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Chiral-$Zn(NTf_2)_2$-Complex-Catalyzed Diastereo- and Enantioselective Direct Conjugate Addition of Arylacetonitriles to Alkylidene Malonates

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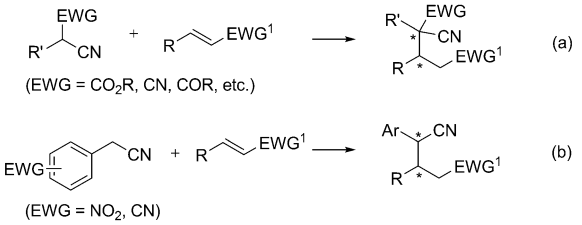
Abstract: Chiral *N,N′*-dioxide/Zn-$(NTf_2)_2$ complexes were demonstrated to be highly effective in the direct asymmetric conjugate addition of arylacetonitriles to alkylidene malonates under mild conditions. A wide range of substrates were tolerated to afford their corresponding products in moderate-to-good yields with high diastereoselectivities (82:18–>99:1 d.r.) and enantioselectivities (81–99% *ee*). The reactions performed well, owing to the high Lewis acidity of the metal triflimidate and a ligand-acceleration effect. The *N,N′*-dioxide also benefited the deprotonation process as a Brønsted base. The catalytic reaction could be performed on the gram-scale with retention of yield, diastereoselectivity, and enantioselectivity. The products that contained functional groups were ready for further manipulation. In addition, a possible catalytic model was proposed to explain the origin of the asymmetric induction.

Keywords: asymmetric catalysis · conjugate addition · enantioselectivity · ligand effects · zinc

Introduction

The addition reaction of carbanions that are stabilized by electron-withdrawing nitrile groups is a useful method for the formation of carbon–carbon bonds. Moreover, this reaction efficiently introduces nitrile groups, which are common functional groups in various bioactive natural products and pharmaceuticals.[1,2] The nitrile group could also undergo transformation into other functional groups, such as amines, amides, and carboxylic acids. Therefore, remarkable attention has been devoted to pursuing efficient methods for the construction of various optically active cyano-containing compounds. Nitrile-stabilized carbanions that are derived from active methylene compounds that contain two electron-withdrawing groups, such as cyanoacetate esters,[3] malononitrile,[4] and cyano ketones,[5] have been extensively investigated in asymmetric nucleophilic addition reactions (Scheme 1a). Comparatively, much less progress has been made in the direct addition of aryl-substituted acetonitriles, owing to the relatively weak acidity and coordination ability of phenylacetonitrile.[6,8a] Strong bases or elevated temperatures are required to grab the α protons.[7] One variant is the incorporation of electron-poor aryl groups onto phenylacetonitrile, which increases the acidity of the α protons,[8,9] thereby allowing the direct nucleophilic addition reaction to proceed under milder reaction conditions (Scheme 1b).



Scheme 1. Representative strategies for the direct conjugate-addition reaction of acetonitrile derivatives. EWG = electron-withdrawing group.

The pioneering work in the direct asymmetric conjugate-addition reaction of nitrophenylacetonitriles to α,β-unsaturated aldehydes was reported by Ruano and co-workers, by using prolinol ethers as organocatalysts.[10] Up to 90% *ee* values and moderate diastereoselectivities were achieved. Subsequently, the Kim group achieved the corresponding reactions between α,β-unsaturated ketones and cinnamaldehyde in moderate diastereo- and enantioselectivities.[11] However, efficient catalyst systems to expand the scope of electrophiles and enhance the stereoselectivity are still desirable and challenging. Benzylidene malonates are classic Michael acceptors. Nevertheless, in the presence of a strong base, the reaction of alkylidene malonates with electron-deficient phenylacetonitriles resulted in the formation of α-cyanostilbene derivatives, instead of the desired adducts.[7c] Herein, we report a direct asymmetric conjugate-addition reaction of arylacetonitriles to a variety of alkylidene malonates. The combination of a chiral *N,N′*-dioxide and zinc(II) triflimidate exhibited high reactivity and stereoinduction,

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thereby generating the targeted adducts in good yields (up to 98%), with excellent diastereoselectivities (up to >99:1 d.r.) and enantioselectivities (up to 99% *ee*). Notably, excess *N,N′*-dioxide was used as a proton scavenger instead of a basic additive in most cases. The triflimidate counterion outperformed triflate and basic ions,[12] which provides an interesting perspective on the use of chiral metal-triflimidate complexes in asymmetric reactions.

Results and Discussion

Initially, our investigation was based on the model reaction between 4-nitrophenylacetonitrile (**1a**, $pK_a = 12.3$)[8b] and diethyl benzylidene malonate (**2a**), with various *N,N′*-dioxide/metal complexes as catalysts.[13] A screening of various metals[14] indicated that few metals worked well with L-ramipril-derived ligand **L1** in CH_2Cl_2 at 35°C (Table 1, entries 1–8). For example, the complexes of $Sc(OTf)_3$, $Y(OTf)_3$, and $Co(acac)_2$ gave low yields. Although the complex of $Ni(acac)_2$, which contained a basic counterion (this might be helpful for the α-deprotonation of arylacetonitrile **1a**),[9] provided the desired product (**3a**) with satisfactory reactivity, albeit with poor enantioselectivity (Table 1, entry 4). Chiral complex **L1**/$Zn(OTf)_2$ afforded higher stereoselectivity than **L1**/$Mg(OTf)_2$, albeit a lower yield of the product (**3a**; Table 1, entry 6 versus entry 5) was obtained. Interestingly, the introduction of a triflimidate counterion, which was highly delocalized and positive charged, appeared to enhance the Lewis acidity of the zinc(II) cation. The **L1**/$Zn(NTf_2)_2$ catalyst afforded an improved yield of 50%, with slightly lower stereoselectivity (87:13 d.r., 71% *ee*; Table 1, entry 8). To improve the reactivity and enantioselectivity of this reaction, various chiral *N,N′*-dioxide ligands were surveyed (Figure 1) on coordination with $Zn(NTf_2)_2$. Notably, bulky substituents at the *ortho* position of the aniline moiety in the ligands had a significant effect on the stereoselectivity and reactivity of the conjugate-addition reaction (Table 1, entries 9–11). Ligands **L2** and **L3**, which contained less-sterically hindered substituents at the phenyl rings, afforded extremely low yields and stereoselectivities (Table 1, entries 9 and 10), whereas ligand **L4**, which was decorated with *tert*-butyl groups, and ligand **L5**, which contained isopropyl groups and a two-carbonic linkage, gave trace amounts of the product with opposite diastereoselectivities (Table 1, entries 11 and 12). With respect to the chiral backbone of the ligands, L-ramipril-derived ligand **L1** exhibited advantages in terms of higher yield and enantioselectivity compared with both ligand **L6**, which was derived from L-proline, and ligands **L7** and **L8**, which were derived from L-pipecolic acid. In addition, these latter two ligands generated the products with reversed enantioselectivity (Table 1, entries 13–15). Moreover, the **L8**/$Zn(NTf_2)_2$ complex promoted the reaction in 40% yield, 96:4 d.r., and 69% *ee* (Table 1, entry 15). To further improve the yield, the concentration of the reaction mixture was investigated. To our delight, the yield was dramatically increased to 99%, with retention of stereoselectivity, on decreasing the volume of solvent (Table 1, entry 16). However, under solvent-free conditions, both the yield and enantioselectivity deteriorated significantly (Table 1, entry 16). Thus, the **L1**/$Zn(NTf_2)_2$ complex and 1.0 M of compound **2a** were chosen to assess other reaction parameters.

The reaction temperature and solvent were found to notably affect the enantioselectivity of this reaction (Table 2). Decreasing the reaction temperature led to higher enantioselectivities and diastereoselectivities (up to 84% *ee* and 92:8 d.r.), but lower yields (Table 2, entries 1–3). Taking the influence of temperature on the activity and enantioselectivity into consideration, 15°C was selected as the optimum temperature. Next, various solvents were tested in the presence of the **L1**/$Zn(NTf_2)_2$ catalyst at 15°C. Aprotic solvents, such as CH_2Cl_2 and toluene, afforded the products in acceptable yields and selectivities (Table 2, entries 1–4). Oxygen-

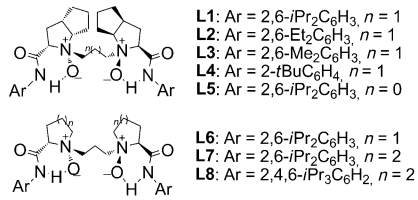
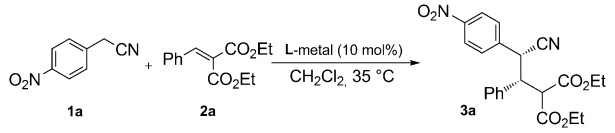


Figure 1. Chiral ligands that were used in the study.

Table 1. Screening of various central metals and ligands in the asymmetric conjugate addition of compound **1a** to compound **2a**.

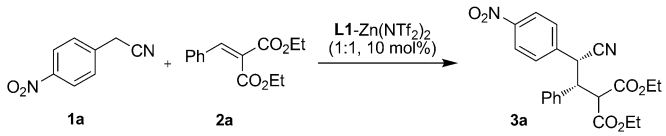


1a 2a 3a

Entry[a]	Ligand	Metal	Yield [%][b]	d.r.[c]	*ee* [%][c]
1	**L1**	$Sc(OTf)_3$	n.r.[d]	–	–
2	**L1**	$Y(OTf)_3$	13	40:60	11
3	**L1**	$Co(acac)_2$	trace	90:10	9
4	**L1**	$Ni(acac)_2$	61	87:13	9
5	**L1**	$Mg(OTf)_2$	51	75:25	41
6	**L1**	$Zn(OTf)_2$	34	95:5	73
7	**L1**	$Zn(ClO_4)_2{\cdot}6H_2O$	15	95:5	74
8	**L1**	$Zn(NTf_2)_2$	50	87:13	71
9	**L2**	$Zn(NTf_2)_2$	15	86:14	9
10	**L3**	$Zn(NTf_2)_2$	n.r.[d]	–	–
11	**L4**	$Zn(NTf_2)_2$	trace	34:66	63
12	**L5**	$Zn(NTf_2)_2$	trace	38:62	39
13	**L6**	$Zn(NTf_2)_2$	12	>99:1	23
14	**L7**	$Zn(NTf_2)_2$	35	92:8	57[e]
15	**L8**	$Zn(NTf_2)_2$	40	93:7	69[e]
16[f]	**L1**	$Zn(NTf_2)_2$	99	87:13	71
17[g]	**L1**	$Zn(NTf_2)_2$	80	85:15	37

[a] Unless otherwise stated, the reactions were carried out with a *N,N′*-dioxide/metal catalyst (1:1, 10 mol%), compound **1a** (0.1 mmol), and compound **2a** (0.1 mmol) in CH_2Cl_2 (0.5 mL) at 35°C for 2 days; [b] yield of the isolated product; [c] determined by HPLC analysis; the *ee* value refers to the *syn* isomer; [d] no reaction; [e] with reversed enantioselectivity; [f] 0.1 mL of the solvent was used; [g] the reaction was performed under solvent-free conditions; acac = acetylacetonate, Tf = trifluoromethanesulfonate.

Table 2. Effects of temperature and solvent on the asymmetric conjugate-addition reaction.



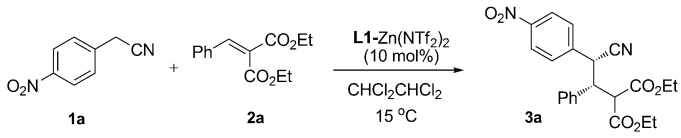
Entry[a]	T [°C]	Solvent	Yield [%][b]	d.r.[c]	*ee* [%][c]
1	35	CH_2Cl_2	99	87:13	71
2	15	CH_2Cl_2	95	92:8	82
3	0	CH_2Cl_2	40	92:8	84
4	15	toluene	66	92:8	78
5[d]	15	Et_2O	trace	n.d.	n.d.
6[d]	15	THF	trace	n.d.	n.d.
7[d]	15	MeOH	trace	n.d.	n.d.
8	15	DMF	20	76:24	0
9	15	$CHCl_3$	61	94:6	88
10	15	CH_2ClCH_2Cl	66	92:8	85
11	15	$CHCl_2CH_2Cl$	70	94:6	87
12	15	$CHCl_2CHCl_2$	60	95:5	92

[a] Reaction conditions: *N,N′*-dioxide-**L1**/$Zn(NTf_2)_2$ (1:1, 10 mol%), compound **1a** (0.2 mmol), and compound **2a** (0.1 mmol) were stirred in solvent (0.1 mL) for 2 days; [b] yield of the isolated product; [c] determined by HPLC analysis; the *ee* value refers to the major isomer; [d] not detected.

containing solvents, such as Et_2O, THF, and MeOH, gave trace amounts of the product (Table 2, entries 5–8). Accordingly, a detailed screen of various haloalkane solvents was conducted (Table 2, entries 9–12). Pleasingly, $CHCl_2CHCl_2$ could further improve the enantioselectivity to 92% *ee*, although the yield was somewhat decreased (60% yield; Table 2, entry 12).

The molar ratio of ligand **L1** to the central metal was another important factor in determining the reactivity of the reaction. As shown in Table 3, it was clear that a small excess of ligand **L1** over $Zn(NTf_2)_2$ had a positive effect on the reaction rate. The optimal ratio of ligand **L1** to $Zn(NTf_2)_2$ was confirmed to be 1.5:1, which gave the product in 98% yield, 95:5 d.r., and 92% *ee* (Table 3, entry 2). Further increasing the ratio of the ligand to the metal resulted in lower yields (Table 3, entry 1). When $Zn(NTf_2)_2$ was present in small excess, the reaction was completely suppressed (Table 3, entry 5). If Et_3N was subjected to the above system, the yield recovered with good diastereo- and enantioselectivities (Table 3, entry 6). These results implied that the *N,N′*-dioxide ligand could assist the deprotonation process as a Brønsted base. In addition, neither $Zn(NTf_2)_2$ or ligand **L1** alone could promote the reaction, which indicated the operation of a ligand-acceleration phenomenon (Table 3, entry 6). Thus, the best results were obtained by using the **L1**/$Zn(NTf_2)_2$ complex (1.5:1, 10 mol%), 4-nitrophenylacetonitrile (**1a**, 0.2 mmol), and diethyl benzylidene malonate (**2a**, 0.1 mmol) in $CHCl_2CHCl_2$ (0.1 mL) at 15°C.

Table 3. Effect of the **L1**/$Zn(NTf_2)_2$ ratio on the asymmetric conjugate-addition reaction.

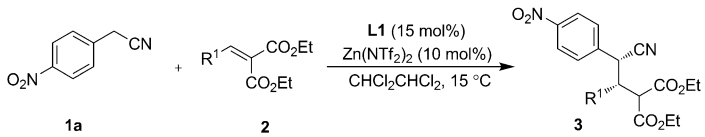


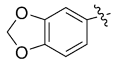
Entry[a]	**L1**/$Zn(NTf_2)_2$	Yield [%][b]	d.r.[c]	*ee* [%][c]
1	2:1	90	96:4	92
2	1.5:1	98	95:5	92
3	1.2:1	90	95:5	92
4	1:1	60	95:5	92
5	0.9:1	n.r.[d]	–	–
6[e]	0.9:1	84	93:7	84
7[f]	–	n.r.[d]	–	–

[a] Reaction conditions, unless otherwise stated: *N,N′*-dioxide-**L1**/$Zn(NTf_2)_2$ (10 mol%), compound **1a** (0.2 mmol), and compound **2a** (0.1 mmol) were stirred in $CHCl_2CHCl_2$ (0.1 mL) at 15°C for 2 days; [b] yield of the isolated product; [c] determined by HPLC analysis; [d] no reaction; [e] 35°C, with Et_3N (0.1 equiv) as an additive; [f] without chiral ligand **L1** or $Zn(NTf_2)_2$.

Under the optimized conditions, an exploration of the scope of the Michael acceptor revealed that a considerable number of alkylidene malonates were well-tolerated. As shown in Table 4, alkylidene malonates with either electron-withdrawing or electron-donating substituents on the aro-

Table 4. Scope of the alkylidene malonate in the asymmetric conjugation-addition reaction of compound **1a**.



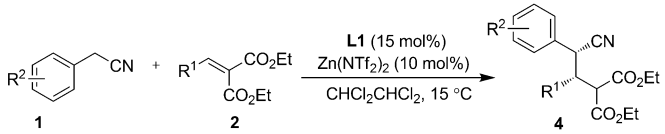
Entry[a]	R^1	Product	t [h]	Yield [%][b]	d.r.[c]	*ee* [%][c]
1	Ph	**3a**	44	98	95:5	92
2	2-FC_6H_4	**3b**	44	96	97:3	98
3	3-FC_6H_4	**3c**	24	98	95:5	93
4	4-FC_6H_4	**3d**	24	98	92:8	88
5	2,6-$F_2C_6H_3$	**3e**	44	90	95:5	99
6	2-ClC_6H_4	**3f**	96	60	98:2	97
7[d]	2-ClC_6H_4	**3f**	40	80	98:2	93
8	3-ClC_6H_4	**3g**	24	98	93:7	91
9	4-ClC_6H_4	**3h**	24	96	92:8	85
10	2,4-$Cl_2C_6H_3$	**3i**	92	75	95:5	93 (1*R*,2*R*)
11	3,4-$Cl_2C_6H_3$	**3j**	24	94	89:11	88
12	3-BrC_6H_4	**3k**	24	90	94:6	93
13	4-BrC_6H_4	**3l**	24	88	93:7	85
14	3-MeC_6H_4	**3m**	44	95	94:6	93
15	4-MeC_6H_4	**3n**	44	94	95:5	92
16	3-$CF_3C_6H_4$	**3o**	24	96	92:8	87
17	4-$CF_3C_6H_4$	**3p**	44	98	94:6	85
18	3-$MeOC_6H_4$	**3q**	48	94	95:5	91
19	4-$MeOC_6H_4$	**3r**	48	70	97:3	91
20		**3s**	48	90	94:6	92
21	2-naphthyl	**3t**	48	96	93:7	92
22[e]	2-thienyl	**3u**	48	80	81:19	81
23[e]	3-thienyl	**3v**	48	85	83:17	81
24[f]	cyclohexyl	**3w**	40	82	83:17	98
25[f]	*i*Pr	**3x**	40	70	88:12	92
26[f]	Et	**3y**	60	55	94:6	97

[a] Reaction conditions, unless otherwise stated: *N,N′*-dioxide-**L1**/$Zn(NTf_2)_2$ (1.5:1, 10 mol%), compound **1a** (0.2 mmol), and compound **2** (0.1 mmol) were stirred in $CHCl_2CHCl_2$ (0.1 mL) at 15°C for 2 days; [b] yield of the isolated product; [c] determined by HPLC analysis; the *ee* value refers to the major isomer; [d] at 35°C; [e] at 0°C; [f] Et_3N (0.1 equiv) was used as an additive.

matic ring provided their corresponding products in good yields and excellent diastereoselectivities and enantioselectivities (up to 98:2 d.r. and up to 99% *ee*; Table 4, entries 1–20). The reactions of substrates with *para*-electron-donating substituents gave slightly higher enantioselectivities than those with *para*-electron-withdrawing substituents (Table 3, entries 15, 19, and 20 versus 4, 9, 13, and 17). The positions of the substituents had a subtle influence on the enantio- and diastereoselectivities: *ortho* substitution was the best, followed by *meta* substitution (Table 4, entries 2–5, 6–11). The yield dropped significantly on increasing the steric bulk of the *ortho* substituents on the substrate, which could be compensated for by raising the reaction temperature, at the expense of slightly lower enantioselectivity (Table 1, entries 6 and 7). Moreover, a fused-ring substrate was well-tolerated, thus providing the addition product (**3t**) in 96% yield, with 93:7 d.r. and 92% *ee* (Table 4, entry 21). In addition, hetero-aryl-containing substrates were also competent for the addition of compound **1a** after lowering the reaction temperature to 0°C (Table 4, entries 22 and 23). Moreover, the reactions of alkyl-substituted substrates were stimulated by the addition of Et_3N, with up to 82% yield, 95:5 d.r., and 98% *ee* (Table 4, entries 24–26 and Supporting Information), as the result of the basicity of Et_3N, which was helpful for the deprotonation of the arylacetonitrile.

The scope of the arylacetonitrile was also explored to investigate the influence of electronic and steric effects of various substituents on the reactivity and stereoselectivity of the reaction (Table 5). 4-Cyanophenylacetonitrile (pK_a = 16.0)[8b] reacted in a similar manner to 4-nitrophenylacetonitrile, albeit in a lower yield (only up to 70%), because of its higher pK_a value than compound **1a** (Table 5, entries 1–4). The results demonstrated that the *para* substituent did not affect the stereoselectivity of the reaction. The reaction between 3-nitrophenylacetonitrile (pK_a = 18.1)[8b] and *para*-substituted alkylidene malonate **2d** gave a relatively higher *ee* value (Table 3, entry 6 versus Table 2, entry 4). Moreover, the reaction of 2-nitrophenylacetonitrile with compound **2** suffered from hindrance from the nitro group, thereby leading to moderate yields and enantioselectivities, but extremely high diastereoselectivities (Table 5, entries 7–9). We also examined the direct conjugate-addition reaction of phenylacetonitrile to compound **2a**. However, the desired product was not obtained; thus, the activation of arylacetonitriles by electron-withdrawing groups was necessary in this catalyst system.

Table 5. Scope of the arylacetonitrile in the asymmetric conjugate addition of compound **1** to compound **2**.



Entry[a]	R^1	R^2	Product	Yield [%][b]	d.r.[c]	*ee* [%][c]
1	Ph	4-CN	**4a**	64	93:7	94
2	2-FC_6H_4	4-CN	**4b**	46	>99:1	98
3	3-FC_6H_4	4-CN	**4c**	70	93:7	91
4	4-FC_6H_4	4-CN	**4d**	60	97:3	87
5[d,e]	Ph	3-NO_2	**4e**	64	83:17	87
6[d,e]	4-FC_6H_4	3-NO_2	**4f**	50	82:18	94
7[e]	Ph	2-NO_2	**4g**	51	>99:1	85
8[e]	3-FC_6H_4	2-NO_2	**4h**	61	>99:1	85
9[e]	4-FC_6H_4	2-NO_2	**4i**	60	>99:1	81
10[e]	Ph	H		n.r.[f]	–	–

[a] Reaction conditions, unless otherwise stated: *N,N'*-dioxide-**L1**/Zn-$(NTf_2)_2$ (1.5:1, 10 mol%), compound **1** (0.2 mmol), and compound **2** (0.1 mmol) were stirred in $CHCl_2CHCl_2$ (0.1 mL) at 15°C for 90 h; [b] yield of the isolated product; [c] determined by HPLC analysis; [d] ligand **L8** was used instead of ligand **L1**; [e] at 35°C, in the presence of 4 Å molecular sieves (10.0 mg); [f] no reaction.

The absolute configuration of the major isomer, *syn*-**3i**, was unambiguously determined to be *R,R* by single-crystal X-ray crystallographic analysis (Figure 2).[15]

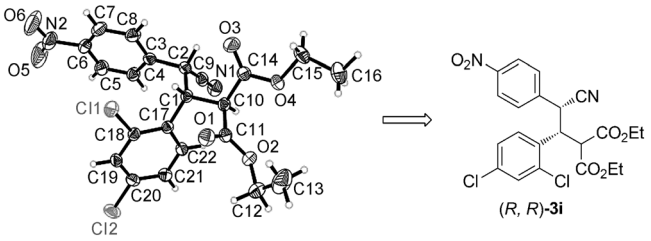
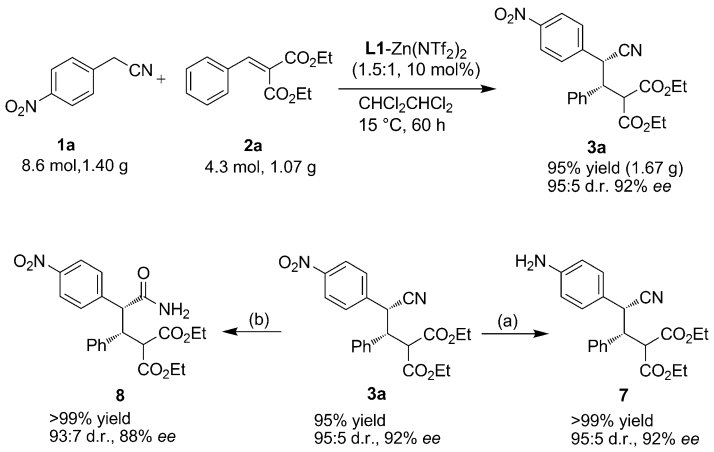


Figure 2. X-ray structure of product **3i**.

We also tested the reaction between ethyl 2-benzylidene-3-oxobutanoate and compound **1a**.[14] The corresponding product was generated in 38% yield, 57:43 d.r., and 82% and 79% *ee* for the two diastereomers. NMR analysis indicated that the β-nucleophilic addition reaction occurred in a highly stereocontrolled manner, whereas the selectivity of the proton-transfer process was low.

To determine the synthetic potential of this catalytic system, the reaction between diethyl benzylidene malonate (**2a**) and compound **1a** was performed on the gram scale under the optimized reaction conditions. Thus, the corresponding adduct (**3a**) was obtained without any loss of yield, diastereoselectivity, or enantioselectivity (Scheme 2). To evaluate the versatility of the functional groups in the product, several transformations started from product **3a** were carried out. The nitro group could be reduced into an amino group with almost complete conversion and retention of the stereoselectivity.[1b] The hydrolysis of the cyano group performed smoothly to afford an amide group in a solution of concentrated sulfuric acid in absolute EtOH.[16]

To gain insight into the reaction mechanism, the relationship between the enantiomeric excess of ligand **L7** and that of product **3a** was investigated (Figure 3).[14] A slightly positive nonlinear effect[17] was observed in either the presence or absence of an amine. The positive nonlinear effect became more obvious at a ligand-to-metal ratio of 1.5:1. These results suggested that minor oligomeric aggregates existed in the reaction system. The catalytic composition was



Scheme 2. Gram-scale synthesis of compound **3a** and its functional transformations: a) H_2 (6 MPa), PtO_2·xH_2O, HCl/EtOH, then K_2CO_3 (pH 9); b) enthanol, conc. H_2SO_4, then aqueous $NaHCO_3$.

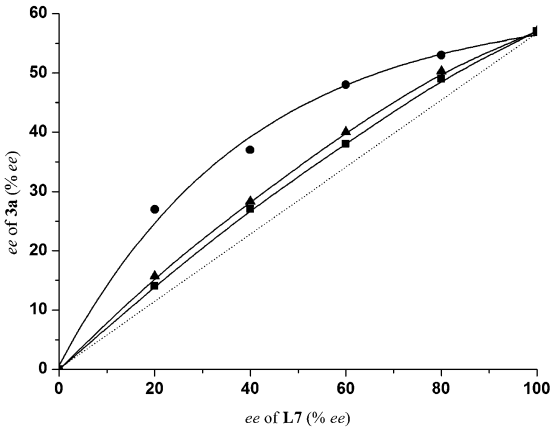


Figure 3. Nonlinear effects in the **L7**/$Zn(NTf_2)_2$-catalyzed reaction between compounds **1a** and **2a**: **L7**/$Zn(NTf_2)_2$ = 1:1 (■); **L7**/$Zn(NTf_2)_2$ = 1:1 (▲) with 0.05 equiv of Et_3N; **L7**/$Zn(NTf_2)_2$ = 1.5:1 (●).

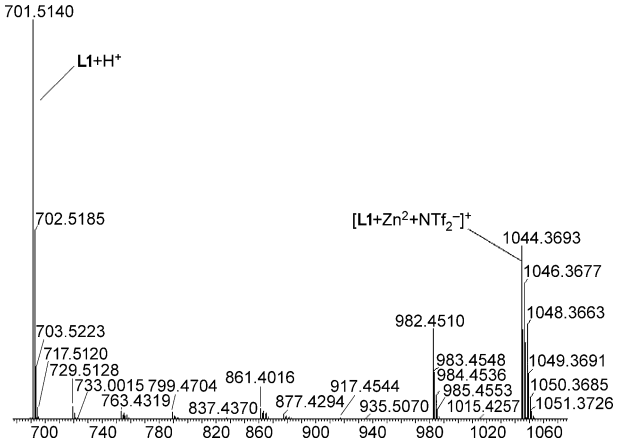
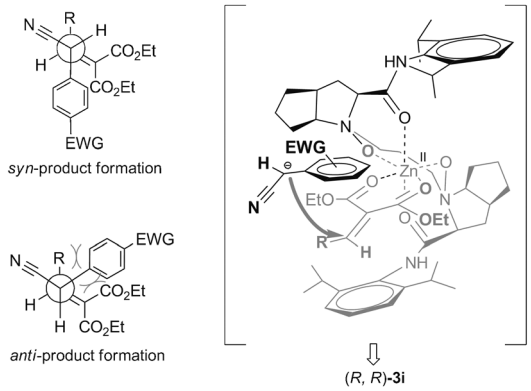


Figure 4. ESI-MS spectrum of the **L1**/$Zn(NTf_2)_2$ catalyst.



Scheme 3. Proposed catalytic model.

also investigated by using ESI-MS. The spectrum of a mixture of ligand **L1** and $Zn(NTf_2)_2$ in a 1.5:1 ratio in $CHCl_2CHCl_2$ at 35 °C showed a signal at *m*/*z* 1044.3693, which was assigned to the complex $[\mathbf{L1}+Zn^{2+}+NTf_2^-]^+$ (*m*/*z* calcd: 1044.3392; Figure 4). This major monomeric complex would function as the most-active and -effective catalytic intermediate.

Based on previous reports[13j,k] and on the absolute configuration of product **3i**, a possible catalytic model is proposed to explain the origin of the high diastereo- and enantioselectivities. As outlined in Scheme 3, the steric hindrance between the aryl group of the arylacetonitrile and the β-substituent and the ester group of the alkylidene malonate resulted in the predominant formation of the *syn* adduct. In the asymmetric process, *N,N′*-dioxide **L1** and alkylidene malonate **2i** coordinated to $Zn(NTf_2)_2$ to form a hexacoordinate intermediate. Assisted by free *N,N′*-dioxide **L1**, a benzylic carbon center was generated, which preferred to attack the *Re* face of Michael acceptor **2i**, thereby generating the observed product, (*R*,*R*)-**3i**.

Conclusion

In summary, we have reported a direct asymmetric conjugate-addition reaction between arylacetonitriles and alkylidene malonates under mild reaction conditions. A chiral *N,N′*-dioxide/zinc(II)-triflimidate complex was found to be efficient for this reaction and the corresponding adducts were afforded in good yields, with high levels of diastereo- and enantioselectivities. The *N,N′*-dioxide also worked as a Brønsted base to activate the arylacetonitriles, thereby providing their corresponding nitrile-stabilized carbanions. The high Lewis acidity of the metal triflimidate, combined with the privileged chiral *N,N′*-dioxide catalysts, are expected to find diverse applications in asymmetric synthesis.

Experimental Section

Typical procedure for the asymmetric conjugate addition of 4-nitrophenylacetonitrile (1a) to diethyl benzylidene malonate (2a): 4-Nitropheny-

lacetonitrile (**1a**, 32.4 mg, 0.2 mmol), $Zn(NTf_2)_2$ (6.3 mg, 0.01 mmol), *N,N′*-dioxide **L1** (10.5 mg, 0.015 mmol), and $CHCl_2CHCl_2$ (0.1 mL) were placed in a dry tube and the mixture was stirred at 35 °C under a N_2 atmosphere for 0.5 h. Then, diethyl benzylidene malonate (**2a**, 24.8 mg, 0.1 mmol) was added and the reaction was stirred at 15 °C and monitored by TLC. After compound **2a** had been completely consumed, the reaction mixture was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 5:1) to afford the desired product (**3a**) as light-yellow oil in 95% yield, 95:5 d.r., and 92% *ee*. The d.r. and *ee* values of compound **3a** were determined by chiral HPLC analysis on a Chiralcel AD-H column. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.8 Hz, 3H), 7.10 (d, J = 6.8 Hz, 2H), 6.90 (d, J = 7.2 Hz, 2H), 4.80 (d, J = 4.0 Hz, 1H), 4.28 (m, 2H), 4.20 (d, J = 11.6 Hz, 1H), 3.88–3.75 (m, 2H), 3.68 (m, 1H), 1.29 (t, J = 6.8 Hz, 3H), 0.81 ppm (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.09, 166.50, 147.64, 140.83, 133.48, 129.11, 129.05, 128.64, 128.43, 123.78, 117.63, 62.61, 61.83, 54.71, 49.44, 40.81, 14.05, 13.55 ppm; HRMS (ESI): *m/z* calcd for $C_{22}H_{22}N_2O_6$: 433.1376 $[M+Na]^+$; found: 433.1378.

Typical procedure for the scale-up reaction: 4-Nitrophenylacetonitrile (**1a**, 1.40 g, 8.6 mmol), $Zn(NTf_2)_2$ (271.0 mg, 0.43 mmol), *N,N′*-dioxide **L1** (451.5 mg, 0.65 mmol), and $CHCl_2CHCl_2$ (4.0 mL) were placed in a dry tube and the mixture was stirred at 35 °C under a N_2 atmosphere for 0.5 h. Then, diethyl benzylidene malonate (**2a**, 1.07 g, 4.3 mmol) was added and the reaction was stirred at 15 °C for 60 h. After removing the solvent under reduced pressure, the reaction mixture was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 5:1) to afford the desired product (**3a**) as a light-yellow oil (1.67 g, 95% yield, 95:5 d.r., 92% *ee*).

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