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Asymmetric Diels–Alder and Inverse-Electron-Demand Hetero-Diels–Alder Reactions of β,γ-Unsaturated α-Ketoesters with Cyclopentadiene Catalyzed by *N*,*N*′-Dioxide Copper(II) Complex

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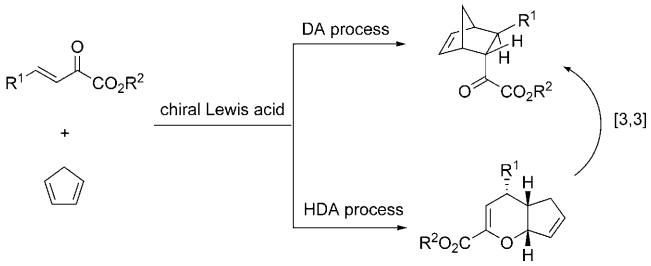
Abstract: Highly enantioselective Diels–Alder (DA) and inverse-electron-demand hetero-Diels–Alder (HDA) reactions of β,γ-unsaturated α-ketoesters with cyclopentadiene catalyzed by chiral *N*,*N*′-dioxide–Cu(OTf)$_2$ (Tf = triflate) complexes have been developed. Quantitative conversion of β,γ-unsaturated α-ketoesters and excellent diastereoselectivities (up to 99:1) and enantioselectivities (up to >99% *ee*) were observed for a broad range of substrates. Both aromatic and aliphatic β,γ-unsaturated α-ketoesters were found to be suitable substrates for the reactions. Moreover, the chemoselectivity of the DA and HDA adducts were improved by regulating the reaction temperature. Good to high chemoselectivity (up to 94%) of the DA adducts were obtained at room temperature, and moderate chemoselectivity (up to 65%) of the HDA adducts were achieved at low temperature. The reaction also featured mild reaction conditions, a simple procedure, and remarkably low catalyst loading (0.1–1.5 mol%). A strong positive nonlinear effect was observed.

Keywords: asymmetric catalysis · chemoselectivity · copper · cycloaddition · *N*,*N*′-dioxide

Introduction

Bridged bicyclic compounds are key structural subunits of numerous natural and unnatural products with a wide range of biological activities.[1] The catalytic asymmetric reactions of α,β-unsaturated carbonyl derivatives and cyclopentadiene have enabled a facile synthesis of these core structures.[2–5] It is important to note that cyclopentadiene not only acts as a 4π component, to give the bridged bicyclic compounds,[6] but can also behave as a dienophile to furnish the inverse-electron-demand hetero-Diels–Alder (HDA)[7–9] cycloadducts when it reacts with β,γ-unsaturated α-ketoesters (Scheme 1).[11–13] The asymmetric HDA process affords ring-fused pyran derivatives with three contiguous stereocenters, which are of particular value in medicinal chemistry.[14] The two products are potentially related to each other by a 3,3-sigmatropic rearrangement.[11b,12a,d,e,13]



Scheme 1. Competing Diels–Alder and hetero-Diels–Alder reactions.

Evans and co-workers presented the first enantioselective example of cyclopentadiene behaving as a dienophile with α,β-unsaturated acyl phosphonates by using chiral oxazoline-copper(II) complexes.[10,11] Subsequently, chiral oxazoline–scandium(III) complexes were applied to the cycloaddition of β,γ-unsaturated α-ketoesters and cyclopentadiene to give HDA adducts as major products with excellent enantioselectivities at extremely low temperature.[13] However, the question of how to improve the chemoselectivity for the DA

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and HDA products has rarely been addressed. Thus, the search for easily accessible and efficient asymmetric catalytic systems that can be applied under mild reaction conditions to obtain the two products with satisfactory stereoselectivity is interesting and challenging. According to initial studies,[6,11–13] it was observed that temperature may play an important role in the chemoselectivity of the reaction, which may provide a degree of chemoselective control. Herein, we present a method that achieves good to high chemoselectivity for the DA adducts and moderate chemoselectivity for the HDA adducts by regulating temperature. Excellent *endo*/*exo* ratios of the DA adducts (up to 99:1) and enantioselectivities (up to >99% *ee*) of the two adducts were observed under mild reaction conditions for a broad range of substrates.

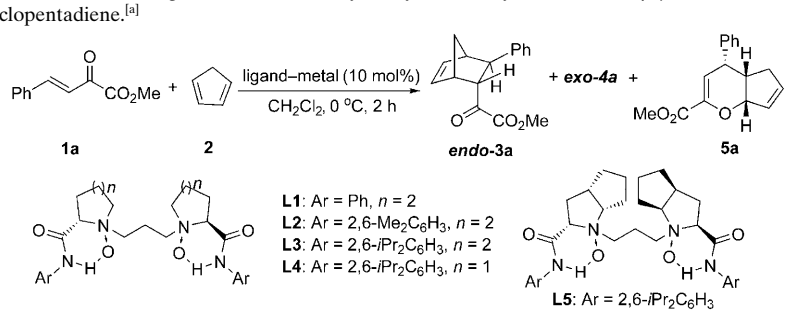
Results and Discussion

As versatile catalysts, chiral *N*,*N*′-dioxide–metal complexes have been superior in many asymmetric reactions.[15] Initially, we examined the cycloaddition reaction of (*E*)-methyl 2-oxo-4-phenylbut-3-enoate (**1a**) with cyclopentadiene (**2**), promoted by *N*,*N*′-dioxide **L1** with various metals, and the significant effect of the central metals on both reactivity and enantioselectivity were noted (Table 1, entries 1–7). As shown in Table 1, only the **L1**–$Cu(OTf)_2$ complex promoted the reaction, with the desired major DA product **3a** being formed in 16% *ee*; the HDA product **5a** was obtained with 40% *ee*, in >99% total yield (Table 1, entry 7). The two sets of isomers derived from the two competitive processes could be easily separated by column chromatography. The effect of the structure of the *N*,*N*′-dioxide ligands, including both the chiral backbone and the steric hindrance of aniline, was then examined (Table 1, entries 8–11). To our delight, a bulkier group at the *ortho* position of aniline, such as methyl, could enhance the enantioselectivity (Table 1, entry 8). More excitingly, *N*,*N*′-dioxide **L3**, which contains bulky 2,6-diisopropyl aniline groups, gave excellent results of more than 99% total yield with 96% *ee* (**3a**) and 99% *ee* (**5a**) (Table 1, entry 9). Furthermore, as in the case of the amino acid backbone, the *N*,*N*′-dioxide **L3**, which was based on L-pipecolic acid, was superior to both L-proline-derived *N*,*N*′-dioxide **L4** and L-ramipril acid derived *N*,*N*′-dioxide **L5**, and afforded the best results (Table 1, entry 9 vs. entries 10 and 11).

Encouraged by the initial results, various solvents were tested in the presence of **L3**–$Cu(OTf)_2$ (10 mol%); the results are listed in Table 2. The important impact of solvent on the enantioselectivity and reactivity of the reaction were thus made apparent. Although the use of acetonitrile gave comparable enantioselectivities for the DA adduct **3a** (90% *ee*) and the HDA adduct **5a** (97% *ee*), it led to a dramatic loss of chemoselectivity for the HDA adduct **5a** (Table 2, entry 2). 1,2-Dichloroethane (DCE) provided good yield (>99%), but the enantioselectivities of both adducts were notably diminished (Table 2, entries 3 vs. 1). Chloroform, tetrahydrofuran, and toluene reduced the catalytic activity of the **L3**–$Cu(OTf)_2$ complex, presumably because of coordination to the central metal (Table 2, entries 4–6). Further studies focusing on the use of ethers as solvent revealed that diethyl ether provided the HDA adduct **5a** with favorable chemoselectivity, but led to low enantioselectivities of the products (Table 2, entry 7). Therefore, dichloromethane was established as the best solvent for the DA and HDA reactions of β,γ-unsaturated α-ketoester with cyclopentadiene (Table 2, entry 1).

The reaction temperature and catalyst loading were then investigated (Table 3). Lowering the temperature led to a clear drop in reactivity and the chemoselectivity for the DA adducts, whereas the enantioselectivity was maintained (Table 3, entries 1–3). When the temperature was increased to 25°C, the reactivity was greatly increased. Moreover, the chemoselectivity for the DA adducts rose to 85% without loss of

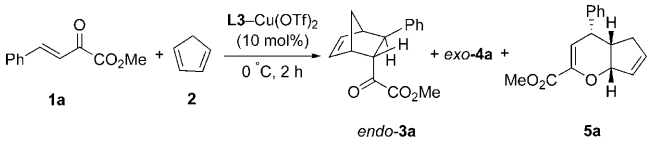
Table 1. Central metal and ligand effects on catalytic asymmetric cycloaddition of β,γ-unsaturated α-ketoester **1a** and cyclopentadiene.[a]



Entry	Ligand	Metal	Yield [%][b]	[**3a**]/[**4a**][c]	*ee* [%][d]	
					3a	**5a**
1	**L1**	$Yb(OTf)_3$	>99	84:16	0	10
2	**L1**	$Y(OTf)_3$	>99	84:16	0	8
3	**L1**	$Ni(acac)_2$	trace	n.d.[e]	n.d.[e]	0
4	**L1**	$Sc(OTf)_3$	>99	96:4	0	0
5	**L1**	$La(OTf)_3$	trace	87:13	11	15
6	**L1**	$[Cu(OTf)]_2$·Tol	>99	96:4	0	26
7	**L1**	$Cu(OTf)_2$	>99	96:4	16	40
8	**L2**	$Cu(OTf)_2$	>99	96:4	31	60
9	**L3**	$Cu(OTf)_2$	>99	96:4	96	99
10	**L4**	$Cu(OTf)_2$	trace	n.d.[e]	n.d.[e]	77
11	**L5**	$Cu(OTf)_2$	trace	n.d.[e]	n.d.[e]	92

[a] Reagents and conditions: 10 mol% **L**/$Cu(OTf)_2$ (1:1), **1a** (0.2 mmol), **2** (200 μL), CH_2Cl_2 (2.0 mL), N_2, 0°C, 2 h. [b] Total yield of **3a**, **4a**, and **5a**. [c] Determined by chiral HPLC analysis, the isomeric configuration of **3** was confirmed by ^1H NMR spectroscopic analysis. [d] Determined by HPLC analysis. [e] Not determined.

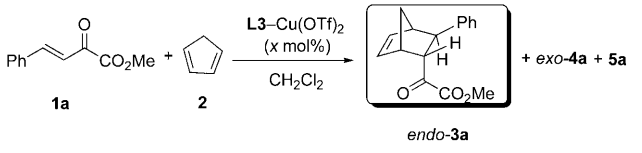
Table 2. Screening of the solvents in the catalytic asymmetric cycloaddition of β,γ-unsaturated α-ketoester **1a** with cyclopentadiene.[a]



Entry	Solvent	Yield [%][b]	[3a+4a]/[5a]	[3a]/[4a][c]	*ee* 3a [%][d]	*ee* 5a [%][d]
1	CH_2Cl_2	>99	50:50	96:4	96	99
2	CH_3CN	>99	80:20	94:6	90	97
3	DCE	>99	51:49	90:10	90	87
4	$CHCl_3$	trace	n.d.[e]	n.d.[e]	59	50
5	THF	trace	n.d.[e]	n.d.[e]	30	40
6	toluene	trace	n.d.[e]	n.d.[e]	35	46
7	Et_2O	>99	20:80	60:40	trace	29

[a] Reagents and conditions: 10 mol% **L3**/$Cu(OTf)_2$ (1:1), **1a** (0.2 mmol), **2** (200 μL), solvent (2.0 mL), N_2, 0 °C, 2 h. [b] Total yield of **3a**, **4a**, and **5a**. [c] Determined by chiral HPLC analysis, the isomeric configuration of **3a** was confirmed by ^{1}H NMR spectroscopic analysis. [d] Determined by HPLC analysis. [e] Not determined.

Table 3. Effect of temperature and catalyst loading on the catalytic asymmetric cycloaddition of **1a** and **2**.[a]



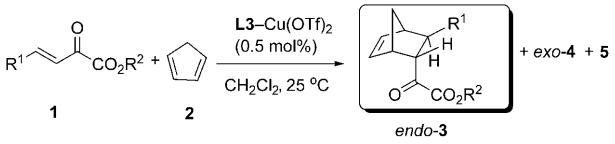
Entry	*T* [°C]	*t*	*x* [mol%]	*ee* 3a [%][b]	[3a]/[4a][c]	[3a+4a]/[5a]
1	0	2 h	10	96	96:4	50:50
2	−20	5 h	10	96	96:4	40:60
3	−45	24 h	10	96	96:4	35:65
4	25	15 min	10	96	96:4	85:15
5	35	15 min	10	82	90:10	89:11
6	25	15 min	1	96	96:4	85:15
7[d]	25	15 min	0.5	96	95:5	85:15
8[e]	25	15 min	0.5	96	95:5	85:15

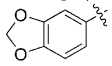
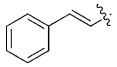
[a] Reagents and conditions: **L3**/$Cu(OTf)_2$ (1:1), **1a** (0.2 mmol), **2** (200 μL), CH_2Cl_2 (2.0 mL), N_2; total yields were all up to >99%. [b] Determined by chiral HPLC analysis. [c] Determined by chiral HPLC analysis, the isomeric configuration of **3a** was confirmed by ^{1}H NMR spectroscopic analysis. [d] Reagents and conditions: **L3**/$Cu(OTf)_2$ (1:1), **1a** (0.4 mmol), **2** (400 μL), CH_2Cl_2 (4.0 mL), N_2. [e] Reagents and conditions: **L3**/$Cu(OTf)_2$ (1:1), **1a** (0.4 mmol), **2** (400 μL), CH_2Cl_2 (4.0 mL), without N_2.

enantioselectivity (96% *ee*) without reducing the *endo*/*exo* ratio (96:4, Table 3, entry 4). A higher chemoselectivity for the DA adducts was achieved at 35 °C, but the enantioselectivity of **3a** decreased significantly (Table 3, entry 5). Reducing the catalyst loading from 10 to 0.5 mol% had no evident influence on the chemoselective formation of the DA adducts, the *endo*/*exo* ratio or the enantioselectivity, and good outcomes (96% *ee*, 95:5 *endo*/*exo* ratio) could be obtained within 15 min (Table 3, entries 6 and 7). It is also notable that the process is tolerant of air and moisture (Table 3, entry 8). Subsequent studies on the reaction parameters, such as substrate concentration (see the Supporting Information), gave the optimal conditions for formation of the DA products: 0.5 mol% **L3**–$Cu(OTf)_2$ complex as the catalyst, 25 °C in dichloromethane (Table 3, entry 7).

Under the optimal conditions, a series of β,γ-unsaturated α-ketoesters proved to be excellent 2π components for this copper(II)-catalyzed cycloaddition reaction, and provided the DA adducts **3** as the major products in high chemoselectivity (up to 94:6) and excellent *endo*/*exo* ratios (up to 99:1) with excellent enantioselectivities (up to 97% *ee*, Table 4).

Table 4. Substrate scope of the asymmetric DA reactions.[a]



Entry	R^1	R^2	[3+4]/[5]	[3]/[4][b]	*ee* 3 [%][c]
1	Ph	Me	85:15	95:5	96
2	Ph	Et	82:18	94:6	95
3	4-MeC_6H_4	Me	85:15	96:4	96
4	4-$MeOC_6H_4$	Me	81:19	96:4	96
5	4-PhC_6H_4	Me	86:14	97:3	95
6		Me	96:4	97:3	97
7		Me	86:14	96:4	96
8	2-naphthy	Me	81:19	96:4	92
9	2-thienyl	Me	90:10	99:1	96
10[d]	2-thienyl	Me	89:11	98:2	92
11	Me	Et	92:8	94:6	96

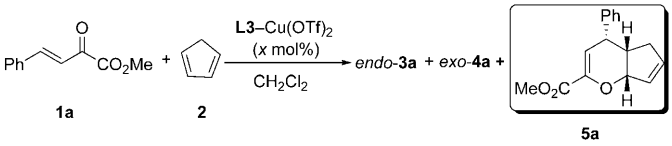
[a] Reagents and conditions: 0.5 mol% **L3**/$Cu(OTf)_2$ (1:1), **1** (0.4 mmol), **2** (400 μL), CH_2Cl_2 (4 mL), N_2, 25 °C, 15 min; total yields were all up to >99%. [b] Determined by chiral HPLC analysis, the isomeric configuration of **3** was confirmed by ^{1}H NMR spectroscopic analysis. [c] Determined by chiral HPLC analysis. [d] Reagents and conditions: 0.1 mol% **L3**/$Cu(OTf)_2$ (1:1), **1a** (2.0 mmol), **2** (2 mL), CH_2Cl_2 (20 mL), N_2.

Both methyl and ethyl esters gave excellent results (Table 4, entries 1 and 2). It was noteworthy that the steric hindrance of the substituent at the aromatic ring had no effect on the enantioselectivities (95–97% *ee*), and up to 94% chemoselectivity for the DA adducts could be obtained (Table 4, entries 3–6). The reactions proceeded well and generated the normal DA product **3** with cinnamyl-substituted substrate in high chemoselectivity with 96% *ee* (Table 4, entry 7). Fused ring and heteroaromatic substrates were also applicable, giving the corresponding products with excellent results (Table 4, entries 8–10). Inspiringly, high DA chemoselectivity (89%) with good enantioselectivity (92% *ee*) was delivered by using as little as 0.1 mol% catalyst (Table 4, entry 10). Moreover, the asymmetric cycloaddition of aliphatic β,γ-unsaturated α-ketoester and cyclopentadiene took place, for the first time, with good chemoselectivity for the DA adducts with 96% *ee* (Table 4, entry 11).

We then aimed to improve the chemoselectivity of the HDA product. As shown in Table 3, we found that lower temperature was favorable for the generation of the HDA

adducts. When the temperature was decreased from −20 to −45 °C, although the reactivity sharply decreased (Table 5), the chemoselectivity for the HDA adduct slightly improved

Table 5. Effect of temperature and catalyst loading on the catalytic asymmetric HDA reaction of **1a** and **2**.[a]



1a 2 5a

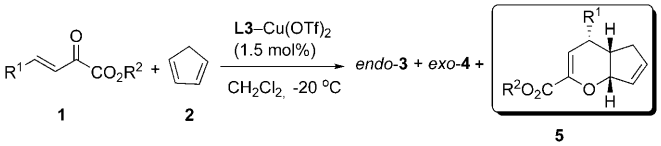
Entry	T [°C]	t [h]	x [mol %]	*ee* **5a** [%][b]	[**5a**]/[**3a**+**4a**]
1	−20	5	10	99	60:40
2	−45	24	10	99	65:35
3	−78	36	10	n.d.[c]	n.d.[c]
4	−20	10	5	99	60:40
5	−20	12	1.5	99	60:40
6[d]	−20	24	0.5	99	60:40

[a] Reagents and conditions: **L3**/Cu(OTf)$_2$ (1:1), **1a** (0.2 mmol), **2** (200 μL), CH_2Cl_2 (2.0 mL), N_2; the total yields were all up to >99 %. [b] Determined by HPLC analysis. [c] Not determined. [d] Reagents and conditions: **L3**/Cu(OTf)$_2$ (1:1), **1a** (0.4 mmol), **2** (400 μL), CH_2Cl_2 (4.0 mL), N_2.

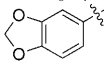
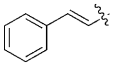
and excellent enantioselectivity (>99 % *ee*, Table 5, entry 2) was maintained. Unfortunately, a further decrease in temperature led to no product formation (Table 5, entry 3). When the catalyst loading was reduced from 10 to 1.5 mol % at −20 °C, the enantioselectivity (>99 % *ee*) and the chemoselectivity for the HDA adduct (60 %) were maintained (Table 5, entries 4 and 5). Moreover, when the catalyst loading was further reduced to 0.5 mol %, similar results could still be obtained, although longer reaction times were required (Table 5, entry 6).[16] Other parameters were also tested, such as substrate concentration, but the results were not further improved (see the Supporting Information). Therefore, optimal reaction conditions for obtaining the HDA products were selected as 1.5 mol % **L3**–Cu(OTf)$_2$ complex as the catalyst, −20 °C in dichloromethane.

Under the optimized conditions, the substrate scope of the HDA reaction was evaluated and the results are summarized in Table 6. As seen for the standard substrate, the reaction of β,γ-unsaturated α-ketoester with an ethyl group worked well, with moderate chemoselectivity and excellent enantioselectivity (Table 6, entries 1 and 2). Regardless of the electronic properties or steric hindrance of the substituent at the aromatic ring of the β,γ-unsaturated α-ketoester, excellent enantioselectivities (>99 % *ee*) and moderate chemoselectivity of the HDA adducts **5** were obtained (Table 6, entries 3–14). (3*E*,5*E*)-Methyl 2-oxo-6-phenylhexa-3,5-dienoate gave the corresponding HDA adduct **5** with up to >99 % *ee*, however, the chemoselectivity was less satisfactory (Table 6, entry 15). Furthermore, moderate chemoselectivity for **5** and excellent enantioselectivities were observed by using condensed-ring and heteroaromatic β,γ-unsaturated α-ketoesters (Table 6, entries 16 and 17). Notably, the catalytic system was also very efficient for the most challenging

Table 6. Substrate scope of the asymmetric HDA reaction.[a]



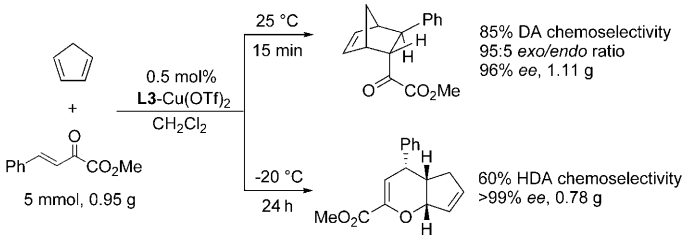
1 2 5

Entry	R^1	R^2	[**5**]/[**3**+**4**]	*ee* [%][b] **3**	*ee* [%][b] **5**
1	Ph	Me	60:40	96	>99
2	Ph	Et	55:45	95	>99
3	4-MeC_6H_4	Me	56:44	96	>99
4	4-$MeOC_6H_4$	Me	56:44	96	>99
5	4-$NO_2C_6H_4$	Me	58:42	n.d.[c]	>99
6	3-$NO_2C_6H_4$	Me	65:35	n.d.[c]	>99
7	4-ClC_6H_4	Me	53:47	n.d.[c]	>99
8	2,4-$Cl_2C_6H_3$	Me	45:55	n.d.[c]	>99
9	3-BrC_6H_4	Me	50:50	n.d.[c]	>99
10	4-BrC_6H_4	Me	55:45	n.d.[c]	>99
11	4-FC_6H_4	Me	53:47	n.d.[c]	>99
12	4-CNC_6H_4	Me	55:45	n.d.[c]	>99
13	4-PhC_6H_4	Me	60:40	95	>99
14		Me	60:40	97	>99
15		Me	22:78	96	>99
16	2-naphthyl	Me	52:48	92	>99
17	2-thienyl	Me	50:50	96	>99
18	Me	Et	46:54	96	>99

[a] Reagents and conditions: 1.5 mol % **L3**/Cu(OTf)$_2$ (1:1), **1** (0.2 mmol), **2** (200 μL), CH_2Cl_2 (2 mL), N_2, −20 °C, 12 h; total yields >99 %. [b] Determined by chiral HPLC analysis. [c] Not determined because no suitable HPLC analytical conditions were found.

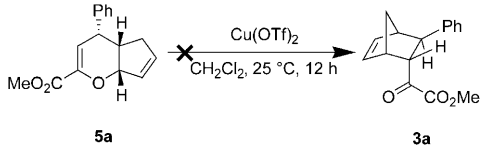
aliphatic substrate, affording the desired HDA adduct in moderate chemoselectivity with more than 99 % *ee* (Table 6, entry 18). In addition, we found that the DA adducts **3** were obtained in moderate chemoselectivity and with good to excellent enantioselectivities at −20 °C (Table 6, entries 1–4 and 13–18).

To further evaluate the synthetic potential of the catalyst system, gram-scale syntheses of the DA adduct **3a** and the HDA product **5a** were performed in the presence of **L3**–Cu(OTf)$_2$ complex as catalyst (0.5 mol %). As shown in Scheme 2, by treatment of 5 mmol starting material under the optimized conditions, the corresponding adducts **3a** and **5a** were obtained without any loss of reactivity, chemoselectivity, or enantioselectivity.



Scheme 2. Gram-scale asymmetric synthesis of **3a** and **5a**.

Under the optimized condition at 25 °C, $Cu(OTf)_2$ did not catalyze the conversion of **5a** into **3a**, which indicated that two distinct pathways dominated at different temperatures in the same catalytic system (Scheme 3). To gain insight into



5a **3a**

Scheme 3. Control reaction of **3a** and **5a**.

the origin of the enantioselectivity, nonlinear effects[17] in the present system were investigated. As shown in Figure 1, strong positive nonlinear effects were observed for both products, suggesting that the reaction system involved a polymeric **L3**–$Cu(OTf)_2$ complex species. Moreover, the strong positive nonlinear effect makes it possible that the high enantioselectivity of the reaction can be achieved by using only a moderate *ee* value for **L3**.

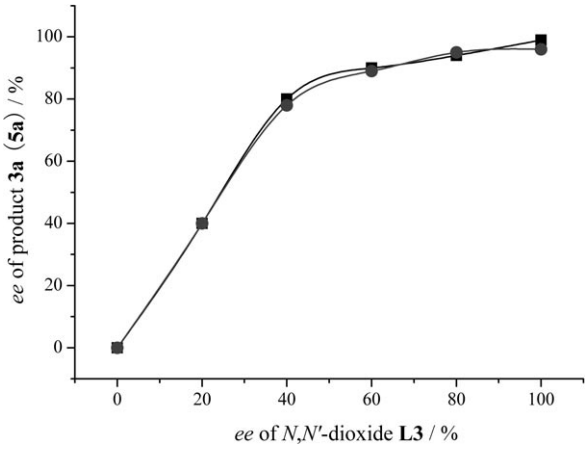


Figure 1. Nonlinear effects in the reaction. ●: DA adduct **3a** obtained at 25 °C, ■: HDA adduct **5a** obtained at −20 °C.

Conclusion

We have developed a catalytic asymmetric cycloaddition reaction between β,γ-unsaturated α-ketoesters and cyclopentadiene that is promoted by an *N*,*N*′-dioxide–$Cu(OTf)_2$ complex. Through regulating the reaction temperature, both normal DA adducts and inverse-electron-demand HDA adducts were obtained in moderate to high chemoselectivity, respectively, with good to excellent enantioselectivities (up to >99 % *ee*). The chemoselectivity for the DA adducts was improved greatly when the reaction was performed at room temperature (25 °C, up to 94 %). In contrast, low temperature was favorable for the chemoselective formation of the HDA adducts (−20 °C, up to 65 %). The reaction also featured mild reaction conditions, a simple procedure, and required remarkably low catalyst loading (0.1–1.5 mol %). Further investigations into the mechanism of this catalytic system are underway.

Experimental Section

General synthesis of DA adduct 3 as major product: A mixture of β,γ-unsaturated α-ketoester (0.4 mmol), $Cu(OTf)_2$ (0.8 mg, 0.002 mmol), and *N*,*N*′-dioxide **L3** (1.3 mg, 0.002 mmol) were added to a test tube under nitrogen and kept at ambient temperature for 0.5 h. Anhydrous CH_2Cl_2 (4.0 mL) was added and the solution was stirred at 25 °C for 0.5 h. Subsequently, cyclopentadiene (400 μL) was added at 25 °C and the reaction mixture was stirred for an additional 15 min. The residue was purified by flash chromatography on silica gel to afford the desired product.

General synthesis of HDA adduct 5 as major product: A mixture of β,γ-unsaturated α-ketoester (0.2 mmol), $Cu(OTf)_2$ (1.1 mg, 0.003 mmol), and *N*,*N*′-dioxide **L3** (2.0 mg, 0.003 mmol) were added to a test tube under nitrogen and kept at ambient temperature for 0.5 h. Anhydrous CH_2Cl_2 (2.0 mL) was added and the solution was stirred at 25 °C for 0.5 h. Subsequently, cyclopentadiene (200 μL) was added at −20 °C and the reaction mixture was stirred for an additional 12 h at −20 °C. The residue was purified by flash chromatography on silica gel to afford the desired product.

General procedure for the scale-up reaction (3a as major product): A mixture of β,γ-unsaturated α-ketoester **1a** (5 mmol, 0.95 g), $Cu(OTf)_2$ (16.2 mg, 0.025 mmol), and *N*,*N*′-dioxide **L3** (9.0 mg, 0.025 mmol) were added to a flask under nitrogen and kept at ambient temperature for 0.5 h. Anhydrous CH_2Cl_2 (50 mL) was added and the solution was stirred at 25 °C for 0.5 h. Subsequently, cyclopentadiene (5.0 mL) was added at 25 °C and the reaction mixture was stirred for an additional 15 min. The residue was purified by flash chromatography on silica gel (ethyl acetate/petroleum ether 1:8) to afford **3a**.

General procedure for the scale-up reaction (5a as major product): A mixture of β,γ-unsaturated α-ketoester **1a** (5 mmol, 0.95 g), $Cu(OTf)_2$ (16.2 mg, 0.025 mmol), and *N*,*N*′-dioxide **L3** (9.0 mg, 0.025 mmol) were added to a flask under nitrogen and kept at ambient temperature for 0.5 h. Anhydrous CH_2Cl_2 (50 mL) was added and the solution was stirred at 25 °C for 0.5 h. Subsequently, cyclopentadiene (5.0 mL) was added under −20 °C and the reaction mixture was stirred for an additional 24 h. The residue was purified by flash chromatography on silica gel (ethyl acetate/petroleum ether 1:8) to afford **5a**.

General procedure for the control reaction: A mixture of HDA product **5a** (0.1 mmol, 25.6 mg) and $Cu(OTf)_2$ (0.6 mg, 0.002 mmol) were added to a test tube. Anhydrous CH_2Cl_2 (1.0 mL) was added and the solution was stirred at 25 °C for 12 h. Under the conditions of the reaction, no interconversion of **3a** into **5a** was observed.

For the methods used to determine the relative and absolute configurations of cycloadducts, see the Supporting Information.

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