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Asymmetric domino Michael–Henry reaction of 1,2-diones with nitroolefins catalyzed by a chiral bisoxazolidine–Ni(acac)$_2$ complex

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ABSTRACT

The asymmetric domino Michael–Henry reaction of 1,2-cyclohexadione with nitroolefins catalyzed by chiral ligand bisoxazolidine **1** and Ni(acac)$_2$ has been developed. This process provided highly functionalized chiral bicycle[3,2,1] octane derivatives with the generation of four new stereogenic centers in high yields (76–99%), and with excellent enantioselectivities (up to 99%) and good diastereoselectivities (up to 9:1) under mild reaction conditions. The procedure presented is simple and makes this method suitable for practical use.

1. Introduction

The formation of carbon—carbon bonds with the control of multiple stereocenters in a single manipulation represents an effective approach for the construction of complex molecules in organic synthesis. Domino reactions are one of the most powerful ways to achieve this aim by assembling complex molecule architecture from relatively simple starting materials without isolating the intermediates.[1] Recently, efforts aimed at the development of asymmetric domino reactions by using chiral organocatalysts have been explored intensively and significant progress has been made.[2] Of the organocatalysts developed, proline derivatives play an important role for this process with high levels of stereoselectivity.[3] However, the domino Michael–Henry reaction[4] of 1,2-diones with nitroolefins, which would lead to unprecedented polyfunctionalized bicycles, has been far less studied. A thorough review of the literature reveals only two examples in which chiral cinchona alkaloid derivatives have been used as organocatalysts for these Michael–Henry reactions and moderate diastereoselectivities and high enantioselectivities were observed.[5] However, the transformation using a chiral metal catalyst has rarely been exploited,[6] and the achievement of high enantioselectivity with low catalyst loading remains an interesting goal.

Bisoxazolidine **1** was first developed by Wolf and has been used as a chiral ligand for metal catalyzed enantioselective alkynylations,[7] alkylations,[8] Henry reactions,[9] Friedel–Crafts reactions,[10] and Reformatsky reactions[11] with high stereoselectivity. In continuation of our research interest in domino reactions,[12] we herein report our recent efforts in the development of Ni(acac)$_2$–bisoxazolidine **1** catalyzed domino Michael–Henry reaction of 1,2-cyclohexadione with nitroolefins giving the desired products bicyclo[3,2,1] octan-8-ones possessing four stereogenic centers in high yields (up to 99%) with moderate diastereoselectivities (dr: up to 9:1) and high enantioselectivities (up to 99% ee).

2. Results and discussion

Initially, the domino Michael–Henry reaction between *trans*-β-nitrostyrene and 1,2-cyclohexadione was selected as a model to examine the effectiveness of bisoxazolidine **1** as a ligand and the results are shown in Table 1. As shown in Table 1, when 5 mol % of Ni(OAc)$_2$ was used as the metal catalyst, the reaction proceeded smoothly in THF at room temperature affording the desired product **4a** in 96% yield with excellent enantioselectivity (97% ee) and moderate diastereoselectivity (dr: 2:1) (entry 1). We also screened other solvents, which had an obvious effect on the stereoselectivity and reactivity of the domino reaction (entries 2–5). When using DMF as the solvent, it gave the product **4a** in high enantio- and diastereoselectivity (entry 3), while *i*-PrOH gave comparable enantioselectivity with relatively low diastereoselectivity, although the reactivity increased dramatically and the reaction was completed in 1 h with 98% yield (entry 5). In order to further optimize the reaction conditions, various metal salts, such as Cu(OAc)$_2$, Zn(OAc)$_2$, and Ni(II) with different counterions, were examined (entries 6–10). We found that the use of Ni(acac)$_2$ showed good catalytic activity with *i*-PrOH and afforded the best results for the reaction in terms of stereoselectivity (ee: 99%, dr: 7:1) and chemical yield (99%) (entry 10). The catalyst loading can be reduced to 3 mol % without significantly compromising the stereoselectivity, but a longer reaction period is

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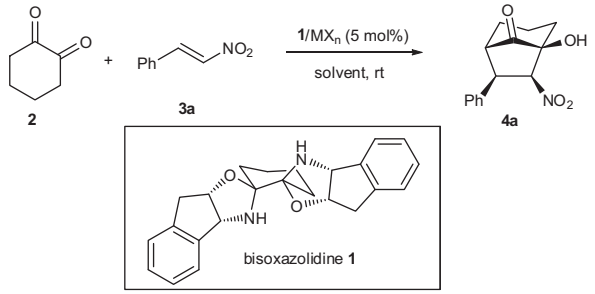
Table 1
Optimization of the domino Michael–Henry reaction conditions of 1,2-cyclohexadione to β-nitrostyrene[a]



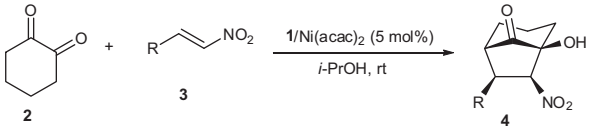
Entry	Solvent	MX_n	T (h)	Yield[b] (%)	dr[c]	ee[d] (%)
1	THF	$Ni(OAc)_2$	12	96	2:1	97
2	DCM	$Ni(OAc)_2$	12	55	2:1	29
3	DMF	$Ni(OAc)_2$	12	88	6:1	97
4	Toluene	$Ni(OAc)_2$	12	49	2:1	69
5	*i*-PrOH	$Ni(OAc)_2$	1	98	4:1	98
6	*i*-PrOH	$NiSO_4$	12	95	6:1	81
7	*i*-PrOH	$Cu(OAc)_2$	12	99	4:1	28
8	*i*-PrOH	$Zn(OAc)_2$	12	89	3:1	62
9	*i*-PrOH	$NiBr_2$	12	89	2:1	58
10	*i*-PrOH	**$Ni(acac)_2$**	**1**	**99**	**7:1**	**99**
11[e]	*i*-PrOH	$Ni(acac)_2$	3	89	7:1	97
12[f]	*i*-PrOH	$Ni(acac)_2$	12	99	7:1	89

[a] Reaction conditions: 1.0 mL of solvent, cyclohexane-1,2-dione **2** (0.6 mmol), nitrostyrene **3a** (0.5 mmol), and 5 mol % of catalyst (**1**: MX_n = 1:1).
[b] Yields of isolated product.
[c] Determined by ^1H NMR spectroscopy.
[d] Determined by chiral HPLC.
[e] 2 mol % of **1** and $Ni(acac)_2$ was used.
[f] 1 mol % of **1** and $Ni(acac)_2$ was used.

needed (entry 11). When the catalyst loading was further reduced to 1 mol %, the reaction was still complete within 12 h with 89% ee. However, the diastereoselectivity was not affected (entry 12).

On the basis of the results summarized in Table 1, the reaction conditions of entry 10 (Table 1) were chosen as the standard reaction conditions in order to study the scope of the domino Michael–Henry reactions using 1,2-cyclohexadione with a series of nitroolefins, and results are summarized in Table 2. From these results, it is obvious that 1,2-cyclohexadione can efficiently undergo domino Michael–Henry reactions with differently substituted nitroolefins in the presence of 5 mol % of catalyst in *i*-PrOH at room temperature to give the desired bicycle[3,2,1] octane derivatives **4a–j** in high yields (76–99%) with good diastereoselectivities (dr up to 9:1) and excellent enantioselectivities (ee: 90–99%). The results in Table 2 also show that the nature of the substitutes on the aryl groups influences both yields and stereoselectivities. For nitroolefins with a 4-halo substitution, both diastereo- and enantioselectivities increased by changing Br to F (entries 2–4). In the case of the 2-bromo substituted nitroolefin, excellent enantioselectivity was also observed (98% ee), but the diastereoselectivity was relatively low (dr: 2:1) (entry 5). The addition of nitroolefins bearing electron-donating groups, heteroaromatic, and naphthyl

Table 2
Asymmetric domino Michael–Henry reaction of cyclohexane-1,2-dione to nitroolefins[a]

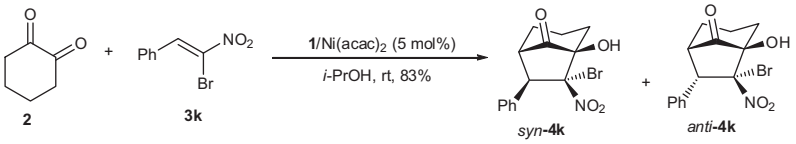


Entry	R	T (h)	Product	Yield[b] (%)	dr[c]	ee[d] (%)
1	Ph	1	**4a**	99	7:1	99
2	4-BrC_6H_4	3	**4b**	88	4:1	92
3	4-ClC_6H_4	3	**4c**	80	7:1	96
4	4-FC_6H_4	4	**4d**	90	9:1	99
5	2-BrC_6H_4	1	**4e**	90	2:1	98
6	4-MeC_6H_4	16	**4f**	98	7:1	91
7	4-$MeOC_6H_4$	16	**4g**	95	7:1	90
8	2-Furyl	16	**4h**	92	4:1	91
9	1-Naphthyl	16	**4i**	94	7:1	91
10	*n*-Butyl	4	**4j**	76	7:1	95

[a] Reaction conditions: 1.0 mL of *i*Pr-OH, cyclohexane-1,2-dione **2** (0.6 mmol), nitroolefin **3** (0.5 mmol), and 5 mol % of catalyst (**1**: $Ni(acac)_2$ = 1:1).
[b] Yields of isolated product.
[c] Determined by ^1H NMR spectroscopy.
[d] Determined by chiral HPLC.

groups also proceeded smoothly and afforded the products in excellent yields and with high diastereo- and enantioselectivities (entries 6–9). Furthermore, the catalyst was also highly effective for the domino reaction of 1,2-cyclohexadione to an aliphatic nitroolefin under standard reaction conditions providing the product **4j** in good yield and excellent enantioselectivity and high diastereoselectivity (entry 10).

In order to determine the absolute stereochemistry of the major enantiomer obtained in this reaction, the reaction of 1,2-cyclohexadione to α-bromonitroolefin **3k** was carried out under standard reaction conditions to afford the desired solid product **4k** in 83% yield with good enantioselectivities for both the *syn*- (92% ee) and *anti*- (90% ee) diastereomers. However, the dr selectivity was low with a *syn*/*anti* ratio of 3:2 (Eq. 1). After the recrystallization, the *syn*-enantiomer **4k** was obtained and its structure was unambiguously determined by an X-ray diffraction study (Fig. 1).[13] Based on the X-ray analysis, the stereochemistry of major enantiomer of the products **4a–j** was assigned as (1*S*,5*S*,6*R*,7*S*).



syn:*anti* = 3:2, ee: 92% (*syn*)
ee: 90% (*anti*)

(1)

3. Conclusion

In conclusion, we have developed a novel and simple catalytic system, chiral bisoxazolidine **1** and an $Ni(acac)_2$ complex, which has efficiently catalyzed the domino Michael–Henry reaction between 1,2-cyclohexadione and a variety of nitroolefins. This method provided highly functionalized chiral products bicycle[3,2,1] octane derivatives with the generation of four new stereogenic centers in high yields, and with excellent enantioselectivities and good diastereoselectivities. The reaction can be carried out under mild conditions and the catalyst loading can be decreased

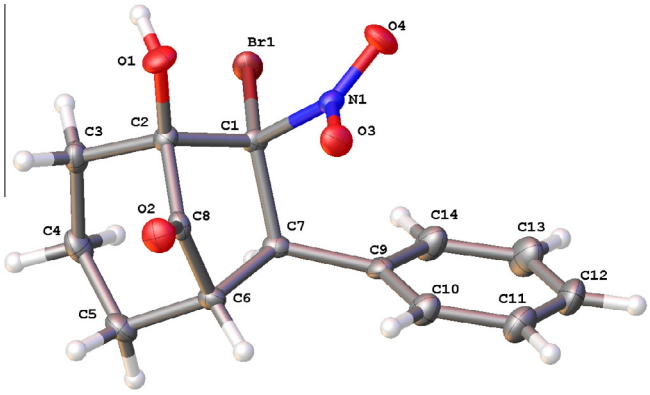


Figure 1. ORTEP representation of **4k**.

to 3 mol % without significantly affecting the stereoselectivity. Further investigations are currently underway to expand the scope and application of this efficient domino process.

4. Experimental

General reaction procedure. To a solution of bisoxazolidine **1** (9.3 mg, 0.025 mmol) in *i*-PrOH (1 mL) were added $Ni(acac)_2$ (6.4 mg, 0.025 mmol), 1,2-cyclohexadione (67.2 mg, 0.6 mmol) and nitroolefin (0.5 mmol). The reaction mixture was stirred at room temperature for the time indicated in Tables 1 and 2. The reaction mixture was concentrated and the residue was purified by flash chromatography (hexane/ethyl acetate = 5:1) to afford the product **4**.

4.1. (1*S*,5*S*,6*R*,7*S*)-1-Hydroxy-7-nitro-6-phenylbicyclo[3.2.1]octan-8-one 4a[6]

Following the general procedure described above, **4a** was obtained after purification by flash chromatography (hexane/ethyl acetate = 5:1) as a colorless oil (99% yield, 99% ee, dr = 7:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.22 (m, 3H), 7.17–7.10 (m, 2H), 4.76 (d, J = 6.0 Hz, 1H), 4.15 (d, J = 5.6 Hz, 1H), 3.42 (br, 1H), 2.80–2.74 (m, 1H), 2.44–2.18 (m, 2H), 2.14–1.90 (m, 3H), 1.80–1.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.7, 142.3, 129.3, 127.8, 126.7, 93.5, 81.7, 51.6, 43.9, 39.7, 36.0, 17.9; HPLC (Chiralcel OJ-H, hexanes/*i*-PrOH, 90:10, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 13.2 min, t_{minor} = 16.1 min.

4.2. (1*S*,5*S*,6*R*,7*S*)-6-(4-Bromophenyl)-1-hydroxy-7-nitrobicyclo-[3.2.1]octan-8-one 4b[6]

Following the general procedure described above, **4b** was obtained after purification by flash chromatography (hexane/ethyl acetate = 8:1) as a colorless oil (88% yield, 92% ee, dr = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.44 (m, 2H), 7.04–6.98 (m, 2H), 4.67 (d, J = 6.4 Hz, 1H), 4.12 (d, J = 6.0 Hz, 1H), 3.22 (br, 1H), 2.78–2.74 (m, 1H), 2.44–2.26 (m, 2H), 2.16–2.06 (m, 1H), 2.04–1.84 (m, 2H), 1.78–1.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.1, 141.2, 132.5, 128.5, 121.9, 93.3, 81.5, 51.4, 43.4, 39.8, 36.0, 17.9; HPLC (Chiralcel OJ-H, hexanes/*i*-PrOH, 90:10, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 44.1 min, t_{minor} = 55.8 min.

4.3. (1*S*,5*S*,6*R*,7*S*)-6-(4-Chlorophenyl)-1-hydroxy-7-nitrobicyclo-[3.2.1]octan-8-one 4c[5b]

Following the general procedure described above, **4c** was obtained after purification by flash chromatography (hexane/ethyl acetate = 8:1) as a colorless oil (80% yield, 96% ee, dr = 7:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.26 (m, 2H), 7.10–7.04 (m, 2H), 4.68 (d, J = 6.4 Hz, 1H), 4.13 (d, J = 6.0 Hz, 1H), 3.22 (br, 1H), 2.78–2.76 (m, 1H), 2.45–2.28 (m, 2H), 2.16–2.04 (m, 1H), 2.03–1.84 (m, 2H), 1.78–1.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.1, 140.7, 133.9, 129.6, 128.1, 93.4, 81.5, 51.5, 43.4, 39.8, 36.0, 17.9; HPLC (Chiralcel OJ-H, hexanes/*i*-PrOH, 95:5, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 18.1 min, t_{minor} = 21.8 min.

4.4. (1*S*,5*S*,6*R*,7*S*)-6-(4-Fluorophenyl)-1-hydroxy-7-nitrobicyclo-[3.2.1]octan-8-one 4d[6]

Following the general procedure described above, **4d** was obtained after purification by flash chromatography (hexane/ethyl acetate = 5:1) as a colorless oil (90% yield, 99% ee, dr = 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15–7.09 (m, 2H), 7.05–6.96 (m, 2H), 4.69 (d, J = 5.6 Hz, 1H), 4.15 (d, J = 5.6 Hz, 1H), 3.28 (br, 1H), 2.78–2.73 (m, 1H), 2.46–2.28 (m, 2H), 2.18–2.05 (m, 1H), 2.02–1.85 (m, 2H), 1.78–1.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.3, 138.1 (J_{C-F} = 3.0 Hz), 128.4 (J_{C-F} = 7.6 Hz), 116.3 (J_{C-F} = 21.3 Hz), 93.6, 81.6, 51.7, 43.2, 39.7, 36.0, 17.9; HPLC (Chiralcel OJ-H, hexanes/*i*-PrOH, 95:5, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 64.3 min, t_{minor} = 61.1 min.

4.5. (1*S*,5*S*,6*R*,7*S*)-6-(2-Bromophenyl)-1-hydroxy-7-nitrobicyclo-[3.2.1]octan-8-one 4e[5b]

Following the general procedure described above, **4e** was obtained after purification by flash chromatography (hexane/ethyl acetate = 8:1) as a colorless oil (90% yield, 98% ee, dr = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.58 (m, 1H), 7.33–7.26 (m, 1H), 7.16–7.10 (m, 1H), 7.01–6.97 (m, 1H), 5.07 (d, J = 6.0 Hz, 1H), 4.78 (d, J = 6.4 Hz, 1H), 3.28 (br, 1H), 2.61 (d, J = 4.8 Hz, 1H), 2.50–2.39 (m, 2H), 2.20–1.93 (m, 3H), 1.82–1.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.3, 140.7, 133.7, 129.3, 128.6, 128.2, 123.7, 91.8, 81.8, 52.5, 43.2, 40.2, 36.4, 17.9; HPLC (Chiralcel OJ-H, hexanes/*i*-PrOH, 90:10, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 25.7 min, t_{minor} = 31.1 min.

4.6. (1*S*,5*S*,6*R*,7*S*)-6-(4-Methylphenyl)-1-hydroxy-7-nitrobicyclo-[3.2.1]octan-8-one 4f[5b]

Following the general procedure described above, **4f** was obtained after purification by flash chromatography (hexane/ethyl acetate = 5:1) as a yellow solid (98% yield, 91% ee, dr = 7:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (d, J = 7.6 Hz, 2H), 7.04–6.99 (m, 2H), 4.73 (d, J = 6.0 Hz, 1H), 4.12 (d, J = 6.4 Hz, 1H), 3.31 (br, 1H), 2.78–2.76 (m, 1H), 2.42–2.36 (m, 2H), 2.30 (s, 3H), 2.14–1.92 (m, 3H), 1.78–1.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.6, 139.4, 137.6, 130.0, 126.6, 93.8, 81.6, 51.7, 43.5, 39.8, 36.0, 21.0, 17.9; HPLC (Chiralcel IA, hexanes/*i*-PrOH, 90:10, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 23.4 min, t_{minor} = 15.5 min.

4.7. (1*S*,5*S*,6*R*,7*S*)-6-(4-Methoxyphenyl)-1-hydroxy-7-nitrobicyclo-[3.2.1]octan-8-one 4g[5b]

Following the general procedure described above, **4g** was obtained after purification by flash chromatography (hexane/ethyl acetate = 5:1) as a colorless oil (95% yield, 90% ee, dr = 7:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 4.72 (d, J = 6.4 Hz, 1H), 4.10 (d, J = 5.6 Hz, 1H), 3.76 (s, 3H), 3.38 (s, 1H), 2.73 (d, J = 2.4 Hz, 1H), 2.44–2.27 (m, 2H), 2.14–2.00 (m, 1H), 2.00–1.90 (m, 2H), 1.77–1.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.7, 159.0, 134.4, 127.8, 114.6, 93.9, 81.6, 55.3, 51.8, 43.2, 39.7, 36.0, 17.9; HPLC (Chiralcel AD-H, hexanes/*i*-PrOH, 80/20, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 22.7 min, t_{minor} = 12.8 min.

4.8. (1*S*,5*S*,6*R*,7*S*)-6-(Furan-2-yl)-1-hydroxy-7-nitrobicyclo-[3.2.1]octan-8-one 4h[6]

Following the general procedure described above, **4h** was obtained after purification by flash chromatography (hexane/ethyl acetate = 5:1) as a colorless oil (92% yield, 91% ee, dr = 4:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.32 (m, 1H), 6.32–6.26 (m, 1H), 6.19–6.16 (m, 1H), 4.92 (d, J = 5.6 Hz, 1H), 4.28 (d, J = 5.6 Hz, 1H), 3.20 (br, 1H), 2.84–2.79 (m, 1H), 2.43–2.27 (m, 2H), 2.14–2.04 (m, 1H), 1.98–1.82 (m, 2H), 1.78–1.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.1, 152.7, 143.1, 110.5, 106.5, 90.2, 81.1, 49.5, 39.8, 37.8, 35.5, 17.9; HPLC (Chiralcel OJ-H, hexanes/*i*-PrOH, 95:5, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 61.0 min, t_{minor} = 102.2 min.

4.9. (1*S*,5*S*,6*R*,7*S*)-1-Hydroxy-6-(naphathalen-2-yl)-7-nitrobicyclo-[3.2.1]octan-8-one 4i[5a]

Following the general procedure described above, **4i** was obtained after purification by flash chromatography (hexane/ethyl acetate = 5:1) as a yellow oil (94% yield, 91% ee, dr = 7:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85–7.78 (m, 3H), 7.63 (d, J = 1.6, 1H), 7.51–7.46 (m, 2H), 7.22–7.17 (m, 1H), 4.86 (d, J = 6.4 Hz, 1H), 4.34 (d, J = 6.4 Hz, 1H), 3.33 (br, 1H), 2.92–2.88 (m, 1H), 2.46–2.34 (m, 2H), 2.20–1.98 (m, 3H), 1.84–1.75 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.6, 139.3, 133.3, 132.6, 129.6, 127.8, 127.7, 126.8, 126.4, 125.7, 124.2, 93.5, 81.7, 51.6, 44.1, 39.9, 36.1, 18.0; HPLC (Chiralcel OJ-H, hexanes/*i*-PrOH, 90:10, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 50.3 min, t_{minor} = 65.6 min.

4.10. (1*S*,5*S*,6*R*,7*S*)-6-Butyl-1-hydroxy-7-nitrobicyclo-[3.2.1]octan-8-one 4j[6]

Following the general procedure described above, **4j** was obtained after purification by flash chromatography (hexane/ethyl acetate = 5:1) as a colorless oil (76% yield, 95% ee, dr = 7:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.38 (d, J = 5.2 Hz, 1H), 3.15 (br, 1H), 2.94 (q, J = 6.8 Hz, 1H), 2.42–2.38 (m, 1H), 2.35–2.30 (m, 1H), 2.20–2.10 (m, 1H), 2.07–1.96 (m, 1H), 1.90–1.80 (m, 3H), 1.68–1.60 (m, 1H), 1.58–1.50 (m, 4H), 1.36–1.20 (m, 2H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.5, 92.0, 81.3, 49.6, 39.8, 38.6, 35.6, 35.5, 28.6, 22.3, 18.0, 13.8; HPLC (Chiralcel OJ-H, hexanes/*i*-PrOH, 90:10, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 14.8 min, t_{minor} = 11.7 min.

4.11. (1*S*,5*S*,6*R*,7*S*)-7-Bromo-1-hydroxy-7-nitro-6-phenylbicyclo-[3.2.1]octan-8-one 4k[6]

Following the general procedure described above, **4k** was obtained after purification by flash chromatography (hexane/ethyl acetate = 5:1) as a yellow solid (83% yield, 92% ee (*syn*), 90% ee (*anti*), dr = 3:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.22 (m, 5H), 4.22 (d, J = 1.6 Hz, 1H), 3.22 (br, 1H), 3.25–3.23 (m, 1H), 2.64–2.54 (m, 1H), 2.30–2.10 (m, 4H), 1.88–1.76 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.6, 134.6, 128.9, 128.7, 128.6, 108.2, 85.1, 57.3, 48.8, 43.9, 36.6, 17.5; HPLC (Chiralcel AD-H, hexanes/*i*-PrOH, 95:5, flow rate = 1.0 mL/min, λ = 254 nm): t_{major} = 28.7 min (*syn*), t_{minor} = 25.9 min (*syn*); t_{major} = 34.8 min (*anti*), t_{minor} = 31.7 min (*anti*).

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