Dynamic Induction of Enantiomeric Excess from a Prochiral Azobenzene Dimer under Circularly Polarized Light.

[円偏光によるプロキラルアゾベンゼン二量体からの鏡像異性体過剰の動的誘起]

A Thesis

Submitted for the Degree of

Doctor of Life Science

By

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Laboratory of Smart Molecules

Transdisciplinary Life Science Course

Graduate School of Life Science

Hokkaido University

Japan, 2015

Dedicated to my teachers,

parents and family…

DECLARATION

I hereby declare that the matter embodied in this thesis entitled **"Dynamic Induction of Enantiomeric Excess from a Prochiral Azobenzene Dimer Under Circularly Polarized Light"** is the result of investigations carried out by me under the supervision of ***Prof. Nobuyuki Tamaoki*** at the Laboratory of Smart Molecule, Transdisciplinary Life Science Course, Graduate School of Life Science, Hokkaido University, Japan and it has not been submitted elsewhere for the award of any degree or diploma.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made whenever the work described has been based on the findings of the other investigators. Any omission that might have occurred by oversight or error of judgments is regretted.

Rijeesh Kizhakidathazhath

CERTIFICATE

I hereby certify that the work described in this thesis entitled **"Dynamic Induction of Enantiomeric Excess from a Prochiral Azobenzene Dimer Under Circularly Polarized Light"** has been carried out by ***Rijeesh Kizhakidathazhath***, under my supervision at the Laboratory of Smart Molecule, Transdisciplinary Life Science Course, Graduate School of Life Science, Hokkaido University, Japan.

Prof. Nobuyuki Tamaoki

(Research Supervisor)

CONTENTS

1. Introduction

Chirality means ‘handedness’ and is a phenomenon that fascinated the scientists for centuries. A molecule is said to be chiral if it can exist as isomers that are non-superimposable on its mirror images , just like right and left hands of human beings. In chemistry, chirality usually refers to the symmetry concept of molecules.[1] Louis Pasteur was the first to realize that the chemistry of life has preferred handedness with the discovery of that salts of tartaric acid exist as mirror image crystals.[2] Later, vant’ Hoff and Le Bel independently recognized the existence of chiral molecules.[3] Now, it is well established that molecular chirality plays a major role in chemistry, biology and pharmaceutical sciences.[4]

The two mirror images of a chiral molecule are referred to as enantiomers. The chemical properties of enantiomers are identical in a symmetrical environment but different in asymmetrical environment. Enantiomers have identical physical properties, but rotate the plane of polarized light in opposite directions and by the same amount. This behavior is called optical activity and it is directly related to the phenomenon of chirality. Chiral substance display optical activity, hence, a pure enantiomer is optically active. An equimolar mixture of two enantiomers shows no optical activity because the effect of both enantiomers on the polarization vector cancels out. Such a mixture is

called racemic mixture or racemate and it is not chiral. The term enantiomeric excess (ee) is used to quantify the composition, if the mixture contains a surplus of one enantiomer.

The process of chiralization implies the transformation of an achiral molecule (molecule possess superimposable mirror images) to chiral one. If the chiralization path takes a single step, then the achiral molecule is termed as prochiral. Prochirality is of particular importance in the treatment of asymmetric synthesis.[4a]

The source of chirality can originate from different types of structural elements: a center, an axis and a plane of chirality. The most common one is center chirality, usually generated when a tetrahedron atom is attached to four different groups. All the amino acids and sugars in living organism display central chirality. Other types are axial chirality, planar chirality and helical chirality. Axial chirality arises when a set of substituents sit in a non-planar arrangement about a chiral axis and mainly observed in biaryl compounds wherein the rotation about the aryl-aryl bond is restricted due to the bulky *ortho* substituents, which gives rise atropisomerism. A molecule possessing two dissymetrically substituted non-coplanar rings (lacking plane of symmetry) results in planar chirality. Biomolecules such as DNA and protein exhibits helical chirality. Helix can be right- or left-handed and are therefore non-superimposable on their mirror

images.[1a], [4a] Figure 1 shows the examples of all different types of chirality.

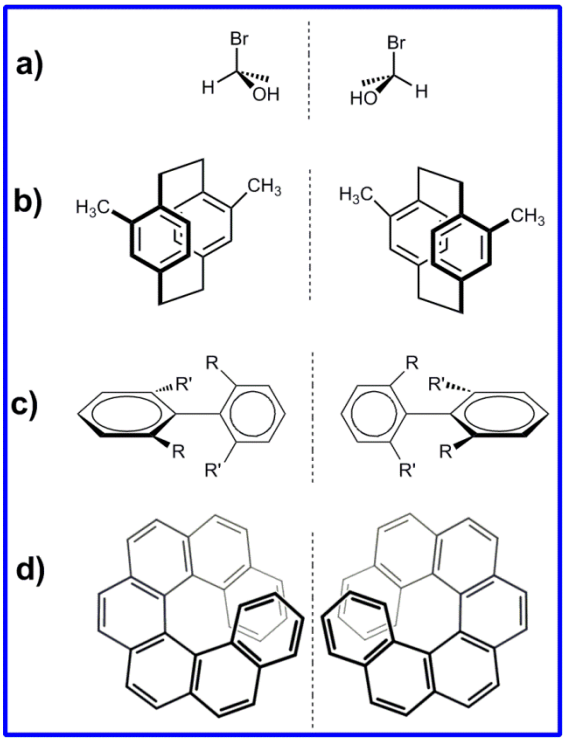


Figure 1: Examples of different type of chirality: a) central chirality: C atom with 4 different substituents; b) planar chirality: cyclophane; c) axial chirality: tetra-substituted biphenyl (atropisomers); d) helical chirality: helicenes.

Homochirality of the essential molecules is one of the fundamental and intriguing aspects of life and has attracted the scientists for a long time.[5-10] The ribose and deoxyribose in RNA and DNA have only D-configuration, whereas the 20 amino acids (except glycine) that form the proteins are of L-configuration.[6] This chiral homogeneity is essential for molecular recognition and replication processes and thus, for the existence of life.[6], [4b] The fundamental questions of how the single

handedness of biomolecules arose in Nature, at what stage of evolutionary process homochirality became dominant, are not yet answered[12] and continue to be a challenging opportunity for many scientists.

Several theories and experiments have been reported to explain the homochirality in Nature.[5-10] Though several physical sources have been proposed to achieve enantiomeric imbalance in molecular systems,[11-12] circularly polarized light (CPL) is the most discussed chiral physical field[12-16] considering the occurrence of strong CPL in a star formation region of the Orion constellation.[17] and believed to be a strongest candidate for explaining the bimolecular homochirality that exists in Nature. In addition, excess of L-amino acids have been found in nonterrestial carbonaceous meteorites, supporting the role of interstellar circularly polarized light in the initial enantiomeric bias.[7], [12], [18]

Circularly polarized light is a chiral electromagnetic radiation exists in pairs of *r*- or *l*-CPL can selectively interact with chiral molecules. The principle of enantiomeric enrichment upon CPL irradiation depends on the differential absorption of *r*- or *l*-CPL by the two enantiomers of an optically active molecule. The degree of preferential excitation is measured by the *g* factor (Kuhn anisotropy factor), which is defined as the normalized difference in molar extinction coefficients between enantiomers toward *l*- or

r-CPL at a particular wavelength.[19]

$$g = (\varepsilon_R - \varepsilon_S)/\varepsilon \quad (1),$$

where ε_R and ε_S are the molar extinction coefficients of each enantiomer toward *l*- or *r*-CPL and $\varepsilon = (\varepsilon_R + \varepsilon_S)/2$. The most sensitive and reliable method to measure optical activity of chiral molecules is circular dichorism (CD). This measures the difference $\Delta\varepsilon$ in the absorption of left- and right-circularly polarized light by an optically active molecule (equation 2).

$$\Delta\varepsilon = \varepsilon_R - \varepsilon_S \quad (2)$$

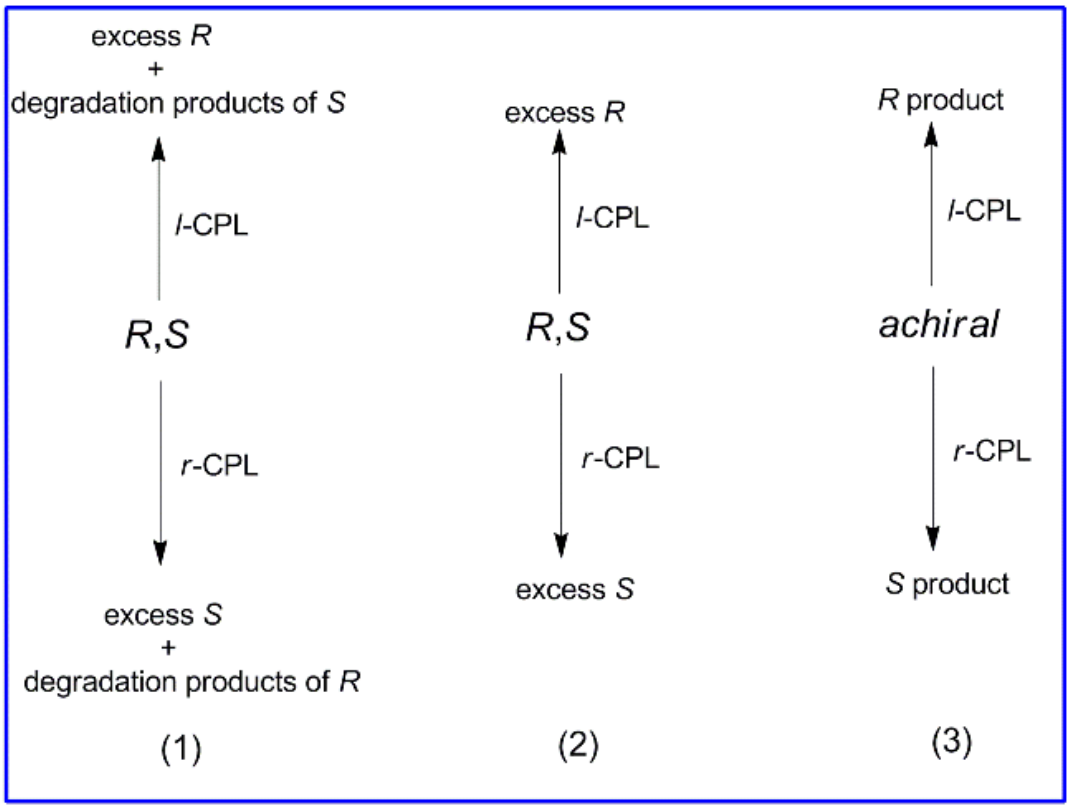
CPL mediated photoreactions have been classified into three categories according to the manner of enantioselective conversions:[12]

(1) Photodestruction- An irreversible process, in which one of the enantiomers is preferentially destroyed to achiral product by *r*- or *l*-CPL and the other remaining enantiomer is enriched.

(2) Photoresolution- A reversible deracemization process of photochemically interconvertible enantiomers. Here the enantiomer which is selectively excited by CPL undergoes racemization and other enantiomer which is less able to absorb *r*- or *l*-CPL will cause enantiomeric excess in the solution. In this process, the irradiation of racemic mixture with *l*-CPL will cause the excess of *R* enantiomer whereas

irradiation with *r*-CPL will accumulate *S* enantiomer (or reverse enantioselectivity takes place).

(3) Asymmetric synthesis- An enantioselective photoreaction leading to the formation an optically active product from a prochiral starting material.



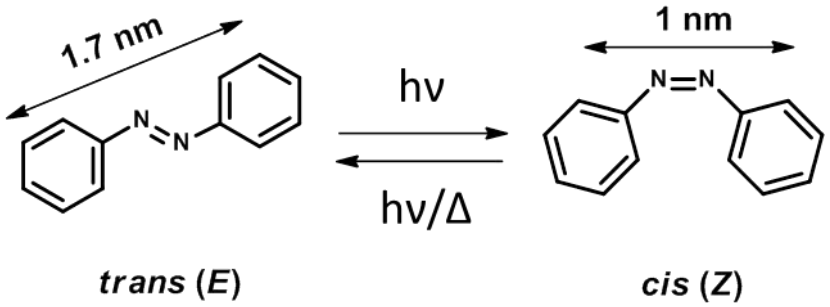
Scheme 1: Three types of CPL-induced enantiodifferentiating photoreactions.[12]

Following studies by vant' Hoff and Le Bel to show that the *r*- and *l*-CPL might be used to induce enantiomeric excess in chemical reactions,[20] several efforts have been made to realize this idea. Kuhn and co-workers succeeded in enantioselective photodestruction of dimethylamide of α-azidopropionic acid.[21] Soon after this study

Mitchel reported optical rotation in the product after the irradiation of humulene nitrosite with CPL.[22] In 1977 Flores et al showed the small enantiomeric excess of racemic chiral compounds including amino acids upon UV-CPL irradiation.[23] Next to photodestruction, Stevenson and Verdieck as well as Norden published papers on photoderacemization of octahedral bidentate Cr^{III} complexes.[24] Later, the groups of Kagan and Kelvin published a series of papers on CPL-induced enantioselective synthesis of helicenes.[25]

The degree of enantiomeric excess obtained in CPL induced photoreactions is too small to be compared with the homochirality in Nature. Thus, amplification of the slight enantiomeric excess induced by CPL is necessary to correlate it with the chiral homogeneity occurring in biomolecules. Soai et al and Shibata et al reported that the small enantiomeric excess by CPL can be converted to enantiomerically pure by asymmetric autocatalysis.[26] Recently Feringa and coworkers also have succeeded in amplification process of a photochromic alkene system via doping in liquid crystals. [27] Regardless of great progress in asymmetric synthesis, there are only a few genuine examples for CPL-induced photoreactions and thus, enantiomeric enrichment of organic compounds using CPL is still continues to be an area of high interest for the researchers.[28-30]

Azobenzene is a well known photochromic compound, undergoes trans→cis isomerization upon irradiation with appropriate wavelength. The reverse *cis→trans* isomerization can be driven by light or occurs thermally in the dark. Azobenzene changes its geometry upon isomerization, makes the molecule to be utilized as a light triggered switch in variety of polymers, surface-modified materials, protein probes, molecular machines, holographic recording devices and metal ion chelators.[31]



Scheme 2: Scheme showing *E-Z* photoisomerization of azobenzene.

Geometric (*E* and *Z*) and stereo (*R* and *S*) isomerisms are usually independent elements of molecular structures, but sometimes they are related to each other. In 1963 Cope et al. reported that *trans* cyclo-octene exists as *R* and *S* enantiomers, whereas *cis* cyclo-octene does not due to its planar ring structure.[32] Recently, we reported an azobenzene tethered naphthalene and dimethyl benzene rotors, in which the *E*-state of the azobenzene show stable and resolvable enantiomers due to their planar chiral nature of the molecules, while the fast racemizing *Z* state made the isolation of enantiomers difficult.[33] The dynamic asymmetry induction by *E-Z* photoisomerization of an

azobenzene from a prochiral azobenzene dimer is a newly introduced concept by our group. In this thesis, the *cis-trans* isomerization of azobenzene upon photoirradiation is successfully utilized for the generation of point, planar and axial chirality.

Although trifold classification was introduced for CPL mediated asymmetric photoreactions, an unequivocal classification is sometime not possible. The main difference between the photoresolution and absolute asymmetric synthesis is whether the chirality itself is generated during the photoreaction or not. In photoresolution, the starting compound is usually racemic mixture of a chiral molecule, which can be converted reversibly to its antipode through a photochemical path. Such reversible enatio-differentiating photoisomerization of chiral molecules using CPL based on the preferential interaction of *r*- or *l*-CPL with one of the enantiomers is known for some compounds.[24],[34] In the past decades few groups have reported dynamic photoresolution using CPL irradiation on sterically overcrowded alkene[27],[35] or bicyclic ketone systems,[36] which undergo photoresolution through a chiral discrimination path from the electronic ground states to a common excited state at which racemization of one of the enantiomers selectively excited by *r*-or *l*-CPL takes place. Recently we have reported photoresolution of bicyclic[37] and monocyclic[33] azobenzene systems by CPL as a chiral source where a ground state of the *cis* form was

used as a common fast racemizing state to which the enantiomers of *trans* form selectively photoisomerized by *l*-or *r*-CPL. In contrast, only one example of asymmetric synthesis with CPL has been reported: for photochemical conversion of nonchiral diarylolefins to chiral helicene derivatives.[25]

In this dissertation, I introduce a new CPL-induced reaction of a nonchiral compound forming a chiral product with an imbalance in the ratio of its enantiomers. In this concept, enantiomeric induction occurs from a prochiral azobenzene dimer through *in situ* formation of a chiral structure upon CPL irradiation at a suitable single wavelength. I propose a new absolute asymmetric synthesis, where enantiomeric imbalance is obtained as a result of an enatio-differentiating photoisomerization path from the photochemically formed enantiomers for one chiral regioisomer to a common ground state of its other non-chiral regioisomers.[38] To the best of my knowledge, this example is the first demonstration of simultaneous induction of chirality and enantiomeric enrichment under CPL irradiation from a prochiral molecule through enantio-differentiating photoisomerization of a photochemically formed chiral structure.

Here, I synthesized a prochiral molecule with the incorporation of two photoisomerizable phenyl azo groups to the ortho positions of benzene ring connected to a naphthalene moiety, **3**. The conformational difference caused by the *E-Z*

photoisomerization of one of the azobenzene moieties substituted to this molecule was successfully utilized for the induction of axial chirality. Recently, our group reported similar studies for central and planar chirality generation in compounds **1** and **2**, respectively.[39][40] In compound **1**, the phenyl azo groups were linked to benzene rings attached to a tetrahedral carbon atom having methyl group and phenyl group, whereas in compound **2**, phenyl azo moieties were introduced as a part of [2.2]paracyclophane. Further, I investigated the possibility of inducing enantiomeric excess in compounds **1**, **2** and **3** by CPL irradiation. The Kuhn anisotropy factor, g calculated from $\Delta\varepsilon$ of photochemically formed chiral structures *EZ* of molecule **1** and **2** were very small resulting the detection of *ee* on CPL irradiation difficult, and was further proved by CD experiments. Interestingly, compound **3** with two photoisomerizable azobenzene on a benzene-naphthalene framework showed reasonably high $\Delta\varepsilon$ and g value, which allowed it to be used in photoresolution study with CPL. Upon *r*-and *l*-CPL irradiation, compound **3** exhibited reversible enantio-differentiating photoisomerization with detectable circular dichorism within a short time.

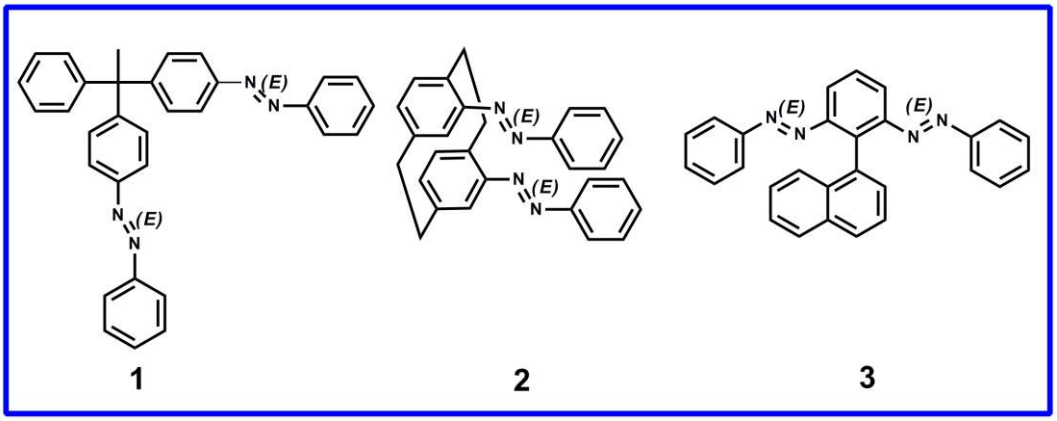
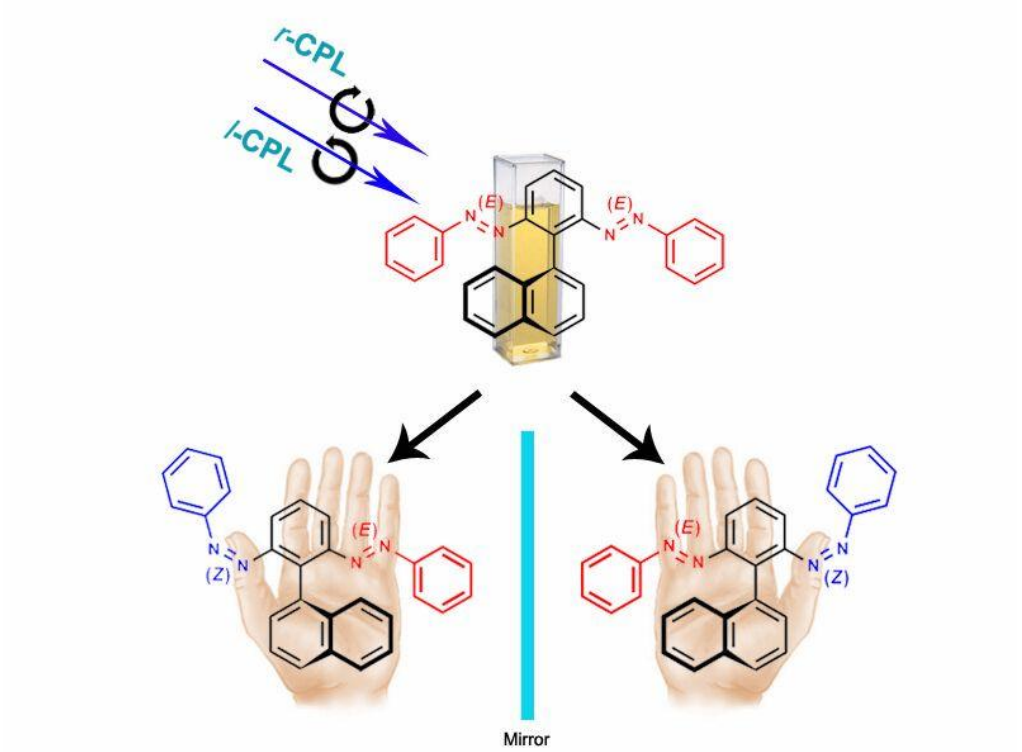


Figure 2: Three different types of prochiral azobenzene dimers.



Scheme 3: Schematic illustration of chirality induction from a prochiral azobenzene dimer **3** upon CPL irradiation.

2. Experimental section

2.1 Materials.

Unless otherwise noted, reagents and solvents were used as received from commercial sources without further purification. Column chromatography was performed on silica gel (60N, spherical, neutral, 40-50 μm), which was purchased from Kanto Chemicals.

2.2 General methods, instrumentation and measurements.

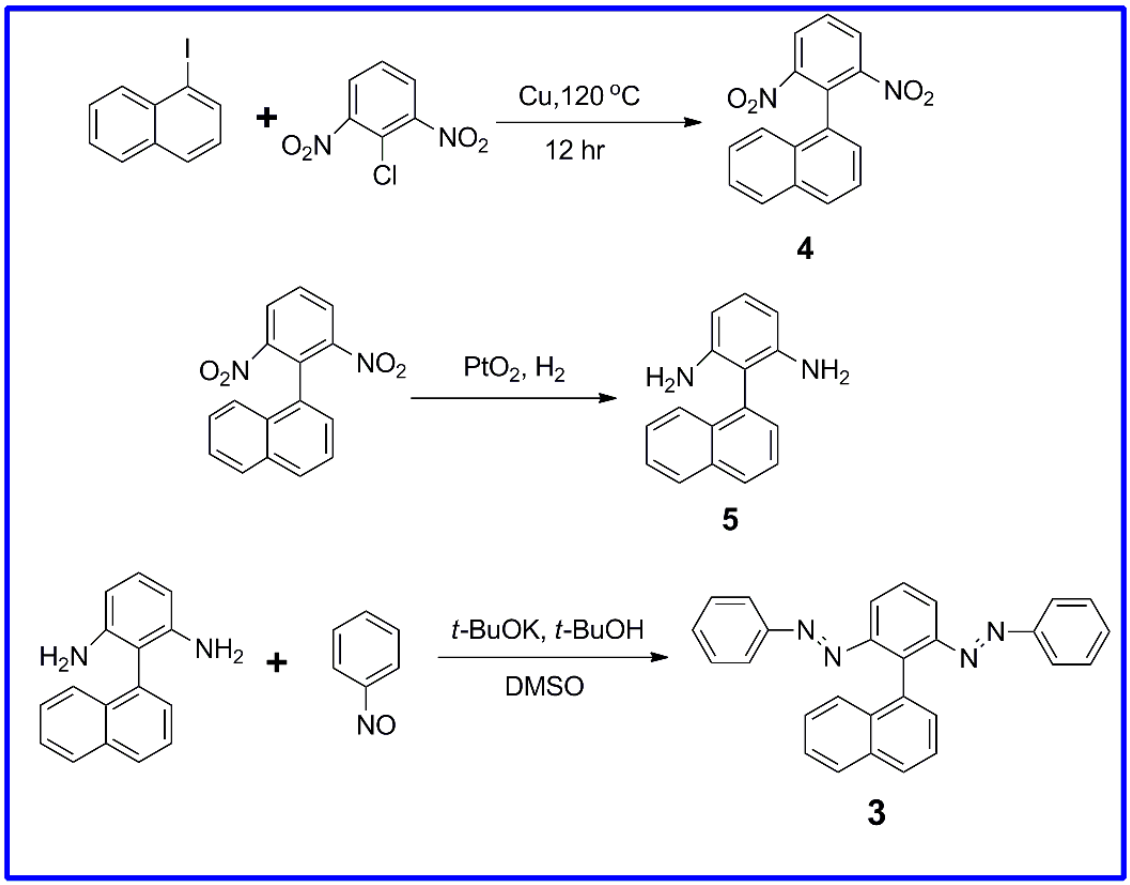
NMR (^{1}H and ^{13}C) spectra were recorded on a JEOL ECX 400 spectrometer using tetramethylsilane as an internal standard. Electronspray ionization mass spectrometry (ESI^{+}) was performed on an AccuTOF (JMS-T100LC; JEOL). Absorption spectra were recorded on an Agilent 8453 spectrophotometer. CD spectra were recorded on a JASCO J-720 spectropolarimeter. Photoisomerization studies were conducted using radiation from a LED source of 365 nm (LED Controller, HAMAMATSU) and super-high-pressure mercury lamp (500W, USHIO Inc.) after passage through 436 nm optical filters (Asahi Spectra Co., Ltd.). High-performance liquid chromatography (HPLC) was conducted on a Hitachi Elite La Chrome HPLC system using a CHIRALPAK IA column (DAICEL Chemical Industries Ltd.). Photo stationary state

compositions were determined by HPLC analysis. The mixture of isopropanol/hexane (2:8) was used as an eluent for HPLC experiments.

2.3 Synthesis.

All of the azobenzene dimers were synthesized in moderate or low yield from their corresponding diamines and nitrosobenzenes and the detailed synthetic process for compound **1** and **2** were described previously.[39],[40] The synthesis of compound **3** was outlined as shown in scheme 1. The parent dinitrobenzene-naphthalene framework was obtained by the crossed Ullmann condensation reaction between 1-iodonaphthalene and 1-chloro-2, 6-dintrobenzene in the presence of copper bronze.[41] The PtO_2/ H_2 reduction of 1-(2,6-dintrophenyl)naphthalene **4** led to the corresponding diamine compound **5** in high yield and confirmed the product formation by NMR and mass analysis.[42] Compound **5** was reported previously as a byproduct while checking the action of hydrazines on β-naphthol in the presence of bisulphite,[43] however, an efficient synthesis and characterization of this diamine **5** has not been discussed so far. I hope it can be used as a starting material for the synthesis of various interesting compounds in material science. The azo units were introduced according to a simple base-catalyzed procedure using nitrosobenzene in the presence of potassium *t*-butoxide

in a *t*-butanol-DMSO solvent mixture and significant amount of diazo compound **3** was isolated.[44]



Scheme 4: Synthetic route to compound **3**.

Compound 4.

1-Chloro-2,6-dintrobenzene (250mg, 1.23mmol), iodonaphthalene (320mg, 1.26mmol) and copper bronze (320, 5.04 mmol), were heated at 120 °C for 12 h (till the dintrochloro benzene spot faded in TLC analysis). After completion of the reaction, the

product was extracted in dichloromethane and washed with water and dried over $MgSO_4$. The solvent was evaporated under vacuum and the product was isolated by column chromatography on silica gel using dichloromethane and hexane (4:6). A pale yellow solid was obtained in 38% yield. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS); δ = 8.16 (d, *J* = 8.2 Hz, 2H), 7.92 (dd, *J* = 8.2, 8.3 Hz, 2H), 7.81 (t, *J* = 8.2 Hz, 1H), 7.49-7.53 (m, 2H), 7.42-7.46 (m, 1 H), 7.33-7.34 ppm (m, 2H).

Compound 5.

Compound **4** (100 mg, 0.34 mmol) was dissolved in 2:1 mixture of ethanol and 1, 4-dioxane (5 ml) and the reaction flask was evacuated and backfilled with argon three times. Added PtO_2 (10 mg, 0.4mmol) under argon atmosphere and changed the atmosphere from argon to hydrogen. The reaction mixture was stirred at room temperature till TLC (mobile phase: 20% ethyl acetate and hexane) shows a single spot, approximately overnight. The catalyst was removed by filtration over celite and evaporated the solvent to dryness under vacuum to yield a brownish solid (71 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{0}C, TMS): δ = 7.90-7.92 (m, 2 H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.58-7.61 (m, 1H), 7.49-7.54 (m, 2H), 7.42-7.46 (m, 1H), 7.07 (t, *J* = 7.9 Hz, 1H), 3.32 ppm (s, 4H); MS (ESI$^+$): m/z: calcd for $C_{16}H_{14}N_2$ $[M+H]^+$: 235.12; found: 235.11

Compound 3.

To a solution of **5** (53 mg, 0.226 mmol) and *t*-BuOK (101 mg, 0.900 mmol) in a mixture of DMSO and *t*-BuOH (4 mL:1 mL) was added nitrosobenzene (96.4 mg, 0.900 mmol) and the reaction mixture was stirred for 12 h, at room temperature. The resulting mixture was poured into a saturated NH_4Cl aqueous solution and extracted with dichloromethane. The organic layer was washed with water and then dried over $MgSO_4$. The solvent was evaporated and the residue was directly column chromatographed over silica gel using dichloromethane and hexane (4: 6) as eluent to get compound **3** as an orange solid (20 mg, 21% yield). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.91- 7.97(m, 4 H), 7.68 (t, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.27-7.46 ppm (m, 13H). ^{13}C NMR (400 MHz, CDCl3, 25 C, TMS); 152.79, 152.12, 139.54, 133.67, 133.61, 133.11, 131.09, 129.94, 129.02, 128.90, 128.49,128.04, 127.94, 127.22, 126.16, 125.97, 125.42, 124.65, 123.15, 123.05, 120.81, 117.83 ppm; MS (ESI^+): m/z calculated for $C_{28}H_{20}N_4$: 413.16 $[M+H]^+$; found: 413.17.

2.4 NMR and Mass Spectra.

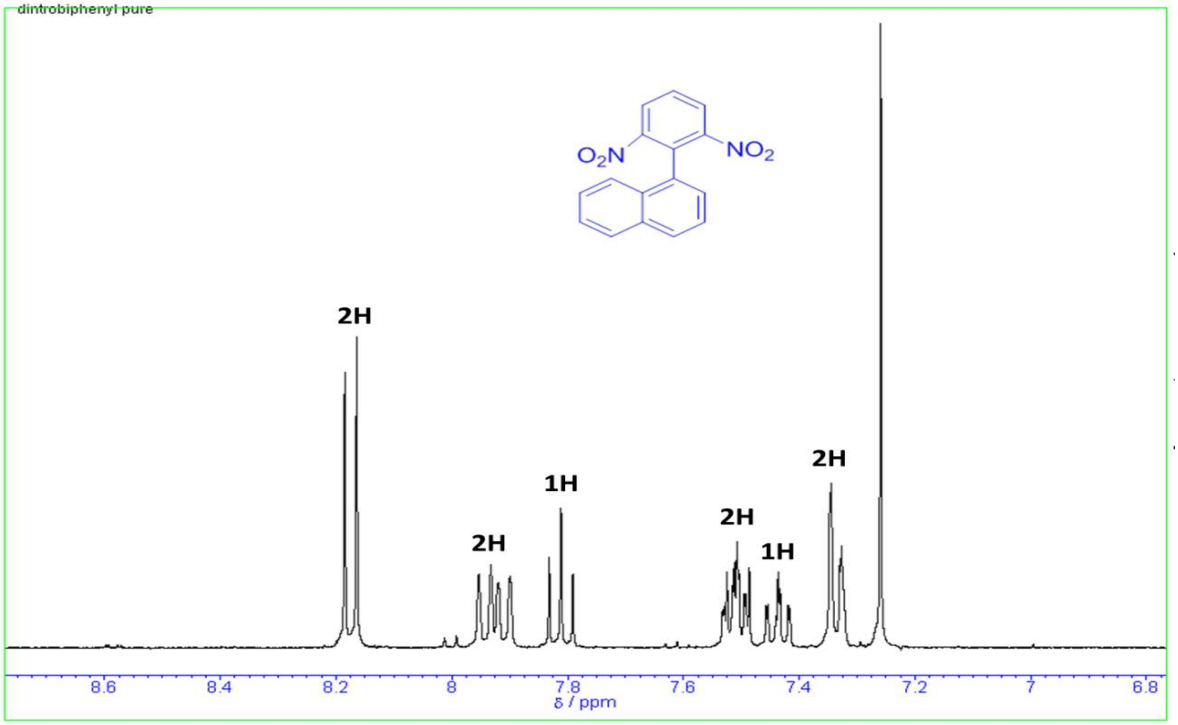


Figure 3: ^{1}H NMR Spectra of compound-**4** in $CDCl_3$ at room temperature

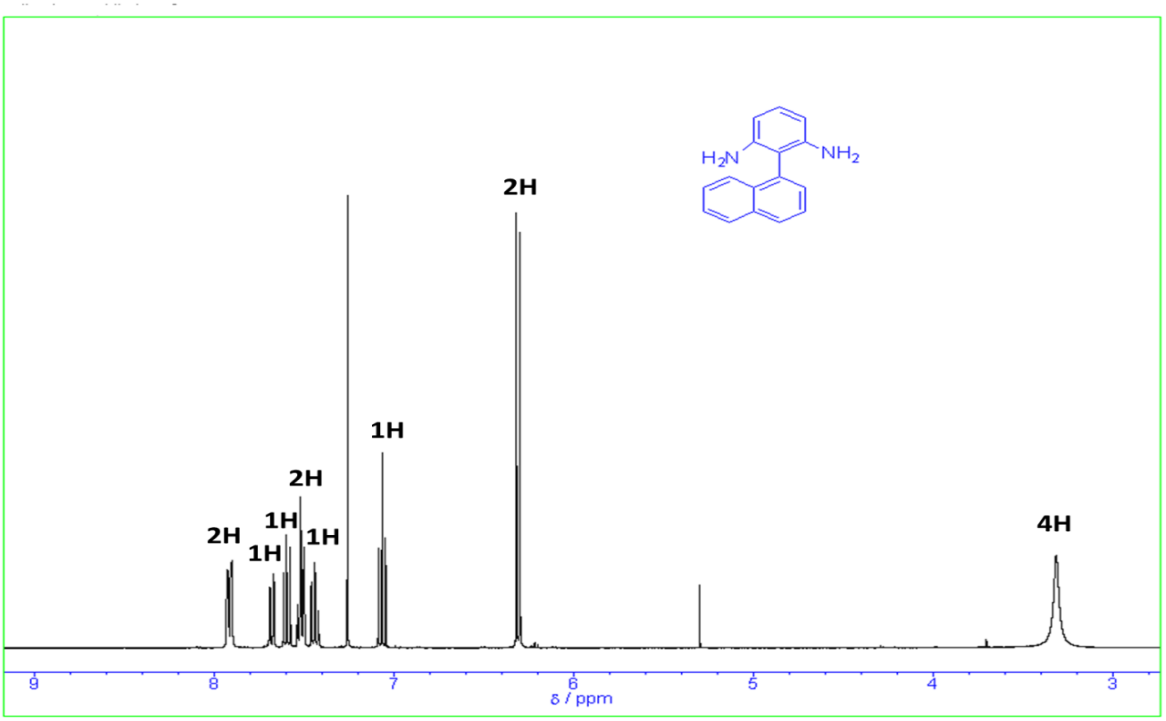


Figure 4: ^{1}H NMR Spectra of compound-**5** in $CDCl_3$ at room temperature

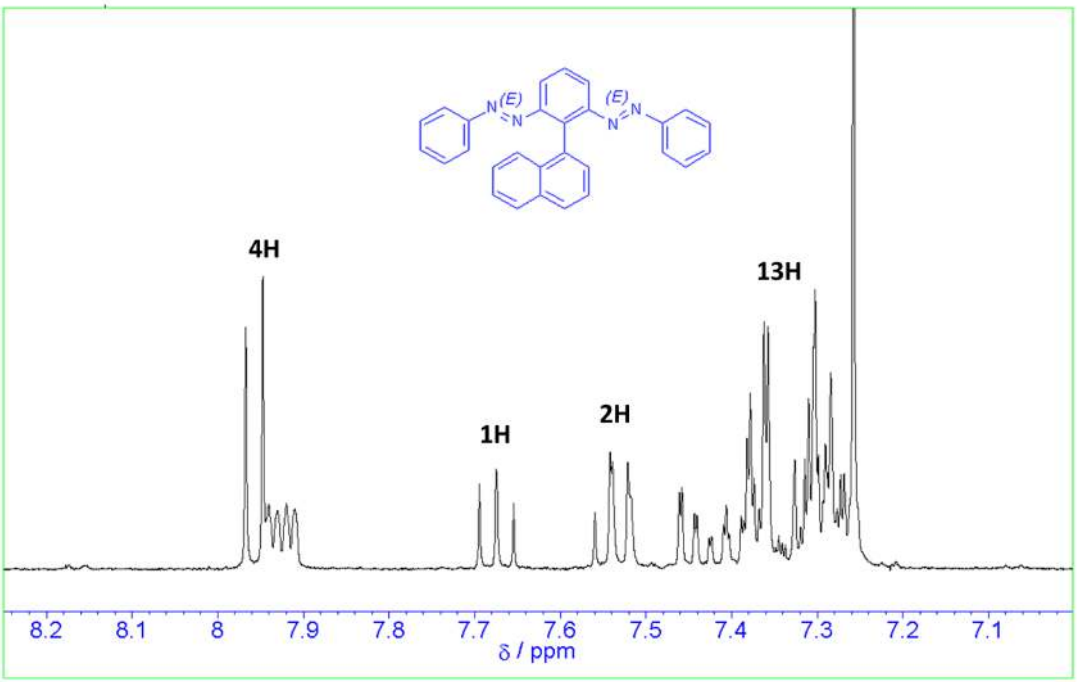


Figure 5: ^{1}H NMR Spectra of compound-**3** in $CDCl_3$ at room temperature

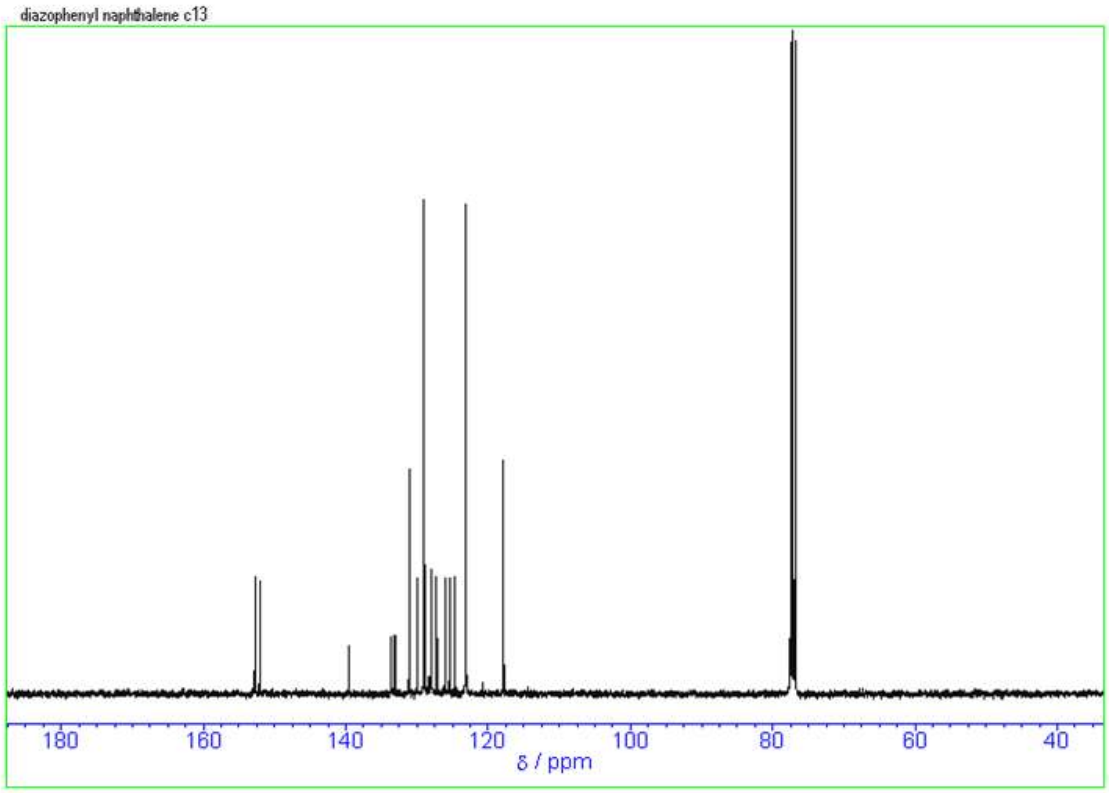


Figure 6: ^{13}C NMR Spectra of compound-**3** in $CDCl_3$ at room temperature

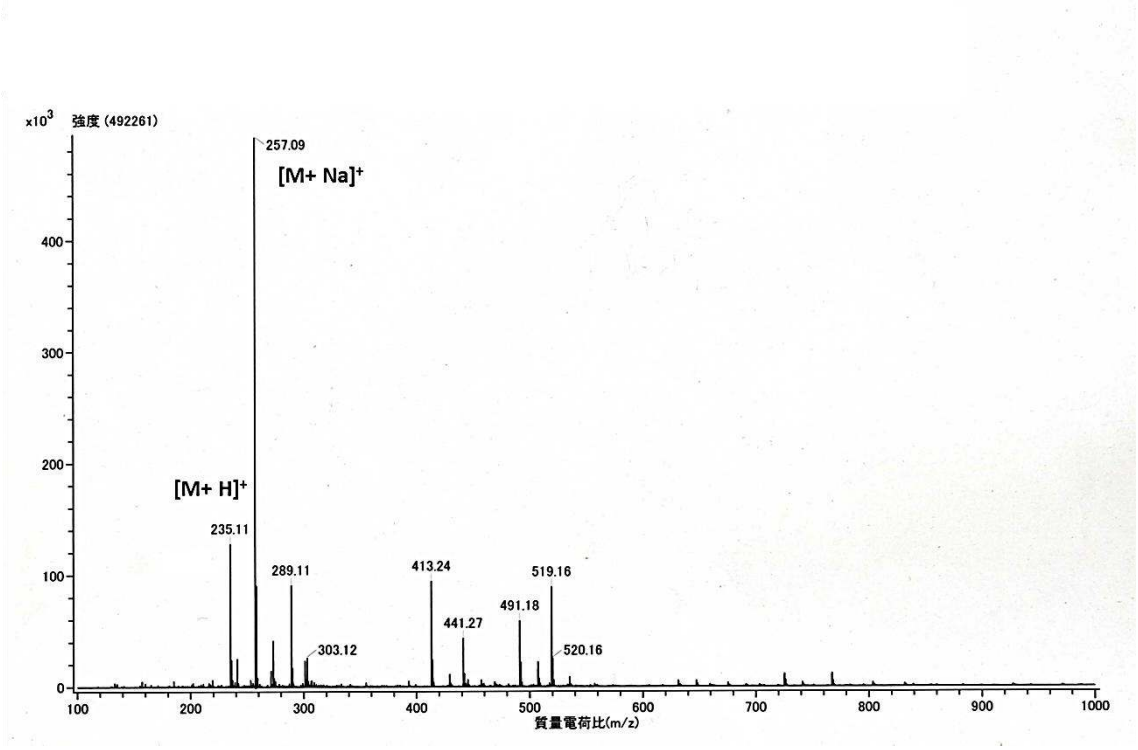


Figure 7: ESI$^+$- Mass Spectra of compound-**5** in methanol at room temperature

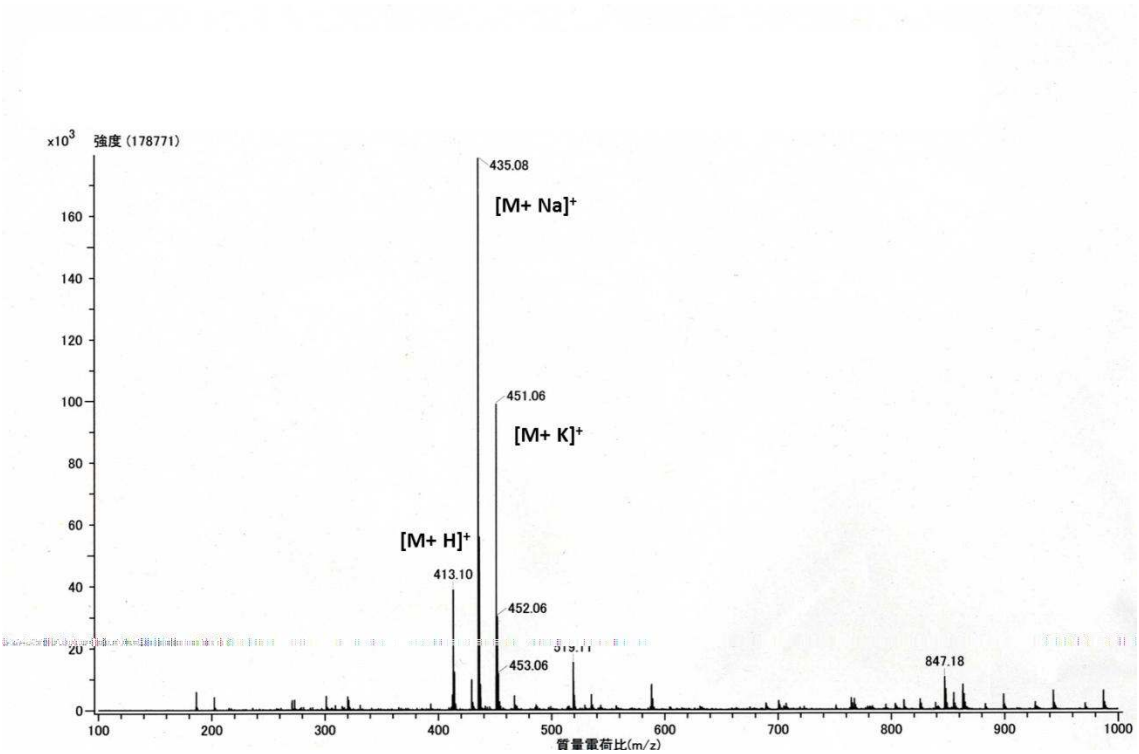


Figure 8: ESI$^+$- Mass Spectra of compound-**3** in methanol at room temperature.

2.5 Single crystal X-ray Analysis.

Single crystal of Compound **3** was mounted on a glass fiber. All measurements were made on a Rigaku R-AXIS RAPID diffractometer using graphite monochromated Mo-Kα radiation (λ = 0.71075 Å). The data were collected at a temperature of -100 °C to a maximum 2θ value of 54.8°. An empirical absorption correction was applied, which resulted in transmission factors ranging from 0.653 to 0.977. The structure was solved by using SIR2004[45] and refined by full matrix least- squares techniques on F^2 using SHELXL-97.[46] The non-hydrogen atoms were refined anisotropically while the hydrogen atoms were refined using the riding model. All the calculations were performed using the CrystalStructure 4.0 (Crystal Structure Analysis Package, Rigaku Corporation, Japan) except for refinement, which was performed using SHELXL-97.[46] The image for the publication was generated using ORTEP-32 software.[47]

2.6 Induced Circular Dichorism by CPL.

The CD instrument was purged with N_2 for at least 20 min; the temperature was set to 25 °C prior to every measurement; spectra were measured between 390 and 625 nm with a standard sensitivity of 100 mdeg, a data pitch of 0.5 nm, a band width of 5 nm, a scanning speed of 20 nm/min, and a response of 2 s, using a quartz cuvette (path

length: 1 cm). Solutions were prepared in MeCN at a concentration of 10^{-3} M; reference CD data were collected in the same solvent. For CPL irradiation, the solution of **3** was kept in the cell holder of the CD spectrometer and irradiated directly with 436-nm light through film filters (TCPR or TCPL; MeCan Imaging, Japan) to produce *r*- or *l*-CPL (about 34 mW/cm^2) for about 15 min, inducing positive and negative CD signals. The filters were alternated to produce *r*- or *l*- CPL to assess the reproducibility of the enrichment of the enantiomers. The intensity of the incident light in the CD spectrometer is lower than 0.16 mW/cm^2 at any wavelengths during the measurement. So the effect of the light during CD measurement on photoisomerization of the compound is negligible.

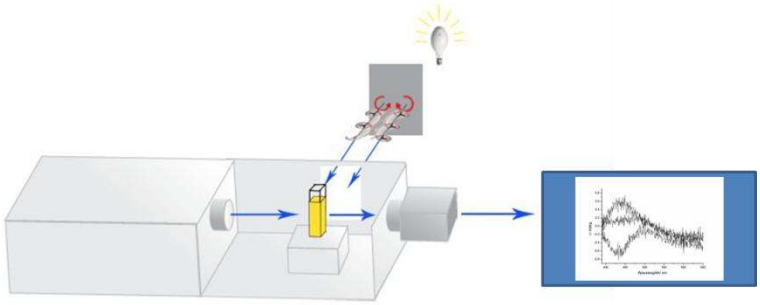


Figure 9: Schematic representation of CPL irradiation set up and induced CD measurement.

The induced spectra were smoothed using adjacent averaging method (θ values of 50 points in 25 nm were used to get the θ value at certain wavelengths). The smoothed spectra were adjusted to zero at 625 nm, assuming the θ value at 625 nm to be zero, and subtracted from the initial spectrum (CD spectrum prior to CPL irradiation) to obtain justified induced CD spectra. Under the same experimental conditions, compounds **1** and **2** did not provide any detectable CD signals after irradiation with *r*- or *l*-CPL.

3. Results and discussion:

3.1 Conformational Analysis.

In this study, I designed a molecule containing azobenzene units that can have *E* or *Z* regioisomeric structures between which transformation is possible by photochemical processes.[48] I synthesized a prochiral molecule **3** by the incorporation of azobenzene as a photo switching component and axis as a chiral generating element. Since the phenyl azo groups are connected symmetrically to core framework (axis), the molecule was 'non-chiral' with two azobenzenes in *E* form and I anticipated that the symmetry breaking can be achieved by the isomerization of a single azobenzene unit upon photo- irradiation. Recently, our group reported the dynamic generation of point and planar chirality in compounds **1**[39] and **2**,[40] respectively, by utilizing the conformational changes caused by the *E-Z* photoisomerization of one of their azobenzene units. To apply our novel concept in axial chiral system, i.e. generation of chirality by *E-Z* photoisomerization of one of the azobenzenes present in the molecule in axial chiral system, I synthesized compound **3** by incorporating two phenyl azo groups at the ortho positions of phenyl ring that was bonded to naphthalene.

The axial chirality of atropisomeric biaryl scaffold has been well discussed in the literature wherein the bulkiness of the dissymmetric substituents in the ortho positions plays a major role in the rotational stability to generate resolvable chiral structures (enantiomers).[49] Thus, while designing compound **3**, I believed that the bulky phenyl azo groups at the ortho positions of benzene connected to naphthalene are sufficient to block the rotation around the central C-C bond and provide conformational stability to the atropisomers that would form upon photoirradiation.

Figure 5 shows ^{1}H NMR spectra of compound **3** at room temperature. Notably the ^{1}H NMR of **3** reveals the structural characteristics in which the expected ortho protons of azobenzene groups upfielded and appeared as muliplet along with the naphthalene protons (δ=7.27-7.46 ppm). The other features of ^{1}H NMR spectra matches with the predicted resonance and were supported by ^{13}C NMR and mass analysis (figure 6 and 8).

The structure of **3** was further confirmed by single crystal X-ray analysis. Crystals were grown from dichloromethane/ hexane solution on slow evaporation method under dark. The analysis of crystal structure reveals that azobenzenes in compound **3** are in thermodynamically stable *trans* form and the phenyl and naphthalene rings are positioned perpendicular to each other reducing the steric clashes

between the orthosubstituted bulky phenyl azo moieties and naphthalene. Moreover, the crystal structure showed that the phenyl azo groups are tilted slightly to the benzene ring to which both the phenyl azo groups are linked probably due to the steric interaction caused by naphthalene. These structural characteristics were comparable with that of atropisomeric ortho substituted biphenyls, in which restricted rotations between two phenyl rings generate atropisomerism and the corresponding atropisomers (enantiomers) were possible to be isolated by chiral HPLC method.[49]

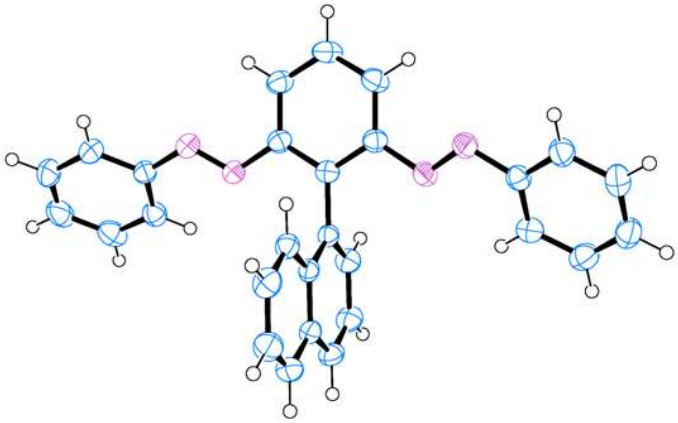


Figure 10: X-ray crystal structure of *EE*-**3.**

3.2 Photochemical Isomerization and Photoinduced Chirality.

Figure 11 shows the changes in the absorption spectrum of compound **3** in acetonitrile before and after irradiation with the light of wavelengths 366 nm and 436 nm at room temperature. The spectrum of compound **3** showed an expected band at 320 nm associated with л-л* transition and a weak band at 453 nm corresponding to n-л* transition (black line). Upon UV irradiation at 366 nm, a gradual decrease in the л-л* band and concomitant increase in the n-л* band confirmed the photoisomerization from *E*-form to *Z*- form in the azobenzene groups (red line). Further irradiation of resulting solution with the light of 436 nm induced reversal of the spectra (blue line). The UV-vis spectral changes observed above were typical for ever known azobenzenes.[31] As our design involved two azobenzene units electronically decoupled through *meta* connection, I expected an independent *E* to *Z* isomerization for each azobenzene unit, which was supported by the seeming isobestic points at 273 nm, 404 nm and 480 nm during the photochromic reactions of compound **3**. The thermal relaxation of photoirradiated solution of **3** at 366 nm was found to occur very slowly (rate constant, $k = 3.15 \times 10^{-6}$ s^{-1} at 30 °C) as observed by change in the absorption spectra in the dark (Figure 12 and 13). Moreover, compound **3** also exhibited a reversible photoisomerization between *cis*-rich and *trans*-rich states by visible light of wavelengths greater than 500 nm (from *trans* to

cis rich state) and 436 nm (from *cis* to *trans* rich state) similar to the ortho-substituted azobenzene derivatives reported recently (Figure 14).[50] Figure 15 and 16 display the changes in the absorption spectrum of compound **1** and **2**, respectively, in acetonitrile before and after irradiation with the light of wavelengths 366 nm and 436 nm at room temperature.

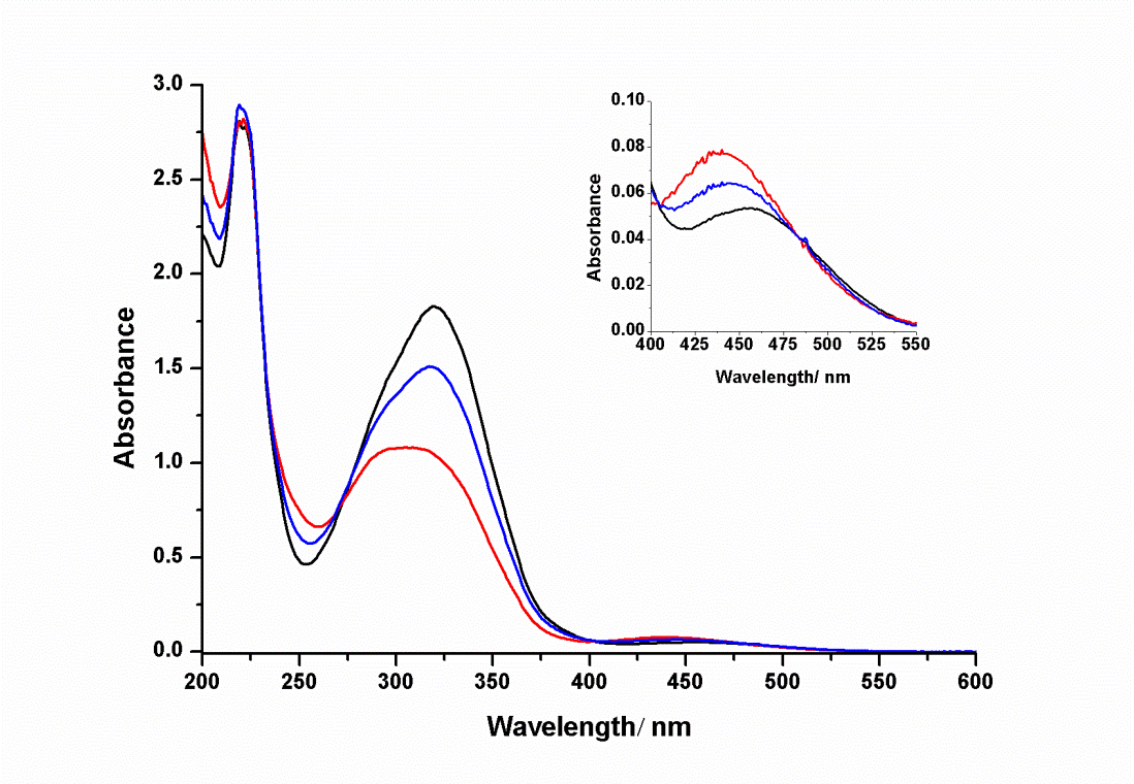


Figure 11: UV-vis spectral changes of acetonitrile solution of **3** (4.69×10^{-4} mol L^{-1}) upon irradiation at room temperature; a) initial state before irradiation (black line); b) Photo stationary state, $PSS_{366\ nm}$ (red line); c) $PSS_{436\ nm}$ (blue line). An enlarged view of n-л* band is shown in the inset.

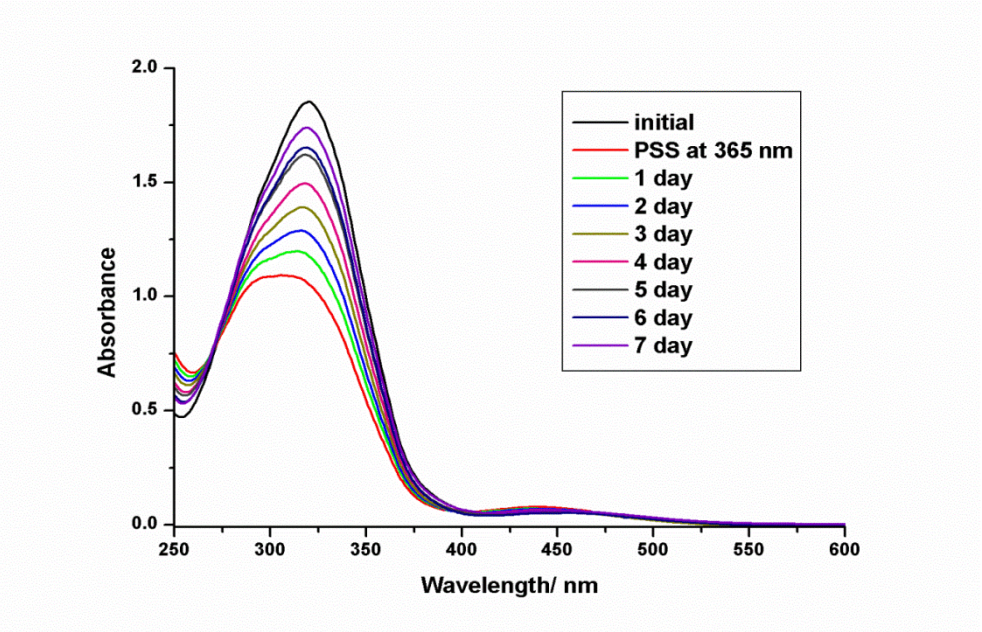


Figure 12: Changes in the UV spectra of acetonitrile solution of **3** ($1.5x10^{-3}$ M) during thermal back isomerization after $PSS_{365\ nm}$ at 30 ^{0}C under dark for 7 days.

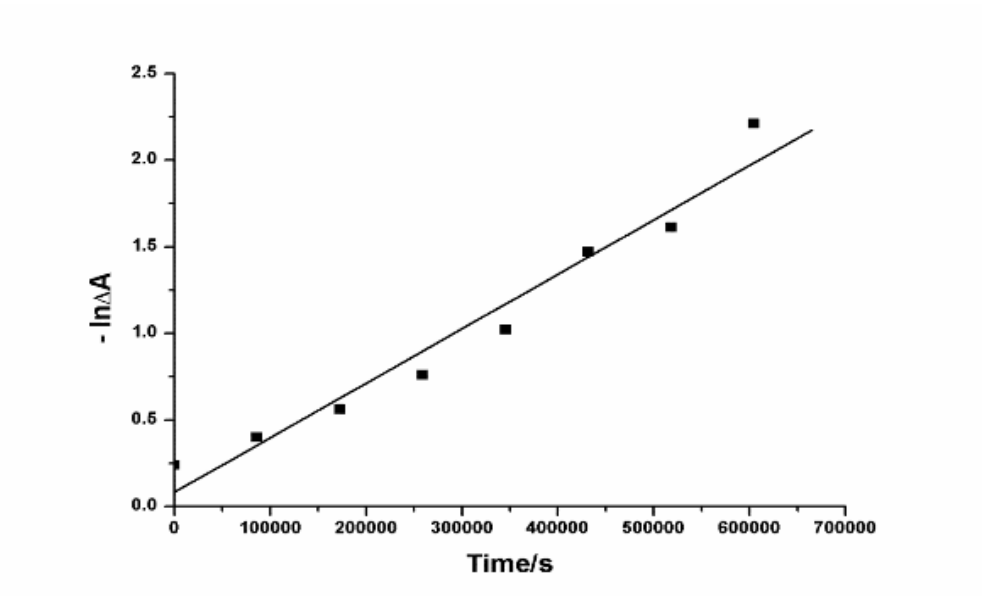


Figure 13: Plot showing linear relationship between logarithm of change in absorbance, ΔA (ΔA is calculated as $\Delta A = A_I - A_t$ from the absorbance at 320 nm of the UV spectra, where A_I is the initial absorbance before irradiation and A_t is the absorbance at time t

after $PSS_{366\ nm}$) and time for **3** after $PSS_{365\ nm}$ at 30 ^{o}C.

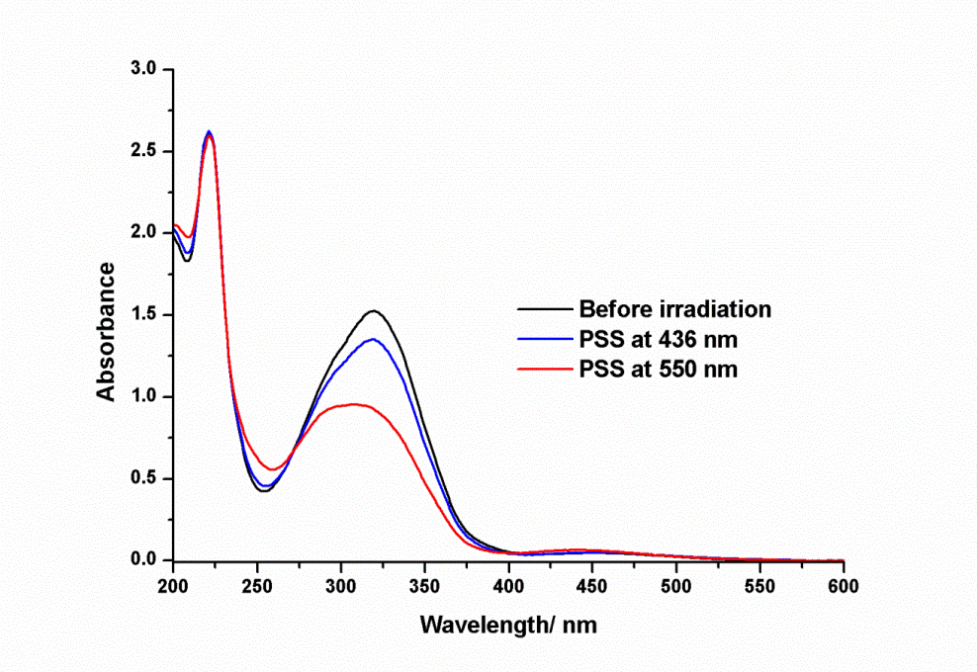


Figure 14: Visible light switching of *EE*-**3**.

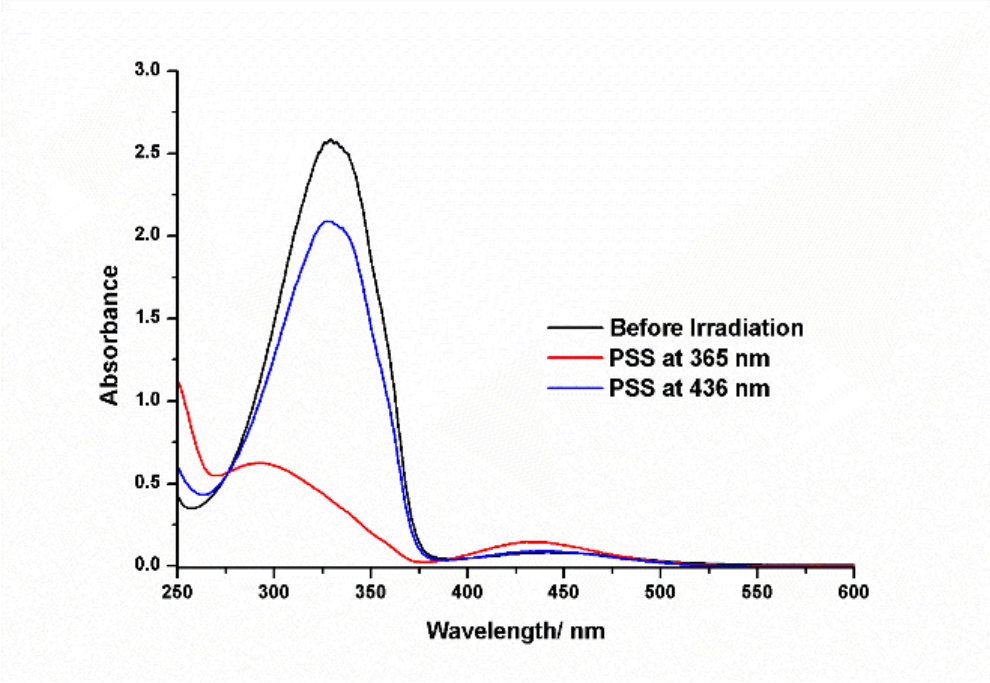


Figure 15: Absorption spectral changes of compound-**1** in acetonitrile (5.1 x 10^{-4} M)

upon irradiation with 365 nm and 436 nm.

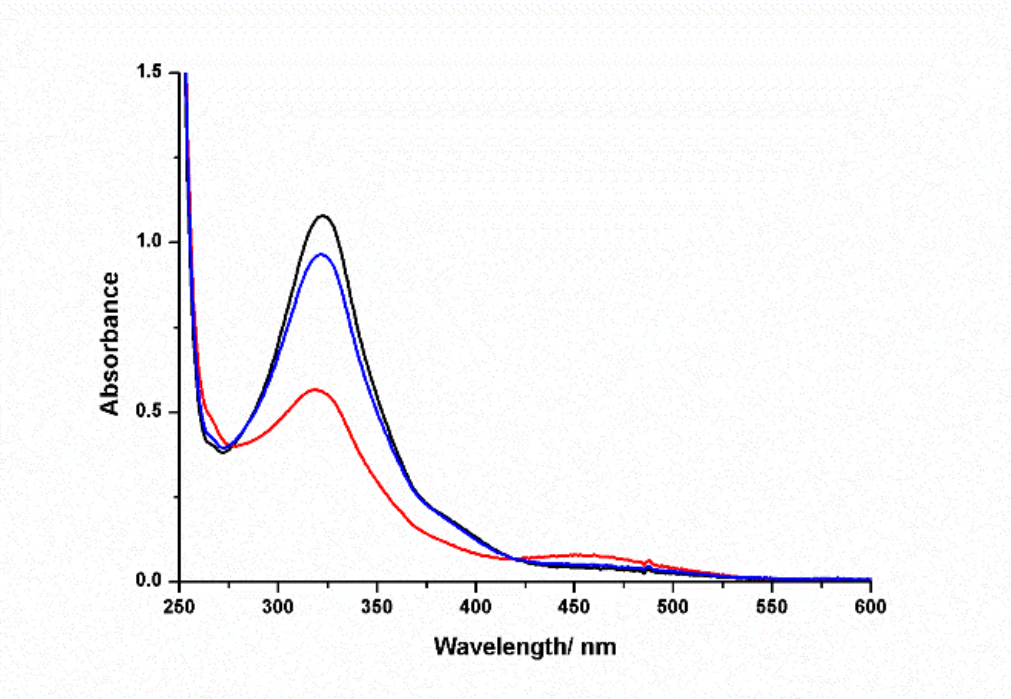


Figure 16: Absorption spectral changes of compound-**2** in acetonitrile (3.69 x 10^{-4} M) upon irradiation with 365 nm and 436 nm.

Figure 17 shows the chiral HPLC elution profile of **3** before and after irradiation. Before irradiation the chromatogram showed a sharp single peak at retention time, Rt = 20.26 min, suggesting that compound **3** initially exists as *EE* form as we have seen in the single crystal X-ray analysis (figure 17a). After 366 nm light irradiation, the chromatogram showed three additional peaks at Rt = 28.24, 32.01 and 57.88 min, along with initial *EE* peak (figure 17b). Subsequent irradiation of the solution at 436 nm reverted the chromatogram characteristics maintaining the second and third peaks equal in the intensity during the irradiations (figure 17c). It is known that *Z* azobenzene

derivatives elutes slowly in normal phase HPLC including chiral HPLC attributing to its polar nature than the corresponding *E* isomer.[51] From these results, the second, third and fourth peaks seemed to be a pair of enantiomers of *EZ*-**3** and *ZZ*-**3** isomers, respectively.[52]

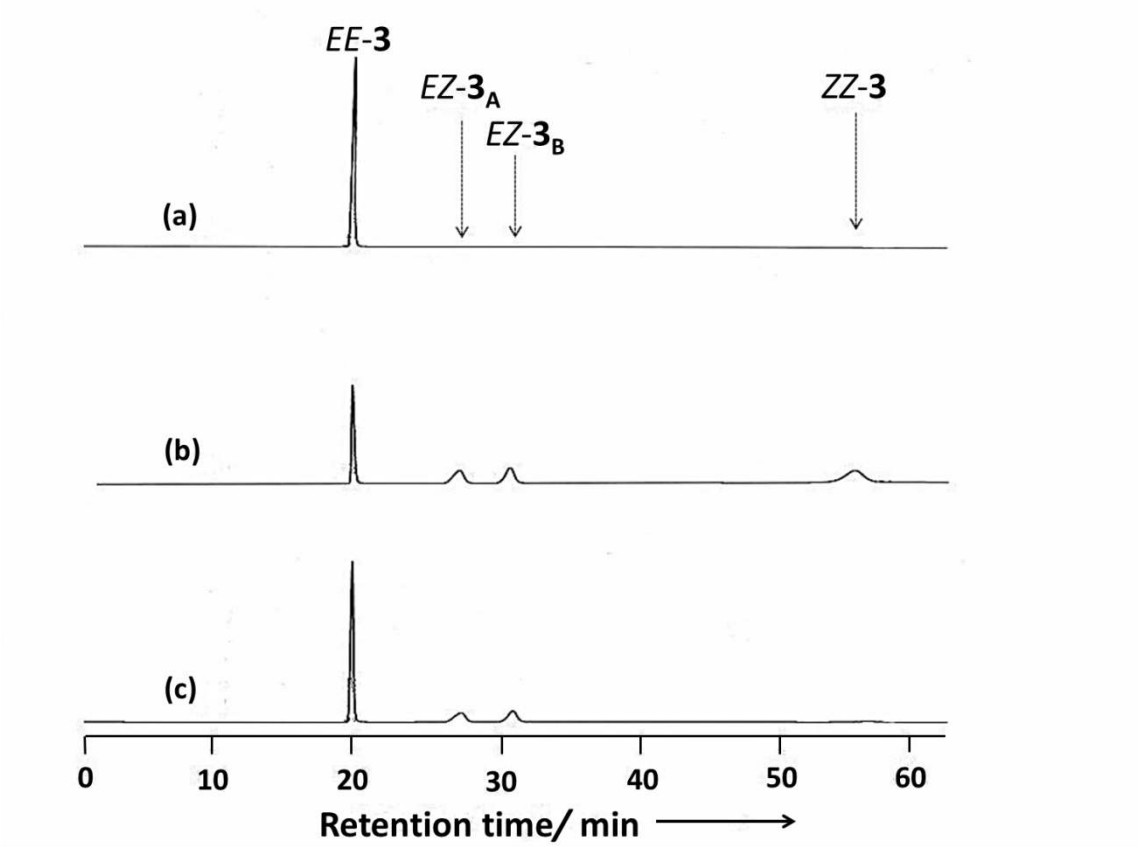


Figure 17: Chromatogram of *EE*-**3**; a) before irradiation, b) the PSS after irradiation at 366 nm, c) the PSS after irradiation at 436 nm monitored by chiral HPLC with a solvent combination of 2:8 (Isopropanol: Hexane), flow rate at 1mL min^{-1}.

To gain further information about the newly formed isomers upon photoirradaition of *EE*-**3**, I isolated second and third fractions of HPLC chromatogram

and measured the CD spectra. The CD spectrum of the second eluted fraction showed three positive bands at 230 nm, 275 nm and 335 nm and three negative bands at 210 nm, 250 nm and 430 nm in acetonitrile solution, and the mirror symmetrical cotton curve was observed for the third fraction (figure 18). The UV-vis absorption spectra of fourth fraction resembled that of *Z* azobenzene derivatives with a characteristic л-л* transition band at 280 nm and n-л* transition band at 436 nm (figure 19).[31] From the aforementioned results and information, I assigned the second and third HPLC peaks as *EZ*-$\mathbf{3_A}$ and *EZ*-$\mathbf{3_B}$, where one of the azobenzene units is in *trans* and other is in *cis* isomeric form but with opposite conformations, whereas the fourth peak as *ZZ*-**3** with both azobenzenes units are in *cis* state.

In order to investigate the possibility of direct thermal racemization between *EZ*-$\mathbf{3_A}$ and *EZ*-$\mathbf{3_B}$, the second eluted *EZ*-$\mathbf{3_A}$ in acetonitrile was kept under dark for one week at room temperature and monitored the thermal back isomerization progress by chiral HPLC. The HPLC analysis did not show the peak for *EZ*-$\mathbf{3_B}$ during the thermal back isomerization from *EZ*-$\mathbf{3_A}$ to *EE* (Figure 20), suggesting that the enantiomers are not thermally interconvertible. The HPLC chromatogram obtained after irradiating *EZ*-$\mathbf{3_B}$ to $PSS_{436\ nm}$ was exactly the same as that of the chromatogram obtained starting from *EE*-**3** at 436 nm PSS (figure 17c). However, the HPLC elution profile obtained for

the photoreaction mixture of *EZ*-**3** before PSS showed unequal peak areas for the *EZ* enantiomers with the appearance of *EE* and *ZZ* peaks (figure 21). These results clearly indicates that the thermally stable *EZ*-$\mathbf{3_B}$ enantiomer racemizes photochemically via nonchiral *EE* or *ZZ* isomeric states.

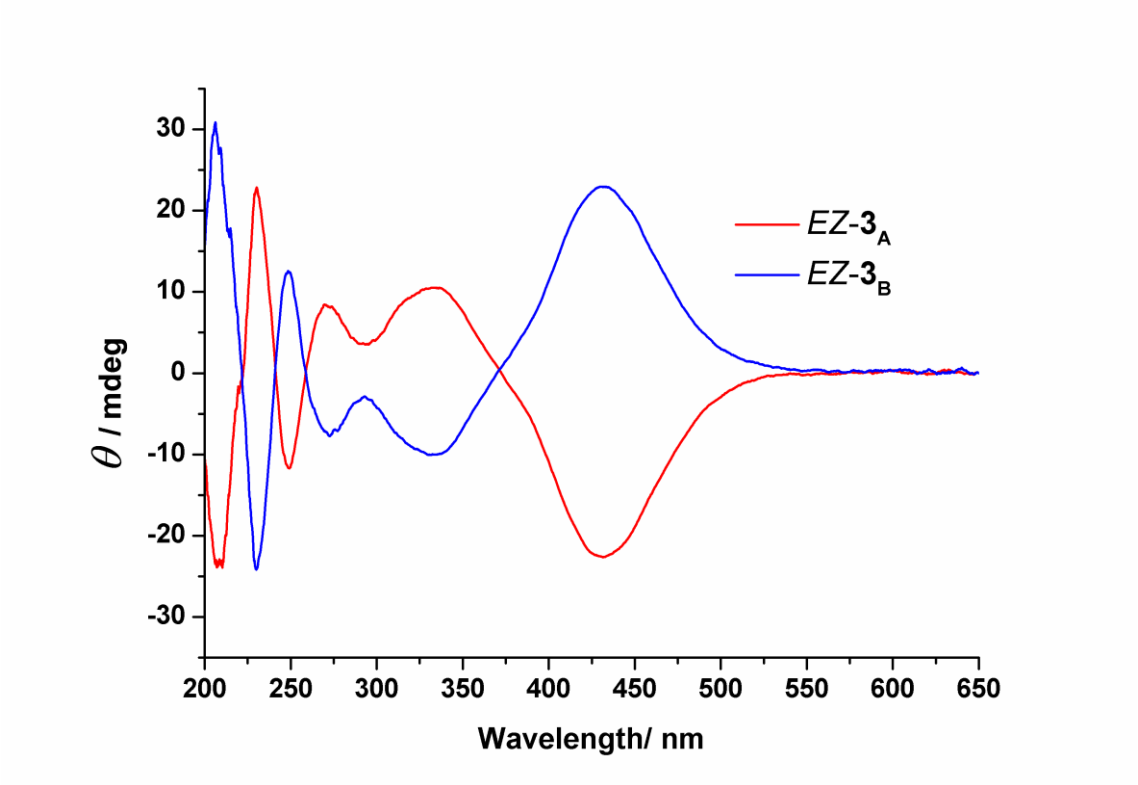


Figure 18: CD spectra of enantiomers *EZ*-**3** in acetonitrile (a) *EZ*-$\mathbf{3_A}$, first eluted enantiomer (red line) and *EZ*-$\mathbf{3_B}$, second eluted enantiomer (blue line). The concentration of the solution was 6.10×10^{-4} mol L^{-1}.

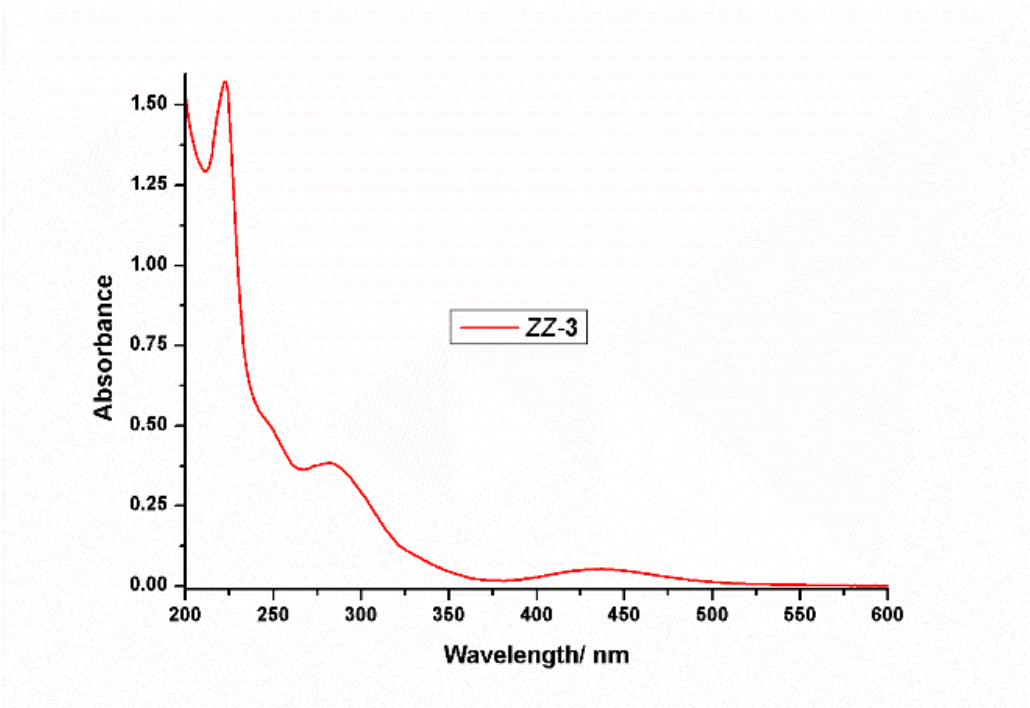


Figure 19: Absorption spectra of *ZZ*-**3** in acetonitrile after HPLC separation.

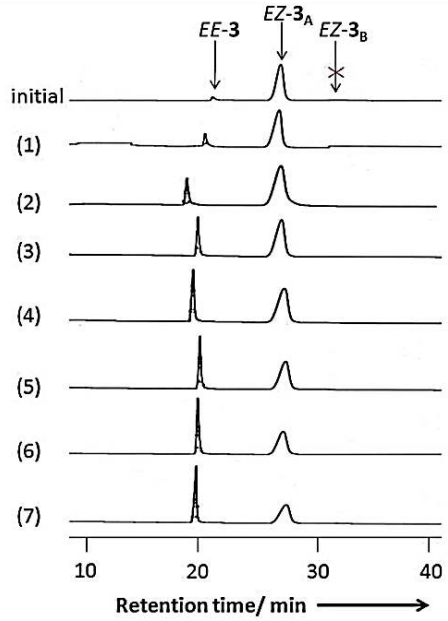


Figure 20: HPLC profile showing no racemization during thermal back isomerization of *EZ*-$\mathbf{3_A}$**,** the first eluted enantiomer of *EZ*-**3** under dark at room temperature over 7

days , where (1)- (7) corresponds to each day chromatogram, respectively.

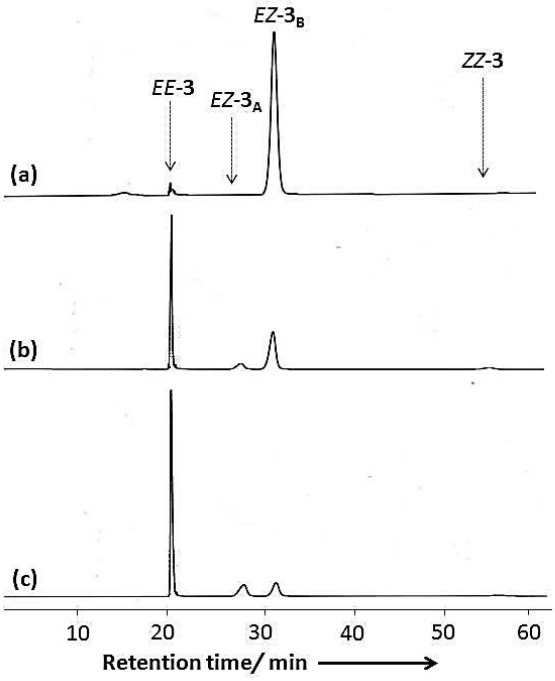
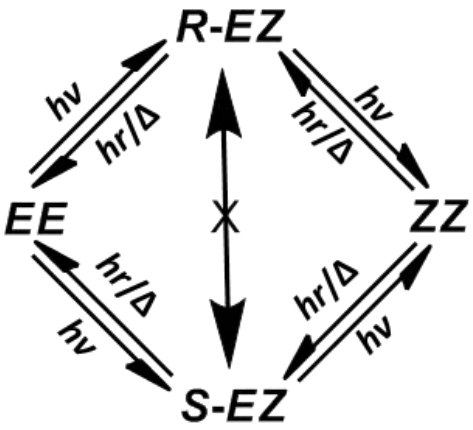


Figure 21: Chromatogram of *EZ*-3_B, the second eluted enantiomer of *EZ*-3 a) before irradiation, b) after 10s irradiation at 436 nm and c) the PSS at 436 nm.

By compiling all the above mentioned results, I propose a possible *EE*↔*ZZ* interconversion pathway through an intermediate chiral *EZ* isomeric state (scheme 5). Upon photoirradiation of *EE* isomer, the independent isomerization of each azobenzene unit produces mixture of *EE*, *EZ*, *ZZ* regio-isomers which are photochemically interconvertible. Among these isomers, the *EZ* isomer formed by the *E-Z* isomerization of single azobenzene unit is chiral and exists as a racemic mixture of *R* and *S* stereoisomers. The *R-EZ* and *S-EZ* stereoisomers do not racemize thermally but

interconvert photochemically through its *EE* or *ZZ* isomeric state. The *ZZ* structure isomerizes either thermally or photochemically to *EE* via monoisomerized *EZ* state (figure 22 and 23).



Scheme 5: Thermal and photochemical isomerization pathway for the azobenzene dimer **3**.

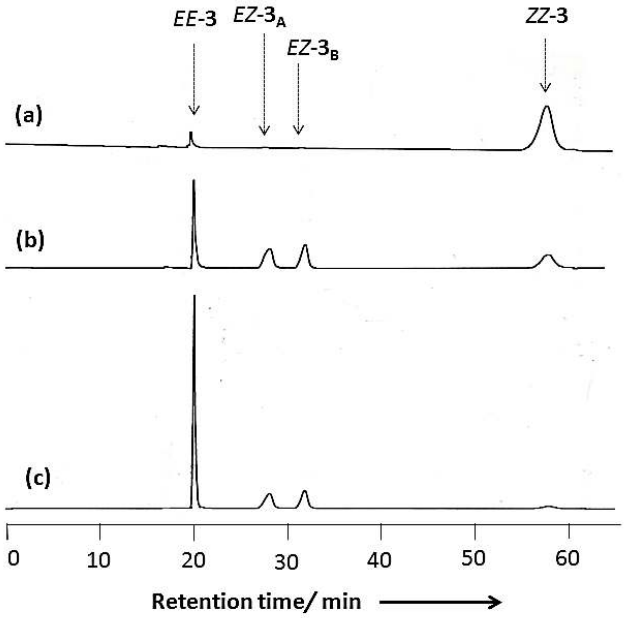


Figure 22: HPLC chromatogram showing *ZZ* to *EE* photoisomerization pathway via *EZ* intermediate a) before irradiation, b) after 10s irradiation at 436 nm and c) the PSS at 436 nm.

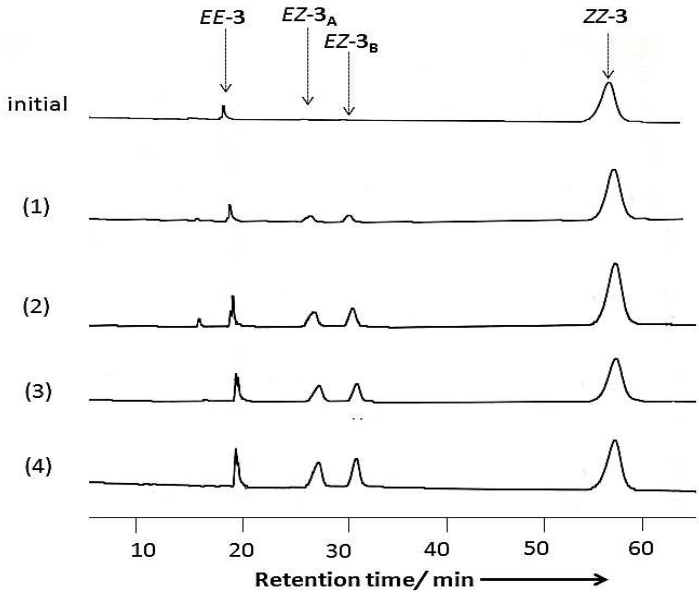


Figure 23: HPLC chromatogram showing *ZZ* to *EE* thermal isomerization via *EZ* intermediate under dark at room temperature over 4 days, where (1)- (4) corresponds to each day chromatogram, respectively.

Then I investigated the complete switching between the chiral and nonchiral structures of **3** by alternate photoirradaition and reflux. As mentioned above compound **3** were in non-chiral *EE* form initially, and the chirality was generated after suitable wavelength light irradiation. After heating the irradiated sample for 1 hour in acetonitrile solvent, the chromatogram peak of *EE*-**3** was fully regenerated with the

disappearance of the peaks corresponding to *EZ*-**3** (Figure 24). Moreover this ON-OFF switching of induced chirality was reproducible for three cycles (Figure 25).

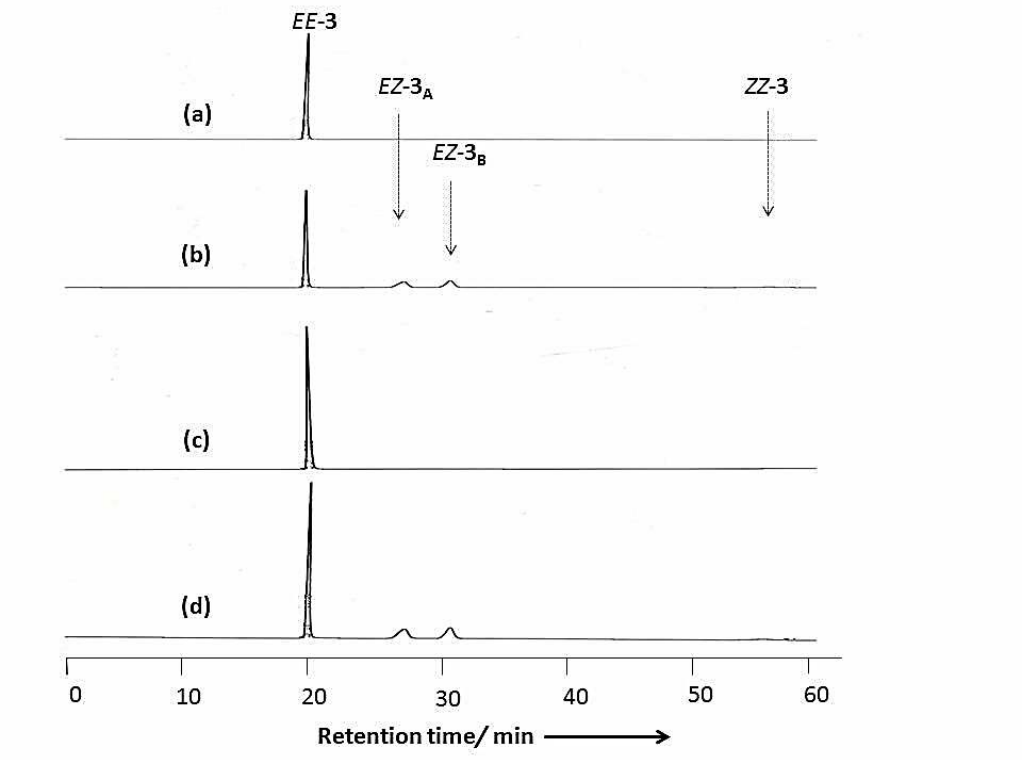


Figure 24: chromatograms of **3** showing ON-OFF switching of asymmetry induction a) before irradiation, b) the PSS after irradiation at 436 nm, c) reflux in acetonitrile and d) the PSS after irradiation at 436 nm.

Introduction of chirality to molecular entities usually involves unidirectional bond breaking or making steps as seen in asymmetric synthesis. Herein, however, I successfully demonstrated the dynamic generation of axial chirality in azobenzene dimer **3**, by *E-Z* photoisomerization of one of the azobenzenes upon photoirradiation, as seen in **1** and **2** for point and axial chirality.

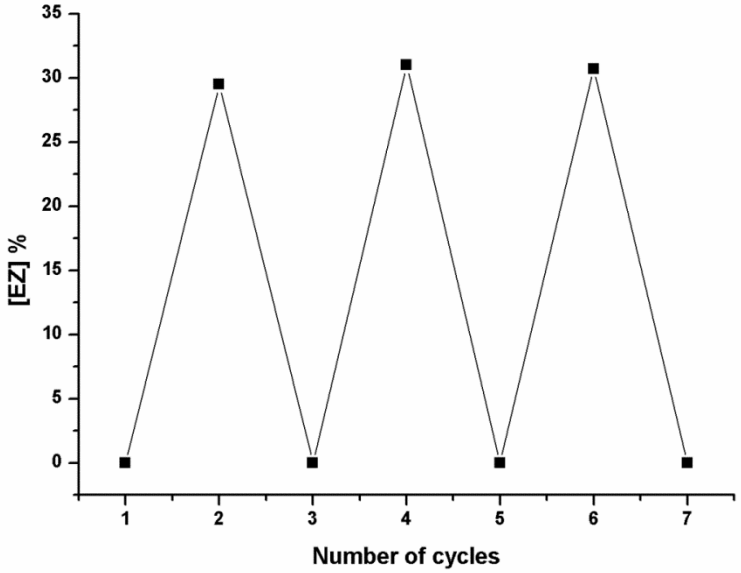
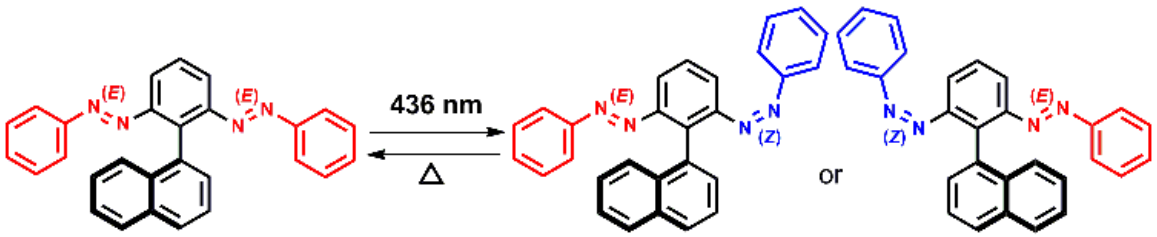


Figure 25: ON -OFF switching of asymmetric induction by alternate irradiation with 436 nm light and reflux in acetonitrile. The EZ-**3** composition at $PSS_{436\ nm}$ was estimated to be 24 % by HPLC studies.



Scheme 6: Schematic representation showing chirality generation in **3** by *E-Z* photoisomerization.

3.3 Photoresolution Induced by CPL.

The ability to induce absolute asymmetric synthesis through the application of CPL, where nonchiral compounds are converted to chiral products with an enantiomeric imbalance, is attractive because it provides a plausible mechanism for the origin of homochirality in bioorganic compounds. The primary goal of my work was to study the feasibility of using compound **1**, **2** and **3** for reactions to form chiral products with enantiomeric excess through the photochemistry of CPL.

I conducted photoresolution experiments for **1**, **2** and **3** by using *r*/*l*-CPL at 436 nm, the wavelength inducing the reasonable high concentration of *EZ* isomers at PSS and showing high $\Delta\varepsilon$ value for the enantiomers of *EZ* and monitored the process by CD spectroscopy in nearly same experimental conditions. In the case of compounds **1** and **2**, we could not observe any induced CD spectra upon *r* or *l*-CPL irradiations (figure 27 and 28). Interestingly, irradiation of prochiral *EE*-**3** in acetonitrile with 436 nm *r*-CPL resulted in a positive CD spectrum within 15 min. This result was confirmed by the observation of opposite CD signal with the same intensity after irradiation of the same sample with *l*-CPL at 436 nm and by the comparison of peak shape and position of the induced spectra with that of one of the pure enantiomers of *EZ*-**3**. Successive irradiation of **3** with *r*-and *l*-CPL at the same wavelength led to CD spectrum changes

between positive and negative signs at the n-л* transition band region (390-625 nm) as shown in (figure 26). Further irradiation with nonpolarized light resulted in an inactive CD spectrum, i.e., a photoracemized state is achieved. This process was reproducible over eight cycles without any deterioration of modulated signals as observed by the CD measurements in independent experiments (figure 26, inset).

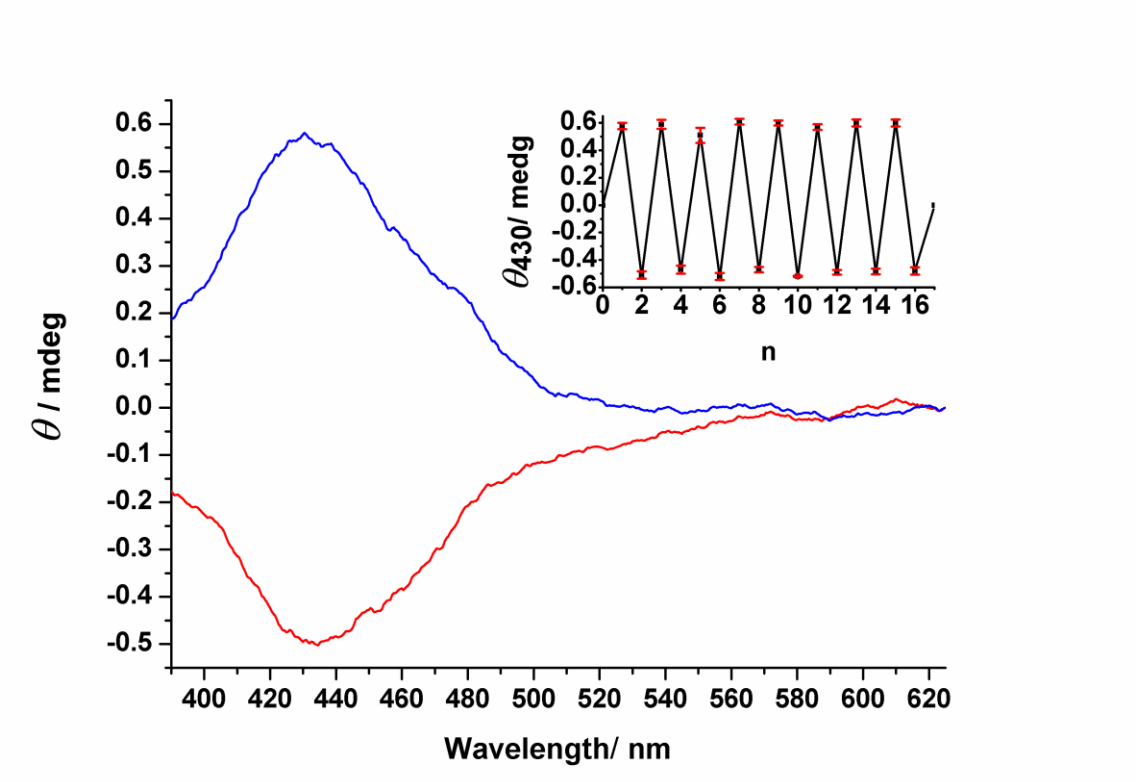


Figure 26: Induced CD spectrum of the acetonitrile solution of **3** upon irradiation with *r* (blue line)- and *l* (red line)-CPL at 436 nm. The inset shows the CD values at 430 nm for a solution of **3** upon alternating irradiation with *r*- and *l*-CPL (n = 1-16) and non-polarized light (n = 17) with a standard error of mean values of three independent

experiments. Due to too high concentration (1.33×10^{-3} M), it was impossible to measure the CD at shorter wavelengths than 390 nm.

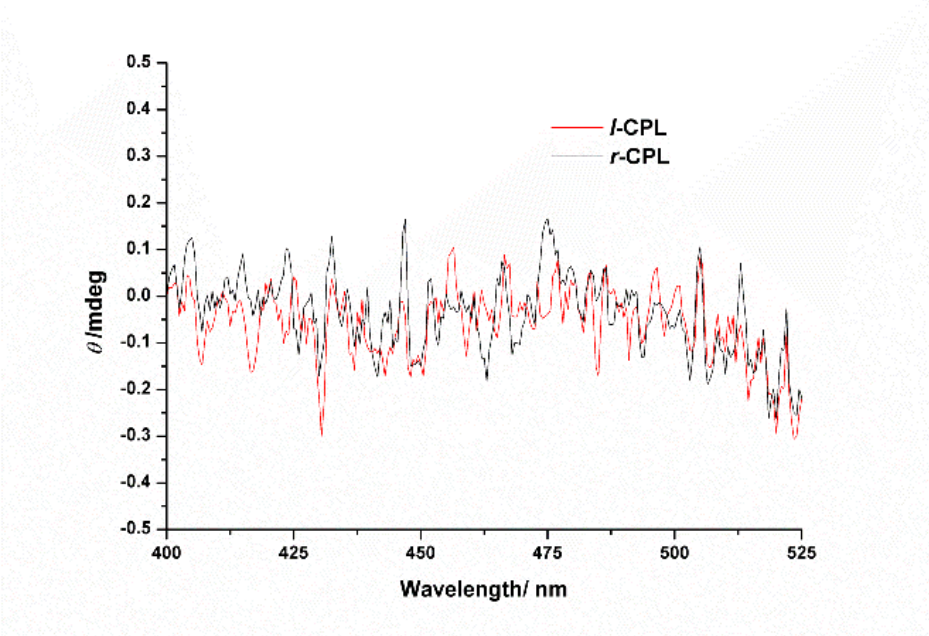


Figure 27: CD spectra of acetonitrile solution of **1** (1.42×10^{-3} M) upon irradiation with *r*-CPL (black line) and *l*-CPL (red line) indicating no induced circular dichorism at PSS_{436}.

I calculated the photoinduced enantiomeric excess (*ee*) using equation (1) from the value of $\Delta\varepsilon_{430}$ (molar circular dichorism at 430 nm) of the pure enantiomer (11.6 L mol^{-1} cm^{-1}) and the induced CD value ($\theta_{430\,nm}$ = 0.5 mdeg) for a 1.33×10^{-3} M solution of **3** in acetonitrile at $PSS_{436\,nm}$, consisting of *EZ*-**3** as 24% (3.2×10^{-4} M) of the total isomers, assuming that the origin of the induced CD in *EZ*-**3** was some imbalance in the concentrations between the *R* and *S* stereoisomers at the photostationary state.

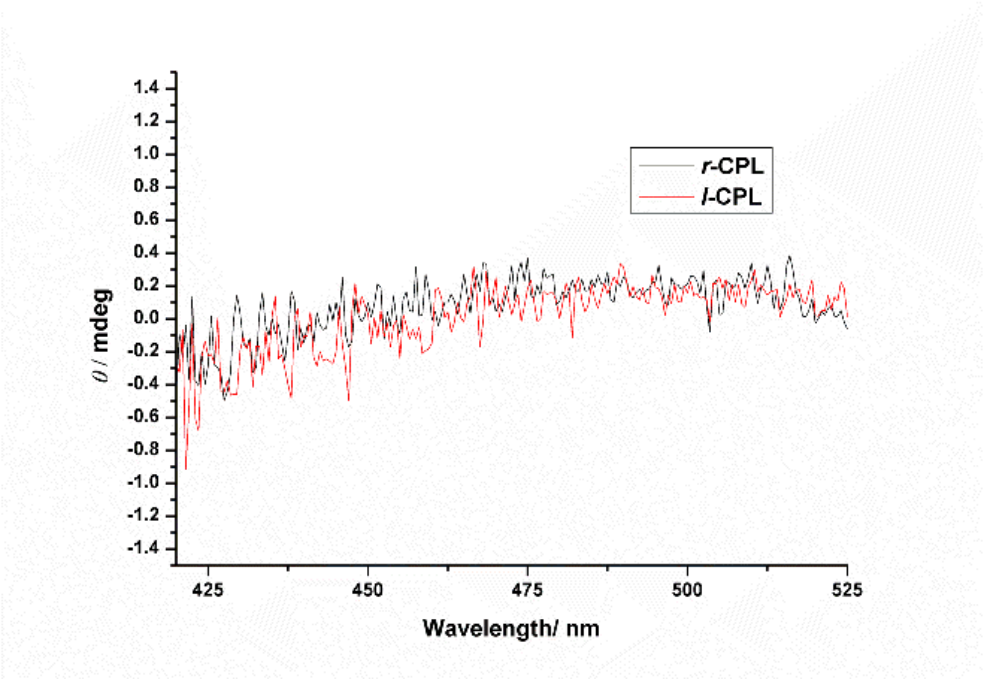


Figure 28: CD spectra of acetonitrile solution of **2** (1.5×10^{-3} M) upon irradiation with *r*-CPL (black line) and *l*-CPL (red line) indicating no induced circular dichorism at PSS_{436}.

$$ee_{PSS} = \{([S] - [R])/([S] + [R])\} \times 100 = 0.4\% \qquad (1)$$

where

$$[S] - [R] = (\text{induced } \theta_{430})/(32{,}980 \times \Delta\varepsilon_{430} \times 1\ \text{cm})$$

$$[S] + [R] = [EZ] \text{ at } PSS_{436\ nm}.$$

By substituting the experimentally obtained values of ε_{436} (1330 L mol^{-1} cm^{-1}) and $\Delta\varepsilon_{436}$ (11.3 L mol^{-1} cm^{-1}) obtained from the CD and UV absorption spectra of the

pure enantiomers of *EZ*-**3** into equation (2), I calculated the theoretical *ee* (*g*/2) to be 0.43% at $PSS_{436\ nm}$. The observed *ee* (ee_{PSS} = 0.4%) for the photoresolution of **3** upon irradiation with *r*- or *l*-CPL was in good agreement with the calculated value.

$$ee_{PSS} = g/2 = \Delta\varepsilon/2\varepsilon \quad (2)$$

I then measured the ε_{436} and $\Delta\varepsilon_{436}$ of *EZ*-**1** and *EZ*-**2** from the UV and CD spectra of pure enantiomers (figure 29, 30, 31 and 32). The *ee* value calculated using equation (2) from the values of ε_{436} (2336 L mol^{-1} cm^{-1}) and $\Delta\varepsilon_{436}$ (0.15 L mol^{-1} cm^{-1}) for *EZ*-**1** was too small (0.003% at 436 nm) to detect by CD instrument and that of *EZ*-**2** calculated from the values of ε_{436} (1907 L mol^{-1} cm^{-1}) and $\Delta\varepsilon_{436}$ (4.2 L mol^{-1} cm^{-1}) was 0.11%. Although the calculated *ee* value of **2** was much higher than **1**, the *EZ* isomeric composition at the $PSS_{436\ nm}$ was found to be very less (12%), making the system not suitable for photochemical deracemization process under CPL. Thus, compound **3** was found to be the most suitable azobenzene dimer for CPL induced photoresolution process owing to its large *g* value (8.5×10^{-3}) and a high [*EZ*] ratio (24%) at $PSS_{436\ nm}$ under CPL irradiation in comparison with **1** and **2**.

Table 1: Absorption, circular dichorism and $[EZ]_{436\,nm}$ datas for azobenzene dimers **1-3** in acetonitrile solution.

Azobenzene dimers	**1**	**2**	**3**
$\Delta\varepsilon_{436}$ ($M^{-1}cm^{-1}$)	0.15	4.28	11.33
ε_{436} ($M^{-1}cm^{-1}$)	2336	1907	1330
g_{436}	5.57×10^{-5}	2.19×10^{-3}	8.51×10^{-3}
Expected ee %	0.004	0.11	0.43
[EZ] % at 436 nm	33	12	24

Absorption and CD spectra used for measuring the chiroptical properties are shown below.

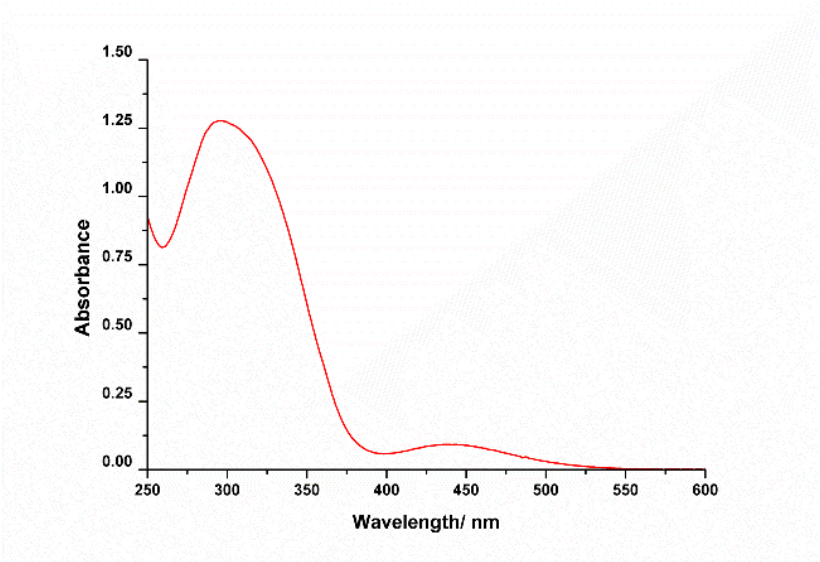


Figure 29: Absorption spectra of *EZ*-$\mathbf{3_A}$ in acetonitrile after HPLC separation. The

identical spectrum was obtained for *EZ*-$\mathbf{3_B}$.

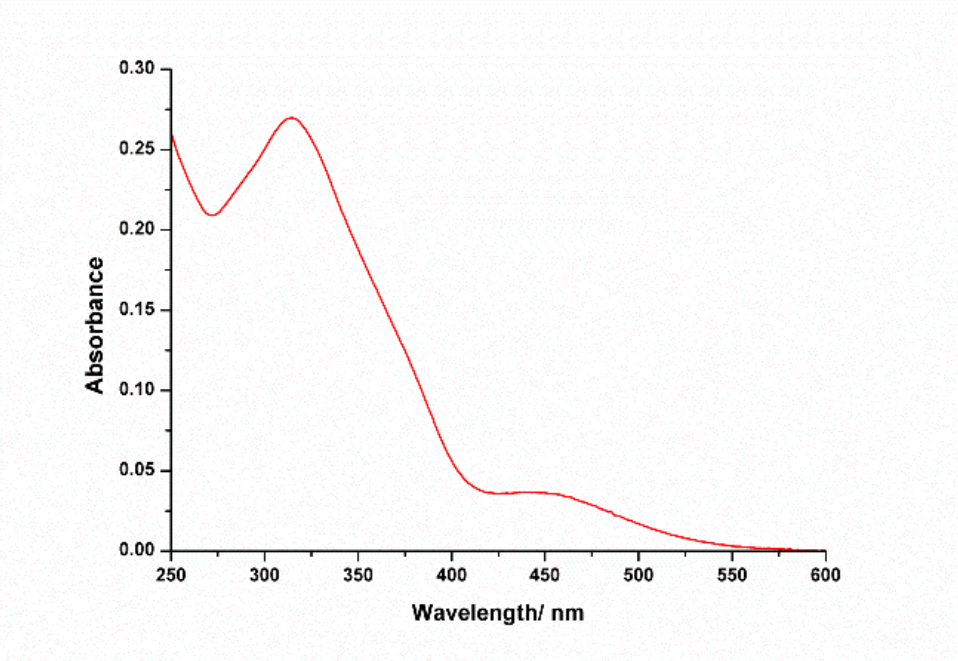


Figure 30: Absorption spectra of *EZ*-$\mathbf{2_A}$ in acetonitrile after HPLC separation. The identic al spectrum was obtained for *EZ*-$\mathbf{2_B}$.

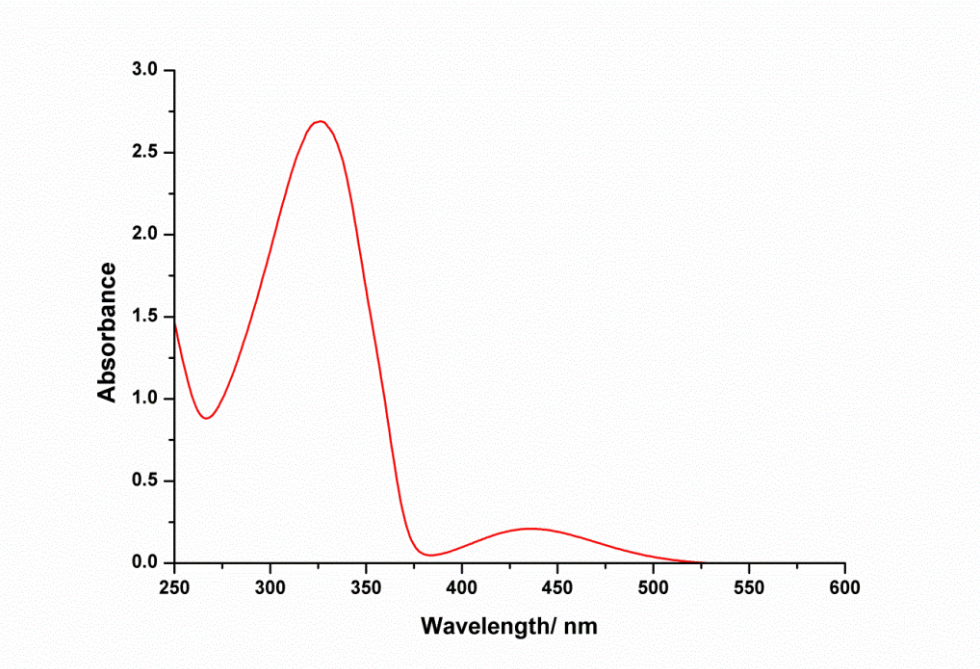


Figure 31: Absorption spectra of *EZ*-$\mathbf{1_A}$ in acetonitrile after HPLC separation. The

identical spectrum was obtained for *EZ*-$\mathbf{1_B}$.

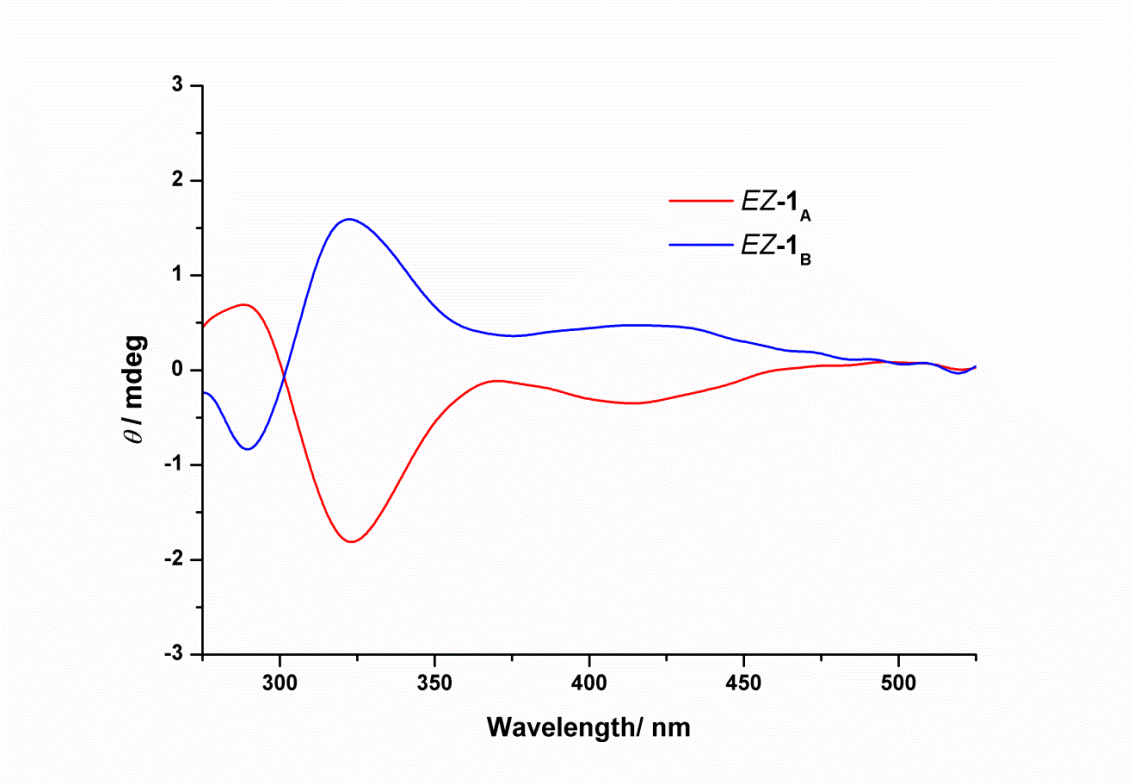


Figure 32: CD spectra of *EZ*-**1** in acetonitrile; first eluted enantiomer, *EZ*-$\mathbf{1_A}$ (red line) and second eluted enantiomer, *EZ*-$\mathbf{1_B}$ (blue line).The concentration of the solution was 1.01×10^{-4} M.

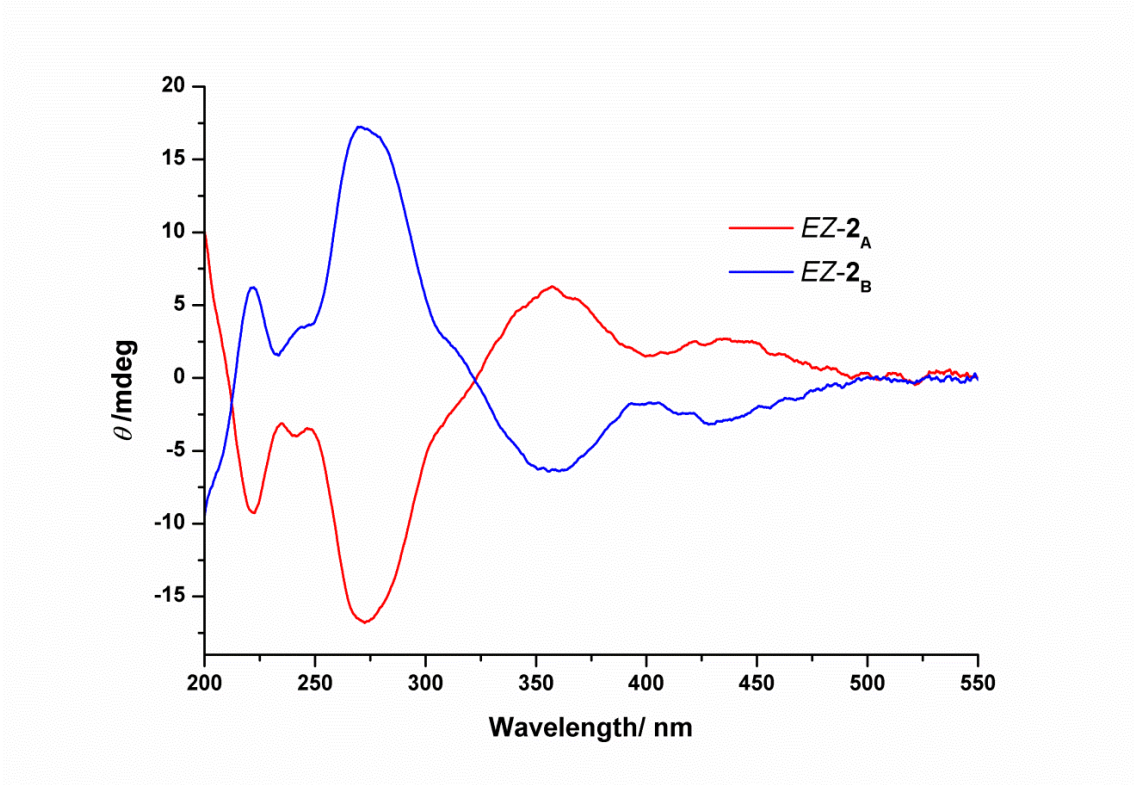


Figure 33: CD spectra of *EZ*-**2** in acetonitrile; first eluted enantiomer, *EZ*-$\mathbf{2_A}$ (red line) and second eluted enantiomer, *EZ*-$\mathbf{2_B}$ (blue line).The concentration of the solution was 1.94×10^{-4} M.

The enantiomeric excess in the photoresolution process is estimated by the following calculation,

The photochemical rate equations in a 1cm cell are

$$\frac{d\,[R-EZ]}{dt} = 1000 I_0 \{(1-10^{-A})/A\}\{(\varepsilon_{EE}\ \phi_{EE\rightarrow EZ}[EE] + \varepsilon_{ZZ}\phi_{ZZ\rightarrow EZ}[ZZ]) - (\varepsilon_{R\text{-}EZ}\phi_{R\text{-}EZ\rightarrow EE}[R\text{-}EZ] + \varepsilon_{R\text{-}EZ}\phi_{R\text{-}EZ\rightarrow ZZ}[R\text{-}EZ])\} \quad (1)$$

$$\frac{d\,[S-EZ]}{dt} = 1000 I_0 \{(1-10^{-A})/A\}\{(\varepsilon_{EE}\ \phi_{EE\rightarrow EZ}[EE] + \varepsilon_{ZZ}\phi_{ZZ\rightarrow EZ}[ZZ]) - (\varepsilon_{S\text{-}EZ}\phi_{S\text{-}EZ\rightarrow EE}[S\text{-}EZ] + \varepsilon_{S\text{-}EZ}\phi_{S\text{-}EZ\rightarrow ZZ}[S\text{-}EZ])\} \quad (2)$$

where [*R-EZ*], [*S-EZ*], [*EE*], [*ZZ*] and $\varepsilon_{R\text{-}EZ}$, $\varepsilon_{S\text{-}EZ}$, ε_{EE}, ε_{ZZ} are concentrations and molar extinction coefficients of *R-EZ*, *S-EZ*, *EE*, *ZZ* isomers, respectively, and $\phi_{EE\rightarrow EZ}$, $\phi_{ZZ\rightarrow EZ}$,

$\phi_{EZ\rightarrow EE}$, $\phi_{EZ\rightarrow ZZ}$ represents the quantum yields of photochemical isomerization from $EE_{\rightarrow}EZ, ZZ_{\rightarrow}EZ$, $EZ_{\rightarrow}EE, EZ_{\rightarrow}ZZ$, respectively.

At the photostationary state,

$$\frac{d\,[R-EZ]}{dt} = \frac{d\,[S-EZ]}{dt} = 0 \quad (3)$$

Then,

$$\varepsilon_{EE}\ \phi_{EE\rightarrow EZ}[\,EE] + \varepsilon_{ZZ}\phi_{ZZ\rightarrow EZ}[\,ZZ] = \varepsilon_{R\text{-}EZ}\ \phi_{R\text{-}EZ\rightarrow EE}[R\text{-}EZ] + \varepsilon_{R\text{-}EZ}\phi_{R\text{-}EZ\rightarrow ZZ}[\,R\text{-}EZ] \quad (4)$$

$$\varepsilon_{EE}\ \phi_{EE\rightarrow EZ}[\,EE] + \varepsilon_{ZZ}\phi_{ZZ\rightarrow EZ}[\,ZZ] = \varepsilon_{S\text{-}EZ}\ \phi_{S\text{-}EZ\rightarrow EE}[S\text{-}EZ] + \varepsilon_{S\text{-}EZ}\phi_{S\text{-}EZ\rightarrow ZZ}[S\text{-}EZ] \quad (5)$$

Equating 4 and 5,

$$\varepsilon_{R\text{-}EZ}\phi_{R\text{-}EZ\rightarrow EE}[R\text{-}EZ] + \varepsilon_{R\text{-}EZ}\phi_{R\text{-}EZ\rightarrow ZZ}[\,R\text{-}EZ] = \varepsilon_{S\text{-}EZ}\phi_{S\text{-}EZ\rightarrow EE}[S\text{-}EZ]+\varepsilon_{S\text{-}EZ}\phi_{S\text{-}EZ\rightarrow ZZ}[S\text{-}EZ] \quad (6)$$

$$\varepsilon_{R\text{-}EZ}[R\text{-}EZ]\,(\phi_{R\text{-}EZ\rightarrow EE}+\phi_{R\text{-}EZ\rightarrow ZZ}) = \varepsilon_{S\text{-}EZ}[S\text{-}EZ]\,(\phi_{S\text{-}EZ\rightarrow EE}+\phi_{S\text{-}EZ\rightarrow ZZ}) \quad (7)$$

Since *R-EZ* and *S-EZ* enantiomers are chemically same, the interconversion quantum yields must be identical for symmetry reasons.
Therefore equation 7 can be written as

$$\varepsilon_{R\text{-}EZ}[R\text{-}EZ] = \varepsilon_{S\text{-}EZ}[S\text{-}EZ] \quad (8)$$

This leads, as $\varepsilon_{R\text{-}EZ} = \varepsilon_{EZ}-(\Delta\varepsilon_{EZ}/2)$ and $\varepsilon_{S\text{-}EZ} = \varepsilon_{EZ}+(\Delta\varepsilon_{EZ}/2)$, to

$$\{\varepsilon_{EZ}-(\Delta\varepsilon_{EZ}/2)\}\,[R\text{-}EZ] = \{\varepsilon_{EZ}+(\Delta\varepsilon_{EZ}/2)\}[S\text{-}EZ] \quad (9)$$

Then, equation 9 can be deduced to,

$$\varepsilon_{EZ}\{\,[R\text{-}EZ]-[S\text{-}EZ]\,\} = (\Delta\varepsilon_{EZ}/2)\,\{[R\text{-}EZ]+[S\text{-}EZ]\} \quad (10)$$

$$([R\text{-}EZ]-[S\text{-}EZ])\,/\,([R\text{-}EZ]+[S\text{-}EZ]) = \Delta\varepsilon_{EZ}/2\varepsilon_{EZ} \quad (11)$$

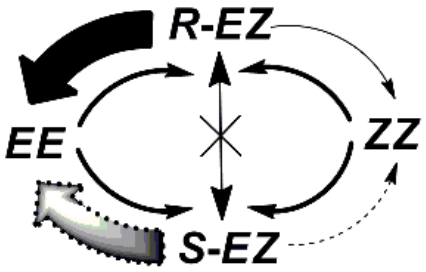
Kuhn anisotropy factor, g is defined as,

$$g = \Delta\varepsilon/\varepsilon \quad (12)$$

from the equations 11 and 12, equation 13 can be obtained,

$$([R\text{-}EZ]-[S\text{-}EZ])\,/\,([R\text{-}EZ]+[S\text{-}EZ]) = g_{EZ}/2 \quad (13)$$

As I already stated, the *EE*, *EZ* and *ZZ* isomers are photochemically interconvertible and establish an equilibrium composition of *EE*, *EZ* and *ZZ* upon photoirradiation. Both the *EE* and *ZZ* isomers are achiral but the *EZ* isomer is chiral and exist as a racemic mixture of *R* and *S* stereoisomers. The reversible photoisomerization from *R*, *S* enantiomers of *EZ* to nonchiral *EE* or *ZZ* states has same efficiency under nonpolarized light irradiation. However, under *r*-or *l*-CPL irradiation the *R* and *S* enantiomers of *EZ* selectively photoisomerizes (solid and dotted arrow) to non-chiral *EE* or *ZZ* ground states. This repeated *EZ* (*R-EZ* or *S-EZ* in scheme 7) to *EE* or *ZZ* enantio-discriminating photoisomerization pathway and the reverse nonenantio-discriminating photoisomerization from *EE* or *ZZ* to *EZ* isomer upon CPL irradiation causes an enantiomeric imbalance in the system at the photostationary state. As a result, a chiral product with a partial enantio-imbalance formed from a nonchiral compound.



Scheme 7. Enatio-differentiating photoisomerization pathways for *EZ* isomer formation

during CPL irradiation with one of CPLs. Solid arrows represent much higher reaction rate of the photoisomerization paths than the corresponding dotted arrows.

There is only one example for absolute asymmetric synthesis using CPL as a chiral source, which are helicenes. In that reaction, *trans*-diarylolefins with different aromatic rings photoisomerized to *cis*-diarylolefins, which existed as mixtures of thermally interconvertible helical enantiomers. Upon further photoabsorption, *cis*-diarylolefins underwent photochemical ring closure to form dihydrohelicenes, which were chemically converted to helicene through oxidation in the presence of iodine.

If absolute asymmetric synthesis is defined as the reaction of an achiral compound to give a chiral product without any sources of chemical chirality, my present CPL-induced reaction for **3** to form a chiral product with enantio-imbalance is seemingly a new absolute asymmetric synthesis using CPL. Actually it is a simultaneous photoresolution process of a photochemically formed racemic mixture. To the best of my knowledge this is the first report of the partial photoresolution of enantiomers formed *in situ* upon photoirradiation of a prochiral molecule by CPL irradiation.

4. Conclusion.

In this study, I have described the design and synthesis of a new class of azobenzene dimers with the symmetric incorporation of two azobenzenes, where photoindued conformational change of one of the azobenzenes was successfully utilized for the generation of asymmetry in the molecules and investigated CPL induced photoresolution. I presented a novel design **3**, where two azobenzenes substituted to the ortho positions of phenyl ring connected to naphthalene induced axial chirality on irradiation with the light of suitable wavelengths. Interestingly, compound **3** has successfully used in reversible enatio-differentiating photoisomerization studies by *r*/*l*-CPL at 436 nm. Here, for the first time, I demonstrated the simultaneous generation of chirality and enantiomeric excess from a non-chiral structure by a single wavelength of CPL irradiation and proposed a new mechanism of CPL photoresolution from the ground states of *R* and *S* enantiomers of *EZ* form to a common ground state of nonchiral *EE* or *ZZ* forms. I believe that such a chiral to nonchiral enantio-differentiating photoisomerization path upon *r*-or *l*-CPL irradiation constitute a molecular model to explain the chiral imbalance in nature through partial photoresolution mechanism and I anticipate the *in situ* generation of chirality from prochirality by light without any complex chemical reaction will be a promising method in optical memory devices

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LIST OF PUBLICATIONS.

1) K. Rijeesh, P.K. Hashim, Shin-Ichiro Noro, Nobuyuki Tamaoki. "Dynamic Induction of Enantiomeric Excess from a Prochiral Azobenzene Dimer under Circularly Polarized Light"**,** *Chem. Sci.*, **2015**, 6, 973-980.

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