to possess an inversion center, the structure has to be disordered. Two alternate orientations for eight of the atoms in each polyether linkage were identified. These atoms were refined with occupancies of 0.5. A ΔF map revealed the inclusion of one molecule of Me_2CO for each "molecule" of $\mathbf{8}\cdot 4\,PF_6$. The non-hydrogen atoms of this solvent were refined isotropically. Hydrogen atoms were placed in calculated positions, assigned isotropic thermal parameters $U(H) = 1.2\,U_{eq}(C)$ $[U(H) = 1.5\,U_{eq}(CMe)]$, and allowed to ride on their parent carbon atoms. The structure was refined by full-matrix least squares based on F^2 to give $R_1 = 0.148$ and $wR_2 = 0.395$ for 557 parameters. The maximum and minimum residual electron densities in the final ΔF map were 1.11 and $-0.48\,e\,Å^{-3}$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100741. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[16] The angles of twist and bowing associated with the bipyridinium units[5a] are 5 and 22°, respectively.

[17] ^1H NMR: $\delta(\alpha$-bipyridinium-H$) = 8.50, 8.63, 8.68, 8.76.8.77, 8.80, 9.14, 9.19$; $\delta(\beta$-bipyridinium-H$) = 7.02, 7.06, 7.23, 7.27, 7.32, 7.34, 7.40, 7.48$.

[18] For a discussion of a very similar process in [2]catenanes, see M. Asakawa, P. R. Ashton, S. E. Boyd, C. L. Brown, R. E. Gillard, O. Kocian, F. M. Raymo, J. F. Stoddart, M. S. Tolley, A. J. P, White, D. J. Williams, *J. Org. Chem.* **1997**, *62*, 877–893.

[19] The temperature-dependent ^1H NMR spectra were analyzed with the coalescence method; values of k_c at T_c were obtained from the approximation $k_c = \pi\Delta\upsilon/2^{1/2}$, where $\Delta\upsilon$ is the limiting value for the difference [Hz] in chemical shifts for the exchanging protons. The Eyring equation was then used to calculate $\Delta G_c^{\neq}$ from k_c at T_c.

[20] The results of spectrophotometric titration were evaluated by a computer-assisted nonlinear least-square curve-fitting program (Ultrafit, Biosoft, Cambridge, **1992**).

[21] The binding constant K_a for the complex formed between TTF and the parent cyclophane cyclobis(paraquat-*p*-phenylene) in MeCN is $7190 \pm 970\,M^{-1}$ $(-\Delta G^\circ = 5.26 \pm 0.07\ kcal\,mol^{-1})$: P.-L. Anelli, M. Asakawa, P. R. Ashton, R. A. Bissell, G. Clavier, R. Gorski, A. E. Kaifer, S. J. Langford, G. Mattersteig, S. Menzer, D. Philp, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, M. S. Tolley, D. J. Williams, *Chem. Eur. J.* **1997**, *3*, 1113–1135. In the case of the $[\mathbf{8}^{4+}\cdot TTF]$ complex $K_a = 200 \pm 10\,M^{-1}$ $(-\Delta G^\circ = 3.14 \pm 0.02\ kcal\,mol^{-1})$. It follows that $\Delta\Delta G^\circ = 2.12\ kcal\,mol^{-1}$; this can be interpreted as the difference in free energy between the two extreme gross conformations of $\mathbf{8}^{4+}$, the self-complexed conformation and the "opened-up" conformation in which the two macrocycles incorporated into $\mathbf{8}^{4+}$ are free to associate with complementary guests.

[22] a) For an excellent review on current developments in molecular switches, see M. D. Ward, *Chem. Ind.* **1997**, 640–645. b) for our most recent publication on molecular switches, see M. Asakawa, P. R. Ashton, V. Balzani, A. Credi, C. Hamers, G. Mattersteig, M. Montalti, A. N. Shipway, N. Spencer, J. F. Stoddart, M. S. Tolley, M. Venturi, A. J. P. White, D. J. Williams, *Angew. Chem.* **1998**, *110*, 357–361; *Angew. Chem. Int. Ed.* **1998**, *37*, 333–337.

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The First Enantioselective Aza-Diels–Alder Reactions of Imino Dienophiles on Use of a Chiral Zirconium Catalyst[**]

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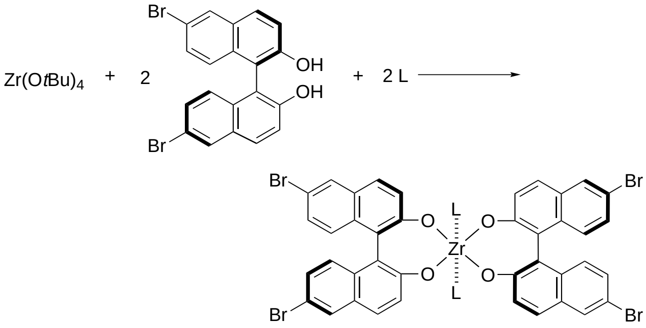
Haruro Ishitani

Asymmetric aza-Diels–Alder reactions provide a useful route to optically active heterocycles such as piperidines and tetrahydroquinolines.[1] Although successful examples of diastereoselective approaches have been reported,[2] there have been few accounts of enantioselective reactions. Yamamoto et al. described elegant enantioselective aza-Diels–Alder reactions of aldimines with Danishefsky's diene on using chiral boron compounds; however, stoichiometric amounts of chiral sources were needed.[3] Quite recently, we reported the first example of a catalytic, enantioselective aza-Diels–Alder reaction of azadienes on using a chiral lanthanide catalyst.[4] While high diastereo- and enantioselectivities were attained in the reaction of azadienes with dienophiles, the products obtained were limited to 8-hydroxytetrahydroquinoline derivatives. Here we report the catalytic, enantioselective aza-Diels–Alder reactions of aldimines (imino dienophiles) with Danishefsky's diene for the synthesis of a wide variety of chiral piperidine derivatives; a chiral zirconium compound was used as catalyst.

The chiral zirconium compound **1**[5] was prepared from $Zr(OtBu)_4$, (*R*)-6,6′-dibromo-1,1′-binaphthol [(*R*)-Br-BINOL, 2 equiv],[6] and the ligand L (2–3 equiv; Scheme 1). The reaction of aldimine **2**, which is obtained from 1-naphthaldehyde and 2-aminophenol (Nap = naphthyl), with Danishefsky's diene **3**[7] was investigated as the model reaction. The ligand and the solvent influenced the yields and enantiose-



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Scheme 1. Synthesis of **1**. L = ligand.

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lectivities strongly (Table 1).[8] 1-Methylimidazole as ligand gave the best results. When the chiral catalyst (10 mol%) was prepared in dichloromethane, the desired aza-Diels–Alder reaction of **2** with **3** proceeded smoothly, but the enantiomeric excess of the adduct was only 40%. On the other hand, the enantioselectivity was improved to 61% *ee* when the catalyst was prepared in benzene by stirring for 1 h at room temperature, the mixture evaporated to remove benzene and *t*BuOH under reduced pressure, and the reaction then carried out in dichloromethane. While use of the bulky diene 4-*tert*-butoxy-2-trimethylsiloxy-1,3-butadiene[9] decreased the selectivity in this case, a higher enantiomeric excess was obtained when the catalyst was prepared in toluene. The best result was finally obtained when the catalyst was prepared and the successive reaction carried out in toluene.[10]

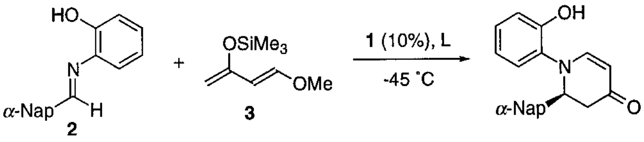
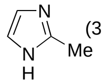
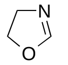
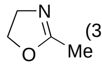


Table 1. Influence of the ligand and the solvent in the reaction of **2** with **3**.

Ligand[a]	Solvent	Yield [%]	*ee* [%]
NMI[b]	CH_2Cl_2	74	40
NMI	1. benzene 2. CH_2Cl_2[c]	81	61
NMI	1. benzene 2. CH_2Cl_2[c]	83[d]	41[d]
NMI	1. toluene 2. CH_2Cl_2[c]	81	71
NMI	toluene	86	82
DMI[e]	toluene	76	59
 (30)	toluene	28	24
 (30)	toluene	86	50
 (30)	toluene	81	46
–	toluene	65	10[f]

[a] 30 mol%, unless noted otherwise. [b] NMI = 1-Methylimidazole. [c] See text. [d] Reaction with 4-*tert*-butoxy-2-trimethylsilyloxy-1,3-butadiene as diene component. [e] DMI = 1,2-dimethylimidazole (20 mol%). [f] Reverse enantioselectivity.

We then examined the influence of the metal (Table 2). Preliminary screening proved that zirconium compounds gave excellent catalytic abilities for the activation of aldimines.[11] Compounds of other Group 4 metals, titanium and hafnium, were screened. A chiral hafnium catalyst gave high yields and enantioselectivities in the model reaction of **2** with diene **3**, whereas lower yields and enantiomeric excesses were obtained with a chiral titanium catalyst.[12]

Table 2. Influence of the metal on the reaction of **2** with **3**.[a]

M	Mol%	Yield [%]	*ee* [%]
Zr	10	86	82
Zr	20	96	88
Hf	10	89	73
Hf	20	96	84
Ti	10	68	39
Ti	20	70	62

[a] Reaction at −45 °C in toluene, catalyst prepared from M(O*t*Bu)$_4$, (*R*)-Br-BINOL (2 equiv), and NMI (3 equiv).

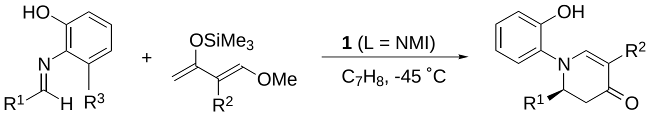
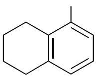
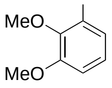
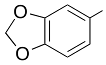


Table 3. Catalytic aza-Diels–Alder reactions.[a, b]

R^1	R^2	Cat. [mol%]	Yield [%]	*ee* [%]
α-Nap	H (**3**)	5	72	67
α-Nap	H (**3**)	10	86	82
α-Nap	H (**3**)	20	96	88
α-Nap	H (**3**)	30	98	89
α-Nap	H (**3**)	50	88	90
α-Nap	Me (**4**)	10	79	89
α-Nap	Me (**4**)	20	93	93
	H (**3**)	10	92	80
o-MeC_6H_4	H (**3**)	10	81	76
o-MeC_6H_4	H (**3**)	20	83	82
o-MeC_6H_4	Me (**4**)	20	97	77
Ph	Me (**4**)	20	83	65
	Me (**4**)	20	95	74
	Me(**4**)	10	80	67
2-thienyl	H (**3**)	10	86	64
c-C_6H_{11}[c]	Me (**4**)	10	47	78
c-C_6H_{11}[c]	Me (**4**)	20	51	86

[a] The absolute configuration was tentatively determined based on the results shown in reference [5]. [b] R^3 = H, unless noted otherwise. [c] R^3 = Me (see text).

Several examples of the catalytic aza-Diels–Alder reactions with the chiral zirconium catalyst are shown in Table 3. In most cases, high chemical yields and good to high enantioselectivities were obtained in the presence of 5–20 mol% of the chiral catalyst.[13] 4-Methoxyl-3-methyl-2-trimethylsiloxy-1,3-butadiene (**4**)[14] also worked well under standard conditions, and the desired 2,3-dihydro-4-pyridone derivatives were obtained in high yields with high enantioselectivities. As for the R^1 group, *ortho*-subsubstituted arenes gave higher selectivities. For example, while the aldimine derived from benzaldehyde (R^1 = Ph) reacted with **4** to afford the corresponding adduct with 65% *ee*, an enantiomeric excess of 74% was obtained in the reaction of the aldimine derived from *o*-tolualdehyde with **4** under the same reaction conditions. The 2-thienyl-substituted aldimine reacted with **3** smoothly to give the corresponding pyridone derivative in a high yield with a good enantiomeric excess.

In the reaction of the cyclohexyl-substituted aldimine with **4**, a low enantiomeric excess of the adduct was observed under standard reaction conditions; the low selectivity was ascribed to the isomerization of the *cis* and *trans* forms of the aldimine. To prevent the isomerization, the aldimine derived from cyclohexanecarbaldehyde and 2-amino-3-methylphenol was used. It was exciting to find that the enantiomeric excess of the corresponding pyridone derivative improved to 86%.

In summary, the first catalytic, enantioselective aza-Diels–Alder reactions of imino dienophiles with Danishefsky's dienes have been achieved on using our original chiral zirconium catalyst. Optically active 2,3-dihydro-4-pyridone derivatives were prepared in high yields with good to high enantiomeric excesses. Further investigations to use the zirconium catalyst in other enantioselective reactions as well as to apply the present enantioselective reactions for the synthesis of biologically active compounds are now in progress.

Experimental Section

A typical experimental procedure is described for the reaction of the aldimine obtained from *o*-tolualdehyde and 2-aminophenol with **3**: 6,6′-Dibromo-1,1′-bi-2-naphthol (0.088 mmol) in toluene (0.5 mL) and *N*-methylimidazole (0.12 mmol) in toluene (0.25 mL) were added to $Zr(OtBu)_4$ (0.04 mmol) in toluene (0.25 mL) at room temperature. The mixture was stirred for 1 h at the same temperature, and then cooled to −45°C. Solutions of the aldimine (0.4 mmol) and **3** (0.6 mmol) in toluene (0.75 mL each) were successively added. The mixture was stirred for 35 h at the same temperature, and saturated $NaHCO_3$ was added to quench the reaction. The aqueous layer was extracted with CH_2Cl_2, and the crude adduct treated with THF/1N HCl (20/1) at 0°C for 30 min. After a usual work-up, the crude product was purified by chromatography on silica gel to give the desired adduct (83%). ^1H NMR ($CDCl_3$): $\delta = 2.10$ (s, 3H), 2.68 (dd, 1H, $J = 7.6$, 16.6 Hz), 3.06 (dd, 1H, $J = 7.6$, 16.6 Hz), 5.15 (d, 1H, $J = 7.5$ Hz), 5.52 (t, 1H, $J = 7.5$ Hz), 6.57 (t, 1H, $J = 7.0$ Hz), 6.76–7.00 (m, 6H), 7.38–7.43 (m, 2H), 9.57 (brs, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 19.0$, 42.7, 58.6, 98.2, 117.1, 119.6, 126.1, 126.2, 126.6, 127.7, 128.3, 130.9, 131.5, 134.8, 136.6, 151.8, 156.8, 192.0; HR-MS calcd for $C_{18}H_{17}NO_2$ [M^+]: 279.1259, found: 279.1271. The optical purity was determined to be 82% *ee* after methylation (MeI, K_2CO_3/acetone) by HPLC analysis with a chiral column. HPLC (Daicel Chiralcel OD, hexane/*i*PrOH (24/1), flow rate 1.0 mL min^{-1}): $t_R = 44.2$ (major enantiomer), $t_R = 50.6$ min (minor enantiomer).

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C_{60} and C_{70} Compounds in the Pincerlike Jaws of Calix[6]arene[**]

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Construction of supramolecular architectures involving electron-deficient fullerenes is of interest in crystal engineering, the synthesis of novel nanostructures, and the development of host–guest chemistry for use in the purification of fullerenes.[1–17] Host molecules that form discrete, albeit inherently weak, complexes with C_{60} and/or C_{70} include

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