Chapter 1

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Bolaamphiphiles are the molecules contain two hydrophilic head groups connected by a hydrophobic chain [1]. The synthesis, hierarchically self-assembled structures and application of bolaamphiphiles has been extensively studied as indicated by the large number of articles [2], reviews [3], and books [4]. The purpose of this chapter is to highlight the brief flavour towards principles, perspectives, and recent development of various amphiphiles and bolaamphiphiles to exploiting the supramolecular self-assemblies for fabrications of soft material towards their increasing potential hi-tech niche application.

1.1 General Overview

Beyond molecular chemistry based on the covalent bond, lies supramolecular chemistry, the chemistry aims at developing highly complex chemical system from components via intermolecular noncovalent interactions [5–7]. The objects of supramolecular chemistry are thus defined on one hand by the nature of the molecular components and on the other by the type of interactions that hold them together by secondary interactions such as hydrogen bonding, electrostatic, π–π stacking interaction, donor–acceptor interactions and metal–ion coordination, etc.

According to Nobel laurite Dr. J. M. Lehn “A supermolecule is an organized, complex entity that is created from the association of two or more chemical species held together by intermolecular forces”.

Over the past few decades, a supramolecular chemistry grown into a major field and has driven numerous developments at the interfaces with biology and physics, as a broad multidisciplinary and interdisciplinary domain providing a highly fertile ground for the synthetic chemists, scientists and researchers because of the fascinating novel molecular materials exhibiting unusual chemical and physical properties, investigating structure and function of biomolecules. Thus, it transcends the traditional divisional boundaries of science and represents a highly
interdisciplinary field. In the early 1960s, the discovery of “crown ethers”, “cryptands”, and “spherands” by Pedersen [8a], Lehn [8b] and Cram [8c] respectively, led to the realization that small, complementary molecules can be made to recognize each other through noncovalent interactions. Such “programmed” molecules can be self-assembled by utilizing these interactions in a definite algorithm to form large supramolecules that have different physicochemical properties than those of the precursor building blocks. Self-assembly of molecular species bridges the gap between the molecular world and nanotechnology. Starting with small building blocks, aggregation can lead to up to several 100th of nanometre-sized domains, which show special properties. Hereby the symmetry of the small building blocks influences the structure of the ensemble and the features of the bulk material.

Supramolecular research developed from its heart, i.e. the examination and understanding of the noncovalent interactions, are often weakly bound and highly dynamic, can be generates a complex architecture, often with a long range order [9]. The various type of general noncovalent interactions presented in figure 1. The knowledge of such noncovalent interactions used to build spontaneously generating well-defined, organised and functional supramolecular complex architecture by self-assembly, to understand the action of biomolecules and to implement function into molecular devices such as sensors [10], molecular transportation [11], mechanical movements and use as supramolecular catalysts [12]. Understanding, inducing, and directing self-processes are key to unravelling the progressive emergence of complex matter. Self-organization is the driving force that led up to the evolution of the biological world from inanimate matter to animate matter and beyond, to ultimately acquire the ability to create new forms of complex matter [13-15]. Clearly, molecular recognition processes are the ideal supramolecular reactions on which the other aspects are based. Cooperative action of multiple interactions leads to an aggregation, which could be results into supramolecular self-assembly. Most often, molecular recognition is not only one noncovalent interaction but the cooperative action of multiple interactions. This refers not only to individual noncovalent bonds, but to the whole shape and the whole electrostatic surface of the molecules involved in the self-assembly process.
Figure 1. Selective and effective recognition is achieved through various combinations of the above mentioned molecular non-covalent interactions.

1.2 Synthetic strategy of naphthalene diimide (NDI) derivatives

The first report on Naphthalene diimide (NDI) was published by Vollmann et al. in 1937. The pioneered work on NDI was initiated in the early 1970s by Hunig et al. [16] but came into culmination in the 1990s as researchers began to realize the potential of NDI as useful precursors in the field of supramolecular chemistry [17-18]. NDI's are generally neutral, planar, chemically robust, redox active compounds usually with high melting points and attracted much attention among the aromatic molecules because of their outstanding photophysical properties in addition to their versatility as supramolecular building blocks. Numerous methods have been developed towards the synthesis of symmetrical 2 and unsymmetrical 4 NDI's (figure 2) using conventional heating in DMF [19], microwave irradiation [20], and careful control of pH [21].

Figure 2. General strategy for synthesis of symmetrical and unsymmetrical NDIs
1.3 Supramolecular self-assemblies of NDIs: A brief review of literature survey

The NDIs are electron deficient aromatic compounds forms n-type semiconducting materials [3] and which are capable of self-organization in combinations with most favourable hydrogen bonding and π-π stacking interactions and are being incorporated into large multi-component assemblies through intercalation. These self-assembled π-conjugated materials could find the potential application [4] in the field of (i) supramolecular electronics as field effect transistors, photovoltaic devices, light emitting diodes and logic gates, (ii) materials sciences for sensing, and development of nano-dimensional soft architecture, (iii) biology for cellular uptake and cell imaging and (iv) medicinal for control release of drugs or its own biological potency.

We discussed here some recent examples of NDI amphiphiles and bolaamphiphiles towards fabricating supramolecular self-assemblies as follows-

1.3.1 Supramolecular self-assemblies of NDI amphiphiles

Elisabetta Iengo et al. [22] described a very efficient metal-mediated strategy of self-assembled non-symmetric triad 5 (NDI, an aluminium (III) porphyrin, and a ruthenium (II) porphyrin, figure 3) for photoinduced charge separation. The photophysics of the triad was investigated in detail using time-resolved spectroscopy in the pico- and nanosecond time domains. The strategy is of great potential interest as, while confining the synthetic effort to the single components, it can give access to a wide range of photoactive systems.

Figure 3. Molecular structure of NDI-porphyrin based non-symmetric triad 5.
George et al. [23] described a mixed donor–acceptor charge-transfer hierarchical self-assembly between dipyrene 6 (donor) and NDI amphiphile 7 (acceptor). Molecular structures of dipyrene 6 foldamer and NDI amphiphile 7 was shown in figure 4. Alternate (mixed) donor–acceptor arrangement of dipyrene 6 and NDI amphiphile 7 through charge transfer mechanism results into self-assembly and leads to fabricate into one-dimensional nanofibers.

![Dipyrane 6 and NDI amphiphile 7](image)

**Figure 4.** Molecular structures of the dipyrene 6 and NDI amphiphile 7 derivative.


![Triethyleneglycol core substituted NDI 8](image)

**Figure 5.** Molecular structure of triethyleneglycol core substituted NDI 8.
Ghosh et al. [25] described the hydrogen-bonding-mediated J-aggregation of a carboxylic acid appended NDI \( \text{NDI } 9 \) amphiphilic chromophore (figure 6), which resulted in white-light emission with a very high fluorescence quantum yield. Morphology of self-assembled material revealed presence of interconnected lamellar aggregates due to synergistic effect of \( \pi-\pi \) stacking and hydrogen bonding among carboxylic acid groups with possibly syn–syn catemer motif.

\[ \text{Figure 6. Molecular structure of NDI } 9 \text{ and illustration of H-bonding model of NDI } 9 \text{ emits white light.} \]

Parquette et al. [26] described the aqueous self-assembly of tube-forming lipid amphiphiles containing an n-type NDI chromophore amphiphiles \( \text{NDI } 10-12 \) appended with L-lysine (figure 7). NDI \( \text{NDI } 10 - 12 \) functionalized with lysine’s results aqueous self-assembly into 1D nanotubes with approximately 4–5 nm, which are among the smallest inner diameters comparable to carbon nanotubes. The nanotube assembly process is remarkably tolerant of head group variations. The versatility of this design strategy promises diverse applications in optoelectronics.
Figure 7. Molecular structures of n-type NDI chromophore amphiphiles 10-12 appended with L-lysine.

1.3.2 Supramolecular self-assemblies of NDI bolaamphiphiles

Sanders et al. [27] described the supramolecular self-assembly of N-Boc-lysine functionalised NDI bolaamphiphile 13 for the construction of helical nanotubes. Such self-assembled helical nanotubes act as selective receptor for condensed aromatic systems and quaternary ammonium ions 14a-b (figure 8) through molecular recognition. The selectivity is based on the relative size of the ion pairs and is a direct measured for the association strength between the nanotubes and ion pairs. These results suggest that the nanotubes have the potential to act as nanoscale reactors in which the effective molarity of the reactants is increased dramatically by complexations within the nanotube cavity.

Figure 8. Structures of L-lysine functionalised NDI 13 and receptor quaternary ammonium ions 14a-b.
Govindaraju et al. [28] demonstrated a bio-inspired design strategy to tune the self-assembly of tryptophan appended NDIs 15 & 16 by minute structural variations, π-π stacking, hydrophobic and metal-π interactions (figure 9). According to him J-type of aggregation induced by hydrophobic-effect while, H-type of aggregation induced by sodium-π interaction of tryptophan appended NDIs, which is confirmed by spectroscopic studies shows structural variations associated with the molecular assembly. The molecular organization has been successfully transformed to nanospheres, particles, nanobelts, fibers and fractals. Such drastic changes in the morphology were gives striking evidence for the importance of non-trivial weak non-covalent forces.

![Figure 9](image9.png)

**Figure 9.** Structures of tryptophane appended NDIs 15 & 16

Parquette et al. [29] synthesized the lysine based NDI bolaamphiphile 17 & 18 (figure 10) for the construction of hierarchical self-assembly of an n-type nanotube. The nanotube assembles via a monolayer nano-ring that further stacks into the nanotube structure. NDI 17 formed a transparent gel in water at concentrations as low as 1 % (w/w), and was stable in the gel state for several months. Transmission electron microscopy (TEM) and atomic force microscope (AFM) revealed the formation of micrometer-long nanotubes with uniform diameters of (12±1) nm. Such nanostructures might be used as components of light-harvesting devices.

![Figure 10](image10.png)

**Figure 10.** Structures of lysine functionalised NDIs 17 & 18.
Ghosh et al. [30] described the spontaneous vesicular assembly of a NDI based non-ionic bolaamphiphile 19 (figure 11) in aqueous medium by using the synergistic effects of π-π stacking and hydrogen bonding. Hydrazide H-bonding functionality of NDI 19 protects these moieties from the bulk water, and resulted in vesicular type of self-assembly. Furthermore, the electron-deficient NDI 19 could engage in donor–acceptor charge-transfer (CT) interactions with a water-insoluble electron rich pyrene leading to inter-vesicular fusion, which eventually resulted in rupturing of the membrane to form 1D fiber.

![Figure 11. Schematic illustration of vesicular and fiber assembly of NDI bolaamphiphile 19.](image)

Zhang et al. [31] described the supramolecular engineering of NDI bolaamphiphile 20 (figure 12), in which different building block can be simply added to the solution stepwise leading to the programmable evolution of the geometry of supra-amphiphiles as well as their self-assembled nanostructures in water. Preliminary, the directional charge-transfer interactions between NDI 20 and naphthalene derivative 21 results into H-shaped supra-amphiphile in water forms 2D nanosheets. Further, by complexations of the H-shaped supra-amphiphiles with pyrene derivatives, the 2D nanosheets transform into ultralong 1D nanofibers.

![Figure 12. Molecular structures of NDI bolaamphiphile 20 and naphthalene derivative 21.](image)
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1.4 Introduction of low-weight molecular gelators (LMWG)

Recently, systematic studies on LMWG have been undertaken, this research field has quickly blossomed and several reviews have been published in the last few years [32]. They can be considered as composite materials made of a three-dimensional (3D) supramolecular network imprisoning a large quantity of liquid. The driving force for the formation of gels can be van der Waals, hydrophobic, fluorophobic, π-π stacking, dipole - dipole, weak coordination interactions, or hydrogen bonds. Such LMWG have been continuously increasing the attention in areas ranging from chemistry and biology to materials science due to their potential applications, such as drug delivery [33], mechanical action [34], hydrophilicity or hydrophobicity modulation [35], optical and electronic effects [36] and so on. Despite a wide range of reported responsive materials, the mostly used stimuli involves are light [36], reaction [33] and heat [37]. Particular, alkanediamide skeleton plays the major contribution to LMWG supramolecular chemistry, which lies in the combination of systematic arrangement of α,ω-head groups and the formation of cooperative hydrogen-bond with intermolecular amide functionality or π-π interactions of terminal substituted groups. The internal connectivity between head groups produces an astonishing chemical and physical stability to gels. Very strong odd-even and chain length effects allow one to manipulate the rigidity of the molecular assemblies. A technical advantage of such compounds may be the low concentration at which aqueous or organic gels are formed and tends to remain straight, allowing for a small bend here and there. Only in three-dimensional crystals or liquid crystal helices do columns of very high curvature appear. During the past few years, the majority of LMWG reported to exhibit gelation ability included amino acids [38], fatty acids [39], carbohydrate [40], surfactants [41], quaternion-amine salts [42], and organometallic salts [43]. Since a number of combinations is allowed to synthesize these supramolecular materials, gels with many more structures and properties. The obtained physical gels are usually degraded by heating or addition of competing molecular components to regenerate the sols. Various materials based on these physical gels are expected, although the research aimed at their possible applications has started only recently.
1.5. Importance of phosphonates and phosphonic acids

Based on the topics discussed in the previous sections, literature survey reveals that very few reports depict, particularly, the use of phosphonate or phosphonic acid in construction of supramolecular nano-dimensional architecture. In medicinal chemistry, phosphonate compounds having own great biological importance often encountered as a bioisosteres of carboxylate in drug design [44]. Nature exhibits variety of phosphate esters and play crucial roles in various naturally occurring biological processes such as cell growth, metabolism, proliferation and differentiation, cell signaling, and gene expression [45]. Research, which bridges between materials chemistry and medicinal chemistry has shown increasing impact in the context of the rapidly developing biochemistry area. Over a short period of time, several design strategies based on phosphorous appended systems for the creation of functional architectures have been developed. Various bolaamphiphiles incorporated with cytidylic acid [46], oligoadenlyic acid [47], thymidylic acid [48], calixarene [49], resorcinarene [50] and porphyrin [51] were identified as most versatile building blocks in supramolecular chemistry. Recently, Iwaura et al. [46] fabricates the supramolecular helical nanofibers in lemon juice biomaterial using cytidylic acid appended bolaamphiphile through self-assembly. Iwaura et al. [47] also reported the self-assembly of a thymidylic acid-appended bolaamphiphile, with heteropolymeric DNA as a template, produced supramolecular helical nanofibers in the presence of specific target DNA. Similarly, Bhosale et al. [51] described the pH dependent molecular self-assembly of octaphosphonate porphyrin results into nanosphere and nanorod construction by carefully control of pH. Schrader et al. [52] investigated that the phosphonic acid motifs act as new hydrogen bonding receptors for guanidium ion recognition have been intensively investigated. In particular, Phosphonic acid group shows remarkable selectivity towards zwitterionic basic amino acids and among them arginine is most attractive because it most often involved in selective protein contacts with DNA and RNA [53]. It plays vital role in living systems for many critical molecular recognition processes, cell division, immune function, hormones releasing and proximate (immediate) precursor of urea, orthinine and agmatine [54].
1.6 Organization of the thesis

This thesis is organized in seven chapters in which chapter-1 explains the brief introduction about amphiphiles, bolaamphiphiles and importance of phosphonates in supramolecular chemistry, followed by synthesis and characterization of the phosphonic acid functionalised amphiphiles and bolaamphiphiles and phosphonate ester linked various hydrophobic alkanediamide derivatives included in chapter-2. The self-assembly properties of both amphiphiles and bolaamphiphiles are discussed in chapter-3 (Part A-D), followed by organogelation properties of phosphonate ester appended hydrophobic alkanediamide derivatives presented in chapter-4. Next, chapter-5 explains about the biological activity of these phosphonated compounds towards cytotoxicity. Synthetic procedures, characterization methods and all relevant spectroscopic data briefly presented in chapter-6 as experimental. The last chapter-7, as annexure was focus on the sensing property of fluorescent chemosensor probe for the sensitive and selective detection of Pb$^{2+}$ and Fe$^{3+}$ metal ions as an annexure.

1.7 References


