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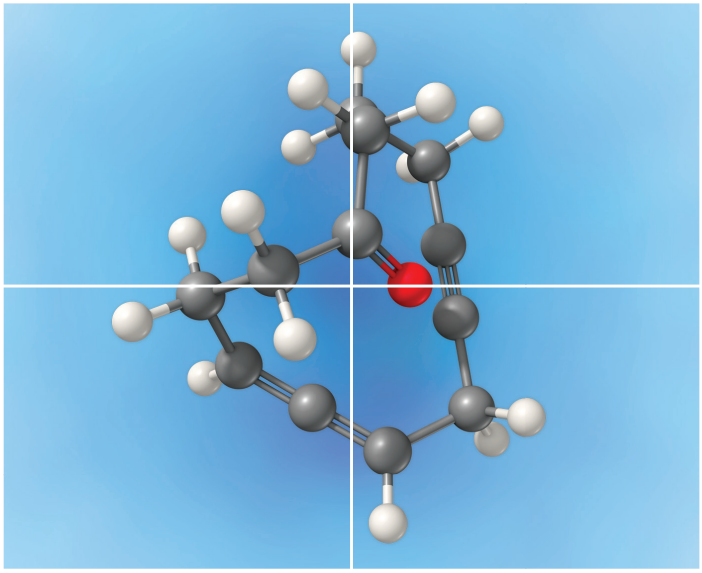

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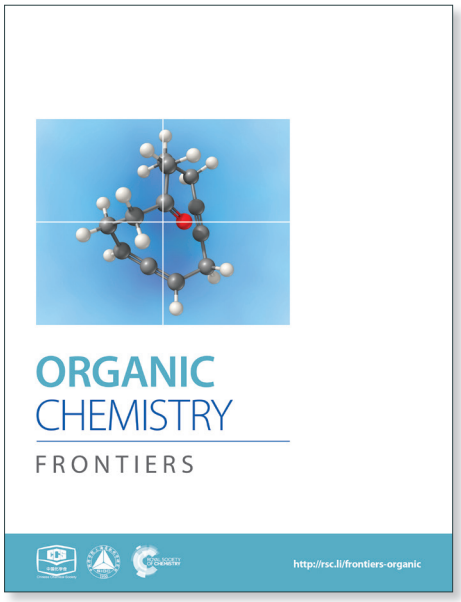

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Stereoselective Intramolecular Cyclopropanation of α-Diazoacetates via Co(II)-Based Metalloradical Catalysis

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Supporting Information Placeholder

ABSTRACT: Co(II) complexes of D_2-symmetric chiral porphyrins have been proven to be effective metalloradical catalysts for the asymmetric intramolecular cyclopropanation of allyl α-diazoacetates. 4-(Dimethylamino)pyridine (DMAP), through positive *trans* effect, plays an important role in the enhancement of the asymmetric induction for the intramolecular cyclopropanation process. This metalloradical catalytic system is suitable for cyclopropanation of allyl α-diazoacetates with varied functional groups and substitution patterns, producing bicyclic products with complete diastereocontrol and good enantiocontrol.

Introduction

Optically pure cyclopropane and cyclopropane-containing polycyclic compounds have been attracting diverse research interests due to not only their fundamental importance, but also their potential synthetic applications.[1] Among different methods, transition metal-catalyzed asymmetric olefin cyclopropanation via carbene transfer has been developed into one of the most versatile methods for the stereoselective construction of these valuable three-membered ring compounds.[2] The intramolecular variation of cyclopropanation allows stereoselective construction of the [n.1.0]bicyclic skeletons, which serves as important intermediates in the synthesis of many interesting biologically active compounds and natural products.[3] As one class of relatively stable and readily available diazo reagents, α-diazoacetates have been widely used for the generation of the carbene species in a number of carbene transfer reactions. The intramolecular cyclopropanation of allyl α-diazoacetates provides a direct way for rapid construction of the bicyclo[3.1.0]hexan-2-one structure. This important transformation, especially the asymmetric version, has been extensively studied over the past decades, which is highlighted by the catalytic systems based on rhodium[4] and ruthenium[5] complexes.

As stable metalloradicals with well-defined open-shell doublet d^7 electronic structure, cobalt(II) complexes of porphyrins [Co(Por)] have been demonstrated as a new class of potent metalloradical catalysts for cyclopropanation reactions.[6] The unprecedented radical pathway initiated by this new system enabled the development of highly asymmetric cyclopropanation of a broad combination of olefin substrates and diazo reagents.[7] Recently, Co(II) complexes of D_2-symmetric chiral porphyrins [Co(D_2-Por*)] were reported to be effective catalysts for the asymmetric intramolecular cyclopropanation of allyl α-diazoacetates with two electron-withdrawing α-groups, namely acceptor/acceptor-substituted diazo reagents.[8] While the Co(II)-catalyzed intramolecular cyclopropanation was shown to be both general and highly stereoselective for various acceptor/acceptor-substituted diazo reagents, only one example of acceptor-substituted allyl α-diazoacetate was examined with the catalytic system for intramolecular formation of the corresponding bicyclo[3.1.0]hexan-2-one via the Co(II)-based metalloradical catalysis (MRC).[9] To assess whether the Co(II)-based MRC would also be generally effective for acceptor-substituted diazo reagents, in addition to the well-demonstrated acceptor/acceptor-substituted diazo reagents, we have performed an systematic investigation on asymmetric intramolecular cyclopropanation of allyl α-diazoacetates.

Results and discussion

We herein report the study of allyl α-diazoacetate derivatives, a representative class of acceptor-substituted diazo reagents, for asymmetric intramolecular cyclopropanation utilizing a "toolbox" of first-generation Co(II)-based metalloradical catalysts (Figure 1).[10] Among them, the Co(II) complex of 3,5-Di^{t}Bu-ChenPhyrin, [Co(**P1**)], with 4-(dimethylamino)pyridine (DMAP) as additive, can effectively catalyze the intramolecular cyclopropanation reactions of allyl α-diazoacetates with a range of functional groups and substitution patterns. The corresponding bicyclo[3.1.0]hexan-2-one derivatives can be produced as a single diastereomer in good to high yields and with significant asymmetric induction.

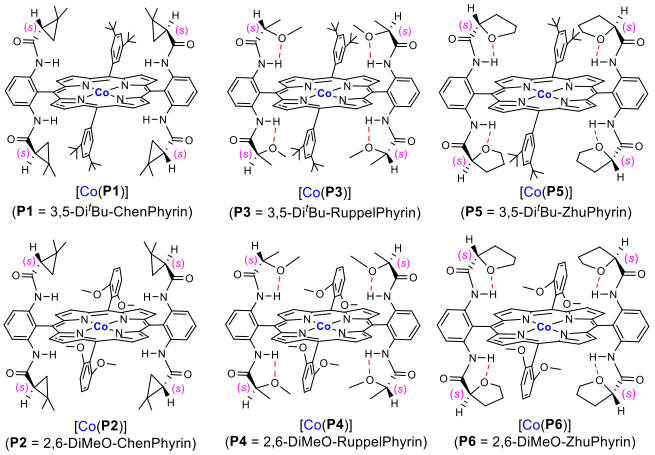
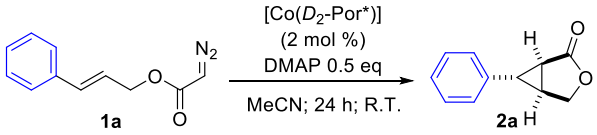


Figure 1. Structures of Co(II) complexes of first-generation D_2-symmetric chiral amidoporphyrins.

Initial experiments were focused on the intramolecular cyclopropanation of cinnamyl α-diazoacetate (**1a**) (Table 1) by utilizing a standard "toolbox" of first-generation metalloradical catalysts

[Co(**P1-P6**)] (Figure 1), which have been proven to be effective for a variety of asymmetric intermolecular cyclopropanation reactions.[7] Applying similar conditions that were optimized for asymmetric intermolecular olefin cyclopropanation with α-diazoacetates, which took the advantage of the positive *trans* effect of DMAP as an additive,[11] it was found that the use of 2 mol % of [Co(**P1**)] (**P1** = 3,5-Di^{t}Bu-ChenPhyrin) could successfully catalyze the cyclopropanation reaction of **1a** in 75% yield with complete diastereocontrol and significant asymmetric induction (entry 1). In the absence of DMAP, the enantioselectivity of the intramolecular cyclopropanation process dropped dramatically while the yield was substantially increased (entry 2). This result demonstrates that the additive DMAP, a potential axial ligand for the Co center, played an important role in enhancing the asymmetric induction for this catalytic intramolecular process. Under the same conditions, the catalyst [Co(**P2**)] (**P2** = 2,6-DiMeO-ChenPhyrin), which contains the same chiral amide units as [Co(**P1**)] but with more sterically hindered non-chiral substituents, appeared to be similarly stereoselective, but less active (entry 3). [Co(**P3**-**P6**)] (Figure 1) represent a subclass of [Co(D_2-Por*)] catalysts with enhanced rigidity in chiral environment due to the presence of intramolecular hydrogen bond in the chiral amide unit. Among them, [Co(**P6**)] was reported to be an excellent catalyst for the asymmetric cyclopropanation of diazosulfones.[7c] These catalysts, however, were found to be ineffective for the intramolecular cyclopropanation of allyl α-diazoacetate **1a** (entries 4–7).

Table 1. Stereoselective Intramolecular Cyclopropanation of Allyl α-Diazoacetate 1a Catalyzed by [Co(D_2-Por*)][a]

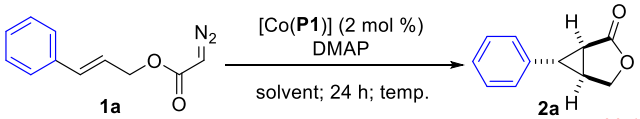


entry	[Co(Por*)]	yield (%)[b]	t:c[c]	ee (%)[d]
1	[Co(**P1**)]	75	>99:1	68
2[e]	[Co(**P1**)]	92	>99:1	40
3	[Co(**P2**)]	53	>99:1	66
4	[Co(**P3**)]	<10	>99:1	ND
5	[Co(**P4**)]	<10	>99:1	ND
6	[Co(**P5**)]	21	>99:1	-7
7	[Co(**P6**)]	NR[f]	-	-

[a] Reactions were carried out in a one-portion protocol using 2 mol % catalyst under N_2 for 24 h with [**1**] = 0.20 M. [b] Isolated yields. [c] Trans/cis ratio determined by ^{1}H NMR. [d] Enantiomeric excess of major diastereomer determined by chiral HPLC. [e] Without DMAP. [f] No reaction.

Using the most active [Co(**P1**)] as the catalyst, the effect of solvents was then examined for the catalytic intramolecular cyclopropanation reaction of allyl α-diazoacetate **1a** (Table 2). The metalloradical cyclopropanation could proceed in a variety of solvents, including coordinating and non-coordinating, aromatic and aliphatic, polar and non-polar as well as halogenated solvents (entries 2–6). The reactivity and stereoselectivity of the cyclopropanation reaction were generally uneffected by the broad range of solvent characteristics, except the non-polar hexanes which provided insufficient solubility. Among the solvents examined, DCM was selected as the solvent of choice as it provided the highest enantioselectivity while retaining a satisfactory yield. Additional experiments were attempted to fine-tune the reaction conditions by optimizing the additive stoichiometry and reaction temperature. It was shown that either decrease or increase in the amount of DMAP led to lower yields and slight decrease in the enantioselectivity (entries 7–9), indicating 0.5 equivalent of DMAP is optimal for the intramolecular reaction, which is consistent with the reported intermolecular reactions.[6a,11] Although lower and higher temperature resulted in increase of the enantioselectivity and yield, respectively (entries 10 and 11), room temperature was chosen to be the optimal since it gave the best overall performance.

Table 2. Solvent and *Trans*-Ligand Effects on [Co(P1)]-Catalyzed Intramolecular Cyclopropanation of Allyl α-Diazoacetate 1a[a]



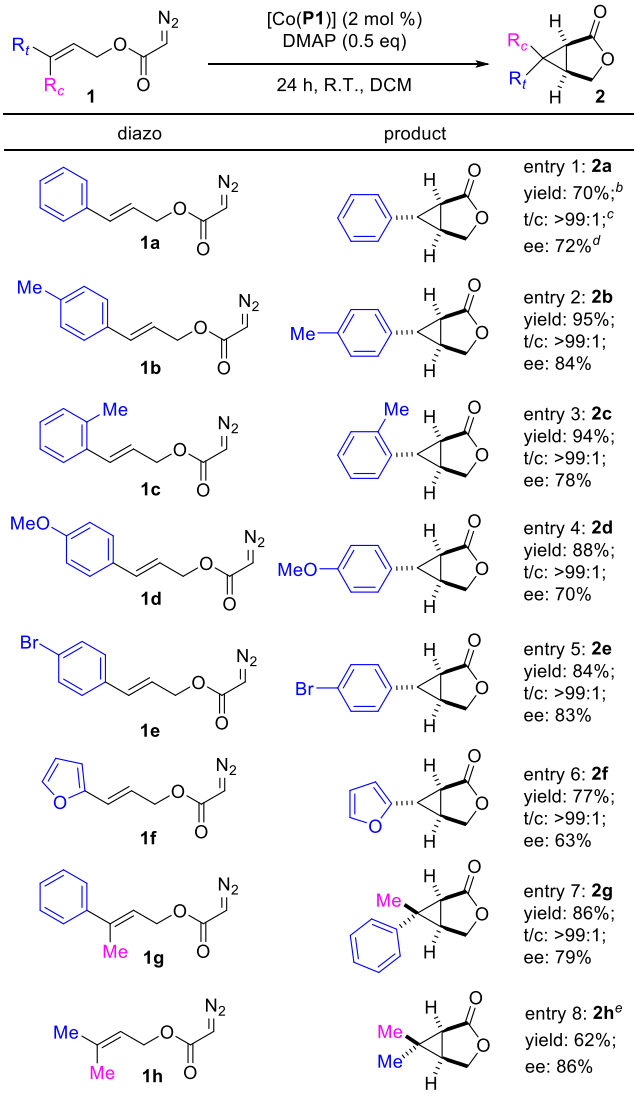
entry	additive (equiv)	solvent	temp.	yield (%)[b]	ee (%)[c]
1	DMAP (0.5)	MeCN	R.T.	75	68
2	DMAP (0.5)	Toluene	R.T.	66	62
3	DMAP (0.5)	PhCl	R.T.	75	61
4	DMAP (0.5)	DCM	R.T.	70	72
5	DMAP (0.5)	Hexanes	R.T.	31	65
6	DMAP (0.5)	EtOAc	R.T.	74	64
7	DMAP (0.5)	DCM	R.T.	70	72
8	DMAP (0.25)	DCM	R.T.	57	68
9	DMAP (0.75)	DCM	R.T.	50	69
10	DMAP (0.5)	DCM	0 °C	37	76
11	DMAP (0.5)	DCM	40 °C	76	64

[a] Reactions were carried out in a one-portion protocol using 2 mol % catalyst under N_2 for 24 h with [**1**] = 0.20 M. Trans/cis ratio determined by ^{1}H NMR. [b] Isolated yields. [c] Enantiomeric excess of major diastereomer determined by chiral HPLC.

Under the optimized reaction conditions, the [Co(**P1**)]-based metalloradical intramolecular cyclopropanation system was found to be applicable for different allyl α-diazoacetates (Table 3). In addition to cinnamyl α-diazoacetate (**1a**) (entry 1), different (*E*)-3-aryl allyl α-diazoacetates with groups that possess different steric and electronic properties on the aromatic ring could also undergo smooth cyclopropanation reactions by [Co(**P1**)] to form the corresponding bicyclic products. For example, α-diazoacetates **1b** and **1c** with para- and ortho-methyl groups, respectively, could be converted to the bicyclic products **2b** and **2c** as single diastereomers in excellent yields with good enantioselectivities (entries 2 and 3). As well, α-diazoacetates **1d** containing an electron-donating MeO-group was shown to be a suitable substrate for the [Co(**P1**)]-catalyzed cyclopropanation process, producing the desired **2d** smoothly with a good level of enantiocontrol (entry 4). The metalloradical cyclopropanation system was shown to also tolerate the presence of halogen atoms in the substrates, as exemplified for the stereoselective formation of brominated bicyclo[3.1.0]hexan-2-one **2e** (entry 5). In addition to allyl α-diazoacetates with aryl substituents, the Co(II)-based catalytic system could be applied to heteroaryl-containing α-diazoacetates, as demonstrated with the intramolecular cyclopropanation of (*E*)-3-(furan-2-yl)allyl α-

diazoacetate (**1f**), which was transformed into 6-(furan-2-yl)-3-oxabicyclo[3.1.0]hexan-2-one (**2f**) in 77% yield with complete diastereocontrol and 63% ee (entry 6). Furthermore, even the sterically demanding tri-substituted olefin-based allyl α-diazoacetates were found to be effective substrates for the intramolecular cyclopropanation via Co(II)-based MRC. For example, the reactions of allyl α-diazoacetates 1**g** and **1h** could be effectively catalyzed by [Co(**P1**)] to form the corresponding 6,6-disubstituted 3-oxabicyclo[3.1.0]hexan-2-one products **2g** and **2h**, respectively, in good yields and stereoselectivities (entries 7 and 8).

Table 3. [Co(P1)]-Catalyzed Enantioselective Intramolecular Cyclopropanation of Allyl α-Diazoacetates[a]



[a] Reactions were carried out in a one-portion protocol using 2 mol % catalyst under N_2 for 24 h with [**1**] = 0.20 M. [b] Isolated yields. [c] Trans/cis ratio determined by ^{1}H NMR. [d] Enantiomeric excess of major diastereomer determined by chiral HPLC. [e] Reaction carried out at 40 ˚C. Reaction under room temperature resulted in 35% yield with 90% ee.

Conclusions

In summary, the Co(II)-based metalloradical system has been proven to enantioselectively catalyze intramolecular cyclopropanation of allyl α-diazoacetates, a representative class of acceptor-substituted diazo reagents. Using readily accessible first-generation metalloradical catalyst [Co(**P1**)], allyl α-diazoacetates have been transformed into [3.1.0]bicyclic structures in good to high yields, with complete diastereocontrol and good asymmetric induction. Together with acceptor/acceptor-substituted diazo reagents,[8] the Co(II)-based intramolecular cyclopropanation has been shown suitable for diazo substrates with a wide range of electronic properties. This feature of broad substrate scope, which is uncommon for catalytic systems involved with electrophilic Fischer-type carbene intermediates, is in good accord with the proposed radical mechanism of the Co(II)-based MRC.[7] Further investigation is currently underway to address remaining issues in asymmetric olefin cyclopropanation, both intermolecular and intramolecular reactions, via Co(II)-based metalloradical catalysis.

Experimental section

General Considerations

All catalytic reactions were performed under nitrogen in oven-dried glassware following standard Schlenk techniques unless otherwise specifically noted. Toluene was distilled under nitrogen from sodium benzophenone ketyl prior to use. Chlorobenzene, acetonitrile, and dichloromethane were dried over calcium hydride under nitrogen and freshly distilled before use. 4 Å molecular sieves were dried in a vacuum oven prior to use. Chemicals were purchased from commercial sources and used without further purification unless specifically noted. Allyl α-Diazoacetates utilized in this study (**1a--h**) were synthesized according to known literature procedures.[12] Thin layer chromatography was performed on Merck TLC plates (silica gel 60 F254). Flash column chromatography was performed with Merck silica gel (60 Å, 230-400 mesh, 32-63 μm). ^{1}H NMR and ^{13}C NMR were recorded on a Varian Inova400 (400 MHz) or a Varian Inova500 (500 MHz) with chemical shifts reported relative to residual solvent. Infrared spectra were measured with a Nicolet Avatar 320 spectrometer with a Smart Miracle accessory. HRMS data was obtained on an Agilent 1100 LC/MS/TOF mass spectrometer. GC/MS measurements were carried out on a Hewitt Packard GCD system. Enantiomeric excess was measured using a Chiraldex G-TA chiral column. Optical rotation was measured on a Rudolf Autopol IV polarimeter. Configuration determined by analogy based upon optical rotation of known compounds in literature.[11]

General Procedure for Intramolecular Cyclopropanation

An oven dried Schlenk tube, that was previously evacuated and backfilled with nitrogen gas, was charged with diazoacetate (0.2 mmol, if solid), catalyst, and DMAP. The Schlenk tube was then evacuated and back filled with nitrogen. The Teflon screw cap was replaced with a rubber septum and 0.5 ml portion of solvent was added followed by diazo (0.2 mmol, if liquid), and the remaining solvent (total 1 mL). The Schlenk tube was then purged with nitrogen for 1 minute and the rubber septum was replaced with a Teflon screw cap. The Schlenk tube was then placed in an oil bath for the desired time and temperature. Following completion of the reaction, the reaction mixture was purified by flash chromatography. The fractions containing product were collected and concentrated by rotary evaporation to afford the compound. In most cases, the product was visualized on TLC using the cerium ammonium molybdate (CAM) stain.

(1*R*,5*S*,6*S*)-6-phenyl-3-oxabicyclo[3.1.0]hexan-2-one (**2a**) was obtained using the general procedure in 70% yield (24.3 mg). $[\alpha]^{20}_D$ = 61 (c = 2.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.21 (m, 3H), 7.05-7.04 (m, 2H), 4.45 (dd, J = 4.8, 9.6 Hz, 1H), 4.39 (d, J = 9.6 Hz, 1H), 2.53-2.49 (m, 1H), 2.33-2.30 (m,

2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 137.1, 128.7, 127.1, 125.9, 69.69, 29.34, 27.36, 26.12. IR (neat, cm^{-1}): 2923 (C-H), 2852 (C-H), 1740 (C=O). HRMS (ESI): Calcd. for $C_{11}H_{11}O_2$ ($[M+H]^+$) m/z 175.0759, Found 175.0765. GC/MS: Chiraldex G-TA (initial temperature: 150 ^{o}C; isothermal for 34 mins; temperature increased 5.0 ˚C per min to a final temperature of 180 ˚C): 72% ee; 19.7 min (major) 21.8 min (minor).

6-(p-tolyl)-3-oxabicyclo[3.1.0]hexan-2-one (**2b**) was obtained using the general procedure in 95% yield (35.9 mg). $[\alpha]^{20}_D$ = 66 (c = 3.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 4.45 (dd, J = 4.8, 9.6 Hz, 1H), 4.40 (d, J = 9.6 Hz, 1H), 2.51-2.48 (m, 1H), 2.32 (s, 3H), 2.30-2.29 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1, 136.8, 134.1, 129.3, 125.8, 69.69, 29.12, 27.24, 25.94, 20.93. IR (neat, cm^{-1}): 2979 (C-H), 2848 (C-H), 1766 (C=O). HRMS (ESI): Calcd. for $C_{12}H_{13}O_2$ ($[M+H]^+$) m/z 189.0915, Found 189.0919. GC/MS: Chiraldex G-TA (initial temperature: 150 ˚C; isothermal for 60 mins; temperature increased 4.0 ˚C per min to a final temperature of 180 ˚C; isothermal for 30 mins): 84% ee; 30.6 min (major) 33.2 min (minor).

6-(o-tolyl)-3-oxabicyclo[3.1.0]hexan-2-one (**2c**) was obtained using the general procedure in 94% yield (35.2 mg). $[\alpha]^{20}_D$ = 24 (c = 1.16, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.13 (m, 3H), 6.95 (d, J = 6.8 Hz, 1H), 4.48 (dd, J = 4.8, 9.6 Hz, 1H), 4.43 (d, J = 9.6 Hz, 1H), 2.58-2.54 (m, 1H), 2.43 (s, 3H), 2.35-2.33 (m, 1H), 2.31-2.29 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 137.5, 134.7, 130.2, 127.3, 126.1, 125.4, 69.68, 27.62, 25.99, 24.59, 19.55. IR (neat, cm^{-1}): 2979 (C-H), 2904 (C-H), 1766 (C=O). HRMS (ESI): Calcd. for $C_{12}H_{13}O_2$ ($[M+H]^+$) m/z 189.0915, Found 189.0905. GC/MS: Chiraldex G-TA (initial temperature: 150 ˚C; isothermal for 60 mins; temperature increased 4.0 ˚C per min to a final temperature of 180 ˚C; isothermal for 30 mins): 78% ee; 25.0 min (major) and 26.9 min (minor).

6-(4-methoxyphenyl)-3-oxabicyclo[3.1.0]hexan-2-one (**2d**) was obtained using the general procedure in 88% yield (36.1 mg). $[\alpha]^{20}_D$ = 62 (c = 0.72, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 4.45 (dd, J = 4.4, 9.6 Hz, 1H), 4.39 (d, J = 9.6 Hz, 1H), 3.81 (s, 3H), 2.49-2.46 (m, 1H), 2.29-2.25 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1, 158.7, 129.0, 127.1, 114.1, 69.69, 55.29, 28.91, 27.18, 25.72. IR (neat, cm^{-1}): 2927 (C-H), 2851 (C-H), 1760 (C=O). HRMS (ESI): Calcd. for $C_{12}H_{13}O_3$ ($[M+H]^+$) m/z 205.0864, Found 205.0868. GC/MS: Chiraldex G-TA (initial temperature: 150 ˚C; isothermal for 60 mins; temperature increased 4.0 ˚C per min to a final temperature of 180 ˚C; isothermal for 30 mins): 70% ee; 66.1 min (major) and 67.8 min (minor).

6-(4-bromophenyl)-3-oxabicyclo[3.1.0]hexan-2-one (**2e**) was obtained using the general procedure in 84% yield (42.3 mg). $[\alpha]^{20}_D$ = 54 (c = 0.70, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 8.4 Hz, 2H), 6.93 (d, J = 8.4 Hz, 2H), 4.45 (dd, J = 4.8, 9.6 Hz, 1H), 4.40 (d, J = 9.6 Hz, 1H), 2.52-2.48 (m, 1H), 2.31-2.26 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 136.2, 131.8, 127.6, 120.9, 69.58, 28.69, 27.23, 26.09. IR (neat, cm^{-1}): 2922 (C-H), 2852 (C-H), 1743 (C=O). HRMS (ESI): Calcd. for $C_{11}H_{10}BrO_2$ ($[M+H]^+$) m/z 252.9864, Found 252.9869. GC/MS: Chiraldex G-TA (initial temperature: 150 ˚C; isothermal for 60 mins; temperature increased 4.0 ˚C per min to a final temperature of 180 ˚C; isothermal for 30 mins): 83% ee; 75.9 min (major) and 79.3 min (minor).

6-(furan-2-yl)-3-oxabicyclo[3.1.0]hexan-2-one (**2f**) was obtained using the general procedure in 77% yield (25.3 mg). $[\alpha]^{20}_D$ = 85 (c = 0.36, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J = 1.2 Hz, 1H), 6.29-6.27 (m, 1H), 6.12 (d, J = 3.2 Hz, 1H), 4.42 (dd, J = 4.8, 9.6 Hz, 1H), 4.36 (d, J = 9.6 Hz, 1H), 2.63-2.60 (m, 1H), 2.42-2.40 (m, 1H), 2.34-2.32 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 149.9, 141.7, 110.6, 106.3, 69.28, 25.15, 24.03, 22.73. IR (neat, cm^{-1}): 2979 (C-H), 2910 (C-H), 1762 (C=O). HRMS (ESI): Calcd. for $C_9H_9O_3$ ($[M+H]^+$) m/z 165.0551, Found 165.0549. GC/MS: Chiraldex G-TA (initial temperature: 150 ˚C; isothermal for 60 mins; temperature increased 4.0 ˚C per min to a final temperature of 180 ˚C): 63% ee; 8.8 min (major) and 9.8 min (minor).

6-methyl-6-phenyl-3-oxabicyclo[3.1.0]hexan-2-one (**2g**) was obtained using the general procedure in 86% yield (32.5 mg). $[\alpha]^{20}_D$ = 71 (c = 0.46, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): 7.33-7.21 (m, 5H), δ 4.51 (dd, J = 5.2, 10.0 Hz, 1H), 4.34 (d, J = 10.0 Hz, 1H), 2.53-2.50 (m, 1H), 2.44-2.43 (m, 1H), 1.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 143.3, 128.7, 127.2, 127.1, 66.54, 31.02, 30.63, 29.32, 15.59. IR (neat, cm^{-1}): 2980 (C-H), 2902 (C-H), 1762 (C=O). HRMS (ESI): Calcd. for $C_{12}H_{13}O_2$ ($[M+H]^+$) m/z 189.0916, Found 189.0922. GC/MS: Chiraldex G-TA (initial temperature: 150 ˚C; isothermal for 60 mins; temperature increased 4.0 ˚C per min to a final temperature of 180 ˚C; isothermal for 30 mins): 79% ee; 16.9 min (minor) and 18.0 min (major).

6,6-Dimethyl-3-oxabicyclo[3.1.0]hexan-2-one (**2h**) was obtained using the general procedure in 35% yield (9.0 mg). $[\alpha]^{20}_D$ = 67 (c = 0.15, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.35 (dd, J = 5.6, 10.0 Hz, 1H), 4.15 (d, J = 10.0 Hz, 1H), 2.05-2.02 (m, 1H), 1.95-1.94 (m, 1H), 1.18 (s, 3H), 1.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 66.52, 30.49, 30.02, 25.20, 14.40. IR (neat, cm^{-1}): 2980 (C-H), 2902 (C-H), 1766 (C=O). HRMS (ESI): Calcd. for $C_9H_9O_3$ ($[M+H]^+$) m/z 127.0759, Found 127.0748. GC/MS: Chiraldex G-TA (initial temperature: 150 ˚C; isothermal for 3 mins; temperature increased 5.0 ˚C per min to a final temperature of 180 ˚C; isothermal for 11 mins): 90% ee; 20.9 min (minor) and 22.3 min (major).

Acknowledgements

We are grateful for financial support by the National Science Foundation (CHE-1152767; X.P.Z.); the National Institutes of Health (R01-GM098777; X.P.Z.), and the Office of Sponsored Awards and Research Support of USC Upstate (J.V.R.).

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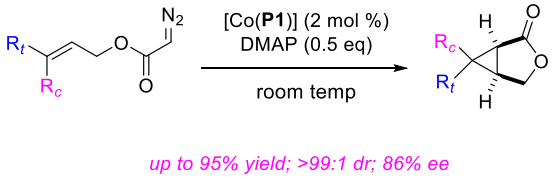

up to 95% yield; >99:1 dr; 86% ee