

学 位 論 文 題 名

Induction and Reversible Switching of Molecular Chirality by Polarized or Non-polarized Light in Azobenzene Derivatives

(アゾベンゼン誘導体における偏光または非偏光照射による
分子キラリティーの誘起および可逆的スイッチング)

学位論文内容の要旨

Chirality which refers to the symmetry concept of molecules has been the topic of interest for chemists since decades, particularly in connection with the homochiral structures in nature along with the increased application in material science and technology. Biomolecules like nucleic acids and proteins in the living organisms exists almost exclusively as single enantiomer, a property that is critical for molecular recognition and replication process and thus seems to be a prerequisite for the origin of life. However, the questions as to where biomolecular homochirality comes from and at what stage in evolutionary process and how one enantiomer gets dominant over the other are not yet answered. One of the ways to answer these is to utilize modern experimental and theoretical work that has done by scientists since the construction of time machine that tells precisely the chain of events that lead to life on the Earth is almost impossible.

The chirality of light (for instance; circularly polarized light (CPL)) is believed to be one of the reason for the origin of amino acid chirality in nature since several theories and experimental observations suggested the existence of both organic molecules in the molecular clouds and substantial CPL in the number of astronomical sources. Moreover, the photoresolution (deracemization process of photochemically interconvertible enantiomers) using CPL is certainly interesting from the view point of laboratory applicability, since CPL is readily generated from linearly polarized light (LPL) in combination with a quarter wavelength plate.

Recently, Feringa *et al* reported reversible photoderacemization with CPL on overcrowded alkene system through chiral discrimination path from electronic ground state to a common excited state. However, chiral discrimination between ground state of two geometrical isomers of a photochromic system is not reported yet. Our interest here is to explore chirality control in photochromic system through a new enantiodiscrimination mechanism at electronic ground state. Specially designed azobenzene system stands as one of the suitable candidate for ground state chiral discrimination since it undergoes enantiodifferentiating photoisomerization on CPL irradiation between

the ground state of *trans* (*E*) and the ground state of *cis* (*Z*) form.

We developed a molecular system based on planar chirality having a photoswitchable benzene rotor in which, CPL irradiation to the racemic mixture of chiral compound leads to the enrichment of one of the enantiomer through a new chiral discrimination path i.e, enantiodifferentiating photoisomerization between ground states of R and S enantiomers of *E* (E_R and E_S) and a common (or fast racemizing) ground state of *Z* form.

In **chapter 2** of the thesis new photo-triggered molecular machines based on planar chiral cyclic azobenzene consisting of a 2,5-disubstituted-1,4-dioxybenzene rotating unit and a 3,3-dioxyazo benzene photoisomerisable moiety bridged together by fixed bismethylene spacers and the induction of molecular chirality by CPL irradiation is described. Among the different kinds of cyclic azobenzenes we synthesized, molecule with 2,5-dimethylbenzene as rotor has been demonstrated as light-controlled molecular brake, wherein free rotation of rotor was completely stopped in *E* isomer, brake ON (rotation OFF) while the rotation was allowed in the *Z* isomer, brake OFF (rotation ON). Molecule with bulkier methoxy substituent on 2,5 positions of benzene rotor showed high conformational restriction on the free rotation of rotor in both *E* and *Z* isomers (brake ON). Compound with fluorine-substituted rotor was observed to be brake OFF irrespective of cavity change by photoisomerization. In addition cyclic azobenzene having 2,5-dimethyl benzene as a rotor was used for the chirality induction studies by CPL. Upon irradiation of a racemate with *r*-or *l*- CPL at 488 nm, we were able to repeatedly perform partial enrichment of S or R enantiomers.

In **chapter 3**, a novel concept for the generation of point chirality directly from a prochiral molecule in azobenzene dimer is described. On suitable wavelength irradiation, *E-Z* photoisomerization of one of the azobenzene moieties turned to generate a difference in substituents around central carbon atom and thus point chirality was induced in the molecule. The enantiomers of induced chiral structures were resolved in chiral HPLC showing circular dichroism with opposite cotton effects. The ON-OFF switching of point chirality was investigated by light irradiation and reflux respectively.

In **chapter 4**, synthesis of new prochiral molecule consisting of two azobenzene moieties attached to 4,15 position of the [2,2]paracyclophane, the induction of planar chirality by light irradiation, and the chiroptical properties obtained after HPLC separations of corresponding enantiomers are described. The asymmetry generated on the [2,2]paracyclophane due to *E-Z* photoisomerization of one of the azobenzene moieties were utilized for the induction of planar chirality in the system.

In this dissertation molecular chirality induction by circularly polarized or non-polarized light irradiation in cyclic or acyclic azobenzene system with a ground state chiral discrimination mechanism is demonstrated. A light controlled molecular machine based on planar chiral cyclic azobenzene and its ON-OFF braking action is also showed. We expect this type of simple azobenzene derivative can represent a model compound, which may explain the asymmetric imbalance of the molecules in nature.

学位論文審査の要旨

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博士学位論文審査等の結果について（報告）

有機化合物における不斉はタンパク質や核酸の二次構造を決定する重要な構造因子であり、また、その二次構造が、生命活動における生体分子機能において鍵となっていることを合わせて考えると、生体分子における不斉の起源について考えることは、生命科学において重要である。生体分子では、アミノ酸における *l* 体、糖における *d* 体のように一方の鏡像異性体のみが主に利用されているが、そのホモキラリティーの起源については未だ明らかになっていない。何らかの物理的な不斉の作用によって、ある不斉有機化合物の鏡像異性体間に濃度差が生じ、それが別の化学的仕組みによって増幅されたと考えられるが、そもそも物理的な不斉の作用で鏡像異性体の濃度差を生じさせる反応の例が少ない。

本論文は、物理的な不斉源として円偏光を用いる光反応に着目し、ラセミ化反応の動的制御という概念に基づき設計した新規化合物により、新しい機構による鏡像異性体選択的光反応を実証し、ホモキラリティーの起源の説明に資することを目的としたものである。

2,5-置換ベンゼンのローター部位とアゾベンゼンからなる光異性化部位を分子内に含む環状分子を合成し、ローター部位の回転運動に対する置換基のサイズとアゾベンゼンの幾何構造の影響を調べた。本化合物では、ローター部位の自由回転が止まるとき、面性不斉によって一對の鏡像異性体が生じる。置換基がメチル基の時、光で制御可能なアゾベンゼンのトランス-シス幾何構造によって、ローターの回転をスイッチすることができた。また、光反応に円偏光を用いることで、一方の鏡像異性体を選択的にかつ繰り返し過剰とすることができた。また別に、 sp^3 炭素にメチル基とフェニル基と2つのアゾベンゼンが置換した化合物を合成し、本化合物が、そのラセミ化反応をアゾベンゼンの光異性化反応で直接スイッチできる新しい化合物であることを示すことに成功した。

これを要するに、著者は、光でスイッチできる幾何異性体のうち一方のみでラセミ化する新規な化合物を合成し、一部の化合物においては、円偏光によって一方の鏡像異性体を過剰とすることに成功したものである。本成果は、全く新しい絶対不斉反応を提案するもので、自然界のホモキラリティーの起源が円偏光である可能性を新たに支持する知見を与えるものであるため、生命科学に貢献するところ大である。

よって著者は、北海道大学博士（理学）の学位を授与される資格あるものと認める。