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[4+2] Cyclization reactions of chiral C_β-substituted Fischer alkenyl carbene complexes: efficient synthesis of enantiopure cyclohexenone and norbornene derivatives

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Abstract—Chiral alkenyl carbene complexes of tungsten(0) **1** and **2**, readily available from the chiral pool, undergo the [4+2] cycloaddition with the Danishefsky diene to provide enantiopure 4-alkenyl-2-cyclohexenone adducts **5** and **7** with high stereoselectivity after treatment of the primary cycloadducts **4** and **6** with TBAF. Cyclopentadiene also cycloadds to carbenes **1** and **2** affording the expected norbornene metal carbene complexes **10** and **12** with remarkable diastereo and face selectivity. Oxidative removal of the metal pentacarbonyl fragment leads to the ester derivatives **11** and **13**. The X-ray structure analysis of two cycloadducts derived from carbenes **1** and **2** has been performed.

1. Introduction

Due to the high electron-accepting power of the pentacarbonylmetal unit, Fischer-type α,β-unsaturated carbene complexes have demonstrated to be excellent partners for different cycloaddition reactions.[1] In particular, the [4+2] cycloaddition of alkenyl carbene complexes toward electron-rich dienes,[2] which emerged two decades ago,[3] reveals some advantages over that based on electron-poor, non-metal dienophiles: (i) the reaction occurs under much milder reaction conditions and, therefore, higher selectivity is attained and (ii) the versatile metal carbene functionality is maintained unaltered in the cycloadduct allowing to undertake further elaboration.[4]

On the other hand, the asymmetric version of this process has not been so widely developed.[5] The most relevant contribution has been delivered by Wulff et al. who found that chiral aminoalkenyl carbene complexes of chromium(0) exhibited very high exo- and facial diastereoselectivity toward 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky's diene).[6] In contrast, chiral alkoxyalkenyl carbene complexes, e.g., carbene complexes derived from (−)-menthol, have been shown to induce modest selectivity.[5,7] In a different approach, the cycloaddition reaction of cyclopentadiene and 2,3-dimethyl-1,3-butadiene with methoxyalkenyl carbenes having a monosaccharide unit (arabinose and galactopyranose) attached to the C-β carbon has been reported to take place with moderate selectivity.[8] In this context, we have focused recently on the potential of tungsten alkenyl carbenes **1** and **2** containing a chiral group—1,3-dioxolane (**1**) and 1,3-dioxane (**2**)—that are readily available from the chiral pool[9] and, importantly, very promising for further elaboration. This type of chiral carbene complexes has been shown to exhibit high selectivity in Michael–Mukaiyama addition[10] and cyclopropanation (Michael type addition/cyclization)[11] reactions with 2-trimethylsilyloxy and 2-methoxyfuran, respectively (Fig. 1).

On the basis of these findings, we have explored the behavior of carbenes **1** and **2** in the Diels–Alder cycloaddition. We report herein that they undergo the [4+2] cycloaddition reaction with 1-methoxy-3-trimethylsilyloxy-1,3-butadiene and cyclopentadiene with good chemical yield and high selectivity. The transformation of the cycloadducts into metal-free derivatives is also undertaken.

2. Results and discussion

First we found that enantiopure tungsten carbene complexes **1** and **2** are highly reactive toward the Danishefsky's diene **3** at low temperature (Scheme 1).[12] Thus, the reaction of the methoxycarbene **1a** (R=Me) with **3** (5 equiv) in toluene

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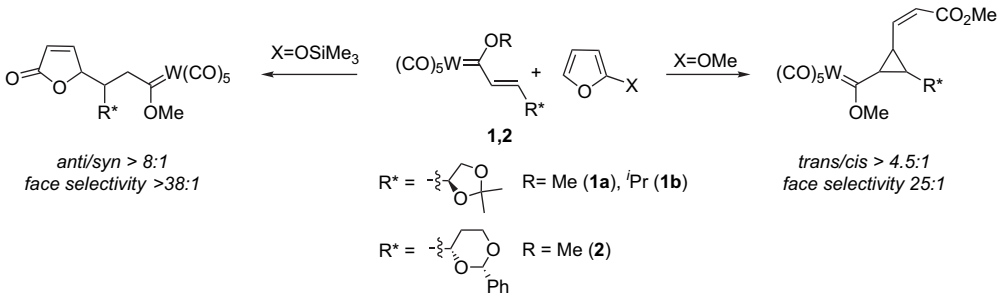
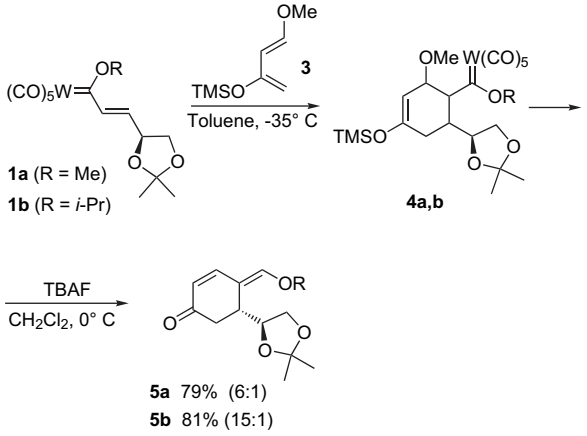


Figure 1.

at −35 °C led to the formation of the expected [4+2] cycloadduct **4a** as a mixture of four diastereoisomers. The complex reaction crude was not analyzed, but it could be transformed into a 6:1 epimeric mixture of cyclohexenones by treatment with tetrabutylammonium fluoride (CH_2Cl_2, 0 °C), in 79% overall yield. Simple flash chromatographic purification permitted the isolation of the major diastereoisomer **5a** in enantiopure form and in high overall yield (64% yield referred to the starting metal carbene complex).

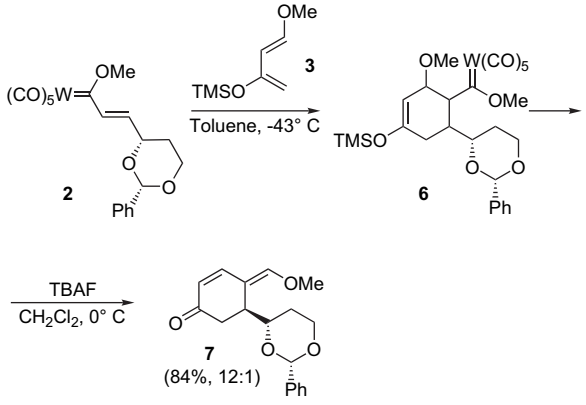


Scheme 1.

Furthermore, the stereoselectivity could be increased by simply using carbene complexes containing a higher steric demanding alkoxy group (Scheme 1). Thus, replacing the methoxy group (carbene **1a**) with the isopropoxy group (carbene **1b**) and conducting the sequence under the same reaction conditions resulted in the formation of the cyclohexenone adduct as a 15:1 epimeric (81% yield).

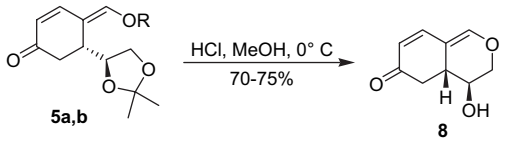
In the same way, the [4+2] cycloaddition of the carbene complex **2** with the diene **3** furnished a mixture of cycloadducts **6** (Scheme 2). Further treatment with TBAF afforded a 12:1 mixture of cyclohexenones (84% yield) from which the major stereoisomer **7** was separated by flash column chromatography (63% overall yield from carbene **2**).

The structure of the cycloadducts **5** and **7** is fully consistent with both the NMR spectral data, including 2D experiments (HMBC, HSQC, and NOESY), and the postulated diene–carbene approach (vide infra). The presence of the chiral auxiliary appendage allowed us to undertake further elaboration and to unambiguously determine the structure of the cycloadducts (Scheme 3). Thus, either cycloadduct **5a** or **5b**



Scheme 2.

was stirred with concd HCl in methanol at 0 °C to afford the enantiopure isochromenone **8** in moderate yield (70% from **5a**; 75% from **5b**), after flash chromatographic purification.[13] (Scheme 3).



Scheme 3.

Compound **8** could be crystallized from a 10:1 pentane/ethyl acetate mixture and its structure confirmed by an X-ray analysis (Fig. 2).

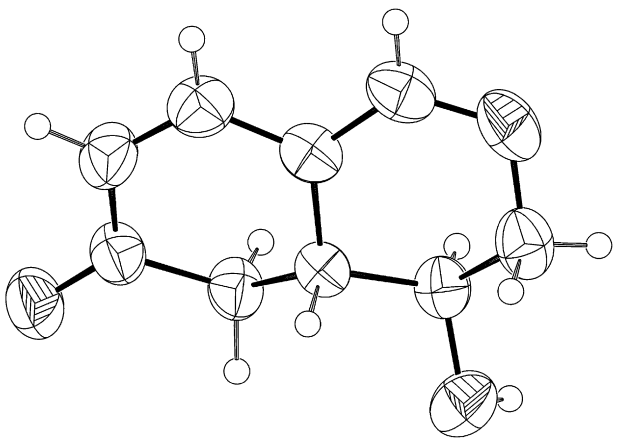
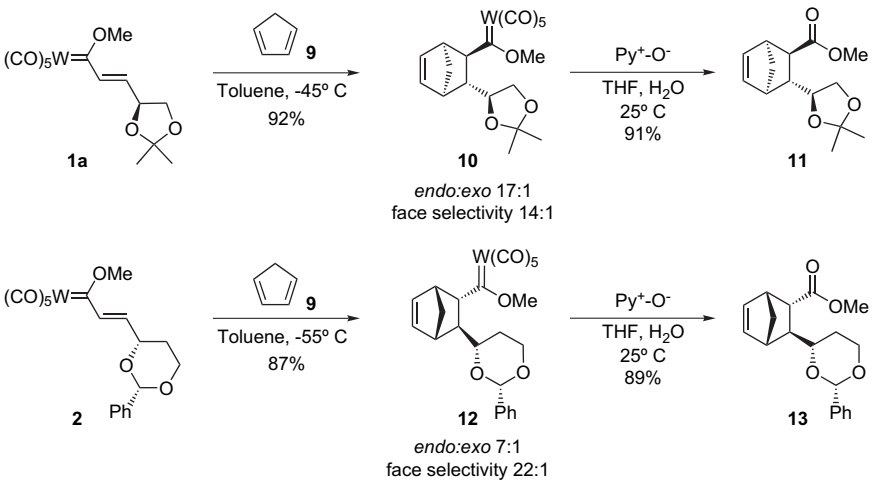


Figure 2.



Scheme 4.

Next we checked the behavior of carbene complexes **1** and **2** as dienophiles toward cyclopentadiene **9** (Scheme 4). It is noticeable that low selectivity has been reported for the [4+2] cycloaddition of cyclopentadiene with, (i) alkenyl carbene complexes derived from chiral alcohols[5] and chiral amines,[5] (ii) alkenyl carbene complexes containing arabinose or galactopyranose units at the C-β position,[8] and (iii) the methyl ester containing the 1,3-dioxolane unit, which is isolobal to carbene **1a**.[14] Thus, the treatment of carbene **1a** (R=Me) with cyclopentadiene **9** (50 equiv) in toluene at −45 °C resulted in the formation of the carbene cycloadduct **10** (92% yield) as the major diastereoisomer. In terms of selectivity, the *endo*/*exo* ratio was found to reach 17:1, while the face stereoselectivity was 14:1. Under similar reaction conditions (toluene, −55 °C), the addition of cyclopentadiene **9** to the carbene complex **2** afforded the cycloadduct **12** in 87% yield and with high selectivity (*endo*/*exo*=7:1, face selectivity 22:1). When the crude mixture of cycloadducts was subjected to flash column chromatography the corresponding cycloadducts **10** and **12** were isolated in good yields (overall yield from carbene complexes **1** and **2**: 80% yield for **10**; 73% yield for **12**) as stereochemically pure compounds.[15] The cycloadducts **10** and **12** were in turn demetalated by oxidation with pyridinium oxide (tetrahydrofuran/water, 25 °C) to provide the corresponding enantiopure esters **11** and **13**, respectively, in 89–91% yields (Scheme 4). Again, the higher efficiency as dienophiles of the alkenyl carbenes with respect to their isolobal esters is evidenced as the cycloaddition of the ester structurally related to carbene **1a** with cyclopentadiene has been reported to produce the cycloadduct **11** as mixture of four diastereoisomers with rather low selectivity.[14]

The structure of compound **12** was determined by an X-ray analysis performed on crystals grown from a hexane solution of racemic cycloadduct (Fig. 3).

The stereoselectivity can be rationalized on the basis of the well-established model for the [4+2] cycloaddition of electron-poor olefins containing the chiral dioxolane unit,[12,14] which has also been assumed in the case of the Michael addition of 2-alkoxyfurans to carbenes **1** and **2**.[10,11] Thus, the approach of cyclopentadiene from the less hindered face of the C=C bond of **1a** in the minimum-energy conformation **A**, would lead to the major isomer **10** (Fig. 4). In the same way, the adduct **12** would arise from the attack of cyclopentadiene **9** to carbene **2** through the conformation **B**.

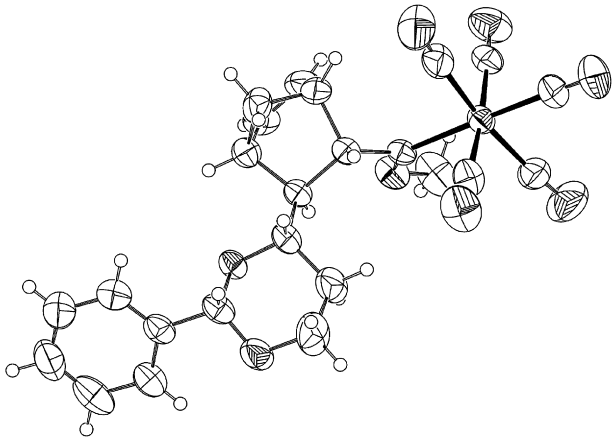


Figure 3.

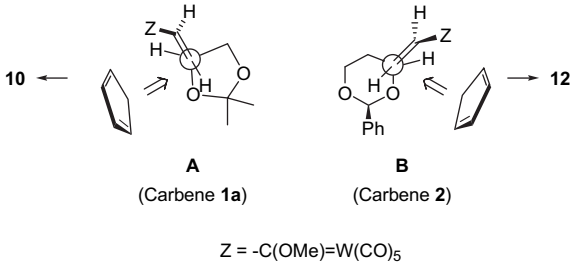


Figure 4.

Regarding the absolute configuration of the newly formed stereogenic centers it should be noted that both chiral moieties are complementary to each other.

3. Conclusions

In conclusion, enantiopure alkenyl carbene complex **1**, readily available from D-glyceraldehyde and methyl(alkoxy)carbene complexes, undergo very efficiently the [4+2]

cycloaddition reaction with typical dienes as Danishefsky's diene and cyclopentadiene to produce cyclohexenone and cyclohexene derivatives with excellent diastereo and face selectivities. This cycloaddition seems to be superior in terms of chemical yield and stereoselectivity over previous examples involving either chiral metal carbene complexes or metal-free dienophiles containing the same chiral auxiliaries. In particular the selectivity found toward cyclopentadiene is noteworthy. In addition, the carbene complex **2** also works well and complements the synthetic usefulness of carbenes **1** in what refers to, (i) elaboration of the auxiliary fragment, and (ii) absolute configuration of the cycloadducts. The presence of both the chiral auxiliary fragment and the metal carbene function in the cycloadducts allows to undertake further synthetic transformations. For instance, the metal elimination on the adducts resulting from Danishefsky's diene furnishes the 4-alkylidene-2-cyclohexenone structure, which appears not to be available at all by direct cycloaddition of the corresponding alkoxyallene.[16] In the same way, the simple hydrolysis of the chiral dioxolane unit offers the way to access the isochromenone skeleton, a component of the coumarin and isocoumarin family, which is extensively present in nature.[17]

4. Experimental

4.1. General methods

All operations were carried out under nitrogen atmosphere using conventional Schlenk techniques. All common reagents were obtained from commercial suppliers and used without further purification unless otherwise indicated. Toluene was distilled from sodium-benzophenone, under a nitrogen atmosphere prior to use. Hexane, ethyl acetate, and methylene chloride were distilled before use. TLC was performed on aluminum-backed plates coated with silica gel 60, with F_{254} indicator. Flash chromatographic columns were carried out on silica gel 60, 230–240 mesh. Optical rotations were determined with a Perkin Elmer 241 polarimeter using a Na lamp; data are reported as follows: $[\alpha]_D^{20}$ (concentration in g per 100 ml, solvent). High-resolution mass spectra were determined on a Finnigan MAT95 spectrometer. NMR spectra were run on Bruker AC-200, AC-300, and AMX-400 spectrometer.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication with numbers: Compound **8** CCDC-635330 and compound **12** CCDC-635331. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

4.1.1. Experimental procedure for the synthesis of the alkenyl carbene 1b. Carbene **1b** was prepared following the established procedure for the synthesis of alkenyl carbene complexes **1a** and **2**.

4.1.1.1. Pentacarbonyl[(*E*)-3-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-(methylethoxy)-2-propenyliden]tungsten(0) (1b). Yield 61%, red oil. R_f=0.59 (hexane/ethyl acetate (5:1). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (d, J=15.0 Hz, 1H), 6.10 (dd, J=15.0 and 5.0 Hz, 1H), 5.75 (hept, J=6.2 Hz, 1H), 4.62 (m, 1H), 4.21 (dd, J=8.3 and 6.8 Hz, 1H), 3.71 (dd, J=8.1 and 7.3 Hz, 1H), 1.54 (d, J=6.2 Hz, 1H), 1.53 (d, J=6.2 Hz, 1H), 1.48 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 321.5 (C), 205.5 (C), 144.4 (CH), 131.3 (CH), 110.3 (C), 87.5 (CH), 75.14 (CH), 68.9 (CH_2), 26.6 (CH_3), 25.3 (CH_3), 22.2 (CH_3). HRMS calcd for $C_{16}H_{18}O_8W$ [M^+]: 522.0506; found: 522.0515.

4.1.2. General procedure for the preparation of cyclohexenones (5 and 7). To a solution of 1 mmol of the corresponding alkenyl carbene **1a**,**1b**, and **2** in 40 ml of toluene at low temperature (see Schemes 1–3), 340 mg (5 mmol) of 1-methoxy-3-trimethylsilyloxy-1,3-butadiene **3** (Danishefsky's diene) was added. After 60 h for **1a** or 72 h for **1b** and **2**, at that temperature, solvents were removed under reduced pressure. At this point, the residue was dissolved in methylene chloride (40 ml) and 2 equiv of tetrabutylammonium fluoride was added at 0 °C. The mixture was allowed to reach room temperature and stirred for two additional hours. At this point, 20 ml of water was added and the mixture extracted with ethyl acetate (3×20 ml) to yield a (6:1), (15:1), and (12:1) diastereomeric mixture of epimers **5a**, **5b**, and **7**, respectively. All three mixtures could be isolated after flash chromatography through inactivated silica gel (hexane/ethyl acetate (2:1)) in 79, 81, and 84%, respective yields. Flash chromatographic purification through inactivated silica gel (hexane/ethyl acetate (2:1)) also allows the isolation of cyclohexenones **5a** and **7**, as enantiopure compounds in 64 and 63% yields from carbenes **1a** and **2**.

4.1.2.1. (*R*)-4-((*Z*)-Methoxymethylen)-5-((*S*)-2,2-dimethyl-(1,3-dioxolan-4-yl))-2-cyclohexenone (5a). Yield 64%, yellowish oil. R_f=0.12 (hexane/ethyl acetate (2:1)). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.90 (d, J=10.0 Hz, 1H), 6.58 (s, 1H), 5.79 (d, J=10.0 Hz, 1H), 4.10 (m, 1H), 3.95 (dd, J=6.2 and 8.2 Hz, 1H), 3.83 (s, 3H), 3.78 (dd, J=6.2 and 8.2 Hz, 1H), 3.24 (m, 1H), 2.81 (d, J=16.2 Hz, 1H), 2.51 (dd, J=6.6 and 16.5 Hz, 1H), 1.41 (s, 3H), 1.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4 (C), 153.5 (CH), 144.7 (CH), 123.4 (CH), 114.6 (C), 109.4 (C), 77.0 (CH), 67.8 (CH_2), 61.1 (CH), 37.6 (CH_2), 36.1 (CH_3), 26.5 (CH_3), 25.2 (CH_3). HRMS calcd for $C_{13}H_{18}O_4$ [M^+]: 238.1200; found: 238.1199. Anal. calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.41; H, 7.63. $[\alpha]_D^{20}$ −21.7 (*c* 0.301, CH_2Cl_2).

4.1.2.2. (*R*)-5-((*S*)-2,2-Dimethyl-(1,3-dioxolan-4-yl))-4-((*Z*)-(methylethoxy)methylen)-2-cyclohexenone (5b). Yield 79% (as a (15:1) epimeric mixture), yellowish oil. R_f=0.42 (hexane/ethyl acetate (2:1)). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.89 (d, J=9.5 Hz, 1H), 6.67 (s, 1H), 5.74 (d, J=10 Hz, 1H), 4.11 (m, 1H), 3.92 (dd, J=6.2 and 8.2 Hz, 1H), 3.79 (dd, J=6.7 and 8.2 Hz, 1H), 3.25 (m, 1H), 2.80 (d, J=16.0 Hz, 1H), 2.50 (dd, J=6.7 and 16.7 Hz, 1H), 1.39 (s, 3H), 1.32 (d, J=7.2 Hz, 3H), 1.31 (d, J=7.2 Hz, 3H), 1.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3 (C), 151.6 (CH), 145.4 (CH), 122.5 (CH), 113.9 (C), 109.1 (C), 77.2 (CH), 76.8 (CH), 68.0 (CH_2), 37.7 (CH_2), 36.0 (CH), 26.4 (CH_3), 25.3 (CH_3), 22.4 (CH_3). HRMS calcd for $C_{15}H_{22}O_4$ [M^+]: 266.1518; found: 266.1510.

4.1.2.3. (*S*)-(5-(2*S*,4*S*)-2-phenyl-1,3-dioxan-4-yl)-4-((*Z*)-methoxymethylen)-2-cyclohexenone (7). Yield 63%,

yellowish oil. R_f=0.43 (hexane/ethyl acetate (2:1)). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46 (m, 2H), 7.35 (m, 3H), 6.91 (d, J=9.8 Hz, 1H), 6.62 (s, 1H), 5.79 (d, J=9.7 Hz, 1H), 5.44 (s, 1H), 4.26 (dd, J=3.9 and 11.2 Hz, 1H), 3.82 (s, 3H), 3.36 (m, 1H), 3.01 (d, J=16.4 Hz, 1H), 2.50 (dd, J=6.6 and 16.6 Hz, 1H), 1.95 (m, 3H), 1.46 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0 (C), 153.9 (CH), 145.0 (CH), 138.5 (C), 128.6 (CH), 128.1 (CH), 126.0 (CH), 123.4 (CH), 114.1(C), 101.1 (CH), 77.6 (CH), 67.0 (CH_2), 61.0 (CH_3), 37.9 (CH), 37.6 (CH_2), 29.2 (CH_2). HRMS calcd for $C_{18}H_{21}O_4$ [M+1]$^+$: 301.1444; found: 301.1443. Anal. calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.72.41; H, 6.67.

4.1.3. Experimental procedure for the synthesis of isochromenone 8. *Method A*: 0.5 mmol of diastereomeric mixture of cyclohexenones **5a** and **5b** was dissolved in 12 ml of 0.1 M solution of HCl in methanol. After stirring this mixture at room temperature for 2 h, solvents were removed under reduced pressure. Chromatographic purification (silica gel, hexane/ethyl acetate (1:1)) yields enantiopure isochromenone **8**, in 72 and 70% yields from cyclohexenones **5a** and **5b**, respectively.

Method B: To a solution of 0.5 mmol of the carbene complexes **1a** and **1b** in 25 ml of toluene at −45 °C, 170 mg (2.5 mmol) of 1-methoxy-3-trimethylsilyloxy-1,3-butadiene was added. After stirring for 60 h at that temperature, solvents were removed under reduced pressure. The residue was dissolved in 12 ml of 0.1 M solution of HCl in methanol. After stirring this mixture at room temperature for 2 h, solvents were removed under reduced pressure. Chromatographic purification (silica gel, hexane/ethyl acetate (1:1)) yields enantiopure isochromenone **8**, in 62 and 66% overall yields from carbenes **1a** and **1b**, respectively.

4.1.3.1. (4*S*,4a*R*)-3,4,4a,5-tetrahydro-4-hydroxyisochromen-6-one (8). White solid, mp=115–117 °C. R_f=0.27 (hexane/ethyl acetate (1:1)). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.02 (d, J=9.3 Hz, 1H), 6.83 (s, 1H), 5.80 (d, J=9.3 Hz, 1H), 4.25 (dd, J=10.5 and 4.2 Hz, 1H), 3.90 (m, 1H), 3.60 (t, J=10.5 Hz, 1H), 3.10 (br s, 1H), 2.90 (dd, J=15.4 and 5.2 Hz, 1H), 2.70 (m, 1H), 2.10 (t, J=14.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6 (C), 149.0 (CH), 145.1 (CH), 122.9 (CH), 110.8 (C), 69.1 (CH), 69.0 (CH_2), 40.1 (CH_2), 38.6 (CH). HRMS calcd for $C_9H_{10}O_3$: 166.0631; found: 166.0630. Anal. calcd for $C_9H_{10}O_3$: C, 65.05; H,6.07. Found: C, 64.90; H, 6.02. $[\alpha]_D^{20}$ +30.6 (*c* 0.627, CH_2Cl_2).

4.1.4. General procedure for the preparation of carbene complexes (10 and 12). To a solution of 1 mmol of tungsten carbene complexes **1** and **2** in 90 ml of toluene at −45 °C or −55 °C (see Scheme 4) 3.3 g (50 mmol) of cyclopentadiene **9** was added. After stirring at that temperature for 95 h solvents were removed under vacuum. The residues were analyzed by ^{1}H NMR spectroscopy and the major diastereoisomer was isolated by column chromatography (silica gel, hexane/ethyl acetate, 10:1) to give the enantiopure carbene complexes **10** and **12**.

4.1.4.1. Pentacarbonyl-[((1*S*,2*R*,3*R*,4*R*)-3-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)bicyclo[2.2.1]hept-5-ene-2-yl)-methoxymethylidene]tungsten(0) (10). Yield 80% (92% mixture of diastereoisomers), orange solid. R_f=0.25 (hexane/ethyl acetate (10:1)). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.31 (m, 1H), 5.69 (dd, J=2.8 and 2.6 Hz, 1H), 4.53 (s, 3H), 4.17 (dd, J=5.0 and 3.1 Hz, 1H), 4.11 (dd, J=7.8 and 6.2 Hz, 1H), 3.97 (m, 1H), 3.50 (s, 1H), 3.33 (dd, J=7.6 and 6.9 Hz, 1H), 1.90 (dq, J=5.1 and 1.5 Hz, 1H), 1.76 (d, J=8.8 Hz, 1H), 1.47(m, 1H), 1.42 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 333.9 (C), 202.3 (C), 197.3 (C), 139.0 (CH), 131.8 (CH), 109.2 (C), 78.5 (CH), 77.6 (CH), 70.3 (CH_3), 69.1 (CH_2), 50.5 (CH), 48.4 (CH), 46.9 (CH_2), 46.3 (CH), 26.8 (CH_3), 25.3 (CH_3). HRMS calcd for $C_{19}H_{22}O_8W$ [M$^+$]: 592.0560; found: 592.0557.

4.1.4.2. Pentacarbonyl-[((1*R*,2*S*,3*S*,4*S*)-3-((2*S*,4*S*)-2-phenyl-1,3-dioxan-4-yl)bicyclo[2.2.1]hept-5-en-2-yl)methoxymethylidene]tungsten(0) (12). Yield 73% (87% mixture of diastereoisomers), orange solid. R_f=0.35 (hexane/ethyl acetate (10:1)). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.5 (5H, m), 6.32 (1H, m), 5.76 (3H, m), 5.53 (1H, s), 4.54 (3H, s), 4.31 (2H, m), 3.97 (1H, m), 3.73 (1H, m), 3.58 (1H, s), 3.23 (1H, m), 2.03 (1H, m), 1.80 (2H, m), 1.50 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 334.1 (C), 202.3 (C), 197.4 (C), 139.2 (CH), 138.5 (C), 131.8 (CH), 128.6 (CH), 128.1 (CH), 125.8 (CH), 100.8 (CH), 79.0 (CH), 77.1 (CH), 70.3 (CH), 66.8 (CH_2), 50.3 (CH_3), 49.6 (CH), 47.3 (CH_2), 44.9 (CH), 30.4 (CH_2). HRMS calcd for $C_{21}H_{20}O_5WNa$ [M−3(CO)+Na]$^+$: 560.0749; found: 560.0746.

4.1.5. General procedure for the oxidation of carbene complexes 10 and 12. Carbene complexes **10** and **12** (0.5 mmol) (or mixture of isomers) were dissolved in 12 ml of a mixture of THF/water (5:1). To this solution 240 mg (2.5 mmol) of pyridine oxide was added and the mixture stirred at room temperature for 15 h. At this point, the mixture was extracted with ethyl acetate (3×10 ml) and the solvents removed under reduced pressure. Chromatographic purification (silica gel) of the residue yields enantiopure norbornenes **11** and **13** as colorless oils.

4.1.5.1. (1*S*,2*R*,3*R*,4*R*)-Methyl 3-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)bicyclo[2.2.1]hept-5-ene-2-carboxylate (11). Yield 91%, colorless oil. R_f=0.30 (hexane/ethyl acetate (5:1)). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.26 (dd, J=5.7 and 3.1 Hz, 1H), 6.02 (dd, J=5.7 and 2.8 Hz, 1H), 3.99 (m, 2H), 3.72 (m, 1H), 3.60 (s, 3H), 3.14 (s, 1H), 2.97 (s, 1H), 2.41 (dd, J=4.8 and 3.5 Hz, 1H), 1.85 (ddd, J=8.9, 4.8, and 1.7 Hz, 1H), 1.56 (d, J=8.8 Hz, 1H), 1.40 (s, 3H), 1.44 (dd, J=3.53 and 1.7 Hz, 1H), 1.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1 (C), 138.3 (CH), 134.1 (CH), 109.0 (C), 79.1 (CH), 68.6 (CH_2), 51.7 (CH_3), 47.4 (CH), 46.8 (CH), 45.9 (CH_2), 45.5 (CH), 44.5 (CH), 26.7 (CH_3), 25.8 (CH_3). HRMS calcd for $C_{14}H_{20}O_4$: 252.1356; found: 252.1364. Anal. calcd for $C_{14}H_{20}O_6$: C, 66.65; H, 7.99. Found: C, 66.64; H, 8.02. $[\alpha]_D^{20}$ −73.9 (*c* 0.33, CH_2Cl_2).

4.1.5.2. (1*R*,2*S*,3*S*,4*S*)-Methyl 3-((2*S*,4*S*)-2-phenyl-1,3-dioxan-4-yl)bicyclo[2.2.1]hept-5-ene-2-carboxylate (13). Yield 89%, colorless oil. R_f=0.55 (hexane/ethyl acetate, 2:1). ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.45 (m, 1H), 6.31 (dd, J=3.6 and 2.1 Hz, 1H), 6.06 (dd, J=3.6 and 1.7 Hz, 1H), 5.52 (s, 1H), 4.31 (dd, J=7.7 and 2.7 Hz, 1H), 3.96 (td, J=7.7 and 1.7 Hz, 1H), 3.74 (m, 2H), 3.66 (s, 3H), 3.17 (d, J=12.2 Hz, 2H), 2.65 (t, J=2.7 Hz, 1H), 1.99 (m,

2H), 1.65 (m, 1H), 1.45 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5 (C). 138.8 (CH), 134.1 (CH), 128.6 (CH), 128.1 (CH), 125.9 (CH), 101.0 (CH), 79.6 (CH), 67.0 (CH_2), 51.6 (CH_3), 48.7 (CH), 47.0 (CH), 46.5 (CH_2), 45.6 (CH), 43.2 (CH), 30.4 (CH_2). HRMS calcd for $C_{19}H_{22}O_4$: 314.1518; found: 314.1513. Anal. calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.30; H, 7.06. $[\alpha]_D^{20}$ +177.2 (*c* 0.32, CH_2Cl_2).

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