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Note

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b02976 • Publication Date (Web): 15 Jan 2018

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Asymmetric conjugate addition of α-cyanoketones to enones using diaminomethylenemalononitrile organocatalyst

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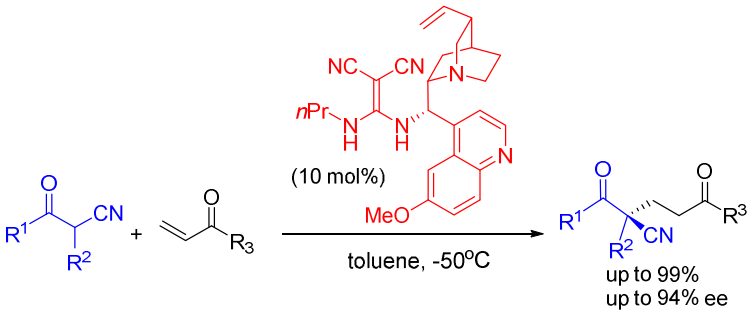
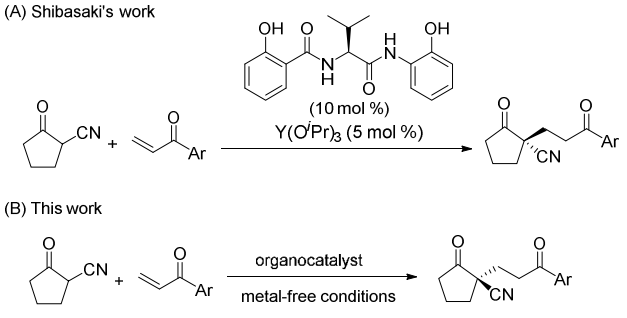


ABSTRACT: A diaminomethylenemalononitrile organocatalyst efficiently catalyzed the asymmetric conjugate addition of α-cyanoketones to vinyl ketones to give the corresponding 1,5-dicarbonyl compounds, which bear an all-carbon quaternary stereogenic center, with high enantioselectivities. This report is the first example of the asymmetric conjugate addition of α-cyanoketones to vinyl ketones using an organocatalyst.

Highly functionalized all-carbon quaternary stereogenic centers are ubiquitous as molecular skeletons in many natural products and biologically active compounds. However, highly reactive reagents and harsh conditions are required to construct them owing to steric hindrance.[1] Therefore, the development of efficient synthesis methodologies for the construction of all-carbon quaternary stereogenic centers under mild reaction conditions is one of the most significant themes of research in modern organic chemistry. Asymmetric conjugate addition using a Michael donor bearing an active methine group is an effective method for the construction of all-carbon quaternary stereogenic centers. In particular, the construction of such centers using organocatalysts has been found to be remarkably attractive with benefits such as environmentally benign properties and mild reaction conditions.[2] Among various Michael donors with active methine groups, α-alkylated α-cyanoketones are valuable because the corresponding conjugate adducts, which bear a highly functionalized all-carbon quaternary stereogenic center, are versatile synthetic intermediates. However, catalytic asymmetric conjugate additions using α-cyanoketones as Michael donors are scarce. In particular, asymmetric conjugate additions of α-cyanoketones using organocatalysts are relatively rare.[3] Chiral 1,5-dicarbonyl-2-cyano derivatives obtained by the asymmetric conjugate addition of α-cyanoketones to aromatic vinyl ketones are valuable building block because they can be easily transformed to enantioenriched spiro-piperidine and bicyclo[3.3.0]octane motif, however, there has been only one pioneering example of the asymmetric conjugate addition using a chiral yttrium catalyst for access to chiral 1,5-dicarbonyl-2-cyano compounds, as reported by Shibasaki et al. (Scheme 1)[4] To the best of our knowledge, there has been no report of the asymmetric conjugate addition of an α-cyanoketone to an aromatic vinyl ketone using an organocatalyst under metal-free conditions. Therefore, the development of the asymmetric conjugate addition of α-cyanoketones to enones using an organocatalyst is highly desirable from the viewpoint of green chemistry.

Scheme 1. Asymmetric conjugate addition of α-cyanoketones to enones



On the other hand, thiourea and squaramide groups, which act as double hydrogen-bond donors, are excellent motifs for asymmetric organocatalysis, and a number of significant asymmetric reactions using chiral organocatalysts bearing thiourea and squaramide groups have been reported by several research groups.[5,6] Recently, we developed organocatalysts bearing a diaminomethylenemalononitrile (DMM) motif as a double hydrogen-bond donor and reported their high catalytic activities in various asymmetric reactions.[7] In this context, to further demonstrate the effectiveness of organocatalysts bearing a DMM unit, we attempted the construction of all-carbon quaternary stereogenic centers by the asymmetric conjugate addition of α-cyanoketones to vinyl ketones using DMM organocatalysts.

Firstly, quinine (**1**), thiourea derivative **2**, and DMM catalysts (**3** and **4**) bearing a chiral cinchona motif (Figure 1) were examined as catalysts for the conjugate addition of 2-oxocyclopentane-1-carbonitrile (**10a**) to 1-phenylprop-2-en-1-one (**11a**) as test reactants at room temperature in CH_2Cl_2 (Table 1). Among the four examined catalysts, **4** was preferred for this conjugate addition to afford the corresponding adduct **12aa**, as it gave an enantiomeric excess (ee) of 54% (entries 1–4). Therefore, it was found that the DMM skeleton was a preferable motif for the organocatalytic reaction between **10a** and **11a** in comparison with the thiourea derivative **2**. When the reaction using **4** was carried out at −50 °C, both the yield and the enantioselectivity were increased (entry 5). The use of the organocatalyst **5**, which bears a simple benzylamine motif, resulted in lower enantioselectivity (entry 6). The organocatalyst **6**, which bears an *n*-butylamine group instead of a benzylamine group, was a good catalyst for the conjugate addition and provided higher stereoselectivity (entry 7). Organocatalysts with alkyl groups of different lengths, namely, *n*-propyl, ethyl, and methyl groups, were examined, and it was found that the organocatalyst **7**, which bears an *n*-propyl group, was the most effective (entries 8–10).

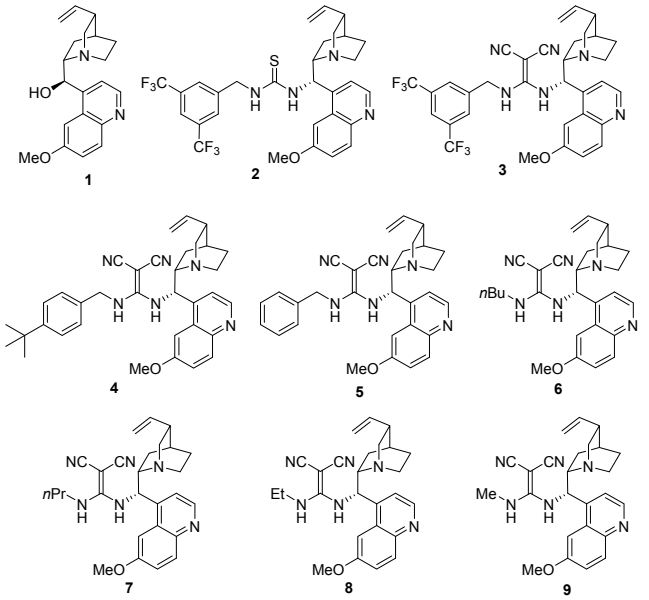
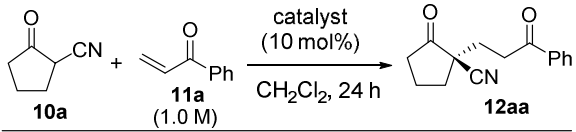


Figure 1. Structure of organocatalysts

Next, we examined the asymmetric conjugate addition using **7** in a representative range of solvents (Table 2). Toluene was found to be the most suitable among the examined solvents, and the enantioselectivity was increased to 89% ee (entries 1–5). When the conjugate addition using **7** was carried out at lower temperatures (−60 and −80 °C), this resulted in decreases in enantioselectivity and yield (entries 6 and 7). To further increase the stereoselectivity, we examined the concentration of the reaction medium (entries 8–10). When the reaction was performed in more dilute solvents, the enantioselectivity tended to increase and reached a maximum at a solvent concentration of 0.2 or 0.3 M (entries 9 and 10). The optimal conditions for the reaction were determined to be as follows: organocatalyst **7** at −50 °C in toluene (0.3 M).

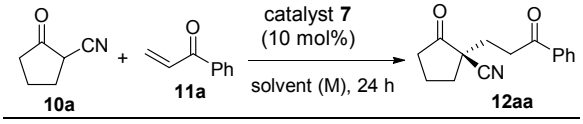
Table 1. Catalyst screening[a]



entry	catalyst	Temp (°C)	% yield[b]	% ee[c]
1	**1**	rt	85	- 10
2	**2**	rt	65	21
3	**3**	rt	75	40
4	**4**	rt	89	54
5	**4**	- 50	94	73
6	**5**	- 50	72	70
7	**6**	- 50	86	82
8	**7**	- 50	86	83
9	**8**	- 50	86	76
10	**9**	- 50	83	40

[a] Reaction conditions: **10a** (0.2 mmol), **11a** (0.2 mmol), catalyst (10 mol %), CH_2Cl_2 (0.2 mL) , 24 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

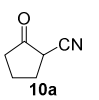
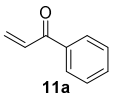
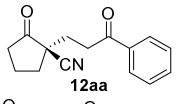
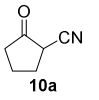
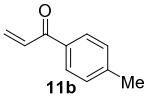
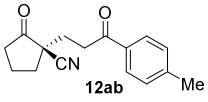
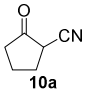
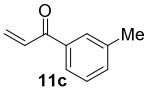
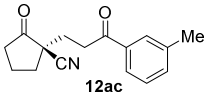
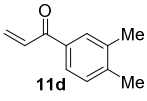
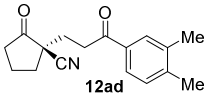
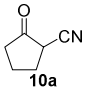
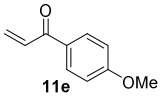
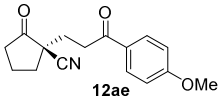
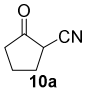
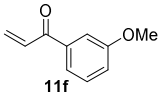
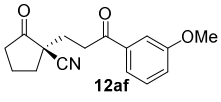
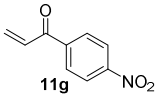
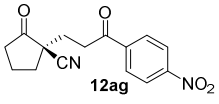
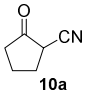
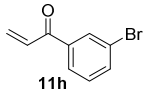
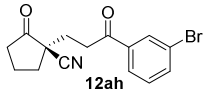
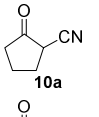
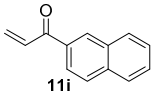
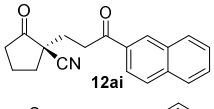
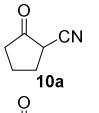
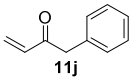
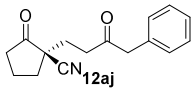
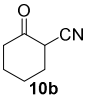
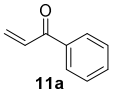
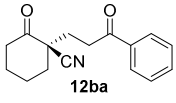
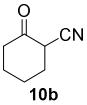
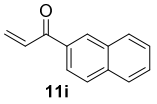
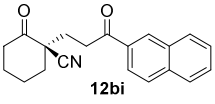
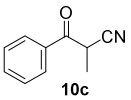
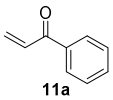
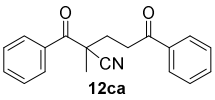
Table 2. Study of reaction conditions[a]



entry	solvent (M)	temp. (°C)	% yield[b]	% ee[c]
1	CH_2Cl_2 (1.0)	-50	86	83
2	THF (1.0)	-50	46	59
3	EtOAc (1.0)	-50	59	67
4	hexane (1.0)	-50	43	28
5	toluene (1.0)	-50	86	89
6	toluene (1.0)	-60	85	89
7	toluene (1.0)	-80	55	84
8	toluene (0.5)	-50	94	92
9	toluene (0.3)	-50	88	94
10	toluene (0.2)	-50	86	94

[a] Reaction conditions: **10a** (0.2 mmol), **11a** (0.2 mmol), catalyst **7** (10 mol %), 24 h. [b] Isolated yield. [c] Determined by chiral HPLC analysis.

Table 3. Asymmetric conjugate additions of α-cyanoketones to enones using organocatalyst **7**[a]

entry	cyanoketone **10**	enone **11**	product **12**	time (h)	% yield[b]	% ee[c]
1	 **10a**	 **11a**	 **12aa**	24	88	94
2	 **10a**	 **11b**	 **12ab**	48	99	88
3	 **10a**	 **11c**	 **12ac**	48	89	92
4[d]	 **10a**	 **11d**	 **12ad**	48	81	91
5	 **10a**	 **11e**	 **12ae**	120	88	90
6	 **10a**	 **11f**	 **12af**	48	99	91
7	 **10a**	 **11g**	 **12ag**	120	99	90
8[d]	 **10a**	 **11h**	 **12ah**	48	80	90
9	 **10a**	 **11i**	 **12ai**	24	92	85
10	 **10a**	 **11j**	 **12aj**	48	13	65
11[d]	 **10b**	 **11a**	 **12ba**	48	74	94
12[d]	 **10b**	 **11i**	 **12bi**	48	75	92
13	 **10c**	 **11a**	 **12ca**	48	62	72
14	**10a**	**11k**	**12ak**	54	95	92
15[e]	**10a**	**11l**	**12al**	96	24[f]	7[g]

[a] Reaction conditions: **10** (0.2 mmol), **11** (0.2 mmol), catalyst **7** (10 mol %), toluene (0.6 mL). [b] Isolated yield.
[c] Determined by chiral HPLC analysis. [d] Catalyst **7** (20 mol%) was used.
[e] *p*-Xylene (0.2 mL) was used as reaction solvent. [f] Ratio of diastereomers is 56:44.
[g] Enantioselectivity of minor isomer is 60% ee.

Once the optimal conditions had been determined, we examined the scope and limitations of the asymmetric conjugate addition of various α-cyanoketones **10** to various vinyl ketones **11** (Table 3). Aromatic vinyl ketones **11b–11f**, which bear methyl and methoxy substituents as representative electron-donating groups on the benzene ring, reacted with the cyclic α-cyanoketone **10a** in the presence of the organocatalyst **7** to afford the corresponding adducts **12aa–12af** in high yields with high enantioselectivities (entries 2–6). The conjugate addition of **10a** to the vinyl ketones **11g** and **11h**, which bear nitro and bromosubstituents, respectively, as representative electron-withdrawing groups, afforded the addition products **12ag** and **12ah**, respectively, with excellent enantioselectivities (entries 7 and 8). The reaction of 1-(naphthalen-2-yl)prop-2-en-1-one (**11i**) with **10a** also proceeded well and afforded the adduct **12ai** with high enantioselectivity (entry 9). The ketone **11j**, as a representative aliphatic vinyl ketone, was a poor substrate and gave a low yield (entry 10). 2-Oxocyclohexane-1-carbonitrile (**10b**), as a representative cyclic α-cyanoketone with a different ring size, reacted with **11a** and **11i** to give the adducts **12ba** and **12bi**, respectively, with excellent enantioselectivities (entries 11 and 12). In the previous report by Shibasaki et al., 2-methyl-3-oxo-3-phenylpropanenitrile (**10c**), as a representative linear α-cyanoketone, was a poor substrate for asymmetric conjugate addition using a rare earth catalyst and gave low yields and low enantioselectivities.[4] However, the reaction of **10c** with **11a** using the organocatalyst **7** afforded the corresponding addition product **12ca** in good yield with high enantioselectivity (entry 13). The conjugate addition of **10a** to **11k**, which bears a thiophene ring, provided the adduct **12ak** in excellent yield with excellent enantioselectivity (entry 14). (*E*)-1-phenylbut-2-en-1-one (**11l**) was poor substrate to provide low yield and low stereoselectivities (entry 15). The stereochemistry of the products was determined by comparison with reported chiral-phase HPLC retention times and optical rotations. The products were selectively obtained with the opposite stereochemistry (*S* configuration) in comparison with the stereochemistry (*R* configuration) reported by Shibasaki et al.[4]

Although no experimental data that indicated the reaction mechanism were obtained, we suggest that the two weakly acidic protons of the DMM motif functioned as a hydrogen-bond donor to activate the carbonyl group of **11**.[8] The coordination of the tertiary amine group in the quinine unit to the enol generated from **10** resulted in highly efficient control of the approach orientations of **10** and **11**.

In conclusion, the DMM organocatalyst **7**, which can be readily prepared, efficiently promoted the asymmetric conjugate addition of α-cyanoketones to aromatic vinyl ketones in toluene to afford the corresponding 1,5-dicarbonyl compounds, which bear an all-carbon quaternary stereogenic center, in high yields with excellent enantioselectivities. This report is the first example of the asymmetric conjugate addition of α-cyanoketones to vinyl ketones using an organocatalyst. Further applications of DMM catalysts to other types of asymmetric reaction and the development of additional novel DMM organocatalysts are currently being investigated in our laboratory.

Experimental Section

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance III Nanobay 400 MHz spectrometer (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR). The chemical shifts are expressed in ppm downfield from tetramethylsilane (δ = 0.00) as an internal standard. Mass spectra were recorded by an electrospray ionization-time of flight (ESI-TOF) mass spectrometer (Micromass LCT). Specific rotations were measured on a Jasco P-1030. Melting points were obtained with Yanaco MP-J3 and are uncorrected. For thin layer chromatographic (TLC) analyses, Merck precoated TLC plates (silica gel 60 F_{254}) were used. Flash column chromatography was performed on neutral silica gel (Kanto Silica gel 60N, 40–50 μm). Organocatalyst **2** was prepared by reported method.[9]

Preparation of organocatalysts 3–9

To a stirred solution of 2-(bis(methylthio)methylene)malononitrile[10] (1.31 g, 7.7 mmol) in THF (29 mL) was added (*S*)-(6-methoxyquinolin-4-yl)((*1S,2S,4S,5R*)-5-vinylquinuclidin-2-yl)methanamine[11] (2.48 g, 7.7 mmol). The mixture was stirred under reflux for 21 h. TLC indicated the reaction was completed, the reaction mixture was cool to room temperature. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel with a mixture of $CHCl_3$ and MeOH affording the crude mono-amine products. To a stirred solution of the crude mono-amine products (1.34 g, 3.0 mmol) in THF (11.4 mL) was added the corresponding amine (6.0 mmol). The mixture was stirred under reflux for 24 h. TLC indicated the reaction was completed, the reaction mixture was cool to room temperature. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel with a mixture of $CHCl_3$ and MeOH affording the compound.

Organocatalyst 3

Yellow powder (817.5 mg, 43%); mp 105-108 °C; $[\alpha]^{27}_D$ = -95.3 °(c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.71 (t, *J* = 10.8 Hz, 1H), 0.88 (m, 1H), 1.24-1.35 (m, 2H), 1.46-1.52 (m, 2H), 1.65 (br s, 1H), 2.10-2.17 (m, 1H), 2.27 (br s, 1H), 2.81 (br d, *J* = 12.2 Hz, 2H), 2.93 (dd, *J* = 13.8, 9.9 Hz, 1H), 3.95 (s, 3H), 4.52 (br d, *J* = 12.7 Hz, 1H), 4.71 (br d, *J* = 14.4 Hz, 1H), 4.99-5.03 (m, 2H), 5.16 (br s, 1H), 5.64-5.72 (m, 1H), 7.18 (d, *J* = 2.6 Hz, 1H), 7.23 (br s, 1H), 7.42 (br d, *J* = 8.3 Hz, 1H), 7.65 (s, 2H), 7.87 (s, 1H), 8.05 (br s, 1H), 8.66-8.83 (br m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =25.5, 26.9, 27.2, 35.4, 38.8, 40.2, 47.8, 53.4, 54.5, 55.6, 63.4, 100.5, 115.3, 117.7, 118.3, 122.2, 122.4, 122.9 (q, $^1J_{C\text{-}F}$ = 272.9 Hz), 128.2, 132.5 (q, $^2J_{C\text{-}F}$ = 33.6 Hz), 132.6, 138.8, 140.4, 141.8, 144.8, 145.4, 147.7, 158.6, 163.7; HRMS (ESI-TOF):Calcd for $C_{33}H_{31}N_6OF_6$ $(M+H)^+$: 641.2464, Found: 641.2471.

Organocatalyst 4

Orange powder (2.4 g, 85%); mp 125-127 °C; $[\alpha]^{29}_D$ = -168.8 °(c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD): δ = 0.93-0.98 (br m, 1H), 1.29 (s, 9H), 1.26-1.33 (m, 2H), 1.62 (br s, 3H), 2.31 (br s, 1H), 2.65 (br s, 1H), 2.79 (br d, *J* = 13.9, 1H), 3.08-3.23 (m, 3H), 3.96 (s, 3H), 4.32(d, *J* = 14.4 Hz, 1H), 4.39 (d, *J* = 14.4 Hz, 1H), 4.93-5.01 (m, 2H), 5.70-5.78 (m, 1H), 6.77 (br s, 2H), 7.19 (br d, *J* = 6.6 Hz, 2H), 7.29 (br s, 1H), 7.47 (dd, *J* = 9.2, 2.2 Hz, 1H), 7.58 (br s, 1H), 8.00 (d, *J* = 9.3 Hz, 1H), 8.56 (d, *J* = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =25.6, 27.1, 27.4, 31.3, 34.6, 34.9, 39.1, 39.9, 48.6, 53.0, 54.9, 55.7, 63.1, 100.7, 115.0, 118.1, 118.6, 122.4, 125.9, 127.8, 132.5, 132.6,

140.8, 142.4, 144.9, 147.7, 151.6, 158.4, 162.9; HRMS (ESI-TOF):Calcd for $C_{35}H_{41}N_6O$ $(M+H)^+$: 561.3342, Found: 561.3316.

Organocatalyst 5

Yellow powder (158.8 mg, 63%); mp 100-103 °C; $[\alpha]^{29}_D$ = -184.8 °(c 1.0, $CHCl_3$); ^1H NMR (400 MHz, CD_3OD): δ = 0.93-0.98 (m, 1H), 1.26-1.33 (m, 2H), 1.63 (br s, 3H), 2.32 (br s, 1H), 2.64-2.72 (m, 1H), 2.77-2.82 (m, 1H), 3.06-3.13 (br m, 1H), 3.06-3.24 (m, 2H), 3.98 (s, 3H), 4.35 (d, *J* =14.5 Hz, 1H), 4.46 (d, *J* =14.7 Hz, 1H), 4.93 (d, *J* = 10.4 Hz, 1H), 4.99 (d, *J* = 17.2 Hz, 1H), 5.75 (ddd, *J* = 17.2, 10.1, 7.3 Hz, 1H), 6.88 (br s, 2H), 7.17-7.24 (m, 3H), 7.29 (d, *J* =3.8 Hz, 1H), 7.47 (dd, *J* = 9.3, 2.6 Hz, 1H), 7.59 (br s, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 8.54 (d, *J* = 4.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.6, 27.1, 27.4, 34.9, 39.1, 40.0, 49.0, 53.2, 54.8, 55.7, 63.1, 100.7, 115.1, 118.1, 118.6, 122.3, 128.0, 128.4, 129.1, 132.5, 135.7, 140.7, 142.2, 145.1, 147.6, 158.5, 163.0; HRMS (ESI-TOF):Calcd for $C_{31}H_{33}N_6O$ $(M+H)^+$:505.2716, Found: 505.2725.

Oganocatalyst 6

White powder (215.2 mg, 91%); mp 93-94 °C; $[\alpha]^{29}_D$ = -191.7 °(c 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ =0.73 (brs, 3H), 0.86-1.12 (m, 6H), 1.39-1.44 (m, 1H), 1.63 (br s, 2H), 1.73 (br s, 1H), 2.35 (br s, 1H), 2.81-2.88 (br m, 2H), 3.04 (br s, 1H), 3.15-3.33 (m, 4H), 3.99 (s, 3H), 4.99 (d, *J* = 10.0 Hz, 1H), 5.01 (d, *J* = 17.0 Hz, 1H), 5.10 (br s, 1H), 5.66-5.74 (m, 1H), 6.40 (br s, 1H), 7.35 (br s, 2H), 7.47 (dd, *J* = 9.1, 1.7 Hz, 1H), 8.11 (d, *J* = 9.2 Hz, 1H), 8.81 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5, 19.6, 25.8, 27.2, 27.7, 31.6, 34.6, 39.3, 40.7, 44.6, 53.2, 55.3, 55.9, 63.0, 100.8, 115.2, 118.3, 119.2, 122.5, 127.2, 132.7, 140.9, 142.5, 145.1, 147.8, 158.7, 163.4; HRMS (ESI-TOF):Calcd for $C_{28}H_{35}N_6O$ $(M+H)^+$:471.2872, Found: 471.2872.

Oganocatalyst 7

Yellow powder (2.0 g, 99%); mp 234-236 °C; $[\alpha]^{29}_D$ = -200.5 °(c 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.62 (t, *J* =7.4 Hz, 3H), 0.87-0.91(m, 1H), 1.07-1.20 (m, 2H), 1.38-1.41 (m, 1H), 1.62 (br s, 2H), 1.72 (br s, 1H), 2.34 (br s, 1H), 2.80-2.87 (m, 2H), 3.09-3.14 (m, 3H), 3.21-3.27 (m, 2H), 3.99 (s, 3H), 4.98 (d, *J* = 13.0 Hz, 1H), 5.01 (d, *J* = 17.2 Hz, 1H), 5.26 (br s, 1H), 5.70 (br s, 1H), 6.80 (br s, 1H), 7.37 (d, *J* = 4.4 Hz, 1H), 7.39 (br s, 1H), 7.45 (dd, *J* = 9.2, 2.3 Hz, 1H), 8.08 (d, *J* = 9.2 Hz, 1H), 8.79 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.8, 22.8, 25.7, 27.2, 27.6, 34.4, 39.2, 40.6, 46.4, 53.2, 55.2, 55.9, 63.0, 100.7, 115.0, 118.4, 118.8, 122.4, 127.4, 132.5, 140.8, 142.6, 145.0, 147.7, 158.6, 163.3; HRMS (ESI-TOF):Calcd for $C_{27}H_{33}N_6O$ $(M+H)^+$:457.2716, Found: 457.2714. Anal. Calcd for $C_{27}H_{32}N_6O$: C,71.03; H, 7.06; N,18.41. Found: C, 70.92; H, 7.06; N, 18.14.

Oganocatalyst 8

White powder (370.2 mg, 28%); mp 227-228 °C; $[\alpha]^{29}_D$ = -212.8 °(c 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ =0.82 (t, *J* =7.2 Hz, 3H), 0.87 (dd, *J* =13.5, 7.2 Hz, 1H), 1.38-1.44 (m, 1H), 1.61-1.65 (m, 2H), 1.74 (br s, 1H), 2.35 (br s, 1H), 2.81-2.88 (m, 2H), 3.05 (br s, 1H), 3.23-3.29 (m, 2H), 3.34-3.43 (m, 2H), 3.99 (s, 3H), 5.00 (d, *J* = 10.0 Hz, 1H), 5.02 (d, *J* = 17.2 Hz, 1H), 5.14 (br s, 1H), 5.66-5.75 (m, 1H), 6.69 (br s, 1H), 7.35 (br s, 2H), 7.47 (dd, *J* = 9.2, 2.2 Hz, 1H), 8.11 (d, *J* = 9.2 Hz, 1H), 8.80 (br s, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.5, 25.7, 27.1, 27.6, 34.4, 39.2, 39.6, 40.6, 53.2, 55.2, 55.9, 62.9, 100.8, 115.1, 118.3, 118.8, 122.4, 127.4, 132.5, 140.8, 142.6, 145.0, 147.7, 158.6, 163.2; HRMS (ESI-TOF):Calcd for $C_{26}H_{31}N_6O$ $(M+H)^+$:443.2559, Found: 443.2553; Anal. Calcd for $C_{26}H_{30}N_6O$: C,70.56; H, 6.83; N,18.99. Found: C,70.33; H, 6.87; N, 18.90.

Oganocatalyst 9

White powder (734.1 mg, 57%); mp: 223-226 °C; $[\alpha]^{29}_D$ = -156.1 °(c 1.0, $CHCl_3$); ^1H NMR (400 MHz, $(CD_3)_2CO$): δ =1.07 (dd, *J* = 13.3, 7.7 Hz, 1H), 1.33-1.40 (m, 1 H), 1.60-1.75 (m, 2H), 2.05 (s, 3H), 2.35 (br s, 1H), 2.82-2.89 (2H), 3.26-3.36 (m, 3H), 4.02 (s, 3H), 4.90 (d, *J* = 10.4 Hz, 1H), 5.00 (d, *J* = 17.1 Hz, 1H), 5.14 (br s, 1H), 5.55 (br s, 1H), 5.81(ddd, *J* = 17.4, 10.4, 7.2 Hz, 1H), 6.93 (br s, 1H), 7.14 (br s, 1H), 7.44 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.64 (d, *J* = 4.5 Hz, 1H), 7.76 (br s, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 8.77 (d, *J* = 4.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 27.2, 27.6, 31.2, 34.6, 39.2, 40.7, 53.8, 55.2, 56.0, 62.7, 101.2, 115.1, 118.3, 118.8, 122.3, 127.1, 132.4, 140.8, 142.7, 145.1, 147.7, 158.5, 164.5; HRMS (ESI-TOF):Calcd for $C_{25}H_{29}N_6O$ $(M+H)^+$:429.2403, Found: 429.2399; Anal. Calcd for $C_{25}H_{28}N_6O$: C,70.07; H, 6.59; N,19.61. Found: C, 69.91; H, 6.60; N, 19.48.

Typical procedure for asymmetric conjugate addition and characterization data of the products (12aa-12al).

To a solution of organocatalyst **7** (9.1 mg, 0.020 mmol), 1-propenylprop-2-en-1-one (**11a**[4], 26.4 mg, 0.20 mmol) in toluene (0.6 mL) were added 2-oxocyclopentane-1-carbonitrile (**10a**[4], 20.0 μL, 0.20 mmol) at -50 °C for 24 h. The reaction mixture was directly purified by flash column chromatography on silica gel with a 3:1 mixture of hexane and ethyl acetate to afford the pure **12aa** (42.5 mg, 88%) as a white solid.

(*S*)-2-Oxo-1-(3-oxo-3-phenylpropyl)cyclopentane-1-carbonitrile (**12aa**)[4]. White solid, 42.5 mg, 88% yield (94% ee). ^1H NMR (400 MHz, $CDCl_3$): δ =2.07-2.18 (m, 4H), 2.32 (ddd, *J* = 5.6, 9.4, 14.6 Hz, 1H), 2.45-2.52 (m, 3H), 3.22 (ddd, *J* = 5.5, 9.5, 18.0 Hz, 1H), 3.41 (ddd, *J* = 5.6, 9.5, 18.0 Hz, 1H), 7.49 (dd, *J* = 7.8, 7.6 Hz, 2H), 7.57-7.61 (m, 1H), 7.98 (dd, *J* = 1.3, 7.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 28.0, 34.0, 35.2, 36.3, 47.9, 118.9, 128.1, 128.7, 133.5, 136.3, 198.0, 209.2; $[\alpha]^{29}_D$ = 9.0° (c 1.0, $CHCl_3$); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a CHIRALPAK IA column (hexane/*i*-PrOH = 90:10 at 1.0 mL/min); λ = 254 nm; t_{major} = 16.2 min, t_{minor} = 14.0 min.

(*S*)-2-Oxo-1-(3-oxo-3-(*p*-tolyl)propyl)cyclopentane-1-carbonitrile (**12ab**)[4]. White solid, 56.3 mg, 99% yield (88% ee). ^1H NMR (400 MHz, $CDCl_3$): δ =2.06-2.18 (m, 4H), 2.31 (ddd, *J* = 5.6, 9.4, 14.6 Hz, 1H), 2.42 (s, 3H), 2.44-2.53 (m, 3H), 3.19 (ddd, *J* = 5.5, 9.6, 18.0 Hz, 1H), 3.38 (ddd, *J* = 5.6, 9.6, 17.9 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.88 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3, 21.8, 28.1, 33.9, 35.3, 36.4, 48.0, 119.0, 128.3, 129.5, 133.9, 144.5, 197.7, 209.3 $[\alpha]^{26}_D$ = 9.3° (c 1.0, $CHCl_3$); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a ChiralCel AD-H column (hexane/*i*-PrOH = 90:10 at 1.0 mL/min); λ = 254 nm; t_{major} = 16.7 min, t_{minor} = 15.2 min.

(*S*)-2-Oxo-1-(3-oxo-3-(*m*-tolyl)propyl)cyclopentane-1-carbonitrile (**12ac**)[4]. White solid, 45.3 mg, 89% yield (92% ee). ^1H NMR (400 MHz, $CDCl_3$): δ =2.04-2.17 (m, 4H), 2.32 (ddd, *J* = 5.6, 9.3, 14.6 Hz, 1H), 2.43 (s, 3H), 2.45-2.52 (m, 3H), 3.21 (ddd, *J* = 5.5, 9.5, 18.0 Hz, 1H), 3.40 (ddd, *J* = 5.5, 9.5, 18.0 Hz, 1H), 7.35-7.41 (m, 2H), 7.77-7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 21.3, 28.0, 34.0, 35.2, 36.3, 47.9, 118.9, 125.3, 128.48, 128.53, 134.2, 136.3, 138.5, 198.1, 209.2; $[\alpha]^{26}_D$ = 8.2° (c 1.0, $CHCl_3$); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a ChiralCel AD-H column (hexane/*i*-PrOH = 90:10 at 1.0 mL/min); λ = 254 nm; t_{major} = 15.3 min, t_{minor} = 14.1 min.

(*S*)-1-(3-(3,4-Dimethylphenyl)-3-oxopropyl)-2-oxocyclopentane-1-carbonitrile (**12ad**)[4]. Colorless oil, 43.4 mg, 81% yield (91% ee). ^1H NMR (400 MHz, $CDCl_3$): δ =2.06-2.17 (m, 4H), 2.27-2.35 (m, 1H), 2.33 (s, 6H), 2.43-2.51 (m, 3H), 3.18 (ddd, *J* = 5.5, 9.5, 17.9 Hz, 1H), 3.37 (ddd, *J* = 5.5, 9.5, 17.9 Hz, 1H), 7.23 (d, *J* = 7.8 Hz , 1H), 7.71 (dd, *J* = 1.7, 7.8 Hz, 1H), 7.74 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 19.8, 20.0, 28.0, 33.8, 35.2, 36.3, 48.0, 119.0, 125.8, 129.2, 129.9, 134.3, 137.1, 143.1, 197.8, 209.2; $[\alpha]^{29}_D$ = 10.0° (c 1.0, $CHCl_3$); Enantiomeric excess of the product was determined by

chiral stationary phase HPLC analysis using a CHIRALPAK IC column (hexane/*i*-PrOH = 2:1 at 1.0 mL/min); λ = 254 nm; t_{major} = 14.3 min, t_{minor} = 15.8 min.

(*S*)-1-(3-(4-Methoxyphenyl)-3-oxopropyl)-2-oxocyclopentane-1-carbonitrile (**12ae**) [4]. White solid, 47.8 mg, 88% yield (90% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ =2.06-2.21 (m, 4H), 2.31 (ddd, *J* = 5.4, 9.4, 14.6 Hz, 1H), 2.42-2.52 (m, 3H), 3.17 (ddd, *J* = 5.6, 9.6, 17.7 Hz, 1H), 3.35 (ddd, *J* = 5.6, 9.6, 17.7 Hz, 1H), 3.38 (s, 3H), 6.95 (d, *J* = 8.8 Hz, 2H), 7.97 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 28.0, 33.5, 35.2, 36.3, 47.9, 55.8, 113.8, 118.9, 129.4, 130.4, 163.8, 196.4, 209.1; $[\alpha]^{26}_D$ = 11.2° (c 1.0, $CHCl_3$); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a ChiralCel AD-H column (hexane/*i*-PrOH = 90:10 at 1.0 mL/min); λ = 254 nm; t_{major} = 35.6 min, t_{minor} = 31.8 min.

(*S*)-1-(3-(3-Methoxyphenyl)-3-oxopropyl)-2-oxocyclopentane-1-carbonitrile (**12af**)[4]. White solid, 54.1 mg, 99% yield (91% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ =2.05-2.18 (m, 4H), 2.32 (ddd, *J* = 5.5, 9.3, 14.6 Hz, 1H), 2.45-2.52 (m, 3H), 3.20 (ddd, *J* = 5.5, 9.5, 18.0 Hz, 1H), 3.39 (ddd, *J* = 5.6, 9.5, 18.0 Hz, 1H), 3.87 (s, 3H), 7.12-7.15 (m, 1H), 7.39 (dd, *J* = 7.9, 7.9 Hz, 1H), 7.48-7.49 (m, 1H), 7.57 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 28.0, 34.1, 35.2, 36.3, 47.9, 55.5, 112.3, 118.9, 120.0, 120.7, 129.7, 137.7, 159.9, 197.8, 209.1; $[\alpha]^{27}_D$ = -2.0° (c 1.0, CH_2Cl_2); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a ChiralCel AD-H column (hexane/*i*-PrOH = 90:10 at 0.8 mL/min); λ = 254 nm; t_{major} = 29.7 min, t_{minor} = 28.5 min.

(*S*)-1-(3-(4-Nitrophenyl)-3-oxopropyl)-2-oxocyclopentane-1-carbonitrile (**12ag**). White solid, 56.5 mg, 99% yield (90% ee). mp 144-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ =2.10-2.21 (m, 4H), 2.35 (ddd, *J* = 5.6, 9.2, 14.6 Hz, 1H), 2.46-2.55 (m, 3H), 3.27 (ddd, *J* = 5.5, 9.3, 18.5 Hz, 1H), 3.50 (ddd, *J* = 5.7, 9.2, 18.5 Hz, 1H), 8.15 (d, *J* = 8.8 Hz, 2H), 8.34 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3, 27.8, 34.6, 35.5, 36.4, 47.6, 118.7, 124.0, 129.2, 140.6, 150.6, 196.5, 209.2; $[\alpha]^{28}_D$ = 28.1° (c 1.0, $CHCl_3$); HRMS (ESI-TOF): Calcd for $C_{15}H_{14}N_2O_4Na$ $(M+Na)^+$: 309.0851, Found: 309.0859; Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a CHIRALPAK IA column (hexane/*i*-PrOH = 80:20 at 0.8 mL/min); λ = 254 nm; t_{major} = 35.3 min, t_{minor} = 32.7 min.

(*S*)-1-(3-(3-Bromophenyl)-3-oxopropyl)-2-oxocyclopentane-1-carbonitrile (**12ah**)[4]. White solid, 51.3 mg, 80% yield (90% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ =2.07-2.19 (m, 4H), 2.32 (ddd, *J* = 5.5, 9.3, 14.6 Hz, 1H), 2.46-2.52 (m, 3H), 3.19 (ddd, *J* = 5.5, 9.4, 18.3 Hz, 1H), 3.40 (ddd, *J* = 5.7, 9.4, 18.3 Hz, 1H), 7.37 (dd, *J* = 7.9, 7.9 Hz, 1H), 7.71-7.73 (m, 1H), 7.89-7.92 (m, 1H), 8.10-8.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 27.8, 34.1, 35.3, 36.3, 47.7, 118.8, 123.1, 126.6, 130.3, 131.1, 136.4, 138.0, 196.6, 209.1; $[\alpha]^{28}_D$ = 10.2° (c 1.0, $CHCl_3$); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a ChiralCel OD-H column (hexane/*i*-PrOH = 90:10 at 1.0 mL/min); λ = 254 nm; t_{major} = 28.1 min, t_{minor} = 22.6 min.

(*S*)-1-(3-(Naphthalen-2-yl)-3-oxopropyl)-2-oxocyclopentane-1-carbonitrile (**12ai**)[4]. White solid, 52.6 mg, 90% yield (89% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ =2.12-2.21 (m, 4H), 2.38 (ddd, *J* = 5.4, 9.4, 14.6 Hz, 1H), 2.48-2.57 (m, 3H), 3.37 (ddd, *J* = 5.5, 9.6, 18.0 Hz, 1H), 3.56 (ddd, *J* = 5.6, 9.6, 17.9 Hz, 1H), 7.56-7.64 (m, 2H), 7.88-7.92 (m, 2H), 8.00-8.04 (m, 2H), 8.52 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3, 28.1, 34.0, 35.3, 36.3, 47.9, 119.0, 123.6, 126.9, 127.8, 128.6, 128.7, 129.7, 129.9, 132.5, 133.6, 135.8, 197.9, 209.2; $[\alpha]^{27}_D$ =24.5° (c 1.0, $CHCl_3$); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a CHIRALPAK IC column (hexane/*i*-PrOH = 2:1 at 1.0 mL/min); λ = 254 nm; t_{major} = 15.3 min, t_{minor} = 17.5 min.

(*S*)-2-Oxo-1-(3-oxo-4-phenylbutyl)cyclopentane-1-carbonitrile (**12aj**)[4]. White solid, 6.5 mg, 13% yield (65% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ =1.87 (ddd, *J* = 5.8, 8.6, 14.5 Hz, 1H), 1.98-2.18 (m, 4H), 2.35-2.43 (m, 3H), 2.70 (ddd, *J* = 5.8, 8.7, 18.4 Hz, 1H), 2.90 (ddd, *J* = 6.2, 8.6, 18.4 Hz, 1H), 3.74 (s, 2H), 7.20-7.36 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 27.6, 35.2, 36.3, 37.3, 47.8, 50.2, 118.8, 127.3, 128.9, 129.5, 133.7, 206.3, 209.2; $[\alpha]^{29}_D$ = -10.1° (c 0.25, $CHCl_3$); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a ChiralCel AD-H column (hexane/*i*-PrOH = 90:10 at 0.8 mL/min); λ = 210 nm; t_{major} = 22.9 min, t_{minor} = 22.0min.

(*S*)-2-Oxo-1-(3-oxo-3-phenylpropyl)cyclohexane-1-carbonitrile (**12ba**). Colorless oil, 38.0 mg, 74% yield (94% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ =1.78-1.97 (m, 3H), 2.02-2.15 (m, 3H), 2.36-2.47 (m, 2H), 2.45-2.56 (m, 1H), 2.84 (ddd, *J* = 5.6, 11.3, 13.6 Hz, 1H), 3.16 (ddd, *J* = 5.1, 10.7, 17.6 Hz, 1H), 3.30 (ddd, *J* = 5.3, 10.9, 17.5 Hz, 1H),7.46-7.52 (m, 2H), 7.56-7.60 (m, 1H), 7.98 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.0, 27.8, 28.1, 34.4, 39.1, 39.3, 51.1, 119.6, 128.1, 128.7, 133.4, 136.4, 198.1, 203.2; $[\alpha]^{29}_D$ = 85.0° (c 1.0, $CHCl_3$); HRMS (ESI-TOF): Calcd for $C_{16}H_{17}NO_2Na$ $(M+Na)^+$: 278.1157, Found: 278.1164; Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a CHIRALPAK IC column (hexane/*i*-PrOH = 90:10 at 0.8 mL/min); λ = 254 nm; t_{major} = 33.8 min, t_{minor} = 36.2 min.

(*S*)-1-(3-(naphthalen-2-yl)-3-oxopropyl)-2-oxocyclohexane-1-carbonitrile (**12bi**)[4]. Colorless oil, 46.0 mg, 60% yield (92% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ =1.79-1.98 (m, 3H), 2.05-2.16 (m, 3H), 2.39-2.44 (m, 1H), 2.46-2.59 (m, 2H), 2.87 (ddd, *J* = 5.6, 11.2, 13.5 Hz, 1H), 3.30 (ddd, *J* = 5.1, 10.7, 17.4 Hz, 1H), 3.43 (ddd, *J* = 5.2, 10.9, 17.5 Hz, 1H), 7.55-7.64 (m, 2H), 7.87-7.92 (m, 2H), 7.99 (d, *J* = 8.0 Hz, 1H), 8.04 (dd, *J* = 1.5, 8.6 Hz, 1H), 8.51(brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.0, 27.8, 28.3, 34.4, 39.2, 39.2, 51.2, 119.7, 123.7, 126.9, 127.8, 128.5, 128.6, 129.6, 129.9, 132.5, 133.7, 135.7, 198.0, 203.3; $[\alpha]^{27}_D$ = 54.6° (c 1.0, $CHCl_3$); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a CHIRALPAK IC column (hexane/*i*-PrOH = 90:10 at 0.8 mL/min); λ = 254 nm; t_{major} = 44.1 min, t_{minor} = 48.3 min.

2-benzoyl-2-methyl-5-oxo-5-phenylpentanenitrile (**12ca**)[4]. White solid, 36.1 mg, 62% yield (72% ee). mp 83-84 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ =1.80 (s, 3H), 2.32 (ddd, *J* = 5.0, 10.8, 14.2 Hz, 1H), 2.71 (ddd, *J* = 5.2, 10.7, 14.2 Hz, 1H), 3.16 (ddd, *J* = 5.1, 10.6, 17.5 Hz, 1H), 3.25 (ddd, *J* = 5.2, 10.8, 17.5 Hz, 1H),7.45-7.67 (m, 6H), 7.95-7.97 (m, 2H), 8.18-8.21 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.5, 32.3, 34.3, 45.4,121.6, 128.1, 128.7, 128.8, 129.4, 133.4, 133.9, 134.0, 136.4, 193.7, 197.8; $[\alpha]^{29}_D$ = -16.8° (c 0.5, $CHCl_3$); HRMS (ESI-TOF): Calcd for $C_{19}H_{18}NO_2$ $(M+Na)^+$: 292.1338, Found: 292.1327; Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a ChiralCel OJ-H column (hexane/*i*-PrOH = 90:10 at 1.0 mL/min); λ = 254 nm; t_{major} = 31.6 min, t_{minor} = 27.4 min.

(*S*)-2-oxo-1-(3-oxo-3-(thiophen-2-yl)propyl)cyclopentane-1-carbonitrile (**12ak**)[4]. White solid, 46.8 mg, 95% yield (92% ee). ^{1}H NMR (400 MHz, $CDCl_3$): δ =2.07-2.17 (m, 4H), 2.31 (ddd, *J* = 5.6, 9.3, 14.6 Hz, 1H), 2.44-2.53 (m, 3H), 3.17 (ddd, *J* = 5.8, 9.5, 17.4 Hz, 1H), 3.34 (ddd, *J* = 5.7, 9.5, 17.4 Hz, 1H), 7.16 (dd, *J* = 3.8, 4.9 Hz, 1H), 7.67 (dd, *J* = 1.1, 4.9 Hz, 1H), 7.80 (dd, *J* = 1.0,3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 28.0, 34.6, 35.2, 36.3, 47.9, 118.8, 128.3, 132.4, 134.1, 143.4, 190.8, 209.0; $[\alpha]^{27}_D$ = 8.9° (c 1.0, $CHCl_3$); Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a ChiralCel AD-H column (hexane/*i*-PrOH = 90:10 at 1.0 mL/min); λ = 254 nm; t_{major} = 24.4 min, t_{minor} = 22.4 min.

2-Oxo-1-(4-oxo-4-phenylbutan-2-yl)cyclopentane-1-carbonitrile (**12al**). White solid, 12.5 mg, 24% yield, diastereomeric ratio (56:44) (7% ee, 60% ee). Major isomer; ^{1}H NMR (400 MHz, $CDCl_3$): δ =1.16

(d, J = 6.7 Hz, 3H), 2.04-2.21 (m, 2H), 2.24-2.31 (m, 1H), 2.39-2.47 (m, 3H), 2.72-2.80 (m, 1H), 2.95 (dd, J = 7.9, 17.8 Hz, 1H), 3.68 (dd, J = 4.2, 17.8 Hz, 1H), 7.46-7.49 (m, 2H), 7.56-7.60 (m, 1H), 7.97 (d, J = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.9, 19.0, 31.7, 33.5, 36.9, 41.1, 52.8, 118.3, 128.1, 128.7, 133.4, 136.7, 198.1, 209.5; $[\alpha]^{26}_D$ = -1.2° (c 0.2, $CHCl_3$); mp 83-85 °C; HRMS (ESI-TOF):Calcd for $C_{16}H_{17}NO_2Na$ $(M+Na)^+$: 278.1157, Found: 278.1152. Minor isomer; ^{1}H NMR (400 MHz, $CDCl_3$): δ =1.17 (d, J = 6.7 Hz, 3H), 2.08-2.20 (m, 3H), 2.36-2.45 (m, 2H), 2.50-2.58 (m, 1H), 2.80 (dt, J = 6.60, 13.1 Hz, 1H), 3.09 (d, J = 6.4 Hz, 2H), 7.48-7.51 (m, 2H), 7.58-7.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2, 19.0, 32.1, 32.9, 37.1, 41.7, 53.2, 118.4, 128.2, 128.8, 133.6, 136.6, 197.7, 208.7; $[\alpha]^{27}_D$ = -21.2° (c 0.2, $CHCl_3$); mp 87-89 °C; HRMS (ESI-TOF):Calcd for $C_{16}H_{17}NO_2Na$ $(M+Na)^+$: 278.1157, Found: 278.1155. Enantiomeric excess of the product was determined by chiral stationary phase HPLC analysis using a ChiralCel OJ-H column (hexane/*i*-PrOH = 90:10 at 1.0 mL/min); λ = 220 nm; Major isomer; t_{major} = 30.7 min, t_{minor} = 62.6 min, Minor isomer; t_{major} = 58.0 min, t_{minor} = 76.0 min.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.
Spectra data, and copies of all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work was supported by JSPS KAKENHI Grant Number 16K08178. The authors would like to thank Enago (www.enago.jp) for the English language review.

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