Chapter

Anion-π Catalysis: A Novel Supramolecular Approach for Chemical and Biological Transformations

Ishfaq Ahmad Rather and Rashid Ali

Abstract

Catalysts by virtue of lowering the activation barrier helps in the completion of a chemical reaction in a lesser amount of time without being themselves consumed. Utilizing the diverse non-covalent interactions in the design and construction of catalysts, recently anion-π interactions were also introduced, giving rise to an emerging field of anion-π catalysis. In the newly constructed anion-π catalysts, significant lowering of activation energy occurs by virtue of anion-π interactions. Till now, several important reactions generating chiral centers have been carried out on the π-acidic surfaces of anion-π catalysts, thereby revealing the significance of anion-π catalysis in the domain of asymmetric synthesis. The motive of this chapter is to highlight the role of anion-π catalysis in asymmetric synthesis and we surely believe that it will offer new opportunities in supramolecular chemistry.

Keywords: anion-π catalysis, anion-π interaction, asymmetric synthesis, cascade reaction, enolate chemistry, naphthalene diimide, fullerene

1. Introduction

From the past few decades, non-covalent interactions have gained the new heights in the domain of catalysis and supported to construct functional systems of fundamental significance. Infact, the application of non-covalent interactions in the field of catalysis are nowadays studied under a separate branch of science known as supramolecular catalysis [1]. By virtue of non-covalent supramolecular interactions, not only the catalytic efficiency of the existed catalysts has been improved but the novel organocatalysts have also been developed [2]. Amongst various supramolecular interactions, the cation-π and anion-π interactions are most promising in the field of catalysis. In cation-π interactions, the cation interacts with π-basic aromatic systems possessing negative quadrupole moment ($Qzz < 0$), whileas in case of recently recognized anion-π interactions, the anion interacts with π-acidic aromatic systems possessing positive quadrupole moment ($Qzz > 0$). For example, benzene ($Qzz = -9B$) is π-basic in nature which makes it suitable to interact with cations through cation-π interactions (**Figure 1**) [3]. However, the interaction of anion with this system looks counterintuitive, as it will lead to repulsion between anion and π-electron cloud of benzene. For this purpose, researchers have

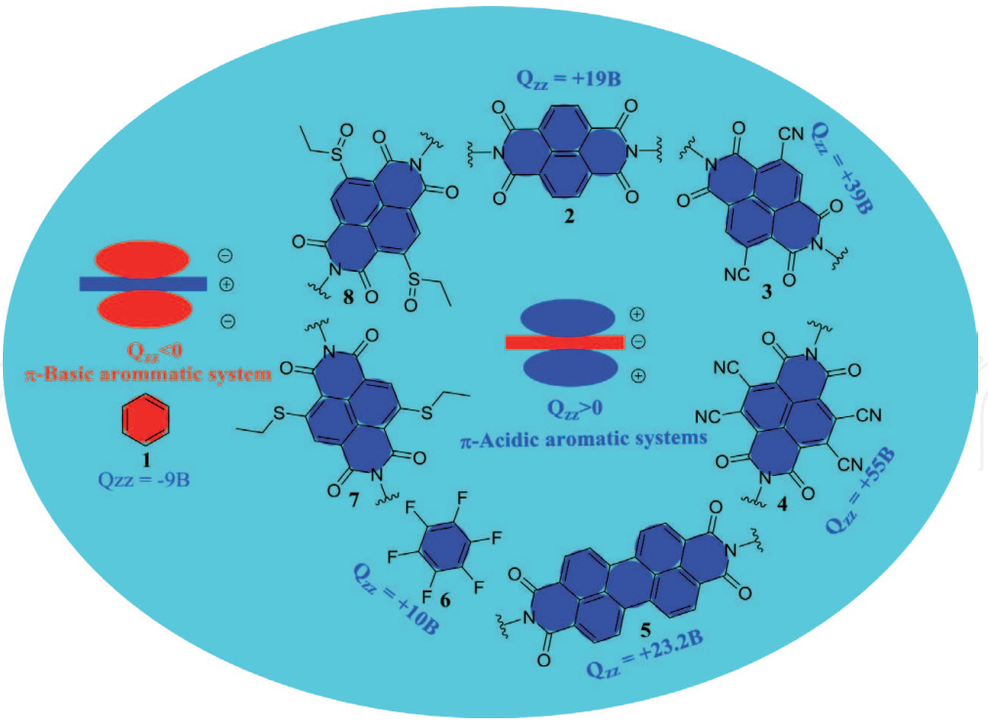


Figure 1.
Structures of diverse π-acidic aromatic systems.

inverted the intrinsic negative Qzz of aromatic systems into positive one (Qzz > 0) by attaching strong electron withdrawing substituents on aromatic systems. By virtue of this, they have generated various π-acidic aromatic scaffolds possessing strong positive quadrupole moment, which in turn interact with diverse anions through anion-π interactions (**Figure 1**) [4].

The recognition of anions is of paramount importance as anions are abundant in nature and play very essential biological role through participation in enzymatic reactions. The transport of anions across biomembranes during different biochemical events makes their recognition even more important [5]. Scientists around the globe are constructing diverse artificial anion receptors, which mimic the function of biosystems and involve anion-π interactions besides other non-covalent interactions in the recognition phenomenon of anions [6]. From the recent theoretical, computational, and experimental investigation, it has been observed that anion-π interactions have shown a promising role in supramolecular catalysis and has given rise to a new concept of anion-π catalysis. The emerging field of anion-π catalysis has not yet much explored in chemistry and until now only few reports are available in literature [7–9]. This is because of the fact that anion-π interactions have recently got experimental evidence, and also there is a dearth of π-acidic aromatic systems being the supreme prerequisite of these interactions [10]. Theoretical and experimental studies have revealed that anion-π catalysis works on the fundamental principle of the stabilization of anionic transition state on π-acidic aromatic surfaces. This stabilization in turn lowers the activation barrier of a particular reaction and hence leads to the formation of a selective desired product quickly under normal reaction conditions [11, 12]. The first evidence of anion-π catalysis came from the Matile's group after carrying out the transmembrane transport of anion by virtue of anion-π interactions [13]. Researchers have developed various anion-π catalysts by adapting different synthetic methodologies [7–9]. It is not feasible herein to discuss such methodologies, but for the convenience of the readers, we have assembled a group of anion-π catalysts used in this chapter (**Figure 2**) [11, 12]. In this chapter, we will discuss the role of these anion-π catalysts in various chemical reactions like

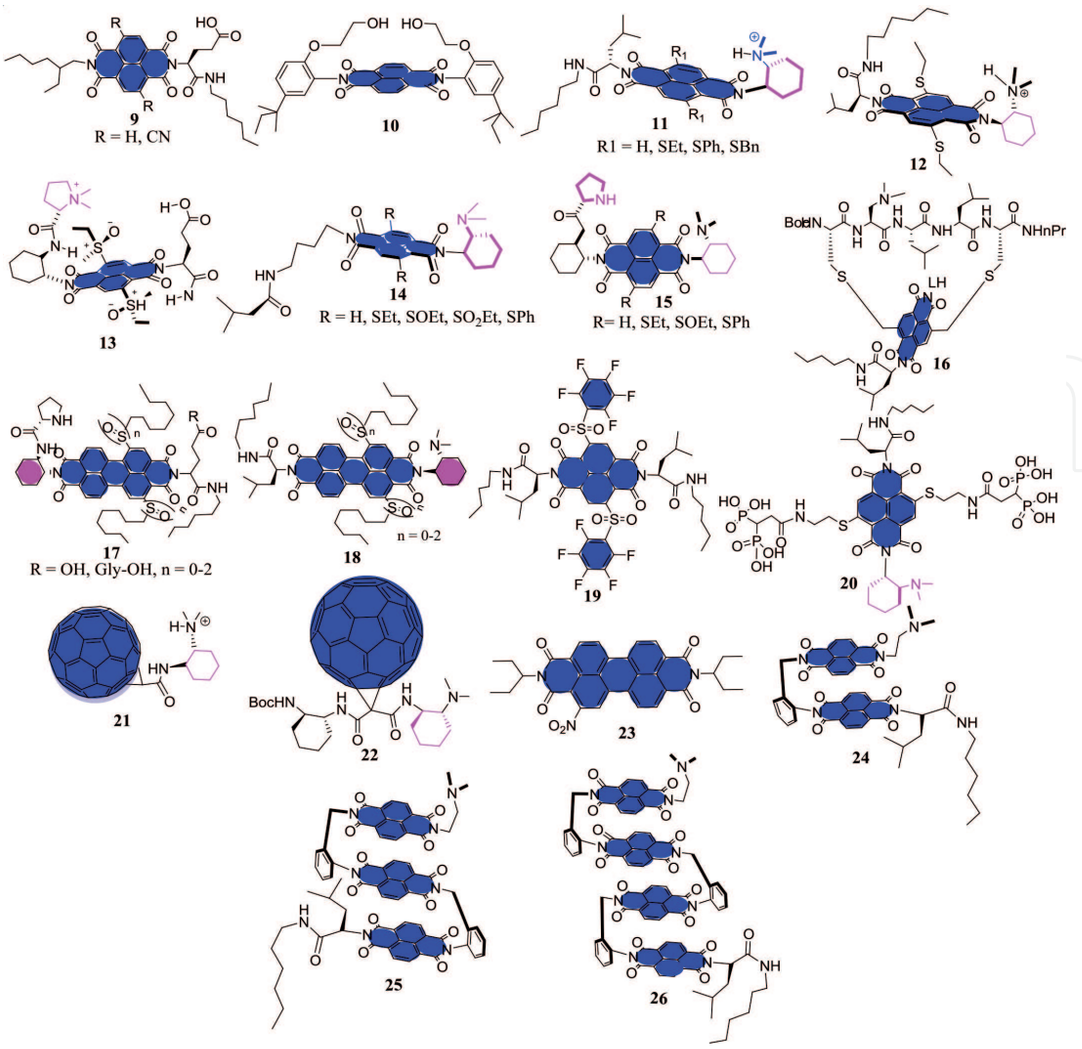


Figure 2.
Structures of various anion-π catalysts used in this chapter.

Kemp elimination, Michael-addition reactions, Diels-Alder reactions, and epoxide ring opening reactions followed by ether and polyether cascade cyclization reactions. Mostly these reactions involve the generation of chiral centers and hence are of prime importance in the arena of asymmetric synthesis.

2. Kemp elimination: a classical tool for anion-π catalysis

The Kemp elimination is a well-known reaction, which involves the abstraction of a proton from the carbon of the benzisoxazole substrate with the help of a catalytic amount of base. This reaction plays an essential biological role and has been documented as an ideal conventional tool for anion-π catalysis by Matile's group. They have carried out this reaction by virtue of the NDI-based anion-π catalysts possessing covalently linked carboxylate base and a solubilizer (alkyl tail) on the π-acidic surface [11]. There occurs the formation of phenolate in the anionic transition-state (**30**) after the proton is abstracted by a covalently attached carboxylate base of NDI based anion-π catalyst (**9**) from the carbon of the substrate (**27**). The anionic transition-state (**30**) acquires stability on the π-acidic surface of catalyst (**9**) by means of anion-π interactions with a magnitude of $\Delta\Delta GTS = 31.8 \pm 0.4$ kJ mol^{-1} along with a catalytic ability of 3.8×10^5 M^{-1} and the transition state recognition (K_{TS}) = 2.7 ± 0.5 μM (**Figure 3**). In order to circumvent the inhibition of the desired

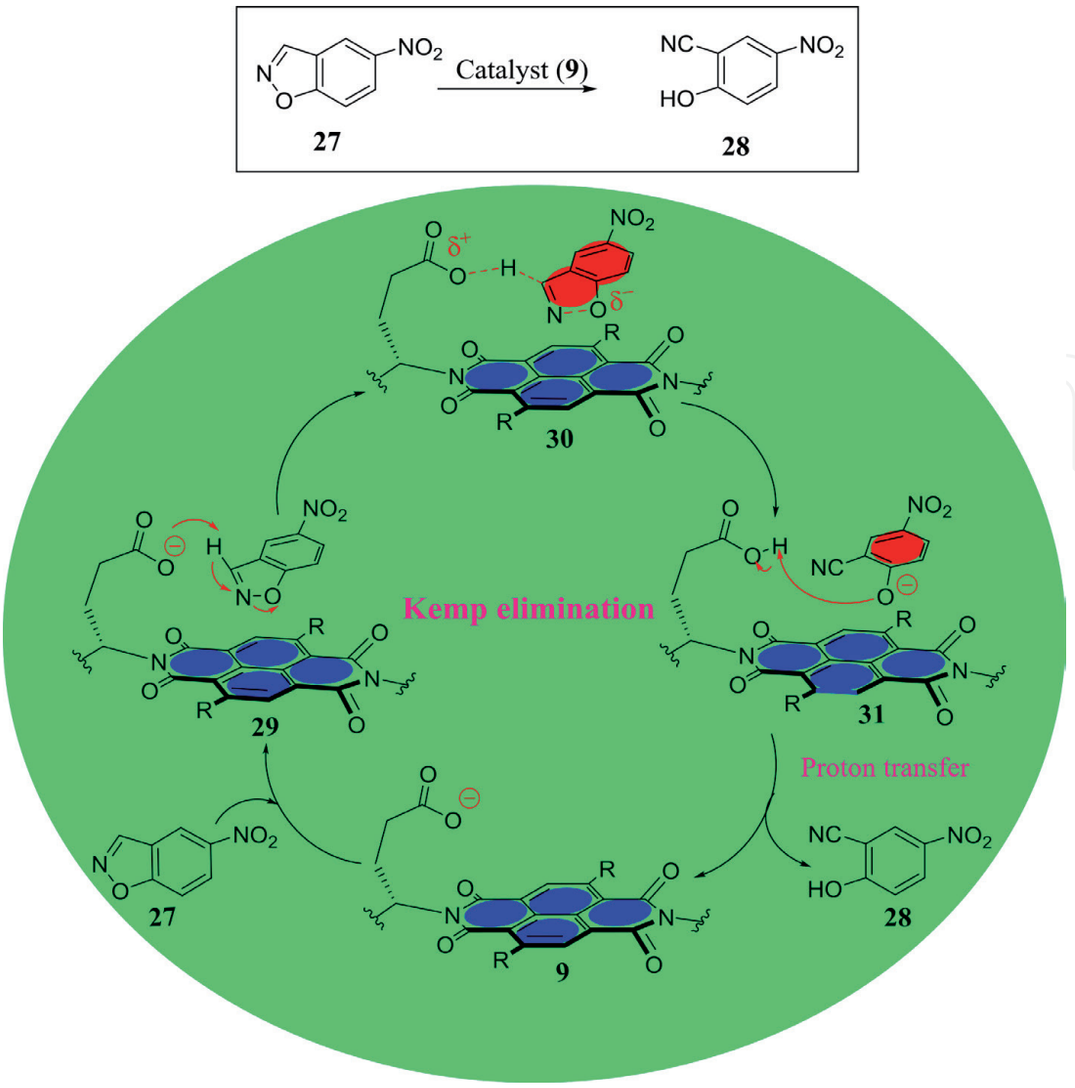


Figure 3.
Schematic illustration of Kemp elimination reaction along with a mechanistic cyclic pathway. Blue color depicts electron deficient and red color implies electron rich.

product, reactive intermediate (**31**) involves protonation of phenolate to yield the desired product **28** with the regeneration of the catalyst (**9**) (**Figure 3**) [11].

3. Michael-addition reactions through anion-π catalysis

Michael-addition, a powerful tool in organic synthesis is a nucleophilic addition reaction which involves the addition of a nucleophile to an *α*,β-unsaturated carbonyl compounds. It is considered as one of the significant atom economic methods to generate enantioselective and diastereoselective C-C bonds under mild reaction conditions. Knowing the fact that enolates play a vital role in both biology as well as chemistry, Matile's group has revealed the role of anion-π catalysis in enolate chemistry. They have computed the catalytic strength of enolate-π interactions by reporting numerous stereoselective Michael addition reactions on NDI based anion-π catalysts (**Figure 4**) [14–17]. From the ^{1}H-NMR studies, a substantial upfield shift of malonate protons has been observed in cases where the malonate group is covalently linked to the π-acidic NDI surface as compared to protons of unbound diethyl malonate group. This in turn leads to enhanced acidity of the associated malonate group by means of anion-π interactions. In fact, this upfield shift display the location of malonate α-protons above the π-acidic surface [15].

On the other hand, experimental studies have revealed that Michael-addition between malonic acid half thioester (**37**) and enolate acceptor **38** fails without anion-π catalyst and hence leads to solely the formation of a decarboxylation product **40**. Fortunately, the presence of anion-π catalyst for the same reaction leads to the formation of an addition product (**39**) selectively in comparison to decarboxylation product (**40**) (**Figure 5**) [16]. Besides these significant catalytic studies of anion-π interactions, the anion-π catalytic domain has now been explored to iminium, [18] enamine, [15] oxocarbenium, and transamination chemistry [19]. Since the Michael addition reactions through enolate chemistry has a significant relevance to several chemical and biological phenomenon, the outcomes of the studies carried out by Matile and teammates can take the domain of organocatalysis to a next level.

By virtue of positive molecular electrostatic potential (MEP), the fullerene (C_{60}) is considered as a potential candidate for anion-π interactions and has recently been introduced in the field of anion-π catalysis. The exceptional selectivity of fullerenes is actually due to localized positive potential areas termed as π-holes (**Figure 6**). By virtue of purest π-system, fullerenes offer a promising role in the exploration of polarizibility significance in a solution-phase anion-π catalysis [20]. Studies based on these facts have revealed a significant improvement in the selective addition of **37** to **38** by means of a fullerene based catalytic dyad **22** as well as catalytic triad **44** (**Figure 6**). Significantly higher selectivity was achieved after intercalating the methyl viologen **45** in between two fullerenes moieties of a catalytic triad **44** [21, 22]. Besides, the addition product selectivity over the decarboxylation product, conjugate addition protonation reaction of **46** and **47** generating 1,3-non-adjacent stereocenters have been also been carried out on the surfaces of anion-π catalyst **21** composed of fullerene (**Figure 6**) [23].

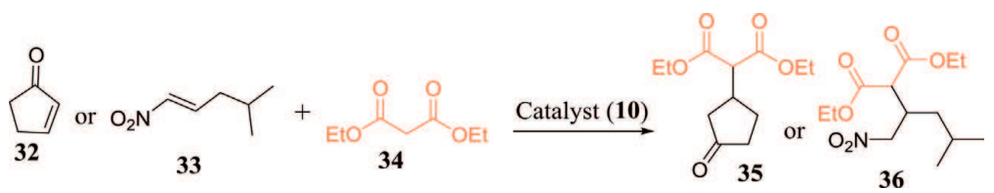


Figure 4.
Schematic representation of Michael addition reaction of **34** *with Michael acceptors (***32** *and* **33***) on the π-acidic NDI surface of* **10***.*

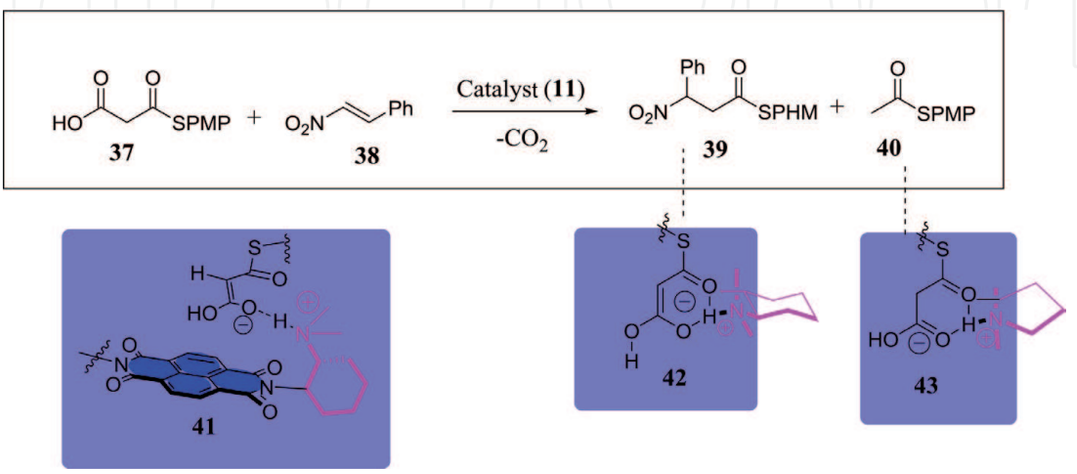


Figure 5.
*Addition (***39***) and decarboxylation (***40***) products in terms of Michael-addition between* **37** *and* **38** *catalyzed by NDI-based anion-π catalyst* **11** *(PMP = p-methoxyphenyl). The molecular structures of transition state (***41***) and of reactive intermediates (***42** *and* **43***) are also given.*

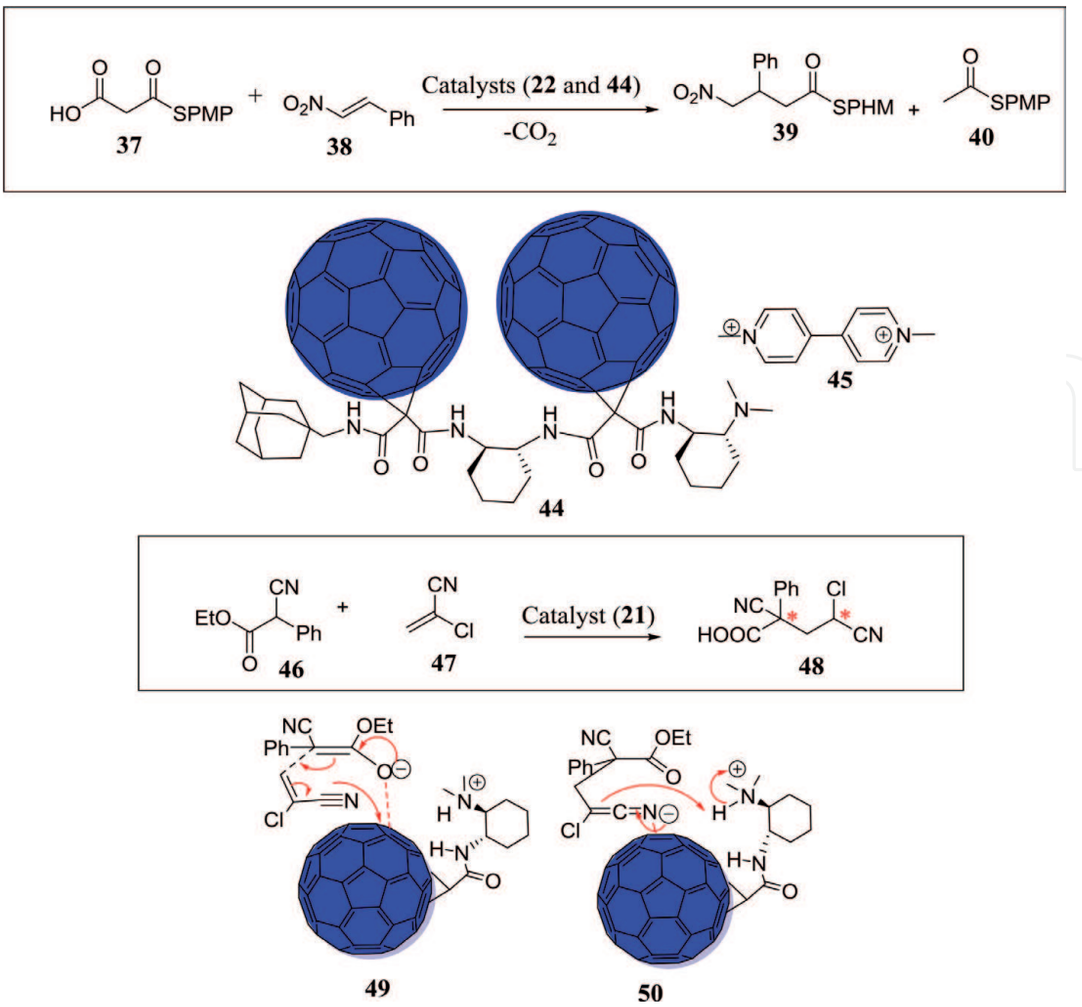


Figure 6.
*Schematic illustration of addition (**39**) and decarboxylation product (**40**) on anion-π catalytic surfaces of fullerenes (**22** and **44**) along with the depiction of conjugate addition protonation reaction and anionic transition state stabilization (**49** and **50**)*

Currently, catalysis by means of an electric field has gained a significant interest in molecular transformations, stereoselectivities, and multistep organic synthesis [24]. Electric fields and potentials besides accelerating the reactions have also been shown to activate the conventional catalysts, enzymes, and catalytic pores [25]. Recent studies have revealed that electric fields can just function as a remote control for anion-π catalysts. It has been observed that immobilization of anion-π catalysts is important before applying the electric field to polarize the π-acidic aromatic systems into an induced dipole (μz), which in turn enhance the stabilization of anionic transition state and intermediate on the catalytic polarizable π-surface (**Figure 7**). In order to fulfill these expectations, a bifunctional anion-π catalyst (**20**) has been designed and synthesized by Matile and coworkers for addition product (**39**) selectivity over decarboxylation product (**40**). In their experimental studies, they have attached two diphosphonate groups in the NDI core of **20** through sulphide substituents in order to immobilize the bifunctional catalyst (**20**) on the surface of indium tin oxide (ITO) (**Figure 7**) [26].

In another event, Matile and teammates have used foldamers (**24–26**) for the Michael addition product selectivity over decarboxylated product and noticed that the selectivity gets increased by increasing the length of stacks, thereby displaying anion-$(\pi)_n$-π catalysis (**Figure 8**) [27]. This is actually due to increase in the electronic communication upon increasing the stack length of foldamers. The catalytic activity dependence on electron-sharing has been found to be superlinear on raising

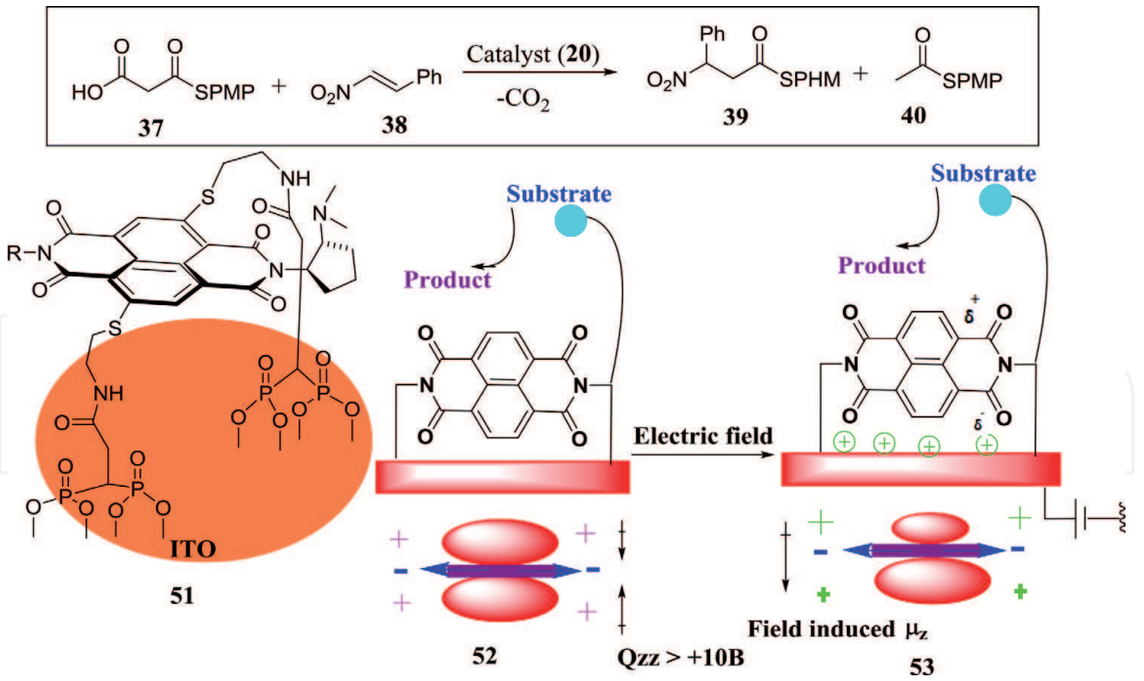


Figure 7.
*Schematic illustration of addition product (**39**) and decarboxylation product (**40**) along with immobilized anion-π catalyst **51** and induced dipole (μz).*

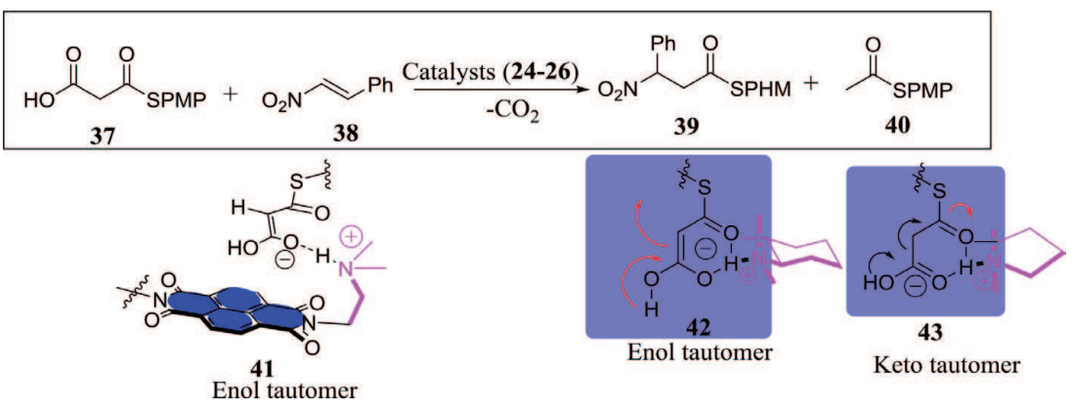


Figure 8.
*Schematic depiction of addition product (**39**) selectivity over decarboxylated product (**40**) by means π-stacked foldamer assisted anion-$(\pi)_n$-π catalysis.*

the stack length. It thus violates sublinear power laws of oligomeric chemistry and reveals the catalytic activity of synergistic amplification over the complete stack [27].

Moreover, quite recently Matile's group has stapled short peptides to NDI-based anion-π catalysts (**16**) in order to generate selective Michael addition product (**39**) over decarboxylative product (**40**) (**Figure 9**). These results regarding anion-π catalysis will serve as an appropriate starting material subsequent to peptides in order to be in operation in larger protein structures and development of anion-π enzymes [28].

Anion-π catalysis play a significant role in the asymmetric synthesis and leads to the generation of chiral isomers selectively. In this regard, the same group has also incorporated NDI moiety in between a carboxylate base and a proline unit for the construction of an anion-π catalyst (**13**). On the π-acidic surface of **13**, they have carried out asymmetric addition of **54** to nitroolefin enamine acceptor **55**. The NDI π-acidic surface helps in the stabilization of transition state of anion near nitronate intermediate by anion-π interactions as can be observed from the structures of

transition states (**59** and **60**) (**Figure 10**). By means of the presence of carboxylate base and proline unit at opposite sides of NDI, it has been found that both the rate of enamine addition and enantioselectivity gets enhanced on increasing the π-acidity of NDI [29, 30]. Thus, it gives an essential indication of the participation of anion-π contacts in stereoselectivity. Moreover, anion-π catalyst (**12**) based on NDI was used for the imine isomerization of undesired achiral substrate **57** to the desired chiral product **58** (**Figure 10**) [18].

On the other occasion, the same group has also carried out asymmetric synthesis on anion-π catalytic surfaces of perylenediimides (PDIs). It has been observed that twist in the π-acidic surface determines the catalytic activity of these PDI-based anion-π catalysts in case of Michael addition reactions of enolates and enamines. This is in contrary to the catalytic activity of NDIs, where reducibility of π-surfaces plays a prominent role. Experimental studies have revealed asymmetric addition of **62** to **38** through PDI-based anion-π catalyst (**17**), which leads to the formation of product **63** containing two chiral centers (**Figure 11**) [31]. Furthermore, the PDI-based anion-π catalyst (**18**) also offers Michael addition product (**39**) selectivity over decarboxylated product (**40**) (**Figure 11**).

In another event, Matile's group has also observed anion-π interactions in anion-π enzymes after preparing anion-π enzyme artificially. They have equipped a range of anion-π catalysts with a water-soluble vitamin known as biotin in order to determine the selectivity of Michael addition product (**39**) over decarboxylation one (**40**) in the chemistry of enolates. [32] Additionally, they screened artificially prepared

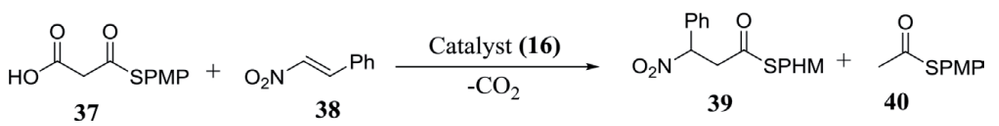
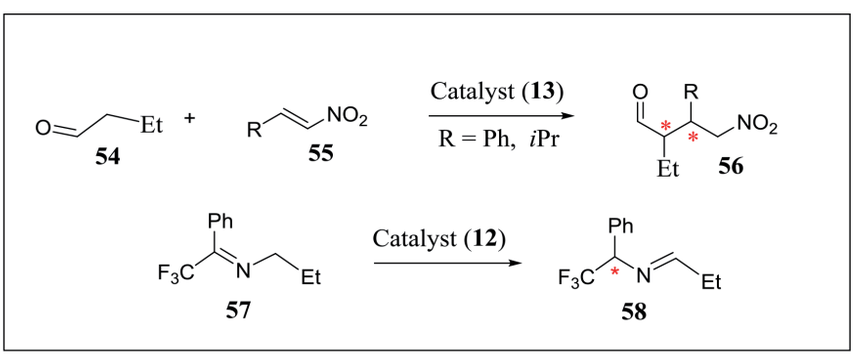


Figure 9.
*Schematic depiction of addition product (**39**) selectivity over decarboxylated product (**40**) by means of peptide stapled NDI-based anion-π catalyst (**16**).*



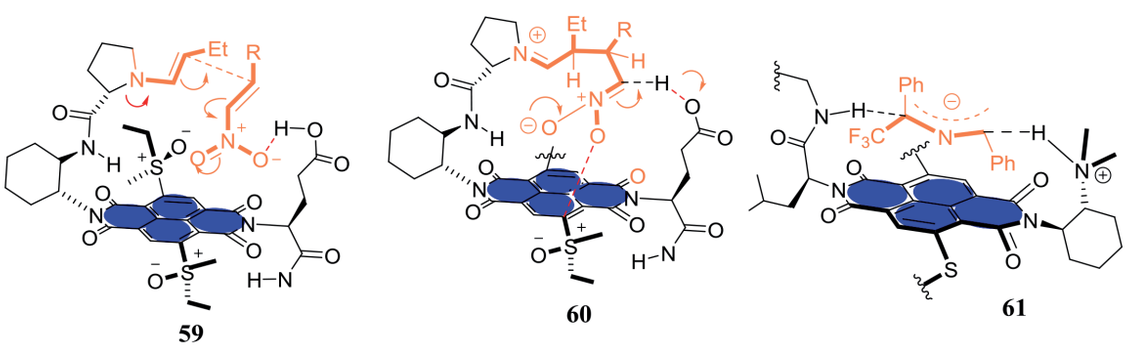


Figure 10.
*Representation of asymmetric addition (**56**) and imine isomerization product (**58**) along with the molecular structures of transition states (**59**–**61**).*

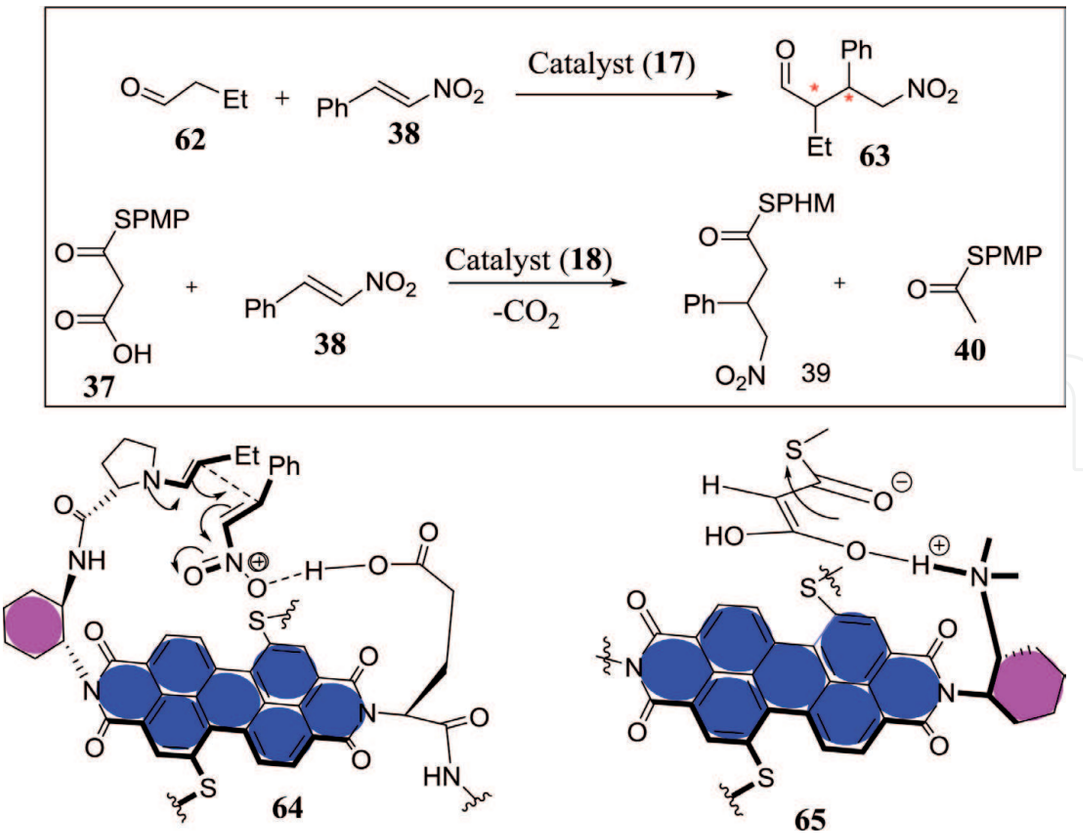


Figure 11.
Asymmetric synthesis of **63** *through PDI-based anion-π catalyst (***17***) and transition state (***64***) depicting formation of C-C bond. Moreover, Michael addition of* **37** *to* **38** *through PDI-based anion-π catalyst (***18***) and a structure of involved transition state (***65***) is also given.*

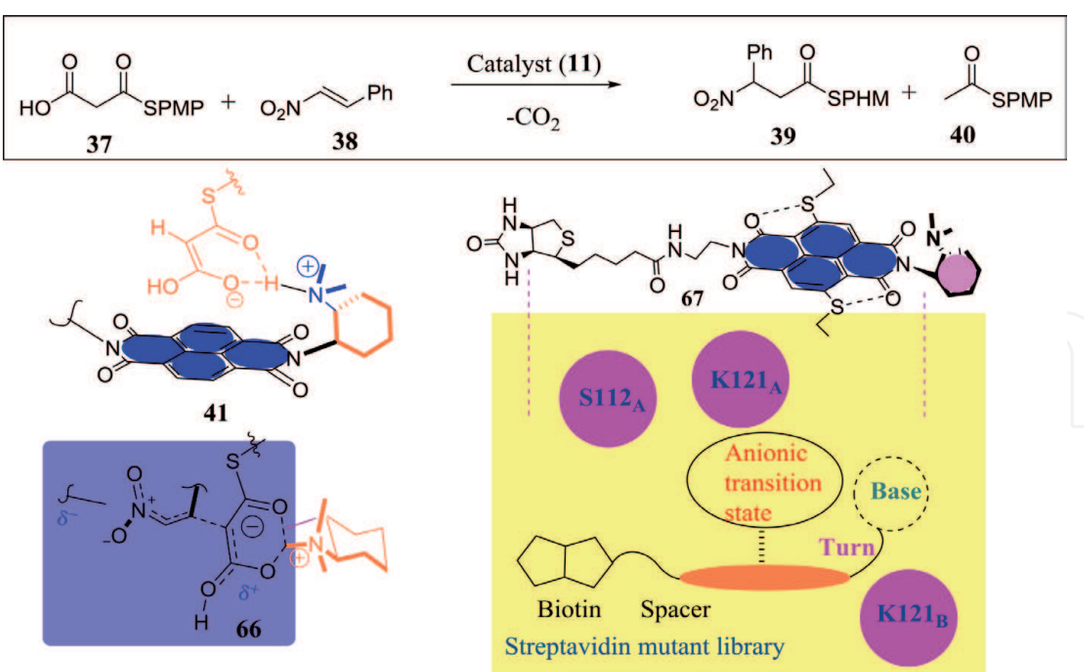
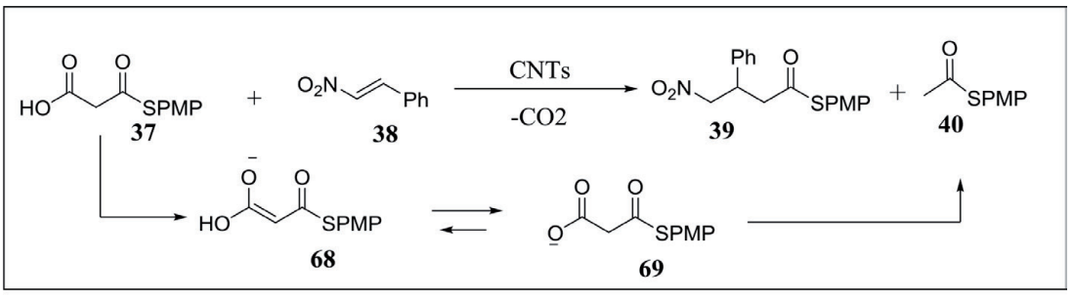


Figure 12.
*Schematic representation of addition (***39***) and decarboxylation product (***40***) by means of anion-π catalyst (***11***). The structures of transition states and reactive intermediates along with the diagrammatic illustration of anion-π enzymes are also given.*

anion-π enzyme against a cluster of the mutants of streptavidin (**Figure 12**). The presence of S112Y mutant leads to desired Michael addition product (**39**) with 95% enantiomeric excess (ee) along with a complete suppression of the decarboxylation



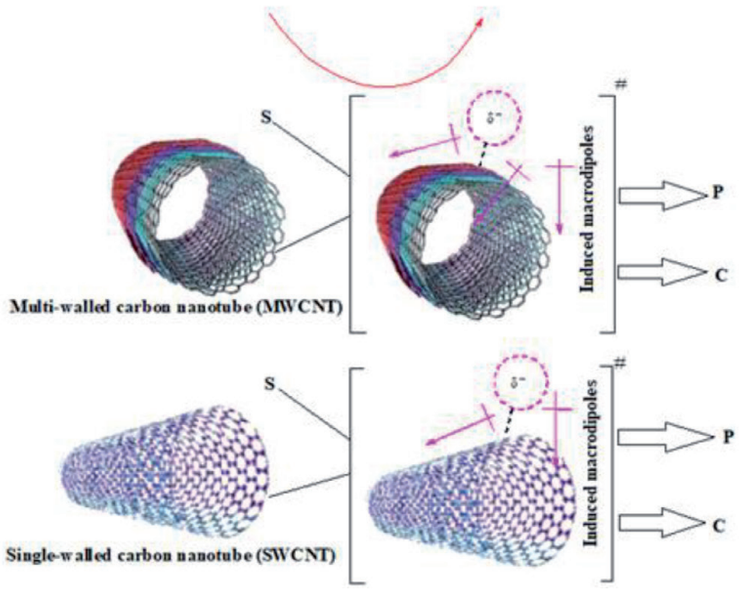


Figure 13.
*Schematic illustration of selective addition product (**39**) on the polarizability induced π-acidic carbon nanotubes (SWCNT and MWCNT).*

product (**40**). The existence of anion-π contacts in proteins has been established through the nitrate inhibition of mutant S112Y. The optimum performance has been found at acidic pH = 3, which clearly indicates that enolate gets formed by virtue of the stabilization on π-acidic surfaces. Moreover, K121 mutant has been found in concurrence with the docking results as far as the function of catalyst composed of tertiary amine is concerned at an ideal pH 3. By means of diverse mutants, it is established that enhancing enantioselectivity continuously agrees with the stabilization of particular transition state [32].

More interestingly, the same group has reported innovative anion-π catalysis on the surfaces of carbon nanotubes and synthesized selective addition products on their π-acidic surfaces (**Figure 13**). Studies have revealed that tertiary amine based multi-walled carbon-nanotubes (MWCNT) display much higher efficiency as compared to single-walled carbon nanotubes (SWCNT). This is by virtue of the fact that between and along the nanotubes of MWCNT, there exists a polarizibility induced π-acidic surfaces [33].

4. Anion-π catalysis in action for Diels-Alder reactions

The Diels-Alder reaction discovered in 1928 (Noble prize 1950), a pericyclic [4 + 2] cycloaddition reaction unites diene and dienophile in an atom economic way to yield corresponding Diels-Alder adducts in a regio- and stereoselective manner. Interestingly, this reaction has been used for the synthesis of a plethora of medicinal as well as other compounds. With these thoughts in mind, Matile's group in recent years has successfully carried out Diels-Alder reactions by means of anion-π catalysts

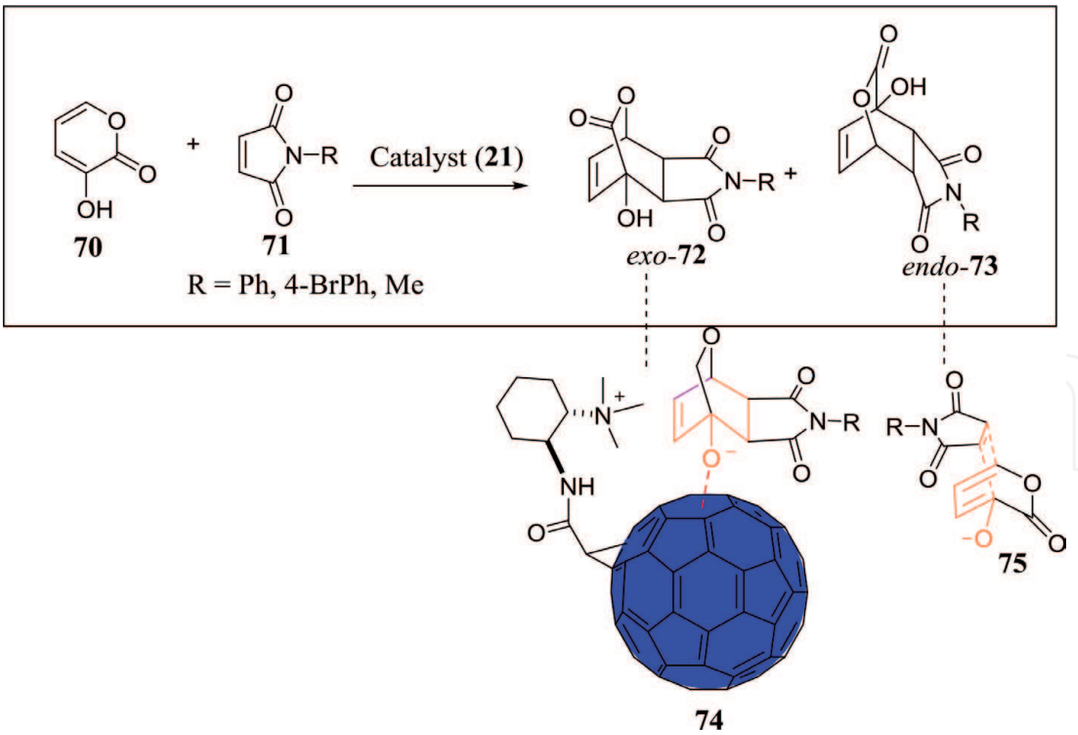


Figure 14.
*Diels-Alder reaction between hydroxypyrone (**70**) and maleimides (**71**) by means of anion-π catalyst (**21**). Moreover, the transition states of exo-**74** and endo-**75** compounds are also given.*

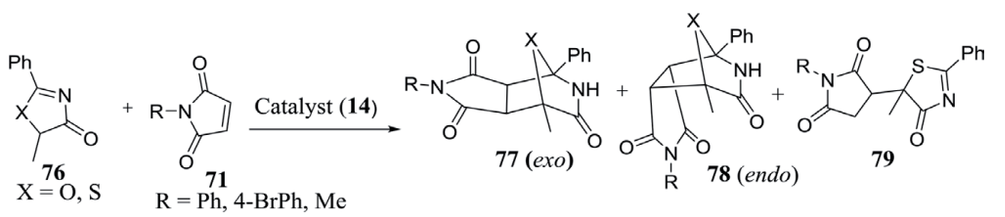


Figure 15.
*Michael product (**77**) catalyzed by triethylaluminium and exo-Diels-Alder product (**79**) catalyzed by anion-π catalyst (**14**).*

based on fullerenes [34]. During the experimental studies, they have got thermodynamically more stable *exo*-products as compared to generally formed *endo*-products by virtue of the *exo*-transition state stabilization as shown in **Figure 14.**

There is no doubt that the main objective of anion-π catalysis is to discover the reactions of indefinite reactivities and the Diels-Alder reactions of anionic nature offers a first indication in this direction. Matile's group has revealed that that the reaction between **76** and **71** catalyzed by triethylaluminium yields Michael adduct **77** as a major compound along with a Diels-Alder side product **78**. Nevertheless, a reaction of concerted cycloaddition nature by means of anion-π catalyst (14) solely offers *exo*-Diels-Alder compound (**79**) (**Figure 15**) [34].

5. Cascade reactions through anion-π catalysis

Cascade reactions are also known as domino or tandem reactions and comprises of at least two simultaneous consecutive reactions. Herein, the preceding reaction develops a chemical functionality on which a subsequent reaction occurs. Such reactions are of vital importance in the synthesis of complex natural products possessing various chiral centers [35]. During these cascade cyclization reactions,

charge displacements are stretched over longer distances. Matile's group has revealed that anion-π catalysis in terms of anion-π interactions is highly capable in the stabilization of these charge displacements. With the help of anion-π catalysis, the cascade reactions on the π-acidic catalytic surface leads to generation of bicyclic asymmetric products possessing four chiral centers (**Figure 16**). Moreover, cascade cyclization reactions through anion-π catalysis are also in action in the generation of asymmetric cyclohexane moieties containing five chiral centers generated in a single step on π-acidic catalytic surface (**Figure 17**). The concept of anion-π catalysis also play a central role in other cascade reactions on the π-acidic aromatic surface. For instance, the reaction of **93** with **94** takes place in a cascade way on the π-acidic aromatic surface (**Figure 18**). The greatest outcome of anion-π catalysis in cascade cyclization reactions is anion-π cinchona fusion catalyst [36].

Epoxide ring opening followed by ether and polyether cascade cyclic reactions are considered as conventional reactions in chemical and biological sciences. Nowadays, these reactions are also considered as attractive tools for anion-π catalysis. To this context, Matile's group has reported some functional systems

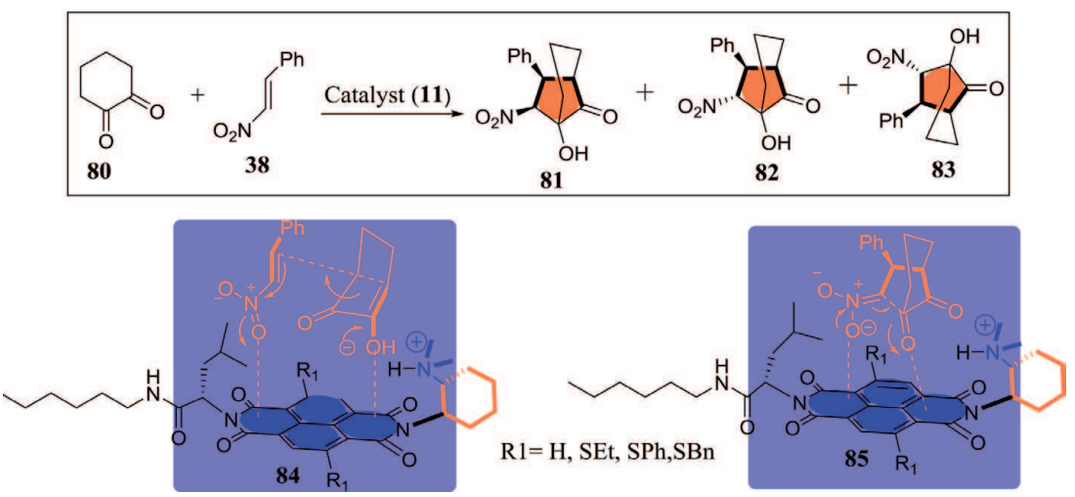


Figure 16.
Schematic representation of the generation of anion-π catalyzed bicyclic cascade products and the structures of involved anion-π transition states.

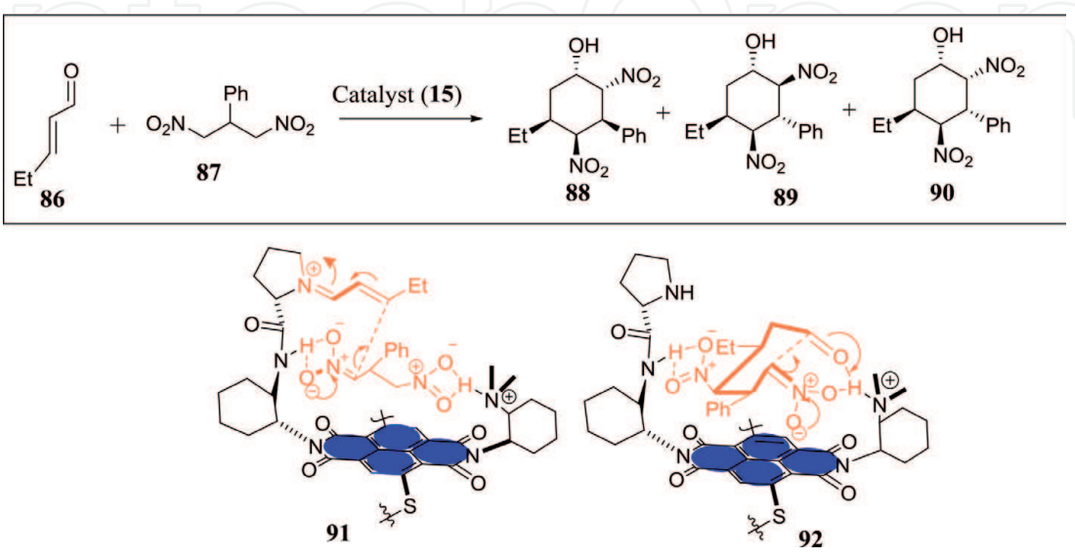


Figure 17.
Schematic illustration of asymmetric anion-π catalyzed cyclohexane rings through cascade cyclisation reaction. Moreover, the structures of anion-π transition states are also given.

Figure 18.
*Schematic depiction of anion-π catalyzed cascade reaction of benzaldehyde derivative (**93**) with ethyl acetoacetate (**94**).*

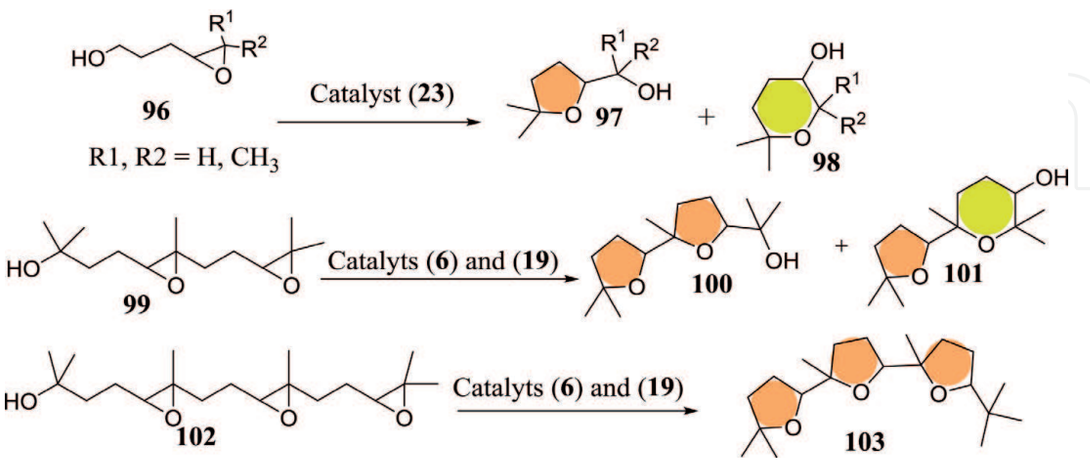


Figure 19.
*Schematic illustration of epoxide ring opening followed by ether and polyether cascade cyclization reactions by virtue of anion-π catalysts (**6**, **19**, and **23**).*

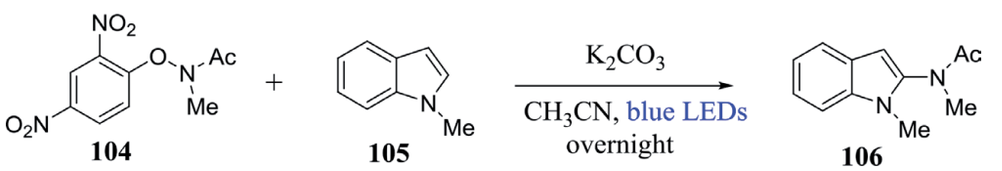


Figure 20.
*Photoamidation reaction between **104** and **105** assisted by anion-π interactions.*

which operate through anion-π interactions and show autocatalysis. Studies have revealed that aromatic π-acidic surfaces involve epoxide ring opening followed by ether cyclization without any activating group (**Figure 19**) [37]. Quite recently, they have also observed exceptional high autocatalysis on the π-acidic surfaces of hexafluorobenzene and substituted NDI's as far as epoxide ring opening followed by cyclisation reactions are concerned. This unique characteristic of autocatalysis not only adds complexity to reaction mechanisms but also offers intriguing perspectives towards future developments [38, 39].

Besides the above-mentioned catalytic relevances of anion-π interactions in the domain of catalysis, amidation reactions driven by light have also been carried out by means of these interactions. It has been observed that anion-π interactions helps in the stabilization of transient complex formed between electron deficient moiety **104** and carbonate or phosphate anion. This complex in turn undergoes cleavage of N-O bond in the presence of light to offer amidyl radical, which is later trapped by heteroaromatic system (**105**) to offer the desired product **106** (**Figure 20**) [40].

6. Conclusions and outlook

Anion-π catalysis in general operates on the fundamental principle of anionic transition state stabilization on π-acidic aromatic surfaces and offers a novel

approach towards diverse molecular transformations. Over the past seven years, steady advancement has been made in the domain of anion-π catalysis with regard to the design of catalyst and the scope of the reaction. Considering the significance of polarizability, it is believed that there will be the emergence of more hidden occurrences of immature anion-π catalysis in the near future. The unconventional anion-π catalysis gains an optimistic outlook from the immense impact of current developments made with conventional cation-π and ion-pairing interactions. It is thus expected that anion-π catalysis will eventually offer new mechanisms and access to new reactivities. However so far, anion-π catalysis fails in the general expectation to produce novel products. Nevertheless, efforts are being carried out all across the globe to meet the general expectations of anion-π catalysis to offer access to novel products with exceptional features, which are far outside the scope of conventional catalysis.

Acknowledgements

We are grateful to DST-SERB New Delhi for financial support (Project File no. ECR/2017/000821). I. A. R. thanks CSIR, New Delhi for the award of the JRF and SRF. R. A. thanks Jamia Millia Islamia, New Delhi for providing the necessary research facilities.

Conflicts of interest

The authors declare no conflicts of interest.

Author details

Ishfaq Ahmad Rather and Rashid Ali*
Organic and Supramolecular Functional Materials Research Laboratory,
Department of Chemistry, Jamia Millia Islamia, New Delhi, India

*Address all correspondence to: rali1@jmi.ac.in

References

[1] P. Ballester, A. Scarso, Editorial: Supramolecular aspects in catalysis, Front. Chem. 2019;7.174. doi:10.3389/fchem.2019.00174.

[2] J.B. Baruah, Principles and advances in supramolecular catalysis, CRC Press, Boca Raton : CRC Press, Taylor & Francis Group, 2019. doi:10.1201/9780429059063.

[3] D.A. Dougherty, The cation-π interaction, Acc. Chem. Res. 2013;46:885-893. doi:10.1021/ar300265y.

[4] I.A. Rather, S.A. Wagay, R. Ali, Emergence of anion-π interactions: The land of opportunity in supramolecular chemistry and beyond, Coord. Chem. Rev. 2020;415:213327. doi:10.1016/j.ccr.2020.213327.

[5] N. Busschaert, C. Caltagirone, W. Van Rossom, P.A. Gale, Applications of supramolecular anion recognition, Chem. Rev. 2015;115:8038-8155. doi: 10.1021/acs.chemrev.5b00099

[6] I.A. Rather, S.A. Wagay, M.S. Hasnain, R. Ali, New dimensions in calix[4]pyrrole: the land of opportunity in supramolecular chemistry, RSC Adv. 2019;9:38309-38344. doi: 10.1039/C9RA07399J

[7] Y. Zhao, Y. Domoto, E. Orentas, C. Beuchat, D. Emery, J. Mareda, N. Sakai, S. Matile, Catalysis with anion-π interactions, Angew. Chemie Int. Ed. 2013;52:9940-9943. doi:10.1002/anie.201305356.

[8] T. Lu, S.E. Wheeler, Quantifying the role of anion-π interactions in anion-π catalysis, Org. Lett. 2014;16:3268-3271. doi:10.1021/ol501283u.

[9] C. Wang, S. Matile, Anion-π catalysts with axial chirality, Chem.- A Eur. J. 2017;23:11955-11960. doi:10.1002/chem.201702672.

[10] M. Giese, M. Albrecht, K. Rissanen, Experimental investigation of anion-π interactions – applications and biochemical relevance, Chem. Commun. 2016;52:1778-1795. doi:10.1039/C5CC09072E.

[11] Y. Zhao, C. Beuchat, Y. Domoto, J. Gajewy, A. Wilson, J. Mareda, N. Sakai, S. Matile, Anion-π catalysis, J. Am. Chem. Soc. 2014; 136:2101-2111. doi:10.1021/ja412290r.

[12] Y. Zhao, Y. Cotelle, L. Liu, J. Lopez-Andarias, A.-B. Bornhof, M. Akamatsu, N. Sakai, S. Matile, The emergence of anion-π catalysis, Acc. Chem. Res. 2018;51:2255-2263. doi:10.1021/acs.accounts.8b00223.

[13] J. Mareda, S. Matile, Anion-π slides for transmembrane transport, Chem. - A Eur. J. 2009;15:28-37. doi:10.1002/chem.200801643.

[14] Y. Cotelle, S. Benz, A.-J. Avestro, T.R. Ward, N. Sakai, S. Matile, Anion-π catalysis of enolate chemistry: Rigidified Leonard turns as a general motif to run reactions on aromatic surfaces, Angew. Chem. 2016;128: 4347-4351. doi:10.1002/ange.201600831.

[15] Y. Zhao, N. Sakai, S. Matile, Enolate chemistry with anion-π interactions, Nat. Commun. 2014;5:3911. doi:10.1038/ncomms4911.

[16] Y. Zhao, S. Benz, N. Sakai, S. Matile, Selective acceleration of disfavored enolate addition reactions by anion-π interactions, Chem. Sci. 2015;6:6219-6223. doi:10.1039/C5SC02563J.

[17] F.N. Miros, Y. Zhao, G. Sargsyan, M. Pupier, C. Besnard, C. Beuchat, J. Mareda, N. Sakai, S. Matile, Enolate stabilization by anion-π interactions: Deuterium exchange in malonate dilactones on π-acidic surfaces,

Chem. - A Eur. J. 2016;22:2648-2657. doi:10.1002/chem.201504008.

[18] L. Liu, Y. Cotelle, A.-J. Avestro, N. Sakai, S. Matile, Asymmetric anion-π catalysis of iminium/nitroaldol cascades to form cyclohexane rings with five stereogenic centers directly on π-acidic surfaces, J. Am. Chem. Soc. 2016;138:7876-7879. doi:10.1021/jacs.6b04936.

[19] L. Liu, S. Matile, Anion-π transaminase mimics, Supramol. Chem. 2017;29:702-706. doi:10.1080/10610278.2016.1258118.

[20] D.S. Sabirov, Polarizability as a landmark property for fullerene chemistry and materials science, RSC Adv. 2014;4:44996-45028. doi:10.1039/C4RA06116K.

[21] J. Lopez-Andarias, A. Frontera, S. Matile, Anion-π catalysis on fullerenes, J. Am. Chem. Soc. 2017;139:13296-13299. doi:10.1021/jacs.7b08113.

[22] J. Lopez-Andarias, A. Bauza, N. Sakai, A. Frontera, S. Matile, Remote control of anion-π catalysis on fullerene-centered catalytic triads, Angew. Chemie Int. Ed. 2018;57:10883-10887. doi:10.1002/anie.201804092.

[23] X. Zhang, L. Liu, J. Lopez-Andarias, C. Wang, N. Sakai, S. Matile, Anion-π catalysis: focus on nonadjacent stereocenters, Helv. Chim. Acta. 2018;101:e1700288. doi:10.1002/hlca.201700288.

[24] S. Shaik, R. Ramanan, D. Danovich, D. Mandal, Structure and reactivity/selectivity control by oriented-external electric fields, Chem. Soc. Rev. 2018;47:5125-5145. doi:10.1039/C8CS00354H.

[25] S. Shaik, D. Mandal, R. Ramanan, Oriented electric fields as future smart reagents in chemistry, Nat. Chem. 2016;8:1091-1098. doi:10.1038/nchem.2651.

[26] M. Akamatsu, N. Sakai, S. Matile, Electric-field-assisted anion-π catalysis, J. Am. Chem. Soc. 2017;139:6558-6561. doi:10.1021/jacs.7b02421.

[27] A.-B. Bornhof, A. Bauza, A. Aster, M. Pupier, A. Frontera, E. Vauthey, N. Sakai, S. Matile, Synergistic anion-$(\pi)_n$-π catalysis on π-stacked foldamers, J. Am. Chem. Soc. 2018;40:4884-4892. doi:10.1021/jacs.8b00809.

[28] A. Pham, S. Matile, Peptide stapling with anion-π catalysts, Chem. – An Asian J. 2020;15:1562-1566. doi:10.1002/asia.202000309.

[29] Y. Zhao, Y. Cotelle, A.-J. Avestro, N. Sakai, S. Matile, Asymmetric anion-π catalysis: enamine addition to nitroolefins on π-acidic surfaces, J. Am. Chem. Soc. 2015; 137:11582-11585. doi:10.1021/jacs.5b07382.

[30] M. Akamatsu, S. Matile, Expanded chiral surfaces for asymmetric anion-π catalysis, Synlett. 2016;27:1041-1046. doi:10.1055/s-0035-1561383.

[31] C. Wang, F.N. Miros, J. Mareda, N. Sakai, S. Matile, Asymmetric anion-π catalysis on perylenediimides, Angew. Chemie Int. Ed. 2016;55:14422-14426. doi:10.1002/anie.201608842.

[32] Y. Cotelle, V. Lebrun, N. Sakai, T.R. Ward, S. Matile, Anion-π enzymes, ACS Cent. Sci. 2016;2:388-393. doi:10.1021/acscentsci.6b00097.

[33] A. Bornhof, M. Vazquez-Nakagawa, L. Rodriguez-Perez, M. Angeles Herranz, N. Sakai, N. Martin, S. Matile, J. Lopez-Andarias, Anion-π catalysis on carbon nanotubes, Angew. Chem. Int. Ed. 2019;58:1-5. doi:10.1002/ange.201909540.

[34] L. Liu, Y. Cotelle, A.-B. Bornhof, C. Besnard, N. Sakai, S. Matile, Anion-π

catalysis of Diels-Alder reactions, Angew. Chemie Int. Ed. 2017;56:13066-13069. doi:10.1002/anie.201707730.

[35] I. Vilotijevic, T.F. Jamison, Epoxide-opening cascades in the synthesis of polycyclic polyether natural products, Angew. Chemie Int. Ed. 2009;48:5250-5281. doi:10.1002/anie.200900600.

[36] L. Liu, Y. Cotelle, J. Klehr, N. Sakai, T.R. Ward, S. Matile, Anion-π catalysis: bicyclic products with four contiguous stereogenic centers from otherwise elusive diastereospecific domino reactions on π-acidic surfaces, Chem. Sci. 2017;8:3770-3774. doi:10.1039/C7SC00525C.

[37] X. Zhang, X. Hao, L. Liu, A.-T. Pham, J. Lopez-Andarias, A. Frontera, N. Sakai, S. Matile, Primary anion-π catalysis and autocatalysis, J. Am. Chem. Soc. 2018;140:17867-17871. doi:10.1021/jacs.8b11788.

[38] M. Paraja, X. Hao, S. Matile, Polyether natural product inspired cascade cyclizations: autocatalysis on π-acidic aromatic surfaces, Angew. Chemie Int. Ed. 59 (2020) 15093-15097. doi:10.1002/anie.202000681.

[39] M. Paraja, S. Matile, Primary anion–π catalysis of epoxide-opening ether cyclization into rings of different sizes: Access to new reactivity, Angew. Chemie Int. Ed. 2020;59:6273-6277. doi:10.1002/anie.202000579.

[40] L. Buglioni, M.M. Mastandrea, A. Frontera, M.A. Pericas, Anion-π interactions in light-induced reactions: Role in the amidation of heteroaromatic systems with activated N -aryloxyamides, Chem. – A Eur. J. 2019;25:11785-11790. doi:10.1002/chem.201903055.