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Asymmetric Baeyer–Villiger Oxidation of 2,3- and 2,3,4-Substituted Cyclobutanones Catalyzed by Chiral Phosphoric Acids with Aqueous H_2O_2 as the Oxidant

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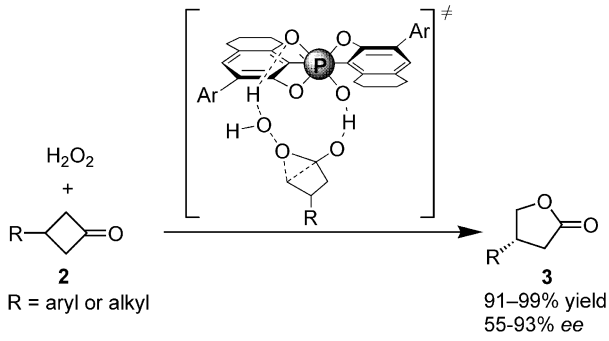
Catalytic asymmetric Baeyer–Villiger (B–V) oxidation of 2,3,4-trisubstituted cyclobutanone (**4**) has been realized by the catalysis of a 1,1′-bi-2-naphthol (BINOL)-derived chiral phosphoric acid (**1j**), which contains bulky 2,4,6-triisopropyl phenyl groups at the 3,3′-positions of the BINOL backbone, using 30 % aqueous H_2O_2 as the oxidant, affording the corresponding γ-lactone (**5**) in 99 % yield with 95 % *ee*. In a divergent kinetic resolution of racemic 2,3-disubstituted bicyclic cyclobutanones (**6**) through asymmetric B–V oxidation, the chiral phosphoric acid **1p** demonstrated excellent catalytic performance, giving a range of regioisomeric chiral lactones in a normal lactone (*nl*)/abnormal lactone (*al*) ratio of up to 2.1:1, with up to 99 % *ee* in the *al* product. It was found that fine tuning of the stereoelectronic properties of the backbone in chiral phosphoric acids is critically important for attaining high levels of enantioselectivity in the catalysis of B–V reactions of different type of cyclobutanones. The present work has provided a convenient approach to the synthesis of a variety of optically active chiral γ-lactones.

Introduction

Baeyer–Villiger (B–V) oxidation[1] represents one of the most important reactions in organic chemistry.[2] The catalytic, enantioselective B–V oxidation of prochiral or racemic ketones using environmentally benign oxidants to give optically enriched lactones has been one of the most challenging transformations in chiral catalysis. Since the first reports were independently made by Strukul and coworkers[3] and Bolm et al.[4] in 1994, a number of chiral metal complexes and organic molecules have been developed as catalysts for the oxidation of various prochiral and/or racemic ketones.[5] However, despite these efforts, wide substrate generality has not yet been achieved in most cases, and excellent enantiocontrol in the reaction is usually achieved mainly by enzymatic systems.[6] On the other hand, considering the oxidants employed in the B–V reaction, only very few chiral catalyst systems are tolerant of aqueous hydrogen peroxide as an environmentally benign oxidant.[3,7] In these regards, we have recently reported the first example of chiral Brønsted-acid-catalyzed asymmetric B–V oxidation of 3-substituted cyclobutanones by using aqueous H_2O_2 as the oxidant, affording a number of chiral γ-lactones in high yields with good to excellent *ee* values (Scheme 1).[8a] A subsequent mechanistic study, which was based on kinetic measurements and theoretical calculations, suggested that the chiral phosphoric acid[8b–8ac] functions as a bifunctional catalyst to simultaneously activate both the reactants and the Criegee intermediate in the reaction, and that the enantioselectivity is largely dependent on the aryl substituents at the 3,3′-positions of the catalyst backbone.[9] With the aim of further demonstrating the potential of this type of catalyst, herein we report asymmetric B–V reactions of a prochiral tricyclic cyclobutanone and a divergent kinetic resolution of racemic bicyclic cyclobutanone derivatives using 30 % aqueous H_2O_2 as the oxidant.



Scheme 1. BINOL-Derived chiral phosphoric-acid-catalyzed enantioselective B–V reaction of 3-substituted cyclobutanones.[8a,9]

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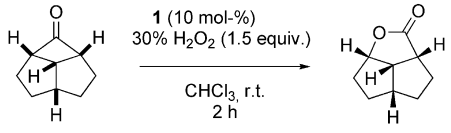
Results and Discussion

Asymmetric B–V Oxidation of Tricyclic Butanone

Tricyclic cyclobutanone **4** has been used as a test prochiral substrate for chemocatalytic asymmetric B–V oxidation, with good to excellent enantioselectivities being achieved in some cases.[10] However, to the best of our knowledge, no report has involved the use of 30% aqueous H_2O_2 for this substrate. A preliminary test of the optimized catalyst **1p** for B–V oxidation of 3-substituted cyclobutanones **2** in our previous communication[8a] revealed that this catalyst only demonstrated moderate enantioselectivity in the oxidation of tricyclic cyclobutanone **4** under the experimental conditions shown in Table 1, affording the corresponding γ-lactone product **5** in 96% yield with 67% *ee* (entry 16). Clearly, the structure of tricyclic cyclobutanone **4** differs significantly from that of 3-substituted cyclobutanones **2**. The above mentioned preliminary result showed that the oxidation of substrates with distinct structural features requires a substrate–catalyst mutual match to realize maximal asymmetric induction and catalytic activity in the reaction. Accordingly, the catalytic performance of a variety of 1,1′-bi-2-naphthol (BINOL)-derived chiral phosphoric acids **1a**–**r** with diverse steric and electronic properties of the 3,3′-substituents and the skeleton (Figure 1) was subsequently examined in the B–V oxidation of tricyclic cyclobutanone **4**; the reaction was performed in $CHCl_3$ at room temperature with a catalyst loading of 10 mol-% by using 1.5 equiv. of 30% aqueous H_2O_2 as the oxidant.

Table 1. Asymmetric B–V oxidation of the tricyclic cyclobutanone **4** in the presence of chiral phosphoric acid **1a**–**q**.[a]



4 **5**

Entry	Cat.	Yield [%][b]	*ee* [%][c]
1	**1a**	97	31
2	**1b**	99	43
3	**1c**	99	19
4	**1d**	99	4
5	**1e**	99	56
6	**1f**	99	32
7	**1g**	95	34
8	**1h**	99	66
9	**1i**	99	29
10	**1j**	99	87
11	**1k**	99	48
12	**1l**	99	68
13	**1m**	99	64
14	**1n**	99	75
15	**1o**	91	69
16	**1p**	96	67
17	**1r**	99	55

[a] Reagents and conditions: 4 (0.1 M in $CHCl_3$), aq. H_2O_2 (30%, 1.5 equiv.), room temp. [b] Yield of isolated product. [c] The enantiomeric excess of **5** was determined by chiral GC (Suplco Beta Dex 225). The absolute configuration of **5** was determined to be 1*S*,4*R*,7*R*,10*S* by comparison of its optical rotation with that reported in the literature.[11c]

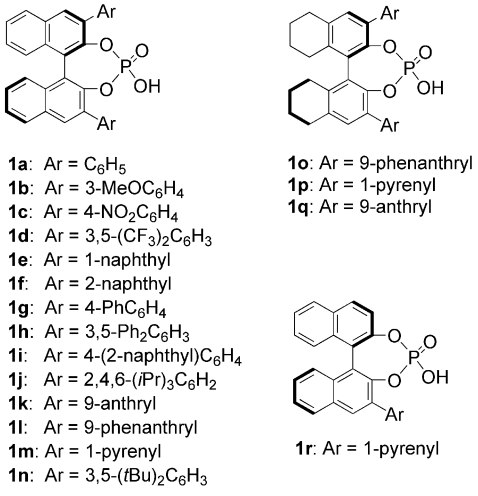
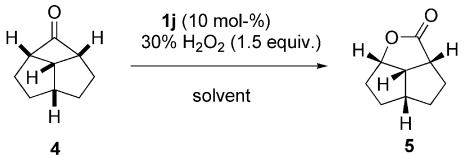


Figure 1. BINOL-derived chiral phoposphoric acids used in this study.

The results are summarized in Table 1. In general, the chiral phosphoric acids constitute a class of efficient catalysts for this reaction, with yields of the lactone product **5** ranging from 91 to 99% in all cases, however, the enantioselectivity varied widely (4–87% *ee*) depending on the detailed structural motifs of the catalyst. Changing the rigid binaphthyl backbone of **1l** or **1m** to the conformationally more flexible H_8-binaphthyl of **1o** or **1p** did not much effect the enantioselectivity (Table 1, entries 12 vs. 15 and 13 vs. 16), and the *ee* values of **5** remained moderate (64–69%) in these cases. On the other hand, the enantioselectivity of the reaction was found to be highly sensitive to slight variations in the stereoelectronic features of the 3,3′-subustitents on the catalyst backbone. Clearly, the incorporation of electron-withdrawing groups into the 3,3′-substituents of the phosphoric acids (**1c** and **1d**) was unfavorable for the reaction, giving lactone **5** with only modest *ee* values (Table 1, entries 3–4). Although the steric bulk of the 3,3′-aryl substituents generally exhibited a beneficial effect on the enantioselectivity (Table 1, entries 1, 5, and 8), the trend was less clear in several cases and the distinct spatial orientation of the substituents seems to also play a role (e.g., entries 5 vs. 6 and 1 vs. 7). Among the phosphoric acids screened for the reaction, **1j**, with the bulky 2,4,6-triisopropyl phenyl groups at the 3,3-positions of the catalyst backbone, was found to be optimal in terms of the enantioselectivity, affording **5** in almost quantitative yield with good enantioselectivity (87% *ee*; Table 1, entry 10).

Further attempts to improve the enantioselectivity of **1j**-catalyzed B–V oxidation of **4** were undertaken by changing the reaction solvent and the reaction temperature. The results are summarized in Table 2. Clearly, both parameters have an impact on the catalytic efficiency and enantioselectivity. Nearly quantitative yields and good *ee* values (84–89%) of the product were obtained for the reactions

Table 2. Solvent and temperature effects on **1j**-catalyzed asymmetric B–V oxidation of tricyclic cyclobutanone **4**.[a]



4 **5**

Entry	Solvent	Temp. [°C]	Time [h]	Yield [%][b]	*ee* [%][c]
1	$CHCl_3$	25	2	99	87
2	CH_2Cl_2	25	2	99	88
3	$ClCH_2CH_2Cl$	25	2	92	87
4	toluene	25	2	99	88
5	$F_3CC_6H_5$	25	2	99	89
6	Et_2O	25	2	99	19
7	*n*-hexane	25	8	92	84
8	toluene	0	12	99	91
9	toluene	–20	12	99	93
10	toluene	–40	24	99	95
11	toluene	–50	24	99	95

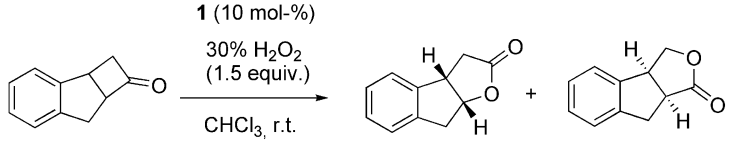
[a] Reagents and conditions: **4** (0.1 M), aq. H_2O_2 (30%, 1.5 equiv.). [b] Yield of isolated product. [c] The enantiomeric excess of **5** was determined by chiral GC on a Suplco Beta Dex 225. The absolute configuration of **5** was determined to be 1*S*,4*R*,7*R*,10*S* by comparison of its optical rotation with that reported in the literature.[11c]

carried out at room temp. in toluene or halogen-containing solvents (Table 2, entries 1–5). Under otherwise identical conditions, the reaction performed in *n*-hexane was more sluggish (Table 2, entry 7), whereas the catalysis in diethyl ether gave lactone **5** with only modest enantioselectivity (19% *ee*; Table 2, entry 6). Although the reaction in toluene took a prolonged period to reach completion at reduced temperatures, this was beneficial for the enantioselectivity as evidenced by the enhanced *ee* values (from 88 to 95%) achieved when the reaction temperature was varied from room temp. to –40 °C (Table 2, entries 4 and 8–10). Further decreasing the temperature to –50 °C gave no further improvement on the *ee* value of the product (Table 2, entry 11).

Asymmetric B–V Oxidation of Racemic Bicyclic Cyclobutanones

Divergent kinetic resolution of racemic cyclobutanones constitutes an important asymmetric B–V transformation.[11] As a result of the combined action of the distinct migratory aptitudes of ketonic alkyls on the substrate and the asymmetric induction of the chiral catalyst, such B–V reactions would usually lead to two regioisomeric lactones

Table 3. Asymmetric B–V oxidation of racemic cyclobutanone **6a** in the presence of chiral phosphoric acid **1a**–**q**.[a]



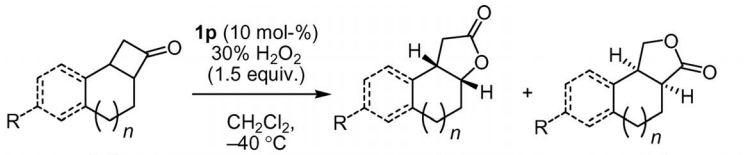
rac-**6a** **7a** (nl) **8a** (al)

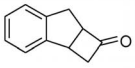
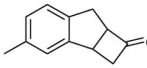
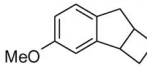
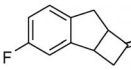
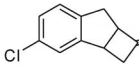
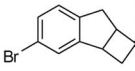
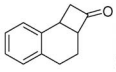
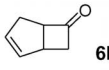
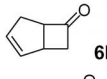
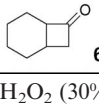
Entry	Cat.	Time [h]	Solvent	Yield [%][b]	*nl*/*al*[c]	*nl*, *ee* [%][d]	*al*, *ee* [%][d]
1	**1a**	24	$CHCl_3$	99	3.7:1	7	–4
2	**1b**	12	$CHCl_3$	99	4.0:1	6	24
3	**1c**	12	$CHCl_3$	99	4.2:1	9	33
4	**1d**	12	$CHCl_3$	99	4.0:1	0	0
5	**1e**	12	$CHCl_3$	99	2.0:1	23	42
6	**1f**	12	$CHCl_3$	99	4.1:1	8	29
7	**1g**	12	$CHCl_3$	99	3.6:1	11	44
8	**1h**	12	$CHCl_3$	99	2.7:1	21	59
9	**1i**	12	$CHCl_3$	99	3.3:1	12	39
10	**1j**	12	$CHCl_3$	99	2.7:1	29	86
11	**1l**	12	$CHCl_3$	99	1.6:1	43	67
12	**1m**	12	$CHCl_3$	99	1.5:1	49	78
13	**1o**	12	$CHCl_3$	99	1.3:1	48	65
14	**1p**	12	$CHCl_3$	99	1.3:1	56	76
15	**1k**	12	$CHCl_3$	99	2.5:1	28	74
16	**1p**	12	CH_2Cl_2	99	1.7:1	47	86
17	**1p**	12	$ClCH_2CH_2Cl$	99	1.6:1	51	84
18	**1p**	12	toluene	99	2.1:1	34	72
19	**1p**	12	$CF_3C_6H_5$	99	2.1:1	37	79
20	**1p**	12	Et_2O	99	4.1:1	9	30
21	**1p**	12	*n*-hexane	94	3.3:1	14	46
22[e]	**1p**	24	CH_2Cl_2	99	2.2:1	38	94

[a] Reagents and conditions: **6a** (0.1 M), aq. H_2O_2 (30%, 1.5 equiv.), room temp. [b] Total yield of isolated products **7a** and **8a**. [c] The ratio of **7a**/**8a** was determined by ^1H NMR spectroscopic analysis of the isolated mixture of the isomeric lactones. [d] The enantiomeric excesses of **7a** and **8a** were determined by chiral HPLC analysis with a Chiralpak OD column; their absolute configurations were not assigned. [e] The reaction was carried out at –40 °C.

in optically enriched forms, sometimes together with unreacted ketone, by kinetic resolution.[12] The product generated by migration of the group that is in accord with migratory aptitude is defined as the normal lactone (abbreviated as *nl*) and the product generated by migration of the group in contravention of the migratory aptitude is thus defined as the abnormal lactone (abbreviated as al).[10e] In fact, asymmetric B–V oxidation of racemic ketones is a well-documented reaction that has previously been in the domain of enzyme catalysis.[6] A variety of chiral transition-metal complexes have also been shown to catalyze such reactions, giving the lactones with high optical purity in some cases.[3,4,7c–7e,10,11] Although significant achievements have been made with metal complex catalysts,[11a,11b,11d,11e,12] to the best of knowledge, the direct use of organocatalysts and aqueous H_2O_2 has never been reported. On the basis of our previous results with the chiral phosphoric acid-catalyzed asymmetric B–V oxidation of 3-substituted cyclobutanones **2**,[8,9] and on the tricyclic cyclobutanone **4** mentioned above, we further explored the possibility of applying this approach to the oxidation of racemic 2,3-disubstituted bicyclic cyclobutanones **6** using chiral phosphoric acid as the catalyst and 30% aqueous H_2O_2 as the oxidant. As shown in Table 3, the chiral phosphoric acid **1b** was found to be efficient in the B–V oxidation of racemic cyclobutanone **6a**, albeit giving low *ee* values (<10%) for both products (**7a** and **8a**; Table 3, entry 1). The normal lactone **7a** is generated by following the migratory aptitude rule and, concomitantly, the abnormal lactone **8a** results from migration of the less substituted carbon atom. Under the stereoelectronic

Table 4. Asymmetric B–V oxidation of racemic bicyclic cyclobutanones **6a**–**j** in the presence of chiral phosphoric acid **1p**.[a]



Entry	6a–j	Time (h)	Yield (%)[b]	nl/al[c]	*ee* (%) (nl, al)[d]
1	 **6a**	24	99	2.2:1	38, 94
2	 **6b**	18	99	2.5:1	36, 95
3	 **6c**	36	99	2.1:1	–, –[f]
4	 **6d**	14	98	4.6:1	24, 99
5	 **6e**	36	99	3.5:1	15, 96
6	 **6f**	17	99	3.1:1	17, 80
7	 **6g**	19	99	3.3:1	28, 97
8	 **6h**	36	99	3.2:1	28, 80
9[e]	 **6h**	12	99	2.2:1	32, 74
10[e]	 **6i**	12	95	4.7:1	18, 85
11[e]	 **6j**	12	85	11.5:1	7, >99

[a] Reagents and conditions: **6** (0.1 M), aq. H_2O_2 (30%, 1.5 equiv.), –40 °C. [b] Total yield of isolated products **7** and **8**. [c] For entries 1–7, the ratio of *nl*/*al* was determined by ^{1}H NMR spectroscopic analysis; for entries 8–11, the ratio of *nl*/*al* was determined by GC analysis. [d] For entries 1–7, the enantiomeric excesses of **7** and **8** were determined by HPLC analysis with a chiral column; for entries 8–11, the enantiomeric excesses of **7** and **8** were determined by GC analysis with a chiral column. The absolute configurations were not assigned. [e] The reaction was carried out at room temp. [f] The peaks were not well-resolved on the HPLC chromatograph.

control of a suitable chiral catalyst, *nl* and/or al might be obtained with good conversion and high *ee* values. Using the racemic bicyclic cyclobutanone **6a** as a model substrate, we subsequently screened the chiral phosphoric acids **1a**–**q** for their ability to catalyze the reaction with 30% H_2O_2 as the oxidant. As shown in Table 3, performing the reactions in chloroform led to complete conversion of the substrates after 12–24 h at room temp., and resulted in the clean formation of **7a** and **8a** in quantitative yields. A moderate to high preference for the *nl* product **7a** (*nl*/*al* = 1.3–4.2) was observed in all cases, which is consistent with the migratory aptitude for B–V reactions. The enantioselectivity for both products varied widely within the series of the chiral phosphoric acid catalysts, ranging from 0–56 for **7a** and 0–86 for **8a**, respectively. For each chiral phosphoric acid, the ratio of the *ee* values of the two regioisomers **7a** and **8a** was approximately equal to the inverse ratio of their relative amounts.[12] Substituents at the 3,3′-positions of the binaphthyl scaffold of the catalyst play a critical role in controlling both regioselectivity and enantioselectivity of this series of reactions, although it is difficult to correlate these selectivities with structural features of the catalyst. Herein, the factors that control the stereoselectivity seem to work in parallel with those discussed above for B–V oxidation of tricyclic ketone **4**, i.e., the 3,3′-substituents at the catalyst backbone should be sufficiently bulky (Table 3, entries 10–14) and adopt a suitable orientation (Table 3, entries 5 vs. 6) to favor good *ee* values for both isomers, whereas the presence of less bulky 3,3′-substituents (Table 3, entries 1 and 2) or some strongly electron-withdrawing groups (Table 3, entries 3 and 4) on the catalyst is disadvantageous for the enantioselectivity. In short, in the presence of catalysts with sterically more encumbering groups (see **1j**–**p**), the products **7a** and **8a** were both obtained in moderate to good *ee* values, together with a somewhat enhanced regioselectivity towards the *al* product (Table 3, entries 10–14).

Solvent and temperature effects on the B–V oxidation of racemic **6a** was further investigated with **1p** as the catalyst under conditions that were otherwise identical to those described above. Whereas the reactions proceeded smoothly in all the tested solvents, both the regioselectivity and the enantioselectivity varied significantly with the solvent used. In general, chlorinated solvents favored both higher enantioselectivity and regioselectivity for the *al* product **8a** (Table 3, entries 14 and 16–17). As expected, the reaction temperature also had a remarkable effect on the regioselectivity and enantioselectivities. When the reaction was carried out at –40 °C, the *ee* value of *al* was enhanced up to 94%, albeit with a concomitant decrease in its proportion in the product mixture (Table 3, entries 16 vs. 22).

A variety of chiral racemic bicyclic cyclobutanone derivatives were then examined as substrates for the asymmetric B–V reactions, which were performed with 0.1 molar equivalent of phosphoric acid **1p** as the catalyst and 1.5 equivalent of 30% aqueous H_2O_2 as the oxidant. The reactions proceeded smoothly in dichloromethane at–40 °C, leading to clean formation of the corresponding normal lactones and abnormal lactones in excellent yields within the specified period of reaction time (Table 4). In all cases, the *nl* products **7a**–**j** were formed as the preferential regioisomers (*nl*/*al* = 2.1 to 11.5), which is in agreement with the migratory aptitude for B–V reactions. Whereas the enantioselectivities for the *nl* products were generally only modest (7–38% *ee*), they were far higher for the corresponding minor *al* isomers **8a**–**j**, which had *ee* values ranging from good to excellent (74–99% *ee*).

Conclusions

The asymmetric B–V oxidation of tricyclic cyclobutanone **4** using 30% aqueous H_2O_2 as the oxidant proceeds smoothly under the catalysis of chiral phosphoric acids to afford the corresponding chiral γ-lactone **5** in quantitative yield with up to 95% *ee*. The chiral phosphoric acids were also found to be efficient catalysts for the asymmetric B–V reaction of various racemic bicyclic cyclobutanone derivatives. The reaction gave a range of chiral lactones with the *nl* products as the major regioisomer in moderate to high *nl*/*al* ratios, whereas the minor *al* isomers could be obtained with good to excellent *ee* values. It was found that fine tuning of the stereoelectronic properties of the backbone in the chiral phosphoric acids is critically important for attaining high levels of enantioselectivity in the catalysis of B–V reactions with different types of cyclobutanones. The present work has provided a convenient approach to the synthesis of a variety of optically active chiral γ-lactones.

Experimental Section

General Methods: NMR spectra were recorded with a Varian Mercury 300 (^{1}H: 300 MHz) or a Varian 400-MR (^{1}H: 400 MHz) spectrometer with samples dissolved in $CDCl_3$. Chemical shifts are expressed in ppm with TMS as an internal standard (δ = 0 ppm) for ^{1}H NMR spectroscopic data. Coupling constants (*J*) are listed in Hertz. HPLC analysis was carried out with a JASCO PU 2089 or a JASCO 1589 instrument. GC analysis was performed with an Agilent 6890N instrument. Unless stated otherwise, all solvents were purified and dried according to standard methods prior to use.

Typical Procedure for the Asymmetric B–V Reaction of Tricyclic Cyclobutanone 4 Catalyzed by Chiral Phosphoric Acid 1j and Aqueous H_2O_2 as Oxidant: A 5-mL Schlenk tube was charged with **1j** (7.5 mg, 0.01 mmol), tricyclic cyclobutanone **4** (14 mg, 0.1 mmol), and toluene (1 mL). The mixture was cooled and stirred at –40 °C before 30% H_2O_2 (17 μL, 0.15 mmol) was added, and the resulting mixture was stirred for 24 h at this temperature. The reaction was quenched by addition of an aqueous solution of Na_2SO_3 (0.1 mL), and the product **5** was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 6:1) in 99% yield. $[\alpha]_D^{20}$ = –66.5 (*c* 0.71, $CHCl_3$), 95% *ee* [ref.[10c] $[\alpha]_D^{20}$ = +62 (*c* 1.0, $CHCl_3$) for (1*R*,4*S*,7*S*,10*R*)-isomer with >98% *ee*]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.94 (dd, *J* = 10.8, 2.8 Hz, 1 H), 3.17–3.20 (m, 1 H), 3.05–3.09 (m, 1 H), 2.62–2.65 (m, 1 H), 2.07–2.18 (m, 3 H), 1.82 (m, 3 H), 1.44–1.54 (m, 2 H) ppm; The enantiomeric excess was determined by chiral GC analysis on a Chiralcel Supelco BETA-DEX 225 column (column temperature = 160 °C, N_2 flow rate = 1.0 mL/min), t_R = 12.4 min (minor), t_R = 13.5 min (major).

Typical Procedure for Asymmetric B–V Reaction of Racemic Bicyclic Cyclobutanones 6a Catalyzed by Chiral Phosphoric Acid 1p and 30% H_2O_2 as Oxidant: A 5-mL Schlenk tube was charged with **1p** (0.01 mmol), racemic cyclobutanone **6a** (0.1 mmol), and CH_2Cl_2 (1 mL). The mixture was cooled and stirred at –40 °C before 30% aqueous H_2O_2 (17 μL, 0.15 mmol) was added, and the resulting mixture was stirred for 12–36 h at this temperature. After completion of the reaction, the residual H_2O_2 was quenched with aqueous Na_2SO_3 (0.1 mL), and the normal lactone **7a** and abnormal lactone **8a** were isolated as a regioisomeric mixture by column chromatography on silica gel (petroleum ether/ethyl acetate, 6:1) in 99% yield. The **7a**/**8a** ratio was determined by comparison of the integration values of the relevant ^{1}H NMR signals at δ = 5.28–5.33 ppm (**7a**) and δ = 4.69 ppm (**8a**) for the isomeric mixture.[10e]

Mixture of Compounds 7a and 8a: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.23–7.29 (m), 5.28–5.33 (m), 4.69 (dd, J = 9.3, 6.3 Hz), 4.53 (dd, J = 9.3, 1.2 Hz), 3.98–4.09 (m), 3.31–3.40 (m), 3.05 (dd, J = 18.0, 9.3 Hz), 2.75 (dd, J = 17.7, 1.2 Hz) ppm. The enantiomeric excess was determined by chiral HPLC analysis on a Chiralpak OD column (hexane/*i*PrOH = 95:5, flow rate: 0.7 mL/min, λ = 214 nm), t_R = 38.3 min (minor) and 53.5 min (major) for the two enantiomers of **7a**, respectively; t_R = 35.7 min (major), 48.3 min (minor) for the two enantiomers of **8a**, respectively. The peak assignments were made by comparison with chromatographs of the corresponding racemic lactones. The absolute configurations for these isomers were not assigned.

Supporting Information (see also the footnote on the first page of this article): Detailed experimental procedure and product characterization for the catalytic asymmetric B–V oxidation of racemic cyclobutanone **6**.

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