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Enantioselective Diels–Alder reaction of *o*-quinodimethanes by utilizing tartaric acid ester as a chiral auxiliary

Motoki Takinami, Yutaka Ukaji* and Katsuhiko Inomata*

Division of Material Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma, Kanazawa, Ishikawa 920-1192, Japan

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Abstract—The asymmetric Diels–Alder reaction of *o*-quinodimethanes, generated from benzocyclobutenols in situ, with fumaric acid esters was achieved by utilizing diisopropyl (*R*,*R*)-tartrate as a chiral auxiliary to afford the corresponding optically active 1,2-*cis*-substituted 1-hydroxy tetrahydronaphthalene derivatives with enantioselectivities up to 83% ee.

1. Introduction

The Diels–Alder reaction of *o*-quinodimethane with olefins is a useful method for constructing the corresponding tetrahydronaphthalene frameworks bearing up to four stereocenters, which are key intermediates for the synthesis of polycyclic compounds,[1] in one step. The Diels–Alder reaction of α-hydroxy *o*-quinodimethane is useful for affording oxygen-functionalized tetrahydronaphthalenes.[2] Although several diastereoselective Diels–Alder reactions of *o*-quinodimethanes have been reported for the synthesis of optically active tetrahydronaphthalenes,[3] there have been only a few enantioselective ones reported,[4] despite the recent development of asymmetric Diels–Alder reactions catalyzed by chiral Lewis acids.[5] We recently designed a novel chiral system utilizing tartaric acid esters and developed asymmetric 1,3-dipolar cycloaddition reactions of nitrile oxides and nitrones, and also asymmetric hetero Diels–Alder reaction of a nitroso compound.[6] Herein, we report an asymmetric Diels–Alder reaction of *o*-quinodimethanes generated in situ from benzocyclobutenols utilizing a tartaric acid ester as a chiral auxiliary.

2. Results and discussion

When diisopropyl (*R*,*R*)-tartrate [(*R*,*R*)-DIPT] is successively treated with butylmagnesium bromide, dialkylzinc, and benzocyclobutenol **1A**, magnesium and zinc bridging intermediate **2** is formed. After the addition of fumaric acid ester **3**, which was anticipated to coordinate to the more Lewis acidic magnesium metal of the intermediate **2**, the intermediary complex **4** containing the *o*-quinodimethane generated by electrocyclic ring-opening reaction is formed, followed by Diels–Alder reaction to afford the corresponding optically active tetrahydronaphthalene(s) **5A** and/or **6A**.

Firstly, the Diels–Alder reaction with diethyl fumarate **3a** was examined in CH_2Cl_2 using dimethylzinc. The cycloaddition proceeded slowly at room temperature to predominantly give 1,2-*cis*-tetrahydronaphthalene **5Aa** as well as 1,2-*trans*-isomer **6Aa** and cyclized lactone **7Aa**. The enantioselectivity of the **5Aa** obtained was determined to be 69% ee by HPLC analysis (Table 1, entry 1). Among the dialkylzincs examined, diisopropylzinc afforded the highest yields and enantioselectivities (entries 1–3). Furthermore, an interval (*t*) between the addition of benzocyclobutenol **1A** and diethyl fumarate **3a** slightly influenced the reaction (entries 3–6). When **3a** was added 30 min after the addition of **1A**, the enantioselectivity was enhanced (entry 5).[7] When the interval was too long, the chemical yield and enantioselectivity were again decreased (entry 6).[8] The effect of solvents was also examined. Reaction in aromatic solvents afforded higher enantioselectivities than that in ether solvents (entries 3, 7–10). Finally, the 1,2-*cis*-tetrahydronaphthalene **5Aa** was produced in 83% ee when the reaction was performed in benzene (entry 11). The bulkiness of the ester groups of the fumarates did not have much influence

* Corresponding authors. Tel.: +81 76 264 5700; fax: +81 76 264 5742 (K.I.); e-mail: inomata@cacheibm.s.kanazawa-u.ac.jp

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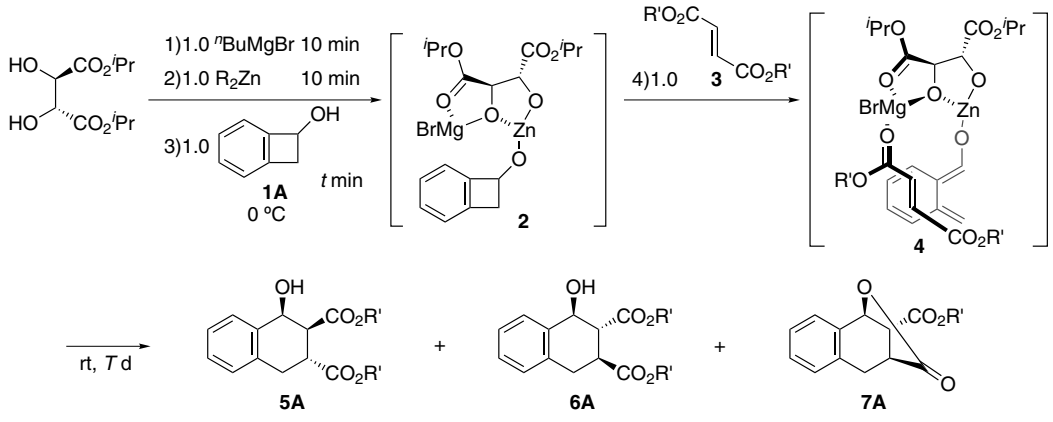
Table 1. Asymmetric Diels–Alder reaction of *o*-quinodimethane generated from benzocyclobutenol (**1A**)



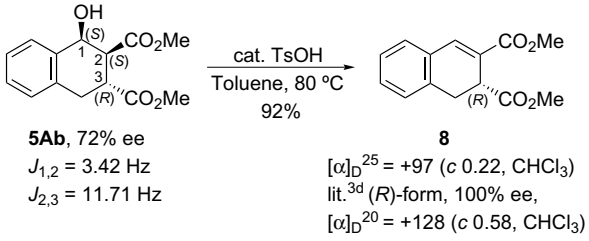
Entry	R	R′	3	Solvent	*t*/min	*T*/d	Products	Total yield of 5A and 6A/%	(5A:6A)[a]	ee/% of 5A[b]	7A/%[c]
1	Me	Et	**a**	CH_2Cl_2	10	5	**Aa**	24	(99:1)	69	5
2	Et	Et	**a**	CH_2Cl_2	10	5	**Aa**	36	(99:1)	69	6
3	^{i}Pr	Et	**a**	CH_2Cl_2	10	5	**Aa**	43	(99:1)	73	4
4	^{i}Pr	Et	**a**	CH_2Cl_2	0	4	**Aa**	47	(93:7)	70	4
5	^{i}Pr	Et	**a**	CH_2Cl_2	30	5	**Aa**	40	(99:1)	77	4
6	^{i}Pr	Et	**a**	CH_2Cl_2	60	3	**Aa**	15	(82:18)	44	7
7	^{i}Pr	Et	**a**	Et_2O	10	3	**Aa**	21	(80:20)	58	14
8	^{i}Pr	Et	**a**	THF	10	5	**Aa**	37	(84:16)	62	13
9	^{i}Pr	Et	**a**	Toluene	10	3	**Aa**	54	(98:2)	76	7
10	^{i}Pr	Et	**a**	Benzene	10	4	**Aa**	52	(96:4)	81	3
11	^{i}Pr	Et	**a**	Benzene	30	3	**Aa**	50	(98:2)	83	3
12	^{i}Pr	Me	**b**	Benzene	30	3	**Ab**	62	(99:1)	75	16
13	^{i}Pr	^{i}Pr	**c**	Benzene	30	3	**Ac**	52	(90:10)	72	4

[a] Ratios were determined by ^{1}H NMR spectra of the crude products.
[b] Optical yields were determined by HPLC analysis (Chiralcel OD-H).
[c] Yields of **7A** were determined by ^{1}H NMR spectra of the crude products.

on the enantioselectivity, but diethyl ester **3a** was the best among the esters examined (entries 11–13).

Next, the Diels–Alder reaction using several benzocyclobutenols was examined as shown in Table 2. 5- or 4-Methoxy substituted benzocyclobutenols **1C** or **1D** afforded the corresponding tetrahydronaphthalene with good enantioselectivities (entries 3 and 4). The introduction of the methoxy group onto the C6 position decreased the enantioselectivity (entry 2). Simultaneous chelation of the MeO group and α-alkoxide oxygen of a quinodimethane may alter the ideal transition state. Chloro-substituted substrates **1E**–**1G** afforded the cycloadduct with moderate enantioselectivities (entries 5–7).

The relative stereochemistry of cycloadducts **5** and **6** was determined by coupling constants between the protons on C1 and C2. That is, the coupling constants $J_{1,2}$ of 1,2-*cis*-isomers **5** [e.g., $J_{1,2} = 3.42$ (**5Aa**), 3.42 (**5Ab**) Hz] were smaller than that of 1,2-*trans*-isomer **6** [$J_{1,2} = 8.54$ (**6Aa**), 8.54 (**6Ab**) Hz].[3e] Furthermore, the ^{1}H NMR spectra of **5Ab** and **6Ab** were identical with reported data.[9] The absolute configuration of the Diels–Alder product **5Ab** was determined to be (1*S*,2*S*,3*R*) by comparing the specific rotation of the dehydrated dihydronaththalene derivative **8** with that of the known (*R*)-**8**.[3d] The absolute configurations of



5Ab, 72% ee
$J_{1,2}$ = 3.42 Hz
$J_{2,3}$ = 11.71 Hz

8
$[\alpha]_D^{25}$ = +97 (*c* 0.22, $CHCl_3$)
lit.[3d] (*R*)-form, 100% ee,
$[\alpha]_D^{20}$ = +128 (*c* 0.58, $CHCl_3$)

other 1,2-*cis*-products **5** were tentatively assigned as (1*S*,2*S*,3*R*).

Although the precise reaction mechanism is still unclear, the plausible transition state is shown in Figure 1 to rationalize the absolute configuration of **5** determined above.

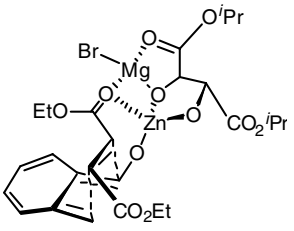
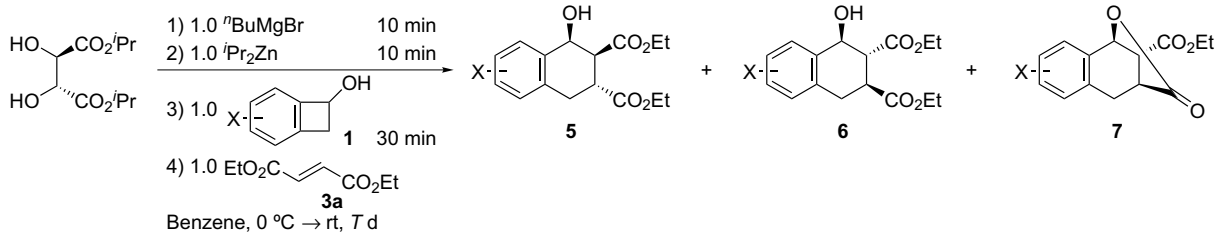


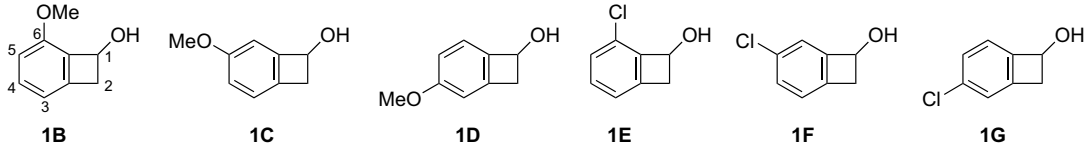
Figure 1.

Table 2. Asymmetric Diels–Alder reaction of several *o*-quinodimethanes generated from the corresponding benzocyclobutenols **1**



Entry	**1**	*T*/d	Total yield of **5** and **6**/%	(**5**:**6**)[a]	ee/% of **5**[b]	**7**/%[c]
1	**1A**	3	50	(98:2)	83	3
2	**1B**	3	33	(99:1)	65	Trace
3	**1C**	4	49	(99:1)	80	4
4	**1D**	4	38	(90:10)	79	Trace
5	**1E**	3	33	(99:1)	54	6
6	**1F**	3	56	(92:8)	68	4
7	**1G**	3	34	(90:10)	66	4

[a] Ratios were determined by ^{1}H NMR spectra of the crude products.
[b] Optical yields were determined by HPLC analysis (Chiralcel OD-H).
[c] Yields of **7** were determined by ^{1}H NMR spectra of the crude products.



3. Conclusion

In conclusion, we have developed a new type of diastereo- and enantioselective Diels–Alder reaction of *o*-quinodimethane generated in situ from benzocyclobutenol by utilizing (*R*,*R*)-DIPT as a chiral auxiliary. This reaction provides a simple and attractive approach to highly functionalized optically active tetrahydronaphthalenes.

4. Experimental

Melting points were determined with a micro-melting apparatus (Yanagimoto Seisakusho) and are uncorrected. The ^{1}H NMR spectra were recorded on a JEOL LA 400 or a LA 300 NMR spectrometer. The chemical shifts of ^{1}H are reported in the δ-scale relative to $Si(CH_3)_4$ ($\delta = 0.00$ ppm) as the internal standards. IR and MS spectra were recorded on a JASCO FT/IR infrared spectrometer and a JEOL SX-102A mass spectrometer, respectively. THF and Et_2O were freshly distilled from sodium diphenylkethyl. All other solvents were distilled and stored over drying agents. Thin-layer chromatography (TLC), flash column chromatography, and recycling HPLC were performed on Merck's silica gel 60 PF_{254} (Art. 7749), Cica-Merck's silica gel 60 (No. 9385-5B), and JAIGL-SIL (s-043-15), respectively.

4.1. Representative procedure for the enantioselective Diels–Alder reaction (Table 1, entry 11)

To a benzene (3 ml) solution of (*R*,*R*)-DIPT (117 mg, 0.5 mmol) was added butylmagnesium bromide (0.5 mmol, 1.0 ml of 0.5 M solution in THF) at 0 °C under an argon atmosphere. The mixture was stirred for 10 min, followed by the addition of diisopropylzinc (0.5 mmol, 0.5 ml of 1.0 M solution in hexane) and after 10 min, a benzene (3 ml) solution of benzocyclobutenol **1A** (60 mg, 0.5 mmol) was added. After stirring for 30 min, a benzene (3 ml) solution of diethyl fumarate **3a** (86 mg, 0.5 mmol) was added and the resulting solution stirred for 3 d at room temperature. The reaction was quenched by the addition of a saturated aq NH_4Cl solution and extracted with AcOEt. The combined extracts were dried over Na_2SO_4 and condensed in vacuo. Separation by TLC (SiO_2, hexane/AcOEt = 5:1) gave **5Aa** contaminated with (*R*,*R*)-DIPT and **1A** and **6Aa**. Further purification by recycling HPLC on silica gel afforded a 98:2 mixture of **5Aa** and **6Aa** (73 mg, 50%). The enantioselectivity of **5Aa** was determined by HPLC analysis using a chiral column (Chiralcel OD-H) to be 83% ee.

4.2. Diethyl (1*S*,2*S*,3*R*)-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 5Aa

Obtained as an oil. $[\alpha]_D^{25} = -121$ (*c* 0.27, EtOH, 83% ee). IR (neat), 3490, 2981, 2934, 1735, 1585, 1492, 1455, 1372, 1317, 1261, 1222, 1188, 1160, 1114, 1065, 1034, 931, 861, 758, 731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 1.30$ (3H, t, $J = 7.07$ Hz), 1.31 (3H, t, $J = 7.07$ Hz), 2.31 (1H, d, $J = 4.64$ Hz), 2.90 (1H, dd, $J = 11.71$, 16.83 Hz), 3.11 (1H, dd, $J = 3.42$, 11.71 Hz), 3.21 (1H, dd, $J = 5.61$, 16.83 Hz), 3.36 (1H, dt, $J = 5.61$, 11.71 Hz), 4.17–4.31 (4H, m), 5.12 (1H, dd, $J = 3.42$, 4.64 Hz), 7.13–7.15 (1H, m), 7.24–7.28 (2H, m), 7.36–7.38 (1H, m). HRMS (FAB)

$(M+Li)^+$, Found: *m/z* 299.1461. Calcd for $C_{16}H_{20}O_5Li$: 299.1471.

4.3. Diethyl (1*R**,2*S**,3*R**)-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 6Aa

Obtained as a solid. Mp 84.5–85.5 °C (recrystallized from benzene). IR (KBr) 3457, 2986, 2940, 2905, 1731, 1714, 1490, 1453, 1417, 1397, 1378, 1350, 1298, 1250, 1192, 1163, 1115, 1099, 1074, 1054, 1042, 1019, 947, 855, 818, 753, 740, 703 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.21$ (3H, t, $J = 7.06$ Hz), 1.24 (3H, t, $J = 7.06$ Hz), 2.68 (1H, d, $J = 6.10$ Hz), 2.91–3.11 (4H, m), 4.04–4.29 (4H, m), 4.92 (1H, dd, $J = 6.10$, 8.54 Hz), 7.03 (1H, d, 7.56 Hz), 7.14–7.21 (2H, m), 7.51 (1H, d, $J = 7.56$ Hz). HRMS (FAB) $(M+Li)^+$, Found: *m/z* 299.1490. Calcd for $C_{16}H_{20}O_5Li$: 299.1471.

4.4. Dimethyl (1*S*,2*S*,3*R*)-1-hydroxy-1,2,3,4-tetrahydronaphtalene-2,3-dicarboxylate 5Ab[9]

Obtained as an oil. $[\alpha]_D^{25} = -89$ (*c* 0.82, EtOH, 75% ee). IR (neat) 3482, 3025, 2953, 2847, 1736, 1585, 1493, 1438, 1377, 1358, 1321, 1264, 1198, 1163, 1115, 1065, 1045, 1014, 943, 920, 876, 850, 819, 781, 763, 732 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 2.26$ (1H, d, $J = 4.88$ Hz), 2.92 (1H, dd, $J = 11.71$, 16.83 Hz), 3.14 (1H, dd, $J = 3.42$, 11.71 Hz), 3.21 (1H, dd, $J = 5.61$, 16.83 Hz), 3.40 (1H, dt, $J = 5.61$, 11.71 Hz), 3.77 (3H, s), 3.80 (3H, s), 5.13 (1H, dd, $J = 3.42$, 4.88 Hz), 7.14–7.16 (1H, m), 7.24–7.30 (2H, m), 7.35–7.38 (1H, m). HRMS (FAB) $(M+Li)^+$, Found: *m/z* 271.1137. Calcd for $C_{14}H_{16}O_5Li$: 271.1158.

4.5. Dimethyl (1*R**,2*S**,3*R**)-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 6Ab[9]

Obtained as a solid. Mp 121.5–122.5 °C (recrystallized from hexane/AcOEt). IR (KBr) 3468, 2954, 2898, 1735, 1707, 1582, 1489, 1440, 1381, 1360, 1327, 1302, 1247, 1208, 1191, 1180, 1116, 1076, 1045, 991, 933, 912, 881, 862, 822, 767, 739, 703 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 2.77$ (1H, d, $J = 6.59$ Hz), 3.01 (1H, dd, $J = 9.27$, 10.49 Hz), 3.05–3.11 (2H, m), 3.16 (1H, dt, $J = 5.61$, 10.49 Hz), 3.73 (3H, s), 3.78 (3H, s), 4.99 (1H, dd, $J = 6.59$, 8.54 Hz), 7.09 (1H, d, $J = 7.07$ Hz), 7.20–7.28 (2H, m), 7.57 (1H, d, $J = 7.56$ Hz). HRMS (FAB) $(M+Li)^+$, Found: *m/z* 271.1173. Calcd for $C_{14}H_{16}O_5Li$: 271.1158.

4.6. Diisopropyl (1*S*,2*S*,3*R*)-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 5Ac

Obtained as an oil. $[\alpha]_D^{25} = -82$ (*c* 0.75, EtOH, 72% ee). IR (neat) 3492, 2980, 2935, 1731, 1585, 1492, 1455, 1375, 1313, 1268, 1190, 1146, 1107, 1065, 1041, 991, 933, 910, 881, 854, 837, 756, 732 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.26$ (6H, d, $J = 6.34$ Hz), 1.29 (6H, d, $J = 6.01$ Hz), 2.27 (1H, br s), 2.85 (1H, dd, $J = 11.71$, 16.59 Hz), 3.09 (1H, dd, $J = 3.66$, 11.47 Hz), 3.18 (1H, dd, $J = 5.61$, 16.59 Hz), 3.29 (1H, ddd, $J = 5.61$, 11.47, 11.71 Hz), 5.01–5.15 (3H, m), 7.12–7.14 (1H, m), 7.23–7.26 (2H, m), 7.35–7.38 (1H, m). HRMS (FAB) $(M+Li)^+$, Found: *m/z* 327.1789. Calcd for $C_{18}H_{24}O_5Li$: 327.1784.

4.7. Diisopropyl (1*R**,2*S**,3*R**)-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 6Ac

Obtained as a solid. Mp 54.5–55.5 °C (recrystallized from benzene/hexane). IR (neat) 3481, 2980, 2936, 1731, 1491, 1455, 1375, 1315, 1268, 1184, 1146, 1107, 1038, 990, 969, 914, 868, 825, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.24$ (3H, d, $J = 6.10$ Hz), 1.26 (3H, d, $J = 6.10$ Hz), 1.28 (3H, d, $J = 6.10$ Hz), 1.29 (3H, d, $J = 6.10$ Hz), 2.89 (1H, d, $J = 6.34$ Hz), 2.96 (1H, dd, $J = 9.27$, 10.25 Hz), 2.98 (1H, dd, $J = 11.47$, 16.10 Hz), 3.07 (1H, dd, $J = 5.12$, 16.10 Hz), 3.10 (1H, ddd, $J = 5.12$, 10.25, 11.47 Hz), 4.93 (1H, dd, $J = 6.34$, 9.27 Hz), 5.02 (1H, h, 6.10 Hz), 5.11 (1H, h, 6.10 Hz), 7.08 (1H, d, $J = 7.07$ Hz), 7.19–7.27 (2H, m), 7.57 (1H, d, $J = 7.32$ Hz). HRMS (FAB) $(M+Li)^+$, Found: *m/z* 327.1783. Calcd for $C_{18}H_{24}O_5Li$: 327.1784.

4.8. Diethyl (1*S*,2*S*,3*R*)-1-hydroxy-8-methoxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 5Ba

Obtained as an oil. $[\alpha]_D^{25} = -55$ (*c* 0.50, EtOH, 65% ee). IR (KBr) 3462, 2982, 2936, 2843, 1724, 1714, 1602, 1588, 1473, 1447, 1432, 1377, 1311, 1279, 1256, 1233, 1182, 1162, 1115, 1091, 1065, 1033, 987, 945, 865, 848, 783, 757, 738 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.30$ (3H, t, $J = 7.07$ Hz), 1.31 (3H, t, $J = 7.08$ Hz), 2.51 (1H, br s), 2.82 (1H, dd, $J = 12.44$, 16.59 Hz), 3.01 (1H, dd, $J = 4.15$, 12.20 Hz), 3.16 (1H, dd, $J = 5.12$, 16.59 Hz), 3.30 (1H, ddd, $J = 5.12$, 12.20, 12.44 Hz), 3.88 (3H, s), 4.18–4.31 (4H, m), 5.43 (1H, d, $J = 4.15$ Hz), 6.75 (1H, d, $J = 7.56$ Hz), 6.76 (1H, d, $J = 8.29$ Hz), 7.22 (1H, m). HRMS (FAB) $(M+Li)^+$, Found: *m/z* 329.1592. Calcd for $C_{17}H_{22}O_6Li$: 329.1576.

4.9. Diethyl (1*R**,2*S**,3*R**)-1-hydroxy-8-methoxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 6Ba

Obtained as a solid. Mp 90.5–91.5 °C (recrystallized from hexane/AcOEt). IR (neat) 3544, 2981, 2938, 2844, 1732, 1588, 1472, 1442, 1396, 1374, 1348, 1254, 1185, 1091, 1020, 924, 862, 782, 749, 678 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.27$ (3H, t, $J = 7.07$ Hz), 1.31 (3H, t, $J = 7.08$ Hz), 2.99–3.13 (4H, m), 3.88 (3H, s), 3.90 (1H, br s), 4.06–4.27 (4H, m), 5.31 (1H, d, $J = 7.56$ Hz), 6.76 (2H, d, $J = 8.29$ Hz), 7.19 (1H, m). HRMS (FAB) $(M+Li)^+$, Found: *m/z* 329.1599. Calcd for $C_{17}H_{22}O_6Li$: 329.1576.

4.10. Diethyl (1*S*,2*S*,3*R*)-1-hydroxy-7-methoxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 5Ca

Obtained as an oil. $[\alpha]_D^{25} = -94$ (*c* 0.77, EtOH, 80% ee). IR (neat) 3502, 2980, 2934, 2841, 1734, 1612, 1505, 1466, 1372, 1309, 1266, 1189, 1163, 1109, 1065, 1037, 942, 922, 880, 858, 818, 771 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.30$ (3H, t, $J = 7.07$ Hz), 1.31 (3H, t, $J = 7.07$ Hz), 2.20 (1H, d, $J = 4.88$ Hz), 2.87 (1H, dd, $J = 11.95$, 16.83 Hz), 3.08 (1H, dd, $J = 3.42$, 11.71 Hz), 3.16 (1H,

dd, $J = 5.61$, 16.83 Hz), 3.34 (1H, ddd, $J = 5.61$, 11.71, 11.95 Hz), 3.79 (3H, s), 4.17–4.30 (4H, m), 5.08 (1H, dd, $J = 3.42$, 4.88 Hz), 6.64 (1H, d, $J = 2.68$ Hz), 6.80 (1H, dd, $J = 2.68$, 8.54 Hz), 7.28 (1H, d, $J = 8.54$ Hz). HRMS (EI) M^+, Found: m/z 322.1415. Calcd for $C_{17}H_{22}O_6$: 322.1416.

4.11. Diethyl (1*R**,2*S**,3*R**)-1-hydroxy-7-methoxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 6Ca

Obtained as a solid. Mp 94.5–96.0 °C (recystallized from hexane/AcOEt). IR (KBr) 3441, 2941, 1730, 1713, 1616, 1578, 1503, 1470, 1397, 1373, 1351, 1296, 1271, 1243, 1198, 1127, 1076, 1053, 1018, 890, 864, 809 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.28$ (3H, t, $J = 7.07$ Hz), 1.30 (3H, t, $J = 7.07$ Hz), 2.71 (1H, br s), 2.96–3.16 (4H, m), 3.78 (3H, s), 4.12–4.28 (4H, m), 4.95 (1H, m), 6.61 (1H, s), 6.81 (1H, d, $J = 8.54$ Hz), 7.47 (1H, d, $J = 8.54$ Hz). HRMS (EI) M^+, Found: m/z 322.1417. Calcd for $C_{17}H_{22}O_6$: 322.1416.

4.12. Diethyl (1*S*,2*S*,3*R*)-1-hydroxy-6-methoxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 5Da

Obtained as an oil. $[\alpha]_D^{25} = -52$ (c 0.28, EtOH, 79% ee). IR (neat) 3483, 2981, 2935, 2839, 1735, 1613, 1584, 1505, 1466, 1443, 1373, 1307, 1264, 1186, 1166, 1112, 1065, 1034, 952, 912, 869, 814, 746, 703 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.29$ (3H, t, $J = 7.07$ Hz), 1.30 (3H, t, $J = 7.07$ Hz), 2.53 (1H, br s), 2.79 (1H, dd, $J = 11.71$, 16.10 Hz), 3.08 (1H, dd, $J = 3.42$, 11.71 Hz), 3.11 (1H, dd, $J = 5.61$, 16.10 Hz), 3.30 (1H, dt, $J = 5.61$, 11.71 Hz), 3.78 (3H, s), 4.16–4.29 (4H, m), 5.05 (1H, d, $J = 3.42$ Hz), 6.82 (1H, dd, $J = 2.68$, 8.54 Hz), 6.89 (1H, d, $J = 2.68$ Hz), 7.03 (1H, d, $J = 8.54$ Hz). HRMS (FAB) $(M+Li)^+$, Found: m/z 329.1585. Calcd for $C_{17}H_{22}O_6Li$: 329.1576.

4.13. Diethyl (1*R**,2*S**,3*R**)-1-hydroxy-6-methoxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 6Da

Obtained as a solid. Mp 88.5–90.0 °C (recystallized from hexane/AcOEt). IR (neat) 3489, 2981, 2935, 2839, 1735, 1614, 1585, 1505, 1466, 1444, 1372, 1307, 1264, 1186, 1166, 1112, 1065, 1034, 975, 952, 913, 870, 815, 771, 746, 703, 659 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.27$ (3H, t, $J = 7.07$ Hz), 1.31 (3H, t, $J = 7.32$ Hz), 2.79 (1H, d, $J = 6.34$ Hz), 2.95 (1H, dd, $J = 10.73$, 16.10 Hz), 2.98 (1H, dd, $J = 9.27$, 10.49 Hz), 3.04 (1H, dd, $J = 5.37$, 16.10 Hz), 3.12 (1H, ddd, $J = 5.37$, 10.49, 10.73 Hz), 3.80 (3H, s), 4.11–4.32 (4H, m), 4.94 (1H, dd, $J = 6.34$, 9.27 Hz), 6.79 (1H, dd, $J = 2.68$, 8.54 Hz), 7.01 (1H, d, $J = 8.54$ Hz), 7.12 (1H, d, $J = 2.68$ Hz). HRMS (FAB) $(M+Li)^+$, Found: m/z 329.1584. Calcd for $C_{17}H_{22}O_6Li$: 329.1576.

4.14. Diethyl (1*S*,2*S*,3*R*)-8-chrolo-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 5Ea

Obtained as an oil. $[\alpha]_D^{25} = -56$ (c 0.54, EtOH, 54% ee). IR (neat) 3501, 2981, 1734, 1595, 1572, 1445, 1372, 1309, 1258, 1187, 1116, 1065, 1031, 939, 901, 867, 781, 733 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.31$ (3H, t, $J = 7.07$ Hz), 1.32 (3H, t, $J = 7.07$ Hz), 2.58 (1H, d, $J = 3.90$ Hz), 2.87 (1H, dd, $J = 12.44$, 16.83 Hz), 3.03 (1H, dd, $J = 3.66$, 12.20 Hz), 3.22 (1H, dd, $J = 5.37$, 16.83 Hz), 3.36 (1H, ddd, $J = 5.37$, 12.20, 12.44 Hz), 4.19–4.30 (4H, m), 5.46 (1H, dd, $J = 3.66$, 3.90 Hz), 7.07 (1H, d, $J = 7.81$ Hz), 7.21 (1H, t, $J = 7.81$ Hz), 7.28 (1H, d, $J = 7.81$ Hz). HRMS (EI) M^+, Found: m/z 326.0926, 328.0885. Calcd for $C_{16}H_{19}O_5{}^{35}Cl$: 326.0921, $C_{16}H_{19}O_5{}^{37}Cl$: 328.0892.

4.15. Diethyl (1*R**,2*S**,3*R**)-8-chloro-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 6Ea

Obtained as a solid. Mp 83.5 °C (recystallized from hexane/AcOEt) IR (neat) 3494, 3064, 2981, 2936, 1733, 1596, 1572, 1447, 1371, 1268, 1200, 1143, 1096, 1027, 963, 897, 860, 811, 780, 741 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.25$ (3H, t, $J = 7.07$ Hz), 1.28 (3H, t, $J = 7.07$ Hz), 2.87 (1H, d, $J = 3.90$ Hz), 2.97–3.04 (1H, m), 3.17–3.24 (2H, m), 3.49 (1H, t, $J = 5.61$ Hz), 4.15–4.22 (4H, m), 5.46–5.48 (1H, m), 7.07 (1H, d, $J = 7.81$ Hz), 7.17 (1H, t, $J = 7.81$ Hz), 7.25 (1H, d, $J = 7.81$ Hz). HRMS (FAB) $(M+Li)^+$, Found: m/z. 333.1088, 335.1091. Calcd for $C_{16}H_{19}O_5{}^{35}ClLi$: 333.1081, $C_{16}H_{19}O_5{}^{37}ClLi$: 335.1085.

4.16. Diethyl (1*S*,2*S*,3*R*)-7-chloro-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 5Fa

Obtained as an oil. $[\alpha]_D^{25} = -57$ (c 0.78, EtOH, 68% ee). IR (neat) 3480, 2981, 2935, 1733, 1488, 1439, 1372, 1306, 1260, 1186, 1125, 1092, 1066, 1030, 940, 871, 812, 770, 742 cm^{-1}. ^1H NMR ($CDCl_3$) $\delta = 1.29$ (3H, t, $J = 7.07$ Hz), 1.30 (3H, t, $J = 7.07$ Hz), 2.59 (1H, d, $J = 4.64$ Hz), 2.86 (1H, dd, $J = 11.22$, 16.83 Hz), 3.11 (1H, dd, $J = 3.66$, 11.22 Hz), 3.16 (1H, dd, $J = 5.61$, 16.83 Hz), 3.35 (1H, dt, $J = 5.61$, 11.22 Hz), 4.17–4.30 (4H, m), 5.04 (1H, dd, $J = 3.66$, 4.64 Hz), 7.08 (1H, d, $J = 8.29$ Hz), 7.23 (1H, dd, $J = 1.95$, 8.29 Hz), 7.37 (1H, d, $J = 1.95$ Hz). HRMS (EI) M^+, Found: m/z 326.0903, 328.0876. Calcd for $C_{16}H_{19}O_5{}^{35}Cl$: 326.0921, $C_{16}H_{19}O_5{}^{37}Cl$: 328.0892.

4.17. Diethyl (1*R**,2*S**,3*R**)-7-chloro-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 6Fa

Obtained as a solid. Mp 106–107.5 °C (recystallized from hexane/AcOEt). IR (KBr) 3454, 2984, 2921, 2851, 1730, 1598, 1576, 1482, 1462, 1445, 1430, 1396, 1373, 1355, 1303, 1254, 1191, 1092, 1053, 1017, 948, 910, 886, 864, 808, 773, 745, 703, 655 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.27$ (3H, t, $J = 7.07$ Hz), 1.30 (3H, t, $J = 7.07$ Hz), 2.95 (1H, d, $J = 6.10$ Hz), 2.96 (1H, dd, $J = 10.49$, 16.59 Hz), 2.99 (1H, dd, $J = 9.27$, 10.25 Hz), 3.06 (1H, dd, $J = 5.61$, 16.59 Hz), 3.14 (1H, ddd, $J = 5.61$, 10.25, 10.49 Hz), 4.11–4.31 (4H, m), 4.93 (1H, dd, $J = 6.10$, 9.27 Hz), 7.03 (1H, d, $J = 8.29$ Hz), 7.18 (1H, dd, $J = 2.20$, 8.29 Hz), 7.58 (1H, d, $J = 2.20$ Hz). HRMS (EI) M^+, Found: m/z 326.0891, 328.0913. Calcd for $C_{16}H_{19}O_5{}^{35}Cl$: 326.0921, $C_{16}H_{19}O_5{}^{37}Cl$: 328.0892.

4.18. Diethyl (1*S*,2*S*,3*R*)-6-chloro-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 5Ga

Obtained as a solid. Mp 84.0–87.0 °C (recystallized from benzene). $[\alpha]_D^{25} = -75$ (*c* 0.51, EtOH, 66% ee). IR (KBr) 3466, 2988, 2939, 1715, 1595, 1475, 1442, 1381, 1342, 1309, 1274, 1228, 1190, 1119, 1085, 1066, 1032, 937, 897, 876, 838, 795, 769, 744, 673 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 1.298$ (3H, t, $J = 7.07$ Hz), 1.302 (3H, t, $J = 7.07$ Hz), 2.47 (1H, d, $J = 5.12$ Hz), 2.88 (1H, dd, $J = 11.22$, 16.83 Hz), 3.10 (1H, dd, $J = 3.42$, 11.47 Hz), 3.16 (1H, dd, $J = 5.61$, 16.83 Hz), 3.35 (1H, ddd, $J = 5.61$, 11.22, 11.47 Hz), 4.18–4.30 (4H, m), 5.07 (1H, dd, 3.42, 5.12 Hz), 7.14 (1H, s), 7.22 (1H, d, $J = 8.29$ Hz), 7.31 (1H, d, $J = 8.29$ Hz). HRMS (EI) M^+, Found: *m*/*z* 326.0924, 328.0884. Calcd for $C_{16}H_{19}O_5{}^{35}Cl$: 326.0921, $C_{16}H_{19}O_5{}^{37}Cl$: 328.0892.

4.19. Diethyl (1*R**,2*S**,3*R**)-6-chloro-1-hydroxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate 6Ga

Obtained as an oil. IR (KBr) 3469, 2982, 2919, 1719, 1597, 1576, 1481, 1437, 1423, 1397, 1377, 1354, 1312, 1293, 1245, 1196, 1165, 1077, 1049, 1021, 892, 868, 836, 806, 786, 753, 697 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) $\delta = 1.28$ (3H, t, $J = 7.15$ Hz), 1.30 (3H, t, $J = 7.15$ Hz), 2.89 (1H, d, $J = 5.14$ Hz), 2.97–3.19 (4H, m), 4.10–4.30 (4H, m), 4.94 (1H, dd, $J = 5.14$, 8.44 Hz), 7.10 (1H, d, $J = 2.20$ Hz), 7.23 (1H, dd, $J = 2.20$, 8.44 Hz), 7.51 (1H, d, $J = 8.44$ Hz). HRMS (EI) M^+, Found: *m*/*z* 326.0916, 328.0903. Calcd for $C_{16}H_{19}O_5{}^{35}Cl$: 326.0921, $C_{16}H_{19}O_5{}^{37}Cl$: 328.0892.

4.20. Ethyl (1*R**,4*R**,10*S**)-1,3,4,5-tetrahydro-3-oxo-1,4-methano-2-benzoxepin-10-carboxylate 7Aa

Obtained as a solid. Mp 116–117 °C (recystallized from benzene). IR (KBr) 2985, 2929, 1782, 1731, 1463, 1434, 1373, 1337, 1313, 1273, 1242, 1208, 1143, 1100, 1023, 998, 957, 943, 876, 858, 820, 778, 752, 729, 695 cm^{-1}. ^1H NMR ($CDCl_3$) $\delta = 0.95$ (3H, t, $J = 7.07$ Hz), 3.08 (1H, d, $J = 17.81$ Hz), 3.31–3.33 (1H, m), 3.51 (1H, dd, $J = 5.37$, 17.81 Hz), 3.77 (1H, t, $J = 5.12$ Hz), 3.90–4.06 (2H, m), 5.43 (1H, d, $J = 5.12$ Hz), 7.12–7.33 (4H, m). HRMS (FAB) M^+, Found: *m*/*z* 247.0951. Calcd for $C_{14}H_{15}O_4$: 247.0970.

4.21. Dehydration of cycloadduct 5Ab

To a toluene (5 ml) solution of tetrahydronaphthalene **5Ab** (27 mg, 0.10 mmol, 72% ee) was added a catalytic amount of *p*-toluenesulfonic acid. Reaction mixture was stirred at 80 °C for 80 min. The reaction mixture was condensed in vacuo. Separation by TLC (SiO_2, hexane/AcOEt = 5:1) gave **8** (23 mg, 91%).

4.22. Dimethyl (*R*)-3,4-dihydronaphtalene-2,3-dicarboxylate 8

Obtained as an oil. $[\alpha]_D^{25} = +97$ (*c* 0.22, $CHCl_3$, 76% ee), {lit.[3d] (*R*)-form: $[\alpha]_D^{20} = +128$ (*c* 0.58, $CHCl_3$)}. IR (neat) 3062, 3000, 2952, 2844, 1713, 1633, 1601, 1572, 1487, 1454, 1435, 1381, 1312, 1205, 1117, 1099, 1080, 1022, 949, 924, 841, 779, 730, 713 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) $\delta = 3.14$ (1H, dd, $J = 8.05$, 16.34 Hz), 3.35 (1H, dd, $J = 3.42$, 16.34 Hz), 3.61 (3H, s), 3.84 (3H, s), 3.88 (1H, dd, $J = 3.42$, 8.05 Hz), 7.18–7.27 (4H, m), 7.65 (1H, s). HRMS (FAB) M^+, Found: *m*/*z* 247.0983. Calcd for $C_{14}H_{15}O_4$: 247.0971.

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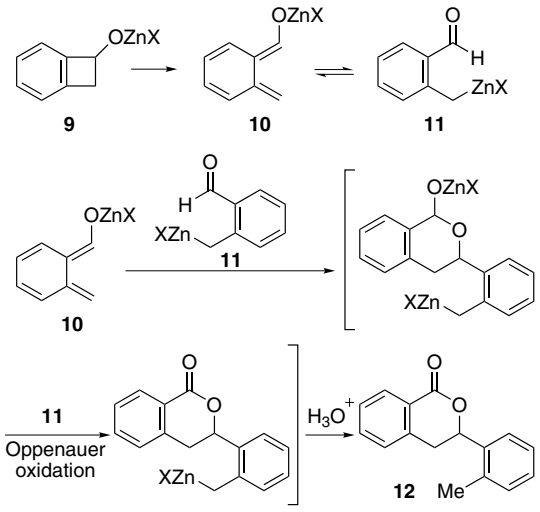
7. When the zinc alkoxide was formed completely by the reaction of benzocyclobutenol **1A** and the reactive isopropylzinc reagent for an appropriate reaction time, the enantioselectivity might be enhanced.
8. When the interval without a dienophile was too long, the production of a slight amount of a by-product **12**, which might have disturbed the ideal reaction pathway, was confirmed. Although the mechanism of the production of **12** was not clear yet, a possible pathway is shown in the following scheme.



9. Supplementary material of Ref. 2d.