Indian Journal of Chemistry
Vol. 64, November 2025, pp. 1079-1088
DOI: 10.56042/ijc.v64i11.22650

Pseudorotaxanes and rotaxanes in the Chemistry curriculum for undergraduate students: A gateway to modern molecular design

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Received 12 August 2025; accepted (revised) 6 October 2025

Design and synthesis of a 24-membered macrocyclic wheel (MC) based [2]rotaxane (ROT) with multiple functional groups are reported. Threading followed by capping strategy has been used to form a mechanically interlocked structure. Initially, metal ion template [2]pseudorotaxane is formed *via* ternary complexations. Thereafter, stoppering *via* Click Chemistry results in [2]rotaxane. The interlocking nature has been established by ESI-MS spectrometry and various 1D and 2D NMR studies. This concept also offers a valuable pedagogical framework for teaching and learning modern chemical design strategies and, the interpretation of various spectroscopic and spectrometric data, along with extensive use of Chem-Draw software for undergraduate students. This article explores the design, synthesis and characterization of pseudorotaxane and rotaxane, importance of interlocked systems in the pedagogy at undergraduate level while aiming towards deeper understanding of modular synthesis and orthogonal reactivity.

Keywords: Upper-division undergraduate level, Supramolecular Chemistry, Non-covalent interactions, Mechanical bond, Rotaxanes

The area of synthesizing multi-functional rotaxanes is getting progressively popular even after 2-3 decades, for their potential uses in multiple dimensions[1]. In this domain, Sauvage and his research group revolutionized the synthesis of MIMs upon introducing the passive metal ion template approach since 1983 (Ref. 1). Although the accumulation of molecular sub-components (*i.e.* wheel, axle, templating agents) required for the preparation of a rotaxane is entropically unfavourable, passive metal ions template directed procedures and associated templating interactions that include, π-π stacking interactions[3], secondary H-bonding interactions[4] are being fruitful to overcome the entropic factor. Sauvage's demonstration of the passive template directed approach was revolutionary because it is based on assembling simple organic building blocks (sub-components) to form three-dimensional threaded structures[5]. These threaded structures (pseudorotaxanes) could be trapped to form interlocked molecules (rotaxanes) in high yield. Many chelating ligand molecules, where metal-ligand interactions play as a bridge between the covalent subcomponents of MIMs, have been reported to date[6]. In the cases described above, appropriate integration of metal chelating centres in the sub-components of pseudorotaxanes results in ternary complexation[7]. Different chelating ligand platforms have been developed, including pincer and[8] scorpionate[9] donor sites in macrocycle or axle backbone to generate the ternary complexes. In the case of metal ion template directed syntheses, upon proper stoppering and de-metallation of the templating agents, precursor pseudorotaxane yields rotaxane[10]. Herein, the metal ion template directed [2]pseudorotaxane and [2]rotaxane formations are reported. Threading followed by capping methodology is demonstrated[11]. Ni(II) ion is used as template for threading and capping is accompanied with azide-alkyne cyclo-addition reaction.

In the year of 2016, the Nobel prize was jointly awarded to Jean-Pierre Sauvage, Sir J. Fraser Stoddart and Bernard L. Feringa for the design and synthesis of molecular machines[12]. Sauvage and Stoddart are renowned for the generation of such tiny machines through mechanically interlocked molecules formation[3,12]. Although it is one of the hot topics of research in Chemistry, the undergraduate curriculum often leaves Supramolecular Chemistry behind[13]. In this context, design, synthetic strategies, structure property relationship behaviour of pseudorotaxanes and rotaxanes have been infrequently revealed in

chemical education literature except the synthesis of Borromean rings[14]. In this context, conceptual foundations of a newly reported interlocked system, teaching strategies, and activity proposals are discussed to help educators introduce this topic at the undergraduate level. This article proposes rotaxanes and/ or mechanically interlocked molecules as an ideal concept for pleasing students with the concept of orthogonality[15], template directed synthesis[16], and modern molecular design thinking in Chemistry.

Pedagogic Objectives for the Study of Multifunctional [2]Pseudorotaxanes and [2] Rotaxane Synthesis

1. **Introduction to Mechanical Bonds and Non-Covalent Interactions in Chemistry**: Undergraduate students can gain a concept of mechanical bonds, which are non-covalent interactions within the mechanically interlocked molecules (MIMs)[18].
2. **Study the Concept of Supramolecular and Host-Guest Chemistry**: Students can investigate the principles of Supramolecular Chemistry, highlighting the template effect—a process where a template such as cations, anions, and even molecular template *via* π-π stacking interactions guides the assembly of interlocked structures like rotaxanes[19].
3. **Improvement of Synthetic Organic Chemistry Knowledge**: This lesson may strengthen the knowledge of synthetic organic Chemistry by studying the approach and strategies involved in constructing complex molecular architectures *i.e.* MIMs[20].
4. **Development of Spectroscopic Analysis Skills**: Students will learn to interpret Nuclear Magnetic Resonance (NMR) and ESI-MS spectrometric data to identify and characterize interlocked compounds and its building blocks. They will become familiar with 2D-NMR tools[21].
5. **Metal Ligand Coordination Chemistry**: This topic will enhance the knowledge about ligating behaviour of the donor atoms and metal ions which depends on the hard-soft concept, and coordination numbers of metal ions[22].

By focusing on the aforementioned objectives, students can build a robust theoretical foundation in the template-directed synthesis and spectroscopic analysis of rotaxanes and pseudorotaxanes, preparing them for advanced studies. This study may encourage them for research in supramolecular and host-guest Chemistry.

Background Concepts for Students

Before approaching to discuss on the design, synthesis, characterisation of the interlocked molecules, students should understand the following key topics:

1. **Supramolecular Chemistry**: It is the study of macromolecular chemical systems formed by the non-covalent interaction of several molecules. The concept of supramolecular or host-guest Chemistry focuses on how molecules recognize, assemble, and function together through hydrogen bonding, metal coordination, van der Waals forces, and π-π stacking interactions, rather than *via* conventional covalent bonds[23].
2. **Mechanically Interlocked Molecules (MIMs)**: **Pseudorotaxanes, Rotaxanes and Non-Covalent Interactions**: The concept of mechanically interlocked molecules had been an attraction of supramolecular chemist since last 2-3 decades and as a consequence of that Stoddart, Sauvage got the Nobel Prize along with Feringa on 2016 for working on it[24]. Pseudorotaxanes are a precursor to synthesise rotaxanes, a mechanically interlocked molecule (MIM). In summary, MIMs are species in which two separate moieties (here rod or dumbbell likes axle molecule and wheel) are conjoined or interlocked with no inter-component covalent bonds[25]. Representative pictures of such complex molecular architectures are shown below.

Pseudorotaxanes are considered the starting backbone for generating interlocked molecules through threading followed by capping method.[11] These are the chemical species on which a rod like axle molecule is surrounded by macrocyclic ligand. The Nomenclature of psedurotaxane depends on how many components (rod-like and wheel-like molecules) are entangled. The nomenclature is based on the number of components in the threaded system without covalent bonds. According to IUPAC, the pseudorotaxane and rotaxane uses the prefix within the third bracket, which indicate the number of components. For example, (i) if there is one axle (or axle with the stopper) and one wheel are present then the species will be called as [2] pseudorotaxane (or, [2]rotaxane) , (ii) if there is one axle (or axle with stopper) and two wheel are present,

then it will be [3]pseudorotaxane (or, [3]rotaxane) and so on[26] (Fig. 1, Fig. 2).

[A] Capping Process

[B] Clipping Process

Pseudorotaxanes are formed *via* cation[27], anion templation[28] and also *via* π-π stacking interaction[29]. Various methods like capping,[11] clipping[30] are common in literature in the context of rotaxane formation. Particularly, where pseudorotaxane formation occurs, and it used as precursor for the formation of rotaxane, capping method is applied[11] (Fig. 3).

3. **Functional Group Transformations and Click Reaction**: Designing of macroscopic components needs various functional group transformations such as substitution reactions[31], imine bond formation[32], imine bond reductions[33], amide formation[34], cyclo-addition reaction[35], *etc*. during the syntheses of wheel and axle. For capping process, Click Chemistry, *i.e*. the copper(I)-catalyzed azide–alkyne cycloaddition reaction, is a common and variously for quick and efficient joining of two or more molecular components with azide and terminal alkyne functionalities. 1,2,3-triazoles forms *via* cycloaddition reaction[36]. This reaction is widely valued due to its mild reaction conditions, high yield, high selectivity, wide-ranging functional group tolerance, and compatibility with biological and materials systems[37]. In recent times, it is a foundation of modular synthesis in chemical biology[37], materials science[38], and Supramolecular Chemistry[39]. Due to the various usage of click reaction including in the medicinal fields, the Nobel Prize was awarded to Carolyn R. Bertozzi, Morten Meldal, and K. Barry Sharpless in the year of 2022 for working on such cyclo-addition reactions[40].
4. **Metal-ligand coordination**: Metal ligand coordination concept is very popular in the field of coordination Chemistry where a chelating multidentate ligand is attached with metal ion with coordinate bonds.
5. **Orthogonal Strategy**: In rotaxane synthesis, an orthogonal strategy involves the usage of distinct and independent chemical reactions to build the components of the pseudorotaxane and/ or rotaxane in spite of having multiple functional groups. This strategy assists the components of interlocked precursors to assemble them *via* target specific reactions or self-sorting. This approach confirms that the formation of one part of the molecule does not hinder the formation or assembly of another part.
6. **Template direct synthesis**: Template-directed synthesis is a method used to create molecules or materials having multiple functional groups by using a template molecules or ions into a desired product. This technique is mostly useful for

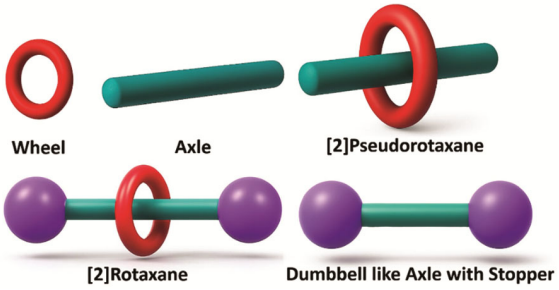


Fig. 1 — Cartoon diagram of Macrocycle, Axle, Axle with Stopper, Pseudorotaxane and Rotaxane

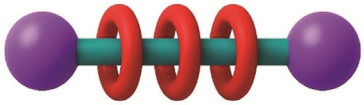


Fig. 2 — Cartoon diagram of [3]Rotaxane

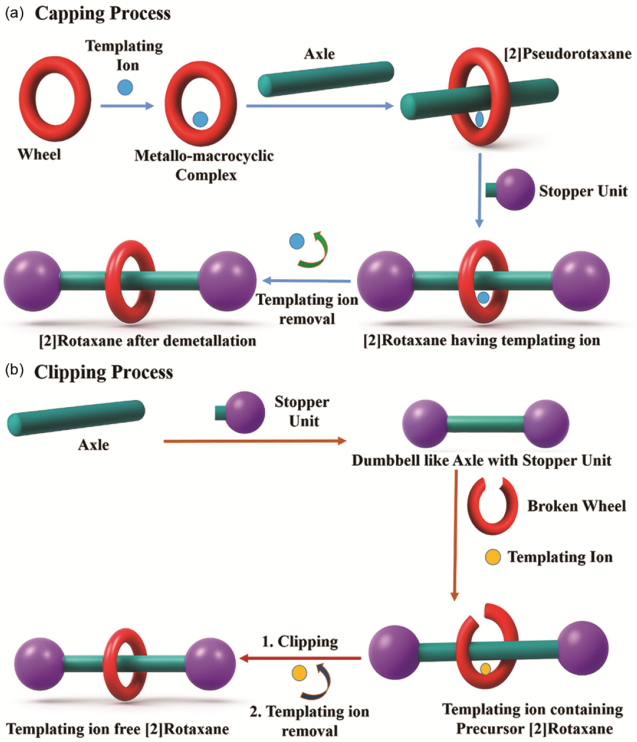


Fig. 3 — Schematic Representation of the various synthetic strategy of Pseudorotaxane, Rotaxane formation via ion templation; [A]: Capping Process; [B]: Clipping Process

producing assemblies that are little difficult to synthesize using traditional methods. In case of interlocked molecules, such templates help to accumulate wheels or axles in proper orientation.

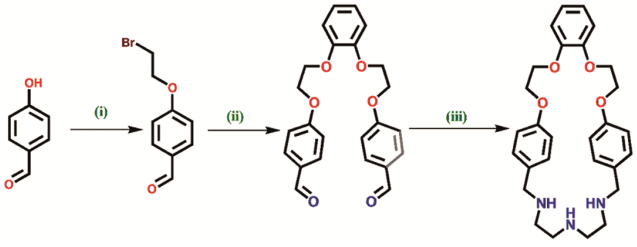
Pedagogical Integration and Learning Outcomes

Students should be able to (i) understand the designing aspects and synthesis of rotaxanes, (ii) understand the concept of mechanical bond formation, (iii) gather knowledge on the topic of application of rotaxanes such as drug delivery, recognition, sensing, catalysis and this area also integrates the concept of organic Chemistry concept accordance to its synthesis part, inorganic Chemistry *via* ion sensing, materials science *via* surface immobilization of MIM's, and chemical biology and thus offering a truly interdisciplinary topic, (iii) analyse spectroscopic data, (iv) apply synthesis knowledge creatively, moving beyond memorization to design-based learning which may assist them for higher order thinking, (v) analyse literature and designing their own systems, students engage in scientific reasoning, literature review, and problem-solving which may develop the research Skill.

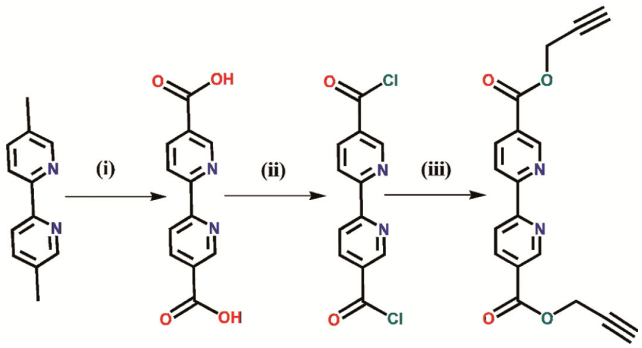
Experimental Overview and Synthetic Strategy:

The metal ion template pseudorotaxanes and further formation of rotaxane *via* capping method is discussed in this article. Details of the synthetic strategies are demonstrated in Schemes 1-5. Formation of wheel *via* high dilution methodology is an interesting for the under graduate students to learn about judicial choice of starting materials and slow addition to avoid polymerisation. The wheel synthesis was followed as mentioned in the report published by Ghosh *et al*. *via* high dilution methodology *via* Scheme 1 [41].

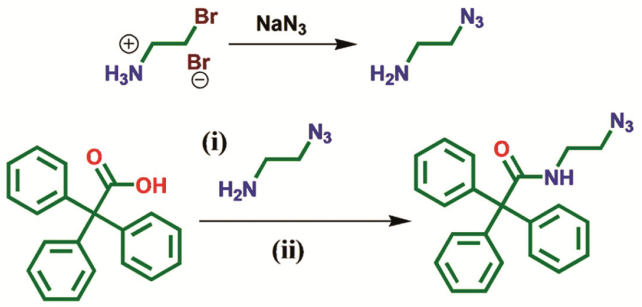
5, 5' dimethyl 2, 2' bipyridine and its derivatives having alkyne end (Fig. 4) is chosen as the linear thread to coordinate with the metallo-macrocycle



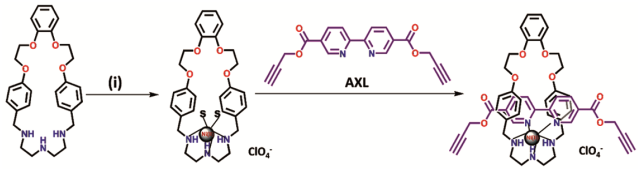
Scheme 1 — Synthesis of Macrocycle(**MC**): (i) 1,2-dibromoethane, K_2CO_3, CH_3CN, reflux; (ii) Catechol, K_2CO_3, DMF, reflux; (iii) diethylenetriamine, $CHCl_3/CH_3OH$, $NaBH_4$



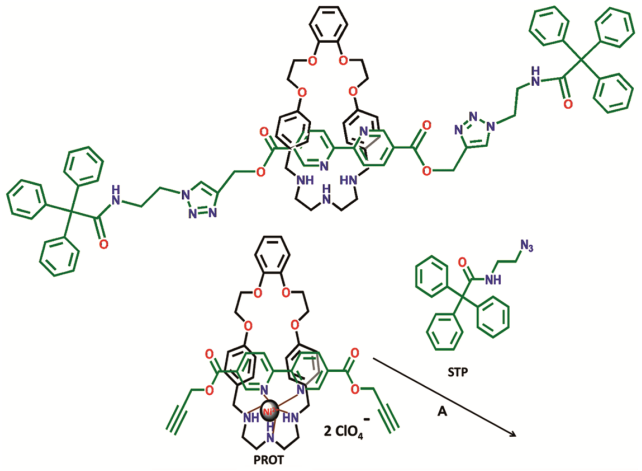
Scheme 2 — (i) $K_2Cr_2O_7$, H_2SO_4, 100°C, reflux, (ii) $SOCl_2$, reflux, then, (iii) 2-propyn-1-ol, Et_3N, 0°C, THF



Scheme 3 — (i) 1-Ethyl-3-(3-dimethylaminopropyl)carbodimide hydrochloride, Hydroxybenztriazole, DMAP, RT, then (ii) 2-amino ethyl azide, 0°C



Scheme 4 — Synthesis of PROT: (i) $Ni(ClO_4)_2$. $6H_2O$ in DCM, Methanol (1:1), S: Solvent molecule



Scheme 5 — Synthetic route of **ROT** starting from the alkyne terminated pseudorotaxane (**PROT**) and azide terminated stopper unit (**STP**), **A**: $Cu(CH_3CN)_4PF_6$, Na_2CO_3, CH_3CN, then demetallation using Na_2EDTA

complexes of **MC** (Fig. 4)*via* [3+2] orthogonal mode of orientation where tris and bis-coordinations are satisfied by the wheel and axle components respectively. A bulky stopper unit having azide terminal (Fig. 4) is chosen to develop rotaxanes upon capping through click reaction. Formation of metal template rotaxane followed de-metallation using strong chelating ligand ethylenediaminetetraacetic acid yielded the [2]rotaxane.

Synthesis of Alkyne terminated axle (AXL): The axle unit was prepared using 5, 5′ dimethyl 2, 2′ bipyridyl as starting material. The methyl group is oxidised using $K_2Cr_2O_7$ in presence of concentrated H_2SO_4. Then the acid is converted to di acid chloride using thionyl chloride. Then, esterification reaction of di acid chloride using propargyl alcohol in presence of triethyl amine results dialkyne terminated axle (AXL) as shown in Scheme 2. Detail synthetic strategy is discussed in the experimental section.

Synthesis of Stopper (STP): The stopper unit is synthesised upon reaction of triphenyl acetic acid with 1 ethyl-3-(3-dimethyl aminopropyl) carbodimide hydrochloride (EDCI) and 1-hydroxy benztriazole (HOBt) as starting material as shown in Scheme 3.

[2]Pseudorotaxane Formation: This bis-alkyne terminated linear type axle molecule AXL is used to synthesise of Ni^{II} templated [2]pseudorotaxanes *via* heteroleptic threaded complexes formation (Scheme 4). The term heteroleptic is used because the metal ion is coordinated by two hetero ligands *i.e*. one wheel and one axle. The [2]pseudorotaxanes (**NiPRT**) are synthesized upon reaction of **MC** (1.0 equivalent) with **AXL** (1.0 equivalent) in presence of $Ni(ClO_4)_2$ (1.0 equivalent) respectively in CH_3OH/CH_2Cl_2 solution at RT.

The ESI-MS spectra of **NiPRT** show prominent peaks at *m*/*z* =953.95 and 427.51that correspond to [**NiPRT**-ClO_4]$^+$, and [**NiPRT**]$^{+2}$ respectively (Fig. 5).

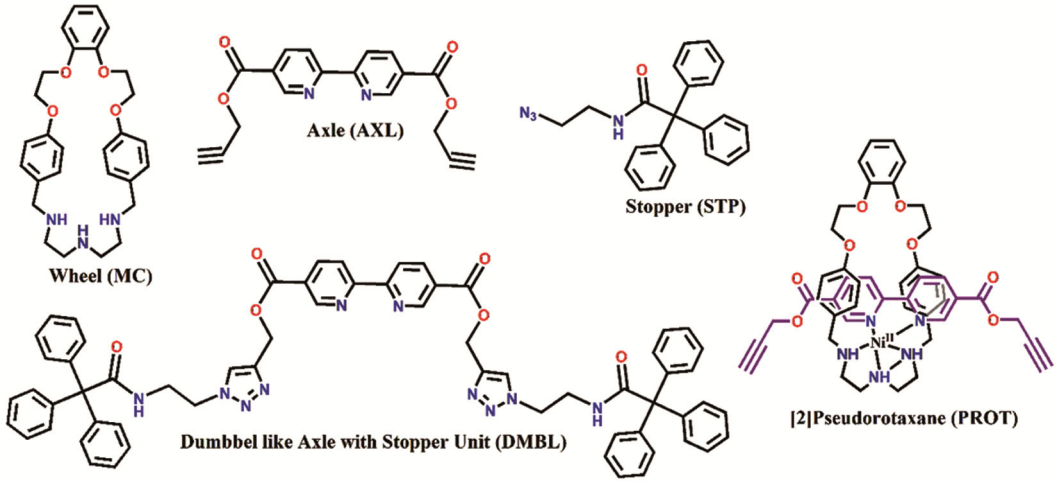


Fig. 4 — Chemical structures of the various parts of interlocked molecules

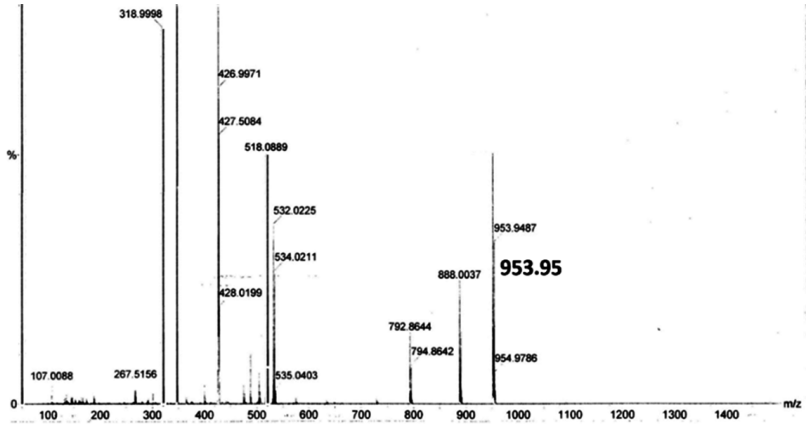


Fig. 5 — ESI-MS Spectrum of [2]Pseudorotaxane

Thus, ESI-MS of **NiPRT** clearly indicates 1:1:1 ternary complexation of wheel, axle and templating ions (Ni^{II}) in [2]pseudorotaxanes.

[2]Rotaxane Formation: Reaction of alkyne terminated **NiPRT** with azide-terminated amide functionalized stopper STP in presence of a catalytic amount of $Cu(CH_3CN)_4PF_6$ followed by *insitu*de-metallation results metal free [2]rotaxane, **ROT** (Scheme 5). [2]Rotaxane **ROT** is purified by column chromatography (SiO_2: 4% CH_3OH in CH_2Cl_2) in 35% yield. Free axle with stopper, **AXL** is also isolated during purification process by column chromatography.

Formation of [2]rotaxane is confirmed by mass spectrometry (ESI-MS), 1D and 2D NMR ROESY NMR spectroscopy experiments. The ESI-MS spectrum of **ROT** shows peaks at *m*/*z* = 1510.30 and 755.63 that correspond to $[\mathbf{ROT}+H]^+$ and $[\mathbf{ROT}+2H]^{2+}$ respectively (Fig. 6).

Comparative ^1H NMR spectra of **wheel (MC)**, axle with stopper **AXL** and [2]rotaxane **ROT** in $CDCl_3$ are shown in Fig. 7. In the spectrum of **ROT**, the triazole C-H proton (H-e) and amide proton (H-h) of the axle component (Fig. 7c) within the interlocked structure are shifted downfield relative to the free **AXL**. These are the indication of the existence of H-bonding interaction within the inter-components of interlocked system. Bipyridine protons H-a, H-b and H-c of the axle and H-5, H-6 protons of the wheel in **ROT** (Fig. 7b) show upfield shifts with respect to its non-interlocked counter parts due to the diamagnetic anisotropy effect (Fig. 7a, Fig. 7c). Such chemical shifts indicate that these protons are present within the shielding region composed of aromatic moieties of the wheel and axle in **ROT** (Fig. 7b). H-7 of wheel (Fig. 7a) and H-d of axle (Fig. 7c) shows upfield shift upon interlocking (Fig. 7b). Additionally, the two sets of methylene protons *i.e.* (H-8, H-9) and (H-3, H-4) of the macrocycle components are appeared almost isochronous in the free wheel (Fig. 7a), upon interpenetration, those are resonating in different ppm values (Fig. 7b) which is indicative of the reduced symmetry of these protons in the interlocked structure of **ROT**.

Two dimensional ^1H-^1H rotating-frame Overhauser effect spectroscopy (ROESY) spectrum displays several through space cross-coupling interactions between the two components of [2]rotaxane. Important interactions include (H-5 and H-a), (H-5 and H-b), (H-5 and H-c), (H-5 and H-d), (H-5 and H-e) and (H-6 and H-a), which indicate that the bipyridine moiety of the axle are close in space into the wheel cavity, which further confirms the interlocked architecture of the **ROT** in solution (Fig. 8).

Hazards

Students must wear an apron and safety goggles before entering the lab. Additionally, they are provided with gloves wherever necessary. Hydrochloric acid (HCl), Sulphuric acid (H_2SO_4) and sodium hydroxide (NaOH) are corrosives and can cause potential skin burns/ irritation and eye damage. Similarly, due to the toxic and volatile nature of some organic solvents like chloroform. diethyl ether, as well as some other reactants, all chemicals must be

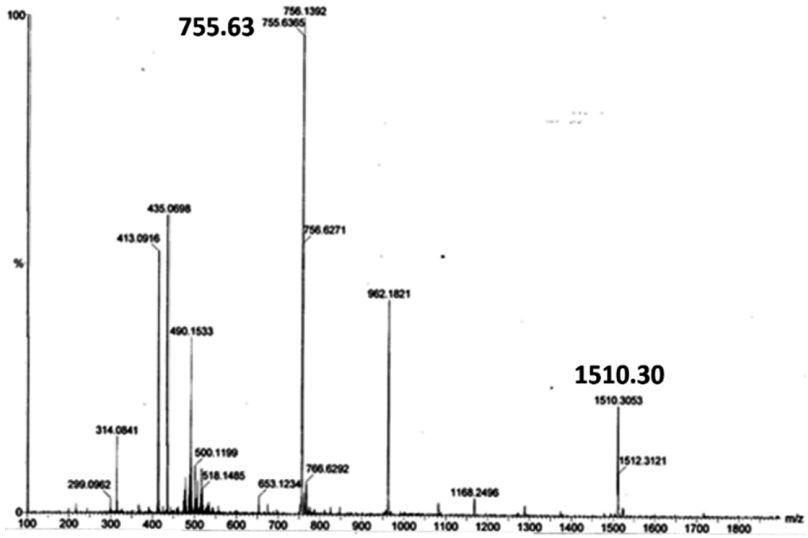


Fig. 6 — ESI-MS Spectrum of [2] Rotaxane

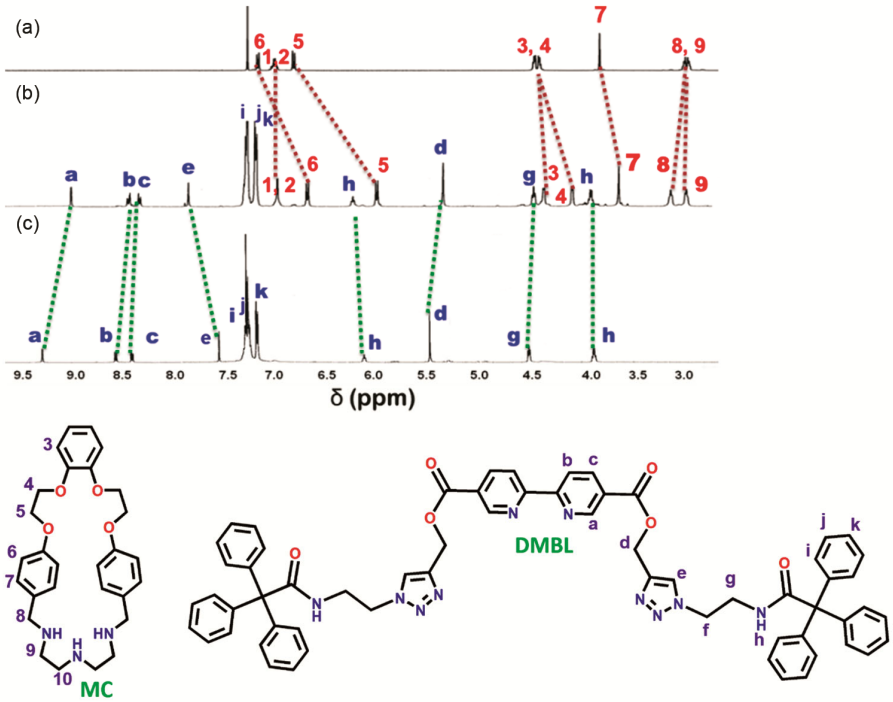


Fig. 7 — Partial stacked ^{1}H NMR spectra (300 MHz) of (a) macrocycle **MC** (top); (b) [2]rotaxane **ROT** (middle); free axle **DMBL** (bottom) in $CDCl_3$ at 298K (the labels correspond to those shown in insert pictures of **MC** and **DMBL**)

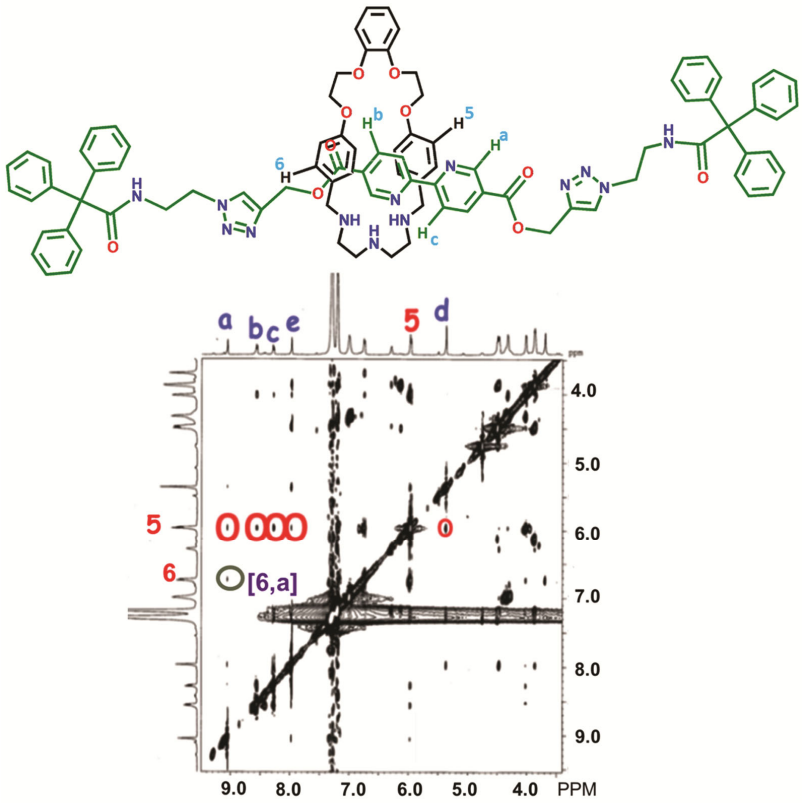


Fig. 8 — ROESY NMR spectrum of ROT (bottom), Chemical drawing showing through space interaction between the different components of the interlocked species (top)

handled cautiously in a well-ventilated fume hood. Safety information for all reagents is available *via* the appropriate Safety Data Sheets[42].

Activity Proposal

The Ministry of Education, Government of India has implemented the NEP 2020 curriculum in which internship and project are mandatory for the under graduate (UG) students with 4 years Chemistry Honours with Research course. The method described herein can be prepared with the involvement of UG students. The internship is mandatory and comprises up to 120 h for a candidate granting participants a certificate and score which is included as an additional merit in their academic records (Academic Bank of Credit). Additionally, a research work has to be carried out at the final year[43]. Throughout the internship and research work tenure, students have ample of opportunities to put the knowledge of classroom theory into practice through specific research and laboratory experiments.

This experiment has been designed to involve the project students in a fragmented way that students can do the experimental work in small groups. Internship students may involve synthesising the interlocked systems' various parts (ring component, axle, metallo-macrocyclic complexes, pseudorotaxane formation, rotaxane formation, purification by column chromatography, *etc*.). During the research period at higher semester, students may change the reaction conditions, solvents to check the variation of yields and reaction times. Some may design their own interlocked systems followed by characterization. Some may involve in the metal ion complexations studies of the interlocked systems *via* absorption spectroscopy. However, all the students should analyse the ESI-MS, NMR, *etc*. spectroscopic data by themselves, and the assessment can be done individually. Seminar Session can be conducted based upon literature reviews followed by presenting of their experimental findings.[13]

Experimental Section

Synthesis of Axle (AXL)

The axle fragments, di-alkyne-di-ester-2,2′-bipyridine [prop-2-ynyl 6-(5-((prop-2-ynyloxy) carbonyl) pyridin-2-yl) nicotinate]is synthesised in good yield in three steps starting from 5,5′-dimethyl 2,2′-bipyridine (Scheme 2). First, 5,5′-dimethyl 2,2′-bipyridine(0.184 g, 1.0 mmol) is oxidized with potassium dichromate (1 g, 3.5 mmol) in presence of sulfuric acid (50 mL), which affords 2,2′ bipyridyl 5,5′-dicarboxylic acid [6-(5-carboxypyridin-2-yl) nicotinic acid] (0.242 g, Yield: 99%) The NMR of this di acid was checked with the literature value as it is a reported compound.[4] Then di acid is reacted with thionyl chloride to synthesis corresponding di-acid chloride [6-(5-(chlorocarbonyl)pyridin-2-yl)nicotinoyl chloride]. This compound was not isolated and the crude was used directly in next step. However, the di acid chloride compound is preserved under vacuum.

Then, to a solution of propargyl alcohol (0.129 g, 0.132 mL, 2.3 mmol) and NEt_3 (0.348 mL, 2.5 mmol) in dry THF (25 mL), 2,2′-bipyridine-5,5′-diacid chloride (281 mg, 1 mmol) dissolved in dry THF (10 mL) was added drop-wise using a pressure equalizing funnel. The mixture was allowed to stir in nitrogen atmosphere at 0°C temperature for 1h, then additional 3h at RT. An off white precipitate was then developed which was filtered. The precipitate was washed with $NaHCO_3$ solution (50 mL), water (100 mL) and dried in vacuum to obtain AXLas an off white solid. Yield 0.256 g, (80%). ESI-MS *(+ve)*: *m/z* Calcd for $C_{18}H_{12}N_2O_4$ $[M+H]^+$, 321.07. Found: 321.06; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.57 (s, 2H, -C*H*), 4.99 (s, 4H, -CH_2), 8.47 (m, 2H, Ar-*H*), 8.61 (d, 2H, *J* =10Hz, Ar-*H*), 9.32 (s, 2H, Ar-*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.2, 75.9, 77.5, 121.8, 126.1, 138.7, 151.1, 158.9, 164.4. Anal. Calcd for $C_{18}H_{12}N_2O_4$: C, 67.50; H, 3.78; N, 8.75. Found: C, 67.87; H, 3.89; N, 8.65%.

Synthesis of STP

To a stirring solution of triphenyl acetic acid [2,2,2-triphenylacetic acid] (576.3 mg, 2.0 mmol, 2.0equivalent.), 1 ethyl-3-(3-dimethyl aminopropyl) carbodimide hydrochloride (383.4.0 mg, 2.0 mmol, 2.0 equivalent) and 1-hydroxy benztriazole (HOBt) (270 mg, 2.0 mmol, 2.0 eqv.) is added in 0.5 min interval and the resulting reaction mixture is stirred for another 1h. After that 2-amino ethyl azide (190 mg, 2.2 mmol, 2.2 eqv.) was added dropwise at ice cold condition. The reaction mixture was stirred additionally for 6h at RT and after that it was evaporated and purified by using silica gel (as stationary phase) column chromatography by using 10% ethyl acetate and pet ether as eluent. Yield 460 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.47 (s, 4H, -CH_2), 6.13 (b, 2H, -*NH*), 7.23-7.33 (m, 15H, Ar-*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.0, 67.5, 75.3, 127.1, 127.9, 130.4, 142.2, 173. Anal. Calcd for

$C_{22}H_{20}N_4O$: C, 74.14; H, 5.66; N, 15.72. Found: C, 74.80; H, 5.26; N, 15.78%.

Synthesis of [2]Pseudorotaxane, PROT:

A solution of $Ni(ClO_4)_2$, $6H_2O$ (36.6 mg, 0.1 mmol) in CH_3OH (5 mL) was added to a solution of **MC** (47.7 mg, 0.1 mmol) in CH_3OH/CH_2Cl_2 (1:1, 5 mL) at RT. The dialkyl axle **AXL** (32.0 mg, 0.1 mmol) was added to this solution. The resultant mixture was stirred for 4h, and the solvent was evaporated. The solid was washed repeatedly with CH_2Cl_2 and dried in vacuum to give pure product **PROT** respectively, yields: 86 mg (80.28%). Complexes were characterized by ESI-MS and elemental analysis. Data for **PROT**: ESI-MS (*+ve* mode) *m/z* Calcd for $C_{46}H_{47}ClN_5NiO_{12}$: 954.23. Found: 953.95. Anal. Calcd for $C_{46}H_{49}Cl_2N_5NiO_{17}$: C, 51.47; H, 4.60; N, 6.52. Found: C, 52.05; H, 4.95; N, 6.89%.

Synthesis of ROT

PROT (214.23 mg, 0.2 mmol) and stopper unit **STP** (142 mg, 0.4 mmol) were suspended in 4mL of 1:1 CH_2Cl_2/CH_3CN solution. Sodium carbonate (0.010 g, 0.10 mmol) was added as a base in solid form, followed by the addition of $Cu(CH_3CN)_4PF_6$ (112 mg, 0.3 mmol) as catalyst in glove box. The reaction was stirred 6h at RT. Then the reaction mixture was evaporated and 20 mL saturated solution of Na_2EDTA in water was added to the crude and stirred for 72h. The solution was poured into 25.0 mL of $CHCl_3$ and washed with water. Then the organic layer was evaporated in reduced pressure to obtain an yellowish solid.The resulting solid was purified by neutral alumina based column chromatography by using 3% CH_3OH/CH_2Cl_2 as eluent to afford 170 mg (56.3%) of the targeted [2]rotaxane, **ROT**, along with free axle.

ROT: ESI-MS (*+ve*): *m/z* Calcd for $C_{90}H_{88}N_{13}O_{10}$ $[M+H]^+$: 1509.68. Found: 1510.30. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.84 (s, 4 H, -CH_2), 2.98 (s, 4H, -CH_2), 3.31 (s, 4H, -CH_2), 3.51 (s, 4H, -CH_2), 3.80 (d, 4H, *J* = 5.6 Hz, -CH_2), 3.99 (b, 4H, CH_2), 4.27 (d, 4H, *J*= 5.6 Hz, -CH_2), 4.38 (b, 4H, -CH_2), 5.28 (s, 4H, -CH_2), 5.96 (d, 4H, *J* = 8.4 Hz, Ar-*H*), 6.19 (b, 2H, -*NH*), 6.66 (d, 4H, *J* = 8.4 Hz, Ar-*H*), 6.96 (s, 4H, Ar-*H*), 7.16-7.30 (m, 30 H, Ar-*H*), 7.85 (s, 2H,-C*H*), 8.36 (d, 2H, *J* = 8.4 Hz, Ar-*H*), 8.47 (d, 2H, *J* = 8.4 Hz, Ar-*H*), 9.05 (s, 2H ,Ar-*H*). Anal. Calcd for $C_{90}H_{87}N_{13}O_{10}$: C, 71.55; H, 5.80; N, 12.05. Found: C, 71.59; H, 5.48; N, 12.89%.

DMBL: ^{1}H NMR ($CDCl_3$, 500 MHz, 298K): δ 3.87 (m, 4 H, -CH_2), 4.51 (m, 4H, -CH_2), 5.47 (s, 4H, -CH_2), 6.11(b, 2H, -*NH*), 7.14-7.28 (m, 30 H, Ar-*H*), 7.53 (s, 2H,-C*H*), 8.39 (d, 2H, *J* = 8.0 Hz, Ar-*H*), 8.55 (d, 2H, *J* = 8.0 Hz, Ar-*H*), 9.26 (s, 2H ,Ar-*H*). Calcd for $C_{62}H_{52}N_{10}O_6$. Found: C, 72.08; H, 5.07; N, 13.56. C, 71.87; H, 4.95; N, 14.01%.

The attempt to record the ^{13}C NMR spectra of the newly synthesised ROT, were unsuccessful due to the low solubility of the compound when a large amount is taken to record ^{13}C NMR and requirement of higher number of scans compared to ^{1}H NMR. Cartoon diagrams of Fig. 1, Fig. 2 and Fig. 3 are drawn using chatgpt upon providing suitable comments from the author and later edited as per the requirements.

Conclusions

The development of synthetic methods of a complex molecules having mechanical bonds has transformed the chemical space in which the supramolecular chemist's community can operate and in deed the chemists are doing so since last 2-3 decades. Multitudes of efficient synthetic strategies like passive[5] and active ion templation[44], H-Bonding[28], π-π stacking[29], Chalcogen Binding[45] interactions have been established. Apart from the traditional application mentioned in the introduction section, these MIMs are increasingly drawn the attention due usage in diverse areas like drug[46] and gene delivery[47], and as components in hydrogels[48] and batteries[49]. Thus, incorporation of the concept of interlocked molecules is very essential in the undergraduate level.

In this article, a new multi component [2]rotaxane has been synthesised. The research activity can be introduced to the undergraduate students of Chemistry for making them familiar with non-covalent interactions or mechanical bond. Incorporation of the theory of rotaxanes, pseudorotaxanes, synthetic strategy of these multicomponent reactions, analysis of various spectroscopic data may help in the internship and research program of the mentioned students.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

Acknowledgements

The author would like to acknowledge School of Chemical Science, Indian Association for the

Cultivation of Science, Kolkata for instrumental support. The author is also grateful to Professor Pradyut Ghosh for his constant support.

Conflicts of Interest

There are no conflicts of interest to declare.

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