

SNAPSHOTS OF SOME TOPICS OF INTEREST OF RECENT NOTABLE
ADVANCES IN CHEMISTRY

*New Trends in Resorcin[4]arenes
Preparation*

Stereoselective (Per)fluoroalkylation of Ketones

Tetrahedral Tetra-Cationic Ionic Liquids

Transparent Ultraviolet-Shielding Polymer Films Using Copper Nanoclusters

Table of contents

- 3 Snapshots of some topics of interest of recent notable advances in chemistry:
- 4 Stereoselective (Per)fluoroalkylation of Ketones
- 6 Tetrahedral tetra-cationic ionic liquids
- 8 New trends in resorcin[4]arenes preparation
- 12 Transparent ultraviolet-shielding polymer films using copper nanoclusters

Snapshots of some topics of interest of recent notable advances in chemistry

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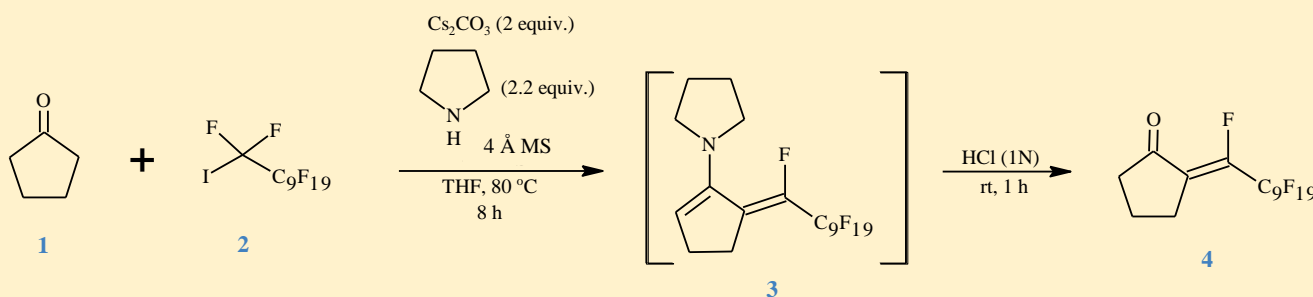
Managing Director / Founder

Stereoselective (Per)fluoroalkylation of Ketones

A facile and transition-metal-free method for the stereoselective synthesis of fluoroalkylated β -fluoroenones from ketones is highlighted. The route features broad substrate diversity with excellent stereoselectivity, and can be further transformed to bioactive molecules.

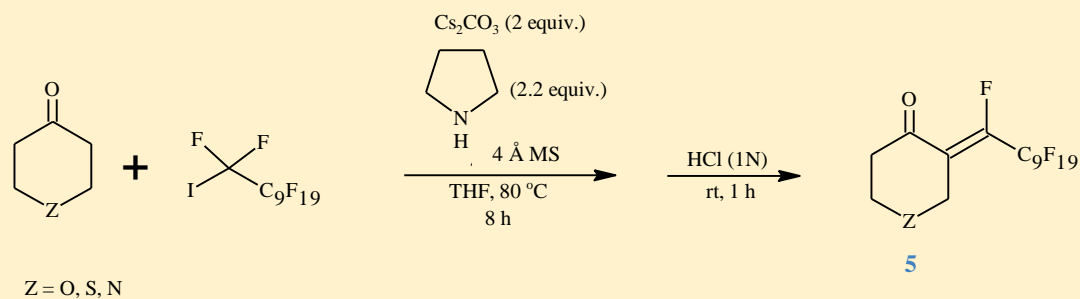
Many of the privileged bioactive molecules possess fluorine atoms. Fluoroalkyl compounds are beneficial because of the versatility of their properties in terms of lipophilicity, metabolic stability, conformation, chemical reactivity etc. More recently, Beller reported the synthesis of stereoselective of β -perfluoroalkylated β -fluoroenones from the reaction of ketones with perfluoroalkyl halides.

The synthesis of β -perfluoroalkylated β -fluoroenones **4** started with cyclopentanone **1** with perfluorodecyl iodide **2** in the presence of Cs_2CO_3 , 4 Å molecular sieves in THF at 80 °C furnishing multi-substituted intermediate **3**, which can be further hydrolyzed to the desired product **4** in moderate to good yields with excellent stereoselectivity (Scheme 1).



Scheme 1. Pyridine-promoted synthesis of β -perfluoroalkylated β -fluoroenones.

Five and six-membered ketones with different substituents and functional groups were compatible with the reaction conditions to yield **5** in moderate to high yields (Scheme 2).



Scheme 2. (Per)fluoroalkenylation of ketones.

Furthermore, the procedure provides easy access to fluorinated and fluoroalkylated bioactive compounds.

Review

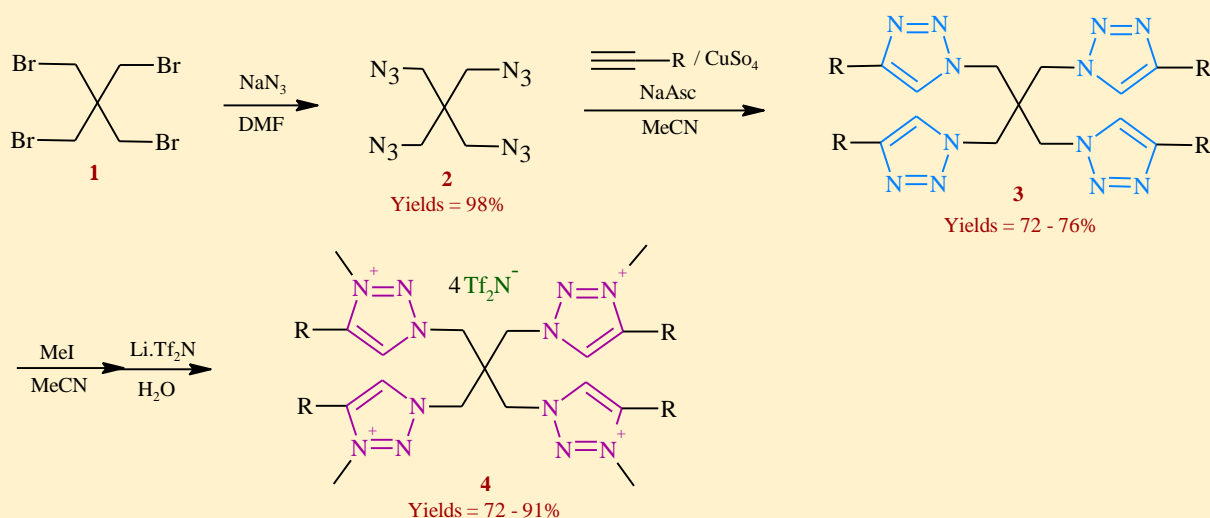
F. Ye, S. Zhang, Z. Wei, F. Weniger, A. Spannenberg, C. Taeschler, S. Ellinger, H. Jiao, H. Neumann, M. Beller, *Eur. J. Org. Chem.*, **2020**, 70–81.

Tetrahedral Tetra-Cationic Ionic Liquids

Tetra-cationic compounds with tetrahedral geometry were installed by introducing four cationic units on a quaternary carbon through $-\text{CH}_2$ -spacer. Cu(I)-catalyzed azide-alkyne cycloaddition reaction followed by quaternization of the triazole unit enabled the synthesis of this compound to overcome the steric crowding around the core.

Ionic liquids are salts in the liquid state around room temperature. They have many potential applications including electrolytes, gas absorbents, solvents, or catalysts. The multi-cation ionic liquids reported thus far were based on linear coupling of the four cationic units. They have some drawbacks such as high viscosity due to higher molecular mass, which, in turn, leads to lower ionic conductivity – a parameter that is crucial for electrolytes. Very recently, Ikeda and Matsushita reported the synthesis of the new tetrahedral tetra-cations containing aromatic heterocycles that feature lower melting point than their aliphatic counterparts due to delocalization of the positive charge.

The tetra-cations were synthesized from pentaerythrityl tetrabromide **1** and 1,2,3-triazolium units through copper-catalyzed cycloaddition of azides to alkynes, which the outstanding feature of the catalytic activity of the copper in producing 1,2,3-triazoles is the fact that many functional groups can be tolerated (Scheme). Then purification of tetra-triazoles **3** followed by quaternization with iodomethane afforded the desired product **4** in high yields.



Scheme . Synthesis of tetrahedral tetra-cation. **Caution:** pentaerythrityl tetra-azide **2** is explosive, thus, it must be handled carefully; used up immediately without storing and mass production must be avoided.

The tetra-cations with ethylene glycol tail were liquids at room temperature, except for **I**. Their ionic conductivities were in the order of 10^{-6} Scm^{-1} at 25 °C, which were relatively low. Low ionic conductivity is related to high viscosity where four positive charges arranged in the proximity of the rigid core are considered to create strong electrostatic field, that leads to high viscosity, and to restrain, in addition, the generation of mobile counter ion contributing to ion conduction.

It was concluded that sterically crowded structure around the pentaerythritol core affects the physical properties of the tetrahedral tetra-cationic ionic liquids, e.g. thermal decomposition property and ionic conductivity.

Review

T. Ikeda, Y. Matsushita, *Chem. Lett.*, **2020**, *49*, 14–16.

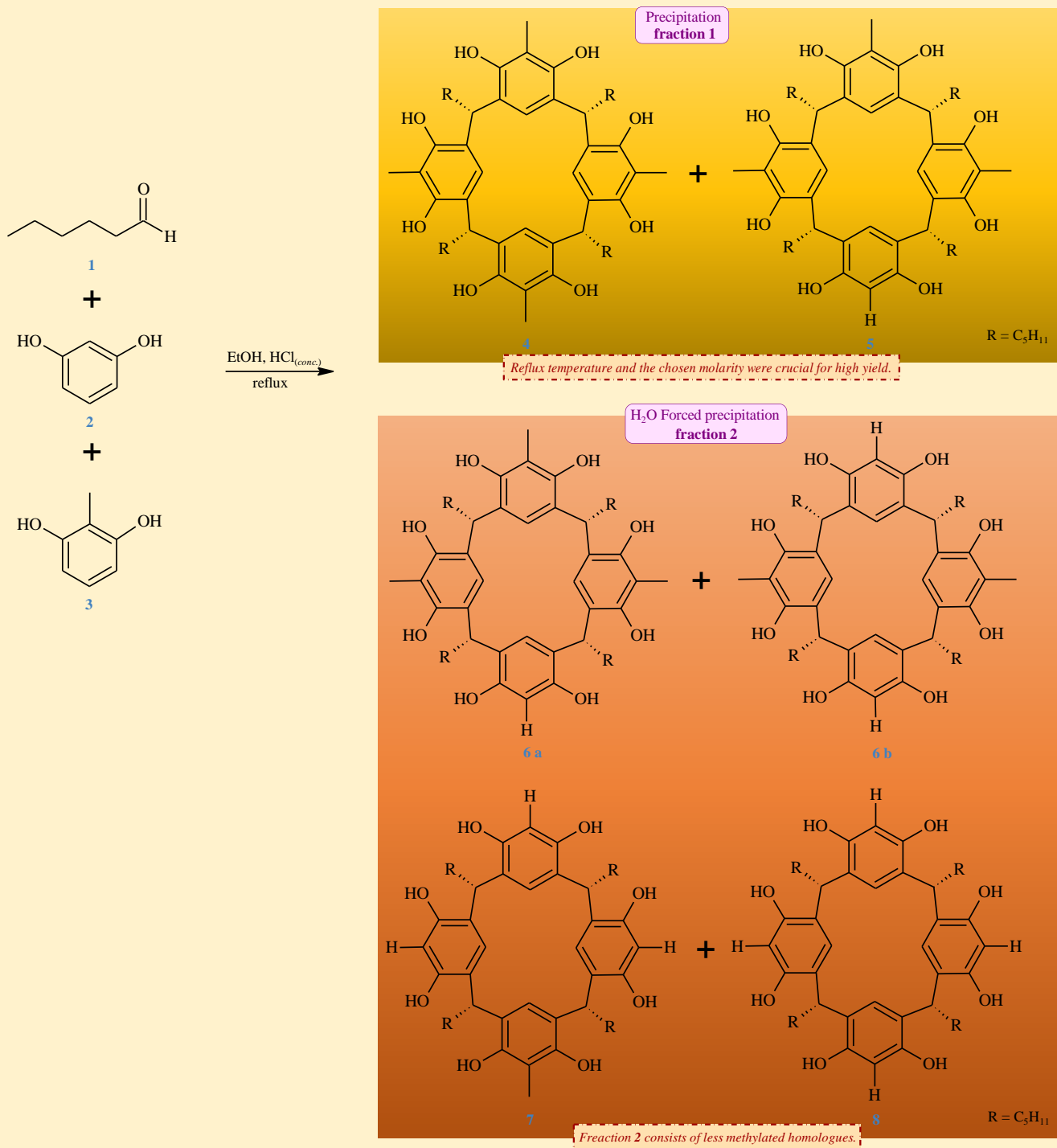
New Trends in Resorcin[4]arenes Preparation

A facile synthesis of mono- and tris-functionalized resorcin[4]arenes is highlighted. Two preparative steps leads to the formation of trimethylresorcin[4]arene. Subsequent functionalization through radicalic bromination affords trisbromomethyl compound, while polar bromination and iodation via mono-lithiated species furnishes the aryl bromide and iodide compounds in excellent yields.

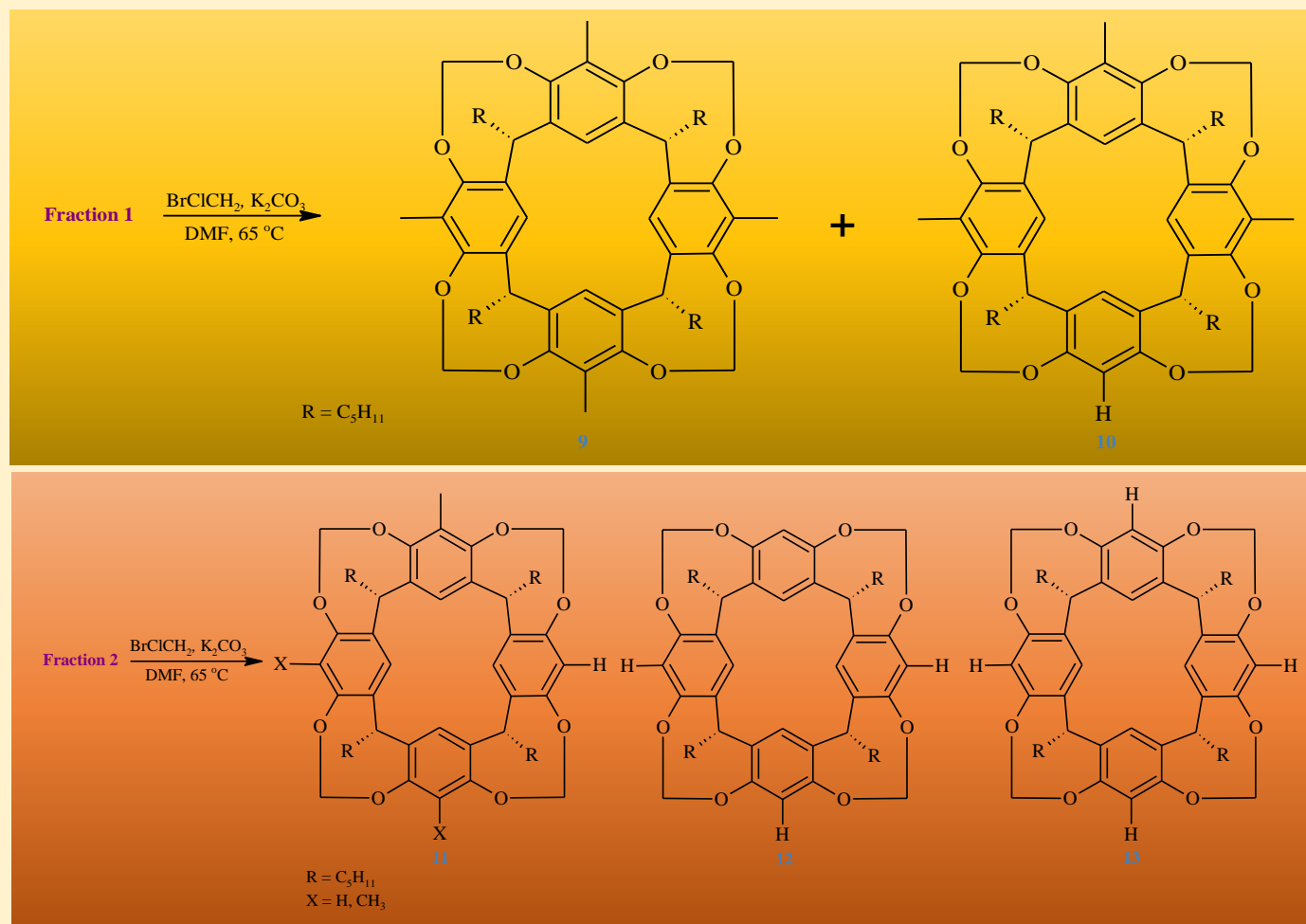
Resorcin[4]arenes constitute important building blocks in supramolecular chemistry. They interact with other molecules forming a host-guest complex, and can be self-assembled into larger supramolecular structures. Their mono- and tri-functionalized compounds form basic structural unit for other molecular recognition scaffolds.

Loose and co-workers demonstrated a short and efficient protocol for the synthesis of these compounds avoiding their dependency on statistics with under- or over-lithiated by-products as a yield diminishing problem. The procedure is accomplished by the co-condensation of resorcinol **2** and 2-methylresorcinol **3** in a mixture of aqueous $\text{HCl}_{(\text{conc.})}$ and ethanol (1:1) followed by slow addition of hexanal **1** in EtOH under elevated temperature (Scheme 1). Two fractions were formed, in which fraction 1 containing isomers **4** and **5** were directly participated from the reaction mixture, while fraction 2 containing less methylated homologues **6-8** were formed by adding water.

After separation of the two fractions, the direct acetalization of these isomers was achieved by using bromochloromethane (BrClCH_2), as methylenating agent, with K_2CO_3 , as the base. Both isomers of fraction 1 (**4** & **5**) formed the fully bridges resorcinarenes **9** and **10** in good yields (up to 30% over two steps based on the amount of methylresorcinol **3**) (Scheme 2). They found that the cyclizing acetalization is enhanced by substituents at the upper-rim, suppressing intermolecular oligomerizations as explained by the high selectivity in cyclizing acetalization of compounds **4** & **5** than the minor congeners **6a** & **6b** as well as the poor yields of isomers **11-13** of fraction 2 comparable to fraction 1.

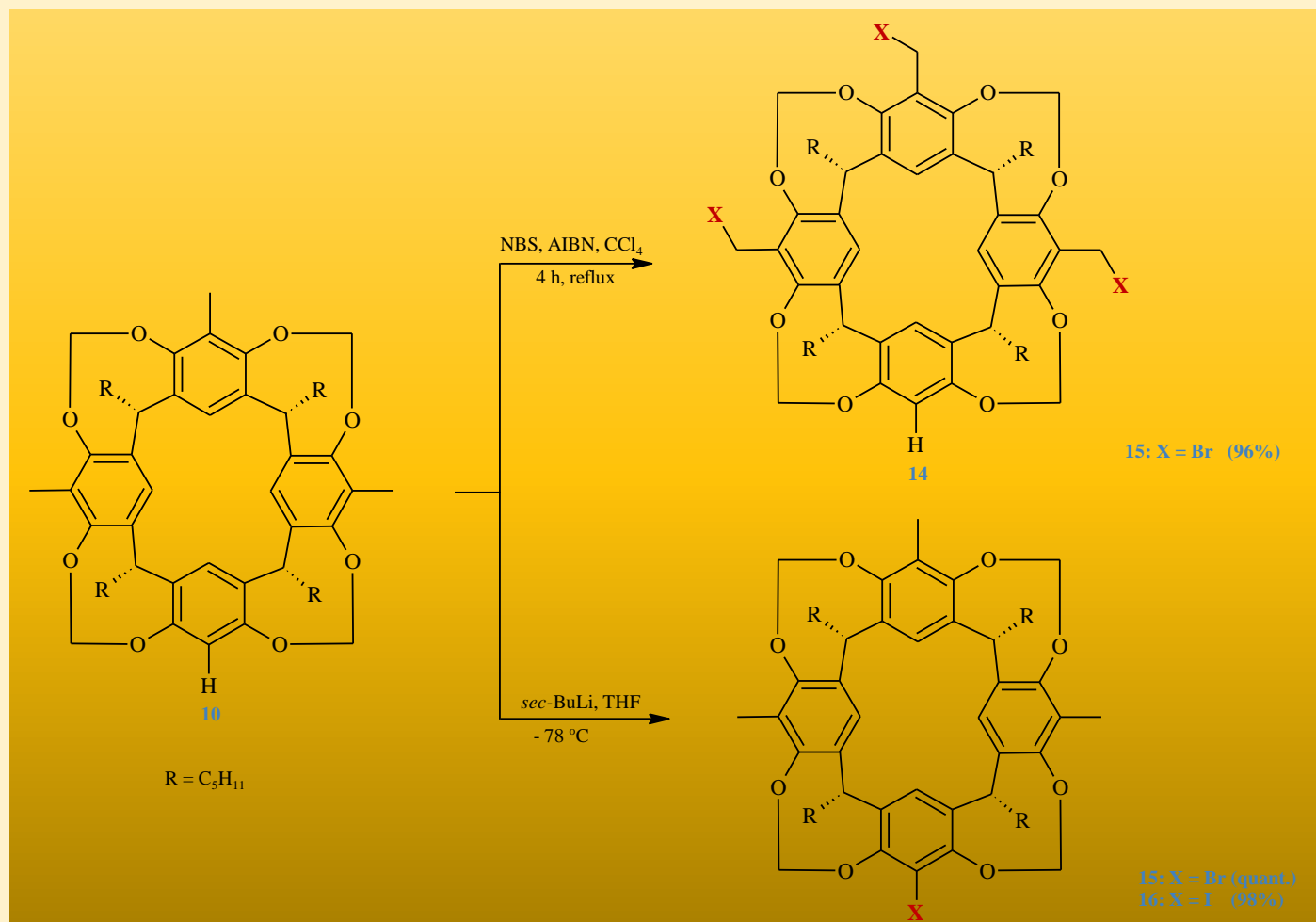


Scheme 1. Condensation reaction and separating of resorcin[4]arenes.



Scheme 2 Acetalization of fraction 1 and fraction 2.

In order to derivatize the methyl groups to create three positively polarized carbon atoms, e.g. available for S_N-type reactions through radical bromination, the halogenation of trimethylated resorcinarene **9** in benzylic position at the upper-rim was proceeded using NBS and AIBN or benzoyl peroxide in CCl₄ as solvent to form the desired product **14** with a yield of 96%. While the mono-derivatization at the phenylic position of **10** was accomplished by employing slow addition of *sec*-butyllithium into the reaction mixture to produce quantitative lithiation at the *ortho*-position. Further derivatization of the lithiated resorcinarenes through bromination using diluted dibromotetrafluoroethane or iodination using elemental iodine afforded the corresponding products **15** & **16** respectively (Scheme 3).



Scheme 3 Orthogonal preparation procedures towards tri- and mono-functionalized resorcinarenes.

The synthesized resorcinarenes can be further employed in S_N -type reactions or transition-metal catalyzed cross-coupling reactions.

Review

D. Loose, A. Aniol, M. Feigel, S. Röhling, G. Dyker, *Eur. J. Org. Chem.*, **2020**, 35–40.

Transparent Ultraviolet-Shielding Polymer Films Using Copper Nanoclusters

A synthetic procedure is described for transparent ultraviolet (UV) shielding polymer films composed of cross-linked polyvinyl alcohol (PVA) and polyvinylpyrrolidone (PVP) incorporated with copper nanoclusters. The composite films show a high UV shielding ability, allowing for transmittance of light in the visible range and possessing good mechanical and thermal properties.

Most of the current used packaging materials for nutrients are transparent polymers which allow UV light to pass through the protective films. Such exposure to UV light may lead to spoil the products or limit the shelf-lifetime of the products as a consequence of undesirable chemical reaction triggered by UV light. Therefore, the development of transparent composite materials that shield UV light, and allow for transmission of visible light, is an attractive research field.

Shi and co-workers reported a procedure to fabricate UV shielding composite films which based on employing ligand-protected metal nanoclusters (NCs) that possess absorption peaks in the UV or blue range, attributed to the inter-band electronic transitions. The composite films consist of a cross-linked PVA and PVP as polymer framework and Cu based nanoclusters, as economically viable inorganic UV absorbers and earth abundant element for large scale applications.

The composite Cu NC based film was synthesized by mixing a proper amount of aqueous solution of PVP with hot PVP solution (80 °C). In the same time Cu NCs was synthesized via reduction of Cu^{2+} by glutathione (GSH) which acts as both ligand and reducing agent, followed by incorporation with the polymers during the dehydration process. Finally, the Cu NC-polymer solution was poured onto the glass substrates, followed by thermal treatment in a vacuum oven to evaporate water until the transparent and free-standing films were obtained (Figure).

The performance of Cu NC based composites were examined for their practical applications in packaging in terms of UV light shielding, thermal stability, flexibility and toxicity. The results revealed that more than 98% of UV light (at 300 nm) could be blocked and more than 45% of light at 500 nm could still be transmitted when 15 mM of Cu^{2+} is used. Furthermore, the composite films showed favourable flexibility, reasonable thermal stability, high stability against UV light exposure, and a slight decrease of cell viability (10% after incubation for 24 h at concentration of 60 $\mu\text{g}/\text{mL}$ determined by the MTS assay on 3T3 fibroblasts).

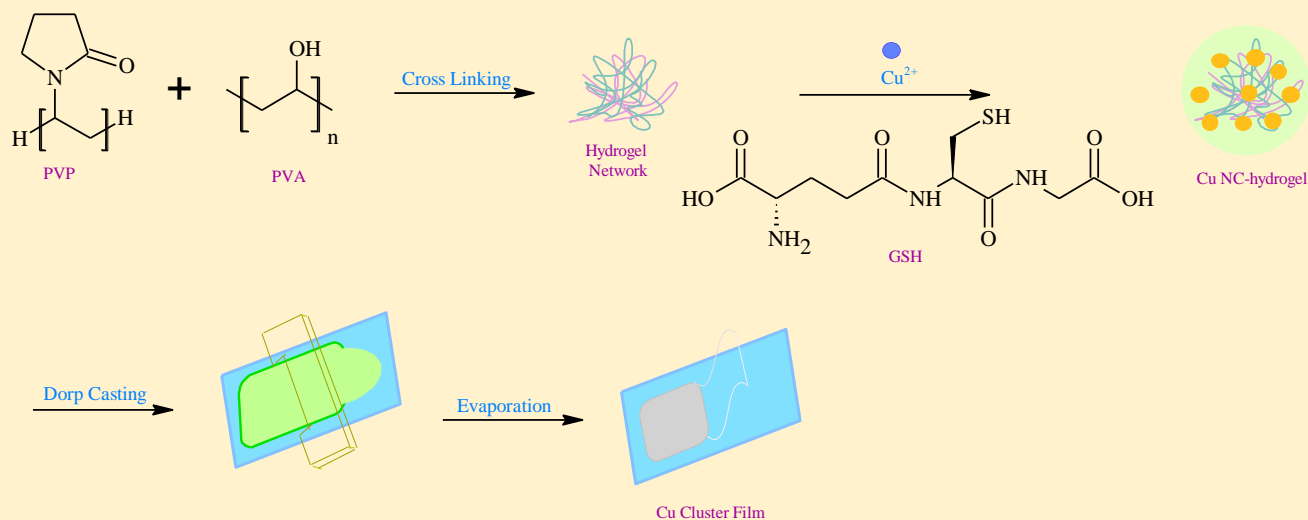


Figure . Schematic illustration of the synthetic pathway of Cu NC based composite polymer films.

Their potential applicability was demonstrated through protection of Rhodamine B dye from photo-degradation.

Review

Y. Shi, X. Zhuang, L. Cao, S. Gou, Y. Xiong, W-F. Lai, Z. Wang, A. L. Rogach, *ChemNanoMat*, **2019**, *5*, 110–115.