# High-Diastereoselective and Enantioselective Cyclopropanation of α,β-Unsaturated Fischer Carbene Complexes: Synthesis of Chiral 1,2-Disubstituted and 1,2,3-Trisubstituted Cyclopropanes

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Reaction of chiral vinylcarbene complexes **1** with *in situ*-generated iodomethyllithium or dibromomethyllithium gives cyclopropylcarbene complexes **4** and **13**, respectively, with high diastereoselectivity (de > 91%). Different enantiopure 1,2-disubstituted and 1,2,3-trisubstituted cyclopropanes are obtained starting from chiral carbene complexes **4** and **13**, respectively.

## Introduction

Transition metal carbene complexes have become valuable reagents for organic synthesis.[1] Among other interesting properties, the synthetic usefulness of these complexes is due to their rich reactivity, showing their own unique types of reactivity. Specifically, cyclopropylcarbene complexes can be transformed into cyclopentenones,[2] cyclopentadienones,[3] cyclopentane-fused oxygen heterocycles,[4] cycloheptadienones,[5] alkenyl halides,[6] and donor−acceptor-substituted cyclopropanes.[7] Moreover, cyclopropylcarbene complexes have been used in other synthetic transformations under thermal[8] or photochemical conditions.[9] However, to the best of our knowledge, the preparation of chiral cyclopropylcarbene complexes is unprecedented.

On the other hand, based on the easy transformation of carbene complexes into different organic compounds,[10] the synthesis of chiral substituted cyclopropylcarbene complexes could open new routes to a wide variety of chiral substituted cyclopropanes. Chiral cyclopropanes are highly useful intermediates in organic synthesis,[11] and the cyclopropane ring is present in a great number of natural products[12] as well as in molecules used as probes in biological processes.[13] For this reason, significant advances have been made in the synthesis of chiral cyclopropanes.[14] However, a total control of the stereoselectivities on the synthesis of 1,2-disubstituted cyclopropanes is still out of reach. Furthermore, reports on an intermolecular enantioselective synthesis of 1,2,3-trisubstituted cyclopropanes are scarce, mainly because

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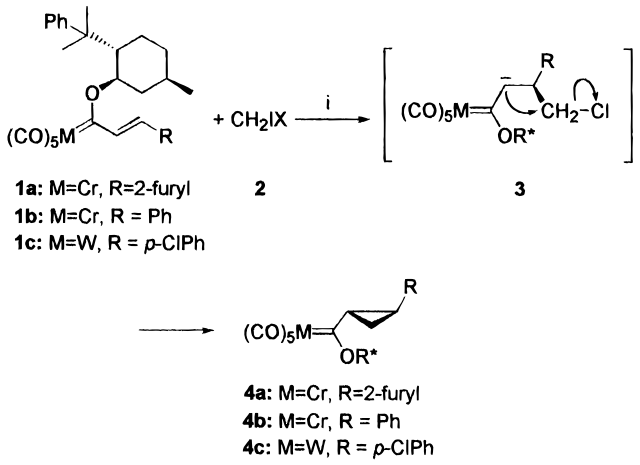
**Scheme 1**[a]




[a] Reagents and conditions: (i) MeLi, THF/diethyl ether, 5 min and then room temperature.

these compounds are generally obtained as diastereoisomeric mixtures with poor enantiomeric excess.[15]

Recently, we have described a methodology for the diastereoselective synthesis of *trans*-substituted chromium cyclopropylmethoxycarbene complexes using chloromethyllithium.[16] In this paper we describe the synthesis of chiral chromium cyclopropylalkoxycarbene complexes **4** and **13**. These compounds are obtained by cyclopropanation of enantiomerically pure chromium alkenyl[((−)-8-phenylmenthyl)oxy]carbene complexes **1** with *in situ*-generated monohalo- or dibromomethyllithium. These processes take place with high-asymmetric induction. Removal of the metal fragment and the chiral auxiliary group leads to enantiopure 1,2-disubstituted or 1,2,3-trisubstituted cyclopropanes, respectively.

## Results and Discussion

**Synthesis of Chiral 1,2-Disubstituted Cyclopropylcarbene Complexes and Their Synthetic Applications.** Treatment of chiral vinylcarbene complexes **1** with chloromethyllithium or iodomethyllithium *in situ* generated at −78 °C gave the corresponding cyclopropylcarbene complexes **4**, with high diastereoselectivity (see the Experimental Section, Scheme 1, and Table 1).

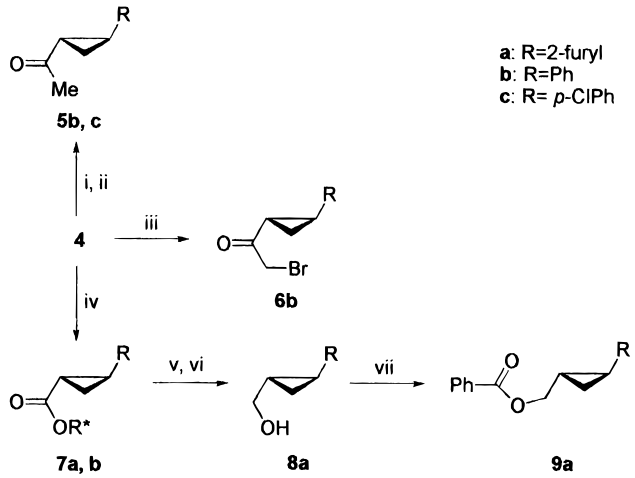
Compounds **1** were obtained by alkylation of tetramethylammonium-derived methylcarbene complex with (−)-8-phenylmenthol and further condensation.[17] Chloromethyllithium or iodomethyllithium were *in situ* generated by treatment of chloroiodomethane or diiodomethane, respectively, with methyllithium. As depicted in Scheme 1, the 1,4-addition of halomethyllithium to vinylcarbene complex **1** would lead to anionic intermediate **3**; spontaneous $\gamma$-elimination of **3** yields the cyclopropylcarbene complex **4**.

**Table 1. Synthesis of Chiral Cyclopropylcarbene Complexes 4**

| | 1 | | 2 | | | |
|---|---|---|---|---|---|---|
| entry | M | R | X | product | yield (%)[a] | de (%)[b] |
| 1 | Cr | 2-furyl | Cl | **4a** | 96 | 74 |
| 2 | Cr | 2-furyl | I | **4a** | 93 | 90 |
| 3 | Cr | Ph | Cl | **4b** | 93 | 77 |
| 4 | Cr | Ph | I | **4b** | 90 | >95 |
| 5 | W | *p*-ClPh | I | **4c** | 95 | >95 |

[a] Isolated yield based on the starting vinylcarbene **1**. [b] Diastereoisomeric excess determined by 300 MHz $^1$H NMR analysis of the crude products **4**.

**Scheme 2**[a]




[a] Reagents and conditions: (i) $CH_2N_2$, diethyl ether, 25 °C, 14 h; (ii) HCl (1 N), 25 °C, 24 h; (iii) $CH_2Br_2$, THF, then LDA (THF), −78 °C, 5 min and then room temperature; (iv) pyridine *N*-oxide, THF, 25 °C, 14 h; (v) $LiAlH_4$, diethyl ether, 35 °C, 14 h; (vi) $H_2O$, 25 °C; (vii) PhCOCl, $Et_3N$, DMAP, $CH_2Cl_2$, 25 °C, 14 h.

Results in Table 1 show that (a) yields of carbene complexes **4** were only moderately affected by the metal in the starting carbene complexes **1**; (b) the reactions of carbene complexes **1** with chloromethyllithium or iodomethyllithium gave essentially the same yields; (c) higher diastereoselectivity (300 MHz, $^1$H NMR spectroscopy) was obtained using iodomethyllithium (entries 2 and 4) instead of chloromethyllithium (entries 1 and 3), which can be explained because iodine is bulkier than chlorine.

To prove the usefulness of this methodology in the synthesis of chiral 1,2-disubstituted cyclopropanes, we have transformed the cyclopropylcarbene complexes **4** into different organic compounds. Thus, treatment of cyclopropylcarbenes **4** with diazomethane[10h] afforded chiral methyl ketones **5**; reaction of **4b** with dibromomethyllithium[18] gave chiral bromomethyl ketone **6b**; treatment of carbene complexes **4** with pyridine *N*-oxide[10c] afforded cyclopropanecarboxylates **7**, and further reduction of **7a** (R = 2-furyl) with $LiAlH_4$ gave the corresponding alcohol **8a** (Scheme 2 and Table 2). Chiral auxiliary was recovered in the synthesis of **5**, **6**, and **8a**.

Except in the oxidation reaction shown at entry 4 (Table 2), all reactions were carried out starting from the cyclopropylcarbene complexes obtained using iodomethyllithium. All transformations proceeded with no detectable epimerization: compounds **5**, **6b**, **7**, and **8a** were obtained with high diastereoselectivity, in agreement

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**Table 2. Synthesis of Chiral 1,2-Disubstituted Cyclopropanes**

| entry | starting compd | product | yield (%)[a] | de (%)[b] |
|---|---|---|---|---|
| 1 | **4b** | **5b** | 75[c] | >98 |
| 2 | **4c** | **5c** | 80 | >98 |
| 3 | **4b** | **6b** | 71[d] | >98 |
| 4 | **4a** | **7a** | 76 | 76 |
| 5 | **4a**[e] | **7a** | 78 | 91 |
| 6 | **4b** | **7b** | 76 | *f* |
| 7 | **7a** | **8a** | 76 | >98 |
| 8 | **8a** | **9a** | 95[g] | >98 |

[a] Isolated yield based on the starting compounds **4**, **7**, and **8a**. [b] Diastereoisomeric excess determined by 300 MHz $^1$H NMR analysis of the crude products **5**−**7**, **8a**, and **9a**. [c] ee = 99%, HPLC (Chiracel OD-H; UV detector at 220 nm, 0.8 mL/min; hexane:2-propanol, 100:1; $t_R$ 13.9 min). [d] ee = 97%, HPLC (Chiracel OD-H; UV detector at 206 nm, 0.8 mL/min; hexane:2-propanol, 100:1; $t_R$ 29.0 min). [e] Compound **4a** was obtained using chloromethyllithium. [f] No de was available from the $^1$H NMR analysis of the crude products. [g] ee = 91%, HPLC (Chiracel OD-H; UV detector at 230 nm, 0.8 mL/min; hexane:2-propanol, 600:1; $t_R$ 32.5 min).

with diastereoisomeric excess (de) of starting compounds **4** and **7a**, respectively.

The enantiomeric purity of chiral 1,2-disubstituted cyclopropanes was determined by chiral HPLC (Chiracel OD-H) analysis. The enantiomeric excess (ee) values of **5b** and **6b** turned out to be 99% and 97%, respectively. Alcohol **8a** could not be resolved using the chiral column Chiracel OD-H; in this case HPLC analysis was carried out with the benzoic ester derivative **9a**, prepared by reaction of **8a** with benzoyl chloride (ee = 91%). All ee determinations were in agreement with the de of the starting cyclopropylcarbene complexes **4**. To realize all the HPLC analyses, racemic mixtures of **5b**, **6b**, and **9a** were prepared to exclude the probability of comigration of both enantiomers in HPLC. Racemic mixtures of **5b**, **6b**, and **9a** were obtained using the same methodology starting from racemic vinylcarbene complexes.[16]

The relative *trans*-configuration in the cylclopropane ring of compounds **4**−**7**, **8a**, and **9a** was established by $^1$H NMR coupling constant analysis.[19] The absolute configuration of these 1,2-disubstituted cyclopropane rings, as depicted in Schemes 1 and 2, was assigned by analogy with the X-ray analysis showed in Figure 1.[20]

The asymmetric induction observed in the cyclopropanation reaction can be explained assuming that in the most stable conformation of **1**, the chiral auxiliary phenyl group shields selectively the double bond (*Re,Re*)-face by $\pi,\pi$-orbital overlap,[21] forcing the nucleophile to approach preferentially from the (*Si,Si*)-face (Chart 1). This model is similar to the "$\pi$-stacking" one proposed by Oppolzer[22] for cuprate additions to enolates and the one depicted by Nakamura[23] to explain the Michael addition diastereoselectivity of enolates of Fischer vinylcarbene complexes.

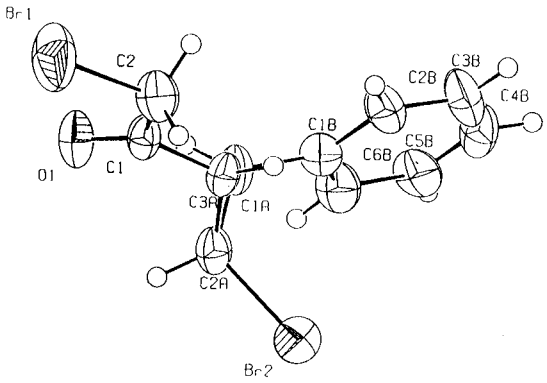
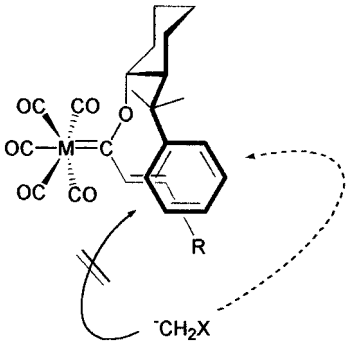



**Figure 1.** Molecular structure of **16** determined by X-ray crystallography.

**Chart 1**




**Synthesis of Chiral 1,2,3-Trisubstituted Cyclopropylcarbene Complexes and Their Synthetic Applications.** Previously to the preparation of enantiopure 1,2,3-trisubstituted cyclopropanes, the diastereoselectivity of this cyclopropanation reaction of achiral $\alpha,\beta$-unsaturated carbene complexes was studied. So, when vinylcarbene complexes **10** reacted with dibromomethyllithium *in situ* generated at −78 °C, 1,2,3-trisubstituted cyclopropylcarbene complexes **13a**,**b** were obtained (Scheme 3 and Table 3). Dibromomethyllithium was *in situ* generated by treatment of dibromomethane with lithium diisopropylamide (LDA). No important differences were observed in the synthesis of **13a** or **13b** starting from chromium or tungsten carbene complex. The proposed mechanism involves the 1,4-addition of dibromomethyllithium to carbene complex **10** and further spontaneous $\gamma$-elimination of intermediate **12**.

1,2,3-Trisubstituted cyclopropylcarbene complex **13a** was transformed into the corresponding ester **14**,[10c] methyl ketone **15**,[10h] and bromomethyl ketone **16**[18] as racemic mixtures using the same methodologies described above. The synthesis of all compounds took place with total diastereoselectivity; thus, 300 $^1$H MHz NMR analysis of reaction crudes shows the presence of one diastereoisomer exclusively. The relative configuration of substituents in the cyclopropane ring, shown in Scheme 3, was assigned on the basis of the value of coupling constants between the cyclopropane protons.[20] So, for example, in racemic **15**, the value of $J_{CHBr-CHPh}$ = 8.1 Hz is in agreement with the *cis*-relationship of the bromine and phenyl substituents; the value of $J_{O=C-CH-CHBr}$ = 3.8 Hz is according to the *trans*-relationship of the bromine and acetyl substituents.

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(20) The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

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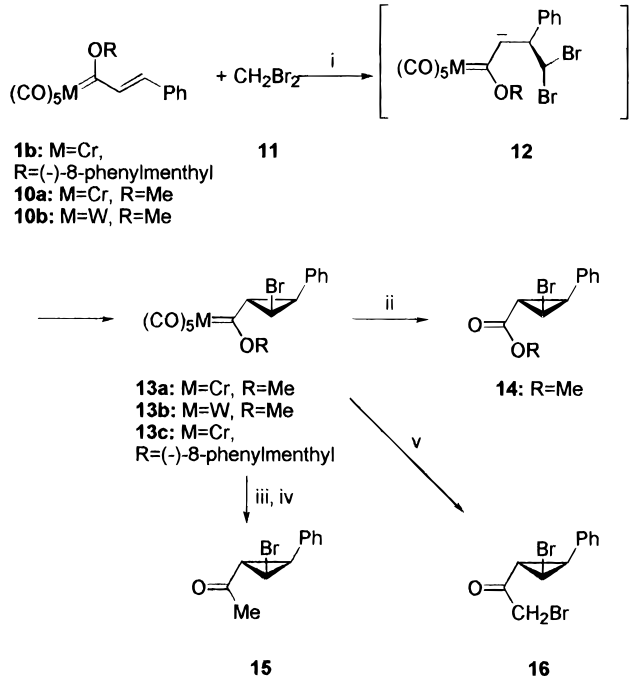
**Scheme 3**[a]




[a] Reagents and conditions: (i) LDA (diethyl ether), THF/diethyl ether, −78 °C, 5 min and then room temperature; (ii) pyridine *N*-oxide, THF, 25 °C, 14 h; (iii) $CH_2N_2$, diethyl ether, 25 °C, 14 h; (iv) HCl (1 N), 25 °C, 24 h; (v) $CH_2Br_2$, THF, then LDA (THF), −78 °C, 5 min and then room temperature.

**Table 3. Synthesis of 1,2,3-Trisubstituted Cyclopropylcarbene Complexes: Obtention of 1,2,3-Trisubstituted Cyclopropanes**

| entry | starting compd | product | yield (%)[a] | de (%)[b] |
|---|---|---|---|---|
| 1 | **10a** | **13a** | 77 | >95 |
| 2 | **10b** | **13b** | 74 | >95 |
| 3 | **1b** | **13c** | 87 | >95 |
| 4 | **13a** | **(±)-14** | 87 | >98 |
| 5 | **13a** | **(±)-15** | 83 | >98 |
| 6 | **13a** | **(±)-16** | 85 | >98 |
| 7 | **13c** | **(+)-15** | 83[c] | >98 |
| 8 | **13c** | **(+)-16** | 76[c] | >98 |

[a] Isolated yield based on the starting compounds **1**, **10**, and **13**. [b] Diastereoisomeric excess determined by 300 MHz $^1$H NMR analysis of the crude products **13**−**16**. [c] ee > 95%, HPLC [Chiracel OD-H; UV detector at (**15**) 220 nm, 0.8 mL/min; (**15**) hexane:2-propanol, 75:1, (**16**) hexane:2-propanol, 10:1; $t_R$ (**15**) 13.3 min, (**16**) 13.7 min].

The synthesis of enantiopure chromium cyclopropylcarbene complex **13c** was achieved starting from the corresponding carbene complex **1b**; its reaction with *in situ*-generated dibromomethyllithium furnished the chiral 1,2,3-trisubstituted cyclopropylcarbene complex **13c** with very high diastereoselectivity (300 MHz $^1$H NMR spectroscopy).

Cleavage of the pentacarbonyl moiety and recovery of chiral auxiliary were performed using diazomethane[10h] or dibromomethyllithium,[18] giving rise to the corresponding chiral methyl ketone **15** or bromomethyl ketone **16**, respectively (Table 3 and Scheme 3). The synthesis of **15** and **16** took place without detectable epimerization (300 MHz $^1$H NMR spectroscopy). The enantiomeric purity of **15** and **16** was determined by chiral HPLC analysis, showing that the synthesis of **13c**, **15**, and **16**, in which three stereogenic centers are generated, proceeds with high enantiomeric excess (ee > 95%). To perform the HPLC analysis, the corresponding racemic mixtures of **15** and **16** were used as standard reference. The absolute configuration of **16**, as depicted in Scheme 3, was established by X-ray analysis (Figure 1).[20] By analogy to this one, the configuration of the rest of the compounds was assigned.

In conclusion, this paper describes a convenient and versatile methodology for the preparation of different enantiopure 1,2-disubstituted and 1,2,3-trisubstituted cyclopropanes with high yield through a simple and rapid cyclopropanation of enantiomerically pure chromium alkenyl[((−)-8-phenylmenthyl)oxy]carbene complexes with *in situ*-generated monohalo- or dibromomethyllithium.

## Experimental Section

**General.** All reactions were conducted under an atmosphere of dry nitrogen using oven-dried glassware and syringes. Temperatures are reported as bath temperatures. Solvents were dried according to established protocols by distillation under nitrogen from appropiate drying agent. Thus, THF and $Et_2O$ were distilled from sodium/benzophenone ketyl and $CH_2Cl_2$ from $P_2O_5$. Solvents used in extraction and purification were distilled prior to use.

Analytical TLC was performed on glass-backed plates coated with silica gel (60 Å) with $F_{254}$ indicator; compounds were visualized with UV light or iodine. Melting points were obtained with open capillary tubes and are uncorrected. $^1$H NMR spectra were recorded at 200 or 300 MHz with TMS ($\delta$ = 0.0) as internal reference. $^{13}$C NMR spectra were recorded at 50 or 75 MHz with $CDCl_3$ ($\delta$ = 76.95) as internal reference. Only the most significant IR absortions and the molecular ions and/or base peaks in MS are given. The enantiomeric purity was determined by chiral HPLC analysis using a Chiracel OD-H column (25 × 0.46 cm).

Reagents were purchased from commercial sources and used without further purification unless otherwise indicated. Pyridine *N*-oxide was freshly sublimated prior to use. The diazomethane solution in diethyl ether was immediately prepared prior to use from *N*-nitrosomethylurea.[24] Silica gel (60 Å) for flash chromatography was purchased from commercial sources (200−450 mesh). Starting vinylcarbene complexes **1** and **13** were prepared according to a published procedure.[25]

**General Procedure for the Preparation of 1,2-Disubstituted Cyclopropylcarbene Complexes 4.** To a −78 °C stirred solution of the corresponding chiral vinylcarbene complex **1** (1 mmol) and chloroiodomethane (0.15 mL, 2 mmol) or diiodomethane (0.16 mL, 2 mmol) in THF (5 mL) and $Et_2O$ (15 mL) was added methyllithium (1.3 mL of 1.5 M solution in $Et_2O$, 2 mmol) dropwise over 5 min. After stirring at −78 °C for 5 min, the mixture was allowed to warm to room temperature and the reaction quenched with silica gel (ca. 2 g). The solvents were distilled (0.1 mmHg), and the residue was subjected to flash column chromatography over silica gel (hexane:AcOEt, 40:1) to provide cyclopropylcarbene complexes **4**.

**Pentacarbonyl{[(1*S*,2*S*)-2-(2-furyl)cyclopropyl]-[((1*R*,3*R*,4*S*)-8-phenylmenthyl)oxy]methylidene}-chromium(0) (4a)**: yellow oil; $R_f$ 0.48 (Hex:AcOEt, 20:1); $^1$H NMR $\delta$ 0.8−1.4 (m, 13 H), 1.6−1.7 (m, 4 H), 1.9−2.0 (m, 1 H), 2.4−2.5 (m, 2 H), 3.6 (ddd, $J$ = 4.0, 5.2, 8.2 Hz, 1 H), 5.3 (td, $J$ = 4.0, 10.5 Hz, 1 H), 6.0 (d, $J$ = 3.2 Hz, 1 H), 6.3 (dd, $J$ = 1.9, 3.1 Hz, 1 H), 7.0−7.3 (m, 6 H); $^{13}$C NMR $\delta$ 21.6, 24.7, 25.4, 23.5, 25.4, 28.8, 31.0, 34.2, 40.3, 50.3, 51.5, 92.5, 105.5, 110.3, 125.3, 125.7, 128.3, 141.2, 150.6, 152.9, 216.5, 223.3, 346.3; IR (neat) 2062, 1917 cm$^{-1}$; MS *m*/*z* 542 ($M^+$, 2), 458 (7), 262 (10), 170 (15), 164 (16), 136 (24), 120 (15), 119 (100), 118 (15),

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105 (79), 91 (70), 79 (18), 77 (20), 55 (12), 52 (17). Anal. Calcd for $C_{29}H_{30}O_7Cr$: C, 64.24; H, 5.57. Found: C, 64.24; H, 5.50.

**Pentacarbonyl{[(1*S*,2*S*)-2-phenylcyclopropyl]-[((1*R*,3*R*,4*S*)-8-phenylmenthyl)oxy]methylidene}-chromium(0) (4b)**: yellow oil; $R_f$ 0.54 (Hex:AcOEt, 21:1); $^1$H NMR $\delta$ 0.8−1.8 (m, 17 H), 2.0−2.1 (m, 1 H), 2.4−2.5 (m, 1 H), 2.8−2.9 (m, 1 H), 3.65 (ddd, $J$ = 3.9, 5.1, 8.1 Hz, 1 H), 5.4 (td, $J$ = 4.1, 10.5 Hz, 1 H), 7.0−7.5 (m, 10 H); $^{13}$C NMR $\delta$ 21.6, 24.0, 25.5, 27.0, 30.3, 31.0, 32.1, 34.2, 40.6, 41.1, 51.6, 53.0, 94.2, 125.4, 125.7, 126.7, 126.8, 128.3, 128.4, 139.3, 151.0, 216.7, 223.3, 346.4; IR (neat) 2058, 1929 cm$^{-1}$; MS $m/z$ 552 ($M^+$, <1), 146 (12), 120 (13), 119 (100), 118 (20), 117 (12), 115 (11), 105 (50), 91 (40), 52 (11). Anal. Calcd for $C_{31}H_{32}O_6Cr$: C, 67.38; H, 5.84. Found: C, 67.02; H, 5.77.

**Pentacarbonyl{[(1*S*,2*S*)-2-(*p*-chlorophenyl)cyclopropyl][((1*R*,3*R*,4*S*)-8-phenylmenthyl)oxy]-methylidene}tungsten(0) (4c)**: yellow oil; $R_f$ 0.60 (Hex:AcOEt, 20:1); $^1$H NMR $\delta$ 0.8−1.8 (m, 17 H), 2.0−2.1 (m, 1 H), 2.4−2.5 (m, 1 H), 2.8−2.9 (m, 1 H), 3.6−3.7 (m, 1 H), 5.4 (td, $J$ = 4.1, 10.5 Hz, 1 H), 7.0−7.5 (m, 9 H); $^{13}$C NMR $\delta$ 22.6, 26.1, 26.7, 27.9, 30.0, 32.1, 32.2, 35.1, 41.2, 44.8, 52.2, 56.7, 95.7, 126.3, 126.7, 129.2, 129.5, 133.4, 138.9, 151.5, 198.7, 203.8, 322.1; IR (neat) 2066, 1931 cm$^{-1}$; HRMS calcd for $C_{31}H_{31}ClO_6W$ 718.131 319, found 718.132 082; MS $m/z$ 718 ($M^+$, 25), 644 (18), 505 (98), 503 (100), 475 (47), 421 (79), 419 (86), 119 (85), 105 (59), 91 (27). Anal. Calcd for $C_{31}H_{31}ClO_6W$: C, 51.79; H, 4.35. Found: C, 51.67; H, 4.29.

**General Procedure for the Preparation of Cyclopropyl Methyl Ketones 5.** Diazomethane (10 mL of a solution in $Et_2O$, 3 mmol) was added to chiral cyclopropylcarbene complexes **4** (0.9 mmol) at 25 °C, and the mixture was stirred for 14 h. Then, the reaction mixture was hydrolyzed with HCl (1 N) and extracted with $Et_2O$ (3 × 10 mL). The combined organic layer was dried ($Na_2SO_4$), filtered, and concentrated *in vacuo*. The crude product mixture was chromatographed on silica gel (hexane:THF, 25:1, for **5b** and hexane:AcOEt, 15:1, for **5c**) to recover chiral auxiliary and provide pure ketones **5**.

**Methyl (1*S*,2*S*)-2-phenylcyclopropyl ketone (5b)**: colorless oil; $R_f$ 0.25 (Hex:AcOEt, 10:1); $[\alpha]^{293}_D$ = +116.2 (*c* 0.785, $CHCl_3$); $^1$H NMR $\delta$ 1.4 (ddd, $J$ = 4.2, 6.6, 8.1 Hz, 1 H), 1.7 (ddd, $J$ = 4.2, 5.1, 9.1 Hz, 1 H) 2.25 (ddd, $J$ = 4.0, 5.1, 8.1 Hz, 1 H), 2.3 (s, 3 H), 2.55 (ddd, $J$ = 4.0, 6.6, 9.1 Hz, 1 H), 7.1−7.3 (m, 5 H); $^{13}$C NMR $\delta$ 18.9, 28.8, 30.6, 32.6, 125.7, 126.2, 128.2, 140.0, 206.7; IR (neat) 1696 cm$^{-1}$; HRMS calcd for $C_{11}H_{12}O$ 160.088 815, found 160.087 967; MS $m/z$) 160 ($M^+$, 25), 117 (100), 115 (43), 91 (28), 43 (35).

**(1*S*,2*S*)-2-(*p*-Chlorophenyl)cyclopropyl methyl ketone (5c)**: colorless oil; $R_f$ 0.44 (Hex:AcOEt, 3:1); $[\alpha]^{293}_D$ = +370.75 (*c* 0.735, $CHCl_3$); $^1$H NMR $\delta$ 1.3 (ddd, $J$ = 4.3, 6.6, 8.2 Hz, 1 H), 1.65 (ddd, $J$ = 4.3, 5.2, 9.1 Hz, 1 H), 2.15 (ddd, $J$ = 4.0, 5.2, 8.2 Hz, 1 H), 2.3 (s, 3 H), 3.45 (ddd, $J$ = 4.0, 6.6, 9.1 Hz, 1 H), 7.0 (d, $J$ = 8.4 Hz, 2 H), 7.2 (d, $J$ = 8.4 Hz, 2 H); $^{13}$C NMR $\delta$ 18.8, 27.9, 30.5, 32.4, 127.1, 128.2, 131.8, 138.6, 206.1; IR (neat) 1697 cm$^{-1}$; HRMS calcd for $C_{11}H_{11}ClO$ 194.049 843, found 194.049 561; MS $m/z$ 196 ($M^+$ + 2, 20), 194 ($M^+$, 60), 153 (30), 151 (91), 125 (19), 116 (57), 115 (82), 43 (100).

**General Procedure for the Preparation of Bromomethyl Cyclopropyl Ketones 6.** To a −78 °C stirred solution of chiral cyclopropylcarbene complex **4** (0.9 mmol) and dibromomethane (0.11 mL, 1.5 mmol) in THF (5 mL) was added LDA [prepared from MeLi (1 mL of 1.5 M solution in $Et_2O$, 1.5 mmol) and diisopropylamine (0.21 mL, 1.5 mmol) in THF (5 mL)] dropwise over 5 min. After stirring at −78 °C for 5 min, the mixture was allowed to warm to room temperature, hydrolyzed with HCl (1 N) and extracted with $Et_2O$ (3 × 10 mL). The solvents were distilled (0.1 mmHg), and the crude product mixture was subjected to flash column chromatography over silica gel (hexane:$Et_2O$, 30:1, for **6b**) to recover chiral auxiliary and provide pure ketones **6**.

**Bromomethyl (1*S*,2*S*)-2-phenylcyclopropyl ketone (6b)**: colorless oil; $R_f$ 0.31 (Hex:AcOEt, 10:1); $[\alpha]^{293}_D$ = +321.2 (*c* 0.55, $CHCl_3$); $^1$H NMR $\delta$ 1.55 (ddd, $J$ = 4.3, 6.8, 8.1 Hz, 1 H), 1.75 (ddd, $J$ = 4.3, 5.2, 9.1 Hz, 1 H), 2.45 (ddd, $J$ = 4.0, 5.2, 8.1 Hz, 1 H), 2.6 (ddd, $J$ = 4.0, 6.8, 9.1 Hz, 1 H), 4.05 (s, 2 H), 7.1−7.4 (m, 5 H); $^{13}$C NMR $\delta$ 19.9, 30.2, 30.7, 34.8, 126.1, 126.8, 128.5, 139.4, 200.1; IR (neat) 1697 cm$^{-1}$; HRMS calcd for $C_{11}H_{11}BrO$ 237.999 338, found 237.999 449; MS $m/z$ 240 ($M^+$ + 2, 4), 238 ($M^+$, 4), 159 (48), 145 (18), 117 (100), 115 (62), 91 (31). Anal. Calcd for $C_{11}H_{11}BrO$: C, 55.25; H, 4.64. Found: C, 55.17; H, 4.58.

**General Procedure for the Preparation of Cyclopropanecarboxylates 7.** To a 25 °C stirred solution of chiral cyclopropylcarbene complex **4** (0.9 mmol) in THF (15 mL) was added pyridine *N*-oxide (0.29 g, 3 mmol). After stirring at 25 °C for 14 h, the mixture was hydrolyzed with HCl (1 N) and extracted with $Et_2O$ (3 × 10 mL). The combined organic layer was dried ($Na_2SO_4$), filtered through Celite, and concentrated *in vacuo* to give pure esters **7**.

**(1*R*,3*R*,4*S*)-8-Phenylmenthyl (1*S*,2*S*)-2-(2-furyl)cyclopropanecarboxylate (7a)**: colorless oil; $R_f$ 0.43 (Hex:AcOEt, 20:1); $[\alpha]^{293}_D$ = +122.6 (*c* 0.61, $CHCl_3$); $^1$H NMR $\delta$ 0.8−1.5 (m, 16 H), 1.6−1.7 (m, 2 H), 1.8−1.9 (m, 1 H), 2.0−2.1 (m, 1 H), 2.2−2.3 (m, 1 H), 4.8 (td, $J$ = 4.4, 10.8 Hz, 1 H), 6.0 (d, $J$ = 3.2 Hz, 1 H), 6.2 (dd, $J$ = 1.9, 3.2 Hz, 1 H), 7.1−7.3 (m, 6 H); $^{13}$C NMR $\delta$ 14.8, 19.0, 21.7, 21.9, 25.0, 26.4, 27.6, 31.1, 34.4, 39.5, 41.6, 50.4, 74.6, 104.9, 110.2, 140.7, 124.9, 125.2, 127.8, 151.3, 153.3, 172.0; IR (neat) 1717 cm$^{-1}$; MS $m/z$ 366 ($M^+$, <1), 214 (13), 152 (41), 135 (13), 119 (100), 107 (32), 105 (63), 91 (95), 81 (16), 79 (51), 78 (20), 77 (60), 55 (19), 53 (14), 41 (23). Anal. Calcd for $C_{24}H_{30}O_3$: C, 78.65; H, 8.25. Found: C, 78.41; H, 8.19.

**(1*R*,3*R*,4*S*)-8-Phenylmenthyl (1*S*,2*S*)-2-phenylcyclopropanecarboxylate (7b)**: colorless oil; $R_f$ 0.47 (Hex:AcOEt, 20:1); $[\alpha]^{293}_D$ = +81.6 (*c* 0.67, $CHCl_3$); $^1$H NMR $\delta$ 0.8−2.2 (m, 21 H), 4.7 (td, $J$ = 4.3, 10.7 Hz, 1 H), 6.9−7.2 (m, 10 H); $^{13}$C NMR $\delta$ 17.3, 21.6, 24.1, 25.2, 25.8, 26.5, 27.6, 31.1, 34.4, 39.6, 41.7, 50.5, 74.6, 124.8, 125.3, 125.9, 126.2, 127.8, 128.2, 140.2, 151.5, 172.6; IR (neat) 1715 cm$^{-1}$; HRMS calcd for $C_{26}H_{32}O_2$ 376.240 230, found 376.240 854; MS $m/z$ 376 ($M^+$, 14), 266 (16), 257 (23), 243 (20), 162 (21), 119 (100), 118 (22), 91 (21), 45 (14).

**(1*S*,2*S*)-[2-(2-Furyl)cyclopropyl]methanol (8a).** To a 0 °C stirred solution of $LiAlH_4$ (0.11 g, 3 mmol) in $Et_2O$ (10 mL) was added a solution of ester **7a** (0.37 g, 1 mmol) in $Et_2O$ (10 mL) dropwise over 15 min. The mixture was refluxed (35 °C) for 14 h. After cooling to 0 °C, $H_2O$ (20 mL) was added. The mixture was extracted with $Et_2O$ (3 × 10 mL). The solvents were distilled (0.1 mmHg), and the crude product mixture was subjected to flash column chromatography over silica gel (hexane:AcOEt, 20:1) to recover chiral auxiliary and provide pure alcohol **8a** as a colorless oil: $R_f$ 0.12 (Hex:AcOEt, 5:1); $[\alpha]^{293}_D$ = +260 (*c* 0.735, $CHCl_3$); $^1$H NMR $\delta$ 0.8−1.0 (m, 2 H), 1.4−1.5 (m, 1 H), 1.75−1.85 (m, 1 H), 3.3 (s br, 1 H), 3.55 (dd, $J$ = 4.5, 6.7 Hz, 2 H), 5.95 (d, $J$ = 3.0 Hz, 1 H), 6.25 (dd, $J$ = 1.7, 3.0 Hz, 1 H), 7.2 (d, $J$ = 1.7 Hz, 1 H); $^{13}$C NMR $\delta$ 11.1, 14.3, 22.5, 65.4, 103.5, 110.1, 140.3, 155.8; IR (neat) 3333, 1024 cm$^{-1}$; HRMS calcd for $C_8H_{10}O_2$ 138.068 080, found 138.068 180; MS $m/z$ 138 ($M^+$, 60), 107 (100), 95 (25), 94 (49), 77 (36).

**(1*R*,2*S*)-[2-(2-Furyl)cyclopropyl]methyl Benzoate (9a).** To a stirred solution of alcohol **8a** (0.1 g, 0.725 mmol) were added benzoyl chloride (0.174 mL, 1.5 mmol), triethylamine (0.209 mL, 1.5 mmol), and a catalytic amount of DMAP. After stirring at 25 °C for 14 h, the mixture was hydrolyzed with $NaHCO_3$ (10%) and extracted with $Et_2O$ (3 × 10 mL). The solvents were distilled (0.1 mmHg), and the crude product mixture was subjected to flash column chromatography over silica gel (hexane:AcOEt, 15:1) to provide pure ester **9a** as a colorless oil: $R_f$ 0.375 (Hex:AcOEt, 10:1); $[\alpha]^{293}_D$ = +37.2 (*c* 0.825, $CHCl_3$); $^1$H NMR $\delta$ 0.9−1.1 (m, 2 H), 1.6−1.7 (m, 1 H), 1.9−2.0 (m, 1 H), 4.25 (d, $J$ = 7.0 Hz, 2 H), 5.95 (dd, $J$ = 0.5, 3.2 Hz, 1 H), 6.2 (dd, $J$ = 1.9, 3.2 Hz, 1 H), 7.2 (d, $J$ = 1.9 Hz, 1 H), 7.3−7.6 (m, 3 H), 8.0−8.1 (m, 2 H); $^{13}$C NMR $\delta$ 11.7, 14.9, 19.1, 27.6, 103.9, 110.2, 128.3, 129.5, 130.1, 132.9, 140.5, 155.2, 166.5; IR (neat) 1715, 1096, 1047 cm$^{-1}$; HRMS calcd for $C_{15}H_{14}O_3$ 242.094 294, found 242.094 790; MS $m/z$ 242 ($M^+$, 38), 136 (17), 129 (66), 105 (100), 91 (30), 77 (48).

**General Procedure for the Preparation of Bromocyclopropylcarbene Complexes 13.** To a −78 °C stirred solution of vinylcarbene complex **1** or **10** (1 mmol) and dibromomethane (0.11 mL, 1.5 mmol) in $Et_2O$ (20 mL) was

added LDA [prepared from MeLi (1 mL of 1.5 M solution in $Et_2O$, 1.5 mmol) and diisopropylamine (0.21 mL, 1.5 mmol) in $Et_2O$ (5 mL)] dropwise over 5 min. After stirring at −78 °C for 5 min, the mixture was allowed to warm to room temperature and the reaction quenched with silica gel (ca. 2 g). The solvents were distilled (0.1 mmHg), and the residue was subjected to flash column chromatography over silica gel (hexane:AcOEt, 40:1) to provide cyclopropylcarbene complexes **13**.

**Pentacarbonyl{[(1*R**,2*S**,3*R**)-2-bromo-3-phenylcyclopropyl]methoxymethylidene}chromium(0) (13a)**: yellow oil; $R_f$ 0.35 (Hex:AcOEt, 10:1); $^1$H NMR $\delta$ 3.3 (dd, $J$ = 6.0, 8.1 Hz, 1 H), 3.9 (dd, $J$ = 3.7, 8.1 Hz, 1 H), 4.15 (dd, $J$ = 3.7, 6.0 Hz, 1 H), 4.9 (s, 3 H), 7.2−7.4 (m, 5 H); $^{13}$C NMR $\delta$ 34.0, 39.8, 55.3, 66.0, 127.6, 128.2, 128.7, 124.4, 215.0, 223.0, 348.6; IR (neat) 2062, 1931 cm$^{-1}$; HRMS calcd for $C_{16}H_{11}BrCrO_6$ 429.914 585, found 429.912 646; MS *m*/*z* 432 ($M^+$ + 2, 25), 430 ($M^+$, 25), 404 (13), 402 (13), 320 (90), 318 (91), 292 (20), 159 (39), 128 (75), 115 (100), 105 (30), 57 (25), 52 (32).

**Pentacarbonyl{[(1*R**,2*R**,3*S**)-2-bromo-3-phenylcyclopropyl]methoxymethylidene}tungsten(0) (13b)**: yellow oil; $R_f$ 0.275 (Hex:AcOEt, 20:1); $^1$H NMR $\delta$ 3.3 (dd, $J$ = 6.0, 8.2 Hz, 1 H), 3.9 (dd, $J$ = 3.4, 8.2 Hz, 1 H), 4.2 (dd, $J$ = 3.4, 6.0 Hz, 1 H), 4.6 (s, 3 H), 7.3−7.5 (m, 5 H); $^{13}$C NMR $\delta$ 33.5, 39.7, 58.8, 69.6, 127.7, 128.3, 128.8, 134.4, 197.0, 203.3, 322.6; IR (neat) 2070, 1915 cm$^{-1}$; HRMS calcd for $C_{16}H_{11}BrO_6W$ 561.923 003, found 561.923 604; MS *m*/*z* 562 ($M^+$, 16), 483 ($M^+$ − Br, 49), 427 (34), 424 (51), 409 (68), 407 (95), 356 (86), 298 (75), 159 (68), 128 (70), 115 (100), 91 (30). Anal. Calcd for $C_{16}H_{31}BrO_6W$: C, 34.13; H, 1.97. Found: C, 34.25; H, 1.94.

**Pentacarbonyl{[(1*S*,2*R*,3*S*)-2-bromo-3-phenylcyclopropyl][((1*R*,3*R*,4*S*)-8-phenylmenthyl)oxy]-methylidene}chromium(0) (13c)**: yellow oil; $R_f$ 0.56 (Hex:AcOEt, 20:1); $^1$H NMR $\delta$ 0.8−2.1 (m, 17 H), 2.45 (dd, $J$ = 6.4, 8.2 Hz, 1 H), 3.3 (dd, $J$ = 3.4, 8.2 Hz, 1 H), 4.0 (dd, $J$ = 3.4, 6.4 Hz, 1 H), 5.3 (td, $J$ = 3.9, 10.7 Hz, 1 H), 7.1−7.5 (m, 10 H); $^{13}$C NMR $\delta$ 21.6, 26.1, 26.6, 27.7, 31.0, 34.2, 34.8, 36.6, 39.7, 44.2, 51.6, 56.5, 93.0, 125.1, 125.6, 127.2, 128.0, 128.1, 129.2, 135.0, 150.4, 216.1, 223.1, 344.6; IR (neat) 2060, 1937 cm$^{-1}$; HRMS calcd for $C_{31}H_{31}BrCrO_6$ 630.074 943, found 630.071 150; MS *m*/*z* 632 ($M^+$ + 2, 19), 630 (19), 548 (21), 546 (21), 119 (100), 105 (37), 91 (23). Anal. Calcd for $C_{31}H_{31}BrCrO_6$: C, 58.96; H, 4.95. Found: C, 58.90; H, 4.88.

**Methyl (1*R**,2*R**,3*S**)-2-Bromo-3-phenylcyclopropanecarboxylate (14).** This compound was prepared, according to the general procedure described above for compounds **7**, from chiral cyclopropylcarbene complex **13a** (0.43 g, 1 mmol) to provide pure ester **14** as a colorless oil: $R_f$ 0.37 (Hex:AcOEt, 10:1); $^1$H NMR $\delta$ 2.45 (dd, $J$ = 3.8, 6.3 Hz, 1 H), 2.95 (dd, $J$ = 6.3, 8.1 Hz, 1 H), 3.5 (dd, $J$ = 3.8, 8.1 Hz, 1 H), 3.8 (s, 3 H), 7.2−7.4 (m, 5 H); $^{13}$C NMR $\delta$ 27.8, 28.8, 31.6, 52.3, 127.4, 128.1, 128.9, 134.3, 171.7; IR (neat) 1730 cm$^{-1}$; HRMS calcd for $C_{11}H_{11}BrO_2$ 253.994 253, found 253.994 215; MS *m*/*z* 256 ($M^+$ + 2, 21), 224 ($M^+$, 21), 197 (58), 195 (65), 175 (67), 131 (20), 116 (38), 115 (100).

**(1*S*,2*R*,3*S*)-2-Bromo-3-phenylcyclopropyl Methyl Ketone (15).** This compound was prepared, according to the general procedure described above for compounds **5**, from chiral cyclopropylcarbene complex **13c** (0.47 g, 0.75 mmol). Purification on silica gel (hexane:AcOEt, 40:1) allowed to recover chiral auxiliary and provided pure ketone **5c** as a colorless oil: $R_f$ 0.28 (Hex:$CH_2Cl_2$, 2:1); $[\alpha]^{293}_D$ = +42.0 (*c* 0.65, $CHCl_3$); $^1$H NMR $\delta$ 2.45 (s, 3 H), 2.75 (dd, $J$ = 3.8, 6.0 Hz, 1 H), 2.95 (dd, $J$ = 6.0, 8.1 Hz, 1 H), 3.7 (dd, $J$ = 3.8, 8.1 Hz, 1 H), 7.25−7.5 (m, 5 H); $^{13}$C NMR $\delta$ 29.8, 31.3, 34.0, 36.4, 127.9, 128.1, 128.8, 134.6, 204.9; IR (neat) 1730 cm$^{-1}$; HRMS calcd for $C_{11}H_{11}BrO$ 237.999 338, found 237.998 288; MS *m*/*z* 239 ($M^+$ + 2, <1), 237 ($M^+$, <1), 159 (77), 116 (39), 115 (96), 43 (100).

**Bromomethyl (1*R*,2*S*,3*R*)-2-Bromo-3-phenylcyclopropyl Ketone (16).** This compound was prepared, according to the typical procedure described above for compounds **6**, from chiral cyclopropylcarbene complex **13c** (0.47 g, 0.75 mmol). Purification on silica gel (hexane:AcOEt, 25:1) allowed to recover chiral auxiliary and provided pure ketone **16** as a white crystalline solid: $R_f$ 0.30 (Hex:AcOEt, 10:1); mp 55−57 °C; $[\alpha]^{293}_D$ = +45.7 (*c* 0.75, $CHCl_3$); $^1$H NMR $\delta$ 3.0−3.05 (m, 2 H), 3.75 (dd, $J$ = 5.1, 6.8 Hz, 1 H), 4.1 (AB system, $J$ = 12.4 Hz, 2 H), 7.25−7.4 (m, 5 H); $^{13}$C NMR $\delta$ 30.4, 34.2, 34.6, 35.2, 127.6, 128.2, 128.9, 134.1, 198.6; IR (neat) 1705 cm$^{-1}$; HRMS calcd for $C_{11}H_{10}BrO$ 236.991 513, found 236.991 394; MS *m*/*z* 316 ($M^+$, <1), 239 ($M^+$ + 2 − Br, 81), 237 ($M^+$ − Br, 81), 197 (52), 195 (54), 158 (36), 129 (41), 116 (85), 115 (100). Anal. Calcd for $C_{11}H_{10}Br_2O$: C, 41.55; H, 3.17. Found: C, 41.45; H, 3.15.

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**Supporting Information Available:** Copies of the $^{13}$C NMR spectra for all compounds (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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