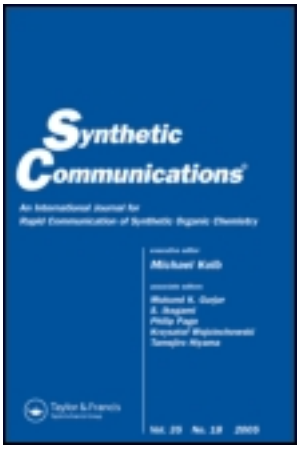

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ASYMMETRIC DIRECT VINYLOGOUS MICHAEL REACTION CATALYZED BY SELF-ASSEMBLED ORGANOCATALYST

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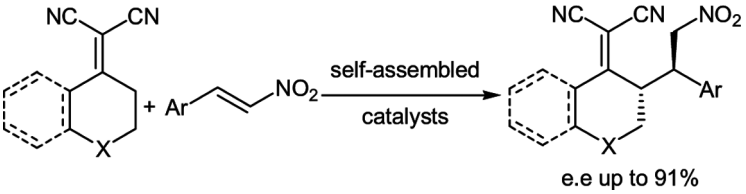
GRAPHICAL ABSTRACT



Abstract *The self-assembled organocatalyst of cinchona alkaloid derivatives and amino acids has been applied to a direct asymmetric vinylogous Michael addition of α,α-dicyanoolefins to nitroolefins; the corresponding products could be obtained in moderate to good yields and enantioselectivities.*

Keywords Dicyanoolefins; enantioselective Michael addition; nitroolefins; organocatalyst; self-assembled

INTRODUCTION

The Michael addition of nucleophiles to electron-deficient olefins is one of the most important carbon–carbon bond-construction strategies in synthetic organic chemistry.[1] Because new stereocenters are often generated, considerable efforts have been devoted to the asymmetric Michael reactions over past decades.[2] Recently, it has been found that α,α-dicyanoolefin compounds can selectively behave as acceptors or vinylogous donors in asymmetric Michael reactions in the presence of organocatalysts, which simultaneously give multifunctional products with two vicinal chiral tertiary carbon centers.[3]

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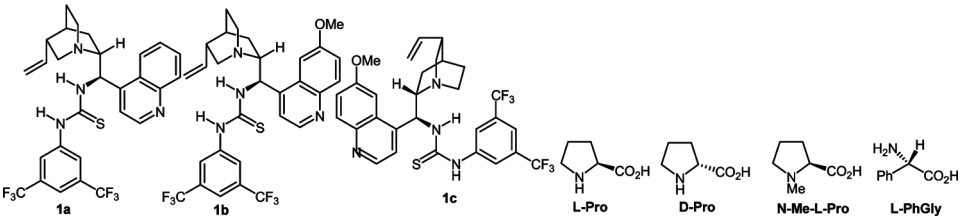
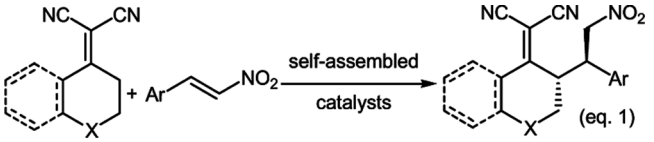


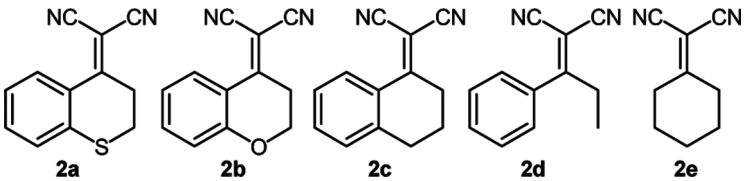
Scheme 1. Representative precatalyst modules.

Nowadays bifunctional organocatalysts possessing thioureas (or ureas) and tertiary amine groups have received special attention, for the double hydrogen-bonding interaction of N–H of thioureas (or ureas) and reactants has been generally recognized as having a specific role in the efficient catalysis and high enantiocontrol.[4] In the presence of such catalysts, the asymmetric direct vinylogous Michael reaction of nitroolefin and α,α-dicyanoolefin could provide one of the most versatile and attractive approaches for the generation of optically active compounds. However, when the cinchona alkaloid derivatives bearing a thiourea functionality were used as the catalysts, only moderate enantioselectivities were achieved in the Michael reaction of nitroolefin and α,α-dicyanoolefin.[3c] Very recently, the concept of self-assembly has been successfully employed to construct combinatorial chiral catalysts.[5] Herein, we report the results of asymmetric direct vinylogous Michael reaction in the presence of self-assembled organocatalyst of cinchona alkaloid derivatives and amino acids [Eq. (1)].



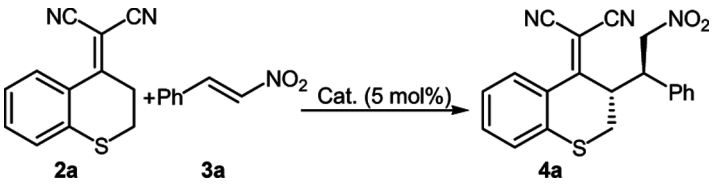
Our initial studies began with reaction of vinyl malononitrile **2a** and nitroolefin **3a** in the presence of a catalytic amount of self-assembled organocatalyst of cinchona alkaloid derivatives **1a–c** and amino acids Schemes 1 and 2. Readily available α-amino acids, such as proline, glycine, alanine, phenylglycine, valine, and phenylalanine, were screened. Some typical results are summarized in Table 1.

The results of the investigation revealed that the reaction could proceed smoothly to yield the desired products in dichloromethane (DCM). However, the enantioselectivities varied greatly depending on the Cinchona alkaloid derivatives



Scheme 2. Structures of vinylmalononitriles **2**.

Table 1. Screening studies of vinylogous Michael addition reaction[a]



2a 3a 4a

Entry	Catalyst	Solvent	Temp. (°C)	Time (h)	Conversion	Ee (%) [b]
1	L-Pro/1a	DCM	rt	30	78	58
2	L-Pro/1b	DCM	rt	30	70	55
3	L-Pro/1c	DCM	rt	30	81	72
4	D-Pro/1a	DCM	rt	30	85	50
5	D-Pro/1b	DCM	rt	30	65	40
6	D-Pro/1c	DCM	rt	30	73	44
7	N-Me-L-Pro/1a	DCM	rt	30	88	18
8	N-Me-L-Pro/1b	DCM	rt	30	86	17
9	N-Me-L-Pro/1c	DCM	rt	30	91	10
10	L-PhGly/1a	DCM	rt	30	41	66
11	L-PhGly/1b	DCM	rt	30	40	44
12	L-PhGly/1c	DCM	rt	30	38	23
13	L-Pro/1c	THF	rt	30	82	89
14	L-Pro/1c	Toluene	rt	30	30	45
15	L-Pro/1c	Acetone	rt	30	70	56
16	L-Pro/1c	EA	rt	30	78	58
17	L-Pro/1c	MeOH	rt	30	91	20
18	L-Pro/1c	Et_2O	rt	30	92	60
19	L-Pro/1c	THF	0	36	64	88

[a]The reaction was carried out on a 0.5-mmol scale.
[b]Determined by chiral HPLC analysis (Chiralcel AS).

and amino acids used (Table 1, entries 1–12). The self-assembled organocatalyst L-Pro (**1c**) proved to be the most promising catalyst, giving the corresponding product with 81% yield and 72% ee at room temperature (Table 1, entry 3).

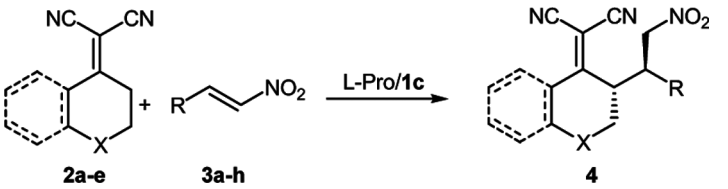
Therefore, the self-assembled organocatalyst L-Pro(**1c**) was selected for the subsequent studies. We next investigated the effect of the reaction medium, reaction temperature, and catalyst loading in the presence of a catalytic amount of L-Pro (**1c**). It was found that the reaction proceeded smoothly in both nonpolar solvent and polar protic solvent. The most encouraging result was obtained when the reaction was carried out in tetrahydrofuran (THF) (Table 1, entry 13). No significant increase in the yield and enantioselectivity (85% yield, 88% ee) was found by increasing the catalyst amount to 10 mol%; however, inferior result (61% yield, 74% ee) was obtained with lower catalyst (2 mol%) loading at the same reaction conditions. By lowering the temperature to 0 °C, the desired product was obtained in comparable ee and poor yield (Table 1, entry 19); for convenience, the reactions for the rest of this study were conducted at room temperature. Therefore, the optimum reaction conditions were achieved by performing the reaction of 1 equiv. of dicyanoolefin with 1.2 equiv. of nitroolefin and 5 mol% catalyst loading at room temperature in THF.

To examine the scope of the direct vinylogous Michael addition reactions in the presence of self-assembled organocatalyst L-Pro(**1c**), a series of α,α-vinylmalononitriles (Scheme) and nitroolefins were evaluated under the optimized reaction conditions, and the results are summarized in Table 2. In most of the cases, the reactions proceeded smoothly to furnish the corresponding products in good yields and high enantioselectivities, and only the *anti*-products were detected in the reactions.

As shown in Table 2, various nitrostyrenes with electron-donating or electron-withdrawing substituents could smoothly react with α,α-dicyanoolefins. Meanwhile, regardless of the alkyl- and aryl- or heteroaryl-substituted nitrostyrenes, the reaction proceeded smoothly to afford the Michael adducts with good diastereoselectivities and enantioselectivities. This method offers several advantages such as good diastereo- and enantioselectivity, good conversions, cleaner reaction profiles, and simple experimental and workup procedures.

A possible mechanism for the enantioselective direct vinylogous Michael addition reaction of vinylmalononitriles to nitrostyrene is shown in Scheme 3. First, a self-assembled organocatalyst was formed by ionic interaction of proline and chiral

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



2a-e **3a-h** **4**

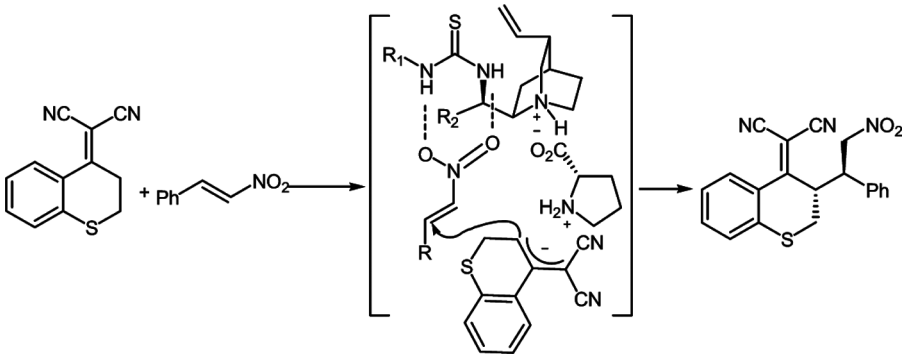
Entry	2	R	Product	Yield (%) [b]	Ee (%) [c]
1	**2a**	Ph (**3a**)	**4aa**	82	89
2	**2a**	4-$MeOC_6H_4$(**3b**)	**4ab**	65	85
3	**2a**	2-Furanyl (**3c**)	**4ac**	58	90
4	**2a**	4-$Me_2NC_6H_4$ (**3d**)	**4ad**	64	91
5	**2a**	i-Propyl (**3e**)	**4ae**	35	61
6	**2b**	Ph (**3a**)	**4ba**	80	88
7	**2b**	4-$MeOC_6H_4$ (**3b**)	**4bb**	62	89
8	**2c**	Ph (**3a**)	**4ca**	78	85
9	**2c**	4-$MeOC_6H_4$ (**3b**)	**4cb**	60	80
10	**2c**	4-$Me_2NC_6H_4$ (**3d**)	**4cd**	56	86
11	**2c**	4-MeC_6H_4 (**3f**)	**4cf**	76	82
12	**2c**	4-ClC_6H_4 (**3g**)	**4cg**	80	88
13	**2c**	4-BrC_6H_4 (**3h**)	**4ch**	81	85
14	**2d**	Ph (**3a**)	**4da**	65	71
15	**2e**	4-$MeOC_6H_4$ (**3b**)	**4eb**	63	63

[a]The reaction was carried out on a 0.5-mmol scale in THF at rt.

[b]Isolated yields.

[c]Determined by chiral HPLC analysis.

[d]All the products are characterized by ^{1}HNMR, ^{13}C NMR, FTIR, and mass spectrometry, and the absolute configurations of products were assigned by comparison with optical rotation and/or retention time on chiral HPLC with the literature value.[3d,3f]



Scheme 3. Possible mechanism of the vinylogous Michael reaction.

thiourea, which incorporated both the proline reaction center and stereocontrolling moiety. Nitroolefin was activated by the double hydrogen-bonding interaction of N–H of chiral thiourea; meanwhile the deprotonation of α,α-dicyanoolefin could occur in the presence of proline. Then vinylogous Michael addition could take place from α,α-dicyanoolefin to nitroolefin, giving the corresponding product with good diastereo- and enantioselectivity.

In summary, we have found that a self-assembled organocatalyst of proline and chiral thiourea can catalyze direct vinylogous Michael reaction at room temperature with good diastereo- and enantioselectivities. These results demonstrate the enormous effect of the thiourea and proline on the reactivity and selectivity. More detailed studies on the mechanism and synthetic applications of this self-assembled catalyst for enantioselective organocatalytic reactions are currently under investigation.

EXPERIMENTAL

Proton nuclear magnetic resonance spectra (^{1}H NMR) and carbon nuclear magnetic resonance spectra (^{13}C NMR) were obtained for solution in $CDCl_3$ with Me_4Si as internal standard on a Bruker Avance DPX 300 spectrometer. Infrared (IR) Spectra were obtained on a Nicolet Fourier tranform (FT)–IR500 spectrophotometer using KBr pellets. Optical rotations were measured in CH_2Cl_2 on a Schmidt + Haensdch polarimeter (Polartronic MH8) with a 1-cm cell (*c* given in g/100 mL). Mass spectral analyses were carried out on a VG 7035 micromass mass spectrophotometer.

General Procedure

A mixture of **2** (0.5 mmol), **3** (0.6 mmol), **1c** (0.025 mmol), and proline (0.02 5 mmol) in THF (1 mL) was stirred for 30 h at rt. Then the reaction was quenched by adding 0.5 mL 1 M HCl. The mixture was extracted with EtOAc and dried with anhydrous sodium sulfate. The crude product was purified by column chromatography on silica gel to give the desired product **4.**

2-[3-(1-Phenyl-2-nitroethyl)-thiochroman-4-ylidene]-malononitrile (4aa)

$[\alpha] = -648$ (c 0.15, $CHCl_3$); ^1H NMR($CDCl_3$, 400 MHz): δ 7.95 (d, $J = 8.0$ Hz, 1H), 7.53–7.27 (m, 8H), 4.73 (dd, $J = 10.0$, 12.6 Hz, 1H), 4.36 (dd, $J = 4.9$, 12.6 Hz, 1H), 3.88–3.81 (m, 1H), 3.77–3.72 (m, 1H), 3.35(dd, $J = 3.2$, 13.9 Hz, 1H), 2.63 (dd, $J = 3.2$, 14.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.4, 137.9, 135.3, 134.6, 130.4, 129.6, 129.1, 127.9, 127.4, 125.4, 124.3, 112.7, 112.5, 83.0, 77.9, 43.5, 41.6, 28.9; IR (KBr): ν 2226, 1556, 1460 cm^{-1}; MS: $C_{20}H_{15}N_3O_2S$ 361.09 $[M]^+$. The enantiomeric ratio was determined by high-performance liquid chromatography (HPLC) on a Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), t minor = 18.756 min, t major = 26.674 min.

2-[3-(1-p-Methoxy-phenyl-2-nitroethyl)-thiochroman-4-ylidene]-malononitrile (4ab)

$[\alpha]_D^{22} = -464$ (c 0.11, EA); ^1H NMR ($CDCl_3$, 400 MHz): δ7.92 (d, $J = 8.2$ Hz, 1H), 7.51 (t, $J = 7.8$ Hz, 1H), 7.34-7.29 (m, 4H), 6.94 (d, $J = 8.8$ Hz, 2H), 4.70 (dd, $J = 10.2$, 12.6 Hz, 1H), 4.34 (dd, $J = 4.8$, 12.6 Hz, 1H), 3.82 (s, 3H), 3.78–3.69 (m, 1H), 3.66–3.58 (m, 1H), 3.34 (dd, $J = 3.2$, 13.8 Hz, 1H), 2.65 (dd, $J = 3.1$, 13.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.6, 143.3, 134.6, 131.6, 130.5, 130.3, 129.6, 129.1, 127.8, 127.4, 125.4, 124.3, 112.8, 112.5, 83.1, 77.8, 55.6, 42.9, 41.6, 28.9; IR (KBr): ν2216, 1640, 1518 cm^{-1}; MS: $C_{21}H_{17}N_3O_3S$ 391.46 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), t minor = 20.156 min, t major = 27.678 min.

2-[3-(1-Furan-2-yl-2-nitroethyl)-thiochroman-4-ylidene]-malononitrile (4ac)

$[\alpha]_D^{22} = -582$ (c 0.11, EA); ^1H NMR($CDCl_3$, 400 MHz): δ 7.91 (d, $J = 8.1$ Hz, 1H), 7.52–7.48 (m, 2H), 7.31–7.24 (m, 2H), 6.45 (d, J 3.9 Hz, 1H), 6.37–6.35 (m, 1H), 4.75 (dd, $J = 9.8$, 12.6 Hz, 1H), 4.31 (dd, J = 4.6, 12.8 Hz, 1H), 3.98–3.84 (m, 1H), 3.84–3.78 (m, 1H), 3.39(dd, $J = 3.4$, 13.9 Hz, 1H), 2.69 (dd, $J = 3.4$, 14.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ170.2, 144.6, 143.7, 134.3, 130.4, 129.1, 127.3, 126.5, 112.8, 111.7, 111.2, 110.8, 82.9, 76.8, 39.8, 37.9, 28.7; IR (KBr): ν 2228, 1562, 1432 cm^{-1}; MS: $C_{18}H_{13}N_3O_3S$ 351.41 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), t minor = 14.856 min, t major = 23.694 min.

2-{3-[1-(4-Dimethylamino-phenyl)-2-nitroethyl]-thiochroman-4-ylidene}-malononitrile (4ad)

$[\alpha]_D^{22} = -388$ (c 0.11, EA); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.02 (d, $J = 8.1$ Hz, 1H), 7.46 (t, $J = 7.7$ Hz, 1H), 7.32 (d, $J = 8.5$ Hz, 1H), 7.29–7.24 (m, 1H), 7.20 (d, $J = 8.5$ Hz, 2H), 6.71 (d, $J = 8.5$ Hz, 2H), 4.68 (dd, $J = 9.6$, 12.1 Hz, 1H), 4.31

(dd, $J = 4.6$, 12.6 Hz, 1H), 3.84-3.68 (m, 2H), 3.32 (dd, $J = 3.2$, 13.9 Hz, 1H), 2.95 (s, 6H), 2.72 (dd, $J = 3.4$, 14.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.8, 150.5, 136.3, 134.5, 130.4, 128.6, 127.4, 125.2, 124.4, 121.9, 112.7, 112.6, 81.9, 78.3, 43.1, 42.3, 40.1, 28.9; IR (KBr): ν 2225, 1623, 1558 cm^{-1}; MS: $C_{22}H_{20}N_4O_2S$ 404.52 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak OD column (20% 2-propanol/hexane, 1 mL/min), t minor = 18.928 min, t major = 29.621 min.

2-[3-(1-Isopropyl-2-nitroethyl)-thiochroman-4-ylidene]-malononitrile (4ae)

$[\alpha]_D^{22} = +201$ (c 0.09, EA); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.85 (d, $J = 8.5$ Hz, 1H), 7.48 (t, $J = 8.2$ Hz, 1H), 7.25–7.18 (m, 2H), 4.42 (dd, $J = 4.6$, 13.2 Hz, 1H), 4.21 (dd, $J = 6.6$, 13.6 Hz, 1H), 3.57–3.46 (m, 2H), 3.23–3.19 (m, 1H), 2.88–2.69 (m, 1H), 2.29–2.20 (m, 1H), 1.04 (d, $J = 6.9$ Hz, 3H), 0.95(d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.3, 137.2, 134.1, 130.9, 126.9, 125.4, 125.2, 112.8, 112.6, 78.9, 74.5, 42.1, 39.8, 29.8, 27.4, 20.7; IR (KBr): ν 2228, 1562, 1438 cm^{-1}; MS: $C_{17}H_{17}N_3O_2S$ 327.42 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak OD column (30% 2-propanol/hexane, 1 mL/min), t major = 10.674 min, t minor = 28.456 min.

2-[3-(1-Phenyl-2-nitroethyl)-chroman-4-ylidene]-malononitrile (4ba)

$[\alpha]_D^{22} = +172$ (c 0.12, EA); ^{1}H NMR($CDCl_3$, 400 MHz): δ 8.25 (d, $J = 8.2$ Hz, 1H), 7.61 (t, $J = 7.8$ Hz, 1H), 7.51–7.44 (m, 3H), 7.39–7.36 (m, 2H), 7.15 (t, $J = 7.7$ Hz, 1H), 7.06 (d, $J = 4.2$ Hz, 1H), 4.87–4.63 (m, 1H), 4.61–4.48 (m, 1H), 4.14–4.05 (m, 2H), 3.76–3.69 (m, 1H), 3.45 (d, $J = 6.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.3, 156.1, 137.7, 135.4, 129.7, 129.1, 128.1, 127.9, 122.5, 118.5, 114.9, 113.1, 112.8, 78.9, 77.5, 66.6, 43.5, 42.9; IR (KBr): ν 2224, 1612, 1556 cm^{-1}; MS: $C_{20}H_{15}N_3O_3$ 345.36 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak OD column (20% 2-propanol/hexane, 1 mL/min), t major = 20.674 min, t minor = 26.756 min.

2-[3-(1-p-Methoxy-phenyl-2-nitroethyl)-chroman-4-ylidene]-malononitrile (4bb)

$[\alpha]_D^{22} = -198$ (c 0.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.18 (d, $J = 8.2$ Hz, 1H), 7.66–7.59 (m, 1H), 7.21 (d, $J = 8.5$ Hz, 2H), 7.19–7.15 (m, 1H), 7.06(d, $J = 8.5$ Hz, 2H), 6.98 (d, $J = 8.3$ Hz, 1H), 4.86–4.78 (m, 1H), 4.48 (dd, $J = 4.8$, 12.6 Hz, 1H), 4.15-4.05 (m, 2H), 3.82 (s, 3H), 3.75–3.69 (m, 1H), 3.41 (d, $J = 6.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.3, 160.2, 156.1, 137.7, 129.7, 127.9, 122.4, 122.5, 118.5, 114.9, 114.8, 113.1, 112.8, 78.8, 77.5, 66.6, 55.5, 43.5, 42.9; IR (KBr): ν 2219, 1612, 1569 cm^{-1}; MS: $C_{21}H_{17}N_3O_4$ 375.39 $[M]^+$; The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), t minor = 24.556 min, t major = 36.678 min.

2-[2-(1-Phenyl-2-nitroethyl)-3,4-dihydro-2H-naphthalen-1-ylidene]-malononitrile (4ca)

$[\alpha]_D^{22} = -178$ (c 0.10, EA); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08 (d, $J = 8.0$ Hz, 1H), 7.62–7.59 (m, 1H), 7.45–7.34(m, 4H), 7.29–7.27 (m, 3H), 4.74-4.68 (m, 1H), 4.46-4.41 (m, 1H), 3.67–3.63 (m, 1H), 3.51–3.44 (m, 1H), 3.08-2.99 (m, 1H), 2.92-2.86 (m, 1H), 2.03–1.95 (m, 1H), 1.84–1.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ174.6, 159.8, 139.5, 136.0, 134.6, 130.1, 129.5, 128.8, 128.7, 127.9, 127.8, 127.4, 113.1, 113.0, 81.1, 78.7, 44.8, 44.5, 25.6, 24.1; IR (KBr): ν 2218, 1624, 1560 cm^{-1}; MS: $C_{21}H_{17}N_3O_2$ 343.41 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), t minor = 19.856 min, t major = 27.678 min.

2-{2-[1-(4-Methoxy-phenyl)-2-nitro-ethyl]-3,4-dihydro-2*H*-naphthalen-1-ylidene}-malononitrile (4cb)

$[\alpha]_D^{22} = -159$ (c 0.14, $CHCl_3$); ^{1}H NMR($CDCl_3$, 400 MHz): δ 8.06 (d, J = 7.8 Hz, 1H), 7.60–7.69 (m, 1H), 7.44–7.33 (m, 2H), 7.19 (d, $J = 6.8$ Hz, 2H), 6.91 (d, $J = 6.8$ Hz, 2H), 4.62 (dd, $J = 10.2$, 12.6 Hz, 1H), 4.40 (dd, $J = 5.2$, 12.6 Hz, 1H), 3.81 (s, 3H), 3.62–3.55 (m, 1H), 3.46–3.40 (m, 1H), 2.92–2.87 (m, 2H), 1.99–1.97 (m, 1H), 1.87–1.84 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.1, 159.8, 139.4, 134.6, 130.1, 129.0, 128.7, 127.8, 127.6, 114.9, 113.1, 113.0, 80.7, 78.6, 55.4, 44.8, 43.7, 25.4, 24.1; IR (KBr): ν 2228, 1608, 1518 cm^{-1}; MS: $C_{22}H_{19}N_3O_3$ 373.48 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), t minor = 24.758 min, t major = 32.694 min.

2-{2-[1-(4-Dimethylamino-phenyl)-2-nitro-ethyl]-3,4-dihydro-2*H*-naphthalen-1-ylidene}-malononitrile (4cd)

$[\alpha]_D^{22} = -110.4$ (c 0.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.04 (d, $J = 8.0$ Hz, 1H), 7.62–7.56 (m, 1H), 7.45–7.33 (m, 2H), 7.10 (d, $J = 8.2$ Hz, 2H), 6.71 (d, $J = 8.2$ Hz, 2H), 4.71–4.63 (m, 1H), 4.42–4.36 (m, 1H), 3.61–3.56 (m, 1H), 3.38–3.31 (m, 1H), 3.05–3.01 (m, 1H), 2.97 (s, 6H), 2.88–2.82 (m, 1H), 1.98–1.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.3, 150.4, 139.8, 134.5, 130.1, 128.8, 128.4, 127.8, 127.1, 113.2, 112.8, 79.9, 78.8, 45.2, 43.8, 40.5, 25.6, 24.5; IR (KBr): ν 2226, 1618, 1562 cm^{-1}; MS: $C_{23}H_{22}N4O_2$ 386.48 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), t minor = 21.766 min, t major = 36.684 min.

2-[2-(1-p-Tolyl-2-nitroethyl)-3,4-dihydro-2h-naphthalen-1-ylidene]-malononitrile (4cf)

$[\alpha]_D^{22} = -192$ (c 0.11, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05 (d, $J = 8.1$ Hz, 1H), 7.61 (t, $J = 7.6$ Hz, 1H), 7.48–7.19 (m, 6H), 4.69–4.62 (m, 1H), 4.42–4.36 (m, 1H), 3.66–3.61 (m, 1H), 3.50–3.45 (m, 1H), 3.05–3.01 (m, 1H), 2.92–2.87 (m, 1H), 2.41 (s, 3H), 2.01–1.97 (m, 1H), 1.87–1.84 (m, 1H); ^{13}C NMR

($CDCl_3$, 100 MHz): δ 175.1, 139.6, 138.6, 134.5, 132.8, 130.2, 129.8, 128.7, 127.8, 127.6, 127.3, 113.2, 113.0, 80.8, 78.6, 44.9, 44.2, 25.6, 24.2, 20.9; IR (KBr): ν 2225, 1558, 1518 cm^{-1}; MS: $C_{22}H_{19}N_3O_2$ 357.42 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), *t* minor = 16.766 min, *t* major = 23.074 min.

2-{2-[1-(*p*-Chloro-phenyl)-2-nitroethyl]-3,4-dihydro-2*H*-naphthalen-1-ylidene}-malononitrile (4cg)

$[\alpha]_D^{22} = -198$ (c 0.12, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.07 (d, *J* = 8.1 Hz, 1H), 7.62–7.59 (m, 1H), 7.44–7.35 (m, 4H), 6.98 (d, *J* = 7.2 Hz, 2H), 4.71–4.67 (m, 1H), 4.49–4.41 (m, 1H), 3.58–3.54 (m, 1H), 3.50–3.42 (m, 1H), 2.94–2.90 (m, 2H), 2.01–1.97 (m, 1H), 1.86–1.81 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.2, 141.1, 134.8, 134.6, 134.4, 130.2, 129.8, 129.2, 128.7, 127.8, 127.5, 113.2, 112.9, 80.9, 79.0, 44.6, 43.8, 25.5, 24.1; IR (KBr): ν 2228, 1578, 1556 cm^{-1}; MS: $C_{21}H_{16}C_lN_3O_2$ 377.92 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), *t* minor = 18.956 min, *t* major = 27.684 min.

2-{2-[1-(*p*-Bromo-phenyl)-2-nitro-ethyl]-3,4-dihydro-2*H*-naphthalen-1-ylidene}-malononitrile (4ch)

$[\alpha]_D^{22} = -186$ (c 0.18, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.08 (d, *J* = 8.0 Hz, 1H), 7.63–7.52 (m, 3H), 7.43–7.32 (m, 2H), 7.11 (d, *J* = 7.2 Hz, 2H), 4.71–4.67 (m, 1H), 4.43–4.41 (m, 1H), 3.62–3.57 (m, 1H), 3.47–3.42 (m, 1H), 2.97–2.93 (m, 2H), 2.02–1.99 (m, 1H), 1.88–1.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.2, 140.2, 135.1, 134.6, 132.8, 130.1, 129.5, 128.8, 127.8, 127.5, 122.9, 113.1, 112.9, 79.9, 77.5, 45.1, 43.8, 25.4, 23.8; IR (KBr): ν 2229, 1582, 1558 cm^{-1}; MS: $C_{21}H_{16}BrN3O_2$ 422.25 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), *t* minor = 25.758 min, *t* major = 32.678 min.

2-(4-Nitro-1,3-diphenyl-butylidene)-malononitrile (4da)

$[\alpha]_D^{22} = -154$ (c 0.15, $CHCl_3$); ^1H NMR($CDCl_3$, 400 MHz): δ 7.65–7.59 (m, 3H), 7.43–7.36 (m, 5H), 7.26–7.19 (m, 2H), 4.72–4.69 (m, 1H), 4.69–4.62 (m, 1H), 3.62–3.58 (m, 2H), 0.98 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 181.6, 135.8, 133.2, 131.6, 129.5, 129.3, 128.6, 128.0, 126.9, 112.1, 111.9, 82.8, 79.2, 47.9, 44.2, 16.9; IR (KBr): ν 2229, 1559, 1498 cm^{-1}; MS: $C_{20}H_{17}N3O_2$ 331.41 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), *t* minor = 18.796 min, *t* major = 22.874 min.

2-{2-[1-(4-Methoxy-phenyl)-2-nitro-ethyl]-cyclohexan-1-ylidene}-malononitrile (4eb)

$[\alpha]_D^{22} = -20.1$ (c 0.15, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.09 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 4.61 (dd, *J* = 12.6, 10.8 Hz, 1H), 4.31 (dd,

$J = 12.6, 4.8$ Hz, 1H), 3.86–3.81 (m, 1H), 3.79 (s, 3H), 3.35–3.32 (m, 1H), 3.09–3.05 (m, 1H), 2.59–2.56 (m, 1H), 2.31–2.19 (m, 1H), 1.711.49 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 185.1, 158.7, 128.9, 127.5, 114.9, 111.2, 110.9, 83.2, 78.8, 55.3, 46.2, 44.1, 31.3, 30.1, 28.8, 19.5; IR (KBr): ν 2228, 1556 cm^{-1}; MS: $C_{18}H_{19}N_3O_3$ 325.38 $[M]^+$. The enantiomeric ratio was determined by HPLC on Chiralpak AS column (20% 2-propanol/hexane, 1 mL/min), t minor = 15.753 min, t major = 40.677 min.

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