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Asymmetric direct vinylogous carbon–carbon bond formation catalyzed by bifunctional organocatalysts

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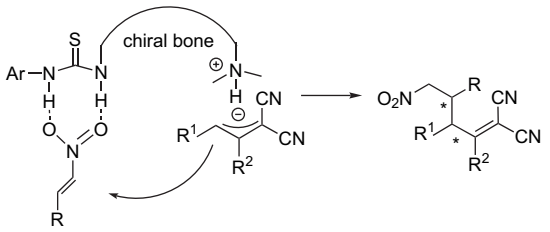
Abstract—The bifunctional chiral thiourea-tertiary amine organocatalysts have been applied to a direct asymmetric vinylogous Michael addition of α,α-dicyanoolefins to nitroolefins with 2–10 mol % catalyst loadings. The electronic properties of the thiourea-based catalysts have significant influences on this reaction. Moderate to excellent enantioselectivities (57–95% ee) have been achieved with low to good isolated yields through fine tuning the structures of the bifunctional organocatalysts. Much better ees were obtained for some α,α-dicyanoolefinic substrates compared with that catalyzed by modified cinchona alkaloids.

1. Introduction

The Michael addition of nucleophiles to electron-deficient olefins represents one of the best studied and versatile carbon–carbon bond construction strategies in synthetic organic chemistry. New stereocenters are often generated, and accordingly the asymmetric conjugate reaction is the subject of intensive research over the past decades.[1] Considerable efforts have been devoted to the Michael reactions by employing α-enolizable carbonyl compounds,[2] nitroalkanes,[3] and organometallic reagents[4] as the nucleophiles, however, expanding the scope of nucleophilic substrates is highly desirable. Recently we have established that the γ-allylic protons of α,α-dicyanoolefins are strongly acidic,[5] and subsequently direct vinylogous[6] additions of α,α-dicyanoolefins to nitroolefins, α,β-unsaturated aldehydes, α,β-unsaturated ketones, and *N*-Boc imines have been successfully developed, giving facile protocols to synthesize various multifunctional products with two vicinal stereocenters.[7] Although excellent enantioselectivity has been achieved in the Michael reactions of α,α-dicyanoolefins and nitroolefins catalyzed by modified cinchona alkaloids,[7a,b] the substrate scope of α,α-dicyanoolefins was generally limited to 1-tetralone derivatives. We envisioned that the catalytic system combining the synergistic activation of both the electrophiles and nucleophiles might improve the stereoselectivity. Recently bifunctional organocatalysts possessing thioureas (or ureas) and tertiary amine groups have received special attention,[8] and a number of highly enantioselective 1,2- or 1,4-addition reactions have been reported in the presence of such catalysts.[9] The double hydrogen-bonding interaction of N–H of thioureas (or ureas) and reactants has been generally recognized to have a specific role in the efficient catalysis and high enantiocontrol. As part of our continuing investigation on thiourea-based organocatalysis,[10] we realized that nitroolefin and α,α-dicyanoolefin should be concertedly activated by the thiourea-tertiary amine catalyst (Scheme 1). Here we would like to present the direct vinylogous Michael addition of α,α-dicyanoolefins to nitroolefins promoted by bifunctional thiourea-tertiary amine catalysts.



Scheme 1. Proposed reaction mode of α,α-dicyanoolefin to nitroolefin catalyzed by bifunctional thiourea-tertiary amine.

2. Results and discussion

Motivated by this idea, we first studied the reaction between α,α-dicyanoolefin **2a**, derived from 1-tetralone, and β-

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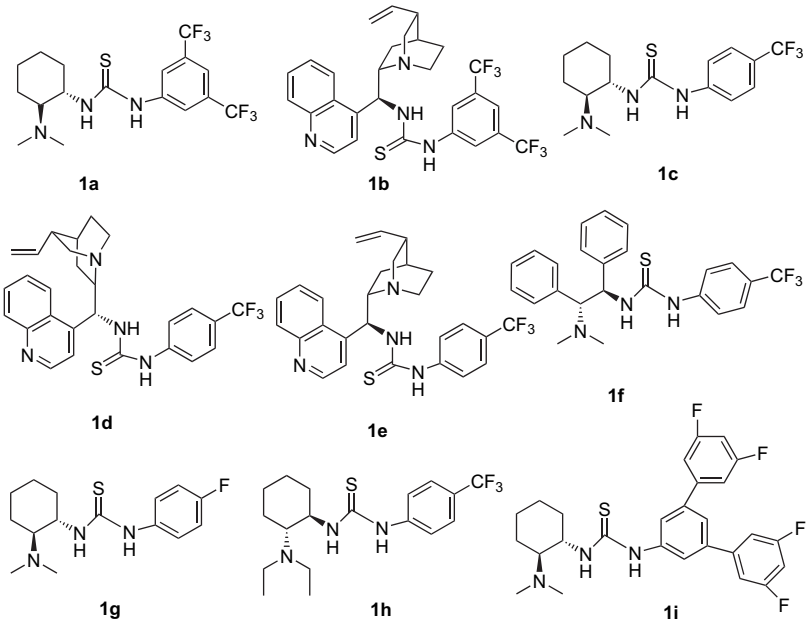
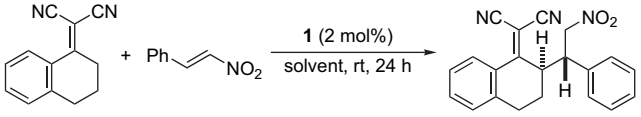


Figure 1. Structures of chiral thiourea-tertiary amine catalysts.

nitrostyrene **3a** in DCM catalyzed by 2 mol % of **1a** bearing a bis(trifluoromethyl)phenyl substituent (Fig. 1) at room temperature. The starting materials were smoothly consumed after 24 h, unfortunately, the desired addition product **4a** with complete anti-selectivity was isolated only in 18% yield due to the formation of large amount of unidentified insoluble byproducts, with 58% ee (Table 1, entry 1). Similar phenomena were observed in the case of catalyst **1b** derived from cinchonidine (entry 2). We ascribed the formation of the byproducts to the polymerization[11] because of the strong electron-withdrawing effects of the thiourea group on nitrostyrene, so better results might be expected in the reactions catalyzed by the thiourea catalysts with lower electron-withdrawing ability.[12] We were pleased to find that the isolated yield was indeed improved, though still low, catalyzed by **1c** with a 4-trifluoromethylphenyl group. More gratifyingly, much higher enantioselectivity (82% ee) was obtained (entry 3). Therefore, other similar bifunctional catalysts **1d**–**1f** with various chiral scaffolds were tested (entries 4–6), and the results were found to be inferior to that of **1c**. In addition, slightly lower ee (78%) was received catalyzed by **1g** with a 4-fluorophenyl substitution compared with that of **1c** (entry 7). The more bulky catalysts **1h** and **1i** also gave lower enantioselectivity in the model reaction (entries 8 and 9). Subsequently, some solvents were screened (entries 10–13), and the ees were dramatically decreased in THF and acetone (entries 12 and 13). Finally we conducted the Michael addition in DCM at 0 °C with 5 mol % of **1c**. The side reactions could be further inhibited, and good isolated yield (64%) was obtained with slightly elevated ee (86%) after 48 h, while some starting material still remained unchanged.

Table 1. Screening studies of vinylogous Michael addition of α,α-dicyanoolefin **2a** to nitrostyrene **3a**[a]



2a **3a** **4a**

Entry	Catalyst	Solvent	*t* (h)	Yield[b] (%)	ee[c] (%)
1	**1a**	DCM	24	18	58
2	**1b**	DCM	24	20	55
3	**1c**	DCM	24	44	82
4	**1d**	DCM	24	37	−68[d]
5	**1e**	DCM	24	64	72
6	**1f**	DCM	24	38	−25[d]
7	**1g**	DCM	24	52	78
8	**1h**	DCM	24	26	−68[d]
9	**1i**	DCM	24	43	65
10	**1c**	Toluene	24	33	83
11	**1c**	DCE	24	53	75
12	**1c**	THF	24	63	36
13	**1c**	Acetone	24	76	48
14[e]	**1c**	DCM	48	64	86

[a] Otherwise noted, the reaction was conducted with 0.12 mmol of **2a** and 0.1 mmol of **3a** in the presence of 2 mol % of **1** in 1 mL solvent at room temperature for 24 h.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis. The absolute configuration was determined by comparison with the authentic sample.[7a]
[d] Product with the opposite configuration was obtained.
[e] At 0 °C with 5 mol % of **1c** for 48 h.

With the optimal reaction conditions in hand, the scope and limitation of the bifunctional thiourea-tertiary amine **1c** catalyzed vinylogous Michael addition were probed using a range of α,α-dicyanoolefins (Fig. 2) and nitroolefins with 5 mol % of **1c**. The results are summarized in Table 2. In general, only one diastereomer was detected in the reactions.

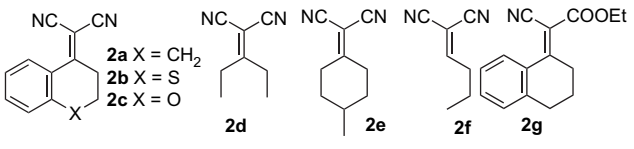


Figure 2. Structures of various α,α-dicyanoolefins.

Table 2. Asymmetric vinylogous Michael addition of α,α-dicyanoolefins **2** to nitroolefins **3**[a]

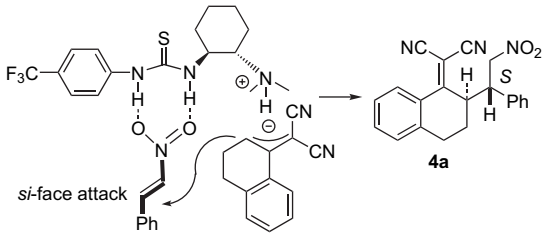
2 **3** **4**

Entry	2	R	T (°C)	t (h)	Conversion of **3**[b] (%)	Yield[c] (%)	ee[d] (%)
1	**2a**	Ph (**3a**)	0	48	77	64 (**4a**)	86
2	**2a**	*p*-MeO–Ph (**3b**)	0	48	60	49 (**4b**)	89
3[b]	**2a**	*p*-Me–Ph (**3c**)	0	48	80	70 (**4c**)	88
4	**2a**	*p*-Cl–Ph (**3d**)	0	48	61	47 (**4d**)	88
5[e]	**2a**	*p*-Cl–Ph (**3d**)	0	24	87	43 (**4d**)	86
6	**2a**	*p*-Br–Ph (**3e**)	0	48	57	45 (**4e**)	89
7	**2a**	*p*-Me_2N–Ph (**3f**)	0	48	72	65 (**4f**)	91
8	**2a**	2-Furanyl (**3g**)	0	48	44	35 (**4g**)	88
9	**2b**	*p*-MeO–Ph (**3b**)	0	24	—	65 (**4h**)	86
10	**2b**	*p*-MeO–Ph (**3b**)	−40	72	63	54 (**4h**)	95
11	**2b**	Ph (**3a**)	−40	72	75	66 (**4i**)	94
12	**2b**	*p*-Me_2N–Ph (**3f**)	−40	72	60	52 (**4j**)	94
13	**2b**	2-Furanyl (**3g**)	−40	72	74	64 (**4k**)	90
14[f]	**2c**	Ph (**3a**)	−10	48	—	89 (**4l**)	85
15[f]	**2c**	Ph (**3a**)	−40	72	45	36 (**4l**)	92
16[f]	**2d**	Ph (**3a**)	0	72	58	31 (**4m**)	63
17[g]	**2e**	Ph (**3a**)	0	72	56	24 (**4n**)	57
18[g]	**2f**	Ph (**3a**)	0	72	77	22 (**4o**)	81
19[e]	**2b**	*i*-Propyl (**3h**)	0	72	85	21 (**4p**)	69

[a] Otherwise noted, the reaction was conducted with 0.12 mmol of **2** and 0.1 mmol of **3** catalyzed by 5 mol % of **1c** in 1 mL DCM.
[b] Conversion was determined based on recovered nitroolefin.
[c] Isolated yield.
[d] Determined by chiral HPLC analysis.
[e] With 10 mol % of (*R*,*R*)-**1c**.
[f] With 5 mol % of (*R*,*R*)-**1c**.
[g] With 10 mol % of **1e**.

Various nitrostyrenes **3a**–**3f** with electron-donating or -withdrawing substituents could smoothly react with α,α-dicyanoolefin **2a** at 0 °C (Table 2, entries 1–7). High enantioselectivities were generally observed, and the isolated yields were moderate due to the incomplete conversion of the substrates after 48 h. Increasing the catalytic loading (10 mol %) did not give better results probably due to the polymerization side reaction (entry 4 vs 5). A good ee was also obtained for furanyl derivative **3g** (entry 8). Sulfur-containing substrate **2b** displayed better reactivity, and good yield with 86% ee was received in the reaction of **3b** at 0 °C after 24 h (entry 9). The reactions of **2b** with nitrostyrenes could be conducted at much lower temperature, and excellent ees (90–95%) were obtained with moderate yields at −40 °C for 72 h (entries 9–12).[13] While a modest ee (74%) was obtained in the reaction of **2c** and nitrostyrene **3a** catalyzed by modified cinchona alkaloid,[7a] current catalytic conditions gave better results, and 85% ee with 89% yield was obtained at −10 °C in 48 h (entry 14). Moreover, the enantioselectivity could be further improved to 92% at −40 °C, while the yield was not satisfying (entry 15). On the other hand, α,α-dicyanoolefins **2d**–**2f** derived from aliphatic ketones and aldehydes were tested at 0 °C with 10 mol % of **1e**. Sluggish reactivity was generally observed, and low isolated yields were obtained. The ee (63%) was moderate in the reaction of acyclic substrate **2d** and **3a** (entry 16). The desymmetrization of cyclic substrate **2e** was attempted, and only one diastereomer with three chiral carbon centers was isolated, while the ee was also poor (entry 17). Notably the aliphatic aldehyde derivative **2f** showed better conversion, and high ee (81%) was achieved while the yield was low (entry 18). The nitroolefin **3h** with alkyl substitution also exhibited low reactivity in the reaction with **2b** in the presence of 10 mol % of **1c**, and a modest ee was obtained (entry 19). In addition, we found that the activated olefin **2g** showed good reactivity with nitrostyrene **3a** catalyzed by **1c**, unfortunately, the racemic product was obtained.[14]

Based on the absolute configuration of **4a**, a plausible catalytic reaction model was proposed.[9d] As outlined in Scheme 2, nitroolefin **3a** and α,α-dicyanoolefin **2a** would be concertedly activated by thiourea and tertiary amine groups. Then vinylogous Michael addition could take place from the *si*-face of **2a**, giving the adduct **4a** with (*S*)-configuration in the benzylic carbon. In addition, trans-structures were generally generated in the exclusive diastereoselectivity owing to the steric reason.



Scheme 2. Transition-state model of vinylogous Michael addition.

3. Conclusion

In conclusion, we have demonstrated that the bifunctional chiral thiourea-tertiary amine compounds were effective organocatalysts in the direct asymmetric vinylogous Michael addition of α,α-dicyanoolefins to nitroolefins. The reactions displayed high regio- and diastereoselectivities, and moderate to excellent enantioselectivities (57–95% ee) have been achieved with low to good isolated yields. Moreover, much better ees were obtained for some α,α-dicyanoolefinic substrates compared with that catalyzed by modified cinchona alkaloids. Moderate enantioselectivities with low yields were obtained using aliphatic α,α-dicyanoolefin or alkyl-substituted nitroolefin as the substrate, and studies are underway to improve these reactions.

4. Experimental

4.1. General

Melting points were determined in open capillaries and are uncorrected. TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (200–300 mesh) eluting with ethyl acetate and petroleum ether. NMR was recorded on Bruker 200, 300 or 400 MHz spectrometers. Chemical shifts are reported in parts per million downfield from tetramethylsilane with the solvent resonance as the internal standard. Enantiomeric excess was determined by HPLC analysis on Chiralpak OD or AS column. DCM was distilled from CaH_2. All other reagents were used as commercially available without purification.

4.1.1. General procedures for the synthesis of bifunctional catalysts 1a–li. To the *N*′,*N*′-disubstituted diamine (2 mmol) in dry DCM (10 mL) was added a solution of aryl isothiocyanate (2.5 mmol) in dry DCM (5 mL). After stirred at room temperature for 2 h, the reaction mixture was concentrated under vacuum. The residue was purified by column chromatography on silica gel (DCM/MeOH) to give the desired thiourea-tertiary amine compound. Catalysts **1a** and **1b** have been reported.[10]

Catalyst ***1c***. Mp: 64–66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.50–7.41 (m, 4H), 4.12 (br s, 1H), 2.76 (br s, 1H), 2.43 (s, 6H), 2.26 (s, 1H), 1.90 (d, J=13.2 Hz, 1H), 1.83 (d, J=12.8 Hz, 1H), 1.71 (d, J=12.8 Hz, 1H), 1.31–1.13 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 180.6, 141.8, 125.9, 123.0, 121.3, 116.8, 67.2, 55.0, 39.8, 32.5, 24.4, 24.3, 22.2; IR (KBr) ν 3275, 2937, 1540, 1325, 1117, 1067, 841, 715 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{22}F_3N_3S$ 345.1487, found 345.1476; $[\alpha]_D^{20}$ +96.0 (*c* 0.1, EtOAc).

Catalyst ***1d***. Mp: 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (d, J=4.4 Hz, 1H), 8.27 (br s, 1H), 8.12 (d, J=8.0 Hz, 1H), 7.69 (t, J=7.2 Hz, 1H), 7.60–7.53 (m, 4H), 7.41 (d, J=14.8 Hz, 2H), 7.30 (d, J=4.4 Hz, 1H), 5.83–5.70 (br s, 2H), 5.26–5.03 (m, 2H), 3.26–3.05 (m, 1H), 2.97–2.83 (m, 4H), 2.33–2.27 (m, 1H), 1.55–1.44 (m, 2H), 1.34–1.12 (m, 1H), 0.93–0.86 (m, 1H), 0.84–0.72 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 181.0, 150.0, 148.6, 141.6, 132.2, 132.0, 130.4, 129.5, 128.7, 128.5, 127.0, 126.3, 123.6, 123.3, 120.7, 119.4, 115.6, 61.6, 48.7, 47.1, 38.8, 37.7, 28.1, 27.2, 25.9, 24.9; IR (KBr) ν 3446, 2928, 1540, 1324, 1118, 1067, 843, 757 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{28}F_3N_4S$ (M+H) 497.1981, found 497.1974; $[\alpha]_D^{20}$ +203.0 (*c* 0.1, EtOAc).

Catalyst ***1e***. Mp: 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.89 (d, J=15.2 Hz, 1H), 8.40 (br s, 1H), 8.16 (d, J=7.6 Hz, 1H), 7.76 (t, J=7.2 Hz, 1H), 7.71–7.69 (m, 4H), 7.43 (d, J=8.4 Hz, 2H), 7.37 (d, J=4.4 Hz, 1H), 5.81 (br s, 1H), 5.71–5.63 (m, 1H), 5.03–4.95 (m, 2H), 3.25–3.15 (m, 3H), 2.80 (br s, 2H), 2.33 (m, 1H), 1.72–1.65 (m, 2H), 1.38–1.31 (m, 1H), 0.98 (br s, 1H), 0.90–0.83 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) 180.7, 150.1, 149.9, 148.6, 140.4, 130.5, 129.4, 129.3, 127.0, 126.8, 126.5, 123.8, 123.6, 123.4, 122.5, 61.5, 56.6, 55.1, 41.2, 39.1, 27.3, 27.1, 25.5; IR (KBr) ν 3280, 2940, 1540, 1324, 1119, 1067, 842, 760 cm^{-1}; HRMS (EI) calcd for $C_{27}H_{27}F_3N_4S$ 496.1909, found 496.1900; $[\alpha]_D^{20}$ −75.0 (*c* 0.1, EtOAc).

Catalyst ***1f***. Mp: 88–90 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 8.07 (s, 1H), 7.61 (d, J=8.4 Hz, 2H), 7.39 (d, J=8.2 Hz, 2H), 7.30–7.24 (m, 3H), 7.15 (br s, 5H), 7.08–7.05 (m, 2H), 5.36 (br s, 1H), 3.76 (d, J=10.8 Hz, 1H), 2.20 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 180.4, 141.1, 139.6, 131.8, 129.9, 125.5, 128.1, 128.0, 127.9, 127.6, 127.4, 126.6, 125.8, 123.6, 122.2, 74.1, 59.3, 40.7; IR (CH_2Cl_2) ν 3264, 2940, 2871, 2835, 2790, 1521, 1456, 1325, 1162, 1125 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{25}F_3N_3S$ (M+H) 444.1716, found 444.1740; $[\alpha]_D^{20}$ +170.5 (*c* 0.4, $CHCl_3$).

Catalyst ***1g***. Mp: 52–54 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.20–7.09 (m, 2H), 7.00–6.95 (m, 2H), 6.87–6.77 (br s, 1H), 3.82 (s, 1H), 2.58 (br s, 1H), 2.30 (t, J=10.8 Hz, 1H), 2.15 (s, 6H), 1.77 (t, J=9.2 Hz, 2H), 1.62 (d, J=13.6 Hz, 1H), 1.31–1.07 (m, 4H), 1.05–0.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 180.2, 163.0, 158.1, 126.9, 126.8, 116.2, 115.8, 66.7, 55.9, 39.8, 32.8, 25.0, 24.5, 21.4; IR (KBr) ν 3222, 2934, 2860, 1508, 1222, 833, 796 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{22}FN_3S$ 295.1518, found 295.1512; $[\alpha]_D^{20}$ +42.5 (*c* 0.2, EtOAc).

Catalyst ***1h***. Mp: 72–74 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.61 (d, J=8.4 Hz, 2H), 7.49 (d, J=8.0 Hz, 2H), 4.02 (br s, 1H), 2.82–2.72 (m, 4H), 2.46 (m, 3H), 1.89 (t, J=14.4 Hz, 2H), 1.76 (d, J=14.4 Hz, 1H), 1.40–1.10 (m, 5H), 1.04 (t, J=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 180.2, 140.9, 126.6, 126.5, 126.4, 123.4, 121.2, 63.7, 55.7, 43.8, 32.5, 29.6, 25.3, 24.4, 23.6, 13.4; IR (KBr) ν 3221, 2934, 2859, 1616, 1523, 1324, 1166, 1122, 1067, 1015, 841, 716, 594 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{27}F_3N_3S$ (M+H) 374.1872, found 374.1878; $[\alpha]_D^{20}$ −91.0 (*c* 0.1, EtOAc).

Catalyst ***1i***. Mp: 122–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.62 (s, 2H), 7.42 (s, 1H), 7.24 (s, 1H), 7.11–7.06 (m, 3H), 6.81–6.73 (m, 2H), 4.28 (br s, 1H), 2.82–2.60 (m, 3H), 2.45 (s, 6H), 2.07–1.87 (m, 2H), 1.76–1.73 (d, J=13.2 Hz, 1H), 1.39–1.31 (m, 2H), 1.27–1.14 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 165.8, 160.6, 143.2, 140.5, 139.5, 122.3, 110.3, 109.7, 103.6, 103.1, 102.6, 66.9, 55.6, 39.8, 32.7, 24.7, 24.4, 21.7; IR (KBr) ν 3445, 2933, 1624, 1591, 1542, 1120, 990, 849 cm^{-1}; HRMS (EI) calcd for $C_{27}H_{27}F_4N_3S$ 501.1862, found 501.1853; $[\alpha]_D^{20}$ +28.0 (*c* 0.2, EtOAc).

4.1.2. General procedure for asymmetric direct vinylogous Michael reaction. Catalyst **1c** (0.005 mmol, 5 mol %), nitroolefin **3** (0.1 mmol), and 4 Å MS (30 mg) were stirred in dry DCM (0.5 mL) and cooled to the desired temperature under argon. Then α,α-dicyanoolefin **2** (0.12 mmol) in dry DCM (0.5 mL) was added. After the stated reaction time, the product was purified by flash chromatography on silica gel (ethyl acetate/petroleum) to give the addition product. The enantiomeric excess was determined by HPLC analysis on chiral column. The absolute configuration of **4a** was determined by comparison with the authentic sample reported early (through ^{1}H NMR and HPLC analysis),[7a] and other products were assigned accordingly. The characterization of the new addition products has been shown below.

4.1.2.1. 2-[3-(1-*p*-Methoxy-phenyl-2-nitroethyl)-thiochroman-4-ylidene]-malononitrile (4h). Mp: 176–178 °C; yield: 54%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.94 (d, J=8.0 Hz, 1H), 7.50 (t, J=8.0 Hz, 1H), 7.32–7.24 (m, 4H), 6.93 (d, J=9.6 Hz, 2H), 4.68 (dd, J=12.8, 10.4 Hz, 1H), 4.33 (dd, J=12.4, 4.8 Hz, 1H), 3.81 (s, 3H), 3.77 (m, 1H), 3.68 (td, J=11.6, 3.2 Hz, 1H), 3.33 (dd, J=14.0, 3.2 Hz, 1H), 2.67 (dd, J=13.6, 3.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 170.8, 143.2, 134.5, 131.6, 130.4, 130.3, 129.5, 129.1, 129.0, 127.4, 126.3, 125.3, 116.7, 114.9, 114.5, 78.1, 55.3, 42.9, 41.8, 29.1, 29.0; IR (KBr) ν 3363, 2208, 1641, 1514, 1286, 1250, 1180, 841, 755 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}N_3O_3SNa$ (M+Na) 414.0833, found 414.0891; $[\alpha]_D^{20}$

+511.0 (*c* 0.10, EtOAc), 95% ee was determined by HPLC on OD column, 40% 2-propanol/hexane, 1.0 mL/min, UV 254 nm, t_{major}=12.3 min, t_{minor}=36.9 min.

4.1.2.2. 2-{3-[1-(4-Dimethylamino-phenyl)-2-nitro-ethyl]-thiochroman-4-ylidene}-malononitrile (4j). Mp: 185–187 °C; yield: 52%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.93 (d, *J*=8.0 Hz, 1H), 7.48 (t, *J*=7.6 Hz, 1H), 7.30 (d, *J*=8.4 Hz, 1H), 7.23–7.27 (m, 1H), 7.18 (d, *J*=8.4 Hz, 2H), 6.69 (d, *J*=8.4 Hz, 2H), 4.66 (dd, *J*=12.0, 9.2 Hz, 1H), 4.32 (dd, *J*=12.4, 4.4 Hz, 1H), 3.65–3.75 (m, 2H), 3.31 (dd, *J*=14.0, 3.2 Hz, 1H), 2.96 (s, 6H), 2.73 (dd, *J*=14.0, 3.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 171.0, 150.6, 136.2, 134.4, 130.4, 128.6, 127.3, 125.1, 124.5, 121.8, 112.7, 112.6, 82.7, 78.2, 42.9, 42.0, 40.3, 29.1; IR (KBr) ν 3429, 2919, 2235, 1615, 1562, 1528, 1435, 1367, 814, 773, 742 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{20}N_4O_2SNa$ (M+Na) 427.1199, found 427.1213; $[\alpha]_D^{20}$ +435.0 (*c* 0.10, EtOAc), 94% ee was determined by HPLC on OD column, 30% 2-propanol/hexane, 1.0 mL/min, UV 254 nm, t_{major}=12.7 min, t_{minor}=39.1 min.

4.1.2.3. 2-[3-(1-Furan-2-yl-2-nitroethyl)-thiochroman-4-ylidene]-malononitrile (4k). Mp: 158–160 °C; yield: 64%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.89 (d, *J*=8.0 Hz, 1H), 7.50–7.45 (m, 2H), 7.30–7.23 (m, 2H), 6.42 (d, *J*=3.2 Hz, 1H), 6.36 (m, 1H), 4.77 (dd, *J*=12.4, 9.6 Hz, 1H), 4.30 (dd, *J*=12.8, 4.8 Hz, 1H), 3.94 (m, 1H), 3.87 (td, *J*=11.2, 3.6 Hz, 1H), 3.41 (dd, *J*=14.0, 3.6 Hz, 1H), 2.73 (dd, *J*=14.0, 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 169.7, 144.3, 143.6, 134.4, 130.3, 129.1, 127.3, 126.4, 125.3, 112.7, 111.7, 111.0, 110.7, 75.8, 39.5, 37.9, 29.7, 29.2, 28.7; IR (KBr) ν 3467, 3346, 2923, 2230, 1561, 1429, 1379, 1016, 777, 756, 735 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{13}N_3O_3SNa$ (M+Na) 374.0570, found 374.0564; $[\alpha]_D^{20}$ +633.0 (*c* 0.20, EtOAc), 90% ee was determined by HPLC on AS column, 30% 2-propanol/hexane, 1.0 mL/min, UV 254 nm, t_{major}=15.1 min, t_{minor}=29.0 min.

4.1.2.4. 2-[3-(1-Phenyl-2-nitroethyl)-chroman-4-yl-idene]-malononitrile (4l). Mp: 108–110 °C; yield: 36%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.25 (d, *J*=8.4 Hz, 1H), 7.61 (t, *J*=7.6 Hz, 1H), 7.45–7.36 (m, 3H), 7.32 (m, 2H), 7.15 (t, *J*=7.6 Hz, 1H), 7.06 (d, *J*=8.4 Hz, 1H), 4.85 (dd, *J*=13.2, 10.4 Hz, 1H), 4.51 (dd, *J*=12.8, 5.2 Hz, 1H), 4.09 (m, 2H), 3.73 (td, *J*=10.8, 5.6 Hz, 1H), 3.31 (d, *J*=11.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 165.2, 156.0, 137.6, 129.6, 129.0, 128.1, 127.9, 122.4, 118.5, 114.9, 113.1, 112.8, 77.5, 66.5, 43.5, 43.0; IR (KBr) ν 3421, 2917, 2223, 1608, 1553, 1480, 1454, 1327, 1259, 1219, 767, 751, 702 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{15}N_3O_3Na$ (M+Na) 368.1006, found 368.1009; $[\alpha]_D^{20}$ −160.0 (*c* 0.10, EtOAc), 92% ee was determined by HPLC on OD column, 40% 2-propanol/hexane, 1.0 mL/min, UV 254 nm, t_{minor}=12.3 min, t_{major}=14.0 min.

4.1.2.5. 2-[2-(1-Phenyl-2-nitroethyl)-2-tolyl-1-ethyl-1-ylidene]-malononitrile (4m). Mp: 92–94 °C; yield: 31%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.42–7.33 (m, 3H), 7.23 (m, 2H), 4.64 (dd, *J*=12.8, 10.4 Hz, 1H), 4.39 (dd, *J*=12.4, 4.8 Hz, 1H), 3.55 (td, *J*=10.8, 4.8 Hz, 1H), 3.38 (m, 1H), 2.73–2.55 (m, 2H), 1.38 (t, *J*=8.0 Hz, 3H), 1.00 (d, *J*=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 187.6, 135.8, 129.5, 128.8, 128.0, 111.4, 111.1, 88.1, 78.6, 47.7, 44.9, 25.7, 16.7, 14.0; IR (KBr) ν 3446, 2986, 2234, 1557, 1435, 1378, 760, 702 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{17}N_3O_2Na$ (M+Na) 306.1213, found 306.1217; $[\alpha]_D^{20}$ +71.4 (*c* 0.14, EtOAc), 63% ee was determined by HPLC on OD column, 40% 2-propanol/hexane, 1.0 mL/min, UV 254 nm, t_{minor}=9.2 min, t_{major}=10.8 min.

4.1.2.6. 2-[2-(1-Phenyl-2-nitroethyl)-4-tolyl-cyclo-hexan-1-ylidene]-malononitrile (4n). Mp: 128–130 °C; yield: 24%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.43–7.33 (m, 3H), 7.25 (m, 2H), 4.64 (dd, *J*=12.4, 10.8 Hz, 1H), 4.34 (dd, *J*=12.8, 4.8 Hz, 1H), 3.87 (td, *J*=10.8, 4.8 Hz, 1H), 3.34 (d, *J*=11.6 Hz, 1H), 3.09 (d, *J*=12.8 Hz, 1H), 2.66 (td, *J*=14.0, 5.6 Hz, 1H), 2.16 (m, 1H), 2.00 (m, 1H), 1.53 (d, *J*=14.0 Hz, 1H), 1.29–1.21 (m, 1H), 1.19–1.09 (m, 1H), 0.81 (d, *J*=6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 184.6, 135.9, 129.5, 128.7, 127.7, 111.3, 110.9, 85.2, 78.4, 46.3, 45.2, 38.0, 36.3, 31.3, 25.8, 20.7; IR (KBr) ν 3382, 2961, 2929, 2235, 1595, 1455, 1379, 763, 701, 599 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{19}N_3O_2Na$ (M+Na) 332.1369, found 332.1372; $[\alpha]_D^{20}$ −30.8 (*c* 0.13, EtOAc), 57% ee was determined by HPLC on AS column, 20% 2-propanol/hexane, 1.0 mL/min, UV 254 nm, t_{major}=12.6 min, t_{minor}=15.3 min.

4.1.2.7. 2-[2-(1-Phenyl-2-nitroethyl)-2-ethyl-1-yl-idene]-malononitrile (4o). Mp: 94–96 °C; yield: 22%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.42–7.33 (m, 3H), 7.19 (m, 2H), 7.14 (d, *J*=11.2 Hz, 1H), 4.64 (dd, *J*=12.8, 9.2 Hz, 1H), 4.54 (dd, *J*=12.8, 6.0 Hz, 1H), 3.57 (m, 1H), 3.01 (m, 1H), 1.57–1.50 (m, 1H), 1.38–1.28 (m, 1H), 0.84 (t, *J*=7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ (ppm) 169.0, 135.6, 129.5, 128.8, 128.0, 111.3, 110.3, 92.1, 78.4, 48.5, 47.3, 29.7, 25.0, 11.2; IR (KBr) ν 3447, 2964, 2927, 2240, 1557, 1383, 1201, 763, 697, 643, 580 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{15}N_3O_2Na$ (M+Na) 292.1056, found 292.1046; $[\alpha]_D^{20}$ −83.3 (*c* 0.03, EtOAc), 81% ee was determined by HPLC on OD column, 20% 2-propanol/hexane, 1.0 mL/min, UV 254 nm, t_{minor}=20.9 min, t_{major}=29.1 min.

4.1.2.8. 2-[3-(1-Isopropyl-2-nitroethyl)-thiochroman-4-ylidene]-malononitrile (4p). Mp: 156–158 °C; yield: 21%; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.80 (d, *J*=8.7 Hz, 1H), 7.42 (t, *J*=8.4 Hz, 1H), 7.19 (m, 2H), 4.38 (dd, *J*=13.5, 3.9 Hz, 1H), 4.16 (dd, *J*=13.5, 6.6 Hz, 1H), 3.56–3.47 (m, 2H), 3.20 (dd, *J*=14.7, 4.2 Hz, 1H), 2.70 (m, 1H), 2.22 (m, 1H), 1.06 (d, *J*=6.9 Hz, 3H), 0.94 (d, *J*=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 171.1, 137.2, 134.0, 130.9, 126.9, 125.3, 125.1, 112.8, 112.6, 74.3, 41.3, 39.9, 29.7, 28.8, 27.3, 20.7, 15.7; IR (KBr) ν 3445, 2965, 2229, 1555, 1434, 768, 737 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}N_3O_2SNa$ (M+Na) 350.0934, found 350.0931; $[\alpha]_D^{20}$ −241.2 (*c* 0.04, EtOAc), 69% ee was determined by HPLC on OD column, 40% 2-propanol/hexane, 1.0 mL/min, UV 254 nm, t_{minor}=7.9 min, t_{major}=30.1 min.

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Supplementary data

HPLC chromatograms of the Michael addition products. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.04.011.

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14. Although the formation of racemic product from **2g** and **3a** catalyzed by **1c** is not clear yet, the following plausible catalytic model might account for the observed results.