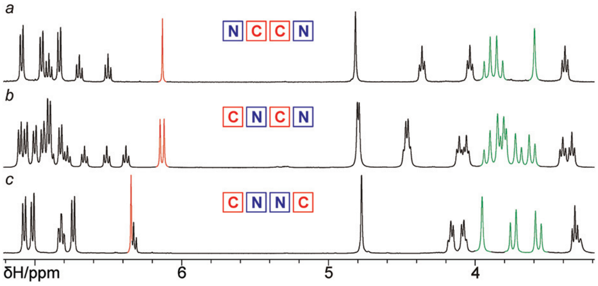


Fig. 4 Parts of the ^{1}H NMR spectra of (a) the calix[4]semitube **17**, (b) calix[4]semitube **24**, and (c) calix[4]semitube **21**; 400 MHz, $CDCl_3$; the signals from the triazole protons are colored red and those from the methylene groups of the calixarene cores are colored green.

triazole protons and three sets of signals from the methylene bridges of three different calixarene cores (Fig. 4b), while for the semitubes **17** (Fig. 4a) and **21** (Fig. 4c) single resonance from the triazole protons and only two sets of signals from the methylene bridges appear in each case.

Similar to the synthesis of the calix[4]semitube **24**, the propargylated bis(calixarene) **23** was reacted with the bis(azide) **13**, which was the synthetic precursor of the bis(calixarene) **23** (Scheme 7). As a result, the triscalixarene semitube **25** having protected acetylene units in the structure was obtained in 25% yield. This allows us to expect that further growth of the tubular architectures will be possible by step-by-step attachment of the bis(azide) **13** to the propargylated semitubes using alternating de-silylation and CuAAC procedures. It seems that the stepwise approach enables more possibilities for the preparation of the long triazolated calix[4]semitubes including those having additional functional groups in the terminal calixarene units, which can be achieved by replacing the propyl groups with the functional ones in the bis(alkyne) **8** or/and in the bis(azide) **4**.

The prepared triscalixarene semitubes of different types seem to be able to form complexes with transition metal cations, which follows from our previous studies on the receptor properties of triazolated calix[4]arenes[9d] as well as from the preliminary data on the complexation ability of the related biscalixarene semitubes towards silver and zinc cations.[8] Still, taking into account the homo/heteroditopic nature of the triscalixarene semitubes and possible inter/intramolecular migrations of the bound cations between the triazole-containing binding sites, the evaluation of their receptor abilities requires the introduction of additional reporter (*e.g.* fluorescent) or other functional/receptor units to the molecules, which can be achieved using the synthetic approaches developed in this work.

Conclusions

We have shown that long triazolated calix[4]semitubes having three calixarene units in the structures can be assembled by using bifunctional and tetrafunctional calixarene azides and alkynes under CuAAC conditions. The four-fold CuAACs between the bifunctional terminal units of the cone or 1,3-alternate shape and the tetrafunctional 1,3-alternate central core have been shown to have limited applicability as condition tuning is required for each of the calixarene combinations, while the separated yields of the targeted assemblies have been modest in most cases. As an alternative, the two-step syntheses of the triscalixarene semitubes, which involved the calix[4]arene bearing two azide groups and two silylated acetylene groups as the key synthone, have been shown to be successfully conducted under similar conditions at each of the two-fold CuAAC steps and have allowed the preparation of the semitubes with different substituents in the terminal units or/and further growth of the semi-tubular assemblies.

It is believed that the obtained results will find application in the development of multitopic tubular hosts having different mutual orientations of the bistriazole cation-binding sites within the molecule, which in turn will allow the creation of stimuli-switchable and other sophisticated supramolecules operating by intramolecular oscillations of a bound cation between the binding sites.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1 (*a*) *Calixarenes 2001*, ed. Z. Asfari, V. Böhmer, J. Harrowfield and J. Vicens, Kluwer Academic, Dordrecht, 2001; (*b*) V. Böhmer, *The Chemistry of Phenols*, ed. Z. Rappoport, John Wiley & Sons, Ltd, Chichester, 2003, pp. 1369–1454; (*c*) *Calixarenes in the Nanoworld*, ed. J. Vicens, J. Harrowfield and L. Baklouti, Springer, Dordrecht, 2007; (*d*) *Calixarenes and Beyond*, ed. P. Neri, J. L. Sessler and M.-X. Wang, Springer International Publishing, 2016.

2 For selected examples of 'classic' biscalixarene receptor molecules joined by at least two linkers, see: (*a*) S. Ullmann, M. Börner, A. Kahnt, B. Abel and B. Kersting, Green-emissive Zn^{2+} complex supported by a macrocyclic Schiff-base/calix[4]arene-ligand: crystallographic and spectroscopic characterization, *Eur. J. Inorg. Chem.*, 2021, 3691–3698; (*b*) M. Gaeta, E. Rodolico, M. E. Fragalà, A. Pappalardo, I. Pisagatti, G. Gattuso, A. Notti, M. F. Parisi, R. Purrello and A. D'Urso, Self-assembly of discrete porphyrin/calix[4]tube complexes promoted by potassium ion encapsulation, *Molecules*, 2021, **26**, 704;

(*c*) S. Ullmann, P. Hahn, P. Mini, K. L. Tuck, A. Kahnt, B. Abel, M. E. G. Suburu, C. A. Strassert and B. Kersting, Mixed-ligand lanthanide complexes supported by ditopic bis(imino-methyl)-phenol/calix[4]arene macrocycles: synthesis, structures, and luminescence properties of $[Ln_2(L_2)(MeOH)_2]$ (Ln = La, Eu, Tb, Yb), *Dalton Trans.*, 2020, **49**, 11179–11191; (*d*) K. Puchnin, M. Andrianova, A. Kuznetsov and V. Kovalev, Field-effect transition sensor for KI detection based on self-assembled calixtube monolayers, *Biosens. Bioelectron.*, 2017, **98**, 140–146; (*e*) S. Moerkerke, V. Malytskyi, L. Marcélis, J. Wouters and I. Jabin, Selective recognition of quaternary ammonium ions and zwitterions by using a biomimetic bis-calix[6]arene-based receptor, *Org. Biomol. Chem.*, 2017, **15**, 8967–8974; (*f*) S. Moerkerke, J. Wouters and I. Jabin, Selective recognition of phosphatidylcholine lipids by a biomimetic calix[6]tube receptor, *J. Org. Chem.*, 2015, **80**, 8720–8726; (*g*) K. Puchnin, D. Cheshkov, P. Zaikin, I. Vatsouro and V. Kovalev, Tuning conformations of calix[4]tubes by weak intramolecular interactions, *New J. Chem.*, 2013, **37**, 416–424; (*h*) K. Puchnin, P. Zaikin, D. Cheshkov, I. Vatsouro and V. Kovalev, Calix[4]tubes: an approach to functionalization, *Chem. – Eur. J.*, 2012, **18**, 10954–10968; (*i*) C.-C. Tsai, I.-T. Ho, J.-H. Chu, L.-C. Shen, S.-L. Huang and W.-S. Chung, Synthesis of 9,10-bis-ketoenaminoanthryl and 9,10-bis-isoxazolylanthryl linked biscalix[4]arenes: atropisomers and molecular recognitions, *J. Org. Chem.*, 2012, **77**, 2254–2262; (*j*) S.-Z. Li, J. Shi, K. Yang and J. Luo, Chemical resolution and chiral recognition of an inherently chiral biscalix[4]arene cone–partial cone conformer, *Tetrahedron*, 2012, **68**, 8557–8563; (*k*) H. Iwamoto, K. Niimi, T. Haino and Y. Fukazawa, Energetics of guest binding to calix[4]arene molecular containers, *Tetrahedron*, 2009, **65**, 7259–7267; (*l*) J. Morales-Sanfrutos, M. Ortega-Muñoz, J. Lopez-Jaramillo, F. Hernandez-Mateo and F. Santoyo-Gonzalez, Synthesis of calixarene-based cavitands and nanotubes by click chemistry, *J. Org. Chem.*, 2008, **73**, 7768–7771; (*m*) G. V. Zyryanov and D. M. Rudkevich, Toward synthetic tubes for NO_2/N_2O_4: design, synthesis, and host-guest chemistry, *J. Am. Chem. Soc.*, 2004, **126**, 4264–4270; (*n*) S. E. Matthews, P. Schmitt, V. Felix, M. G. B. Drew and P. D. Beer, Calix[4]tubes: a new class of potassium-selective ionophore, *J. Am. Chem. Soc.*, 2002, **124**, 1341–1353; (*o*) P. Schmitt, P. D. Beer, M. G. B. Drew and P. D. Sheen, Calix[4]tube: a tubular receptor with remarkable potassium ion selectivity, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 1840–1842.

3 For selected examples of bis(thiacalixarenes) joined by at least two linkers, see: (*a*) A. A. Muravev, E. A. Trushina, A. T. Yakupov, S. E. Solovieva and I. S. Antipin, Ag-selective nanotubes based on bisthiacalix[4]arene with ethylene sulfide bridges, *Dokl. Chem.*, 2019, **487**, 212–214; (*b*) F. Yang, F. Yin, H. Guo, Z. Huang and X. Zhang, Syntheses and cations complexation properties of novel thiacalix[4]-1,3-aza-crown and bisthiacalix[4]-1,3-aza-crown, *J. Inclusion Phenom. Macrocyclic Chem.*, 2010, **67**, 49–54; (*c*) V. Bhalla, J. N. Babu, M. Kumar, T. Hattori and S. Miyano, Synthesis and binding studies of novel thiacalixpodands and bisthiacalixarenes having O,O″-dialkylated thiacalix[4]arene unit(s) of 1,3-alternate conformation, *Tetrahedron Lett.*, 2007, **48**, 1581–1585; (*d*) C. Pérez-Casas and T. Yamato, 1,3-Alternate-thiacalix[4]arene-based dimer: synthesis and inclusion behavior, *Chem. Eng. Commun.*, 2006, **193**, 1185–1193; (*e*) V. Bhalla, M. Kumar, H. Katagiri, T. Hattori and S. Miyano, Synthesis and binding studies of novel bisthiacalix[4]arenes with diimime linkages, *Tetrahedron Lett.*, 2005, **46**, 121–124; (*f*) V. Csokai, B. Balázs, G. Tóth, G. Horváth and I. Bitter, Unprecedented cyclisations of calix[4]arenes under the Mitsunobu protocol. Part 3: Thiacalix[4]crowns versus dimers, *Tetrahedron*, 2004, **60**, 12059–12066; (*g*) V. Csokai, A. Grün and I. Bitter, Unprecedented cyclisations of calix[4]arenes with glycols under the Mitsunobu protocol. Part 1: A new perspective for the synthesis of calixcrowns, *Tetrahedron Lett.*, 2003, **44**, 4681–4684; (*h*) S. E. Matthews, V. Felix, M. G. B. Drew and P. D. Beer, Thiacalix[4]tube: synthesis, X-ray crystal structure and preliminary binding studies, *New J. Chem.*, 2001, **25**, 1355–1358.

4 For selected examples of bis(calixpyrroles) joined by at least two linkers, see: (*a*) R. Molina-Muriel, J. R. Romero, Y. Li, G. Aragay and P. Ballester, The effect of solvent on the binding of anions and ion-pairs with a neutral [2]rotaxane, *Org. Biomol. Chem.*, 2021, **19**, 9986–9995; (*b*) S. Xiong, F. Chen, T. Zhao, A. Li, G. Xu, J. L. Sessler and Q. He, Selective inclusion of fluoride within the cavity of a two-wall bis-calix[4]pyrrole, *Org. Lett.*, 2020, **22**, 4451–4455; (*c*) R. Molina-Muriel, G. Aragay, E. C. Escudero-Adán and P. Ballester, Switching from negative-cooperativity to no-cooperativity in the binding of ion-pair dimers by a bis(calix[4]pyrrole) macrocycle, *J. Org. Chem.*, 2018, **83**, 13507–13514; (*d*) J. R. Romero, G. Aragay and P. Ballester, Ion-pair recognition by a neutral [2]rotaxane based on a bis-calix[4]pyrrole cyclic component, *Chem. Sci.*, 2017, **8**, 491–498; (*e*) A. Galán, E. C. Escudero-Adán and P. Ballester, Template-directed self-assembly of dynamic covalent capsules with polar interiors, *Chem. Sci.*, 2017, **8**, 7746–7750; (*f*) W. Wu, Z. Tian, S. Wang, C. Peng, H. Liu, S. Dai and D.-e. Jiang, Design of calix-based cages for CO_2 capture, *Ind. Eng. Chem. Res.*, 2017, **56**, 4502–4507; (*g*) Q. He, M. Kelliher, S. Bähring, V. M. Lynch and J. L. Sessler, A bis-calix[4]pyrrole enzyme mimic that constrains two oxoanions in close proximity, *J. Am. Chem. Soc.*, 2017, **139**, 7140–7143; (*h*) I. Saha, J. H. Lee, H. Hwang, T. S. Kim and C.-H. Lee, Remarkably selective, non-linear allosteric regulation of anion binding by a tetracationic calix[4]pyrrole homodimer, *Chem. Commun.*, 2015, **51**, 5679–5682; (*i*) V. Valderrey, E. C. Escudero-Adán and P. Ballester, Highly cooperative binding of ion-pair dimers and ion quartets by a bis(calix[4]pyrrole) macrotricyclic receptor, *Angew. Chem., Int. Ed.*, 2013, **52**, 6898–6902; (*j*) V. Valderrey, E. C. Escudero-Adán and P. Ballester, Polyatomic anion assistance in the assembly

of [2]pseudorotaxanes, *J. Am. Chem. Soc.*, 2012, **134**, 10733–10736.

5 For selected examples of bis(calixresorcinarenes), see: (*a*) W. Wang, K. Su, E.-S. M. El-Sayed, M. Yang and D. Yuan, Solvatomorphism influence of porous organic cage on C_2H_2/CO_2 separation, *ACS Appl. Mater. Interfaces*, 2021, **13**, 24042–24050; (*b*) Q. Xiao, W.-W. Haoyang, T. Lin, Z.-T. Li, D.-W. Zhang and J.-L. Hou, Unimolecular artificial transmembrane channels showing reversible ligand-gating behavior, *Chem. Commun.*, 2021, **57**, 863–866; (*c*) D. Danielsiek and G. Dyker, An adaptive resorcinarene hemicarcerand, *Eur. J. Org. Chem.*, 2021, 1026–1034; (*d*) K. Harada, R. Sekiya and T. Haino, Folding and unfolding of acetoxy group-terminated alkyl chains inside a size-regulable hemicarcerand, *J. Org. Chem.*, 2021, **86**, 4440–4447; (*e*) K. Tamaki, A. Ishigami, Y. Tanaka, M. Yamanaka and K. Kobayashi, Self-assembled boronic ester cavitand capsules with various bis(catechol) linkers: cavity-expanded and chiral capsules, *Chem. – Eur. J.*, 2015, **21**, 13714–13722; (*f*) M. Vazdar, A. S. Mitchell, R. N. Warrener and D. Margetić, High pressure promoted exchange of guests from hemicarceplexes, *Tetrahedron*, 2015, **71**, 550–553; (*g*) S. Bringmann, R. Brodbeck, R. Hartmann, C. Schäfer and J. Mattay, Anthracene-resorcin[4]arene-based capsules: synthesis and photoswitchable features, *Org. Biomol. Chem.*, 2011, **9**, 7491–7499; (*h*) N. K. Beyeh, A. Valkonen and K. Rissanen, Piperazine bridged resorcinarene cages, *Org. Lett.*, 2010, **12**, 1392–1395.

6 For selected examples of hybrid multimacrocycles from the calixarene family, see: (*a*) S. K. Kim, V. M. Lynch, B. P. Hay, J. S. Kim and J. L. Sessler, Ion pair-induced conformational motion in calix[4]arene-strapped calix[4]pyrroles, *Chem. Sci.*, 2015, **6**, 1404–1413; (*b*) B. Sadhu, M. Sundararajan, G. Velmurugan and P. Venuvanalingam, Elucidating the structures and cooperative binding mechanism of cesium salts to the multitopic ion-pair receptor through density functional theory calculations, *Dalton Trans.*, 2015, **44**, 15450–15462; (*c*) S. K. Kim, V. M. Lynch and J. L. Sessler, Cone calix[4]arene diethyl ester strapped calix[4]pyrrole: a selective receptor for the fluoride anion, *Org. Lett.*, 2014, **16**, 6128–6131; (*d*) S. K. Kim, V. M. Lynch, N. J. Young, B. P. Hay, C.-H. Lee, J. S. Kim, B. A. Moyer and J. L. Sessler, KF and CsF recognition and extraction by a calix[4]crown-5 strapped calix[4]pyrrole multitopic receptor, *J. Am. Chem. Soc.*, 2012, **134**, 20837–20843; (*e*) P. Thiampanya, N. Muangsin and B. Pulpoka, Azocalix[4]arene strapped calix[4]pyrrole: a confirmable fluoride sensor, *Org. Lett.*, 2012, **14**, 4050–4053; (*f*) I.-W. Park, S.-K. Kim, M.-J. Lee, V. M. Lynch, J. L. Sessler and C.-H. Lee, Calix[4]pyrrole–calix[4]arene–crown-5 conjugate with flexible linkers as a model for a selective ion-pair container, *Chem. – Asian J.*, 2011, **6**, 2911–2915; (*g*) S. K. Kim, J. L. Sessler, D. E. Gross, C.-H. Lee, J. S. Kim, V. M. Lynch, L. H. Delmau and B. P. Hay, A calix[4]arene strapped calix[4]pyrrole: an ion-pair receptor displaying three different cesium cation recognition modes, *J. Am. Chem. Soc.*, 2010, **132**, 5827–5836; (*h*) M. H. Patel and P. S. Shrivastav, Casting heteracalixarenes from calixarene templates: a unique synthetic strategy, *Chem. Commun.*, 2009, 586–588; (*i*) J. L. Sessler, S. K. Kim, D. E. Gross, C.-H. Lee, J. S. Kim and V. M. Lynch, Crown-6-calix[4]arene-capped calix[4]pyrrole: an ion-pair receptor for solvent-separated CsF ions, *J. Am. Chem. Soc.*, 2008, **130**, 13162–13166; (*j*) F. Yang, X. Zhao, H. Guo, J. Lin and Z. Liu, Syntheses and extraction properties of novel biscalixarene and thiacalix[4]arene hydrazone derivatives, *J. Inclusion Phenom. Macrocyclic Chem.*, 2008, **61**, 139–145; (*k*) E. Khomich, M. Kashapov, I. Vatsouro, E. Shokova and V. Kovalev, Substituent control of potassium and rubidium uptake by asymmetric calix[4]-thiacalix[4]tubes, *Org. Biomol. Chem.*, 2006, **4**, 1555–1560.

7 (*a*) V. G. Organo, V. Sgarlata, F. Firouzbakht and D. M. Rudkevich, Long synthetic nanotubes from calix[4]arenes, *Chem. – Eur. J.*, 2007, **13**, 4014–4023; (*b*) V. G. Organo and D. M. Rudkevich, Emerging host–guest chemistry of synthetic nanotubes, *Chem. Commun.*, 2007, 3891–3899; (*c*) E. Wanigasekara, A. V. Leontiev, V. G. Organo and D. M. Rudkevich, Supramolecular, calixarene-based complexes that release NO gas, *Eur. J. Org. Chem.*, 2007, 2254–2256; (*d*) V. G. Organo, A. V. Leontiev, V. Sgarlata, H. V. R. Dias and D. M. Rudkevich, Supramolecular features of calixarene-based synthetic nanotubes, *Angew. Chem., Int. Ed.*, 2005, **44**, 3043–3047; (*e*) V. Sgarlata, V. G. Organo and D. M. Rudkevich, A procedure for filling calixarene nanotubes, *Chem. Commun.*, 2005, 5630–5632; (*f*) S. K. Kim, J. Vicens, K.-M. Park, S. S. Lee and J. S. Kim, Complexation chemistry. Double- and multi-1,3-alternate-calixcrowns, *Tetrahedron Lett.*, 2003, **44**, 993–997; (*g*) S. K. Kim, J. K. Lee, S. H. Lee, M. S. Lim, S. W. Lee, W. Sim and J. S. Kim, Silver ion shuttling in the trimer-mimic thiacalix[4]crown tube, *J. Org. Chem.*, 2004, **69**, 2877–2880; (*h*) A. Ikeda and S. Shinkai, Multiple connection of 1,3-alternate-calix[4]arenes. An approach to synthetic 'Nano-tubes', *J. Chem. Soc., Chem. Commun.*, 1994, 2375–2376.

8 A. Gorbunov, N. Ozerov, M. Malakhova, A. Eshtukov, D. Cheshkov, S. Bezzubov, V. Kovalev and I. Vatsouro, Assembling triazolated calix[4]semitubes by means of copper(I)-catalyzed azide–alkyne cycloaddition, *Org. Chem. Front.*, 2021, **8**, 3853–3866.

9 For our studies on the features and applications of CuAAC in calixarene chemistry, see: (*a*) A. Gorbunov, D. Cheshkov, V. Kovalev and I. Vatsouro, Copper(I)-catalyzed cycloaddition of azides to multiple alkynes: a selectivity study using a calixarene framework, *Chem. – Eur. J.*, 2015, **21**, 9528–9534; (*b*) A. Gorbunov, N. Sokolova, E. Kudryashova, V. Nenajdenko, V. Kovalev and I. Vatsouro, Chiral heteroditopic baskets designed from triazolated calixarenes and short peptides, *Chem. – Eur. J.*, 2016, **22**, 12415–12423; (*c*) B. Bolshchikov, S. Volkov, D. Sokolova, A. Gorbunov, A. Serebryannikova, I. Gloriozov, D. Cheshkov, S. Bezzubov, W.-S. Chung, V. Kovalev and I. Vatsouro, Constructing bridged multifunctional calixarenes by intramolecular

indole coupling, *Org. Chem. Front.*, 2019, **6**, 3327–3341; (*d*) A. Gorbunov, J. Kuznetsova, K. Puchnin, V. Kovalev and I. Vatsouro, Triazolated calix[4]arenes from 2-azidoethylated precursors: is there a difference in the way the triazoles are attached to narrow rims?, *New J. Chem.*, 2019, **43**, 4562–4580; (*e*) A. Gorbunov, J. Kuznetsova, I. Deltsov, A. Molokanova, D. Cheshkov, S. Bezzubov, V. Kovalev and I. Vatsouro, Selective azide–alkyne cycloaddition reactions of azidoalkylated calixarenes, *Org. Chem. Front.*, 2020, **7**, 2432–2441; (*f*) A. Gorbunov, A. Iskandarova, K. Puchnin, V. Nenajdenko, V. Kovalev and I. Vatsouro, A route to virtually unlimited functionalization of water-soluble *p*-sulfonatocalix[4]arenes, *Chem. Commun.*, 2020, **56**, 4122–4125; (*g*) S. Bezzubov, K. Ermolov, A. Gorbunov, P. Kalle, I. Lentin, G. Latyshev, V. Kovalev and I. Vatsouro, Inherently dinuclear iridium(III) meso architectures accessed by cyclometalation of calix[4]arene-based bis(aryltriazoles), *Dalton Trans.*, 2021, **50**, 16765–16769.

10 Z.-G. Luo, Y. Zhao, F. Xu, C. Ma, X.-M. Xu and X.-M. Zhang, Synthesis and thermal properties of novel calix[4]arene derivatives containing 1,2,3-triazole moiety *via*, K_2CO_3-catalyzed 1,3-dipolar cycloaddition reaction, *Chin. Chem. Lett.*, 2014, **25**, 1346–1348.

11 Z. Asfari, A. Bilyk, C. Bond, J. M. Harrowfield, G. A. Koutsantonis, N. Lengkeek, M. Mocerino, B. W. Skelton, A. N. Sobolev, S. Strano, J. Vicens and A. H. White, Factors influencing solvent adduct formation by calixarenes in the solid state, *Org. Biomol. Chem.*, 2004, **2**, 387–396.

12 W. Xu, J. J. Vittal and R. J. Puddephatt, Propargyl calix[4]arenes and their complexes with silver(I) and gold(I), *Can. J. Chem.*, 1996, **74**, 766–774.

13 S. Cecioni, R. Lalor, B. Blanchard, J.-P. Praly, A. Imberty, S. E. Matthews and S. Vidal, Achieving high affinity towards a bacterial lectin through multivalent topological isomers of calix[4]arene glycoconjugates, *Chem. – Eur. J.*, 2009, **15**, 13232–13240.

14 V. A. Burilov, N. A. Epifanova, E. V. Popova, S. F. Vasilevsky, S. E. Solovieva, I. S. Antipin and A. I. Konovalov, Regioselective synthesis of 1,2,3-triazolyl derivatives of calix[4]arenes based on 1,3-dipolar cycloaddition, *Russ. Chem. Bull.*, 2013, **62**, 767–772.

15 The CIF file has been deposited with the Cambridge Crystallographic Data Centre: CCDC 2157422.† Details of X-ray diffraction measurements are provided in the ESI.†