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Scope of Research
The research interests of the laboratory include the development of advanced molecular transformation, total synthesis of biologically active products, and molecular recognition. Programs are active in the areas of asymmetric alkylation of carbonyl compounds based on “memory of chirality”, nucleophilic catalysis for fine organic syntheses, synthesis of unusual amino acids and nitrogen heterocycles, regioselective functionalization of carbohydrates, synthesis and properties of homochiral oligonaphthalenes, and the structural and functional investigation of heterochiral oligomers.

Research Activities (Year 2009)
Publication

Presentations
Binaphthyl Surrogates Possessing a Metal Center Directly Bound to the Chiral Axis, 34th Symposium on


Grants
Furuta T, Synthesis of Functionalized Artificial Phospholipids for Investigation of Membrane Related Biosystems, Grant-in-Aid for Scientific Research (C), 1 April 2008–31 March 2011.
Yoshimura T, Syntheses of Natural Products via Memory of Chirality, Grant-in-Aid for Young Scientists (B), 1 April 2007–31 March 2009.
Discrimination of Distal Enantiotopic Hydroxy Groups by Organocatalysis

Asymmetric desymmetrization of meso-1,2-diols, meso-1,3-diols, and prochiral 1,3-diols have been well established. However, the corresponding reactions of 1,5-diols and the longer analogues have rarely been developed because of their extreme difficulty. We have developed organocatalytic asymmetric lactonization of α-symmetric 1,9-diols via discrimination of distal enantiotopic hydroxy groups with ~12 Å distance in between. Treatment of 2 with 10 mol% of 1 in the presence of t-Bu(i-Pr)NMe followed by benzyol chloride gave 3 in 92% ee and 91% yield.

Figure 1.

Catalytic Kinetic Resolution of Axially Chiral Binaphthylamines

Nonenzymatic catalytic kinetic resolution of racemic amines has been extremely limited because uncatalyzed non-selective acylation competes significantly with catalyzed enantioselective acylation. We have developed the kinetic resolution of (+)-2,2'-disubstituted-1,1'-binaphthyl-8,8'-diamines with chiral \( \sigma \)-symmetric organocatalyst 4. Treatment of the racemic aromatic amines with isobutyric anhydride in the presence of 10 mol% of 4 gave recovered unacylated amines in 86–98% ee at 61–71% conversion, which corresponds to the selectivity factor (\( \delta \)), 15–24. Based on the temperature-dependence of the enantioselectivity of the kinetic resolution, \( \Delta \Delta H^* \) and \( \Delta \Delta S^* \) between the acylation reactions for the fast-reacting (S)-isomer and the slow-reacting (R)-isomer were determined to be ~2.9 kcal/mol and ~7.8 kcal/mol, respectively. We assume that the acylation of the fast-reacting (S)-isomer proceeds via intermolecular hydrogen bonding between the catalyst and the NH group of the (S)-isomer, where the reacting amino group is located close to the carbonyl group of the acyl-pyridinium intermediate. On the other hand, the hydrogen bonding between the catalyst and the slow-reacting (R)-isomer does not make the reacting NH group close to the carbonyl group, so that the (R)-isomer is expected to undergo direct acylation of the amino group without hydrogen-bonding interaction.

Figure 2.

Asymmetric Synthesis of Multisubstituted \( \beta \)-Lactams from \( \alpha \)-Amino Acids

A method for asymmetric synthesis of multisubstituted \( \beta \)-lactams via intramolecular conjugate addition of the enolates derived from amino acid derivatives has been developed. Precursors 5 for \( \beta \)-lactam synthesis were readily prepared from \( \alpha \)-amino acids via introduction of \( p \)-methoxyphenyl group into the nitrogen, acylation of the resulting amine with maleic anhydride, followed by esterification. Treatment of 5 (R=CH\( \text{Ph} \)) with cesium carbonate in ethanol at 0°C for 1 h gave a 1:1 mixture of cis- and trans-6 in 95% and 96% ee, respectively, in a combined yield of 94%. Treatment of diastereomerically pure trans-6a (R=CH\( \text{Ph} \), 96% ee) with cesium carbonate in ethanol at 20°C for 10 h gave a 12:1 mixture of cis- and trans-6a in 90% and 89% ee, respectively. Similarly, diastereomerically pure cis-6a (R=CH\( \text{Ph} \), 92% ee) gave a 13:1 mixture of cis- and trans-6a in 84% and 77% ee, respectively, on treatment with cesium carbonate in ethanol at 20°C for 10 h. Thus, diastereoselectivity of the \( \beta \)-lactam formation was found to be thermodynamically controlled.

Figure 3.

Yoshimura T, Asymmetric Total Synthesis of Bioactive Natural Products via Planar Chiral Enolate, Grant-in-Aid for Young Scientists (B), 1 April 2009–31 March 2011.

Awards

Uruno Y, Best Poster Award, “The Creation of a Peptide[2]catenane and \( \alpha \),\( \alpha \)-Peptide Catalysts Based on Alternating \( \alpha \),\( \alpha \)-Peptide Architecture”, The 29th Seminar on Synthetic Organic Chemistry for Young Scientists, Kobe, 24 November 2009.


Uruno Y, Impressive Poster Presentation Award, “Toward the Development of Unique Materials Based on Alternating \( \alpha \),\( \alpha \)-Peptide Architecture”, The 5th Host Guest Chemistry Symposium, Utsunomiya, 30 May 2009.