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REVIEW ARTICLE

Helicenes synthesis and their Potential Applications

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Abstract:
Helicenes represent a class of polycyclic compounds characterized by an angular configuration, resulting in a helical conformation. These compounds can feature ortho-fused aromatic or heteroaromatic rings. In instances where an alkyl hexane exhibits more than five aromatic rings ($n > 5$), distinct consistent enantiomers, P (left-handed) and M (right-handed), may emerge. The intrinsic chiral structure of helicenes, combined with extended p-conjugation, yields notable electrical circular dichroism (ECD) spectra and substantial optical rotations (ORs). Hexapole helicenes, synthesized through (2+2+2) cyclic reactions of aryne precursors generated by palladium, consist of six [5] helicene substructures, resulting in potential 20 stereoisomers. Selectively obtaining HH-1, the second isomeric form, HH-2, becomes the more stable isomer through quantitative isomerization (HH2) under heat conditions, as predicted by density functional theory (DFT) calculations. Chiral high-performance liquid chromatography (HPLC) effectively separates HH-2's two enantiomers. Kinetic investigations into the isomerization, based on DFT calculations, HPLC, and H1 NMR absorption spectroscopy from HH-1 to HH-2, along with an enantiomerically accelerated racemization of enantiomerically purified HH-2, were conducted. In this review, the most recent developments in this area of study are outlined.

Keywords: Helicenes; Enantiomers; Circular dichroism; Antimitotic action.

1. Introduction

Meisenheimer and Witte reported the first helicenes in 1903. There hasn't been much progress on organic helicenes throughout the following few decades. However, in the 1950s, helicenes chemistry began to gain traction when Newman and associates developed their synthesis and separation methods [1]. The molecules of carbon called helicenes are created by ortho-analling benzene. They are phenanthrene analogues of benzene [2, 3] .This kind of benzene ring arrangement invariably results in face-to face overlap. One common illustration is the heptahelicene or helicene. The usual helix structure along with chirality are the results of these interactions. Such compounds' great optical activity is one of their most distinctive features.. More recently, helicenes' vibrating circular dichroism (VCD) has been studied. [4]. To relieve the internal tension brought on by an increasing number of rings, these molecules take on the distinctive screw shape. The article that follows and concentrates a chemically mediated synthesis of helicenes and helicene-like compounds .Numerous helicenes applications have been researched. [5] More thorough research is required in these situations to fully explore an opportunity of helicenes in various application domains. It is therefore very necessary in this context to develop novel and effective synthesis methods for helicenes.

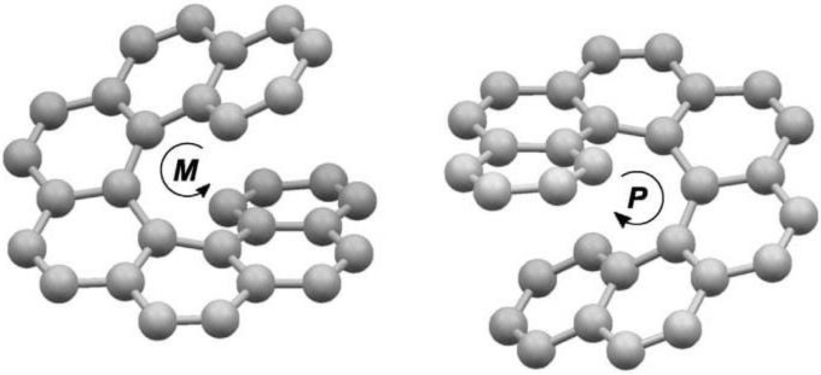

Figure 1 Heptahelicene

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2. Synthesis of helicenes

2.1. Helicenes Synthesis through double carbon and hydrogen Arylation process catalysed by palladium

Palladium catalyzed a double Carbon-Hydrogen arylation process by Z,Z-bis-(bromostilbene)s to synthesizes helicenes(5) and (6)in moderate excellent yields. This technique can be used to synthesize helicenes with substituents that lack electrons. This approach to helicenes synthesis is both efficient and useful. [6] The progress of helicene synthesis, however, still has a lot of opportunity. We have devised a substitute for helicene synthesis, catalyzed double C-H arylation synthesis with palladium using Z,Z-bi-(stilbene)s, as part of our programmed to discover effective techniques for the synthesis of helical compounds. Using rhodium or palladium as a catalyst with CH arylation, there is no need to pre-activate bonding components, making it an effective approach for synthesizing heterocycles. A few recent papers on C-H arylation catalysed by Pd. [7, 8] So, using Pd catalyst, we first looked at the C-H arylation process for producing 1,2-dimethoxy-phenanthrene

Table 1. Helicene synthesis using arylation process

Entry	Palladium cat.	T (^{0}c)	Solvent	Base	Yield (%)
1	$PdCl_2$(dppf)	90	DMSO	Potassium acetate	37
2	$PdCl_2$(dppf)	130	DMSO	Potassium acetate	55
3	$PdCl_2$(dppf)	130	DMF	Potassium acetate	51
4	$PdCl_2$(dppf)	130	DMA	Potassium acetate	62
5	$PdCl_2(PhCN)_2$	130	DMA	Potassium acetate	51
6	$Pd(OAc)_2$	130	DMA	Potassium acetate	68
7	$Pd(OAc)_2$	130	DMA	Potassium carbonate	99

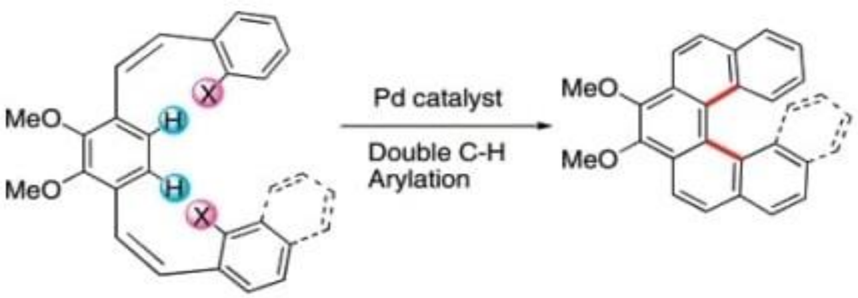

Figure 2 Helicene Synthesis using arylation process

2.2. The Formation of Helicenes using Diels-Alder Process

In the late 1990s, Stara, Stary and other researchers applied them to the production of helicenes.. Because of their twisted structure, helicenes have an intrinsic torsional strain. It takes some additional energy to construct such a distorted structure, but they are not greatly destabilised because the strain is dispersed throughout the entire molecule. However, since [2 + 2 + 2] cyclo-isomerization of πelectron complexes is a strongly exergonic process, it is ideally suited to this requirement. It was demonstrated by computational investigations that the corresponding dienetriynes' [2 + 2 + 2] cyclo-isomerization yields the creation of helicenes. Utilizing cobalt as mediators the production of pyridazino helicenes via cycloisomerization of nitriles [9, 10]

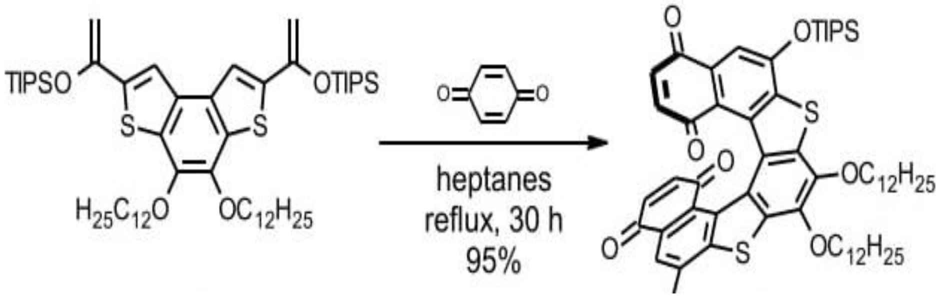

Figure 3 Helicenes synthesis using Diels -Alder cycloaddition

3. Applications

3.1. Antimitotic action

There are few instances of the helicene scaffold directly and explicitly engaging with biological targets that are useful to therapy. The most effective helicenes for medicinal chemistry target specific DNA topologies such as selective helicenes B/Z,DNA binding. Furthermore, G-quadruplex DNA . (24). All eukaryotic cells utilize microtubules (MTs), internal protein scaffolds, to facilitate mechanical activities such as cell motility, act as motor protein cargo transport pathways, and divide cells by dividing their chromosomes. (25). A huge noncovalent polymer of the α/β-tubulin "monomer" protein, MTs undergo constant remodeling in cells to perform their intended roles through carefully timed cycles of polymerization and depolymerization. (26). By preventing cell division, or mitosis, MT inhibitors have an antiproliferative effect. We measured the vitality of the HeLa human cervical carcinoma cell line after 40 hours in order to investigate the antiproliferative properties of HA1.At low micromolar doses, it was discovered that HA1 inhibits around 40% of normal cell growth and has a sigmoid dosage response curve with a good state which a Hillslope common for compounds that depolymerize tubulin also. [11]

3.2. Other uses

The African willow species Combretum caffrum is the source of Combretastatin A-4 (CA4), which has been shown to have especially encouraging anti-tubulin action. Furthermore, helicenes have a wide range of uses, such as asymmetric catalysis, due to association of a completely conjugated arrangement with a spiral arrangement. chemical switches. Pigments, emitters of circularly polarized light, Spheronics (predicated on spin selectivity caused by chirality). electrical equipment made of organic materials. Although helicenes are finding more and more uses in synthesis and materials research, chemical biology has not given these scaffolds enough attention. For the resolution of helicenes with carboxylic acid functionalities chiral amines like alkaloids are used Ammonium salts that are diastereoisomeric are created in this manner. An chiral acid chloride among others like chloride of camphanoyl esterified with helicenes that have a hydroxyl function. [12]. A Selective precipitation is used to separate the resultant diastereomeric esters. These operations are also performed on a big scale. Not all crystallisation is selective. Racemization of smaller helicenes can happen readily at ambient temperature or even a little bit higher. Under such circumstances,optical resolution is facilitated by the use of HPLC. HH^{o}2 is the most stable isosomer, while HH1 is the second most stable isosomer, according to DFT calculations (Figure 4). HH 1's stereoselective formation's specifics, however, are still unknown.

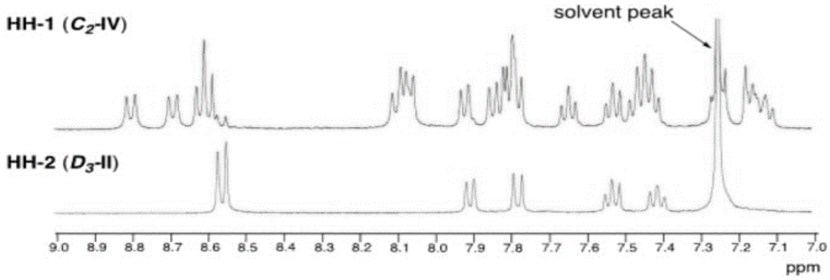

Figure 4. ^{1}H NMR spectra in toluene -d8 of HH-1 (the colour of green) and HH-2 (brown) in toluene-d$_8$

4. Conclusion

The synthesis of helicenes is detailed in this study, employing [2+2+2] cyclization catalyzed by Pd. The initial helicene was designed with a targeted protein in mind, aiming for therapeutic applications, specifically anti-mitotic activity. Its bioactivity has been confirmed at doses pertinent to cells and validated through systematic live cell imaging. Furthermore, recent advancements, qualities, and applications of these helicenes have been discussed in light of their promising attributes

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Author's short biography

Sai Venkat Tarigoppala

Sai Venkat Tarigoppala is a student of B pharmacy whose research focuses on contextualising the effects of force of helicenes. His conducting investigations is based on a synthesis of anti-mitotic action, function and uses. His goal was to use his curiousity and self motivation to further enhance his valuable skills for the pharmacy sector.