Chapter 1

Introduction

1.1 Introduction

Chirality plays a crucial role in life-sustaining processes and therefore asymmetric synthesis has become a central research theme in the field of organic chemistry. Although a lot of research has been focussed earlier on the chemistry of molecules with sp^3 chiral center, other features such as axial chirality, helical chirality, and planar chirality (Figure 1) have been recently investigated for their potential use in synthesis, in asymmetric catalysis, and as chiral perturbers. Axially chiral compounds, unlike molecules that feature central chirality (point chirality), lack stereogenic center(s) yet exist as enantiomers. Atropisomers belong to this class of chiral compounds; however, in this case the enantiomers exist due to the restricted rotation around a single bond.

Pasteur proposed that the optical activity of chiral compounds is due to enantiomorphism of the molecular configuration.[1] Later, Van't Hoff and Le Bell showed that the optical activity in all known chiral compounds could be correlated with the presence of an asymmetric carbon atom in the molecule. Subsequently, several scientists have discovered that a molecule could be chiral without the presence of an asymmetric (sp^3) carbon. For the first time Christie and Kenner reported the "optical activity due to axial chirality" in 1922, this type of enantiomerism was observed in the resolution of 6,6'-dinitro-2,2'-diphenic acid *via* fractional crystallization with a chiral resolving agent (as diastereomeric Brucine salt). In the molecule the phenyl rings lie perpendicular in order to minimise steric interactions between the four *ortho* substituents. Rotation about the biphenyl bond was significantly restricted and interconversion between the two isomers was slow enough to allow their resolution and it was later called as "Atropisomerism". The term atropisomerism originates from the Greek *a* means not and *tropos* means turn and it was coined by Richard Kuhn[1] in 1933 to describe molecules with a chiral axis maintained by hindered rotation about a single bond.

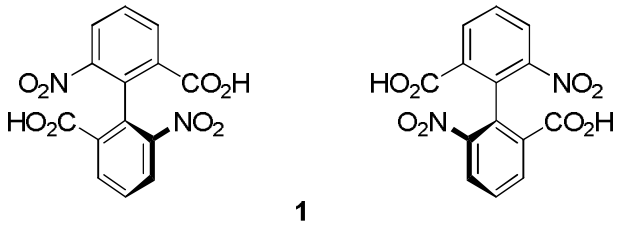

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Figure 1: First example of isolated atropisomeric molecules

Atropisomerism is a class of stereoisomerism that arises from hindered rotation around a bond (axis of chitality) that result in molecules which exist as a mixture of stable, isolable

atropisomers. Structural features, for example bulky substituents or strained rings, may increase the barrier to rotation between two distinct conformations to allow the separation of the atropisomers. The phenomenon of axial chirality relies on the rotational stability about a single bond. While the stereoselective synthesis of compounds containing one or more stereogenic centre has emerged as one of the most important fields in chemistry. However, the scenario has changed with the recognition that the configuration at a biaryl axis can be a decisive factor in governing the pharmacological properties of bioactive compounds[3] and that axial chirality is the fundamental aspect of useful reagents and catalysts in asymmetric synthesis.[4]

The biaryl structure is joined by a carbon-carbon (sp^2-sp^2) single bond, and it is the rotation about this bond which is affected by steric interactions. The most common room temperature atropisomeric compounds are biphenyls and binaphthyls.

In general, there are two necessary requirements for axial chirality in biaryl molecules,

1. An axis resistant to rotation.

2. The presence of different substituents on both sides of the axis; for example in Figure **2**, A ≠ B and C ≠ D.

When the positions *ortho* to this bond are occupied by three or four bulky substituents, free rotation around the axis may be restricted and the biaryl system is locked into a specific conformation. If A = C and B = D, the molecule has C_2 symmetry but is still chiral. Axial chirality can also occur from non-equivalence of *meta* substituents.

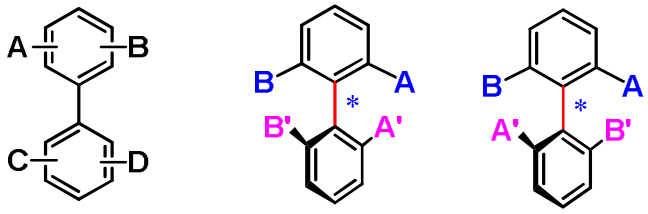


Figure 2: Conditions for axial chirality in biaryls.

Mono *ortho* substituted biaryls do not form stable atropisomers at room temperature[1] whereas di-*ortho* substituted biphenyls are difficult to resolve unless the substituents are large. However, di-*ortho* substituted biphenyl **2** and 1,1'-binapthyl **3** can be resolved.

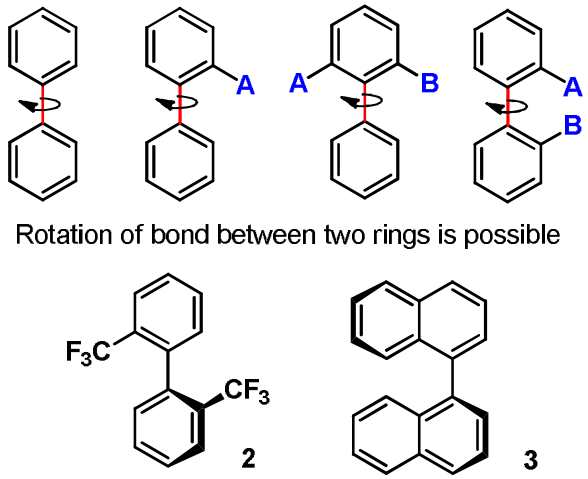


Figure 3: Effect of *ortho* substituents (mono and di) in biaryls.

Tri *ortho* substituted biaryls generally have short half life and often racemizes at room temperature, particularly if at least one of the *ortho* substituents is small (e.g. fluorine or methoxy). If all three groups are large in size, then the racemisation is slow. Biphenyl **4** has a barrier of rotation of 125 kJ/ mol at room temperature.

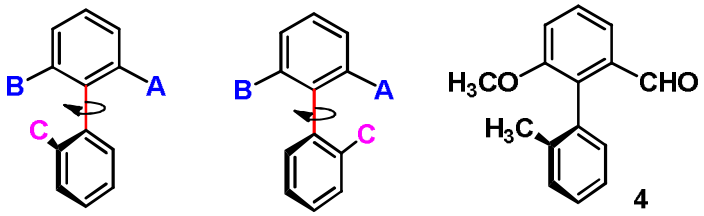


Figure 4: Effect of *ortho* substituents (tri) in biaryls.

Biaryls with four *ortho* substituents are virtually guaranteed to be atropisomeric at room temperature even if the substituents are small as in tetrafluorobiphenyl **5**. The barriers to rotation can be very high as in the chiral auxiliary BINOL **6** allowing conformational stability even at high temperatures.

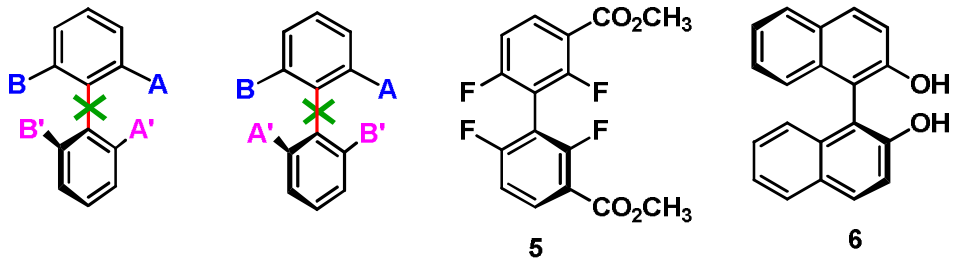
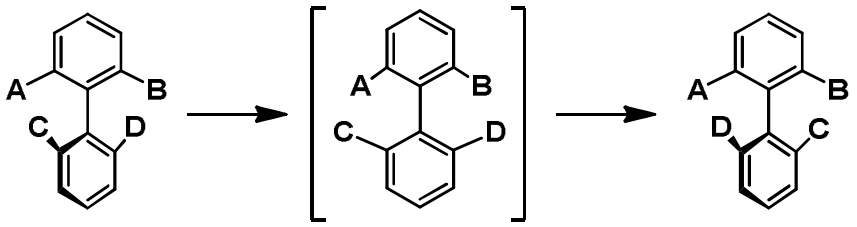


Figure 5: Effect of *ortho* substituents (tetra) in biaryls.

Apart from the *ortho* substituent, *meta* substitution also help the restriction of rotation along the C-C bond (e.g. **5**).

The rate of racemisation depends upon the size of the substituents, larger the substituent, the slower the rate of racemisation. It roughly follows van der Waals radii. The order is; I>Br>CH_3>Cl>NO_2>CO_2H>F>H. The two *ortho* substituents on the two rings of the biphenyl can point to each other, and so there is some interaction which increases with increasing van der Waals radii.

The aryl-aryl bond rotation is clearly evident in the *ortho*-substituted biphenyl systems (Scheme 1) where with the increase in the bulkiness of the *ortho*-groups, the barrier to interconversion of the two isomers also increases. The transition between the two enantiomers will produce a state in which the aryl rings are coplanar and there is an energy difference associated with this interaction. Therefore the isomers arrange perpendicularly giving two atropisomeric molecules.



Scheme 1

Three major factors govern value of the minimum free energy barrier to rotation, $\Delta G^{\ddagger}$;

a. The combined steric demands of the substituents in proximity to the axis;
b. The length and rigidity of bridges (if present); and
c. The mechanisms involved in isomerisation.

In case of some atropisomers, isolation is impossible due to a low energy barrier between the two enantiomers and thus they interconvert rapidly at room temperature. Oki proposed that the atropisomers should be separable if they exhibit a half life of at least 1000 s (16.7 min) at a given temperature.[3] Thus for compounds that are atropisomeric at room temperature isolation of the individual conformers is possible. The minimum free energy barrier to rotation needed to achieve atropisomerism varies with temperature, $\Delta G^{\ddagger}_{200K}$ = 61.6 kJ/mol, $\Delta G^{\ddagger}_{300K}$ = 93.5 kJ/mol, $\Delta G^{\ddagger}_{350K}$ = 109 kJ/mol. The calculated energy barrier where atropisomers can be isolated at room temperature is approximately

85 kJ/mol. When the barrier of rotation between the interconversion of atropisomers becomes higher than this value, they can be separated by conventional chromatographic techniques. Nevertheless if the barrier of rotation is less than 85 kJ/mol then the isomers can be detected by NMR spectroscopy, DFT calculations and other analytical methods.

1.2 Types of Atropisomers

Atropisomers are often broken down into several classes based on the type of hybridisation of the atom involved in the hindered rotation or by the type of bonds around which rotation is blocked (Figure 6).

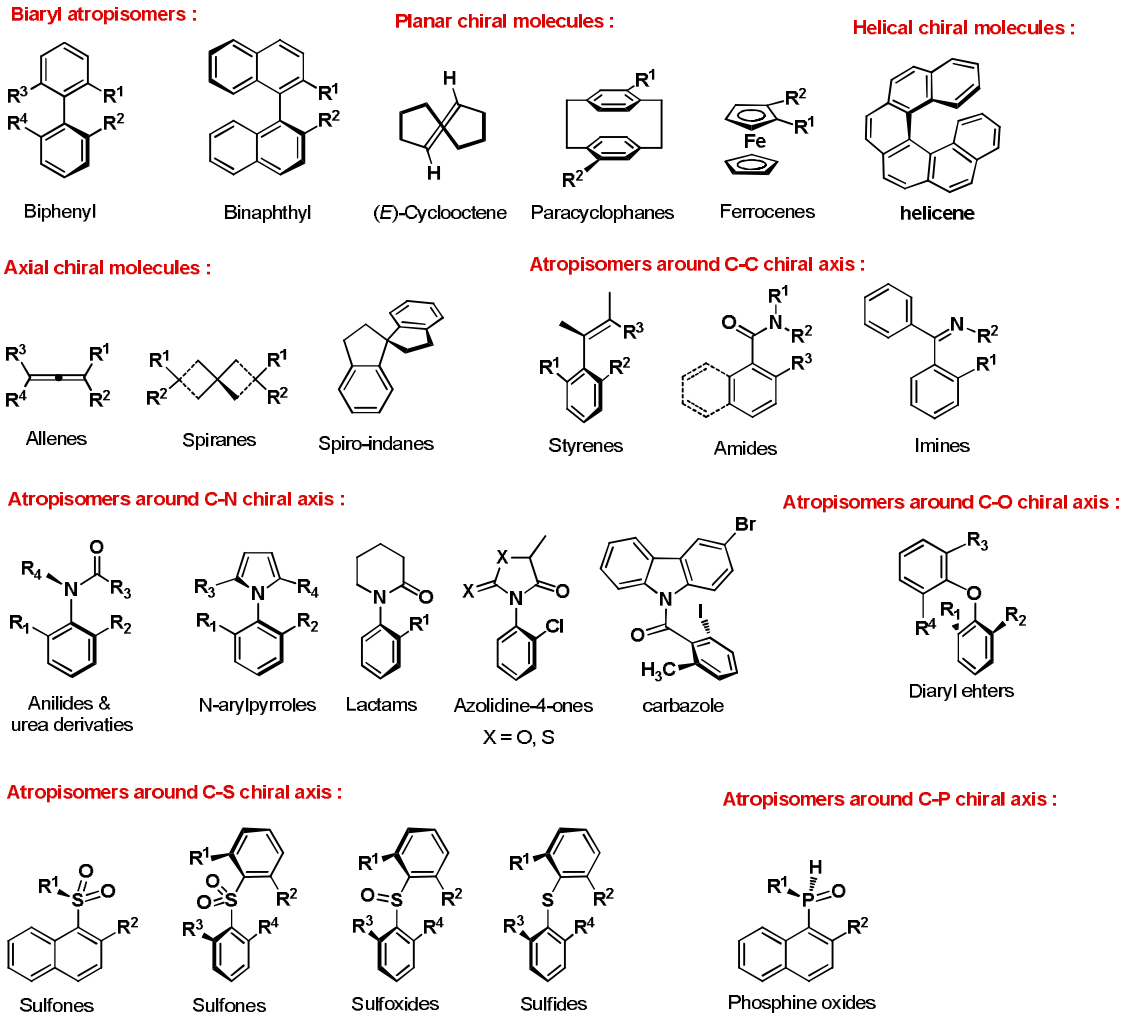


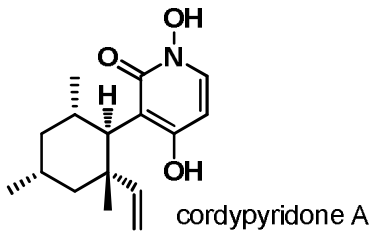
Figure 6: Various Forms of Chiralities

Based on Hybridisation

Atropisomers can be classified based on the hybridization of the atoms around the chiral axis i.e. 1) sp^2 - sp^2 2) sp^2 - sp^3 3) sp^3 - sp^3.

The first and most common class is the sp^2 - sp^2 family. Most of the atropisomers included in this class and were biaryls, tri or tetra *ortho* substituted compounds. The best known group of compounds of this class of atropisomers are the binaphthyl derivatives, which are commonly known as BINOL and BINAP.

The second is sp^2 - sp^3 class. It is rarely observed in some natural products for example cordypyridone A **7** and in aromatic molecules with bulky di-tertiary-butyl alcohol **8** groups. And the last is sp^3 - sp^3 class which is usually only formed in non-natural systems especially designed to hinder the free rotation. This type of atropisomerism shown in triptycene systems **9**.[5]



cordypyridone A

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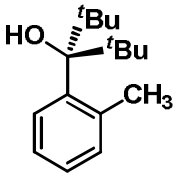

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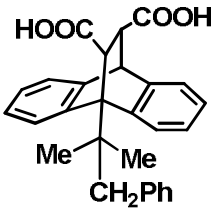

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Figure 7

Based on Bond Rotation

The restriction of rotation is not limited to just Ar–Ar covalent bond. The other type of atropisomers includes molecules, ones having restriction of rotation between:

a) the carbon of aromatic ring and carbon of carbonyl group about the **C-CO** bond of benzamides, [6]

b) the carbon of aromatic ring and nitrogen of amide group about **C-N** bond of anilides[7,8] and urea derivatives[9]

c) the **C-O** bond of ethers[10,11]

d) the **C-S** bond of sulfones[12,13]

A number of these non-biaryl atropisomers such as diaryl ethers, diaryl ureas, anilides, benzamides and thioamides, *N*-aryl carbamates, aryl sulphides and sulfones, *N*-arylpyrroles, indoles and 2',6'-disubstituted *N*-benzoyl carbazole derivatives were found to exhibit atropisomerism[14] as shown in Figure 6.

1.3 Atropisomers in Natural products and its importance in biological systems

The phenomenon of atropisomerism is not artificial but a number of natural compounds have such conformationally restricted stereogenic axis. Since last few years, the importance of axially chiral molecules has become more significant in the field of natural product synthesis because of widespread occurrence in nature and biologically active molecules. A common examples of sp^2-sp^2 class or Ar-Ar (C-C) type are bis naphthalene containing natural products gossypol **10** and kotanin **11** isolated from cotton seed plants.[15] Gossypol exists as two atropisomers due to restricted rotation about the biaryl bond. Racemic Gossypol used as an adjuvant in post-operative bladder cancer and the contraceptive effect appears to be associated with the (-)-Gossypol, while toxic effects (cardiac toxicity in cattle) appear to be associated with the (+)-Gossypol. Vancomycin **12** contains three types of stereo elements i.e. two chiral planes and a stereogenic biaryl axis, and it is biologically active as an antibiotic, originally isolated by Eli Lilly in 1956.[16] Knipholone[17] **13** has only axial chirality, and particularly *M* configured isomer shows good antimalarial[18] and antitumor activities.[19] Mastigophorene A **14**, a C_2-symmetric bisphenol, is known to stimulate nerve growth.[20] The natural products of Cordypyridone A[21] and its atropisomer Cordypyridone B belongs to sp^2-sp^3 class. The two molecules are formally diastereomers and conformationally stable at room temperature, which interconvert only on heating. The axially chiral natural products are not limited to C-C-coupled (Ar-Ar) biaryl compounds but other type of heteroaryl C-N bond is also found, e.g. in (*M*)-Murrastifoline-F [22] **15** and Marinopyrrole **16** (Figure 8).

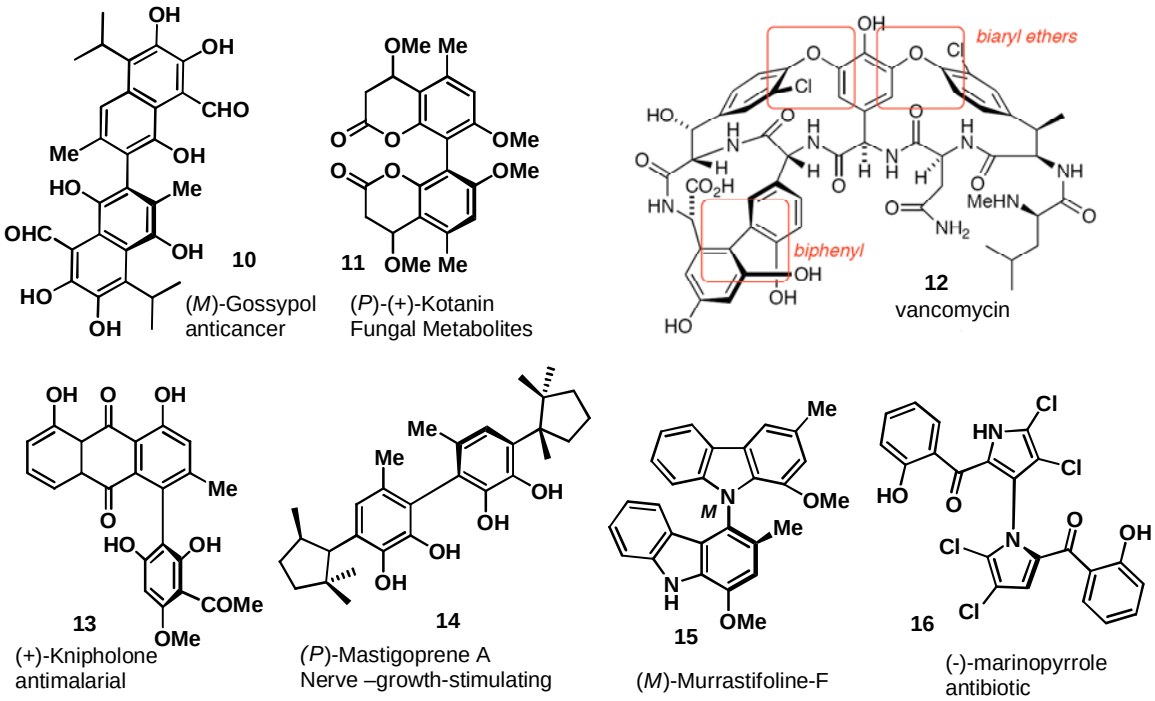


Figure 8

The importance of the configuration of the chiral axis in biological activity is demonstrated by the two isomeric 3-cyanocyproheptadine compounds **17** and **18**, which have been synthesized and resolved into enantiomeric atropisomers (Figure 9).[18b] Compound **17** was shown to be a potent antipsychotic agent, whereas its corresponding atropisomeric enantiomer **18** was virtually inactive.

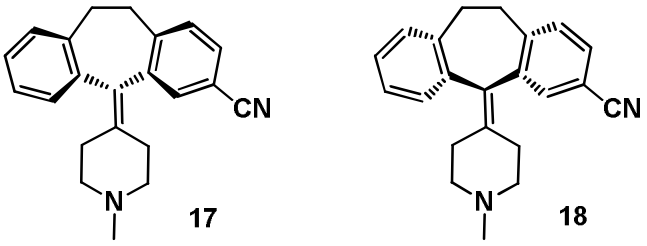


Figure 9

1.4 Assignment of absolute configuration in chiral biaryl

The absolute axial configuration (atropisomers) can be denoted by analysis of a Newman projection along the biaryl axis (Figure 10). The atropisomers are usually defined by the chirality rule, viz., *R* (or R_a) and *S* (or S_a) nomenclature using Cahn-Ingold-Prelog rules,[23] it is also often represented in terms of helicity rules, viz. *P* (positive helix) and *M* (negative helix) nomenclature. The analysis is done by following the shortest 90° path

from the substituent of highest priority at the proximal ring to the highest-ranking one at the distal ring (i.e. here from OH to OH'). If this 90° turn is counter clockwise as in **19**, the absolute configuration is R_a or *M* (for minus); if it is clockwise as in **19**-ena, then the descriptor is S_a or *P* (for plus).[24]

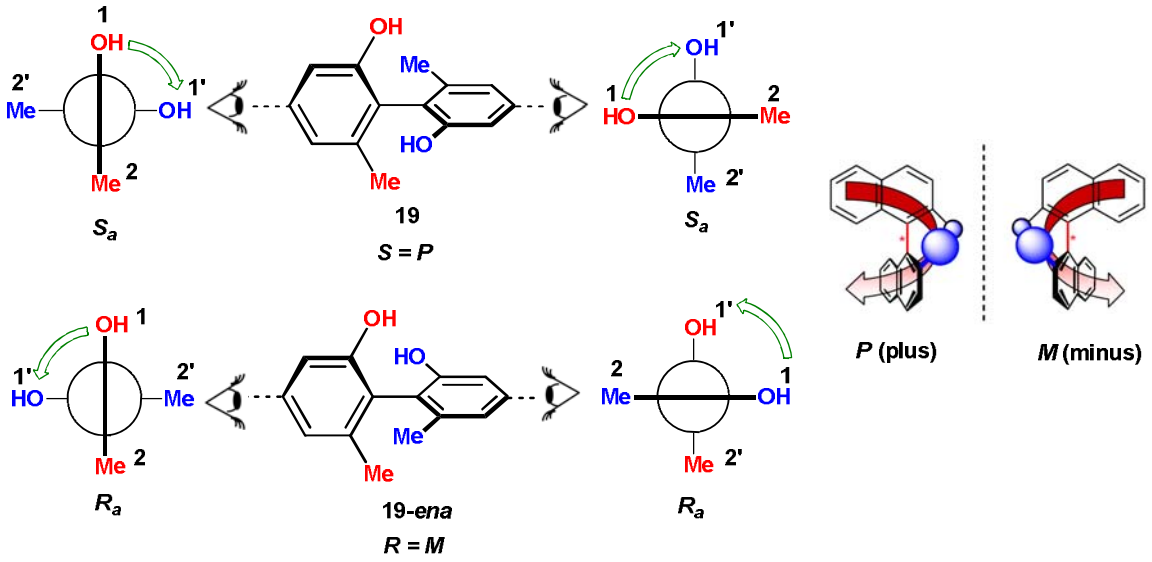


Figure 10

1.5 Synthesis of Atropisomers

Though the first observation on atropisomerism was recognized in 1922, most of the atropisomeric compounds synthesized later were not investigated in the framework of atropisomerism. This may be due to the lack of appreciation of the importance of axial chirality in atropisomeric compounds. After isolation of several atropisomeric natural products such as alkaloids, coumarins, flavonoids, peptides, polyketides, polymers, ligand, terpenes, these compounds were studied for their biological activity. Many compounds also incorporate biaryl building blocks, and these can be used as chiral reagents, chiral phases for chromatography and chiral liquid crystals as well as the use of biphenyls as chiral ligands for metals. Subsequent work led to a better understanding of the importance of atropisomers/axial chirality leading to greater study of atropisomeric compounds.[25, 26] Biaryl compounds are important synthetic molecules, with the key step being the formation of the bond between the two aromatic segments of the biaryl.

However, as the last few decades have witnessed major progress in this field, we feel that a general update of this research is of interest. Consequently, in this thesis we will be discussing the synthesis and application of atropisomeric molecules. For easy

understanding in the field of atropselective synthesis this part is divided into four major sections (Chart 1). Section I includes the stereoselective construction of biaryl linkages whereas Section II concerns the access to chiral biaryls *via* construction of (an)aromatic ring(s). Section III deals with stereoselective transformation of prochiral or racemic biaryls. Finally Section IV presents an interesting example of the synthesis of optically enriched biaryls relying on a central-to-axial chirality transfer. For a more detailed understating of these synthetic routes and concepts, an excellent review article has been published.[27]

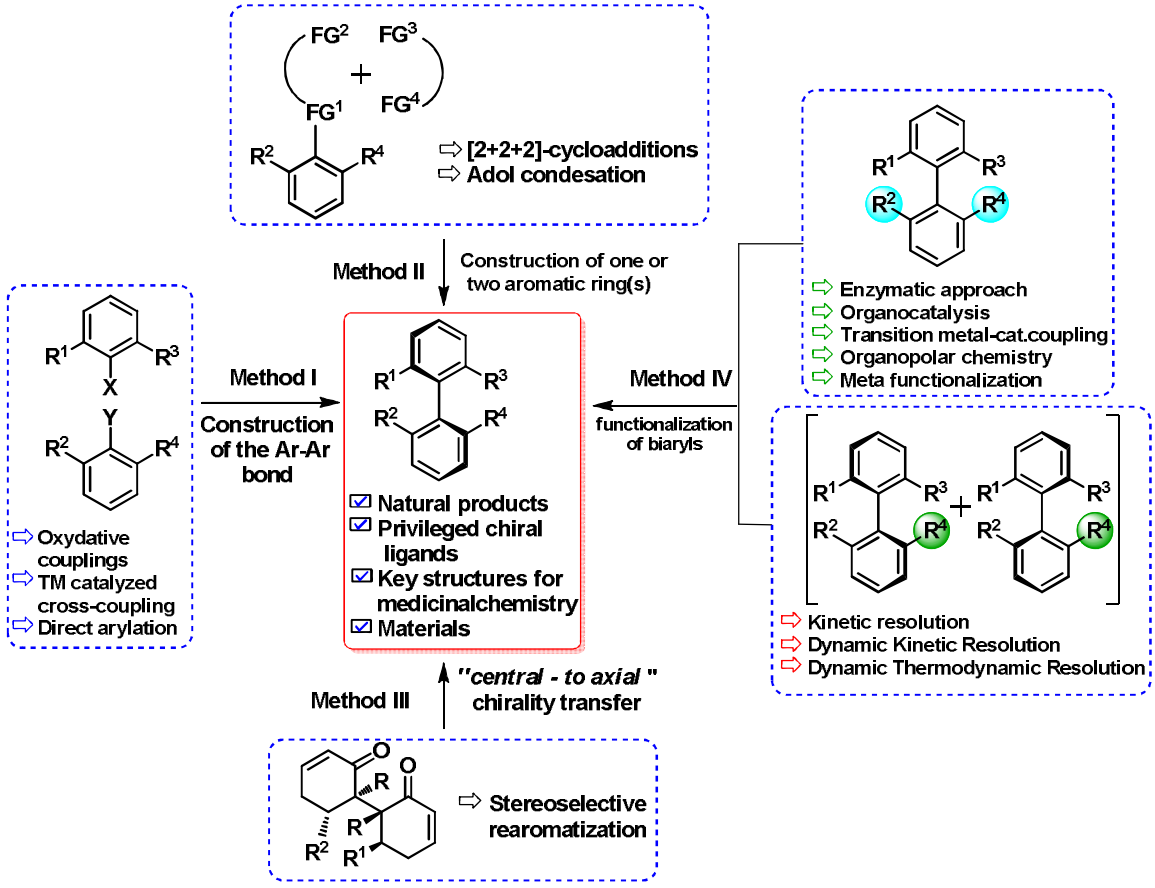


Chart 1

1.5.1 Construction of the Ar-Ar bond

The Ar–Ar couplings approach is most useful method for synthesis of atropisomeric biaryl compounds. The atropselective aryl-aryl coupling step is the one where the construction of the axis occurs simultaneously with the asymmetric induction by diastereo- and enantioselective approaches (Scheme 2). It is important to keep in mind that the construction of a configurationally stable biaryl compound is, by definition, a

sterically challenging operation, which often requires "forcing'' conditions to provide the coupled products in reasonable yields. This, on the other hand, can cause a concomitant atropisomerization at the axis, hence leading to diminished atroposelectivities. Thus, care has to be taken that the reaction conditions employed are still mild enough not to interfere with the stereochemical of the biaryl axis.

Diastereoselective biaryl couplings have been realized by three different strategies:

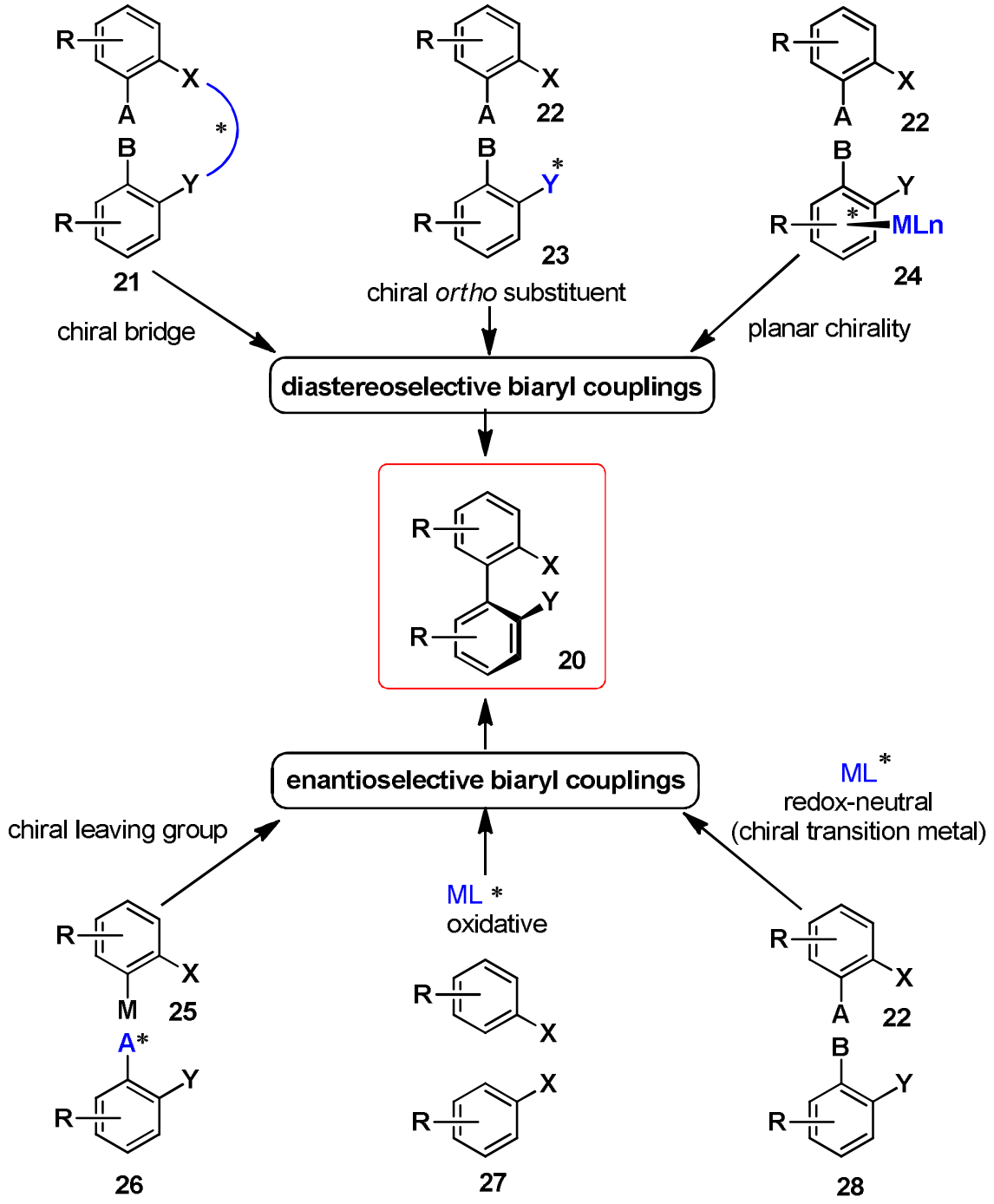
1. Intramolecular Coupling with Chiral Tethers.
2. Intermolecular Coupling with Chiral *ortho* Substituents.
3. Intermolecular Coupling with the Element of Planar Chirality.

Enantioselective approach also has three different types of strategies:

4. Intermolecular Coupling with Chiral Leaving Groups.
5. Oxidative Homocoupling in the Presence of Chiral Additives.
6. Redox-Neutral Cross-Coupling Catalyzed by Chiral Metal Complexes.

Diastereoselective biaryl couplings have been realized by three different strategies: The simplest involves the incorporation of a chiral bridge (often sourced from the chiral pool) to prelink the two aryl substrates, subsequently permitting a favorable intramolecular reaction (**21** to **20**),[28] Diastereoselective intermolecular coupling reactions can be effected by utilizing arenes that are modified by a chiral auxiliary, normally in one of the *ortho* positions next to the coupling site as in **22** + **23** to **20**,[29] or by using a removable chiral element, for example, in the form of planar-chiral η^6- chromium complexes as for **22** + **24** to **20**.[30]

An overall enantioselective approach has been achieved by employing a chiral leaving group, as in **26**, which is eliminated in the coupling step **25** + **26** to **20**,[31] enantioselective biaryl coupling will also result if the stereochemical information is induced through a chiral additive. Both stoichiometric and catalytic oxidative dimerizations have been realized with metal-based reagents (e.g. with Cu) by using chiral ligands, usually amino ligands, to induce the axial configuration **27** + **27** to **20**.[32] Furthermore, based on redox-neutral couplings **22** + **28** to **20**.[33]

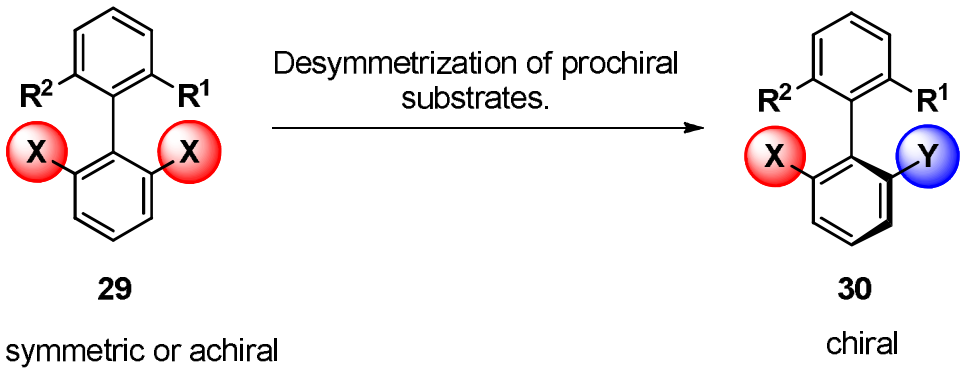


Scheme 2

1.5.2 Stereoselective functionalization of racemic biaryls compounds

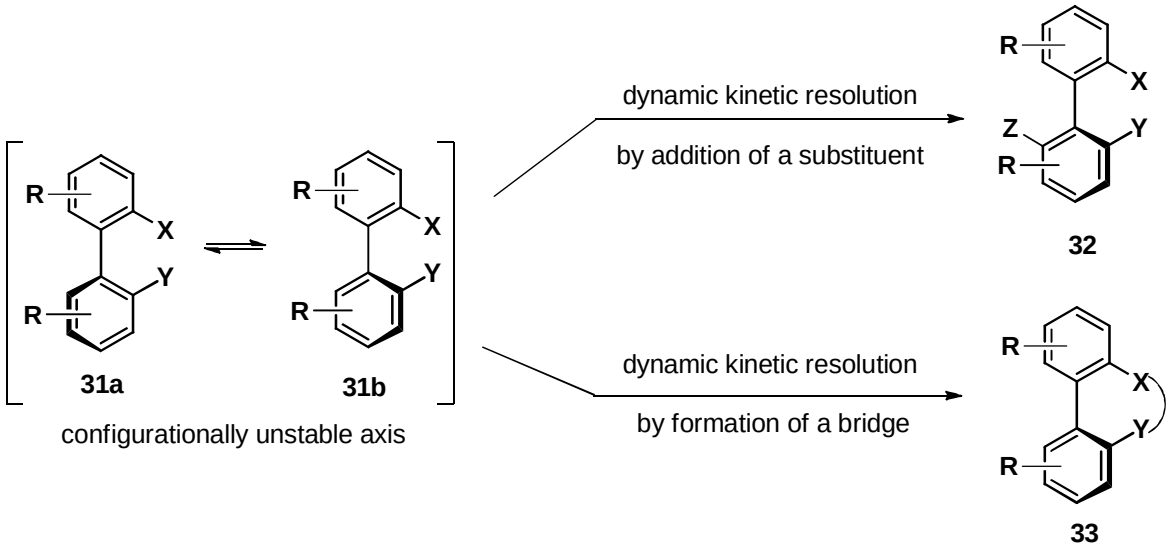
Besides the conventional approach of direct atroposelective biaryl coupling described in the preceding section, this method describes conceptually simplest way to produce chiral biaryl compounds from configurationally labile biaryl species, in an enantiomer-differentiating manner. In this method construction of the target biaryl species is carried

out over two separate steps: a nonstereoselective C-C coupling reaction and a second step that finally establishes the absolute configuration at the biaryl axis. This concept permits optimization of each of the two steps independently. For such an introduction of the stereochemical information at a preformed axis, the biaryl substrate has to be either rotationally hindered but achiral or chiral but configurationally unstable. The first criterion is met if (at least) one of the two aromatic portions is constitutionally symmetric, as in **29** (Scheme 3). An enantiotopos-differentiating transformation of one substituent (here X to Y) will reduce the symmetry and, thus lead to axially chiral biaryl products of type **30**.[34]



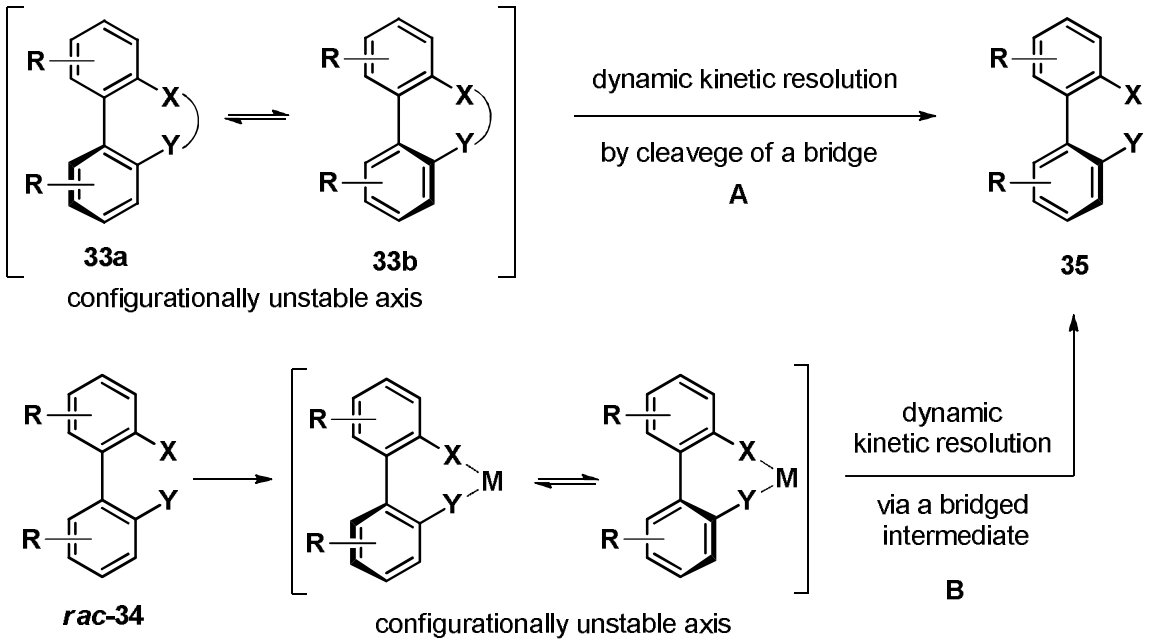
Scheme 3

Nonsymmetric biaryl compound **31** was achiral owing to rapid atropisomeric interconversion can be used as substrates for dynamic kinetic resolution. One option, though rarely used, is the atropoenantiomer-differentiating introduction of another *ortho* substituent, which establishes and simultaneously "locks" the axial conformation as in **32** (Scheme 4).[35] Alternatively, atropoenantiomer-differentiating bridging of the two aromatic halves of **31** delivers axially chiral biaryl species of the type **33** if this process is associated with an increase in the rotational barrier sufficient to reach configurational stability (Scheme 5).[36] Vice versa, the cleavage of a short bridge that causes configurational instability, as in 33a to 33b, allows an elegant access to axially chiral biaryl products (Scheme 5A).



Scheme 4

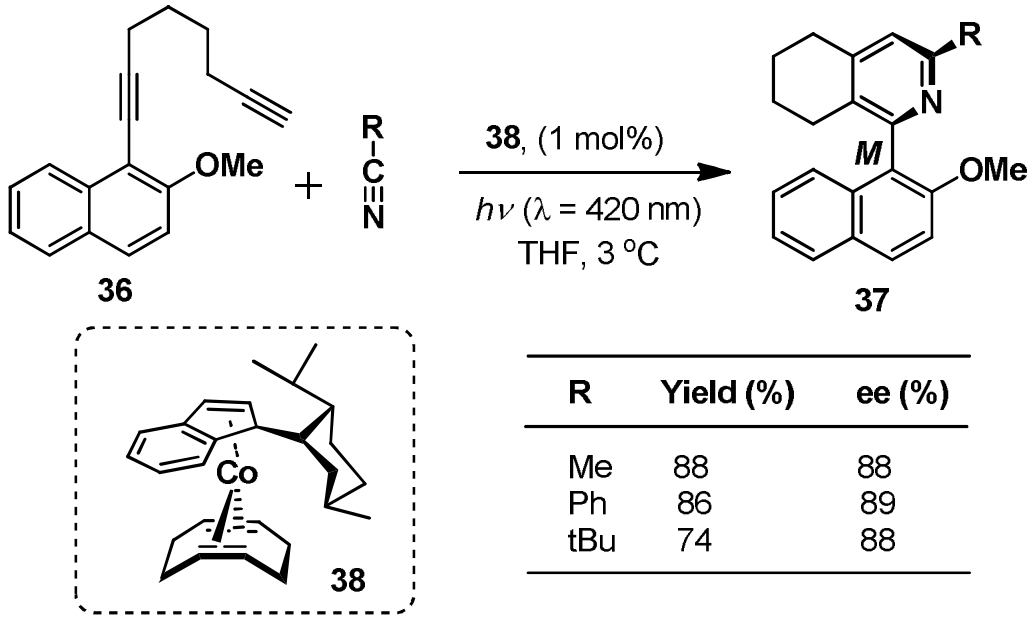
Moreover, biaryl compounds that are configurationally stable under normal conditions can undergo atropodiastereomerization if transiently bridged by a transition metal; this protocol can be used for the dynamic kinetic resolution of biaryl species that are stereochemically stable under ordinary conditions, for example, rac-**34** to chiral **35** (Scheme 5B)[37].



Scheme 5

1.5.3 Atropisomerism via construction of aromatic ring(s)

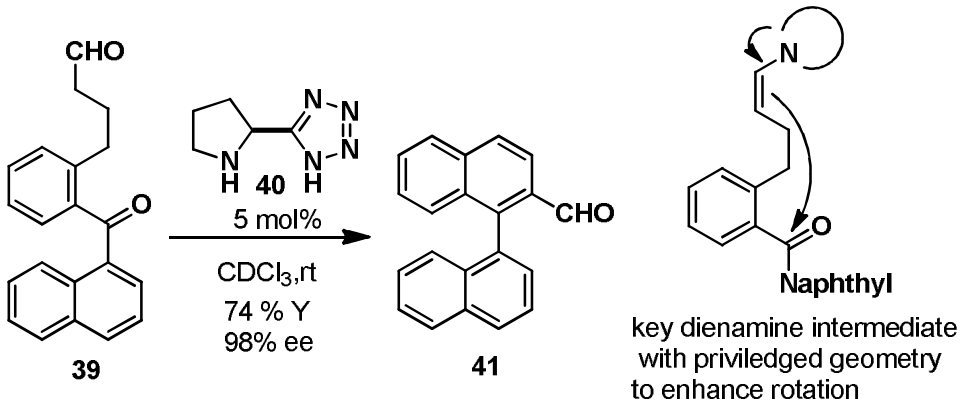
Besides the more classical direct asymmetric coupling reactions (Scheme 3) and the atroposelective transformations on already prepared biaryl systems, a fundamentally new strategy for the construction of chiral biaryl compounds has emerged recently. In this concept, a preformed aryl-C single bond is transformed atroposelectively into the biaryl axis upon construction of the second arene ring from an aryl C substituent (Scheme 6 & 7). Thus, the groups of Gutnov and Heller synthesized axially chiral 2-aryl pyridines by a catalytic asymmetric [2+2+2] cycloaddition.[38] The reaction of the 1-naphthyl diyne **36** with alkyl or aryl nitriles in the presence of the cobalt catalyst **38** (Scheme 6) gave the pyridines (*M*)-**37** in good yield and optical purity.



R	Yield (%)	ee (%)
Me	88	88
Ph	86	89
tBu	74	88

Scheme 6: Atropoenantioselective synthesis of the 1-aryl-5,6,7,8 tetrahydroisoquinolines (*M*)-**37** by asymmetric [2+2+2] cycloaddition.

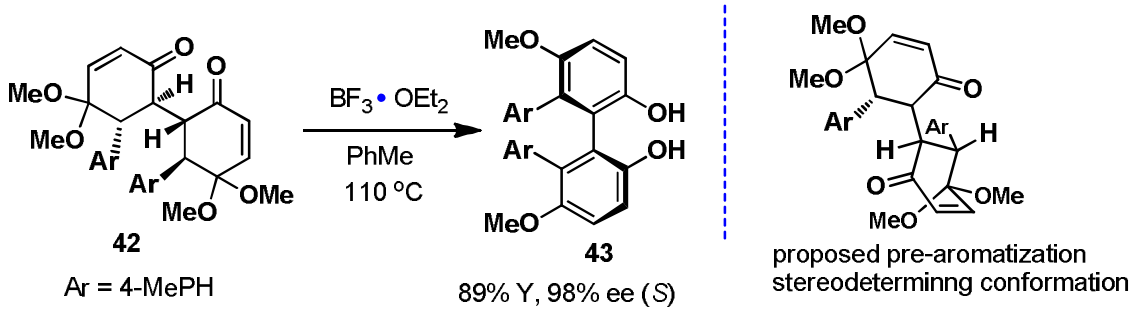
In 2014 Sparr *et al.* adopted a distinct, biosynthetically inspired route toward atroposelective biaryls implying a (2-pyrrolidinyl)-tetrazole catalyzed aldol condensation cascade reaction (Scheme 7).[39] The secondary chiral amine **40** will undergo an activation *via* dienamine formation and further catalyse the aldol reaction leading to the formation **41** in excellent atropselectivity and chemical yield.



Scheme 7

1.5.4 Stereoselective rearomatization: ''central-to-axial chirality exchange''

Thomson and collaborators[40] have developed a reaction where the stereogenic centres present on the substrate should promote an efficient central-to-axial chirality transfer and thus delivering atropisomerically enriched moieties. This research group assumed that under aromatization conditions, highly sterically congested bicyclic diones **42** bearing four stereogenic carbons might be converted into an axially chiral biphenol **43** (Scheme 8). The aromatization occurs without rotation around the central carbon–carbon bond and thus the configuration of the axial chirality can be reliably predicted.

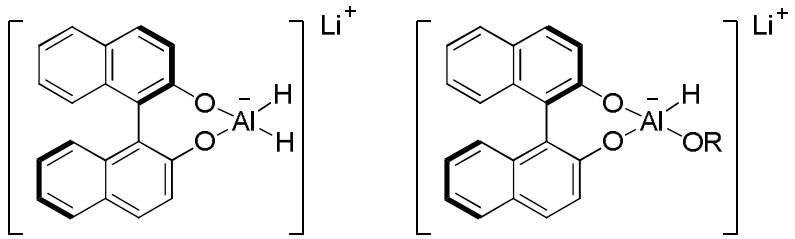


Scheme 8: Synthesis of biphenols by traceless central-to-axial chirality exchange

1.6 Applications of Atropisomers

Asymmetric synthesis has become a major topic of synthetic chemistry in the past two decades and today is probably the most important field of organic synthesis. The subject has especially become critical due to the discovery of correlation of chirality and the specific properties of optically pure medicines as compared to their racemic forms. An important tool for the introduction of a chiral centre to a molecule is asymmetric catalysis. This is commonly achieved through organometallic and coordination chemistry

by employing chiral ligands, in particular, axially chiral phosphorus-based ligands. Among a wide variety of asymmetric reactions, enantioselective reduction of prochiral carbonyl compounds is one of the most extensively studied transformations.[41] A standard method of this type involves the use of metal hydride complexes bearing chiral alkoxy or amino ligands. In this area several reagents have been developed, in particular by modification of lithium aluminium hydride. The first generation of this catalyst is 2,2'-dihydroxy-l,1'-binaphthyl-lithium aluminum hydride (*R*)-BINAL-H **44** prepared by mixing $LiAlH_4$ and an equimolar amount of enantiomerically pure l,l'-bi-2-naphthol (BINOL) in tetrahydrofuran (THF), gave a very poor enantiomeric excess (2%) in the reduction of prochiral acetophenone. Replacement of either hydrogen by an ethoxy group produces a modified aluminium hydride reagent. The reduction of prochiral alkyl phenyl ketones with three equivalents of this modified reagent, BINAL-H **45**, gave excellent enantiomeric excess (Figure 11).[42]



(*R*)-BINAL-H **44**

Modified (*R*)-BINAL-H **45**

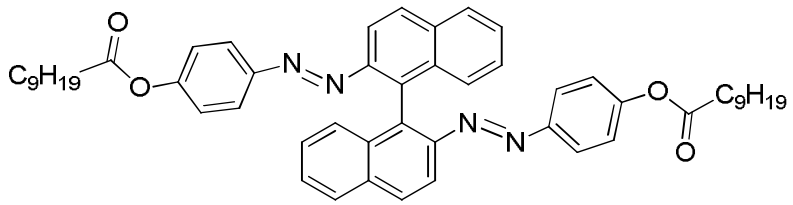
Figure 11

Derivatives of BINOL have been successfully employed in other important transformations such as the epoxidation of olefins,[43] oxidation of sulphides,[44] Diels-Alder reactions[45] and catalytic asymmetric Michael additions.[46]

Today, the design and synthesis of chiral phosphine ligands plays a central role in the development of highly enantioselective transition metal catalyzed asymmetric reactions. In fact, slight change in conformational, steric, and electronic properties of the chiral ligands can often lead to dramatic variations in reactivity and enantioselectivity. For atropisomeric diphosphines, for example, a small variation in the dihedral angle of the ligands can have a significant impact on the reactivity and selectivity of reactions.[47] Although atropisomeric biaryl phosphines have been used effectively as chiral ligands, for many asymmetric reactions, the design of new non biaryl atropisomeric chiral ligands had been extensively developed in last few years. The angled aromatic rings serve as a

useful scaffold for the attachment of metal coordinating heteroatoms and the complex formed with transition metal is one of the most useful catalysts in modern organic asymmetric synthesis.

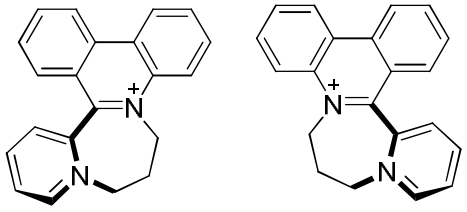
Apart from the most common application of atropisomers (chiral ligands, chiral auxiliaries), there are other applications of this kind of molecule in several areas of chemistry and technology. For example nanotechnology, molecular machines and molecular switches are subjects of continuous interest. Chiral molecular switches seem particularly attractive because they undergo reversible transformations connected to changes in the chiral response of the system under the influence of external factors. A typical example is the isomerization of an azo group when irradiated with light of the right frequency. Photochemically driven chiral switches seem promising for several technological applications.[48] Because axially chiral binaphthyl shows strong exciton in Circular Dichroism (CDs) and has large helical twisting power (which expresses the ability of a chiral solute to twist a nematic phase), they are suitable to be used in controlling the phase behaviour of liquid crystals. Gottarelli et al have reported the synthesis and study of diazo-derivative of (*R*)-,2,2-diamino-l,l'-binaphthyl **46** as liquid crystalline molecule (Figure 12).[49]



46

Figure 12

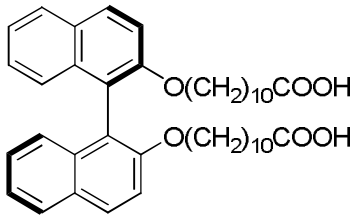
Chirality is an important phenomenon in many chemical and biological processes, playing a key role in the assembly of supramolecular structures and also recognition of biomolecules. The development of deoxyribonucleic acid (DNA) binding agents as nano probes of the structure of nucleic acid has gained considerable importance. Amongst several fluorescent molecules known to bind with DNA, atropisomeric luminescent viologens **47** is known to interact with DNA. It is also observed that (*S*) enantiomer of **47** has greater affinity for DNA as compared to (*R*)-**47**.[50]



47-(*S*) **47**-(*R*)

Figure 13

Apart from the application in biological systems, atropisomers are also known to have applications in material chemistry. Axially chiral molecules are known to show applications in the field of colloidal chemistry. Bai et al. have reported the synthesis of compound **48** and it was found to shown amphiphilic properties[51] and was used in the study of assembly behaviour.[52]



48

Figure 14

Although a significant amount of research has been conducted in the area of atropisomers over the past few years, additional investigations are required to effect further advances in and search newer applications in the field of asymmetric synthesis and in material chemistry.

In chapter 2, we have synthesized a series of atropisomeric *ortho*-substituted terphenyls. This chapter is divided into two sections. Section 1 describes the synthesis and attempted resolution of conformational isomers. Whereas in section 2 we will be explaining that all compounds showed conformational behaviour at room temperature as observed from the ^{1}H-NMR and the barrier to rotation for all synthesized compounds was measured by analyzing the variable temperature ^{1}H-NMR spectra. Thermodynamic data and barrier to rotation for all the *ortho* terphenyl derivatives has been summarized.

In chapter 3, we will be discussing how the atropisomeric binapthalene derivatives will be transformed to helicene and helicene like molecules. This chapter is mainly

divided into three sections. In section 1, we will be discussing the synthesis, resolution and determination of configuration of binapthalene compounds. Whereas in section 2 we will describe the synthesis of helicene like molecules from atropisomeric binaphthalene intermediates. The molecules have been subjected to the study of their Circularly Polarized Luminescence (CPL), which is the emission analogue of CD, to further investigate the influence of the helical like structure of the compounds on the chiroptical properties. Section 3 will be discussing the synthesis of hetero helicene molecules from atropisomeric molecules, and its resolution and the optical, thermal properties were studied.

Chapter 4 will be explained miscellaneous atropisomeric molecules. This chapter further divided into two sections. Section 1 will be described atropisomeric biphenyls derivatives have been synthesized and studied for their possible Micheal reaction as application. In section 2 describes our efforts to make a chiral axis of target benzil molecules. During the synthesis of benzil axis we isolated unexpected product and we have proposed mechanism to explain the formation of products from benzil.

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