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A Scope of Chiral Cyclopropanations of Various α-functionalized Diazoketone Derivatives with Styrene Catalyzed by *p-Nitro* Ru(II)-*diphenyl*-Pheox Complex

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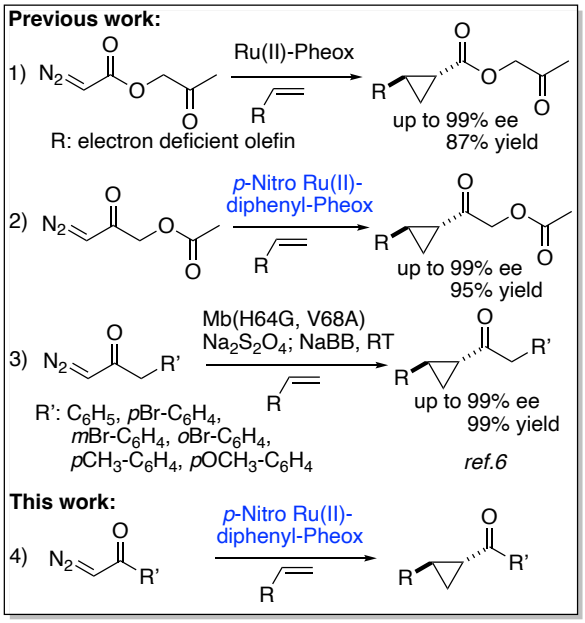
Abstract: Following the success of the first intermolecular cyclopropanations of diazo acetoxy acetone with olefins using a novel *p-nitro*-Ru(II)-*diphenyl*-Pheox catalyst, other α-functionalized diazoketones have synthesized using the same reaction conditions. Consequently, chiral cyclopropyl products were formed with excellent yield (up to 87% yield), high diastereoselectivity (up to 99:1), and high enantioselectivity (up to 90% ee).

Keywords: Asymmetric synthesis; Cyclopropanation; Ru(II)-Pheox; Diazoketones; *p-nitro*-Ru(II)-diphenyl-Pheox; Carbene transfer.

1. INTRODUCTION

A chiral cyclopropane ring is an important cyclic structural motif in pharmaceuticals and bioactive natural products, garnering significant interest in the fields of organic and pharmaceutical chemistry.[1] There have been reports of highly stereoselective cyclopropanation of diazoacetates with olefins via carbene transfer catalyzed by copper, rhodium, ruthenium, cobalt, and Ir complexes.[2]

Previously, we reported on the Ru(II)Pheox-catalyzed asymmetric cyclopropanation of numerous olefins, including vinyl carbamates, allenes, and α, β-unsaturated carbonyl compounds. Ru(II)Pheox complexes exhibited effective catalysis towards a series of optically active cyclopropane derivatives containing electron-rich olefins, allenes, and electron-deficient olefins.[3] In addition, succinimidyl- and ester-functionalized diazoacetates were found to be effective carbene sources in the highly stereoselective cyclopropanation of different olefins. [4] We hypothesized that the C=O group of succinimidyl diazoacetate or acetonyl diazoacetate, which coordinates with Ru after forming a carbene-metal complex, may be responsible for the increase in stereoselectivity. Since the distance between the carbonyl group and another acetyl-based carbonyl group is the same, we would expect the same effect on the stereoselectivity, which could result in a cyclopropyl ketone moiety with strong stereoselectivity. We reported the first catalytic asymmetric synthesis of a ketone carbene precursor based on an acetonyl acetate skeleton using *p-nitro*- Ru(II)-*diphenyl*-Pheox as the chiral catalyst.[5] Superior yields (up to 95%)



Scheme 1: Research Background

as well as excellent diastereoselectivities (up to 99:1) and enantioselectivities (up to 99:1). A recent study reported a highly stereoselective cyclopropanation of olefin with diazo ketones using biocatalysts.[6] Currently, diazo ketone-catalyzed decompositions with high enantioselectivity are attracting more interest. Furthermore, optically active cyclopropyl ketone moieties are found in natural products with important physiological properties,[7] such as the natural product bisgersolanolide [8] and approved anticancer drugs larotaxel [9] and prasugrel (anticoagulant).[10] Thus, we

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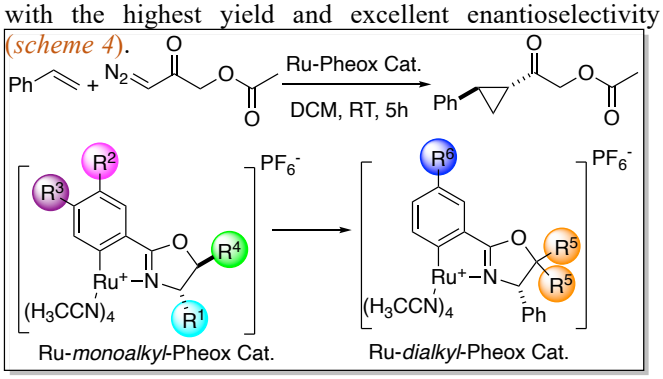
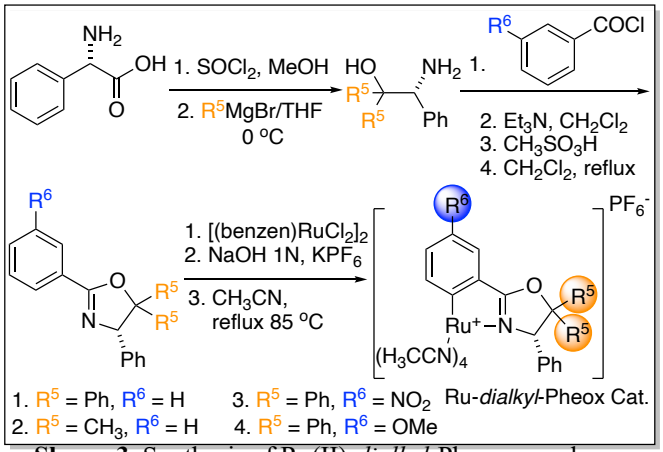
now report that *p-nitro*-Ru(II)-*diphenyl*-Pheox can also catalyze an asymmetric reaction of styrene with other types of diazo ketones, thereby expanding the substrate scope for chiral cyclopropyl ketone products (*Scheme 1*).

2. RESULTS AND DISCUSSION

Here, we summarize the previous report on the reaction of styrene with diazo acetoxy acetone using *p*-nitro-Ru(II)-diphenyl -Pheox as a chiral catalyst. [5] Initially, we examined Ru(II)-*monoalkyl*-Pheox derivatives as catalysts for the aforementioned reaction, but they only provided moderate to high reactivities and moderate to good stereoselectivities up to 73% yield and 75% ee. Subsequently, we improved these catalysts and discovered that Ru(II)-*dialkyl*-Pheox derivatives could increase both stereoselectivity and yield (*scheme 2*). The *p-nitro*-Ru(II)-*diphenyl*-Pheox complex exhibited the highest activity and enantioselectivity among the series of catalysts that we evaluated (*scheme 3*), then found that in the series of catalysts that we carried out, the bulky *p*-nitro-Ru(II)-*diphenyl*-Pheox complex had highest activity, and enantioselectivity. Next, we optimized the reaction in various solvents and temperatures using *p-nitro*-Ru(II)-*diphenyl*-Pheox as the catalyst. We found dichloromethane to be the most effective solvent among those examined, and the catalytic cyclopropanation proceeded at –50 °C for 5 h with the highest yield and excellent enantioselectivity (*scheme 4*).

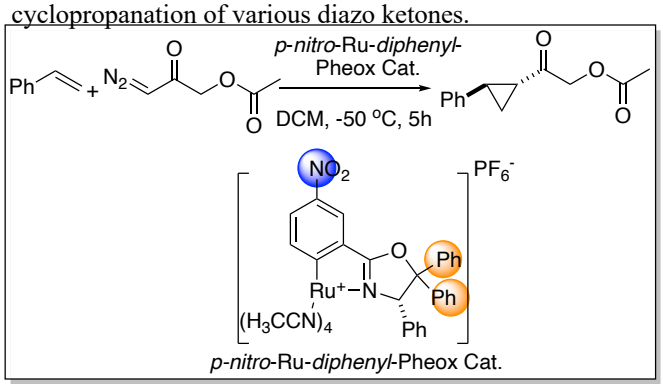


Scheme 2. Process of choosing the suitable catalyst



Sheme 3. Synthesis of Ru(II)-*dialkyl*-Pheox complexes

Except for our isolated highly enantioselective cyclopropanation example involving an acceptor-only diazo ketone reagent,[5] we discovered that diazo ketones had been underutilized in transition metal catalyzed carbene transfer reactions.[11] As a result, we attempted to broaden the scopes of the substrates, concentrating on the asymmetric cyclopropanation of various diazo ketones.



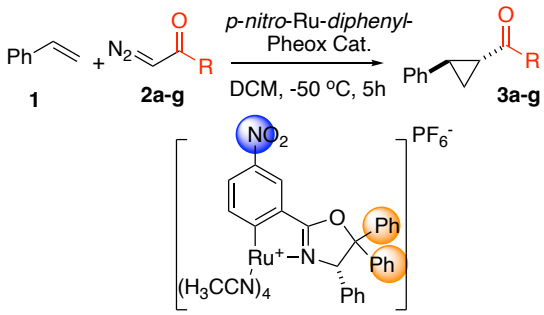
Scheme 4. Optimization of reaction condtions

To examine other functional groups on diazo ketone in the asymmetric cyclopropanation reaction, various diazo ketones **2a-g** were examined under the aforementioned optimization conditions, with the expectation that this strategy could provide an additional means of diversifying the cyclopropyl ketone products (*Table 1*). Initially, a diverse set of diazo ketones were synthesized from the corresponding bromoacetates by treating them with *N,N'*-ditosylhydrazine with moderate to excellent yields;[12] this procedure produced the desired carbene donor reagents with up to 94% yield.

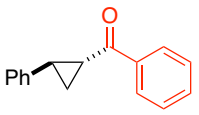
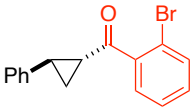
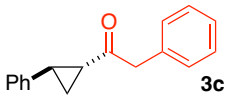
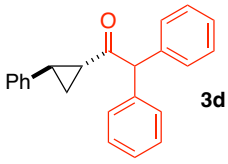
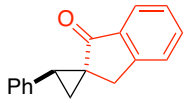
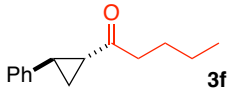
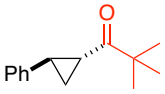
Notably, a variety of alkyl diazo ketone analogs could be processed by *p*-nitro-Ru(II)-*diphenyl*-pheox catalyst to afford the corresponding cyclopropanes **3a-g** in up to 87% yield, with excellent *trans*-selectivity (>99% de)(*) and moderate to good enantioselectivity (41 to 90% ee) (*entries 1-7*). In addition to the previously reported catalytic asymmetric cyclopropanation of α-diazoacetophenone with styrene using Halterman iron porphyrins which afforded 67% yield and 76% ee,[11b] and chiral ruthenium porphyrins, which afforded 57% yield and 83% ee,[11a] chemo catalytic protocols for asymmetric cyclopropanations are employed to investigate various diazo ketones **3c-g** as carbene precursors. The cyclopropyl product (**3a**) of -diazoacetophenone with styrene using *p*-nitro-Ru(II)-diphenyl-Pheox was obtained with 80% yield and 80% enantioselectivity, according to our findings. Intriguingly, the reaction involving a simple carbene donor, such as butyl diazo ketone (**2f**), yielded **3f** in moderate yield and with high enantioselectivity (see entry 6: 95% de, 90% ee).

Notably, the bulky carbene donors **2d, 2e,** and **2g** could be obtained through the *p-nitro*-Ru(II)-*diphenyl*-Pheox catalyst to afford the corresponding cyclopropanes **3d, 3e,** and **3g** (see entries 4, 5, and 7) with high yield (up to 85%) and moderate enantioselectivity (65%, 65%, and 41% ee). These results, when combined with those from a previous report [5] demonstrate the remarkable tolerance of the *p-nitro*-Ru(II)-*diphenyl*-Pheox catalyst for accepting various diazo ketone reagents to produce a wide range of cyclopropyl ketones with high stereoselectivity.

Table 1. Asymmetric cyclopropanation of funtionalized diazoketones.



p-nitro-Ru-*diphenyl*-Pheox Cat.

Entry	**3a-g**	Yield [%][a]	d.r[b]	-ee [%][c]
1	 **3a**	80	96:4	80/75 Trans/Cis
2	 **3b**	87	99:1	86
3	 **3c**	70	90:10	89/88 Trans/Cis
4	 **3d**	85	97:3	65
5	 **3e**	62	99:1	65
6	 **3f**	45	95:5	90
7	 **3g**	60	92:8	41

[a] Isolated yield. [b] Determined by ^{1}H NMR analysis, the enantioselectivty for trans product only. [c] Determined by chiral HPLC analysis.

Given the importance of optically active cyclopropane rings as pharmacophores in drug molecules and biologically active natural products, our research suggests that diazo ketones could be a promising class of carbene donor reagents for this application. As a result of the versatile reactivity of carbonyls and their unique reactivity imparted to the α-functionalized group, cyclopropane product diversification is afforded multiple opportunities.

3. EXPERIMENTAL SECTION

General Information

All reactions were performed under an argon atmosphere unless otherwise noted. Dichloromethane (CH_2Cl_2) was purchased from Kanto Chemical Co., Inc. Acetonitrile was purchased from Wako Pure Chemical Industries, Ltd.. All reactions were monitored by thin layer chromatography (TLC), glass plates pre-coated with silica gel Merck KGaA 60 F254, layer thickness 0.2 mm. All the staring materials are commercially available and were used without further purification unless otherwise noted. The products were visualized by irradiation with UV light or by treatment with a solution of phosphomolybdic acid, a solution of a $KMnO_4$ or a solution of *p*-anisaldehyde. Column chromatography was performed using silica gel (Merck, Art. No.7734). ^{1} H NMR (500 MHz, 400 MHz), ^{13}C NMR (126, 100 MHz) were recorded on JEOL JNM-ECX500, JEOL JM-ECS400 spectrometer. Chemical shifts are reported in ppm (δ) relative internal tetramethylsilane (0.00 ppm) in $CDCl_3$. Optical rotations were performed with a JASCO P-1030 polarimeter at the sodium D line (1.0 ml sample cell). DART mass (positive mode) analyses were performed on a LC-TOF JMS-T100LP.

3.1. Synthesis of various diazo ketones

Procedure for the synthesis of diazo ketones **2a**[13], **2b**[14], **2c**[15], **2d**[16], **2e**[17], **2f**[18], **2g**[19] were prepared according to literature procedures.

2-diazo-1-phenylethan-1-one 2a[13]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.72 (m, 2H), 7.57-7.50 (m, 1H), 7.43 (dd, *J* = 6.8, 4.5 Hz, 2H), 5.93 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 186.4, 136.6, 132.7, 128.7, 126.7, 54.2.

1-(2-bromophenyl)-2-diazoethan-1-one 2b[14]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (m, 1H), 7.45 (d, *J* = 6.9 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.30 (m, 1H), 5.72 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.82, 139.54, 133.71, 131.81, 129.00, 127.51, 119.23, 57.48.

1-diazo-3-phenylpropan-2-one 2c[15]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (s, 2H), 5.17 (s, 1H), 7.25-7.39 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 48.5, 55.6, 127.7, 129.3, 129.8, 135.4, 193.4

3-diazo-1,1-diphenylpropan-2-one 2d[16]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.45 (m, 10H), 5.23 (s, 1H), 4.92 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.77, 138.95, 129.17, 128.86, 127.49, 62.35, 56.24.

2-diazo-2,3-dihydro-1H-inden-1-one 2e[17]

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, J=7.3, 1H); 7.54 (t, J=7.2, 1H); 7.40 (d, J=7.3, 1H); 7.39 (t, J=7.2, 1H); 4.02 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 188.4; 143.2; 137.3; 133.1; 127.8; 125.3; 122.6; 28.6.

1-diazohexan-2-one 2f[18]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.22 (s, 1H), 2.29 (t, *J* = 6.8, 2H), 1.10-1.18 (m, 4H), 0.92 (t, *J* = 4.20, 3H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.48, 54.15, 40.78, 27.15, 22.30, 13.55.

1-diazo-3,3-dimethylbutan-2-one 2g[19]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (s, 1H), 1.12 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.85, 52.98, 42.48, 26.99

3.2. Synthesis of (*S*)-2-(3-nitrophenyl)-4,5,5-triphenyl-4,5-dihydrooxazole

Procedure for the synthesis of (***S***)-diphenylphenylglycinol[20] first. (*S*)-2-(3-nitrophenyl)-4,5,5-triphenyl-4,5-dihydrooxazole with following data:

$[\alpha]_D^{27.2}$ = –2.66 (c 1.04, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (d, *J* = 1.91 Hz, 1H), 8.54 (d, *J* = 7.64 Hz, 1H), 8.41 (d, *J* = 8.41 Hz, 1H), 7.68–7.73 (m, 3H), 7.44 (t, *J* = 7.64 Hz, 2H), 7.36 (t, *J* = 7.64 Hz, 1H), 7.06–7.10 (m, 3H), 6.97–7.03 (m, 7H), 6.20 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.27, 148.53, 144.20, 139.93, 138.01, 134.39, 129.85, 129.54, 128.75, 128.50, 128.48, 127.97, 127.59, 127.46, 127.03, 126.75, 126.58, 126.37, 123.58, 95.31, 72.92 ppm.

IR (neat) ν 3087, 2926, 2316, 1951, 1659, 861 cm^{-1}

HRMS (DART) calcd for $C_{27}H_{21}N_2O_3$ $[M+H]^+$: 421.15522 found: 421.15520.

3.3. Synthesis of *p*-nitro-Ru(II)-*diphenyl*-Pheox catalyst

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 2.14 Hz, 1H), 8.07 (d, *J* = 8.24 Hz, 1H), 7.97 (dd, *J* = 2.44, 2.44 Hz, 1H), 7.76 (d, *J* = 7.63 Hz, 2H), 7.41 (t, *J* = 7.63 Hz, 2H), 7.28 (t, *J* = 7.63 Hz, 1H), 7.15 (d, *J* = 7.02 Hz, 2H), 6.96–7.11 (m, 8H), 5.95 (s, 1H), 3.08 (s, 3H), 2.28 (s, 3H), 1.95 (s, 3H), 1.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.89, 143.47, 139.14, 136.99, 135.55, 129.38, 128.90, 128.59, 128.11, 127.76, 127.53, 127.25, 126.38, 126.22, 122.62, 122.01, 121.81, 121.31, 119.73, 98.39, 76.61, 4.16, 3.86, 3.33, 3.15 ppm.

IR (neat) ν 3235, 2931, 2278, 1628, 1323, 840 cm^{-1}.

3.4 Typical procedure for catalytic asymmetric cyclopropanation of styrene with various diazo ketones

A solution of diazo ketones **3a-g** (0.2 mmol, 1.0 equiv.) in CH_2Cl_2 (2.0 mL) was slowly added to a mixture of *p*-nitro-Ru(II)-*diphenyl*-Pheox (0.01 mmol) as catalyst and olefin (1.0 mmol, 5.0 equiv.) in CH_2C1_2 (2.0 mL) for 4 h under argon atmosphere and the suspended reaction mixture was designed at -50 ºC. After the addition completed, the reaction mixture was continuously stirred for 1 h at the same temperature. The reaction was monitored by TLC. Upon completion, solvent was removed and the residue was purified by column chromatography on silica gel eluted with EtOAc/n-Hexane to give the cyclopropanation products. The *trans*/*cis* ratio was determined from the crude ^{1}H NMR spectra, and the enantioselectivity was determined by chiral HPLC analysis.

Phenyl(2-phenylcyclopropyl)methanone 3a[11a-b]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 9.56 Hz, 2H, Ar–**H**), 7.55 (m, 1H, Ar–**H**), 7.46 (t, *J* = 7.64 Hz, 2H, Ar–**H**), 7.31 (t, *J* = 7.64 Hz, 2H, Ar–**H**), 7.17–7.25 (m, 3H, Ar–**H**), 2.90 (ddd, *J* = 4.20, 5.35, 8.03 Hz, 1H, OCC**H** (cyclopropane)), 2.66 (ddd, *J* = 4.20, 6.50, 9.17 Hz, 1H, Ar–C**H** (cyclopropane)), 1.93 (ddd, *J* = 4.20, 5.35, 9.17 Hz, 1H, CH**H** (cyclopropane)), 1.56 (ddd, *J* = 4.20, 6.88, 8.03 Hz, 1H, C**H**H (cyclopropane)). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.68, 140.58, 137.78, 133.02, 128.67, 128.63, 128.21, 128.18, 126.71, 126.67, 126.33, 126.29, 30.09, 29.42, 19.36 ppm.

The ee was determined chiral HPLC analysis. Column (Chiral AD), UV detector 220 nm, eluent: Hexane/IPA = 60/1, Flow rate: 0.5 ml/min. $[\alpha]_D^{23.9}$ = –1.61 (c 0.72, $CHCl_3$)

(2-bromophenyl)(2-phenylcyclopropyl)methanone 3b

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.63 Hz, 1H, Ar–**H**), 7.45 (d, *J* = 7.93 Hz, 1H, Ar–**H**), 7.30 (m, 7H, Ar–**H**), 2.79 (ddd, *J* = 3.97, 7.02, 10.38 Hz, 1H, OCC**H** (cyclopropane)), 2.70 (ddd, *J* = 3.97, 5.35, 8.54 Hz, 1H, Ar–C**H** (cyclopropane)), 1.97 (ddd, *J* = 4.27, 7.02, 8.54 Hz, 1H, CH**H** (cyclopropane)), 1.59 (ddd, *J* = 4.27, 5.19, 10.38 Hz, 1H, C**H**H (cyclopropane)). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.83, 31.80, 33.64, 119.33, 126.28, 126.75, 127.52, 128.61, 129.12, 131.79, 133.68, 140.06, 142.12, 202.29.

HRMS (DART) calcd for $C_{16}H_{14}BrO$ $[M+H]^+$: 301.02280 found 301.02280.

IR (neat) ν 3061, 3029, 2923, 1681, 1213, 749 cm^{-1}.

The ee was determined chiral HPLC analysis. Column (Chiral ODH), UV detector 220 nm, eluent: Hexane/IPA = 140/1, Flow rate: 0.5 ml/min. $[\alpha]_D^{23.9}$ = –2.57 (c 1.28, $CHCl_3$).

2-phenyl-1-(2-phenylcyclopropyl)ethan-1-one 3c[6]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.34 (m, 8H, Ar–**H**), 7.17–7.34 (m, 8H, Ar–**H**), 7.0 (d, *J* = 6.88 Hz, 2H, Ar–**H**), 2.50 (ddd, *J* = 4.20, 6.88, 9.17 Hz, 1H, OCC**H** (cyclopropane)), 3.87 (s, 2H, OCC**H$_2$**), 2.21 (ddd, *J* = 4.20, 5.35, 8.03 Hz, 1H, Ar–C**H** (cyclopropane)), 1.68 (ddd, *J* = 4.20, 5.35, 9.17 Hz, 1H, CH**H** (cyclopropane)), 1.34 (ddd, *J* = 4.20, 6.50, 8.03 Hz, 1H, C**H**H (cyclopropane)). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.48, 140.24, 134.22, 129.62, 128.84, 128.52, 127.10, 126.62, 126.34, 51.10, 31.86, 29.78, 19.18 ppm.

HRMS (DART) calcd for $C_{17}H_{17}O$ $[M+H]^+$: 237.12794 found 237.12790.

IR (neat) ν 3061, 3028, 1694, 1603, 1397, 1069, 698 cm^{-1}.

The ee was determined chiral HPLC analysis. Column (Chiral AD), UV detector 220 nm, eluent: Hexane/IPA = 100/1, Flow rate: 1.0 ml/min. 89% *ee* (*trans*), 88% *ee* (*cis*). $[\alpha]_D^{25.9}$ = –1.54 (c 0.65, $CHCl_3$).

2,2-diphenyl-1-(2-phenylcyclopropyl)ethan-1-one 3d

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.35 (m, 13H, Ar–**H**), 6.95 (d, *J* = 7.02 Hz, 2H, Ar–**H**), 7.21 (t, *J* = 7.26 Hz, 1H, Ar–**H**), 5.29 (s, 1H, OCC**H$_2$**), 2.56 (ddd, *J* = 4.27, 7.02, 9.46 Hz, 1H, OCC**H** (cyclopropane)), 2.23 (ddd, *J* = 3.97, 6.71, 7.93 Hz, 1H, Ar–C**H** (cyclopropane)), 1.75 (ddd, *J* = 3.97, 6.95, 9.16 Hz, 1H, CH**H** (cyclopropane)), 1.36 (dt, *J* = 3.97, 6.71, 9.47 Hz, 1H, C**H**H (cyclopropane)). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.73, 140.13, 138.46, 138.41, 129.31, 129.26, 128.86, 128.74, 128.49, 127.35, 127.27, 126.64, 126.47, 65.55, 32.81, 30.45, 19.41 ppm.

HRMS (DART) calcd for $C_{23}H_{21}O$ $[M+H]^+$: 313.15924 found 313.15920.

IR (neat) ν 3060, 3027, 1698, 1088, 1070, 698 cm^{-1}.

The ee was determined chiral HPLC analysis. Column (Chiral AD), UV detector 220 nm, eluent: Hexane/IPA = 120/1, Flow rate: 1.0 ml/min. $[\alpha]_D^{1.56}$ = –3.2716 (c 1.56, $CHCl_3$).

2-phenylspiro[cyclopropane-1,2'-inden]-1'(3'H)-one 3e[22]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.41 Hz, 1H), 7.53 (t, *J* = 7.26 Hz, 1H), 7.38 (t, *J* = 7.26 Hz, 2H), 7.30–7.33 (m, 3H), 7.13 (d, *J* = 6.88 Hz, 2H), 3.00 (d, *J* = 17.58 Hz, 1H,), 2.92 (t, *J* = 7.26 Hz, 1H), 2.79 (d, *J* = 17.58 Hz, 1H), 1.99 (q, *J* = 4.59 Hz, 1H), 1.69 (q, d = 4.59 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.73, 140.13, 138.46, 138.41,129.31, 129.26, 128.86, 128.74, 128.49, 127.35, 127.27, 126.64, 126.47, 65.55, 32.81, 30.45, 19.41 ppm.

The ee was determined chiral HPLC analysis. Column (Chiral IC3), UV detector 220 nm, eluent: Hexane/IPA = 9/1, Flow rate: 1.0 ml/min. $[\alpha]_D^{22.7}$ = –1.00 (c 0.47, $CHCl_3$).

1-(2-phenylcyclopropyl)pentan-1-one 3f

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08–7.29 (m, 5H, Ar–**H**), 2.58 (t, *J* = 7.26 Hz, 2H, $OCCH_2$), 2.49 (ddd, *J* = 4.20, 6.50, 9.17 Hz, 1H, OCC**H** (cyclopropane)), 2.19 (ddd, *J* = 4.20, 5.35, 8.41 Hz, 1H, Ar–C**H** (cyclopropane)), 1.57–1.67 (m, 3H, C**H**H (cyclopropane), $OCCH_2C\mathbf{H_2}$), 1.31–1.37 (m, 3H, CH**H** (cyclopropane), $C\mathbf{H_2}CH_3$), 0.903 (t, *J* = 7.26 Hz, 3H, $C\mathbf{H_3}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.35, 140.60, 128.57, 126.67, 126.13, 43.86, 32.27, 28.88, 26.16, 22.46, 18.92, 13.94 ppm.

HRMS (DART) calcd for $C_{14}H_{19}O$ $[M+H]^+$: 203.14359 found 203.14360.

IR (neat) ν 2957, 2931, 1697, 1399, 1065, 697 cm^{-1}.

The ee was determined chiral HPLC analysis. Column (Chiral OD), UV detector 220 nm, eluent: Hexane/IPA = 60/1, Flow rate: 0.5 ml/min. $[\alpha]_D^{23}$ = –1.3679 (c 0.53, $CHCl_3$).

2,2-dimethyl-1-(2-phenylcyclopropyl)propan-1-one 3g

Trans– product: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.26 Hz, 2H, Ar–**H**), 7.21 (t, *J* = 7.26 Hz, 1H, Ar–**H**), 7.11 (d, *J* = 7.26 Hz, 2H, Ar–**H**), 2.42 (ddd, *J* = 4.20, 6.50, 9.17 Hz, 1H, OCC**H** (cyclopropane)), 2.37 (ddd, *J* = 3.82, 5.35, 8.03 Hz, 1H, Ar–C**H** (cyclopropane)), 1.63 (ddd, *J* = 4.20, 5.35, 9.03 Hz, 1H, C**H**H (cyclopropane)), 1.35 (ddd, *J* = 4.20, 6.50, 8.03 Hz, 1H, CH**H** (cyclopropane)), 1.20 (s, 9H, C-($C\mathbf{H_3}$)$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.61, 140.68, 128.57, 126.51, 126.34, 44.11, 29.79, 29.21, 27.81, 26.31, 18.57 ppm. IR (neat) ν 2965, 1690, 1365, 1068, 697 cm^{-1}.

HRMS (DART) calcd for $C_{14}H_{19}O$ $[M+H]^+$: 203.14359 found 203.14360.

The ee was determined chiral HPLC analysis. Column (Chiral OJH), UV detector 220nm, eluent: Hexane/IPA = 50/1, Flow rate: 1.0 ml/min. $[\alpha]_D^{22.9}$ = –0.4206 (c 0.26, $CHCl_3$).

CONCLUSION

We designed and developed highly stereoselective cyclopropanations of olefin with various α-functionalized diazo ketone reagents with excellent yield (up to 87% yield), diastereoselectivity (up to 99:1), and enantioselectivity (up to 90% ee) based on our experimental evidence on the stereoinduction mechanism in p-nitro-Ru(II)-diphenyl-Pheox complex catalyzed during the cyclopropyl reactions. This work contributes to the availability of various new and useful enantioenriched cyclopropyl ketones, found in pharmaceutically significant natural and synthetic products.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest, financial or otherwise.

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