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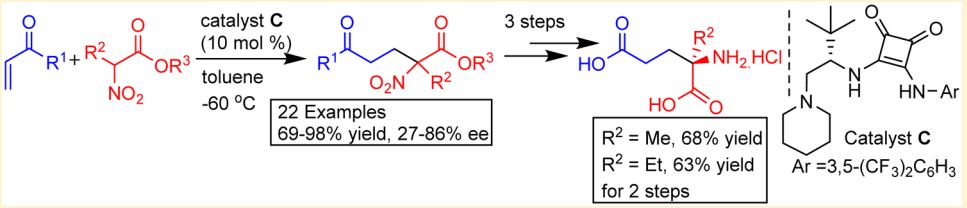
Enantioselective Synthesis of Quaternary α-Amino Acids via L-*tert*-Leucine-Derived Squaramide-Catalyzed Conjugate Addition of α-Nitrocarboxylates to Enones

Kalisankar Bera, Nishikant S. Satam, and Irishi N. N. Namboothiri*

Department of Chemistry, Indian Institute of Technology Bombay, Mumbai 400 076, India

Supporting Information



ABSTRACT: Enantioselective Michael addition of tertiary α-nitroesters to β-unsubstituted vinyl ketones has been carried out in the presence of an L-*tert*-leucine-derived squaramide as organocatalyst. The products, quaternary α-nitroesters, were formed in excellent yield and moderate to good ee's in most cases. Scale-up of the reaction and synthetic applications of the products, including transformation to representative quaternary α-amino acids, have also been demonstrated.

Quaternary α-amino acids are considerably resistant to chemical and enzymatic degradation due to their conformational and configurational stability and are useful building blocks in the synthesis of novel peptides and proteins possessing well-defined biological properties.[1] Quaternary α-amino acids were found to be mechanism-based inhibitors of pyridoxal phosphate-dependent enzymes and an integral part of bioactive natural products sphingofungins E and F, myriocin and altemicidin, to name a few (Figure 1).[2]

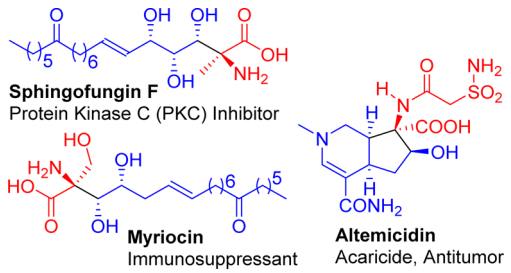


Figure 1. Quaternary α-amino acid containing bioactive natural products.

Approaches to enantioenriched quaternary α-amino acids include resolution, chiral auxiliary based, and catalytic asymmetric synthesis.[3−6] Catalytic asymmetric approaches involving α-alkylation of tertiary α-amino/iminocarboxylates, addition of C-centered nucleophiles to ketimines, α-amination of tertiary α-carboxylates, and addition of tertiary α-nitrocarboxylates to various Michael acceptors have been reviewed recently.[6]

Among the above approaches, α-functionalization of tertiary α-nitrocarboxylates via 1,4-addition, 1,2-addition and alkylation in the presence of suitable chiral catalysts is a convenient means of generating enantioenriched quaternary α-amino acids.[6] As for 1,4-addition, catalytic asymmetric addition of α-nitrocarboxylates to enones,[7−9] enamides,[10] nitroalkenes,[11] vinyl phosphonates,[12] vinyl sulfones,[13] and azodicarboxylates[14] afforded the corresponding quaternary α-amino acids or their precursors. Addition of α-nitrocarboxylates to β-unsubstituted enones has been reported to take place in the presence of (*R*)-ALB, resulting in the adducts with low to moderate ee (5−80%) with only two products possessing >50% ee and in the presence of peptides delivering just two products with 0 and 50% ee.[7] A similar reaction in the presence of a quinine-derived catalyst led to the adduct in 90% ee for which a single example exists in the literature.[8] Isolated examples for the reaction of β-substituted enones with α-nitrocarboxylate in the presence of chiral thiourea catalysts giving products with moderate to good enantioselectivities and with an α-fluoro-α-nitrocarboxylate in the presence of cinchoninamine providing the products in moderate diastereoselectivities but excellent enantioselectivities have also been reported.[9]

Recently, we reported the enantioselective synthesis of quaternary α-aminophosphonates[15−17] and α-nitrosulfones[18,19] via conjugate addition of tertiary α-nitrophosphonates and α-nitrosulfones, respectively, to various Michael acceptors such as enones, vinyl sulfones, and acrylates. While cinchona-derived thiourea and squaramide catalysts turned out to be very effective in most cases,[15−18] an amino acid (L-*tert*-leucine) derived squaramide was the catalyst of choice for the conjugate addition of nitrosulfones to acrylates and acrylamides.[19] In

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continuation of our efforts, we intended to investigate the synthesis of quaternary α-amino acids or their precursors via conjugate addition of tertiary α-nitrocarboxylates to β-unsubstituted enones. This is also because of the limited success encountered in such reactions earlier in terms of enantioselectivity and substrate scope.

We envisioned that organocatalysts possessing a chiral Broensted basic core, a tertiary amine, and a Brönsted acid appendage such as thiourea[20] or squaramide[21] which proved their efficiency in recent years and in our own recent endeavors would be suitable for the above purpose. To our knowledge, there are only two reports for the application of amino acid derived squaramide in asymmetric reactions.[19,22]

We began our experiments by treating *p*-tolyl α-nitropropanoate **2a** as the nucleophile with enone **1a** as the Michael acceptor in the presence of 10 mol % of quinine−squaramide **C1** as the catalyst in toluene at −60 °C (Figure 2 and Table 1).

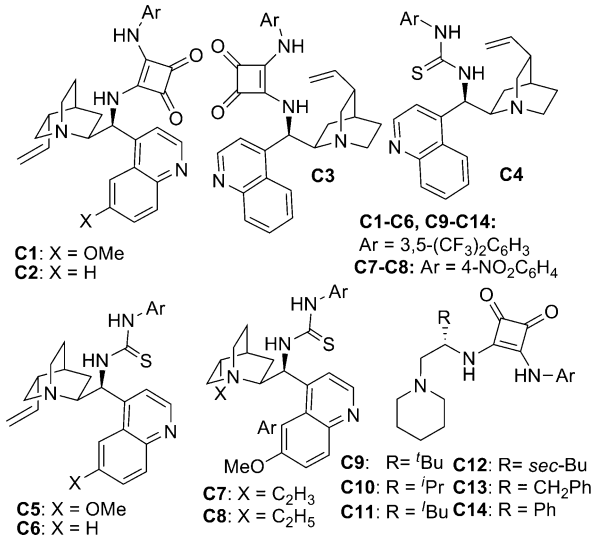
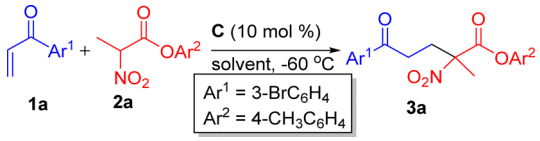


Figure 2. Catalysts screened.

The desired Michael adduct **3a** was isolated in excellent yield (94%) and good enantioselectivity (76% ee, entry 1). Later, several cinchona-based squaramides **C2**−**C3**, thioureas **C4**−**C8**, and amino acid derived squaramides **C9**−**C14** were screened as organocatalysts for the reaction between enone **1a** and nitroester **2a** in toluene at −60 °C (Figure 2 and Table 1, entries 2−14). Though all the squaramide and thiourea catalysts were quite effective in providing the Michael adduct **3a** in excellent yield (≥90%), the enantioselectivities were only moderate to good in most cases (53−79% ee, entries 2−8 and 10−14). However, with *tert*-leucine-derived squaramide **C9** as the catalyst, the Michael adduct **3a** was isolated in excellent yield (95%) and good ee (82%, entry 9). In order to further improve the enantioselectivity, other reaction parameters such as temperature and solvent were evaluated (entries 15−19). Although the reaction was complete in 12 h at higher temperature (−25 °C), the selectivity dropped to 78% ee (entry 15). At this juncture, possible enhancement of enantioselectivity by screening other solvents such as xylene, mixture of mesitylene and xylene, dichloromethane, and THF was attempted in the presence of 10 mol % of *tert*-leucine−squaramide **C9** (entries 16−19). This resulted in the formation of the Michael adduct **3a** with moderate to good enantioselectivity (50−76% ee, entries 16−19). Thus, 10 mol % of *tert*-leucine-derived squaramide **C9** as the catalyst in toluene at −60 °C turned out to be the optimal conditions for our reaction (Table 1, entry 9).

Table 1. Catalyst Screening and Solvent Optimization

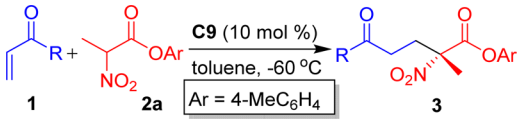


entry	C[a]	solvent	time (h)	% yield[b]	% ee[c]
1	**C1**	toluene	15	94	76
2	**C2**	toluene	15	93	73
3	**C3**	toluene	15	90	53[d]
4	**C4**	toluene	15	94	79
5	**C5**	toluene	15	92	74[d]
6	**C6**	toluene	15	94	76
7	**C7**	toluene	15	91	70
8	**C8**	toluene	15	91	76
9	**C9**	**toluene**	**18**	**95**	**82**
10	**C10**	toluene	18	93	76
11	**C11**	toluene	18	94	65
12	**C12**	toluene	18	94	78
13	**C13**	toluene	18	92	66
14	**C14**	toluene	18	92	67
15[e]	**C9**	toluene	12	94	78
16	**C9**	xylene	18	94	76
17	**C9**	mesitylene: xylene[f]	18	94	68
18	**C9**	CH_2Cl_2	18	90	67
19	**C9**	THF	18	92	50

[a]Catalyst. [b]After silica gel column chromatography. [c]ee determined by chiral HPLC. [d]Opposite enantiomer. [e]Reaction performed at −25 °C. [f]Ratio 85:15.

Having optimized the reaction conditions, the scope of enones **1** and nitroesters **2** was investigated (Tables 2−4). At

Table 2. Scope of Enones 1



entry	**1**, R	**3**	time (h)	% yield[a]	% ee[b]
1	**1a**, 3-BrC_6H_4	**3a**	18	95	82
2	**1b**, 4-BrC_6H_4	**3b**	20	97	75
3	**1c**, 4-ClC_6H_4	**3c**	20	94	77
4	**1d**, 2-ClC_6H_4	**3d**	20	97	35
5	**1e**, 4-CNC_6H_4	**3e**	15	90	74
6	**1f**, 4-$NO_2C_6H_4$	**3f**	15	88	69
7	**1g**, Ph	**3g**	25	94	72
8[c]	**1h**, 4-MeC_6H_4	**3h**	25	85	75
9	**1i**, 4-$OMeC_6H_4$	**3i**	30	97	76
10	**1j**, 2-Naphthyl	**3j**	20	95	71
11	**1k**, 2-thienyl	**3k**	24	89	68
12	**1l**, Styrenyl	**3l**	25	91	73
13	**1m**, *c*-C_6H_{11}	**3m**	40	69	37
14	**1n**, CH_3	**3n**	72	76	27

[a]After silica gel column chromatography. [b]ee determined by chiral HPLC. [c]Also performed on gram scale between **1h** (9.3 mmol, 1.357 g) and **2a** (6.2 mmol, 1.297 g) in the presence of **C9** (5 mol %) at −60 °C to afford **3h** in 82% (1.810 g) yield and 75% ee.

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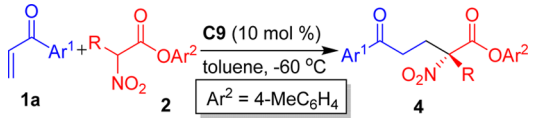
first, taking nitroester **2a** as the representative Michael donor, various substituted enones **1a−m** have been screened, and the results are summarized in Table 2. In general, the reactions were complete in 15−30 h to afford the quaternary α-nitrocarboxylates **3** in very good to excellent yields (85−97%) and moderate to good enantioselectivities (68−82%). However, longer reaction time (40−72 h) and moderate yield (69−76%) and low ee (27−37%) were encountered in the case of products **3m,n**, which resulted from alkyl vinyl ketones **1m,n** (entries 13 and 14). The ee was low (35%), despite excellent yield (97%) for product **3d** as well, which resulted from *ortho*-substituted aryl vinyl ketone **1d** (entry 4). There was no major substituent effect as enones bearing weakly and strongly electron-withdrawing groups **1a−c** and **1e,f**, respectively, reacted equally well with nitroester **2a** to afford the products **3a−c** and **3e,f** in 88−97% yield and 69−82% ee (entries 1−3, 5, and 6). Similarly, enones bearing electroneutral and weakly and strongly electron-donating substituents **1g−i**, respectively, afforded the products **3g−i** in excellent yield (85−97%) and good selectivity (72−76% ee, entries 7−9). Representative examples of fused aryl, heteroaryl, and styrenyl enones, **1j−l**, respectively, also reacted well with nitroester **2a** to deliver the products **3j−l** in 89−95% yield and 68−73% ee (entries 10−12). Notably, the reaction between dienone **1l** and nitroester **2a** was 100% regioselective in that **2a** reacted selectively with the β-unsubstituted olefin moiety in the presence of β-substituted olefin moiety in dienone **1l** and furnished the Michael adduct **3l** in 91% yield and 73% ee (entry 12). To evaluate the practical utility of the asymmetric Michael addition of α-nitrocarboxylate **2** to enone **1**, a reaction of representative substrates **2a** with **1h** was performed on gram scale (entry 8). Gratifyingly, the desired Michael adduct **3h** was formed in 82% yield (1.810 g) and 75% ee even with 5 mol % of catalyst **C9**.

Subsequently, the scope of α-nitrocarboxylates **2** was investigated with a representative enone **1a** (Table 3). Thus,

Table 3. Scope of α-Alkyl Group in Nitroesters 2



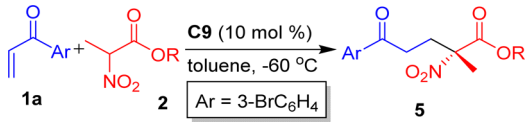
entry	2, R	Ar^1	4	time (d)	% yield[a]	% ee[b]
1	**2b**, Et	3-BrC_6H_4	**4a**	2	87	83
2	**2c**, *n*-Pr	3-BrC_6H_4	**4b**	3	92	86
3	**2d**, *n*-Bu	3-BrC_6H_4	**4c**	3	94	83
4	**2e**, *i*-Pr	3-BrC_6H_4	**4d**	4	88	69
5	**2b**, Et	4-MeC_6H_4	**4e**	3	85	77

[a]After silica gel column chromatography. [b]ee determined by chiral HPLC.

α-nitrocarboxylates bearing a linear alkyl chain reacted smoothly with enone **1a** to furnish quaternary α-nitrocarboxylates **4a−c** in high yields (87−94%) and good enantioselectivities (83−86%, entries 1−3). However, α-nitrocarboxylate **2e** bearing a branched alkyl chain provided the desired Michael adduct **4d** only in moderate enantioselectivity (69% ee) albeit in very good yield (88%, entry 4).

Further scope of nitroester **2** was investigated by changing the ester group from *p*-tolyl to other representative aryl (*o*-tolyl), arylalkyl (Bn), and alkyl (Et) groups (Table 4). While the yields in these cases remained consistently excellent (93−98%), the enantioselectivities varied appreciably (43−78%).

Table 4. Scope of Ester Group in Nitroesters 2



entry	2, R	5	time (h)	% yield[a]	% ee[b]
1	**2f**, 2-MeC_6H_4	**5a**	18	93	78
2	**2g**, Bn	**5b**	18	97	61
3	**2h**, Et	**5c**	24	98	43

[a]After silica gel column chromatography. [b]ee determined by chiral HPLC.

For instance, as in the case of most of the entries in Tables 2 and 3, aryl ester **2f** furnished the product **5a** with good enantioselectivity (78%, entry 1). On the other hand, the ee dropped to 61% in the case of benzyl ester **5b** (entry 2) and 43% in the case of alkyl ester **5c** (entry 3).

In the proposed mechanism, the nitrocarboxylate **2**, after deprotonation by the piperidine moiety of the catalyst **C9**, is stabilized by the squaramide moiety through H-bonding. At the same time, the protonated piperidine activates the enone **1** by hydrogen bonding giving rise to the favored transition state (Figure 3). Michael addition of the stabilized nitronate **2**

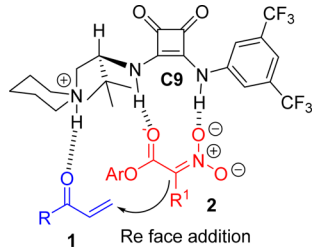


Figure 3. Proposed transition state.

through its *Re* face to the activated enone **1** delivers the desired conjugate adduct **3**, **4**, or **5** in enantioenriched form and regenerates the catalyst **C9**.[23]

Finally, the synthetic applications of the products were demonstrated using representative quaternary α-nitroesters **3h** and **4e** (Scheme 1). Baeyer−Villiger oxidation of **3h** and **4e** provided the nitrodiesters **6a,b** in excellent (84−92%) yield. Treatment of diesters **6a** with excess (4 equiv) benzylamine in THF under reflux led to the formation of diamide **8** again in 92% yield. On the other hand, while attempts to synthesize monoamide using 1.2 equiv of benzylamine, under otherwise identical conditions, furnished a mixture of **7** and **8**, selective synthesis of cyclic imide **7** in 62% yield could be achieved by carrying out the reaction in toluene under reflux. The nitroimide **7** was further subjected to reduction using Zn/HCl at room temperature to afford aminoimide **9** in 85% yield. It may be noted that the enantioselectivities remained similar within experimental error for all these compounds. More importantly, the diesters **6a,b** were transformed in one pot to their amino acids **11a,b**, as their hydrochloride salts, via base-mediated hydrolysis followed by nitro group reduction using Zn/HCl in 63−68% overall yields for two steps.

The absolute configuration of **3h** was assigned as *R* based on its conversion to (*R*)-2-methylglutamic acid **11a** (Scheme 1). The absolute configuration of other analogues was assigned by analogy.

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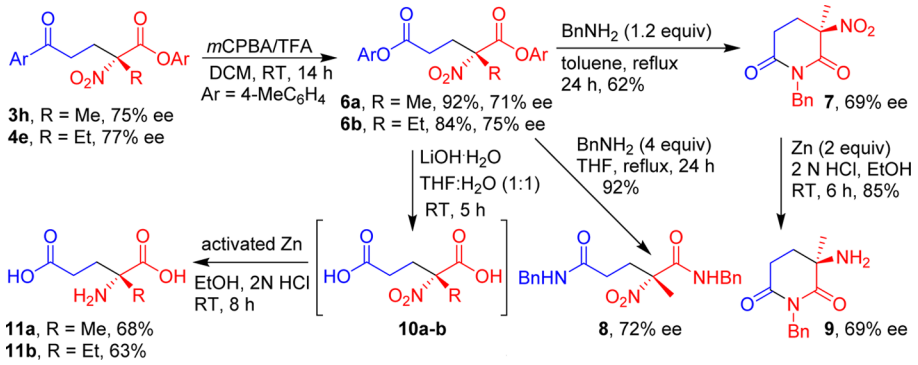
Scheme 1. Synthetic Applications of the Michael Adducts



In conclusion, we have developed the first general and efficient method for the enantioselective Michael addition of α-nitrocarboxylates to various α-unsubstituted vinyl ketones in the presence of a *tert*-leucine-derived squaramide organocatalyst. The conjugate adducts, quaternary α-nitroesters, were isolated in high yields and moderate to good enantioselectivities in most cases. The feasibility of scale up of the enantioselective conjugate addition without any appreciable drop in yield and selectivity and transformation of the products to quaternary α-amino acids and cyclic quaternary α-amino imides have been successfully demonstrated. Design and synthesis of more efficient chiral organocatalysts that would further improve the enantioselectivities will be part of our future endeavors.

EXPERIMENTAL SECTION

General Methods. The melting points recorded are uncorrected. NMR spectra (^{1}H and ^{1}H decoupled ^{13}C) were recorded with TMS as the internal standard. The coupling constants (J values) are given in hertz (Hz). High-resolution mass spectra were recorded under ESI Q-TOF conditions. Enantioselectivities were determined using chiral HPLC equipped with a PDA-detector. Specific rotations were measured for solutions of samples of known concentrations in a suitable solvent using a polarimeter equipped with a sodium vapor lamp. Catalysts **C1**−**C11** were prepared by literature methods.[24,25] Bromoesters **14a**−**g** and nitroesters **2a**−**g** are new and were prepared by a general procedure reported in the literature.[26] Nitroester **2h** and its precursor bromoester **14h**[26] as well as enones **1a**−**n**[27] are known compounds.

General Procedure for the Preparation of Catalysts C12−14. To a solution of 3-methoxy-4-(arylamino)cyclobut-3-ene-1,2-dione **15** (1.017 g, 3.00 mmol) in dry DCM (15 mL) was slowly added a solution of amine **16**[25] (3.00 mmol) in dry DCM (10 mL) at rt. The reaction mixture was stirred for 4 h, and the resulting precipitate was isolated by filtration. The residue was washed with ether (10 mL) and dried in vacuo to afford catalyst **C** as a white solid.

*3-(3,5-Bis(trifluoromethyl)phenylamino)-4-((2S,3R)-3-methyl-1-(piperidin-1-yl)pentan-2-ylamino)cyclobut-3-ene-1,2-dione (**C12**):* colorless solid; yield 1.208 g, 82%; mp 215−216 °C; IR (film, cm^{-1}) 3200 (m), 3150 (m), 2939 (vs), 2790 (w), 1799 (s), 1663 (s), 1583 (vs), 1456 (vs), 1379 (vs), 1327 (w), 1276 (vs), 1183 (s), 1170 (m), 1129 (s), 942 (m), 882 (m), 748 (m); ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.87 (t, overlaps with d, J = 8.2 Hz, 3H), 0.88 (d, overlaps with t, J = 7.2 Hz, 3H), 1.05−1.19 (m, 1H), 1.23−1.52 (m, 7H), 1.53−1.65 (m, 1H), 2.12−2.27 (unresolved m, 2H), 2.29−2.40 (m, 2H), 2.39−2.50 (m, 2H), 4.15 (br unresolved, 1H), 7.50−7.65 (br unresolved, 2H), 8.04 (s, 2H), 10.07 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 11.3, 15.2, 23.9, 24.2, 25.7, 37.6, 54.4, 56.2, 60.4, 114.5, 117.9, 123.2 (q, J_{C-F} = 271.0 Hz), 131.4 (q, J_{C-F} = 33.0 Hz), 141.2, 161.8, 170.4, 180.2, 184.6; MS (ES+, Ar) m/z (rel intensity) 493 ([MH + 1]$^+$, 21), 492 ([MH]$^+$, 100); HRMS (ES+, Ar) calcd for $C_{23}H_{28}F_6N_3O_2$ (MH$^+$, 100) 492.2083, found 492.2080; $[\alpha]^{25}_D$ +7.03 (c 0.5, acetone).

*(S)-3-(3,5-Bis(trifluoromethyl)phenylamino)-4-(1-phenyl-3-(piperidin-1-yl)propan-2-ylamino)cyclobut-3-ene-1,2-dione (**C13**):* colorless solid; yield 1.024 g, 65%; mp 248−250 °C; IR (film, cm^{-1}) 3180 (m), 3140 (m), 3026 (w), 2940 (s), 1800 (s), 1661 (s), 1575 (vs), 1463 (vs), 1377 (vs), 1280 (vs), 1223 (w), 1189 (s), 1130 (s), 944 (w), 884 (m), 749 (m); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.25−1.35 (m, 2H), 1.36−1.46 (m, 4H), 2.19−2.32 (br unresolved, 2H), 2.34−2.47 (m, 4H), 2.76 (ABqd, J = 13.8, 8.3 Hz, 1H), 2.94 (ABqd, J = 13.8, 5.0 Hz, 1H), 4.47 (br unresloved, 1H), 7.11−7.32 (m, 5H), 7.60 (s overlap with br s, 1H), 7.61 (br s overlap with singlet, 1H), 8.00 (s, 2H), 10.09 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.9, 25.6, 53.7, 54.4, 62.7, 114.7, 118.0, 123.2 (q, J_{C-F} = 271.0 Hz), 126.4, 128.4, 129.3, 131.4 (q, J_{C-F} = 34.0 Hz), 137.8, 141.1, 161.9, 170.0, 180.2, 184.5; MS (ES+, Ar) m/z (rel intensity) 527 ([MH + 1]$^+$, 36), 526 ([MH]$^+$, 100); HRMS (ES$^+$, Ar) calcd for $C_{26}H_{26}F_6N_3O_2$ (MH$^+$, 100) 526.1924, found 526.1923; $[\alpha]^{25}_D$ −49.65 (c 0.5, DMSO).

*(S)-3-(3,5-Bis(trifluoromethyl)phenylamino)-4-(1-phenyl-2-(piperidin-1-yl)ethylamino)cyclobut-3-ene-1,2-dione (**C14**):* colorless solid; yield 1.196 g, 78%; mp 230−233 °C; IR (film, cm^{-1}) 3205 (s), 3032 (w), 2938 (vs), 2855 (w), 2791 (w), 1797 (vs), 1667 (s), 1575 (vs), 1455 (vs), 1376 (vs), 1330 (m), 1274 (vs), 1174 (s), 1124 (s), 997 (w), 941 (m), 884 (m), 746 (w), 728 (w), 698 (m), 683 (w); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.29−1.38 (m, 2H), 1.38−1.50 (m, 4H), 2.35 (br unresolved, 2H), 2.50−2.63 (m, 3H), 2.73−2.82 (m, 1H), 5.36 (br unresloved, 1H), 7.28−7.34 (br m, 1H), 7.36−7.41 (m, 4H), 7.65 (s, 1H), 8.04 (s, 2H), 8.16 (br s, 1H), 10.19 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.8, 25.5, 54.1, 55.6, 64.2, 114.7, 118.1, 123.2 (q, J_{C-F} = 271.0 Hz), 126.5, 127.7, 128.7, 131.3 (q, J_{C-F} = 33.0 Hz), 140.6, 141.0, 162.3, 169.6, 180.5, 184.5; MS (ES+, Ar) m/z (rel intensity) 513 ([MH + 1]$^+$, 36), 512 ([MH]$^+$, 100), 293 (5), 217 (7); HRMS (ES$^+$, Ar) calcd for $C_{25}H_{24}F_6N_3O_2$ (MH$^+$, 100) 512.1767, found 512.1766; $[\alpha]^{26}_D$ −17.08 (c 0.5, acetone).

Preparation of 2-Bromoesters 14.[26] To a stirred solution of 2-bromocarboxylic acid **12** (23.0 mmol) was added oxalyl chloride (4.0 mL, 46.0 mmol) slowly, and the reaction mixture was stirred for 2 h at 60 °C. Then the excess oxalyl chloride was removed by distillation, and the desired 2-bromo acid chloride **13** was isolated. Pyridine (1.89 mL, 23.5 mmol) was added dropwise at −10 °C to the stirred solution of 2-bromo acid chloride **13** (19.5 mmol) and phenol or benzyl alcohol (17.5 mmol) in toluene (50 mL). The reaction mixture was stirred overnight. After the completion of the reaction (as monitored by TLC), the mixture was diluted with ice−water (100 mL). The aqueous layer was extracted with toluene (2 × 50 mL). The combined organic layer was washed with water (50 mL) and dried over anhyd sodium sulfate. The solvent was removed in vacuo, and the crude 2-bromoester **14** was purified by silica gel column chromatography using ethyl acetate−petroleum ether (4%) as eluent.

*p-Tolyl 2-bromopropanoate (**14a**):* colorless liquid; yield 3.201 g, 78%; IR (neat, cm^{-1}) 2927 (w), 1739 (vs), 1615 (w), 1514 (s), 1448 (m), 1339 (w), 1242 (m), 1198 (m), 1167 (w), 1073 (w), 985 (w), 818 (s), 509 (w); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.97 (d, J = 6.9 Hz, 3H), 2.39 (s, 3H), 4.63 (q, J = 6.9 Hz, 1H), 7.04 (d, J = 8.3 Hz, 2H), 7.15 (d, J = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 21.6,

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39.9, 120.8, 130.2, 136.1, 148.4, 169.1; MS (ES+, Ar) m/z (rel intensity) 268 ([MNa + 3]$^+$, 10), 267 ([MNa + 2]$^+$, 97), 266 ([MNa + 1]$^+$, 10), 265 ([MNa]$^+$, 100), 221 (75), 223 (15); HRMS (ES+, Ar) calcd for $C_{10}H_{11}BrO_2Na$ (MNa^+, 100) 264.9835, found 264.9831.

*p-Tolyl 2-bromobutanoate (**14b**):* colorless liquid; yield 3.701 g, 70%; IR (neat, cm^{-1}) 2959 (s), 2928 (vs), 2859 (m), 1760 (vs), 1507 (w), 1254 (w), 1222 (w), 1198 (m), 1166 (w), 1133 (w), 1108 (w), 1019 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, J = 7.3 Hz, 3H), 2.17 (dquin, J = 14.7, 7.3 Hz, 1H), 2.29 (dquin, J = 14.7, 7.3 Hz, 1H), 2.39 (s, 3H), 4.40 (t, J = 7.3 Hz, 1H), 7.03 (d, J = 8.3 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 21.1, 28.5, 47.4, 120.9, 130.2, 136.1, 148.4, 168.6; MS (ES+, Ar) m/z (rel intensity) 282 ([MNa + 3]$^+$, 11), 281 ([MNa + 2]$^+$, 99), 280 ([MNa + 1]$^+$, 11), 279 ([M + Na]$^+$, 100), 275 (15), 259 (15); HRMS (ES+, Ar) calcd for $C_{11}H_{13}BrO_2Na$ (MNa^+, 100) 278.9991, found 278.9998.

*p-Tolyl 2-bromopentanoate (**14c**):* colorless liquid; yield 3.999 g, 73%; IR (neat, cm^{-1}) 2928 (vs), 2859 (m), 1760 (vs), 1508 (w), 1464 (w), 1251 (w), 1198 (m), 1166 (w), 1133 (w), 1105 (w), 1019 (m), 813 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (t, J = 7.4 Hz, 3H), 1.44−1.56 (m, 1H), 1.56−1.68 (m, 1H), 2.04−2.25 (m, 2H), 2.36 (s, 3H), 4.44 (t, J = 7.9 Hz, 1H), 7.01 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 20.8, 21.0, 36.8, 45.6, 120.9, 130.1, 136.1, 148.4, 168.7; MS (ES+, Ar) m/z (rel intensity) 296 ([MNa + 3]$^+$, 14), 295 ([MNa + 2]$^+$, 97), 280 ([MNa + 1]$^+$, 14), 279 ([M + Na]$^+$, 100), 285 (14), 249 (10); HRMS (ES+, Ar) calcd for $C_{12}H_{15}BrO_2Na$ (MNa^+, 100) 293.0148, found 293.0146.

*p-Tolyl 2-bromohexanoate (**14d**):* colorless liquid; yield 4.299 g, 78%; IR (neat, cm^{-1}) 2956 (vw), 1742 (vs), 1498 (w), 1447 (m), 1380 (w), 1336 (m), 1270 (m), 1218 (m), 1156 (s), 1072 (w), 993 (w), 948 (vw), 752 (m), 698 (w), 603 (vw); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, J = 7.0 Hz, 3H), 1.36−1.52 (m, 3H), 1.53−1.64 (m, 1H), 2.05−2.17 (m, 1H), 2.18−2.29 (m, 1H), 2.37 (s, 3H), 4.43 (t, J = 7.4 Hz, 1H), 7.02 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 21.0, 22.1,29.5, 34.6, 45.8, 120.9, 130.1, 136.0, 148.4, 168.7; MS (ES+, Ar) m/z (rel intensity) 310 ([MNa + 3]$^+$, 13), 309 ([MNa + 2]$^+$, 96), 308 ([MNa + 1]$^+$, 13), 307 ([M + Na]$^+$, 100), 281 (10), 263 (10); HRMS (ES+, Ar) calcd for $C_{13}H_{17}BrO_2Na$ (MNa^+, 100) 307.0304, found 307.0304.

*p-Tolyl 2-bromo-3-methylbutanoate (**14e**):* colorless liquid; yield 4.011 g, 73%; IR (neat, cm^{-1}) 2928 (vs), 1760 (vs), 1507 (w), 1464 (w), 1198 (m), 1166 (w), 1133 (w), 1019 (m), 813 (w), 509 (w); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (d, J = 6.6 Hz, 3H), 1.22 (d, J = 6.6 Hz, 3H), 2.38 (s overlaps with m, 3H), 2.36−2.45 (m overlaps with s, 1H), 4.26 (d, J = 8.1 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.2, 20.2, 21.1, 32.6, 54.3, 120.9, 130.2, 136.1, 148.4, 168.4; MS (ES+, Ar) m/z (rel intensity)) 296 ([MNa + 3]$^+$, 14), 295 ([MNa + 2]$^+$, 99), 294 ([MNa + 1]$^+$, 14), 293 ([M + Na]$^+$, 100), 281 (5); HRMS (ES+, Ar) calcd for $C_{12}H_{15}BrO_2Na$ (MNa^+, 100) 293.0148, found 293.0144.

*o-Tolyl 2-bromopropanoate (**14f**):* colorless liquid; yield 3.501 g, 74%; IR (neat, cm^{-1}) 3030 (w), 2982 (w), 2929 (w), 2866 (w), 1760 (vs), 1584 (vw), 1490 (w), 1462 (vw), 1445 (w), 1380 (vw), 1339 (m), 1246 (m), 1223 (s), 1173 (m), 1141 (s), 1111 (m), 1071 (vw), 1043 (w), 985 (vw), 942 (vw), 895 (vw), 840 (vw), 773 (m), 748 (s), 713 (w), 678 (vw), 532 (vw); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (d, J = 6.9 Hz, 3H), 2.24 (s, 3H), 4.63 (q, J = 6.9 Hz, 1H), 7.04 (dd, J = 7.9, 0.9 Hz, 1H), 7.13−7.30 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 21.8, 39.7, 121.5, 126.6, 127.2, 130.3, 131.5, 149.0, 168.7; MS (ES+, Ar) m/z (rel intensity) 268 ([MNa + 3]$^+$, 8), 267 ([MNa + 2]$^+$, 96), 266 ([MNa + 1]$^+$, 8), 265 ([M + Na]$^+$, 100), 243 (1), 221 (10); HRMS (ES+, Ar) calcd for $C_{10}H_{11}BrO_2Na$ (MNa^+, 100) 264.9835, found 264.9831.

*Benzyl 2-bromopropanoate (**14g**):* colorless liquid; yield 3.599 g, 76%; IR (neat, cm^{-1}) 3066 (vw), 3035 (vw), 2955 (vw), 2930 (vw), 2869 (vw), 1741 (vs), 1498 (vw), 1447 (m), 1380 (m), 1336 (m), 1270 (m), 1218 (m), 1155 (s), 1096 (w), 1072 (m), 1058 (m), 1029 (vw), 993 (w), 948 (vw), 916 (vw), 752 (m), 698 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.85 (d, J = 6.9 Hz, 3H), 4.41 (q, J = 6.9 Hz, 1H), 5.20 (s, 2H), 7.32−7.43 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 40.0, 67.6, 128.2, 128.5, 128.7, 135.2, 170.1; MS (ES+, Ar) m/z (rel intensity) 268 ([MNa + 3]$^+$, 9), 267 ([MNa + 2]$^+$, 99), 266 ([MNa + 1]$^+$, 9), 265 ([M + Na]$^+$, 100), 250 (5), 221 (3); HRMS (ES+, Ar) calcd for $C_{10}H_{11}BrO_2Na$ (MNa^+, 100) 264.9835, found 264.9839.

Preparation of Nitroesters 2.[26] To a stirred solution of $NaNO_2$ (0.945 g, 14.2 mmol) in DMSO (20 mL) was added phloroglucinol (1.034 g, 8.7 mmol) followed by 2-bromoester **14** (8.27 mmol) at 0 °C. After completion of the reaction (as monitored by TLC), the mixture was diluted with diethyl ether (50 mL) and ice−water (50 mL). The aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic layer was washed with water (50 mL) and dried over anhyd sodium sulfate. The solvent was removed in vacuo, and the crude 2-nitroester **2** was purified by silica gel coloumn chromatography using ethyl acetate and petroleum ether (8%) as eluent.

*p-Tolyl 2-nitropropanoate (**2a**):* colorless liquid; yield 1.249 g, 69%; IR (neat, cm^{-1}) 2926 (w), 1770 (vs), 1561 (vs), 1506 (m), 1450 (m), 1389 (w), 1359 (w), 1315 (w), 1194 (vs), 1175 (s), 1112 (w), 1084 (w), 1019 (w), 904 (w), 874 (w), 843 (w), 816 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.93 (d, J = 7.1 Hz, 3H), 2.36 (s, 3H), 5.41 (q, J = 7.1 Hz, 1H), 7.01 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 21.0, 83.3, 115.2, 120.7, 130.1, 130.3, 136.7, 147.8, 164.0; MS (ES+, Ar) m/z (rel intensity) 233 ([MNa + 1], 3), 232 ([MNa]$^+$, 100), 221 (1), 201 (1), 181 (1); HRMS (ES+, Ar) calcd for $C_{10}H_{11}NO_4Na$ (MNa^+, 100) 232.0580, found 232.0581.

*p-Tolyl 2-nitrobutanoate (**2b**):* colorless liquid; yield 1.299 g, 67%; IR (neat, cm^{-1}) 3037 (w), 2979 (s), 2944 (m), 2884 (w), 1770 (vs), 1561 (vs), 1507 (s), 1460 (m), 1439 (m), 1373 (w), 1289 (m), 1192 (vs), 1174 (vs), 1103 (m), 1091 (m), 962 (m), 841 (s), 812 (s), 790 (s), 510 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (d, J = 7.1 Hz, 3H), 2.29−2.55 (m overlaps with s, 2H), 2.38 (s, overlaps with m, 3H), 5.28 (dd, J = 8.8, 5.9 Hz, 1H), 7.01 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 21.1, 24.2, 89.4, 120.7, 130.3, 136.7, 147.8, 163.4; MS (ES+, Ar) m/z (rel intensity) 247 ([MNa + 1], 3), 246 ([MNa]$^+$, 53), 153 (100); HRMS (ES+, Ar) calcd for $C_{11}H_{13}NO_4Na$ (MNa^+) 246.0737, found 246.0739.

*p-Tolyl 2-nitropentanoate (**2c**):* colorless liquid; yield 1.499 g, 73%; IR (neat, cm^{-1}) 2927 (vs), 1771 (vs), 1564 (vs), 1508 (w), 1374 (w), 1265 (w), 1195 (m), 1170 (w), 1109 (m), 1020 (w), 804 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (t, J = 7.4 Hz, 3H), 1.46−1.59 (m, 2H), 1.99−2.31 (m, 1H), 2.35 (s, overlaps with m, 3H), 2.34−2.47 (m, overlaps with s, 1H), 5.32 (dd, J = 9.2, 5.8 Hz, 1H), 6.99 (d, J = 8.5 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.5, 19.2, 21.1, 32.4, 88.0, 120.7, 130.3, 136.7, 147.9, 163.5; MS (ES+, Ar) m/z (rel intensity) 260 ([MNa]$^+$, 100), 216 (49), 102 (10); HRMS (ES+, Ar) calcd for $C_{12}H_{15}NO_4Na$ (MNa^+, 100) 260.0893, found 260.0893.

*p-Tolyl 2-nitrohexanoate (**2d**).* colorless liquid; yield 1.511 g, 73%; IR (neat, cm^{-1}) 2927 (s), 1771 (s), 1564 (s), 1507 (vw), 1374 (vw), 1266 (vw), 1196 (w), 1169 (w), 1108 (w), 1019 (w), 803 (vw), 508 (vw); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, J = 7.1 Hz, 3H), 1.37−1.53 (m, 4H), 2.24−2.35 (m, 1H), 2.38 (s, overlaps with m, 3H), 2.36−2.48 (m, overlaps with s, 1H), 5.33 (dd, J = 9.1, 5.7 Hz, 1H), 7.02 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 21.0, 22.1, 27.8, 30.2, 88.2, 120.7, 130.3, 136.7, 147.9, 163.5; MS (ES+, Ar) m/z (rel intensity) 274 ([MNa]$^+$, 100), 164 (1), 132 (4); HRMS (ES+, Ar) calcd for $C_{13}H_{17}NO_4Na$ (MNa^+, 100) 274.1050, found 274.1043.

*p-Tolyl 3-methyl-2-nitrobutanoate (**2e**):* colorless liquid; yield 1.295 g, 63%; IR (neat, cm^{-1}) 2927 (vs), 1771 (vs), 1564 (vs), 1508 (w), 1374 (w), 1266 (w), 1196 (m), 1170 (w), 1109 (w), 1020 (w), 804 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (d, J = 6.9 Hz, 3H), 1.20 (d, J = 6.9 Hz, 3H), 2.35 (s, 3H), 2.73−2.86 (m, 1H), 5.12 (d, J = 8.9 Hz, 1H), 7.01 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 18.9, 21.0, 30.5, 93.5, 120.7, 130.3, 136.6, 147.8, 162.7; MS (ES+, Ar) m/z (rel intensity) 276 ([M+K]$^+$, 10), 260 ([M + Na]$^+$, 100), 216 (50), 132 (5), 102 (9); HRMS (ES+, Ar) calcd for $C_{12}H_{15}NO_4Na$ (MNa^+, 100) 260.0893, found 260.0892.

*o-Tolyl 2-nitropropanoate (**2f**):* colorless liquid; yield 1.299 g, 72%; IR (neat, cm^{-1}) 2982 (m), 1770 (vs), 1563 (vs), 1490 (m), 1449 (m), 1389 (m), 1360 (w), 1316 (w), 1222 (s), 1172 (vs), 1110 (m), 1084

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(w), 750 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96 (d, J = 7.1 Hz, 3H), 2.20 (s, 3H), 5.46 (q, J = 7.1 Hz, 1H), 7.05 (dd, J = 7.9, 1.7 Hz, 1H), 7.17−7.27 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 16.0, 83.2, 121.3, 127.1, 127.3, 130.1, 131.6, 148.6, 163.5; MS (ES+, Ar) m/z (rel intensity) 233 ([MNa + 1], 8), 232 ([MNa]$^+$, 100), 221 (4); HRMS (ES+, Ar) calcd for $C_{10}H_{11}NO_4Na$ (MNa$^+$, 100) 232.0580, found 232.0582.

*Benzyl 2-nitropropanoate (**2g**):* colorless liquid; yield 1.402 g, 78%; IR (neat, cm^{-1}) 3035 (w), 2965 (w), 1753 (vs), 1562 (vs), 1498 (w), 1455 (m), 1392 (w), 1361 (w), 1315 (w), 1267 (w), 1195 (m), 1121 (w), 1085 (w), 1027 (m), 874 (w), 751 (m), 698 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80 (d, J = 7.1 Hz, 3H), 5.24 (q, J = 7.1 Hz, 1H), 5.25 (s, 2H), 7.32−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 68.6, 83.3, 128.5, 128.9, 129.0, 134.4, 165.1; MS (ES+, Ar) m/z (rel intensity) 233 ([MNa + 1], 12), 232 ([MNa]$^+$, 100), 221 (20), 204 (22), 181 (31), 162 (45), 145 (32), 125 (10), 102 (14); HRMS (ES+, Ar) calcd for $C_{10}H_{11}NO_4Na$ (MNa$^+$, 100) 232.0580, found 232.0581.

General Procedure for the Addition of Nitroesters 2 to Enones 1. To a solution of nitroester **2** (0.5 mmol) and catalyst **C9** (24.55 mg, 0.05 mmol) in toluene (0.5 mL) was added enone **1** (0.75 mmol, dissolved in 0.5 mL toluene) at −60 °C. The reaction mixture was stirred at the same temperature and monitored by TLC. The solvent was evaporated in vacuo, and the residue was purified by silica gel column chromatography using EtOAc−petroleum ether (10−30%, gradient elution) as eluent to afford pure **3**, **4**, or **5**. All the fractions containing the product were combined, and the solvent was removed in vacuo in order to avoid any self-disproportionation of enantiomers (SDE) during column chromatography.[28]

*p-Tolyl (R)-5-(3-bromophenyl)-2-methyl-2-nitro-5-oxopentanoate (**3a**):* colorless solid; yield 200 mg, 95%; mp 77−78 °C; IR (film, cm^{-1}) 3040 (w), 2919 (w), 1771 (vs), 1694 (s), 1550 (s), 1506 (w), 1416 (vw), 1387 (vw), 1349 (w), 1311 (vw), 1251 (s), 1224 (m), 1204 (m), 1117 (m), 1068 (w), 914 (vw), 890 (vw), 778 (m), 683 (w), 556 (vw), 508 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.01 (s, 3H), 2.35 (s, 3H), 2.73, 2.80 (ABqdd, J = 12.6, 9.2, 5.9 Hz, 2H), 3.13, 3.20 (ABqdd, J = 15.0, 9.2, 5.9 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.35 (t, J = 7.9 Hz, 1H), 7.70 (ddd, J = 7.9, 1.8, 0.9 Hz, 1H), 7.87 (ddd collapsed to dt, J = 7.9, 1.4 Hz, 1H), 8.07 (dd collapsed to t, J = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 22.5, 30.9, 33.4, 92.2, 120.7, 123.3, 126.7, 130.3, 130.5, 131.2, 136.5, 136.7, 138.1, 147.9, 166.0, 196.1; MS (ES+, Ar) m/z (rel intensity) 445 ([MNa + 3]$^+$, 16), 444 ([MNa + 2]$^+$, 99), 443 ([MNa + 1]$^+$, 16), 442 ([MNa]$^+$, 100), 439 (24), 437 (24), 422(11), 420 (12); HRMS (ES+, Ar) calcd for $C_{19}H_{18}BrNO_5Na$ (MNa$^+$, 100) 442.0261, found 442.0261; $[\alpha]^{25}_D$ −8.49 (c 1.0, $CHCl_3$); HPLC Chiralcel OD-H (petroleum ether/i-PrOH = 90/10, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 22.0 min, t_R (minor) = 23.8 min; 82% ee.

*p-Tolyl (R)-5-(4-bromophenyl)-2-methyl-2-nitro-5-oxopentanoate (**3b**):* colorless solid; yield 204 mg, 97%; mp 86−88 °C; IR (film, cm^{-1}) 2921 (w), 1774 (vs), 1692 (vs), 1584 (w), 1551 (vs), 1507 (w), 1421 (vw), 1388 (m), 1348 (w), 1314 (w), 1249 (m), 1201 (m), 1162 (w), 1117 (m), 1064 (w), 989 (vw), 888 (vw), 802 (m), 786 (w), 755 (w); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.02 (s, 3H), 2.37 (s, 3H), 2.75, 2.81 (ABqdd, J = 15.0, 9.4, 5.7 Hz, 2H), 3.14, 3.22 (ABqdd, J = 17.7, 9.4, 5.7 Hz, 2H), 7.01 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.6 Hz, 2H), 7.84 (d, J = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 22.6, 31.1, 33.3, 92.3, 120.7, 128.9, 129.7, 129.7, 130.3, 132.3, 135.1, 136.7, 147.9, 166.0, 196.5; MS (ES+, Ar) m/z (rel intensity) 445 ([MNa + 3]$^+$, 19), 444 ([MNa + 2]$^+$, 100), 443 ([MNa + 1]$^+$, 19), 442 ([MNa]$^+$, 100), 437 (9); HRMS (ES+, Ar) calcd for $C_{19}H_{18}BrNO_5Na$ (MNa$^+$, 100) 442.0261, found 442.0261; $[\alpha]^{25}_D$ −11.68 (c 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 258 nm), t_R (major) = 27.4 min, t_R (minor) = 29.4 min; 75% ee.

*p-Tolyl (R)-5-(4-chlorophenyl)-2-methyl-2-nitro-5-oxopentanoate (**3c**):* colorless solid; yield 176 mg, 94%; mp 108−109 °C; IR (film, cm^{-1}) 2920 (vw), 1778 (vs), 1690 (vs), 1587 (w), 1572 (w), 1549 (vs), 1509 (m), 1389 (m), 1314 (vw), 1242 (s), 1209 (s), 1166 (w), 1116 (m), 1104 (w), 1091 (m), 979 (w), 889 (w), 804 (m), 788 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 3H), 2.35 (s, 3H), 2.72, 2.79 (ABqdd, J = 15.0, 9.1, 6.0 Hz, 2H), 3.12, 3.20 (ABqdd, J = 17.7, 9.1, 6.0 Hz, 2H), 6.99 (d, J = 8.5 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.89 (d, J = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 22.5, 31.0, 33.3, 92.3, 120.7, 129.2, 129.6, 130.3, 134.7, 136.7, 140.1, 147.9, 166.0, 196.3; MS (ES+, Ar) m/z (rel intensity) 400 ([MNa + 2]$^+$, 29), 399 ([MNa + 1]$^+$, 16), 398 ([MNa]$^+$, 100), 393 (11), 376 (25), 329 (8); HRMS (ES+, Ar) calcd for $C_{19}H_{18}ClNO_5Na$ (MNa$^+$, 100) 398.0766, found 398.0766; $[\alpha]^{25}_D$ −12.32 (c 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 258 nm), t_R (major) = 25.5 min, t_R (minor) = 27.4 min; 77% ee.

*p-Tolyl (R)-5-(2-chlorophenyl)-2-methyl-2-nitro-5-oxopentanoate (**3d**):* colorless oil; yield 182 mg, 97%; IR (neat, cm^{-1}) 2935 (m), 1768 (vs), 1703 (s), 1590 (w), 1553 (vs), 1507 (m), 1434 (w), 1389 (vw), 1347 (w), 1265 (m), 1240 (m), 1194 (vs), 1172 (s), 1115 (m), 1074 (w), 985 (vw), 805 (vw), 757 (s), 739 (s), 705 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.35 (s, 3H), 2.78 (ABqdd, J = 15.0, 8.0, 6.6 Hz, 2H), 3.17 (ABqdd, J = 18.0, 8.0, 6.6 Hz, 2H), 6.99 (d, J = 8.6 Hz, 2H), 7.19 (d, J = 8.6 Hz, 2H), 7.33 (ddd, J = 7.5, 6.3, 2.3 Hz, 1H), 7.37−7.44 (m, 2H), 7.48 (ddd, J = 7.5, 1.3, 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 22.3, 31.0, 37.6, 92.2, 120.7, 127.3, 129.2, 130.3, 130.8, 131.1, 132.3, 136.7, 138.7, 147.9, 166.0, 200.5; MS (ES+, Ar) m/z (rel intensity) 401 ([MNa + 3]$^+$, 6), 400 ([MNa + 2]$^+$, 32), 399 ([MNa + 1]$^+$, 19), 398 ([MNa]$^+$, 100), 393 (28), 376 (27), 329 (15); HRMS (ES+, Ar) calcd for $C_{19}H_{18}ClNO_5Na$ (MNa$^+$, 100) 398.0766, found 398.0765; $[\alpha]^{25}_D$ −4.64 (c 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 97/3, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 32.7 min, t_R (minor) = 34.4 min; 35% ee.

*p-Tolyl (R)-5-(4-cyanophenyl)-2-methyl-2-nitro-5-oxopentanoate (**3e**):* colorless solid; yield 165 mg, 90%; mp 75.5−77.5 °C; IR (film, cm^{-1}) 2926 (w), 2232 (w), 1768 (vs), 1696 (s), 1607 (vw), 1554 (vs), 1507 (m), 1459 (w), 1405 (w), 1390 (w), 1348 (w), 1292 (w), 1243 (m), 1194 (s), 1172 (m), 1116 (m), 1062 (vw), 1019 (vw), 992 (w), 846 (m), 808 (m), 737 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.00 (s, 3H), 2.34 (s, 3H), 2.72, 2.79 (ABqdd, J = 15.0, 9.1, 5.9 Hz, 2H), 3.17, 3.26 (ABqdd, J = 18.0, 9.1, 5.9 Hz, 2H), 6.98 (d, J = 8.3 Hz, 2H) 7.18 (d, J = 8.3 Hz, 2H), 7.76 (d, J = 8.6 Hz, 2H), 8.03 (d, J = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 22.6, 30.9, 33.7, 92.1, 116.9, 117.9, 120.6, 128.6, 130.3, 132.8, 136.8, 139.2, 147.8, 165.9, 196.2; MS (ES+, Ar) m/z (rel intensity) 390 ([MNa + 1]$^+$, 19), 389 ([MNa]$^+$, 100), 221 (9), 181 (9); HRMS (ES+, Ar) calcd for $C_{20}H_{18}N_2O_5Na$ (MNa$^+$, 100) 389.1108, found 389.1108; $[\alpha]^{25}_D$ −15.36 (c 1.0, $CHCl_3$); HPLC Chiral cell AD-H (petroleum ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 64.7 min, t_R (minor) = 55.2 min; 74% ee.

*p-Tolyl (R)-2-methyl-2-nitro-5-(4-nitrophenyl)-5-oxopentanoate (**3f**):* colorless solid; yield 170 mg, 88%; mp 94−95 °C; IR (film, cm^{-1}) 2925 (w), 1768 (s), 1697 (m), 1604 (w), 1555 (vs), 1528 (s), 1508 (m), 1389 (w), 1347 (s), 1319 (w), 1244 (m), 1194 (s), 1171 (m), 1116 (m), 1019 (vw), 991 (vw), 856 (m), 806 (w), 742 (m); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.01 (s, 3H), 2.35 (s, 3H), 2.74, 2.81 (ABqdd, J = 15.0, 9.2, 5.7 Hz, 2H), 3.21, 3.30 (ABqdd, J = 18.0, 9.2, 5.7 Hz, 2H), 6.99 (d, J = 8.3 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 8.10 (d, J = 8.9 Hz, 2H), 8.30 (d, J = 8.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 22.7, 31.0, 34.0, 92.1, 120.6, 124.1, 129.3, 130.3, 136.8, 140.7, 147.9, 150.7, 165.9, 196.1; MS (ES+, Ar) m/z (rel intensity) 410 ([MNa + 1]$^+$, 21), 409 ([MNa]$^+$, 100), 404 (14), 387 (3); HRMS (ES+, Ar) calcd for $C_{19}H_{18}N_2O_7Na$ (MNa$^+$, 100) 409.1006, found 409.1009; $[\alpha]^{25}_D$ −15.51 (c 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 90/10, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 60.7 min, t_R (minor) = 72.3 min; 69% ee.

*p-Tolyl 2-methyl-2-nitro-5-oxo-5-phenylpentanoate (**3g**):* colorless solid; yield 160 mg, 94%; mp 93−94 °C; IR (film, cm^{-1}) 3036 (vw), 2926 (w), 1775 (vs), 1688 (vs), 1598 (w), 1582 (w), 1550 (vs), 1506 (w), 1459 (w), 1421 (vw), 1389 (w), 1347 (vw), 1321 (vw), 1247 (m), 1210 (m), 1200 (m), 1186 (m), 1161 (w), 1118 (m), 1102 (w), 888 (w), 747 (m), 690 (w); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.02 (s, 3H), 2.37 (s, 3H), 2.78, 2.84 (ABqdd, J = 15.0, 9.2, 5.9 Hz, 2H),

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3.18, 3.24 (ABqdd, J = 17.6, 9.2, 5.9 Hz, 2H), 7.02 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 7.49 (t, J = 7.3 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.98 (d, J = 7.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 22.5, 31.1, 33.3, 92.4, 120.7, 128.2, 128.9, 130.3, 133.7, 136.4, 136.7, 148.0, 166.1, 197.5; MS (ES+, Ar) m/z (rel intensity) 364 ([MNa]$^+$, 100), 301 (15); HRMS (ES+, Ar) calcd for $C_{19}H_{19}NO_5Na$ (MNa^+, 100) 364.1155, found 364.1154; $[\alpha]^{25}_D$ −10.58 (c 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 27.4 min, t_R (minor) = 29.9 min; 72% ee.

*p-Tolyl (R)-2-methyl-2-nitro-5-oxo-5-p-tolylpentanoate (**3h**):* colorless solid; yield 151 mg, 85%; mp 101−102 °C; IR (film, cm^{-1}) 2925 (w), 1779 (s), 1682 (s), 1606 (w), 1552 (vs), 1510 (w), 1420 (w), 1389 (w), 1308 (vw), 1245 (m), 1214 (m), 1115 (w), 890 (w), 784 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 3H), 2.35 (s, 3H), 2.41 (s, 3H), 2.74, 2.81 (ABqdd, J = 15.0, 9.0, 6.2 Hz, 2H), 3.12, 3.19 (ABqdd, J = 17.4, 9.0, 6.2 Hz, 2H), 7.00 (d, J = 8.4 Hz, 2H) 7.19 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 21.8, 22.4, 31.1, 33.1, 92.4, 120.7, 128.3, 129.5, 130.3, 133.9, 136.6, 144.5, 147.9, 166.1, 197.1; MS (ES+, Ar) m/z (rel intensity) 379 ([MNa + 1]$^+$, 17), 378 ([MNa]$^+$, 100), 373 (11), 356 (21), 309(5); HRMS (ES+, Ar) calcd for $C_{20}H_{21}NO_5Na$ (MNa^+, 100) 378.1312, found 378.1315; $[\alpha]^{25}_D$ −11.25 (c 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 90/10, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 23.6 min, t_R (minor) = 25.5 min; 75% ee.

*p-Tolyl (R)-5-(4-methoxyphenyl)-2-methyl-2-nitro-5-oxopentanoate (**3i**):* colorless solid; yield 180 mg, 97%; mp 94−95 °C; IR (film, cm^{-1}) 2937 (w), 1778 (vs), 1679 (s), 1603 (s), 1577 (s), 1550 (vs), 1510 (m), 1424 (w), 1390 (w), 1313 (w), 1256 (vs), 1247 (vs), 1213 (s), 1179 (s), 1116 (m), 1061 (vw), 1034 (w), 892 (w), 808 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 3H), 2.35 (s, 3H), 2.74, 2.80 (ABqdd, J = 15.0, 9.1, 6.1 Hz, 2H), 3.09, 3.16 (ABqdd, J = 17.3, 9.1, 6.1 Hz, 2H), 3.87 (s, 3H), 6.94 (d, J = 8.9 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.94 (d, J = 8.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 22.4, 31.2, 32.8, 55.7, 92.5, 114.0, 120.7, 129.5, 130.3, 130.5, 136.6, 148.0, 163.9, 166.1, 196.0; MS (ES+, Ar) m/z (rel intensity) 395 ([MNa + 1]$^+$, 19), 394 ([MNa]$^+$, 100), 373 (8), 372 (40), 325 (7); HRMS (ES+, Ar) calcd for $C_{20}H_{21}NO_6Na$ (MNa^+, 100) 394.1261, found 394.1258; $[\alpha]^{25}_D$ −13.55 (c 1.0, $CHCl_3$); HPLC Chiral cell AD-H (petroleum ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 258 nm), t_R (major) = 39.3 min, t_R (minor) = 37.5 min; 76% ee.

*p-Tolyl (R)-2-methyl-5-(naphthalen-2-yl)-2-nitro-5-oxopentanoate (**3j**):* colorless solid; yield 186 mg, 95%; mp 117−118.2 °C; IR (film, cm^{-1}) 3060 (w), 2924 (w), 1778 (vs), 1681 (vs), 1628 (vw), 1596 (vw), 1548 (vs), 1508 (m), 1470 (vw), 1439 (vw), 1418 (vw), 1389 (w), 1352 (w), 1254 (m), 1240 (m), 1206 (m), 1185 (w), 1117 (m), 1062 (w), 866 (w), 825 (w), 814 (w), 798 (w), 745 (w); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.37 (s, 3H), 2.84, 2.90 (ABqdd, J = 15.0, 9.3, 5.8 Hz, 2H), 3.32, 3.38 (ABqdd, J = 17.4, 9.3, 5.8 Hz, 2H), 7.04 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 7.58 (t, J = 8.0 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 7.90 (d, partially overlaps with d, J = 8.0 Hz, 1H), 7.92 (d, partially overlaps with d, J = 8.7 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 8.04 (dd, J = 8.7, 1.6 Hz, 1H), 8.49 (d, J = 1.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 22.5, 31.2, 33.3, 92.4, 120.7, 123.8, 127.1, 127.9, 128.8, 129.8, 130.0, 130.3, 132.6, 133.7, 135.9, 136.7, 148.0, 166.1, 197.4; MS (ES+, Ar) m/z (rel intensity) 415 ([MNa + 1]$^+$, 24), 414 ([MNa]$^+$, 100), 409 (4); HRMS (ES+, Ar) calcd for $C_{23}H_{21}NO_5Na$ (MNa^+) 414.1312, found 414.1313; $[\alpha]^{25}_D$ −12.52 (c 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 41.6 min, t_R (minor) = 43.8 min; 71% ee.

*p-Tolyl (R)-2-methyl-2-nitro-5-oxo-5-(thiophene-2-yl)pentanoate (**3k**):* colorless solid; yield 154 mg, 89%; mp 111−112 °C; IR (film, cm^{-1}) 3093 (vw), 2925 (vw), 1778 (vs), 1668 (vs), 1551 (vs), 1519 (m), 1506 (m), 1442 (w), 1423 (m), 1413 (m), 1389 (m), 1347 (w), 1311 (w), 1245 (vs), 1203 (s), 1162 (w), 1117 (m), 1103 (w), 1083 (w), 887 (vw), 860 (vw), 813 (vw), 802 (vw), 732 (m), 726 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.35 (s, 3H), 2.74, 2.80 (ABqdd, J = 15.0, 9.0, 6.2 Hz, 2H), 3.09, 3.16 (ABqdd, J = 17.0, 9.0, 6.2 Hz, 2H), 6.99 (d, J = 8.3 Hz, 2H), 7.13 (dd, J = 5.0, 3.8 Hz, 1H), 7.19 (d, J = 8.3 Hz, 2H), 7.66 (dd, J = 5.0,1.1 Hz, 1H), 7.74 (dd, J = 3.8, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 22.4, 31.1, 33.9, 92.3, 120.7, 128.4, 130.3, 132.4, 134.3, 136.7, 143.4, 147.9, 166.0, 190.4; MS (ES+, Ar) m/z (rel intensity) 371 ([MNa + 1]$^+$, 40), 370 ([MNa]$^+$, 100), 365 (11), 349 (6), 348 ([MH]$^+$, 19); HRMS (ES+, Ar) calcd for $C_{17}H_{18}NO_5S$ (MH^+) 348.0900, found 348.0904; $[\alpha]^{25}_D$ −10.42 (c 1.0, $CHCl_3$); HPLC Chiralcel OD-H (petroleum ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 258 nm), t_R (major) = 36.1 min, t_R (minor) = 38.1 min; 68% ee.

*(E)-p-Tolyl (R)-2-methyl-2-nitro-5-oxo-7-phenylhept-6-enoate (**3l**):* colorless solid; yield 167 mg, 91%; mp 129−130 °C; IR (film, cm^{-1}) 2918 (w), 1776 (s), 1659 (s), 162 (m), 1544 (vs), 1574 (vw), 1508 (m), 1389 (w), 1241 (m), 1206 (m), 1179 (m), 1117 (m), 979 (w), 744 (m), 690 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.35 (s, 3H), 2.65−2.80 (m, 2H), 2.81−2.97 (m, 2H), 6.74 (d, J = 16.3 Hz, 1H), 7.0 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.37−7.45 (m, 3H), 7.55 (dd, J = 6.8, 2.9 Hz, 2H), 7.59 (d, J = 16.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 22.4, 30.9, 35.3, 92.4, 120.7, 125.6, 128.6, 129.2, 130.3, 130.9, 134.3, 136.7, 143.6, 147.9, 166.1, 197.3; MS (ES+, Ar) m/z (rel intensity) 391 ([MNa + 1]$^+$, 17), 390 ([MNa]$^+$, 100), 385 (10), 381 (6), 368 (33), 321 (4) 221 (6); HRMS (ES+, Ar) calcd for $C_{21}H_{21}NO_5Na$ (MNa^+) 390.1312, found 390.1309; $[\alpha]^{25}_D$ −12.64 (c 1.0, $CHCl_3$); HPLC Chiralcel OD-H (petroleum ether/i-PrOH = 97/3, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 54.3 min, t_R (minor) = 48.9 min; 73% ee.

*p-Tolyl (R)-5-cyclohexyl-2-methyl-2-nitro-5-oxopentanoate (**3m**):* colorless solid; yield 120 mg, 69%; mp 64−66 °C; IR (film, cm^{-1}) 2932 (vs), 2856 (m), 1773 (vs), 1710 (vs), 1533 (vs), 1508 (m), 1450 (m), 1388 (w), 1347 (w), 1237 (m), 1195 (m), 1169 (m), 1146 (w), 1114 (m), 1081 (w), 1019 (w), 887 (w), 859 (w), 844 (w), 809 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11−1.41 (m, 5H), 1.61−1.71 (m, 1H), 1.72−1.88 (m, 4H), 1.91 (s, 3H), 2.29−2.41 (m, overlaps with singlet, 1H), 2.35 (s, overlaps with m, 3H), 2.49−2.73 (m, 4H), 6.97 (d, J = 8.3 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 22.3, 25.7, 25.9, 28.6, 28.6, 30.6, 35.0, 51.0, 92.3, 120.7, 130.3, 136.6, 147.9, 166.0, 211.3; MS (ES+, Ar) m/z (rel intensity) 371 ([MNa + 1]$^+$, 21), 370 ([MNa]$^+$, 100), 348 ([MH]$^+$, 6), 301 (4); HRMS (ES+, Ar) calcd for $C_{19}H_{26}NO_5$(MH^+) 348.1805, found 348.1805; $[\alpha]^{25}_D$ −3.64 (c 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 98/2, flow rate 0.25 mL/min, λ = 216 nm), t_R (major) = 64.3 min, t_R (minor) = 68.1 min; 37% ee.

*p-Tolyl (R)-2-methyl-2-nitro-5-oxohexanoate (**3n**):* colorless solid; yield 106 mg, 76%; mp 64−66 °C; IR (film, cm^{-1}) 2366 (vw), 1773 (vs), 1718 (s), 1546 (s), 1507 (m), 1353 (w), 1238 (s), 1197 (vs), 1197 (vs), 1162 (m), 1117 (m), 1056 (vw), 886 (vw), 803 (w), 511 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (s, 3H), 2.18 (s, 3H), 2.35 (s, 3H), 2.49−2.73 (m, 4H), 6.99 (d, J = 8.9 Hz, 2H), 7.19 (d, J = 8.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 22.4, 30.2, 30.5, 38.0, 92.2, 120.7, 130.3, 136.7, 147.9, 166.0, 205.8; MS (ES+, Ar) calcd for $C_{14}H_{17}NO_5Na$ (MNa^+) 302.0999, found 302.0988; $[\alpha]^{25}_D$ −2.05 (c 1.0, $CHCl_3$); HPLC Chiralpack ADH (petroleum ether/i-PrOH = 97/3, flow rate 0.5 mL/min, λ = 220 nm), t_R (major) = 30.5 min, t_R (minor) = 39.9 min; 27% ee.

*p-Tolyl (R)-5-(3-bromophenyl)-2-ethyl-2-nitro-5-oxopentanoate (**4a**):* colorless solid; yield 188 mg, 87%; mp 84−85 °C; IR (film, cm^{-1}) 3066 (vw), 2968 (m), 2935 (m), 2877 (w), 1767 (s), 1693 (s), 1552 (vs), 1507 (m), 1421 (w), 1349 (w), 1264 (w), 1194 (vs), 1168 (m), 1125 (w), 1068 (vw), 1019 (vw), 997 (vw), 878 (vw), 783 (m), 739 (w), 680 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 3H), 2.35 (s, 3H), 2.45 (ABqq, J = 15.1, 7.6 Hz, 2H), 2.71, 2.78 (ABqdd, J = 15.1, 9.6, 5.5 Hz, 2H), 3.06, 3.17 (ddd, J = 17.9, 9.6, 5.5 Hz, 1H), 3.17 (ddd, J = 17.9, 9.6, 5.5 Hz, 1H), 6.98 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.35 (t, J = 7.9 Hz, 1H), 7.70 (ddd, J = 7.9, 1.7, 0.9 Hz, 1H), 7.85 (ddd collapsed to dt, J = 7.9, 1.3 Hz, 1H), 8.06 (dd collapsed to t, J = 1.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.4, 21.1, 28.1, 28.9, 33.3, 96.1, 120.8, 123.3, 126.8, 130.3, 130.5, 131.2, 136.5, 136.7, 138.1, 147.9, 165.5, 196.2; MS (ES+, Ar) m/z (rel intensity) 459 ([MNa + 3]$^+$, 15), 458 ([MNa + 2]$^+$, 76), 457 ([MNa +

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1]$^+$, 15), 456 ([MNa]$^+$, 77), 367 (18), 302 (17), 301 (100), 149 (7); HRMS (ES+, Ar) calcd for $C_{20}H_{20}BrNO_5Na$ (MNa^+) 456.0417, found 456.0412; $[\alpha]^{25}_D$ −8.77 (*c* 0.75, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/*i*-PrOH = 97/3, flow rate 0.3 mL/min, λ = 244 nm), t_R (major) = 56.4 min, t_R (minor) = 59.5 min; 83% ee.

*p-Tolyl (R)-5-(3-bromophenyl)-2-nitro-5-oxo-2-propylpentanoate (**4b**):* colorless solid; yield 206 mg, 92%; mp 86−87 °C; IR (film, cm^{-1}) 3066 (w), 2968 (m), 2935 (m), 2877 (w), 1767 (s), 1693 (s), 1591 (w), 1552 (vs), 1507 (m), 1421 (m), 1348 (w), 1299 (w), 1264 (w), 1194 (vs), 1168 (m), 1125 (m), 1068 (w), 1019 (w), 997 (w), 878 (vw), 783 (m), 739 (w), 680 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (t, *J* = 7.3 Hz, 3H), 1.38−1.52 (m, 2H), 2.32−2.41 (m, overlaps with s, 2H), 2.35 (s, overlaps with m, 3H), 2.71, 2.79 (ABqdd, *J* = 15.2, 9.6, 5.6 Hz, 2H), 3.06, 3.17 (ABqdd, *J* = 17.8, 9.6, 5.6 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.70 (ddd, *J* = 7.9, 1.9, 0.9 Hz, 1H), 7.86 (ddd collapsed to dt, *J* = 7.9, 1.4 Hz, 1H), 8.06 (dd collapsed to t, *J* = 1.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 17.4, 21.0, 28.6, 33.3, 37.5, 95.6, 120.7, 123.3, 126.7, 130.3, 130.5, 131.2, 136.5, 136.7, 138.1, 147.9, 165.6, 196.2; MS (ES+, Ar) *m*/*z* (rel intensity) 473 ([MNa + 3]$^+$, 18), 472 ([MNa + 2]$^+$, 100), 471 ([MNa + 1]$^+$, 19), 470 ([MNa]$^+$, 93), 395 (8), 367 (27), 301 (18); HRMS (ES+, Ar) calcd for $C_{21}H_{22}BrNO_5Na$ (MNa^+) 470.0574, found 470.0577; $[\alpha]^{25}_D$ −5.44 (*c* 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/*i*-PrOH = 97/3, flow rate 0.5 mL/min, λ = 244 nm), t_R (major) = 30.3 min, t_R (minor) = 32.1 min; 86% ee.

*p-Tolyl (R)-2-(3-(3-bromophenyl)-3-oxopropyl)-2-nitrohexanoate (**4c**):* colorless solid; yield 217 mg, 94%; mp 84−86 °C; IR (film, cm^{-1}) 3066 (vw), 2968 (m), 2934 (m), 2877 (w), 1767 (s), 1693 (vs), 1591 (vw), 1552 (vs), 1507 (m), 1441 (w), 1421 (m), 1348 (m), 1264 (w), 1194 (vs), 1168 (m), 1125 (m), 1068 (w), 1019 (w), 997 (w), 878 (w), 783 (m), 739 (w), 680 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, *J* = 7.0 Hz, 3H), 1.32−1.49 (m, 4H), 2.34−2.41 (m, overlaps with s, 2H), 2.35 (s, overlaps with m, 3H), 2.71, 2.78 (ABqdd, *J* = 15.2, 9.6, 5.6 Hz, 2H), 3.05, 3.17 (ABqdd, *J* = 17.8, 9.6, 5.6 Hz, 2H), 6.99 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.70 (ddd, *J* = 7.9, 2.0, 1.0 Hz, 1H), 7.86 (ddd collapsed to dt, *J* = 7.9, 1.5 Hz, 1H), 8.06 (dd collapsed to t, *J* = 1.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 21.0, 22.7, 25.9, 28.6, 33.3, 35.2, 95.7, 120.7, 123.3, 126.7, 130.3, 130.5, 131.2, 136.5, 136.7, 138.1, 147.9, 165.6, 196.2; MS (ES+, Ar) *m*/*z* (rel intensity) 487 ([MNa + 3]$^+$, 22), 486 ([MNa + 2]$^+$, 93), 485([MNa + 1]$^+$, 21), 484 ([MNa]$^+$, 100); HRMS (ES+, Ar) calcd for $C_{22}H_{24}BrNO_5Na$ (MNa^+) 484.0730, found 484.0731; $[\alpha]^{25}_D$ −5.30 (*c* 0.8, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/*i*-PrOH = 97/3, flow rate 0.5 mL/min, λ = 244 nm), t_R (major) = 26.6 min, t_R (minor) = 28.5 min; 83% ee.

*p-Tolyl (R)-5-(3-bromophenyl)-2-isopropyl-2-nitro-5-oxopentanoate (**4d**):* colorless oil; yield 197 mg, 88%; IR (neat, cm^{-1}) 3066 (w), 2968 (m), 2935 (m), 2877 (w), 1767 (s), 1693 (s), 1592 (w), 1552 (vs), 1507 (m), 1467 (w), 1441 (w), 1422 (m), 1349 (w), 1264 (w), 1194 (vs), 1168 (m), 1125 (m), 1068 (w), 1019 (w), 784 (m), 739 (w), 680 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (d, *J* = 6.8 Hz, 3H), 1.22 (d, *J* = 6.8 Hz, 3H), 2.34 (s, 3H), 2.71−2.78 (m, 2H), 2.82 (septet, *J* = 6.8 Hz, 1H), 3.12, 3.23 (ABqdd, *J* = 17.9, 8.9, 6.4 Hz, 2H), 7.00 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.69 (ddd, *J* = 7.9, 1.9, 0.9 Hz, 1H), 7.86 (ddd collapsed to dt, *J* = 7.9, 1.4 Hz, 1H), 8.06 (dd collapsed to t, *J* = 1.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.0, 18.3, 21.1, 28.5, 33.8, 35.1, 99.3, 120.8, 123.3, 126.7, 130.3, 130.5, 131.2, 136.5, 136.7, 138.2, 147.8, 165.1, 196.5; MS (ES+, Ar) *m*/*z* (rel intensity) 473 ([MNa + 3]$^+$, 23), 472 ([MNa + 2]$^+$, 94), 471 ([MNa + 1]$^+$, 22), 470 ([MNa]$^+$, 100), 465 (9); HRMS (ES+, Ar) calcd for $C_{21}H_{22}BrNO_5Na$ (MNa^+) 470.0574, found 470.0570; $[\alpha]^{25}_D$ −8.26 (*c* 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/*i*-PrOH = 97/3, flow rate 0.5 mL/min, λ = 244 nm), t_R (major) = 23.0 min, t_R (minor) = 30.5 min; 69% ee.

*p-Tolyl 2-ethyl-2-nitro-5-oxo-5-(p-tolyl)pentanoate (**4e**):* colorless solid; yield 467 mg, 85%; mp 75−77 °C; IR (film, cm^{-1}) 2981 (vw), 2368 (vw), 1762 (vs), 1552 (m), 1508 (w), 1356 (vw), 1194 (vs), 1167 (s), 1018 (vw), 799 (w), 738 (m), 511 (vw); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, *J* = 7.5 Hz, 3H), 2.35 (s, 3H), 2.39−2.52 (m, 2H), 2.68, 2.82 (ddd, *J* = 19.2, 9.5, 6.0 Hz, 2H), 3.02, 3.19 (ddd, 19.2, 9.5, 6.0 Hz, 2H), 6.98 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.85 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.4, 21.1, 21.9, 28.3, 28.8, 33.0, 96.3, 120.8, 126.5, 128.4, 129.6, 130.3, 134.0, 136.6, 144.8, 147.9, 165.6, 197.2; MS (ES+, Ar) calcd for $C_{21}H_{23}NO_5Na$ (MNa^+) 392.1468, found 392.1468; $[\alpha]^{25}_D$ −8.59 (*c* 1.0, $CHCl_3$); HPLC Phenomenex Celluose-1 (petroleum ether/*i*-PrOH = 97/3, flow rate 0.5 mL/min, λ = 220 nm), t_R (major) = 40.6 min, t_R (minor) = 43.6 min; 77% ee.

*o-Tolyl (R)-5-(3-bromophenyl)-2-methyl-2-nitro-5-oxopentanoate (**5a**):* colorless solid; yield 78 mg, 93%; mp 60−61 °C; IR (film, cm^{-1})3066 (w), 2936 (w), 1767 (s), 1693 (s), 1554 (vs), 1491 (vw), 1448 (vw), 1422 (w), 1389 (vw), 1347 (w), 1300 (vw), 1242 (w), 1222 (w), 1170 (m), 1120 (s), 1069 (w), 780 (w), 750 (m), 706 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (s, 3H), 2.20 (s, 3H), 2.75, 2.84 (ABqdd, *J* = 15.1, 9.0, 6.0 Hz, 2H), 3.14, 3.21 (ABqdd, *J* = 17.8, 9.0, 6.0 Hz, 2H), 7.05 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.15−7.26 (m, 3H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.71 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.87 (dt, *J* = 7.9, 1.1 Hz, 1H), 8.07 (t, *J* = 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1, 22.5, 31.0, 33.4, 92.2, 121.3, 123.3, 126.7, 127.1, 127.3, 130.1, 130.5, 131.2, 131.7, 136.6, 138.1, 148.6, 165.6, 196.1; MS (ES+, Ar) *m*/*z* (rel intensity) 445 ([MNa + 3]$^+$, 77), 444 ([MNa + 2]$^+$, 100), 443 ([MNa + 1]$^+$, 72), 442 ([MNa]$^+$, 100), 441 (46), 439 (28), 437(74), 432 (22); HRMS (ES+, Ar) calcd for $C_{19}H_{18}BrNO_5Na$ (MNa^+, 100) 442.0261, found 442.0261; $[\alpha]^{25}_D$ −5.32 (*c* 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/*i*-PrOH = 98/2, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 29.9 min, t_R (minor) = 31.7 min; 78% ee.

*Benzyl (R)-5-(3-bromophenyl)-2-methyl-2-nitro-5-oxopentanoate (**5b**):* colorless sticky oil; yield 81 mg, 97%; IR (neat, cm^{-1}) 3065 (w), 1751 (m), 1691 (m), 1552 (vs), 1456 (w), 1422 (vw), 1348 (w), 1300 (w), 1266 (m), 1202 (w), 1184 (w), 1127 (m), 1099 (w), 776 (m), 739 (s), 701 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.85 (s, 3H), 2.56−2.70 (m, 2H), 2.95−3.01 (m, 2H), 5.24 (s, 2H), 7.27−7.37 (m, 6H), 7.69 (ddd, *J* = 7.9, 1.8, 0.9 Hz, 1H), 7.76 (ddd collapsed to dt, *J* = 7.9, 1.4 Hz, 1H), 7.98 (dd collapsed to t, *J* = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 30.8, 33.4, 68.7, 92.1, 123.2, 126.7, 128.6, 128.9, 129.0, 130.4, 131.2, 134.5, 136.4, 138.1, 167.0, 196.1; MS (ES+, Ar) *m*/*z* (rel intensity) 445 ([MNa + 3]$^+$, 9), 444 ([MNa + 2]$^+$, 42), 443 ([MNa + 1]$^+$, 9), 442 ([MNa]$^+$, 43), 393 (5), 302 (16), 301 (100), 279(3), 149 (3); HRMS (ES+, Ar) calcd for $C_{19}H_{18}BrNO_5Na$ (MNa^+, 100) 442.0261, found 442.0266; $[\alpha]^{25}_D$ + 1.71 (*c* 0.57, $CHCl_3$); HPLC Chiral cell OD-H (petroleum ether/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 19.8 min, t_R (minor) = 20.8 min; 61% ee.

*Ethyl (R)-5-(3-bromophenyl)-2-methyl-2-nitro-5-oxopentanoate (**5c**):* colorless solid; yield 70 mg, 98%; mp 58.5−60 °C; IR (film, cm^{-1}) 2987 (w), 2944 (w), 1750 (s), 1684 (s), 1549 (vs), 1466 (w), 1443 (w), 1416 (w), 1389 (w), 1348 (w), 1299 (w), 1267 (m), 1228 (w), 1187 (m), 1132 (w), 1115 (w), 1013 (w), 773 (s), 745 (w), 680 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7.1 Hz, 3H), 1.85 (s, 3H), 2.60, 2.68 (ABqdd, *J* = 15.0, 8.5, 6.4 Hz, 2H), 3.05, 3.10 (ABqdd, *J* = 17.8, 8.5, 6.4 Hz, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.70 (ddd, *J* = 8.0, 1.8, 1.0 Hz, 1H), 7.86 (ddd collapsed to dt, *J* = 8.0, 1.4 Hz, 1H), 8.06 (dd collapsed to t, *J* = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.4, 30.8, 33.4, 63.2, 92.1, 123.3, 126.7, 130.5, 131.2, 136.5, 138.1, 167.2, 196.3; MS (ES+, Ar) *m*/*z* (rel intensity) 383 ([MNa + 3]$^+$, 15), 382 ([MNa + 2]$^+$, 99), 381 ([MNa + 1]$^+$, 17), 380 ([MNa]$^+$, 100), 360 (19), 358 (19), 313(9), 311 (9), 301 (8); HRMS (ES+, Ar) calcd for $C_{14}H_{16}BrNO_5Na$ (MNa^+, 100) 380.0104, found 380.0106; $[\alpha]^{25}_D$ + 1.58 (*c* 1.0, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 19.4 min, t_R (minor) = 20.5 min; 43% ee.

General Procedure for the Baeyer−Villiger Oxidation of 3h and 4e. To a stirred solution of *m*-chloroperbenzoic acid (55−75%, 11.25 mmol, 1.94 g) in dichloromethane (9 mL) at rt was added TFA (7.3 mmol, 562 μL), and stirring was continued for 6 h. A solution of ketone **3h** (483 mg, 1.36 mmol) or **4e** (502 mg, 1.36 mmol) in dichloromethane (3 mL) was added to the reaction mixture, and

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stirring was continued for another 14 h at rt. The reaction mixture was diluted with ether (15 mL), washed with satd aqueous sodium sulphite (20 mL), sodium bicarbonate (20 mL), and brine (10 mL), and dried over anhyd sodium sulfate. The organic layer was concentrated in vacuo, and the residue was purified by silica gel column chromatography using EtOAc−petroleum ether (5%) as eluent to afford the ester **6**.

*Di-p-tolyl (R)-2-methyl-2-nitropentanedioate (**6a**):* colorless solid; yield 461 mg, 92%; mp 120 °C; IR (film, cm^{-1}) 2921 (w), 1764 (vs), 1555 (s), 1507 (m), 1446 (vw), 1389 (vw), 1347 (vw), 1296 (vw), 1196 (s), 1167 (m), 1147 (w), 1115 (w), 1046 (vw), 1017 (vw), 942 (vw), 841 (w), 809 (w); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.0 (s, 3H), 2.34 (s, 3H), 2.44 (s, 3H), 2.69−2.86 (m, 4H), 6.94 (d, J = 8.4 Hz, 2H), 7.0 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.25 Hz, 2H), 7.20 (d, J = 8.25 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 21.1, 22.2, 29.3, 31.8, 92.0, 120.7, 121.2, 130.2, 130.4, 135.9, 136.8, 148.0, 148.4, 165.8, 170.6; MS (ES^+, Ar) m/z (rel intensity) 394 (MNa^+, 100), 241 (45); HRMS (ES^+, Ar) calcd for $C_{20}H_{21}NO_6Na$ (MNa^+, 100) 394.1261, found 394.1261; $[\alpha]^{25}_D$ −10.98 (c 0.5, $CHCl_3$); HPLC Chiralpack cellulose-2 (petroleum ether/i-PrOH = 90/10, flow rate 0.5 mL/min, λ = 216 nm), t_R (minor) = 16.7 min, t_R (major) = 18.5 min; 71% ee.

*Di-p-tolyl (R)-2-ethyl-2-nitropentanedioate (**6b**):* colorless solid; yield 439 mg, 84%; mp 122−124 °C; IR (film, cm^{-1}) 2982 (w), 1762 (vs), 1552 (s), 1507 (m), 1355 (vw), 1194 (vs), 1167 (s), 824 (w), 508 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 3H), 2.35 (s, 3H), 2.36 (s, 3H), 2.49 (ABqq, J = 14.5, 7.3 Hz, 2H), 2.68- 2.79 (m, 4H), 6.95 (d, J = 8.5 Hz, 2H), 7.01 (d, J = 8.5 Hz, 2H), 7.19 (t, J = 8.2 Hz, 2H), 7.20 (d, J = 8.2 Hz, 2H);^{13}C NMR (125 MHz, $CDCl_3$) δ 8.3, 21.0, 21.1, 28.4, 28.8, 29.2, 95.8, 120.8, 121.2, 130.2, 130.4, 135.9, 136.7, 148.0, 148.4, 165.8, 170.6; MS (ES^+, Ar) calcd for $C_{21}H_{23}NO_6Na$ (MNa^+, 100) 408.1418, found 408.1420; $[\alpha]^{25}_D$ −7.110 (c 1.0, $CHCl_3$); HPLC Phenomenex cellulose-2 (petroleum ether/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 216 nm), t_R (major) = 23.6 min, t_R (minor) = 25.5 min; 75% ee.

*(R)-1-Benzyl-3-methyl-3-nitropiperidine-2,6-dione (**7**).* To a solution of ester **6** (200 mg, 0.54 mmol) in toluene (5 mL) was added benzylamine (70 μL, 0.64 mmol, 1.2 equiv), and the mixture was refluxed for 24 h. The mixture was concentrated in vacuo, the residue was dissolved in EtOAc (15 mL), and the organic layer was washed with 1 N HCl (2 × 5 mL), dried over anhyd sodium sulfate, and concentrated in vacuo. The obtained residue was purified by silica gel column chromatography using EtOAc−petroleum ether (30−40%) as eluent to afford the amide **7**: colorless liquid; yield 122 mg, 62%; IR (film, cm^{-1}) 3412 (m), 2925 (w), 1736 (m), 1686 (vs), 1552 (vs), 1496 (w), 1454 (w), 1392 (w), 1377 (m), 1173 (s), 1081 (w), 753 (m), 700 (m); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.90 (s, 3H), 2.19 (ddd, J = 16.4, 13.1, 7.8 Hz, 1H), 2.62−2.89 (m, 3H), 4.98, 5.06 (ABq, J = 14.0 Hz, 2H), 7.22−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8, 29.1, 29.8, 44.4, 88.7, 127.9, 128.7, 128.8, 136.3, 166.0, 169.8; HRMS (ES^+, Ar) calcd for $C_{13}H_{14}N_2O_4Na$ (MNa^+, 100) 285.0844, found 285.0846; $[\alpha]^{25}_D$ + 8.61 (c 0.5, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 250 nm), t_R (major) = 11.9 min, t_R (minor) = 13.3 min; 69% ee.

*(R)-N,N′-Dibenzyl-2-methyl-2-nitropentanediamide (**8**).* To a solution of ester **6** (200 mg, 0.55 mmol) in THF (5 mL) was added benzylamine (235 μL, 2.15 mmol, 3.9 equiv), and the mixture was refluxed for 24 h. The mixture was concentrated in vacuo, the residue was dissolved in EtOAc (15 mL), and the organic layer was washed with 1 N HCl (2 × 5 mL), dried over anhyd sodium sulfate, and concentrated in vacuo. The residue was purified by silica gel column chromatography using EtOAc−petroleum ether (85−90%) as eluent to afford the amide **8**: colorless solid; yield 165 mg, 92%; mp 114 °C; IR (film, cm^{-1}) 3413 (brvs), 3333 (br vs), 1659 (vs), 1651 (vs), 1548 (s), 1267 (vw), 1028 (vw), 740 (m), 700 (w); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.82 (s, 3H), 2.18−2.32 (m, 2H), 2.53−2.68 (m, 2H), 4.40 (d, J = 5.4 Hz, 2H), 4.45 (d, J = 5.4 Hz, 2H), 5.73 (brs, 1H), 6.78 (brs, 1H), 7.22−7.37 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.2, 31.2, 33.1, 44.0, 44.4, 93.7, 127.9 × 2, 128.0, 129.0 × 2, 137.3, 138.0, 166.3, 170.9; MS (ES^+, Ar) m/z (rel intensity) 408 (MK^+, 98), 392 (MNa^+, 100), 370 MH^+, 55); HRMS (ES^+, Ar) calcd for $C_{20}H_{24}N_3O_4$ (MH^+, 100) 370.1761, found 370.1751; $[\alpha]^{25}_D$ +5.70 (c 0.5, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 90/10, flow rate 0.5 mL/min, λ = 250 nm), t_R (major) = 29.6 min, t_R (minor) = 34.6 min; 72% ee.

*(R)-3-Amino-1-benzyl-3-methylpiperidine-2,6-dione (**9**).* To a solution of compound **7** (132 mg, 0.5 mmol) in EtOH (10 mL) at 0 °C was added activated Zn (894 mg, 13.76 mmol) followed by 1 N HCl (4 mL). The reaction mixture was stirred for 5 h at rt. Then, the reaction mixture was filtered through Celite and concentrated in vacuo. The residue was dissolved in EtOAc (15 mL), and the organic layer was washed with water (2 × 5 mL), dried over anhyd sodium sulfate, and concentrated in vacuo to afford the amide **9**: colorless liquid; yield 98 mg, 85%; IR (film, cm^{-1}) 3407 (br vs), 3336 (br vs), 2927 (w), 1652 (s), 1548 (s), 739 (m), 700 (w); ^{1}H NMR (400 MHz, $CDCl_3$) 1.90 (s, 3H), 2.19 (ddd, J = 16.4, 13.1, 7.8 Hz, 1H), 2.62−2.89 (m, 3H), 4.98, 5.06 (ABq, J = 14.0 Hz, 2H), 7.22−7.42 (m, 5H); ^{13}C NMR (100 MHz, MeOD) δ 24.1, 30.3, 30.5, 44.6, 56.1, 128.5, 129.3, 129.6, 138.5, 173.0, 177.3; HRMS (ES^+, Ar) calcd for $C_{13}H_{17}N_2O_2$ (MH^+, 100) 233.1285, found 233.1284; $[\alpha]^{25}_D$ +7.34 (c 0.5, $CHCl_3$); HPLC Chiralpack IC (petroleum ether/i-PrOH = 90/10, flow rate 0.5 mL/min, λ = 250 nm), t_R (major) = 22.9 min, t_R (minor) = 24.7 min; 69% ee.

General Procedure for the Ester Hydrolysis and Nitro Group Reduction of 6. To a stirred solution of diester **6** (186 mg of **6a** or 193 mg of **6b**, 0.5 mmol) in THF (5.0 mL) and H_2O (3.0 mL) was added LiOH·H_2O (38 mg, 1.0 mmol), and the mixture was stirred at room temperature for 6 h. The mixture was acidified with 1 N HCl and extracted with Et_2O (3 × 20 mL). The organic layer was concentrated in vacuo to afford the diacid **10**. Activated Zn (894 mg, 13.76 mmol) was added to a solution of crude diacid **10** (95 mg of **10a** or 103 mg of **10b**, 0.5 mmol) in EtOH (10 mL) and was added 1 N HCl (4 mL) at 0 °C to room temperature. The reaction mixture was stirred for 5 h at room temperature. Then the reaction mixture was filtered through Celite, and the filtrate was concentrated in vacuo to afford amino acid hydrochloride **11**.

*(R)-2-Methylglutamic acid hydrochloride (**11a**):*[29] colorless solid; yield 55 mg, 68%; mp 142−144 °C (lit.[29] mp 143−148 °C); IR (KBr, cm^{-1}) 3382 (s), 3076 (br s), 1688 (br s), 1603 (s), 1463 (m), 1407 (m), 1375 (m), 1328 (w), 1295 (m), 1246 (m), 1128 (s), 1035 (m), 905 (w), 842 (w), 787 (w), 772 (w), 603 (s), 546 (s), 467 (m); ^{1}H NMR (500 MHz, D_2O) δ 1.47 (s, 3H), 2.02−2.19 (m, 2H), 2.34−2.52 (m, 2H); ^{13}C NMR (125 MHz, D_2O) δ 22.1, 29.1, 31.9, 60.7, 175.8, 177.1; HRMS (ES^+, Ar) calcd for $C_6H_{11}NO_4K$ (MK^+, 100) 200.0320, found 200.0320; $[\alpha]_D^{25}$ −8.91 (c 0.36, H_2O; lit.[29] $[\alpha]_D^{23}$ −10.00, c 0.36, H_2O).

*(R)-2-Amino-2-ethylpentanedioic acid hydrochloride (**11b**):*[29] colorless solid; yield 55 mg, 63%; mp 167−169 °C (lit.[29] mp 169−174 °C); IR (KBr, cm^{-1}) 3032 (br s), 2130 (m), 1607 (br s), 1400 (s), 1361 (s), 1295 (m), 1238 (m), 1187 (m), 1133 (m), 1004 (vw), 943 (w), 917 (vw), 846 (s), 769 (w), 669 (s), 535 (s); ^{1}H NMR (500 MHz, D_2O) δ 1.05 (t, J = 8.5 Hz, 3H), 2.46 (q, J = 7.3 Hz, 2H), 2.62 (br d, J = 6.1 Hz, 2H), 2.70 (br d, J = 6.1 Hz, 2H); ^{13}C NMR (100 MHz, D_2O) δ 8.4, 22.1, 29.1, 31.9, 60.7, 175.8, 177.1; HRMS (ES^+, Ar) calcd for $C_7H_{13}NO_4K$ (MK^+, 100) 214.0476, found 214.0475; $[\alpha]_D^{25}$ +1.4 (c 0.42, H_2O; lit.[29] $[\alpha]_D^{23}$ +1.9 (c 0.42, H_2O).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00543.

NMR spectra and HPLC profiles for all the new/relevant compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: irishi@iitb.ac.in.

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Notes

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