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Rh_2(*S*-PTAD)$_4$-catalyzed asymmetric cyclopropenation of aryl alkynes

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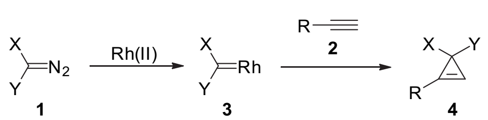
ABSTRACT

Rh_2(*S*-PTAD)$_4$ is an effective catalyst for the asymmetric cyclopropenation of aryl alkynes using a siloxyvinyldiazoacetate as the carbenoid precursor. Upon deprotection of the silyl protecting group, highly enantioenriched cyclopropenes bearing geminal acceptor groups can be accessed. These cyclopropenes undergo regioselective rhodium(II)-catalyzed ring expansion to furans.

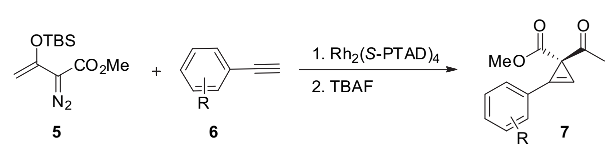
1. Introduction

Cyclopropenes are important synthetic targets[1] because of their broad utility as intermediates in organic synthesis and their occurrence in a variety of natural products.[2–4] One of the most generally useful methods for the synthesis of cyclopropenes is the metal catalyzed reaction of diazo compounds **1** with alkynes **2** (Scheme 1). These reactions proceed via metal carbenoid intermediates **3**, which then cyclopropenate the alkynes to form **4**.



Scheme 1. Rhodium-catalyzed cyclopropenation.

The reactivity of metal carbenoids is greatly influenced by the nature of the substituents on the carbenoid. Consequently, reviews of metal carbenoids often classify the carbenoids into three distinct groups, the acceptor carbenoids, the acceptor/acceptor carbenoids and the donor/acceptor carbenoids. Rhodium-catalyzed asymmetric intermolecular cyclopropenation[5] with acceptor- and donor/acceptor carbenoids are now well-established processes, and high levels of asymmetric induction can be achieved.[6] In contrast, the asymmetric synthesis of cyclopropenes containing two acceptor groups by the carbenoid approach is less developed.[7,8] High asymmetric induction has only been achieved when one of the acceptor groups is a cyano group.[9,10] In this paper we describe an indirect method for the asymmetric synthesis of cyclopropenes **7** bearing two carbonyl acceptor groups by reaction of siloxyvinyldiazoacetate **5** with alkynes **6** (Scheme 2).[11]



Scheme 2. Synthesis of cyclopropenes bearing two acceptor groups.

A further objective of this study is to illustrate the interplay between diazoacetoacetate **9** and siloxyvinyldiazoacetate **5**, which is readily formed from **9**.[12] Nitrogen extrusion from **9** generates the acceptor/acceptor carbenoid **10**, whereas **5** generates the donor/acceptor carbenoid **8**. Acceptor/acceptor carbenoids are highly electrophilic intermediates, whereas the reactivity of donor/acceptor carbenoids is greatly modulated by the influence of the donor group.[5a,13] Hence, it is possible to use **5** as a surrogate for **9** when the high reactivity of the acceptor/acceptor carbenoid **9**, precludes its successful utilization in a particular reaction (Scheme 3).

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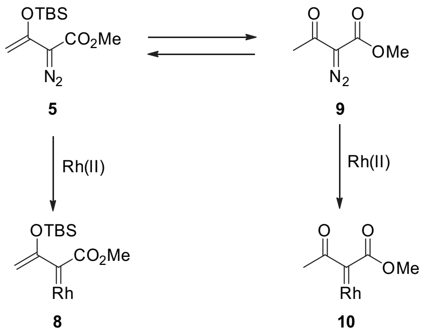
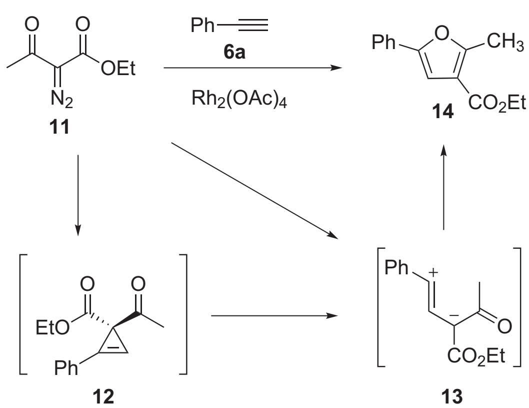


Scheme 3. Relationship between **5** and **9**.

2. Results and discussion

One of the challenges of conducting cyclopropenation reactions with the diazoacetoacetate **9** is the tendency of this system to react via zwitterionic intermediates, leading to two different reaction pathways.[14] This type of behavior has been reported in the rhodium acetate-catalyzed reaction of **11** with phenylacetylene **6a**, which instead of forming the cyclopropene **12** generated the furan **14** (Scheme 4).[15] The formation of **14** could, in principle, arise from a zwitterionic intermediate **13** formed directly from the reaction of the carbenoid with the alkyne or by ring-opening of an initially formed cyclopropene **12**.



Scheme 4. Proposed mechanism for the Rh(II)-catalyzed formation of furan **14**.

In order to explore whether it would be possible to conduct an asymmetric cyclopropenation of phenylacetylene with diazoacetoacetate **9**, a series of reactions were conducted, varying the catalyst and solvent. When $Rh_2(Oct)_4$ was used as catalyst, only the furan product **15** was formed as seen in the ^1H NMR of the crude reaction mixture. The product was isolated in 97% yield and the structure of **15** was confirmed by X-ray crystallography.[16] In an attempt to isolate a cyclopropene product **7a**, the reaction was conducted at −45 °C. Indeed, ^1H NMR analysis of the crude reaction showed a mixture of cyclopropene **7a** and the furan **14**.

Different reactivity was observed when chiral dirhodium complexes, $Rh_2(S\text{-DOSP})_4$, and $Rh_2(S\text{-PTAD})_4$, were used as catalysts (Fig. 1). In these cases, the cyclopropene product **7a** was formed as the major product in about 70% yield in reactions conducted at room temperature. The cyclopropenes, however, were formed in very poor enantiomeric excess for both catalysts even when the reaction was conducted at −45 °C (Table 1).

Since enantiomerically enriched cyclopropenes could not be directly accessed using diazo compound **9** as carbenoid precursor, we turned our attention to siloxyvinyldiazoacetate **5** because in principle, the cyclopropenyl ketone could be accessed upon deprotection of the silyl protecting group. Several chiral catalysts were also surveyed for this particular reaction to form cyclopropene **16** and the results are shown in Table 2.

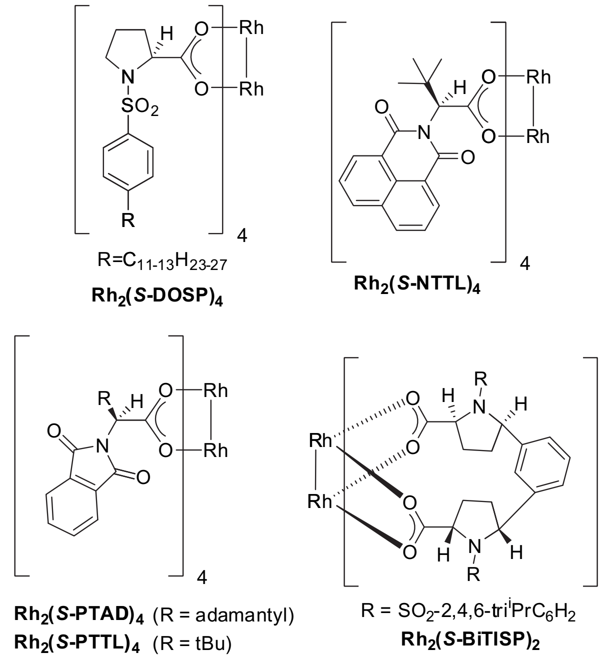
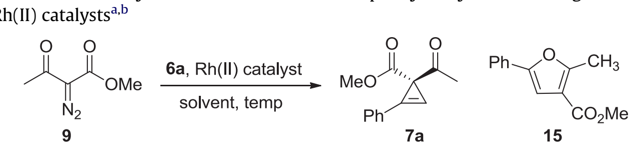


Fig. 1. Structures of chiral dirhodium catalysts $Rh_2(S\text{-DOSP})_4$, $Rh_2(S\text{-PTAD})_4$, $Rh_2(S\text{-NTTL})_4$, $Rh_2(S\text{-PTTL})_4$, and $Rh_2(S\text{-biTISP})_2$.

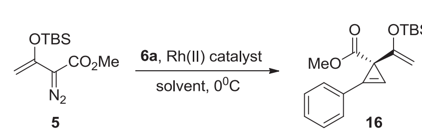
Table 1
Reaction of methyl diazoacetoacetate **9** and phenylacetylene **6a** using different Rh(II) catalysts[a,b]



Entry	Catalyst[c]	Solvent	Temp (°C)	% Yield 7a	% Yield 15	% ee
1	$Rh_2(Oct)_4$	DCM	23	—	97	—
2	$Rh_2(Oct)_4$	DCM	−45	61	24	—
3	$Rh_2(S\text{-PTAD})_4$	DCM	23	74	9	<5
4	$Rh_2(S\text{-PTAD})_4$	DCM	−45	66	—	<5
5	$Rh_2(S\text{-DOSP})_4$	Pentane	23	73	17	7
6	$Rh_2(S\text{-DOSP})_4$	Pentane	−45	69	—	11

[a] Reaction conditions: 0.5 mmol scale of **6a** used, reaction time: 3 h.
[b] Diazoacetate **15** (2 equiv) used.
[c] Catalyst (2 mol %) loading.

Table 2
Reaction of siloxyvinyldiazoacetate **5** and phenylacetylene using different Rh(II) catalysts[a,b]

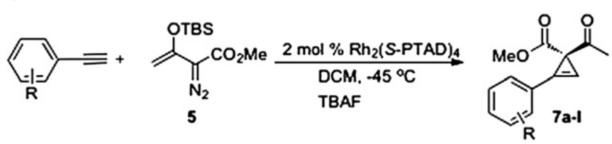


Entry	Catalyst[c]	Solvent	% Yield	% ee[d]
1	$Rh_2(R\text{-DOSP})_4$	Pentane	41	−51
2	$Rh_2(S\text{-PTAD})_4$	DCM	93	94
3	$Rh_2(S\text{-NTTL})_4$	DCM	93	88
4	$Rh_2(S\text{-PTTL})_4$	DCM	91	90
5	$Rh_2(S\text{-BiTISP})_2$	Pentane	43	58

[a] Reaction conditions: 0.5 mmol scale of **6a** used, reaction time: 2 h.
[b] Diazoacetate **5** (2 equiv) used.
[c] Catalyst (2 mol %) loading.
[d] Negative ee value means opposite sense of enantioinduction.

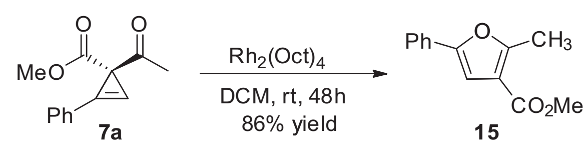
The prolinate-based catalyst Rh_2(*R*-DOSP)$_4$ and the bridged catalyst Rh_2(*S*-BiTISP)$_2$ both performed poorly in terms of yield and enantioselectivity. Excellent yields and enantioselectivities were obtained using the structurally related catalysts Rh_2(*S*-NTTL)$_4$ and Rh_2(*S*-PTTL)$_4$. All of the catalysts gave the same sense of enantioinduction as Rh_2(*S*-PTAD)$_4$. These results are consistent with previous studies on asymmetric reactions with siloxyvinyldiazoacetate **5**. We have reported that Rh_2(*S*-PTAD)$_4$ was a very effective catalyst in asymmetric tandem cyclopropanation/Cope rearrangement reactions with **5**.[17] Muller had observed that Rh_2(*S*-NTTL)$_4$ is better than Rh_2(*S*-DOSP)$_4$ in intermolecular cyclopropanation with siloxyvinyldiazoacetate **5**. The absolute configuration of the cyclopropene **16** was not rigorously determined and was tentatively assigned based on the results reported by Müller and co-workers[18] and our previous work on rhodium-catalyzed cyclopropenation with alkynes and styryldiazoacetates.[6e] The optimized conditions for the one-pot cyclopropenation/deprotection of arylacetylenes was found to be slow addition of the diazo compound (over 2 h) to a dichloromethane solution of Rh_2(*S*-PTAD)$_4$ (2 mol %) and the alkyne at −45 °C. The silyl protecting group can be removed in situ by adding excess amount of TBAF after complete addition of the diazoacetate solution to the reaction mixture. Under the optimized conditions, the substrate scope of the cyclopropenation reaction was investigated. Various aromatic acetylenes were used as trapping agent (Table 3) and results showed that the reaction is generally compatible with substituted arylacetylenes **6** affording cyclopropenyl ketones **7** in moderate to excellent yields (77–94% yield) and excellent enantioselectivities (93–99% ee). Clean cyclopropenation and no benzylic C–H insertion were observed using *p*-ethylethynylbenzene (entry 4) and TBS-protected *o*-ethynylbenzylalcohol (entry 12) as substrates, which showed that cyclopropenation can occur in a highly selective manner. Selective monoycyclopropenation of diynes in the case of was also possible (entries 9 and 10). Electron rich arylacetylenes, such as *p*-ethynylanisole and 2-ethynylnaphthalene also afforded highly enantiopure cyclopropenes, however, these products were too unstable for full characterization and are not included in the table.[19] The absolute configuration of the cyclopropene **7** was not rigorously determined and was tentatively assigned based on the results reported by Müller and co-workers[18] and our previous work on rhodium-catalyzed cyclopropenation with alkynes and styryldiazoacetates.[6e] With the cyclopropenyl ketones in hand, the feasibility of Rh(II)-catalyzed ring expansion of the cyclopropenyl ketones to furans was investigated. Cyclopropene **7a** in DCM was stirred in the presence of Rh_2(Oct)$_4$ at 23 °C (Scheme 5). ^{1}H NMR analysis of the crude reaction mixture after 2 h showed small amounts of furan product. After 48 h of stirring proton NMR analysis showed near complete conversion of the cyclopropene to the furan product. The product was isolated by flash chromatography and the pure furan product was obtained in 86% yield. In the absence of Rh_2(Oct)$_4$, the cyclopropene did not undergo ring expansion to the corresponding furan. This result demonstrates that indeed the cyclopropene undergoes a Rh(II)-catalyzed rearrangement to the furan product. However, the rearrangement is slower than a typical rhodium-catalyzed cyclopropenation, which means the reaction between diazoacetoacetate **9** and phenylacetylene **6a** is more likely to undergo a mechanism involving zwitterionic intermediates instead of a rearrangement of an initially formed cyclopropene (Scheme 5).

Table 3
Rh_2(*S*-PTAD)$_4$-catalyzed cyclopropenation of various alkynes and siloxylvinyldiazoacetate **5**[a,b]



Entry	R	Product	% Yield	ee %
1	H	**7a**	83	98
2	*o*-Me	**7b**	80	98
3	*p*-Me	**7c**	86	93
4	*p*-Et	**7d**	90	97
5	*P*-tBu	**7e**	87	98
6	*P*-Br	**7f**	92	95
7	*p*-Ph	**7g**	88	98
8	*m*-CF_3	**7h**	94	93
9	*p*-Ethynyl	**7i**	85	94
10	*m*-Ethynyl	**7j**	88	97
11	*p*-F, *m*-Me	**7k**	77	97
12	*o*-CH_2OTBS	**7l**	94	99

[a] Reaction conditions: 0.5 mmol of alkyne, 1.0 mmol of TBAF used.
[b] Diazoacetate **5** (2 equiv) used.



Scheme 5. Rh(II)-catalyzed rearrangement of cyclopropenes **7a** to furan **15**.

3. Conclusion

In summary, siloxyvinyldiazoacetates were found to be effective carbenoid precursors for highly enantioselective Rh_2(*S*-PTAD)$_4$-catalyzed cyclopropenation reactions with arylacetylenes. A new class of optically active cyclopropenes with quaternary carbon bearing germinal acceptor groups is now readily accessible. Cyclopropenyl ketone was also found to undergo a regioselective Rh(II)-catalyzed ring expansion to furans.

4. Experimental section

4.1. General

General methods for spectral and analytical procedures and X-ray crystallographic data for **15** are described in Supplementary data.

4.2. General procedure for Rh(II)-catalyzed decompositions of methyl diazoacetoacetate 9 in the presence of phenylacetylene

A mixture of alkyne (0.5 mmol) and Rh_2(Oct)$_4$ (0.01 mmol) was dissolved in 1 mL of dichloromethane and stirred at indicated temperature under an atmosphere of argon. Diazoacetoacetate **9** (1.0 mmol) in 10 mL dichloromethane was then added to the reaction mixture via syringe pump over 2 h. After the complete addition, the reaction mixture was stirred for additional 1 h and the reaction mixture was concentrated in vacuo. The residue was purified on silica using 10:1 hexane/diethyl ether followed by 1:1 hexane/EtOAc as eluents to give the desired product/s.

4.3. General procedure for Rh(II)-catalyzed decompositions of siloxyvinyldiazoacetate 5 in the presence of acetylenes

A mixture of alkyne **6** (0.5 mmol) and Rh_2(*S*-PTAD)$_4$ (0.01 mmol) was dissolved in 1 mL of dichloromethane and stirred at −45 °C under an atmosphere of argon. Siloxyvinyldiazoacetate **5** (1.0 mmol) in 10 mL dichloromethane was then added to the reaction mixture via syringe pump over 2 h. After the complete addition, the reaction mixture was stirred for additional 20 min followed by addition of TBAF (1.0 mmol) in one portion. The reaction mixture was further stirred at 23 °C followed by aqueous work-up. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified on silica using 10:1 hexane/diethyl ether followed by 1:1 hexane/EtOAc as eluents to afford the desired cyclopropenyl ketones.

*4.3.1. Methyl 2-methyl-5-phenylfuran-3-carboxylate (**15**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) afforded as white solid. Mp 55–57 °C; R_f 0.72 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J=7.2 Hz, 2H), 7.34 (t, J=7.2 Hz, 2H), 7.23 (t, J=7.2 Hz, 1H), 6.84 (s, 3H), 3.80 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 164.6 (C), 158.9 (C), 151.9 (C), 130.2 (C), 128.9 (CH), 127.8 (CH), 123.8 (CH), 115.3 (C), 105.6 (CH), 51.5 (CH_3), 14.0 (CH_3); IR (neat) 2951, 1715, 1614, 1440, 1230, 1096, 907, 729, 690 cm^{-1}; ESI-HRMS: (M+H) m/z, found: 217.0820; calcd ($C_{13}H_{13}O_3$): 217.0858;

*4.3.2. Methyl (R)-1-(1-((tert-butyldimethylsilyl)oxy)vinyl)-2-phenylcycloprop-2-enecarboxylate (**16**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) afforded **16** in 93% yield (154 mg) as a yellowish oil. R_f 0.74 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (m, 2H), 7.38 (m, 3H), 6.95 (s, 1H), 4.29 (d, J=0.4 Hz, 1H), 4.17 (d, J=0.4 Hz, 1H), 3.67 (s, 3H), 0.88 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 174.3 (C), 158.9 (C), 130.4 (CH), 130.1 (CH), 128.9 (CH), 125.6 (C), 117.3 (C), 99.4 (CH), 90.6 (CH), 52.2 (CH_3), 25.7 (CH_3), −4.6 (CH_3) (CH_3); IR (neat) 2951, 2929, 2857, 1725, 1623, 1297, 1242, 1056, 1013, 832, 696 cm^{-1}; ESI-HRMS: (M+H) m/z, found: 330.1610; calcd ($C_{19}H_{26}O_3Si$): 330.1651; HPLC: ADH, 1% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 21.1 min (minor), 26.3 min (major), 94% ee with Rh_2(*S*-PTAD)$_4$.

*4.3.3. Methyl (R)-1-acetyl-2-phenylcycloprop-2-enecarboxylate (**7a**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7a** in 83% yield (90 mg) as a yellow oil. R_f 0.30 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.59 (m, 2H), 7.42 (m, 3H), 6.98 (s, 1H), 3.69 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 206.1 (C), 172.0 (C), 130.9 (CH), 130.4 (CH), 129.2 (CH), 124.1 (C), 113.3 (C), 96.5 (CH), 52.3 (CH_3), 40.7 (C), 28.1 (CH_3); IR (neat) 3139, 2952, 1721, 1693, 1274, 1229, 697 cm^{-1}; ESI-HRMS: (M+H) m/z, found: 217.0820; calcd ($C_{13}H_{13}O_3$): 217.0858; HPLC: ADH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 10.6 min (major), 11.3 min (minor), 98% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +10.9 (*c* 1.0, $CHCl_3$).

*4.3.4. Methyl (R)-1-acetyl-2-(o-tolyl)cycloprop-2-enecarboxylate (**7b**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7b** in 80% yield (92 mg) a as yellow oil. R_f 0.33 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J=7.6 Hz, 1H), 7.30 (m, 3H), 6.99 (s, 1H), 3.71 (s, 3H), 2.52 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 206.2 (C), 172.0 (C), 140.5 (CH), 131.2 (CH), 130.9 (CH), 130.6 (CH), 126.5 (CH), 123.0 (C), 112.4 (C), 98.1 (CH), 52.3 (CH_3), 39.8 (C), 28.1 (CH_3), 20.2 (CH_3); IR (neat) 3138, 2953, 2853, 1720, 1694, 1273, 1208, 723 cm^{-1}; ESI-HRMS: (M+H) m/z, found: 231.0976; calcd ($C_{14}H_{15}O_3$): 231.1016; HPLC: ADH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 8.6 min (major), 9.8 min (minor), 98% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +6.8 (*c* 1.0, $CHCl_3$).

*4.3.5. Methyl (R)-1-acetyl-2-(p-tolyl)cycloprop-2-enecarboxylate (**7c**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7c** in 86% yield (99 mg) as a yellow oil. R_f 0.36 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, J=8.0 Hz, 2H), 7.23 (d, J=8.0 Hz, 2H), 6.82 (s, 1H), 3.68 (s, 3H), 2.36 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 206.4 (C), 172.1 (C), 141.5 (CH), 130.5 (CH), 129.9 (CH), 121.3 (C), 113.3 (C), 95.1 (CH), 52.3 (CH_3), 40.7 (C), 28.1 (CH_3), 21.8 (CH_3); IR (neat) 3139, 2952, 1720, 1693, 1275, 1229, 820 cm^{-1}; ESI-HRMS: (M+H) m/z, found: 231.0976; calcd ($C_{14}H_{15}O_3$): 231.1016; HPLC: ODH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 10.6 min (major), 11.3 min (minor), 98% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +11.8 (*c* 1.0, $CHCl_3$).

*4.3.6. Methyl (R)-1-acetyl-2-(4-ethylphenyl)cycloprop-2-enecarboxylate (**7d**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7d** in 90% yield (109 mg) as a yellow oil. R_f 0.42 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J=6.8 Hz, 2H), 7.26 (d, J=8.8 Hz, 2H), 6.85 (s, 1H), 3.71 (s, 3H), 2.68 (q, J=7.2 Hz, 2H), 2.22 (s, 3H), 1.25 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 206.4 (C), 172.1 (C), 147.7 (CH), 130.6 (CH), 128.8 (CH), 121.5 (C), 113.3 (C), 95.1 (CH), 52.4 (CH_3), 40.7 (C), 29.1 (CH_2), 28.1 (CH_3), 15.5 (CH_3); IR (neat) 3140, 2966, 1723, 1694, 1276, 1230, 837 cm^{-1}; ESI-HRMS: (M+H) m/z, found: 245.1133; calcd ($C_{15}H_{17}O_3$): 245.1172; HPLC: ADH, 2% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 37.4 min (major), 40.2 min (minor), 97% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +7.8 (*c* 1.0, $CHCl_3$).

*4.3.7. Methyl (R)-1-acetyl-2-(4-(tert-butyl)phenyl)cycloprop-2-enecarboxylate (**7e**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7e** in 87% yield (118 mg) as a yellow oil. R_f 0.45 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J=8.4 Hz, 2H), 7.47 (d, J=8.4 Hz, 2H), 6.83 (s, 1H), 3.71 (s, 3H), 2.22 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 206.4 (C), 172.1 (C), 154.5 (CH), 130.3 (CH), 126.3 (CH), 121.3 (C), 113.2 (C), 95.2 (CH), 52.4 (CH_3), 40.7 (C), 35.2 (C), 31.3 (CH_3), 28.1 (CH_3); IR (neat) 3139, 2957, 1721, 1696, 1270, 1229, 838 cm^{-1}; ESI-HRMS: (M+H) m/z, found: 273.1446; calcd ($C_{17}H_{21}O_3$): 273.1484; HPLC: ADH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 10.8 min (major), 13.1 min (minor), 98% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +4.8 (*c* 1.0, $CHCl_3$).

*4.3.8. Methyl (R)-1-acetyl-2-(4-bromophenyl)cycloprop-2-enecarboxylate (**7f**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7f** in 92% yield (137 mg) as a yellow oil. R_f 0.38 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J=8.4 Hz, 2H), 7.41 (d, J=8.4 Hz, 2H), 6.93 (s, 1H), 3.69 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 205.9 (C), 171.8 (C), 132.6 (CH), 131.8 (CH), 125.5 (C), 123.1 (C), 112.5 (C), 97.2 (CH), 52.5 (CH_3), 40.6 (C), 28.3 (CH_3); IR (neat) 3141, 2951, 1721, 1694, 1273, 1227, 827 cm^{-1}; ESI-HRMS: (M+H) m/z, found: 294.9925; calcd ($C_{13}H_{12}BrO_3$): 294.9964; HPLC: ADH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 18.3 min (major), 20.9 min (minor), 95% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +16.9 (*c* 1.0, $CHCl_3$).

*4.3.9. Methyl (R)-2-([1,1′-biphenyl]-4-yl)-1-acetylcycloprop-2-enecarboxylate (**7g**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7g** in 88% yield (129 mg) as a yellow oil. R_f 0.33 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.64 (m, 4H), 7.57 (m, 2H), 7.42 (m, 2H), 7.37 (m, 1H), 6.93 (s, 1H), 3.72 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 206.2 (C), 172.0 (C), 143.8 (CH), 140.2 (CH), 130.9 (CH), 129.2 (CH), 128.3 (CH), 127.9 (CH), 127.4 (CH), 122.9 (C), 113.1 (C), 96.3 (CH), 52.4 (CH_3), 40.8 (C), 28.2 (CH_3); IR (neat) 3139, 3030, 2951, 1721, 1693, 1274, 1229, 843, 696 cm^{-1}; ESI-HRMS: (M+H) m/z, found: 293.1133; calcd ($C_{19}H_{17}O_3$): 293.1172; HPLC: ADH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 23.2 min (major), 27.5 min (minor), 98% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +1.6 (*c* 1.0, $CHCl_3$).

*4.3.10. Methyl (R)-1-acetyl-2-(3-(trifluoromethyl)phenyl)cycloprop-2-enecarboxylate (**7h**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7h** in 94% yield (138 mg) as a yellow oil. R_f 0.42 (hexane/EtOAc 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.75 (d, J=7.6 Hz, 1H), 7.79 (d, J=8.0 Hz, 1H), 7.59 (t, J=7.6 Hz, 2H), 7.08 (s, 1H), 3.74

(s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 205.7 (C), 171.6 (C), 133.5 (CH), 132.0 (C, q, J=130.4 Hz), 129.9 (CH), 127.4 (CH), 127.0 (CH), 125.1 (C), 112.1 (C), 98.6 (CH), 52.5 (CH_3), 40.7 (C), 28.4 (CH_3); IR (neat) 3139, 2952, 1721, 1693, 1274, 1229, 697 cm^{-1}; ESI-HRMS: (M+H) *m/z*, found: 285.0694; calcd ($C_{14}H_{11}F_3O_3$): 285.0733; HPLC: ADH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 4.5 min (major), 7.1 min (minor), 98% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +1.7 (*c* 1.0, $CHCl_3$).

*4.3.11. Methyl (R)-1-acetyl-2-(3-ethynylphenyl)cycloprop-2-enecarboxylate (**7i**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7i** in 88% yield (106 mg) as a yellow oil. R_f 0.41 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (t, J=1.6 Hz, 1H), 7.55 (m, 2H), 7.41 (t, J=7.6 Hz, 1H), 6.98 (s, 1H), 3.73 (s, 3H), 3.15 (s, 1H), 2.27 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 205.9 (C), 171.8 (C), 134.3 (CH), 133.8 (CH), 130.6 (CH), 129.3 (CH), 124.5 (C), 123.5 (C), 112.5 (C), 97.5 (CH), 82.5 (C), 78.8 (CH), 52.5 (CH_3), 40.7 (C), 28.4 (CH_3); IR (neat) 3284, 3142, 2952, 1721, 1694, 1274, 1224, 1045, 799 cm^{-1}; ESI-HRMS: (M+H) *m/z*, found: 217.0820; calcd ($C_{13}H_{13}O_3$): 217.0858; HPLC: ADH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 10.6 min (major), 11.3 min (minor), 98% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +6.8 (*c* 1.0, $CHCl_3$).

*4.3.12. Methyl (R)-1-acetyl-2-(4-ethynylphenyl)cycloprop-2-enecarboxylate (**7j**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7j** in 85% yield (102 mg) as a yellow oil. R_f 0.45 (hexane/EtOAc 8:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (app t, J=8.8 Hz, 4H), 7.00 (s, 1H), 3.72 (s, 3H), 3.23 (s, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 205.9 (C), 171.8 (C), 132.9 (CH), 130.3 (CH), 124.7 (C), 124.3 (C), 112.7 (C), 97.6 (CH), 83.0 (C), 79.9 (CH), 52.5 (CH_3), 40.7 (C), 28.3 (CH_3), 21.8 (CH_3); IR (neat) 3293, 3142, 2953, 1723, 1694, 1274, 1230, 907, 727 cm^{-1}; ESI-HRMS: (M+H) *m/z*, found: 241.0820; calcd ($C_{15}H_{13}O_3$): 241.0859; HPLC: ADH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 17.9 min (major), 19.3 min (minor), 93% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +2.1 (*c* 1.0, $CHCl_3$).

*4.3.13. Methyl (R)-1-acetyl-2-(4-fluoro-3-methylphenyl)cycloprop-2-enecarboxylate (**7k**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7k** in 77% yield (96 mg) as a yellow oil. R_f 0.39 (hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, J=8.0 Hz, 2H), 7.23 (d, J=8.0 Hz, 2H), 6.82 (s, 1H), 3.68 (s, 3H), 2.36 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 206.1 (C), 171.9 (C), 164.1 (C), 161.6 (C), 133.7 (CH), 129.9 (CH, J=35.2 Hz), 126.3 (C, J=72.8 Hz), 120.1 (C), 116.1 (CH, 94.4 Hz), 112.5 (C), 95.5 (CH), 52.4 (CH_3), 40.8 (C), 28.2 (CH_3), 14.6 (CH_3); IR (neat) 3139, 2955, 1719, 1693, 1274, 1229, 697 cm^{-1}; ESI-HRMS: (M+H) *m/z*, found: 249.0882; calcd ($C_{14}H_{13}FO_3$): 249.0921; HPLC: ADH, 10% *i*-PrOH/hexane, 1 ml min^{-1}, UV 254 nm, t_R: 17.8 min (major), 20.2 min (minor), 97% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +7.9 (*c* 1.0, $CHCl_3$).

*4.3.14. Methyl (R)-1-acetyl-2-(2-(((tert-butyldimethylsilyl)oxy)-methyl)-phenyl)cycloprop-2-enecarboxylate (**7l**).* Purification by silica gel chromatography eluting with hexane/Et_2O (10:1) then hexane/EtOAc (1:1) afforded **7l** in 94% yield (169 mg) as a yellow oil. R_f 0.69 (hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J=7.6 Hz, 1H), 7.48 (t, J=7.6 Hz, 1H), 7.31–7.43 (m, 2H), 6.95 (s, 1H), 4.98 (s, 2H), 3.72 (s, 3H), 2.25 (s, 3H), 0.98 (s, 9H), 0.14 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 206.0 (C), 171.9 (C), 143.4 (CH), 131.1 (CH), 130.9 (CH), 127.4 (CH), 126.5 (CH), 120.5 (C), 111.1 (C), 98.6 (CH), 62.7 (CH_2), 52.4 (CH_3), 39.9 (C), 28.2 (CH_3), 26.1 (CH_3), 18.6 (C), −5.1 (CH_3); IR (neat) 3139, 2954, 2885, 2856, 1724, 1693, 1254, 1122, 1079, 837, 757 cm^{-1}; ESI-HRMS: (M+H) *m/z*, found: 217.0820; calcd ($C_{13}H_{13}O_3$): 217.0858; HPLC: ASH, 10% *i*-PrOH/hexane, 0.7 ml min^{-1}, UV 254 nm, t_R: 8.4 min (major), 10.3 min (minor), 99% ee with Rh_2(*S*-PTAD)$_4$; $[\alpha]_{D^{23}}$ +7.2 (*c* 1.0, $CHCl_3$).

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Supplementary data

Detailed experimental for the compounds, X-ray crystallographic data for **15**, HPLC traces for all chiral compounds and ^{1}H NMR and ^{13}C NMR spectra for all new compounds are described in Supplementary data. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.04.029.

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