aliquot with an internal standard (cyclohexanol in phosphate buffer), and then calibrating the measured relative area in the chromatogram with their corresponding response factors. The reaction was monitored for 24 h.

Control Experiments: No chiral alcohol product was formed in the absence of the HLADH enzyme, while no ketone was reduced to alcohol in the presence of the model cofactors **1** and **4**. The latter result shows that **1** and **4** preferentially bind to the Cp*Rh center in the presence of the ketone, and they are reduced regioselectively to their 1,4-NADH derivatives **3** and **5**, all in the absence of HLADH.

General Procedure (Oxidation): NAD^+ (83.58×10^{-3} mmol) or NAD^+ models **1** or **4** and HLADH (10 units) were placed in a 10-mL Schlenk flask, and Schlenk techniques were used to deoxygenate the solid mixture. Under positive argon pressure, potassium phosphate buffer (5 mL, 100 mM, pH 7.04, deoxygenated) and (*S*)-2-pentanol (83.58×10^{-3} mmol) were added successively through a syringe. The reaction flask was immediately capped securely with a glass stopper and shaken by using a shaker at room temperature. The progress of the reaction was monitored by means of GC, and the product, 2-pentanone, was identified by comparing the retention time with that of an authentic sample. The oxidation of (*R*)-2-pentanol was also tested under the same conditions, and its reaction rate was found to be much slower than that of (*S*)-2-pentanol. The relative rates of (*S*)- and (*R*)-2-pentanol in the first 24 hr were ~4:1. Additionally, the reactions were found to reach equilibrium after ~60 h (in the case of (*S*)-2-pentanol), at which point both 2-pentanol and 2-pentanone were present in the reaction mixture in a ratio of ~40:60. The same procedure described in the example with NAD^+ was followed with the water soluble model **4**. Both racemic 2-pentanol and (*S*)-2-pentanol were tested, and similar results were obtained as stated in the case of NAD^+, except that the reaction rate became slower after 24 h.

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Transfer of Chiral Information through Achiral Ion Recognition by a Novel Pseudocrown Ether with a Binaphthyl Moiety

Tatsuya Nabeshima,* Akihiro Hashiguchi, Toshiyuki Saiki, and Shigehisa Akine

Chiral products obtained from metabolic processes are often used as reactants for subsequent asymmetric reactions in different chiral environments.[1] Not only chemical reactions but also physical events, such as the selective transport of chiral substrates, require chiral communication between the molecules engaged in the chiral process. Thus, transfer, transduction, modulation, and amplification of chiral information are essential issues for all chiral phenomena. These processes, however, are usually regulated by chiral molecules. Hence, the regulation of such chiral events by an achiral species is extremely fascinating and important.

Allostery and feedback are good examples of the transfer of molecular information, and they regulate many biological events that are linked to each other.[2] These regulating processes play an important role in controlling the function of proteins and they are effective for triggering a certain cascade of reactions in which molecular information is transferred and/or amplified. Many artificial allosteric receptors have recently been reported in which their function is regulated by a single effector, although multistep response to several different stimuli should be very useful for constructing cascade systems[3] and molecular logic devices.[4, 5]

Here we report that podand **1**[6] dually responds to external stimuli, its conversion to a pseudocrown ether complex $[Cu^I(\mathbf{1})]$, and the transfer of chiral information in $[Cu^I(\mathbf{1})]$ by achiral guests, namely alkali metal ions. Precursor

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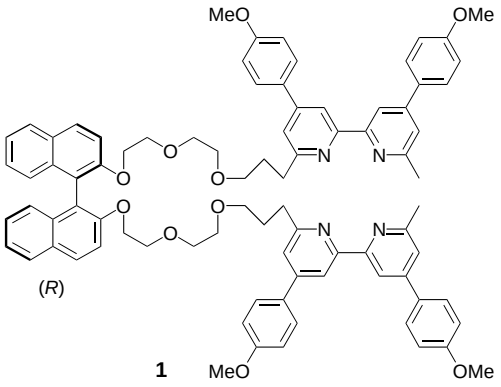

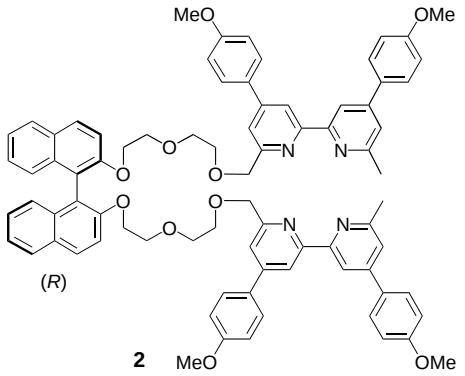

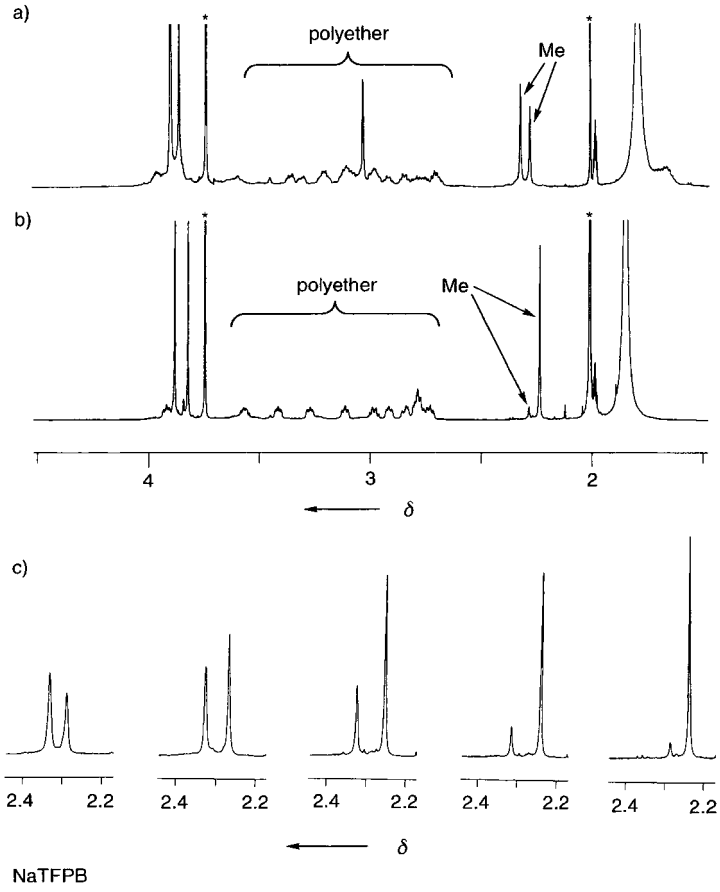

Figure 1. ^{1}H NMR spectra of [Cu^I(**1**)] in a mixture of $CDCl_3$ and CD_3CN (95:5): a) [Cu^I(**1**)]TFPB; b) [Cu^I(**1**)]TFPB and four equivalents of NaTFPB; c) The signals for the picolyl methyl groups in the absence and presence of NaTFPB (0.25–4 equiv). * denotes solvent signals.

1 for the pseudocrown ether complex possesses two polyether chains that connect the (*R*)-1,1′-binaphthyl and 2,2′-bipyridine moieties. If 1:1 complexation of **1** with a Cu^I ion occurs, the desired host [Cu^I(**1**)] with a cyclic binding site for an alkali metal ion is produced. There are two diastereomers of [Cu^I(**1**)], that is, a helical and nonhelical structure.

Quantitative formation of the red [Cu^I(**1**)] complex was ascertained by UV/Vis and ^{1}H NMR spectroscopies.[6, 7] A metal-to-ligand charge-transfer (MLCT) absorption characteristic of a tetrahedral Cu^I–bipyridine complex[7] appeared at 480 nm upon addition of Cu^I ions. The isotope distribution observed in the electrospray ionization (ESI) mass spectrum for [Cu^I(**1**)] is in good agreement with the theoretical pattern. This geometry is also supported by new signals for the methyl protons adjacent to the bipyridine moieties appearing upfield in the ^{1}H NMR spectrum.[7b,c] UV/Vis (1,2-dichloroethane:CH_3CN 50:1) and ^{1}H NMR ($CDCl_3$:CD_3CN:CD_3OD 47:3:50) titrations indicate the quick formation of a stable complex between **1** and a Cu^I ion. There are two signals in the ^{1}H NMR spectrum arising from the picolyl methyl protons which can be assigned to the two diastereomers. Consequently, the ratios of the diastereomers can be calculated to be 42:58[8] and 43:57 for [Cu^I(**1**)] and [Cu^I(**2**)], respectively.

Significant changes in the ^{1}H NMR spectrum of [Cu^I(**1**)] (Figure 1) were observed on addition of NaTFPB ($TFPB^-$: tetrakis[3,5-bis(trifluoromethyl)phenyl]borate). In particular, the chemical shifts of the resonances attributed to the polyether chains changed drastically, which indicates that the Na^+ ion complexes inside the cavity of the pseudocrown ether of [Cu^I(**1**)]. Analysis of the resulting complex by ESI-MS also suggests the formation of the ternary complex of **1**, Cu^I, and Na^+. In a more polar solvent ($CDCl_3$:CD_3OD 4:1), however, an excess amount (2 equiv) of Na^+ ions resulted in no significant changes in the ^{1}H NMR spectrum. The addition of nBu$_4$NTFPB had no effect on the spectra. This result is explained by the nBu$_4$NTFPB ion being too large to coordinate with [Cu^I(**1**)], as judged by the inspection of a CPK model. In contrast to [Cu^I(**1**)], the addition of Na^+ and K^+ ions caused no spectral changes to [Cu^I(**2**)], thus showing that the complex had practically no affinity for Na^+ and K^+ ions. This remarkable selectivity of [Cu^I(**1**)] and its respective affinity, relative to [Cu^I(**2**)], probably results from the smaller electrostatic repulsion between the Na^+ and Cu^I ions and/or from the higher flexibility of the polyether chains as a consequence of the longer trimethylene spacers between the polyether chain and the bipyridine units. The ratio of the two signals for the picolyl methyl protons in the ^{1}H NMR spectrum of [Cu^I(**1**)] increased considerably in proportion to the amount of Na^+ added. One diastereomer was formed slightly more favorably (42:58) in the absence of Na^+ ions. However, the distribution of the diastereomers was reversed in the presence of excess Na^+ ions (4 equiv), and the other isomer formed predominately (89:11). It is noteworthy that the ratio is independent of the concentration (1.0–8.0 mM) of

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[Cu^{I}(**1**)]. This fact again indicates that the two signals do not come from *n*:*n* oligomeric products but from the two 1:1 isomers. Thus, the increase in the ratio reflects the higher affinity of one diastereomer toward Na^+ ions than that of the other. The changes in the ratio and chemical shifts of the signals for the methyl protons were analyzed by nonlinear regression to give the association constants (K_a) between [Cu^{I}(**1**)] and Na^+. The K_a value of one diastereomer is 15 times larger than that of the other. The effective coordination of the polyether moieties in [Cu^{I}(**1**)] to an Na^+ ion induced a conformational change, and thus a shift in the equilibrium between the diastereomers. The enhancement of the diastereomeric excess (77 %, 4 equiv of Na^+) in [Cu^{I}(**1**)] clearly shows that the chirality of the (*R*)-1,1′-binaphthyl moiety is transferred to the tetrahedral Cu^{I}–bipyridine complex by complexation with an Na^+ ion, which acts not only as an achiral guest but also as a mediator of chiral information. It is notable that the addition of [18]crown-6 to a mixture of **1**, Cu^{I}, and Na^+ (1:1:2) decreased the diastereomeric ratio to the original value obtained in the absence of Na^+ ions. This effect is attributed to the removal of the Na^+ ion from the cavity of the pseudocrown ether. The addition of K^+ ions (4 equiv) has a smaller effect on the ratio of diastereoisomers (85:15), and the ratio was even smaller with Cs^+ ions (66:34). The dependency of the ratio on the size of the alkali metal ions suggests there is a dipole–ion interaction between the guests and the pseudocrown ring.

Preferential formation of one diastereomer of [Cu^{I}(**1**)] was also shown by CD spectroscopy (Figure 2). The complex [Cu^{I}(**1**)] itself exhibited very weak Cotton effects (almost CD silent) in the region of the MLCT band. However, positive and negative Cotton effects were distinctly observed in the presence of Na^+ ions, which is consistent with the predominant formation of the right-handed, (that is, helical) structure.[9] The formation of a 1:1 complex between [Cu^{I}(**1**)] and Na^+ was evident from monitoring the increase in the CD intensity.[10] ^{1}H NMR spectroscopic studies have shown that the helical diastereomer of the pseudocrown ether binds Na^+ ions even more strongly than the other (Scheme 1). Inspection

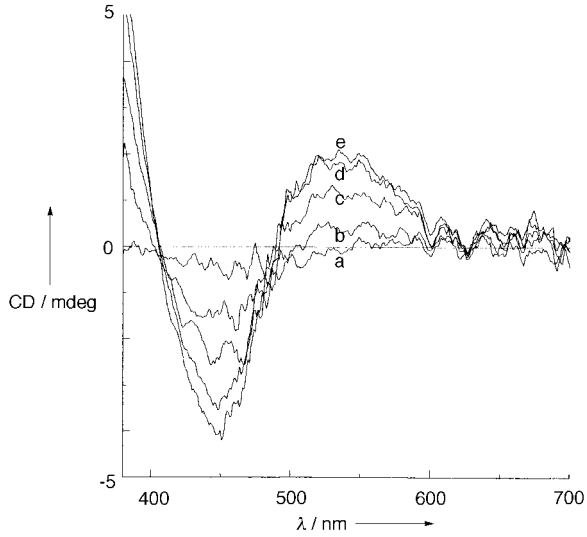
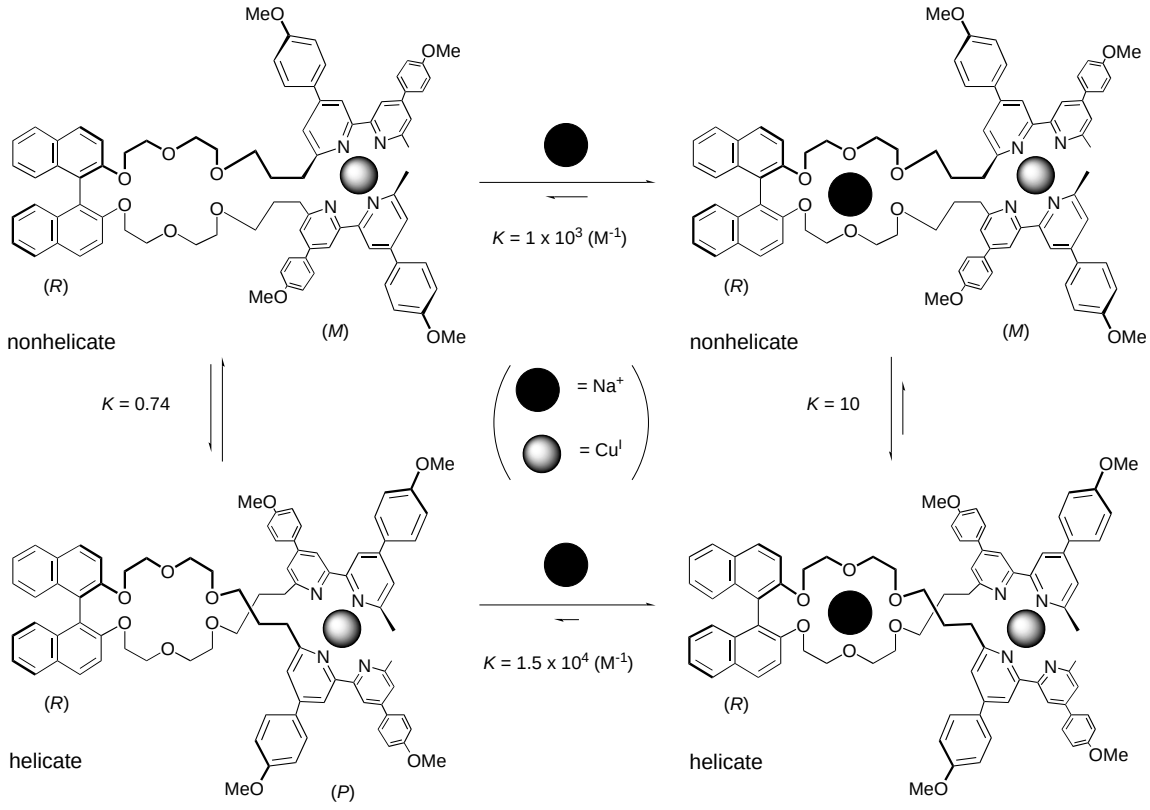


Figure 2. CD Spectral Changes of [Cu^{I}(**1**)]TFPB by the addition of NaTFPB in a mixture of CH_2ClCH_2Cl and CH_3CN (95:5) at 25 °C. Concentration of [Cu^{I}(**1**)]TFPB = 2.0 mM. a) NaTFPB: 0 equiv; b) NaTFPB: 0.25 equiv; c) NaTFPB: 0.50 equiv; d) NaTFPB: 1.0 equiv; e) NaTFPB: 2.0 equiv.



Scheme 1. Transfer of chiral information from the binaphthyl moiety to the [Cu^{I}(bpy)$_2$] complex of **1**. bpy = 2,2′-bipyridine.

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of CPK models suggested that the helical structure is more compact and rigid, and that the helicate provides a more favorable binding site for Na^+ ions than the nonhelicate. Finally, the observation of a modulation of the CD intensity in the MLCT region indicates that this system works as an AND device for CD output by utilizing coordination and chiral information: The Cu^I and Na^+ ions act as the input signals[4, 5] and there is only a CD response if the system receives both input signals.

All the spectral data obtained indicate unambiguously that there is an efficient and intramolecular transfer of chiral information from the binaphthyl moiety to the [Cu^I-bipyridine] complex through the coordination of an achiral Na^+ ion. This complexation makes the pseudocrown ring more rigid than in the Na^+-free [Cu^I(**1**)] complex. This rigidity results in a significant reduction in the loss of chiral information from the binaphthyl unit to the Cu^I complex through the polyether spacers and results in effective chiral communication being achieved.

Helicates such as the [Cu^I(**1**)] complex are also considered to be strong candidates for intermolecular chirality transfer since helical metal complexes have a high potential for chiral recognition and interaction with helical biomolecules such as DNA[11] and proteins with an α-helical structure. A preliminary experiment showed that [Cu^I(**1**)] bound to amino acid derivatives, thus an interaction with proteins can be expected. We are currently investigating chiral information transfer systems by using an achiral mediator for chirality.

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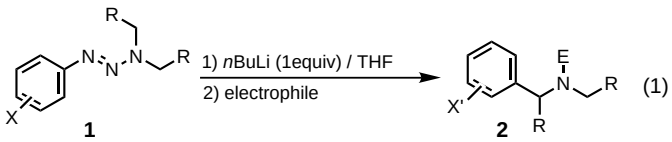
α-Lithiation of 1-Aryl-3,3-dialkyltriazenes and Intramolecular Conversion to Benzylamine and Tetrahydrobenzotriazine Derivatives**

Keiji Nishiwaki,* Takashi Ogawa, and Keizo Matsuo*

1-Aryl-3,3-dialkyltriazenes are utilized in many ways in organic syntheses, for example, as protective groups for aniline derivatives,[1] as precursors of benzyne,[2] as well as in diazo coupling,[3] Sandmeyer–Gattermann reactions,[4] and hydroxylation of positive ion exchange resins.[5] Recently, Nicolaou et al. showed that aryltriazenes can be used in the construction of aryl ethers, and applied this method to the synthesis of vancomycin.[6] In combinatorial chemistry, triazenes were used as linkers in solid-phase synthesis[7] and as alkylating polymers in solution-phase synthesis.[8] Haley et al. reported thermal cyclization of triazenes.[9]

Here we report on the transformation of l-aryl-3,3-dialkyltriazenes into benzylamines and dearomatized compounds, which involves a novel intramolecular carbon–carbon bond-forming reaction in which a lithiated alkyl group on the nitrogen atom in the 3-position[10] attacks the aromatic ring as a nucleophile.

The triazenes were prepared in good yields from the corresponding primary aromatic amines by standard methods ($NaNO_2$/HCl, then addition of the respective amine). The general procedure for the transformation of the triazenes into benzylamines is as follows. The triazenes were treated with *n*BuLi (1 equiv) in THF at 0 °C for 1 h, followed by the addition of electrophiles to produce the corresponding benzylamine derivatives [Eq. (1)]. The results are summarized in Table 1. The addition of Boc_2O instead of H_2O as an electrophile greatly increased the yield (entries 1 and 3). When *o*- and *p*-methylphenyltriazenes were treated as above, *m*-methylbenzylamine was formed in both cases, but the yield of the product was superior in the latter case (entries 6–8). Some *p*-substituted triazenes were transformed into *m*-substituted benzylamine derivatives (entries 9–12). In the case of the *m*-substituted triazenes, mixtures of *o*- and *p*-methylbenzylamine derivatives were obtained, but *p*-derivatives were formed predominantly (entries 7 and 13). The *m*-methoxy- and *m*-fluorophenyltriazenes produced *o*-substitut-



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