

# KEKULENE: THE SUPER BENZENE

## Abstract

Since Kekulé's proposal of the cyclic structure of benzene, aromaticity—a basic notion in organic chemistry has been of particular interest to chemists as a way to explain the stability of cyclic conjugated  $\pi$ -electron systems. A particular aromatic stabilizing mechanism, the  $\pi$ -conjugation in two concentric macrocyclic conjugation routes labelled as [18]-annulene and [30]-annulene, has been suggested for kekulene ( $C_{48}H_{24}$ ), a prototype cycloarene. There has been much discussion about this alleged "super-aromaticity" for many years. According to a different model, kekulene has six disjoint aromatic sextets, which satisfies Clar's rule that benzoid compounds should have as many disjunct aromatic benzene rings as possible and as few double bonds as possible. Since its discovery, different groups demonstrated different routes to synthesize this highly conjugated system. Though it has long extended conjugation, still a big debate is there for last few decades about its aromatic nature. In this book chapter, electronic nature, aromaticity and different synthetic techniques of kekulene will be discussed.

**Keywords:** Kekulene, macrocyclic conjugation, Huckel discovery

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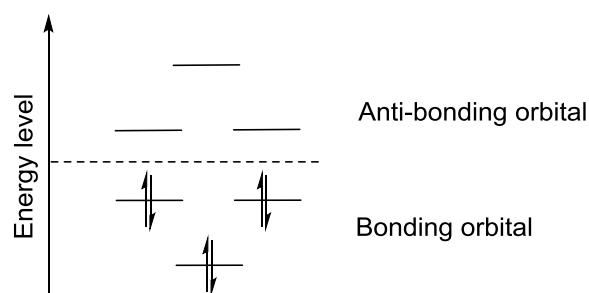
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## I. WHAT IS AROMATICITY?<sup>1</sup>

Sir Erich Hückel, a chemist and physicist from Germany, devised a theory to assist assess whether an aromatic property will be present in a planar ring molecule. This rule is widely used to determine aromaticity in monocyclic conjugated compounds, known as Hückel aromatic rule. According to this definition, an aromatic compound is a planar monocyclic conjugated system with  $(4n + 2)$  delocalized  $\pi$ -electrons (where  $n = 0, 1, 2, \dots$ ). A compound is thought to be exceptionally stable if all of its bonding molecular orbitals are filled with paired electrons, according to Hückel's Molecular Orbital Theory. Aromatic compounds are quite stable since this is true. With aromatic compounds, the lowest energy molecular orbital has 2 electrons while the following  $n$  energy levels each have 4 electrons,



**Figure 1:** Molecular Orbital Diagram of Benzene

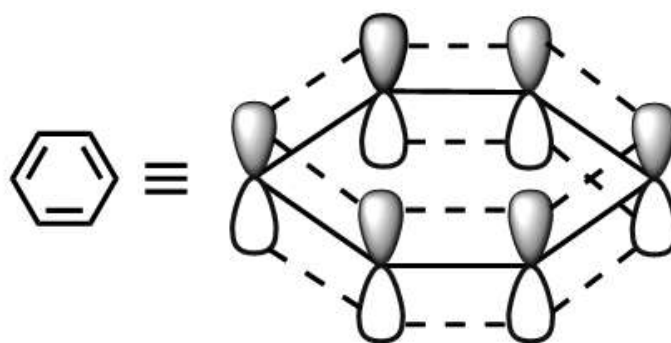
filling all bonding orbitals and leaving no anti-bonding orbitals unoccupied. This results in  $4n+2$  electrons overall (figure 1).

### 1. Conditions for Aromaticity

- The molecule should be cyclic.
- The molecule must be planar.
- There should be  $(4n+2)$   $\pi$ -electrons in the molecule ( $n$  might be 0 or any positive integer).
- The whole molecule must have uninterrupted conjugation.

If any molecule fulfills those above criteria, but instead of having  $(4n+2)$   $\pi$ -electrons contains  $4n\pi$  electrons, they are classified as anti-aromatic compound (for example, cyclobuta-1,3-diene etc.). If any molecules fill up all those above criteria, but instead of being planar they are non-planar, they are classified as non-aromatic compounds (for example, cyclodeca-1,3,5,7,9-pentaene etc.)

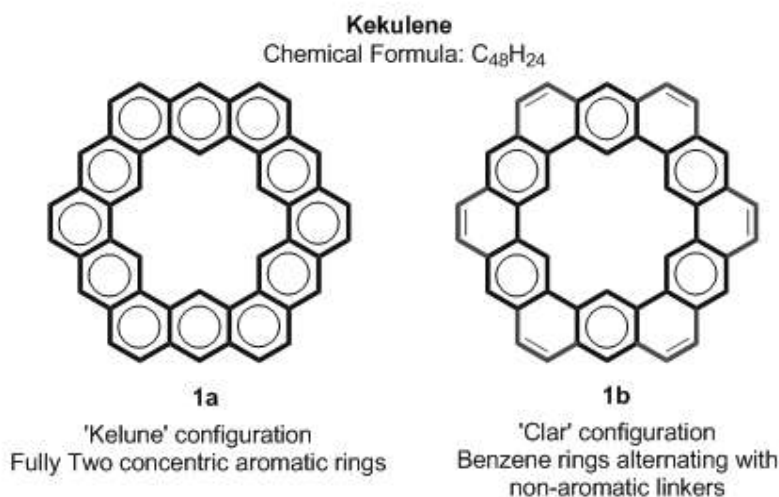
One of the most studied aromatic compounds, is benzene having molecular formula of  $C_6H_6$ . It is a monocyclic aromatic compound having planar shaped cyclic system with  $6\pi$ -electrons. Benzene is a hexagonal, cyclic and planar system having  $6\pi$ -electronic system. All the carbon atoms are  $sp^2$  hybridized and C-C-C bonds angles are  $120^\circ$ . Each carbon atom contains a unhybridized empty p-orbital, which form the  $\pi$ -electron cloud over and below the ring. All the six  $\pi$ -electrons are delocalized through this electron cloud. This most accepted cyclic structure of benzene was proposed by Kekule in 1865 (figure 2).



**Figure 2:**  $\pi$ -Orbitals of Benzene

## II. WHAT IS KEKULENE?

Due to the uniqueness of their molecular and electrical structures, cyclo-arenes<sup>2</sup> are a fascinating family of polycyclic aromatic hydrocarbons (PAHs) that have captured the attention of scientists for decades.<sup>3</sup> They make excellent venues for examining fundamental issues surrounding the idea of aromaticity, particularly those pertaining to the distribution of  $\pi$ -electrons in complicated aromatic systems.<sup>4</sup> Since cyclo-arenes are used as models for graphene pores,<sup>5</sup> interest in them has recently grown. Kekulene is the most analysed member of this series. It is categorised as a [12]-circulene with the formula  $C_{48}H_{24}$ . After its discovery, it was named in the honor of famous scientist August Kekulé, who proposed the most well accepted structure of benzene. Kekulene is mainly famous for its novel structure and electronic properties. Since its discovery, determination of its structure is one of the most debatable topics in last few decades.<sup>6</sup> After several analysis, several structures were proposed. Among them, ‘Kekulene’ and ‘Clar’ configurations are of special interest (figure 3). ‘Clar’ configuration is proposed having six benzene-like rings connected via vinyl groups in non- aromatic rings and bridging bonds. On the other hand, in ‘kekulene’ configuration, two radial single bonds connect two concentric aromatic rings (18 inner, 30 outer electrons) to form a fully annulenoid structure.



**Figure 3:** ‘Kekule’ and ‘Clar’ Structure of Kekulene

### III. IS KEKULENE IS A SUPER-AROMATIC SYSTEM?

Since the discovery of kekulene, there is a long debate about the electronic nature and aromaticity of kekulene. Several research groups demanded several facts and gave proofs against their theory. It has been unclear if the cyclic annellation of benzene rings in kekulene results in an increase in thermodynamic stability.

On kekulene, Cioslowski and colleagues performed complex ab initio molecular orbital computations, they observed that, contrary to what would be predicted from localised structures of tiny benzenoid hydrocarbons, kekulene has a higher thermodynamic stability.<sup>7</sup> A super-aromatic stabilisation energy is one name for this type of stabilisation energy. As a thermodynamic stability brought on by macrocyclic conjugation along the cyclic array of benzene rings, they described super-aromaticity. Kekulene must be viewed as both a benzenoid and a subclass of annulenoid species if it is totally super-aromatic in this sense. Aromaticity often results from the cyclic conjugation of one electron. In a conjugated system, aromaticity results from every feasible cyclic route. In chemical graph theory, these cyclic routes are known as ring components or circuits. The circuits around the inner cavity in kekulene must be in charge of super-aromaticity. If so, how much do these circuits affect the kekulene's stability or aromaticity?

In order to clarify the super-aromaticity of kekulene, Aihara and group used several graph-theoretical approaches to it and related polycyclic aromatic hydrocarbons (PAHs) in this study.<sup>8</sup> They very sensitively gauge the level of super-aromaticity using one of the techniques. They performed several theoretical calculations, like topological energy resonance energy, circuit resonance energy, additive nodal increments etc. Calculating the total  $\pi$ -electron energy of kekulene provides clear proof that the compound lacks super-aromaticity. In this case, a hypothetical molecule called super-antiaromatic kekulene was created by flipping the sign of the resonance integral for two of the C-C bonds in kekulene. The selection of these two bonds must be deliberate. The outer and inner peripheries of each link must be at the same location. Additionally, both must be benzene ring members of the same ring. There are several methods to select two bonds that satisfy these requirements. But in every way, kekulene is a typical benzenoid hydrocarbon.

### IV. DIFFERENT SYNTHETIC APPROACHES OF KEKULENE

Since its discovery several attempts were made in different labs throughout the world. In 1978, it was first synthesised by Staab and Diederich, which is regarded as a milestone discovery in the study of aromatic chemistry.<sup>9</sup> They started from *m*-xylene (**2**). When *m*-xylene is treated with concentrated nitric acid, it converts to its di-nitro derivative **3**. Presence of double nitro group in the same benzene ring makes the benzylic protons highly acidic. Upon condensation reaction with benzaldehyde in presence of piperidine, di-nitro compound **3** is converted to compound **4**. Reduction of compound **4** under palladium-charcoal converts it to compound **5**. After that treatment of compound **5** with amyl nitrite converts it to 5,6,8,9-tetrahydrobenzo[*m*]tetraphene (**6**). The reaction goes via the formation of diazonium salt. Treating compound **6** with para-formaldehyde in presence of hydrobromic acid/polyphosphoric acid mixture it furnishes dibromo derivative **7**. After treatment with thiourea followed by refluxing under basic condition converts it to (5,6,8,9-tetrahydrobenzo[*m*]tetraphene-3,11-diyl)dimethanethiol (**9**). It is used as the main precursor for kekulene synthesis (figure 4).

Step 1:

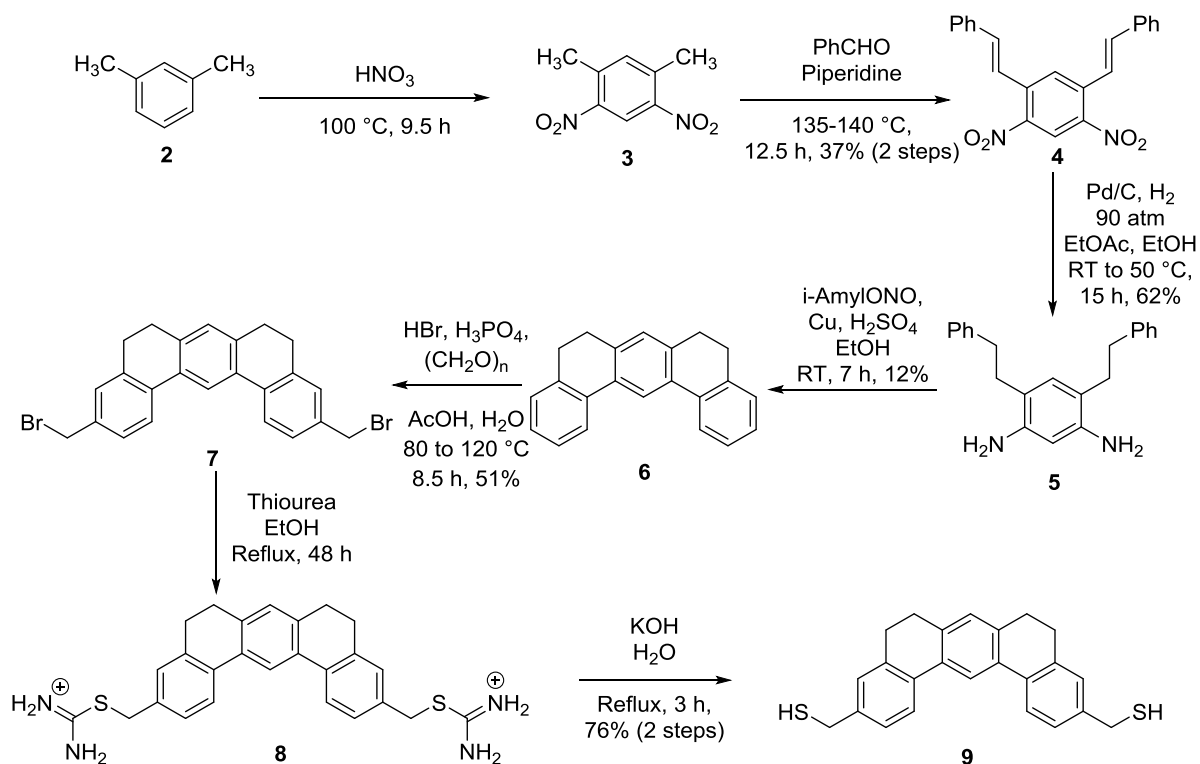
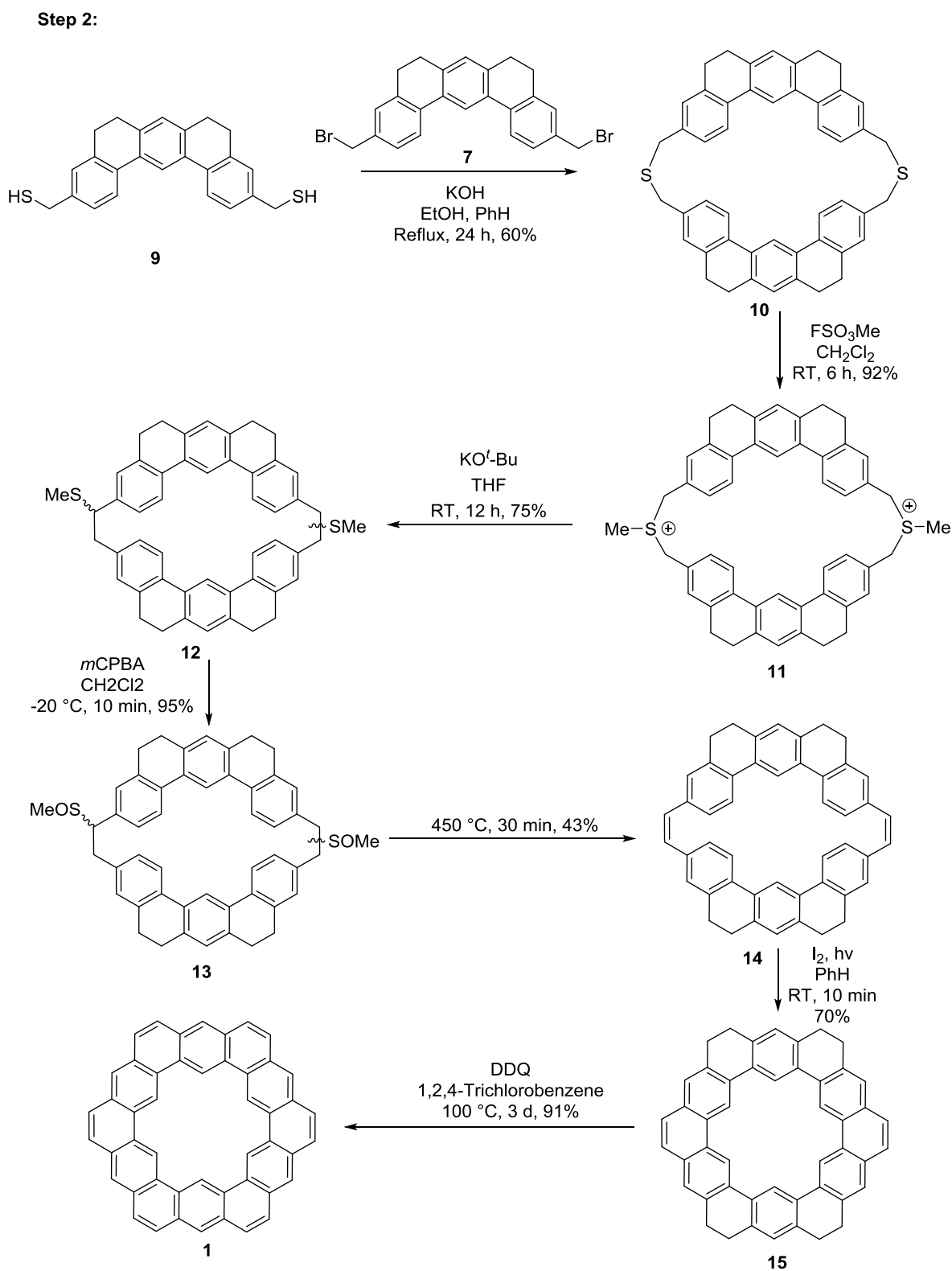


Figure 4: Staab and Diederich synthesis of Kekulene, Part-1

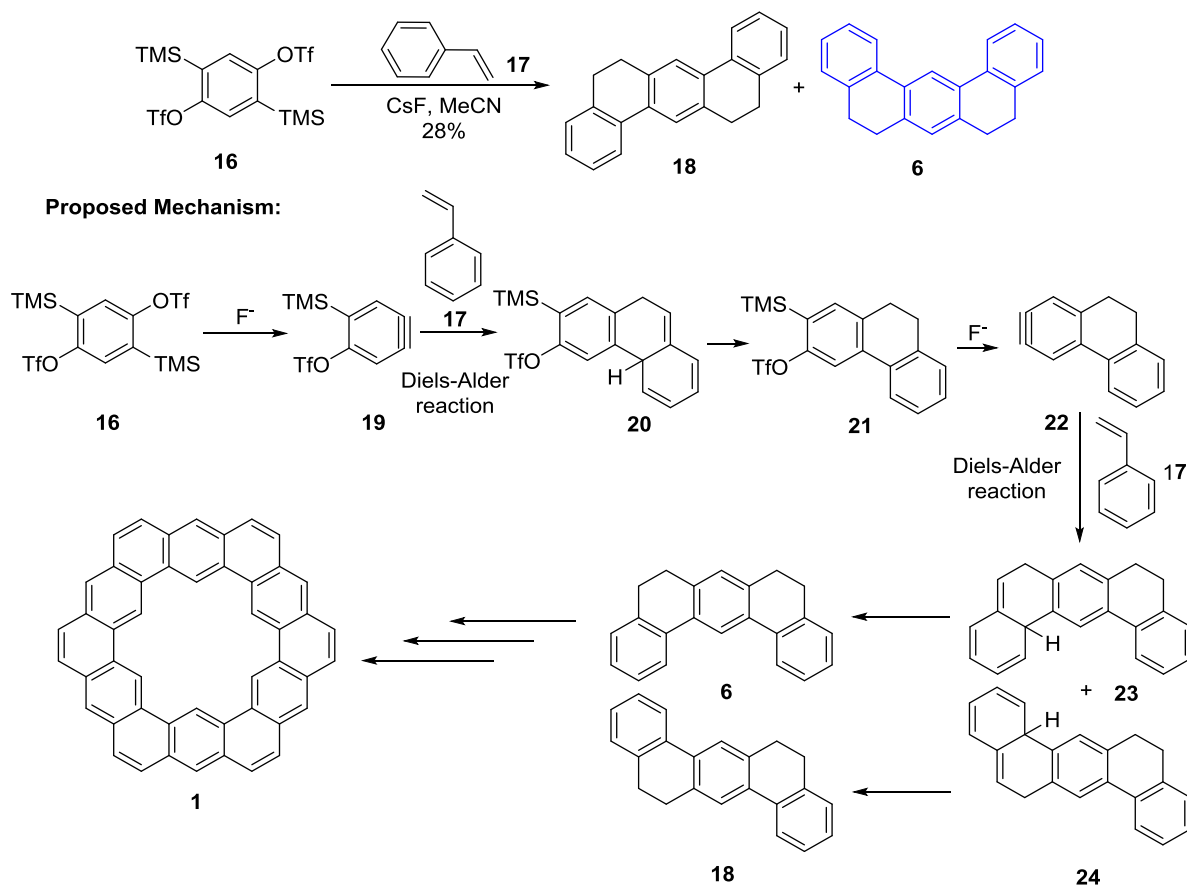
Compound **9** is coupled with compound **7** in presence of KOH to form macrocyclic derivative **10**, which further treated with  $\text{FSO}_3\text{Me}$  followed by potassium *t*-butoxide converts it compound **12** via Stevens rearrangement. Compound **12** is further treated with oxidising agent *m*CPBA followed by treatment at very high temperature (around  $450\text{ }^\circ\text{C}$ ) converts it to compound **14**. Finally, compound **14** is treated with  $\text{I}_2$  under photochemical condition followed by oxidation with DDQ to furnish kekulene (**1**) (figure 5).



**Figure 5:** Staab and Diederich synthesis of Kekulene, Part-2

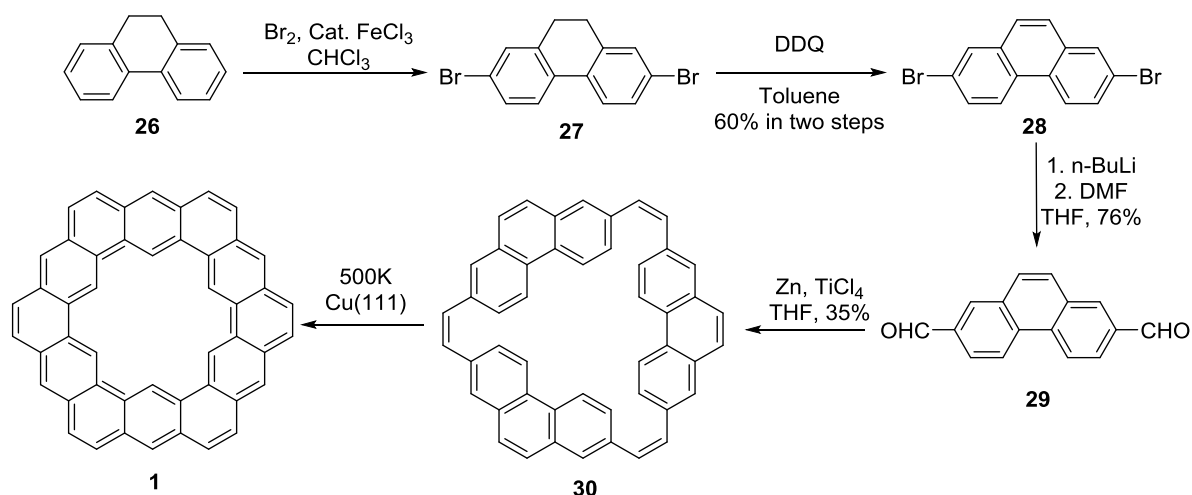
The main drawback of Staab and Diederich synthesis of kekulene is the synthesis of 5,6,8,9-tetrahydrobenzo[m]tetraphene intermediate (**6**), which is used as the main precursor. It is synthesized in multiple steps and in very low yield (overall yield after four steps is

around 2.5%). But compound **6** can be synthesized through a quicker and more efficient pathway, demonstrated by Pérez group (figure 6).<sup>10</sup> In this protocol, bistriflate derivative **16** acts as a source of benzyne derivative (**19**) in presence of fluoride ion, which further react with styrene (**17**) in a Diels-Alder reaction fashion to provide compound **20**. Again, it undergoes another benzyne derivative (**22**) formation in presence of fluoride and again undergoes Diels-Alder reaction to produce compound **6** and its isomer (**18**) in relatively high yield (28%). Staab and Diederich already demonstrated the synthesis of kekulene (**1**) using 5,6,8,9-tetrahydrobenzo[*m*]tetraphene (**6**) as the precursor.



**Figure 6:** Synthesis of Kekulene via Benzyne Intermediate

Tautz and group showed another step-economical as well as atom-economical protocol to synthesize kekulene (**1**) (figure 7).<sup>11</sup> According to this developed protocol, kekulene (**1**) can be easily synthesized through only five steps taking 9,10-dihydrophenanthrene (**26**) as the precursor. Bromination of it using liquid bromine in presence of catalytic amount of ferric chloride produces 2,7-dibromo-9,10-dihydrophenanthrene (**27**) as the sole product. Further, it was oxidized by DDQ to get fully aromatized compound 2,7-dibromophenanthrene (**28**) exclusively. Bromine group abstraction by *n*-butyl lithium followed by treatment with *N,N*-dimethyl formamide furnished corresponding formyl derivative phenanthrene-2,7-dicarbaldehyde (**29**) exclusively. Treating phenanthrene-2,7-dicarbaldehyde (**29**) with zinc and TiCl<sub>4</sub>, followed by heating in presence of Cu metal at 500 K, furnishes kekulene (**1**).

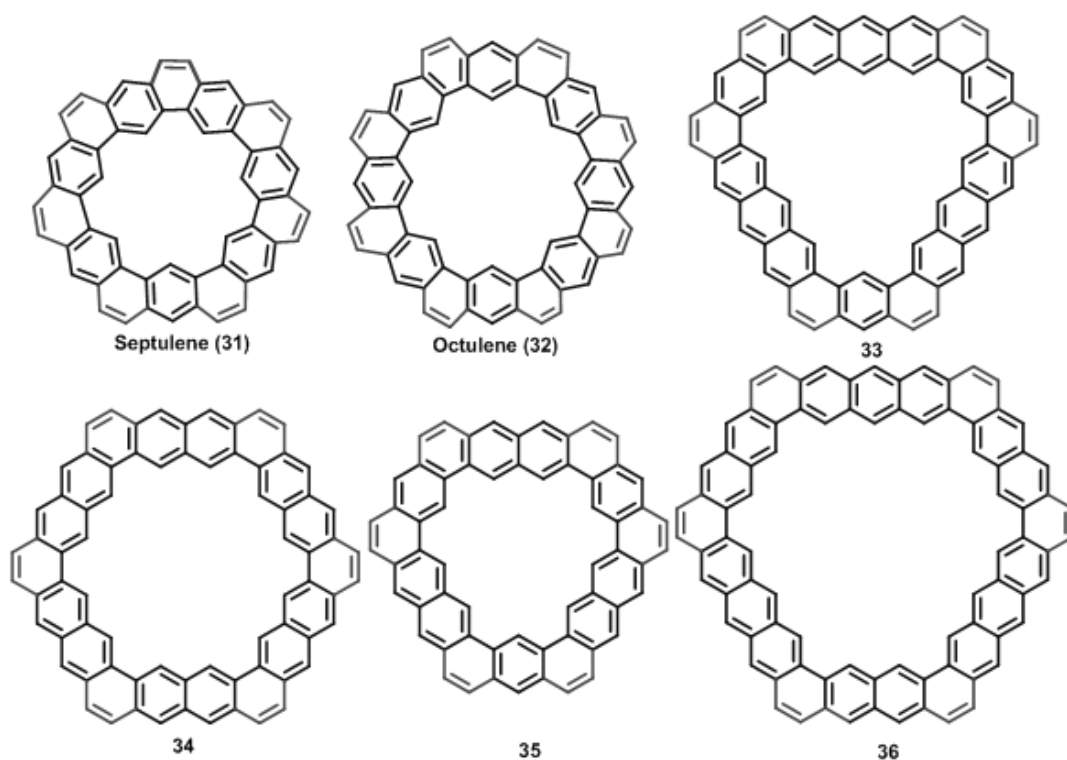


**Figure 7:** Synthesis of Kekulene using 9,10-dihydrophenanthrene

## V. EXPANDED KEKULENE

As per the description of Staab and Diederich, "Cycloarenes" are polycyclic aromatic compounds in which fully annulated macrocyclic systems are present and enclose a cavity into which carbon-hydrogen linkages point through a mix of angular and linear annulations of benzene units. Those are member of  $D_{6h}$  symmetry groups. After the discovery of synthetic protocol and electronic properties of kekulene, several research groups attempted to find procedure to synthesize extended kekulene systems (figure 8).<sup>12</sup> One of the extended kekulene analogue is septulene, which is a heptagonal analogue of kekulene developed in 2012.<sup>13</sup> The molecule exhibits a low solubility and an electrical structure resembling that of kekulene. Their 'Clar' structures explain this commonality. The resemblance does not—and in fact, cannot—follow from their 'Kekule' structures, which fundamentally vary because to the odd or even number of atoms in their inner and outer annuli. 'Clar' structures, not 'Kekule' structures, should be utilised to depict bonding in polycyclic aromatic compounds, as Septulene conclusively shows it. Using a fold-in synthesis technique, Stepien et al. synthesised kekulene and its higher analogue Octulene in 2016, both of which are soluble in common organic solvents.<sup>14</sup> This new hydrocarbon macrocycle has a sizable core circuit with 24 members that is peripherally fused to 24 benzene rings. The  $\pi$ -conjugated surface is significantly hyperbolically distorted by such an arrangement. Using photophysical techniques, the effects of distortion in Octulene were investigated. The results showed a smaller electronic band gap and more flexibility in the  $\pi$  system. Consequently, a productive synthesis technique for aryl-substituted kekulene and Octulene derivatives was also discovered by the Wu group in 2020. While this is going on, other comparable structures, including extended coronoids, which have been synthesised in solution or on the surface, have been seen to exhibit unique electrical properties from the single-chain cycloarenes.<sup>15</sup>



**Extended Kekulene derivatives  
(Class of higher cycloarenes)****Figure 8:** Expanded Kekulene Systems**VI. CONCLUSION**

After the Huckel discovery of the criteria of aromaticity, several compounds are tested to understand their aromatic nature. Several higher conjugated systems were examined and used in material science etc. for their huge conjugation. The most common aromatic system which was examined thoroughly, was benzene. In last few decades, synthesis and aromatic property examination of polycyclic aromatic hydrocarbon kekulene is a debating as well as most interesting topic in science. Since the discovery of kekulene more than thirty years ago, theoretical chemistry in this area has developed significantly more than synthetic chemistry, making it possible to quantitatively assess the conjugation circuits of  $\pi$ -electrons in kekulene-related compounds. limited number of chemicals made accessible for research. Although super-aromatic influence cannot be completely ruled out on the basis of magnetic property, the majority of experimental and theoretical research were concentrated on kekulene, showing its Clar's sextet image. However, the recent synthesis of Septulene and its higher analogues have revealed a novel element of the conjugation circuit for benzenoid kekulene-related compounds. Further higher conjugated systems have been synthesized and their aromatic properties are also examined.

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