Group 6 Heteroatom- and Non-Heteroatom-Stabilized Carbene Complexes. β,β'- and α,β,β'-Annulation Reactions of Cyclic Enamines

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Abstract: Cyclization reactions of group 6 Fischer carbene complexes with cyclopentanone and cyclohexanone enamines are described. Enamine **3a** undergoes thermal α,β,β'-annulation with alkenylcarbene complexes **1** and **2** (THF, 60 °C), affording semibullvalenes **5**. The metalate intermediates **6**, resulting from β,β'-annulation of the enamines **3a** and **4a**, were quantitatively formed by running the reaction in hexane at room temperature. Acid-promoted demetalation of **6** afforded *endo*-2-bicyclo[3.2.1]octen-8-ones **7** and *endo/exo*-2-bicyclo[3.3.1]nonen-9-ones **8** (*endo/exo* = 5:1). Using (*S*)-methoxymethylpyrrolidine-derived enamines **3b** and **4b,c** allowed highly enantioenriched cycloadducts *endo*-(+)-**7** as well as *endo*-(−)-**8** and *exo*-(−)-**8** to be accessed. The non-heteroatom-stabilized carbene complex **10** was formed from complex **6** by Me$_3$SiOTf-promoted elimination of the methoxy group, characterized by ^{13}C NMR, and transformed into the organic compounds **7**, **7**-*d*, and **11** as well as into bicyclo[3.2.1]octan-2,8-diones **14** and cycloheptanones **15**. On the basis of this sequence, enantioenriched cycloheptanones (+)-**15** were efficiently prepared in one pot from carbene complexes **2** and enamine **3b** (51−55% yield, 91−96% ee). Extension of this work to simple Fischer carbene complexes **16** allowed an appropriate way to generate the nonstabilized pentacarbonyl[(phenyl(alkyl)carbene]tungsten complex **17** to be designed, for which the thermal and chemical behavior leading to compounds **18**−**21** is described.

Introduction

The synthesis of polyclyclic molecules following short and stereoselective routes constitutes one of the main challenges in synthetic organic chemistry. In particular, much work has been devoted to the design of efficient routes to [3.2.1] and [3.3.1] bicyclic molecular skeletons.[1] A straightforward entry into these frameworks can be envisaged by reaction of appropriate C3-synthons with cyclic ketones via α,α'-annulation,[2] or with their enamine derivatives via β,β'-annulation.[3] For instance, a number of two-step processes based on α-alkenylation or α-alkynylation of cyclic ketones followed by induced ring closure have been disclosed.[2] In addition, apart from the elegant [3+3]-cyclization

of nitroallylic esters and enamines discovered by Seebach,[3a] no highly enantioselective approaches have been reported.[2f,3b]

Despite the fact that transition-metal complexes have played a paramount role in the area of carbocyclization reactions,[4] [3+3]-carbocyclization approaches mediated or assisted by transition metals remain almost unexplored.[5,6]

On the other hand, the great potential of Fischer carbene complexes in carbocyclization reactions has been demonstrated in the last few years.[7] In particular, alkenyl(alkoxy)carbene complexes have become valuable C3-synthons in a number of carbo- and heterocyclization reactions.[8] For instance, we found that tungsten alkenylcarbene complexes readily undergo [3+2]-

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(2) For selenium-induced ring closure, see: (a) Nicolaou, K. C.; Pfefferkorn, J. A.; Cao, G.-Q.; Kim, S.; Kessabi, J. *Org. Lett.* **1999**, *1*, 807. For Hg^{2+}-mediated ring closure, see: (b) Frontier, A. L.; Raghavan, S.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1997**, *119*, 6686. (c) Huang, H.; Forsyth, C. J. *J. Org. Chem.* **1995**, *60*, 5746. For Pd(II)-mediated ring closure, see: (d) Kende, A. S.; Roth, B.; Sanfilippo, P. J.; Blacklock, T. J. *J. Am. Chem. Soc.* **1982**, *104*, 1784 and 5808. For free-radical ring closure, see: (e) Cole, B. M.; Han, L.; Snider, B. B. *J. Org. Chem.* **1996**, *61*, 7832. For enantioselective free-radical ring closure, see: (f) García-Ruano, J. L.; Rumbero, A. *Tetrahedron: Asymmetry* **1999**, *10*, 4427.

(3) (a) Seebach, D.; Missbach, M.; Calderari, G.; Eberle, M. *J. Am. Chem. Soc.* **1990**, *112*, 7625. (b) Butkus, E.; Stoncius, A. *Synlett* **1999**, 234. (c) Byeon, C.-H.; Hart, D. J.; Lai, C.-S.; Unch, J. *Synlett* **2000**, 119. (d) Buono, F.; Tenaglia, A. *J. Org. Chem.* **2000**, *65*, 3869.

(4) (a) Frühauf, H.-W. *Chem. Rev.* **1997**, *97*, 523. (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49.

(5) For an isolated example involving Fischer alkenyl carbene complexes, see: Barluenga, J.; Tomás, M.; Rubio, E.; López-Pelegrín, J. A.; García-Granda, S.; Pérez-Priede, M. *J. Am. Chem. Soc.* **1999**, *121*, 3065.

(6) For a two-step [3+3]-annelation, see: Ward, D. E.; Gai, Y.; Kaller, B. F. *J. Org. Chem.* **1995**, *60*, 7830.

(7) Recent reviews: (a) Wulff, W. D. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: New York, 1995; Vol. 12, p 469. (b) Herndon, J. W. *Tetrahedron* **2000**, *56*, 1257. (c) Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271. (d) Barluenga, J.; Fañanás, F. J. *Tetrahedron* **2000**, *56*, 4597. (e) Sierra, M. A. *Chem. Rev.* **2000**, *100*, 3591. (f) de Meijere, A.; Shirmer, H.; Duetsch, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3964.

(8) For recent work in this field, see for instance: (a) Barluenga, J.; Martínez S.; Suárez-Sobrino, A.-L.; Tomás, M. *J. Am. Chem. Soc.* **2001**, *123*, 11113. (b) Kagoshiima, H.; Okamura, T.; Akiyama, T. *J. Am. Chem. Soc.* **2001**, *123*, 7182. (c) Barluenga, J.; Alonso, J.; Rodríguez, F.; Fañanás, F.-J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2459.
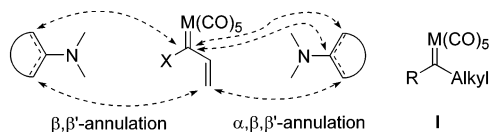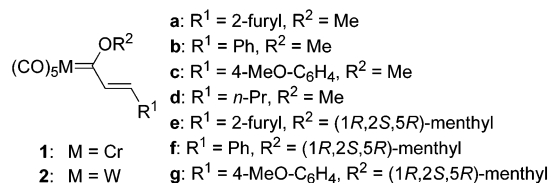
Figure 1.

Figure 2.

cycoaddition toward enamines derived from acyclic ketones and aldehydes to produce substituted 2-cyclopentenones and cyclopentanones, respectively, in a diastereoselective and enantioselective way.[9]
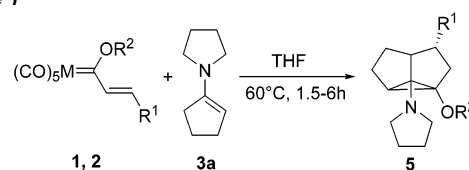
Herein, we present our results on the *β,β′*-annulation ([3+3]-cyclization) and *α,β,β′*-annulation reactions of cyclopentanone and cyclohexanone enamines with Fischer alkenylcarbene complexes (Figure 1).[10] On the basis of such work, a preliminary study on the potential of non-heteroatom-stabilized alkylcarbene complexes of type **I** is first reported in the second part of this paper (Figure 1).

The present study has been undertaken using (i) pentacarbonyl[alkenyl(alkoxy)]carbene complexes of chromium(0) (**1**) and tungsten(0) (**2**), (ii) cyclopentanone enamines derived from pyrrolidine (**3a**) and (*S*)-2-methoxymethylpyrrolidine (**3b**), and (iii) cyclohexanone enamines derived from pyrrolidine (**4a**), (*S*)-2-methoxymethylpyrrolidine (**4b**), and (*S*)-2-(1-methoxymethylethyl)pyrrolidine (**4c**) (Figure 2).

Results and Discussion

[3+3]-Cyclization of Carbene Complexes 1 and 2 and Enamines 3 and 4. First, 1-pyrrolidinylcyclopentene **3a** was reacted with chromium or tungsten alkenylcarbene complexes **1a−c** or **2a−c** in THF at 60 °C for 1.5 h to furnish substituted semibullvalenes **5a−c** in nearly 90% yield after column chromatography purification (Scheme 1).[11] This one-step polycyclization reaction gives ready access to the complex structure **5** and entails the formation of three carbon−carbon bonds and five stereogenic centers with complete control of selectivity[12] in a process that has no precedents in the chemistry of metal
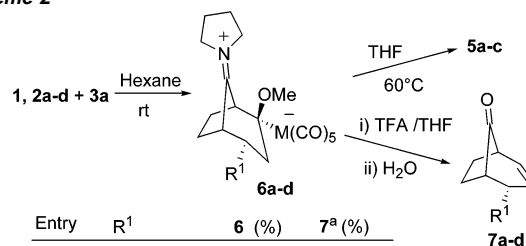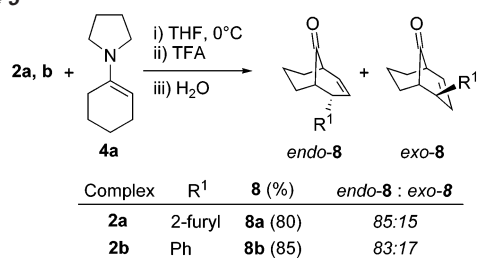
(9) Barluenga, J.; Tomás, M.; Ballesteros, A.; Santamaría, J.; Brillet, C.; García-Granda, S.; Piñera-Nicolás, A.; Vázquez, J. T. *J. Am. Chem. Soc.* **1999**, *121*, 4516.
(10) Preliminary communication: Barluenga, J.; Ballesteros, A.; Santamaría, J.; Bernardo de la Rua, R.; Rubio, E.; Tomás, M. *J. Am. Chem. Soc.* **2000**, *122*, 12874.
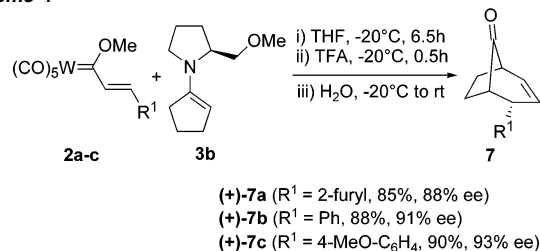(11) In general, both chromium (**1**) and tungsten (**2**) carbene complexes have been found to work equally well. The preparation of (+)-**7**, (±)-**8**, and enantiorenriched **8** has been undertaken using tungsten carbenes **2**.
(12) The connectivity and relative stereochemistry of compounds **5** were clearly elucidated by HMQC, HMBC, and NOESY NMR experiments.

Scheme 1

Entry	R[1]	R[2]	5 (%)
a	2-furyl	Me	**5a** (85)
b	Ph	Me	**5b** (88)
c	4-MeO-C₆H₄	Me	**5c** (a)
e	2-furyl	(1*R*,2*S*,5*R*)-menthyl	**5e** (70)
f	Ph	(1*R*,2*S*,5*R*)-menthyl	**5f** (73)
g	4-MeO-C₆H₄	(1*R*,2*S*,5*R*)-menthyl	**5g** (a)

[a] Attempted purification led to decomposition.

Scheme 2

Entry	R[1]	6 (%)	7[a] (%)
a	2-furyl	**6a** (95)	**7a** (87)
b	Ph	**6b** (94)	**7b** (89)
c	4-MeO-C₆H₄	**6c** (97)	**7c** (91)
d	*n*-Pr	**6d** (b)	**7d** (60)[c]

[a] Yield from carbene complexes **1,2**.
[b] Not determined, but **6d** was characterized and transformed into **7d**.
[c] 4:1 endo/exo mixture

carbene complexes. Additionally, when the chiral, nonracemic chromium carbene complexes **1e−g**, derived from (−)-menthol, and **3a** were heated in THF at 60 °C for 6 h the cycloadducts **5e−g** were formed as a single diastereoisomer and isolated in fairly good yields.

At this point we decided to run further experiments that might shed light onto this complex process. First, we replaced the solvent with a much less polar solvent such as hexane. Interestingly, conducting the reaction of complexes **1a−d** and **2a−d** and enamine **3a** in hexane at room temperature resulted in quantitative precipitation of the metal complexes **6a−d** (Scheme 2). We observed that these metalate complexes **6** are actually the intermediate species for the formation of semibullvalenes **5** from carbene complexes **1** and **2** since **6a−c** could be smoothly transformed into **5a−c** by heating in THF at 60 °C for 1.5 h. Moreover, it was important from a synthetic point of view to find that, alternatively, compounds **6** can be transformed very efficiently into bicyclo[3.2.1]oct-2-en-8-ones **7** by treatment with TFA/THF at 0 °C followed by warming in the presence of water (Scheme 2). This process takes place with high yield in most cases (60−91% overall yield from the starting carbene complexes), the *endo* stereoisomer being the sole isomer detected.

The whole transformation can also be effected in a one-pot fashion without isolation of the corresponding metalate complex **6**. This is exemplified in Scheme 3 for the preparation of bicyclo[3.3.1]non-2-en-9-ones **8**. Thus, tungsten carbene complexes **2a,b** were consecutively reacted with cylohexanone enamine **4a** in THF at 0 °C, treated with TFA at the same temperature, and allowed to reach room temperature in the

Scheme 3

Complex	R^1	8 (%)	*endo*-8 : *exo*-8
2a	2-furyl	**8a** (80)	85:15
2b	Ph	**8b** (85)	83:17

Scheme 4

(+)-**7a** (R^1 = 2-furyl, 85%, 88% ee)
(+)-**7b** (R^1 = Ph, 88%, 91% ee)
(+)-**7c** (R^1 = 4-MeO-C$_6$H$_4$, 90%, 93% ee)

Scheme 5

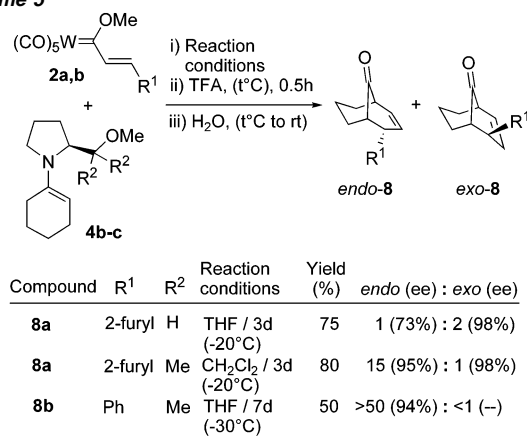| Compound	R^1	R^2	Reaction conditions	Yield (%)	*endo* (ee) : *exo* (ee)
8a	2-furyl	H	THF / 3d (-20°C)	75	1 (73%) : 2 (98%)
8a	2-furyl	Me	CH$_2$Cl$_2$ / 3d (-20°C)	80	15 (95%) : 1 (98%)
8b	Ph	Me	THF / 7d (-30°C)	50	>50 (94%) : <1 (--)

presence of water to furnish a ca. 5:1 mixture of *endo*-**8** and *exo*-**8** cycloadducts (80−85% yield) which were separated by routine column chromatography.

Once the diastereoselective [3+3]-cyclization leading to racemic cycloadducts was effiently delineated, we focused on the asymmetric synthesis of bicyclo[3.2.1]octenone and bicyclo-[3.3.1]nonenone derivatives **7** and **8**. Although the first attempts using menthol-derived carbene complexes **1e−g** and **2e−g** were unsuccessful, it was a delight to find that this goal could be accomplished very efficiently by using chiral cyclopentanone enamines derived from readily available (*S*)-2-methoxymethylpyrrolidine (Scheme 4). Thus, stirring a solution of tungsten carbene complexes **2a−c** and cyclopentanone enamine **3b** (THF, −20 °C, 6.5 h) followed by TFA quenching and warming with water resulted in the diastereoselective formation of the enantiomerically enriched *endo*-cycloadducts **7**. Column chromatography purification gave pure **7** in 85−90% yield and high enantiomeric excess (88−93% ee) as determined by chiral HPLC (Chiracel OB-H and OJ columns). The absolute configuration of **7c** was determined by X-ray analysis (vide infra).

Enantiopure cyclohexanone enamines **4b,c** were also tested toward tungsten complexes **2a,b** (Scheme 5). We found that these enamines are fairly less reactive than the cyclopentanone analogues and their cycloaddition reaction to **8** required longer reaction times. On the other hand, the *endo/exo* and *face*

Scheme 6
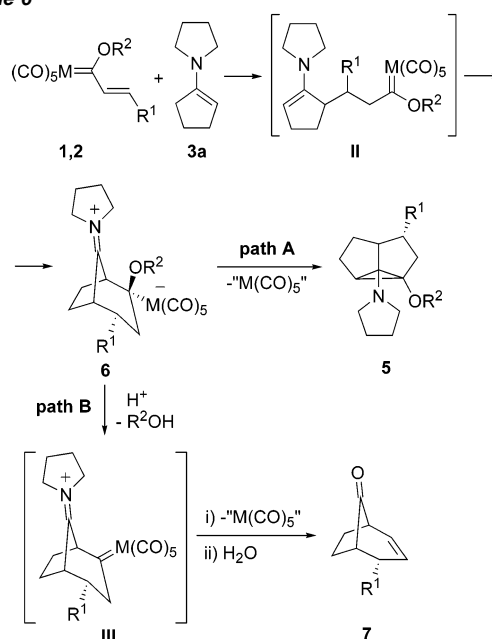
selectivity of the process was highly dependent on the reaction conditions and even on the substituent R^1 of the carbene complex. Thus, the reaction of **2a** (R^1 = 2-furyl) and methoxymethylpyrrolidine enamine **4b** (THF, −20 °C, 72 h) yielded the cycloadduct **8a** (75% yield) as a 1:2 mixture of *endo/exo* isomers. *Endo* and *exo* isomers could be separated by column chromatography, affording pure *endo*-(−)-**8a** (73% ee) and *exo*-(−)-**8a** (98% ee). On the contrary, the corresponding *endo* isomer was efficiently formed with very high face selectivity if the reaction was run in dichloromethane as solvent and the more sterically demanding enamine **4c** was used. Thus, the reaction between carbene complex **2a** and enamine **4c** (CH$_2$Cl$_2$, −20 °C, 72 h) afforded *endo*-(−)-**8a** in good yield and with high selectivity (80%, *endo*-(−)-**8a**:*exo*-(−)-**8a** = 15:1, 95% ee for *endo*-(−)-**8a**).[13] When this reaction was carried out at −50 °C, both the *endo*-(−)-**8a**:*exo*-(−)-**8a** ratio and the ee of *endo*-(−)-**8a** increased to >20:1 and 98%, respectively, though the chemical yield dropped to 52%. The formation of the cycloadduct **8b** (R^1 = Ph) could be achieved with excellent stereoselectivity (*endo*-(−)-**8b**:*exo*-**8b** > 50:1, 94% ee) and in moderate chemical yield (50%) by performing the reaction of carbene **2b** and enamine **4c** in THF (−30 °C, 7 days). All the enantiomeric excesses for compounds **8** were determined by chiral HPLC (Chiracel OJ).

Proposed Mechanism. We think that the formation of semibullvalene derivatives **5** and the [3+3]-cycloadducts **7** from carbene complexes **1** and **2** and enamines **3** can be rationalized as depicted in Scheme 6. First, 1,4-addition of the C$_\beta$-enamine to the electrophilic alkene carbene complex would produce the Michael adduct **II**.[14] The conversion of this intermediate **II** into the final semibullvalene structure **5** implies simply the intramolecular cyclopropanation of an electron-rich carbon−carbon double bond, specifically the C$_\alpha$–C$_\beta$ double bond of the newly formed enamine, by a Fischer carbene complex. In this particular sense, the isolation of the zwitterionic species **6** does represent an unprecedented feature for supporting the accepted polar
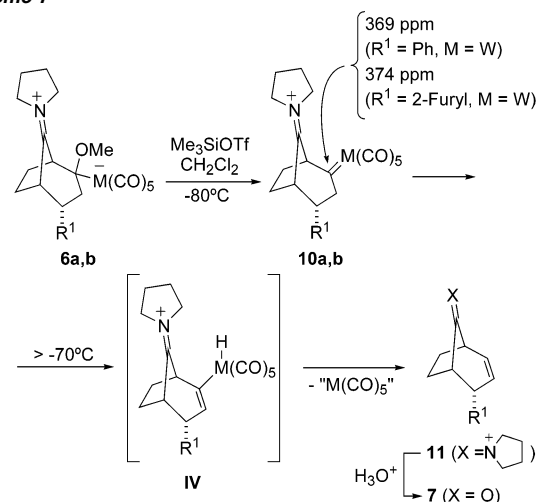
(13) The replacement of enamine **4c** with **4b** led to poorer selectivity toward *endo*-**8a** (*endo*:*exo* = 5:1, 83% ee).

pathway for the cyclopropanation reaction of electron-rich alkenes, such as enamines, by Fischer carbene complexes (path A).[15] Moreover, the *endo* orientation of the $M(CO)_5$ fragment precludes the cyclopropanation reaction to involve the participation of a metallacyclobutane species, but rather backside attack of the carbanion-type metal-bonded carbon to the iminium function is thought to occur.[16] Second, the formation of the cycloadducts **7** deserves particular attention (path B). Thus, in agreement with previous observations,[17] one would suggest that the metalate complex **6** might suffer acid-induced elimination of methanol to form an elusive non-heteroatom-stabilized carbene species, **III**, which would then undergo β-hydrogen elimination and reductive metal elimination to yield **7** after hydrolysis of the imonium function.
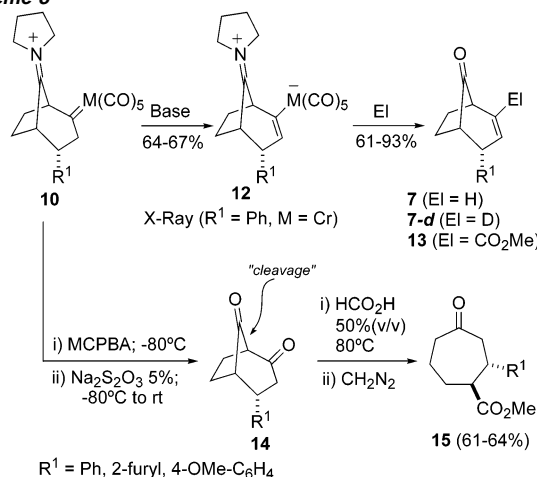
Non-Heteroatom-Stabilized Tungsten Carbene Complexes. Although group 6 non-heteroatom-stabilized carbene complexes lacking α-hydrogen atoms (such as phenyl and diphenylcarbene derivatives) are well-known organometallic reagents,[18] the chemistry of the alkyl analogues is extremely limited due to their high instability.[19] In an elegant study,[19a] Casey et al. reported some years ago that pentacarbonyl[phenyl-(methyl)carbene]tungsten(0), which was generated from the stabilized phenyl(methoxy)carbene complex by successive treatment with MeLi and HCl, decomposed whithin 30 min at −78 °C, giving rise to a mixture of styrene and 1-methyl-1,2-diphenylcyclopropanes. We now provide some evidence of this type of complex and apply it to the selective ring opening of the 8-bicyclo[3.2.1]octanone skeleton **7** to racemic and enantioenriched cycloheptanones.

Racemic complexes **6a,b** were treated at −80 °C with trimethylsilyl triflate in dichloromethane to generate, after 30 min, the nonstabilized carbene complexes **10a,b**,[20] for which the significant carbene resonates at 369 (**10a**, R^1 = Ph, M = W) and 374 (**10b**, R^1 = 2-furyl, M = W) ppm in the ^{13}C NMR spectrum (Scheme 7). These complexes were found to be fairly stable below −80 °C, but they quantitatively decompose above

(14) Evidence for the formation of this intermediate comes from the isolation of the adduct **9** in the reaction of pentacarbonyl[2-methylpropenylidene-(methoxy)]tungsten complex and enamine **3a**. The initially formed carbene complex undergoes metal elimination, affording the enol ether **9** when subjected to SiO_2 treatment.

(15) Casey, C. P.; Cesa, M. C. *Organometallics* **1982**, *1*, 87.
(16) See: Brookhart, M.; Liu, Y.; Goldman, E. W.; Timmers, D. A.; Williams, G. D. *J. Am. Chem. Soc.* **1991**, *113*, 927. In our case, despite the fact that the *endo* stereochemical orientation of the anion metal center of **6** is exclusively observed both in the solid state and in THF-d_8 solution, an *endo−exo* equilibration cannot be definitively ruled out.
(17) (a) Casey, C. P.; Brunsvold, W. R. *Inorg. Chem.* **1977**, *16*, 391. (b) Rudler, H.; Audouin, M.; Parlier, A.; Martin-Vaca, B.; Goumont, R.; Durand-Réville, T.; Vaissermann, J. *J. Am. Chem. Soc.* **1996**, *118*, 12045.
(18) (a) Casey, C. P.; Burkhardt, T. J. *J. Am. Chem. Soc.* **1973**, *95*, 5833. (b) Casey, C. P.; Polichnowski, S. M.; Shusterman, A. J.; Jones, C. R. *J. Am. Chem. Soc.* **1979**, *101*, 7282. (c) Fischer, H.; Mauz, E.; Jaeger, M.; Fisher, R. *J. Organomet. Chem.* **1992**, *427*, 63. (d) Fischer, H.; Hofmann, J. *Chem. Ber.* **1991**, *124*, 981. (e) Fischer, H.; Zeuner, S.; Ackermann, K. *J. Chem. Soc., Chem. Commun.* **1984**, 684. (f) Pfeiffer, J.; Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2828. (g) Pfeiffer, J.; Nieger, M.; Dötz, K. H. *Eur. J. Org. Chem.* **1998**, *1011*, 1. (h) The catalytic cyclopropanation of alkenes via (2-furyl)carbene complexes of group 6 has been reported very recently; see: Miki, K.; Nishino, F.; Ohe, K.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 5260.
(19) (a) Casey, C. P.; Albin, L. D.; Burkhardt, T. J. *J. Am. Chem. Soc.* **1977**, *99*, 2533. (b) For $M(SnPh_3)(CO)_2(=CMePh)(\eta$-$C_5H_5)$, (M = Mo, W), see: Winter, M. J.; Woodward, S. *J. Chem. Soc., Chem. Commun.* **1989**, 457.
(20) We found that dry acids, e.g., TFA and HBF_4, are also effective for the formation of **10**.
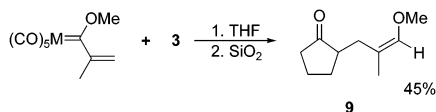
Scheme 7

Scheme 8

−70 °C to the imonium salt **11**, via carbon-to-metal hydrogen shift to species **IV** and metal elimination. Compounds **11** were not isolated but hydrolyzed to ketones **7**.

Because of the high electron-acceptor nature of the $(CO)_5M$ fragment,[21] the C_α–H deprotonation of **10** occurs readily with different organic bases (pyridine, triethylamine, etc.) (Scheme 8). Thus, the reaction of **6** with Me_3SiOTf to generate **10** as above, followed by addition of Et_3N (2 equiv, −80 °C), gave rise to the metalate **12**, which in turn underwent efficient protonation (H_2O), deuteration (D_2O), or methoxycarbonylation (I_2/MeOH)[22] to afford, after imonium hydrolysis, **7**, **7-d**, and **13**, respectively. Surprisingly, the metal carbene complex **10** does not cyclopropanate the pyrrolidine enamine **3a**, but low-temperature deprotonation (CH_2Cl_2, −80 °C) to the imonium metalate complex **12** again takes place (Scheme 8).[23] Moreover, the carbene functionality of **10** could be oxidized to the corresponding carbonyl group. This was accomplished ef-

(21) For alkoxycarbene complexes, see: (a) Bernasconi, C. F.; Leyes, A. E.; Ragains, M. L.; Shi, Y.; Wang, H.; Wulff, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 8632. (b) Bernasconi, C. F.; Sun, W. *J. Am. Chem. Soc.* **2002**, *124*, 2299.
(22) For the methoxycarbonylation of tungsten(0) methoxymetalated complexes, see: Fuchibe, K.; Iwasawa, N. *Tetrahedron* **2000**, *56*, 4907.
(23) Alkylidene complexes of tungsten(0) stabilized as pyridinium ylides are able to cyclopropanate electron-rich alkenes. See: (a) Rudler, H.; Durand-Réville, T. *J. Organomet. Chem.* **2001**, *617−618*, 571. (b) Reference 17b. (c) Martín-Vaca, B.; Durand-Réville, T.; Audouin, M.; Rudler, H. *Synthesis* **1998**, 1534. (d) Martín-Vaca, B.; Rudler, H. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3119.

Scheme 9
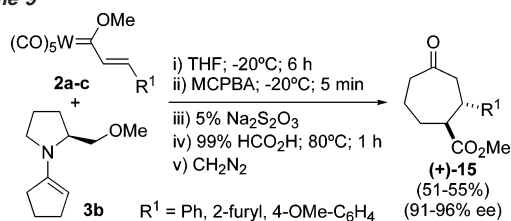
ficiently by low-temperature addition of MCPBA to the complex **10**, generated as above, followed by warming to room temperature in the presence of 5% $Na_2S_2O_3$ to furnish the diketones **14**. Those compounds were not chromatographed, but we became highly interested in the transformation of this bicyclic framework **14** into the cycloheptane ring.[24] Therefore, we focused on the retro-Claisen-type reaction of the 1,3-diketones **14** and found that their treatment with aqueous methanoic acid (50% v/v) at 80 °C followed by esterification with CH_2N_2 resulted in the formation of racemic cycloheptanones **15** in acceptable yields (61−64% from **6**) and with complete regioselectivity by cleavage of the C_1–C_8O bond.

This procedure could be improved when applied to the enantioenriched systems in the sense that the whole reaction sequence was shortened and carried out in a one-pot fashion from the starting carbene complexes **2** (Scheme 9). Thus, tungsten complexes **2a**−**c** were treated with chiral, nonracemic (R = CH_2OMe) pyrrolidine enamine **3b** in THF at −20 °C for 6 h. The resulting solution was stirred at the same temperature with MCPBA for 5 min followed by addition of 5% $Na_2S_2O_3$ and stirring at room temperature for 2 min.[25] Methanoic acid was then added and the mixture heated at 80 °C for 1 h, extracted with Et_2O, and treated with CH_2N_2. The reaction crude product was purified by column chromatography to provide substituted 4-methoxycarbonylcycloheptanones **15** in good overall yields (51−55% yield from **2**) and with very high enantioselectivity (91−96% ee) determined by chiral HPLC (Chiracel OB-H).[26]

Taking advantage of the methodology depicted, preliminary studies on simple carbene complexes, for instance, pentacarbonyl[phenyl(methoxy)carbene]tungsten complex **16**, were done (Scheme 10). Thus, the treatment of **16** with alkyllithiums RCH_2-Li (R = H, n-Pr) at 0 °C in THF followed by cooling to −80 °C and addition of Me_3SiOTf resulted presumably in the generation of carbene complexes **17**. This species was not characterized but was allowed (i) to reach room temperature to furnish alkenes **18** (61−67% yield, E:Z = 1:1), (ii) to react with pyridine oxide at −80 °C to afford phenones **19** (40−45% yield), (iii) to react with MeOH/Et_3N/I_2 at −80 °C to yield methyl 2-phenylalkenoates **20** (70−74% yield, E:Z = 1:5), and (iv) to reach room temperature in the presence of aqueous 1 M NaOH/Et_4NBr to give the stable tetraethylammonium alkenylmetalate **21** (R = H, 32% yield, mp 95−98 °C dec), which was fully characterized.

(24) The attempts were at the beginning based on the Baeyer−Villiger oxidation/lactone hydrolysis sequence of the bicyclic ketones **7**, but regioisomeric mixtures of hydroxycycloheptenecarboxylic acids, resulting from the insertion of oxygen into both C_1−C_8O and C_5−C_8O bonds, were systematically obtained using various procedures and reaction conditions.
(25) It should be noted that MCPBA plays a 2-fold role: (i) acid-catalyzed generation of the nonstabilized carbene complex and (ii) oxidation of the carbene function as it is formed, which allows the carbene to be generated at −20 °C.
(26) The corresponding cyclopentanone ring, arising from cleavage of the C_1–C_2O bond, was formed in negligible amounts (<5%).
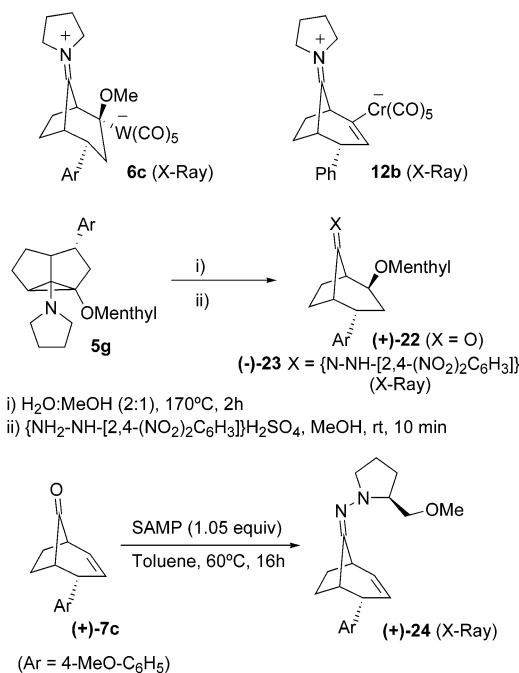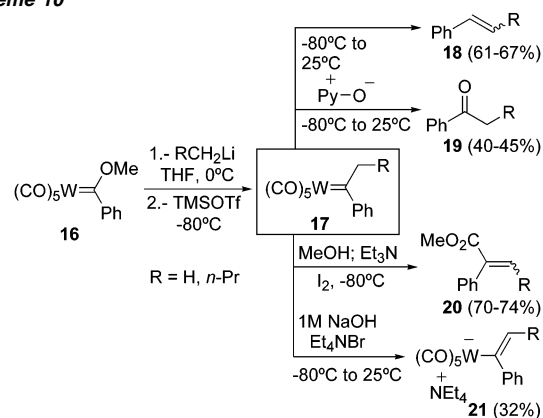
Figure 3.

Scheme 10

Structural Characterization. The structural analysis of all the compounds is based on spectroscopic data (^{1}H and ^{13}C NMR spectra, IR spectra, and MS spectra) and elemental analyses (see the Experimental Section). In addition, the unambiguous characterization by X-ray analysis has been done for compounds **6c**, **12b**, **23**, and **24** (Figure 3).

Thus, metalate complex **6c** was crystallized by diffusion of hexane into a tetrahydrofuran solution, and **12b** was crystallized in dichloromethane at −20 °C. Compound **23** was synthesized by thermal ring opening of **5g** (H_2O/MeOH (2:1), 170 °C, 2 h) to the ketone **22** followed by derivatization with 2,4-dinitrophenylhydrazine to hydrazone (−)-**23**, which was crystallized from methanol. To ascertain its absolute configuration, ketone (+)-**7c** was reacted with (S)-(1-amino-2-methoxymethyl)-pyrrolidine (SAMP) and the resulting hydrazone **24** crystallized from pentane at −20 °C.

Conclusions

Fischer alkenylcarbene complexes of chromium and tungsten are very useful C3-synthons for the [3+3]-cycloaddition reaction toward cyclopentanone and cyclohexanone enamines, allowing a simple, one-step protocol for the diastereo- and enantioselec-

tive synthesis of functionalized bicyclo[3.2.1]octane and bicyclo-[3.3.1]nonane skeletons to be designed.[27] On the other hand, the novel α,β,β′-anulation reaction of cyclopentanone enamines and alkenylcarbene complexes described here represents the shortest thermal access to tricyclo[3.3.0.0²,⁸]octanes (semibullvalene derivatives),[28] systems known to be precursors of molecules of interest, e.g., triquinanes.[29] The isolation of key intermediates has permitted, not only the confirmation of the polar pathway for the cyclopropanation of enamines by Fischer carbene complexes, but more importantly the realization that nonstabilized alkylcarbene complexes are not elusive species, but that they can be generated and subjected to various transformations. Specifically, we have shown that non-heteroatom-stabilized pentacarbonyl(bicyclo[3.2.1]octan-2-ylidene)-tungsten(0) complexes **10** are readily accessible, via methoxy displacement from the corresponding methoxymetalate complexes **6**. The potential of this type of carbene makes possible the one-pot synthesis of enantioenriched 3,4-disubstituted cycloheptanones **15** from Fischer carbene complexes and cyclopentanone enamines. The strategy shown here is also applicable to simple non-heteroatom-stabilized alkylcarbene complexes, as illustrated in the generation of **17** from **16** and its transformations into compounds **18−21**. In conclusion, we think that the results shown here may open the door to the synthetic use of alkyl nonstabilized group 6 carbene complexes.[30]

Experimental Section[31]

Reaction of Carbene Complex 1 or 2 with Cyclopentanone Pyrrolidine Enamine 3a. Synthesis of Semibullvalenes 5. To a solution of carbene complex **1** or **2** (1 mmol) in THF (50 mL) was added at room temperature 178 mg (1.3 mmol) of cyclopentanone pyrrolidine enamine **3a**. The reaction mixture was heated at 60 °C for 1.5 h (**5a−c**) or 6 h (**5e−g**). Removal of solvent at reduced pressure and column chromatography (hexanes−ethyl acetate−triethylamine, 20:1:1) afforded the semibullvalenes **5** as pale yellow oils.

Data for Compound 5a. From pentacarbonyl[(*E*)-2-(2-furyl)ethyl-(methoxy)carbene]tungsten (**2a**). Yield: 85%. ¹H NMR (CDCl₃, 400 MHz): δ 1.1 (dd, 1H, *J* = 7.1, 12.5 Hz), 1.4 (m, 1H), 1.55 (m, 1H), 1.7 (d, 1H, *J* = 6.5 Hz), 1.8 (m, 4H), 2.05 (m, 1H), 2.1 (dd, 1H, *J* = 10.8, 13.0 Hz), 2.4 (dd, 1H, *J* = 10.3, 13.0 Hz), 2.8 (m, 4H), 3.0 (t, 1H, *J* = 7.1 Hz), 3.35 (s, 3H), 3.4 (m, 1H), 6.0 (m, 1H), 6.25 (m, 1H), 7.3 (m, 1H). ¹³C NMR (CDCl₃, 100 MHz): δ 23.9 (2 CH₂), 25.0 (CH₂), 30.7 (CH₂), 32.8 (CH₂), 36.8 (CH), 42.4 (CH), 45.2 (CH), 51.2 (2 CH₂), 56.4 (CH₃), 68.1 (C), 75.6 (C), 105.3 (CH), 109.6 (CH), 140.9 (CH), 156.0 (C). HRMS (*m/z*): calcd for C₁₇H₂₃NO₂ 273.1729, found 273.1718. Anal. Calcd for C₁₇H₂₃NO₂: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.77; H, 8.58; N, 5.09.

Data for Compound 5e. From pentacarbonyl[(*E*)-2-(2-furyl)ethyl-[(1*R*,2*S*,5*R*)-menthyloxy]carbene]tungsten (**2e**). Yield: 70%. [α]²⁰_D =

(27) The bicyclo[3.3.1]nonan-2-one skeleton is the central part of a number of terpenes. For instance, see refs 2a−d.

(28) (a) For the arene−alkene photocyclization, see: Wender, P. A.; Siggel, L.; Nuss, J. M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 5, pp 645−673. (b) For the oxadi-π-methane rearrangement of bicyclo[2.2.2]octenones to semibullvalenes, see: Lee, T.-H.; Rao, P. D.; Liao, C.-C. *Chem. Commun.* **1999**, 801.

(29) Singh, V. *Acc. Chem. Res.* **1999**, *32*, 324.

(30) Rudler et al. have reported that the reduction of alkoxycarbene complexes with dihydropyridine generates a different type of nonstabilized group 6 carbene complexes, which are stabilized and characterized as pyridinium ylides. See refs 23a−d. Specific nonstabilized carbene complexes of tungsten(0) have been reported to be formed via nucleophilic *endo*-attack of the carbonyl oxygen/imine nitrogen of the *o*-alkynylphenyl ketone/*N*-(*o*-alkynylphenyl)imine derivatives; see, respectively: (a) Iwasawa, N.; Shido, M.; Kusama, H. *J. Am. Chem. Soc.* **2001**, *123*, 5814. (b) Kusama, H.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2002**, *124*, 11592.

(31) General information, experimental procedures, and spectral data for compounds not described here are provided in the Supporting Information.

−0.184 (*c* 0.43, CH₂Cl₂). ¹H NMR (CDCl₃, 300 MHz): δ 0.8 (d, 3H, *J* = 7.0 Hz), 0.85 (d, 3H, *J* = 7.0 Hz), 0.95 (d, 3H, *J* = 6.5 Hz), 0.7−1.0 (m, 2H), 1.1 (dd, 1H, *J* = 6.9, 12.1), 1.3−1.7 (m, 8H), 1.85 (m, 4H), 2.0−2.3 (m, 4H), 2.45 (dd, 1H, *J* = 10.0, 12.6 Hz), 2.8 (m, 4H), 3.05 (t, 1H, *J* = 7.1 Hz), 3.45 (m, 2H), 6.0 (m, 1H), 6.25 (m, 1H), 7.3 (m, 1H). ¹³C NMR (CDCl₃, 75 MHz): δ 16.0 (CH₃), 20.8 (CH₃), 22.5 (CH₃), 23.2 (CH₂), 24.0 (2 CH₂) 24.9 (CH₂), 25.3 (CH), 31.4 (CH), 31.5 (CH₂), 32.3 (CH₂), 34.4 (CH₂), 39.7 (CH), 40.6 (CH₂), 42.7 (CH), 46.2 (CH), 47.2 (CH), 51.0 (2 CH₂), 65.2 (C), 71.0 (C), 76.7 (CH), 105.3 (CH), 109.7 (CH), 140.8 (CH), 156.2 (C). HRMS (*m/z*): calcd for C₂₆H₃₉NO₂ 397.2981, found 397.2968; Anal. Calcd for C₂₆H₃₉NO₂: C, 78.54; H, 9.89; N, 3.52. Found: C, 79.02; H, 9.97; N, 3.49

Reaction of Carbene Complex 1 or 2 with Cyclopentanone Pyrrolidine Enamine. Synthesis of Complexes 6. To a solution of carbene complex **1a−d** or **2a−d** (1 mmol) in hexane (40 mL) at room temperature was added 151 mg (1.1 mmol) of cyclopentanone pyrrolidine enamine in hexane (10 mL). The reaction mixture was stirred for 2 h. Filtration of the yellow solid and washing with hexane (2 × 15 mL) yielded complexes **6** as solids.

Data for Compound 6a. From **2a**. Yield: 95%. Yellow solid. Mp: 105−110 °C dec. ¹H NMR (THF-*d₈*, 300 MHz): δ 1.8−1.9 (m. 1H), 2.05−2.45 (m, 7H), 2.65 (m, 1H), 2.7 (dd, 1H, *J* = 4.4, 15.8 Hz), 3.25 (br d, 1H, *J* = 7.0 Hz), 3.35 (s, 3H), 3.7−3.8 (m, 1H), 3.95 (dd, 1H, *J* = 1.7, 6.6 Hz), 4.05−4.25 (m, 3H), 4.35−4.45 (m, 1H), 6.3 (m, 1H), 6.45 (m, 1H), 7.5 (d, 1H, *J* = 1.3 Hz). ¹³C NMR (THF-*d₈*, 50 MHz): δ 22.2 (CH₂) 26.9 (2 CH₂), 28.1 (CH₂), 40.5 (CH₂), 47.5 (CH), 50.4 (CH), 54.6 (CH₃), 54.9 (CH₂), 55.8 (CH₂), 64.8 (CH), 108.2 (CH), 108.3 (C), 112.1 (CH), 143.5 (CH), 157.1 (C), 201.4 (C), 206.0 (CO), 206.2 (4 CO). FAB-MS (*m/z*): 598 (M⁺ + 1). Anal. Calcd for C₂₂H₂₃-NO₇W: C, 44.24; H, 3.88; N, 2.35. Found: C, 44.02; H, 3.61; N, 2.30.

Data for Compound 6c. From pentacarbonyl[(*E*)-2-(4-methoxy-phenyl)ethyl(methoxy)carbene]tungsten (**2c**). Yield: 97%. Yellow solid. Mp: 89−91 °C dec. ¹H NMR (THF-*d₈*, 300 MHz): δ 1.7 (m. 1H), 2.0−2.45 (m, 7H), 2.5 (br s, 1H), 2.6 (dd, 1H, *J* = 4.3, 15.6 Hz), 3.05 (br d, 1H, *J* = 6.8 Hz), 3.3 (s, 3H), 3.6−3.7 (m, 1H), 3.8 (s, 3H), 3.9 (d, 1H, *J* = 6.9 Hz), 4.0−4.2 (m, 3H), 4.3−4.5 (m, 1H), 6.9 (d, 2H, *J* = 8.7 Hz), 7.25 (d, 2H, *J* = 8.7 Hz). ¹³C NMR (THF-*d₈*, 75 MHz): δ 21.6 (CH₂) 26.9 (2 CH₂), 28.3 (CH₂), 41.6 (CH₂), 50.4 (CH), 54.5 (CH₃), 54.6 (CH₂) 55.1 (CH), 55.8 (CH₂) 56.5 (CH₃), 64.8 (CH), 108.3 (C), 115.7 (2 CH), 130.4 (2 CH), 135.6 (C), 160.9 (C), 201.5 (C), 206.0 (CO), 206.2 (4 CO); FAB-MS (*m/z*): 638 (M⁺ + 1). Anal. Calcd for C₂₅H₂₇NO₇W: C, 47.11; H, 4.27; N, 2.20. Found: C, 47.41; H, 4.51; N, 2.11.

Synthesis of Bicyclo[3.2.1]oct-2-en-8-ones 7. Method A: Hydrolysis of Complexes 6. To a solution of complex **6** (1 mmol) in THF (40 mL) at 0 °C was added 1 mL of trifluoroacetic acid in THF (10 mL). The reaction mixture was stirred for 10 min, 10 mL of H₂O was added, and the solution was allowed to reach room temperature and stirred for an additional 2 h. The mixture was extracted with methylene dichloride (3 × 30 mL) and the organic layer washed with 20 mL of a saturated solution of sodium hydrogen carbonate and 20 mL of water. The resulting solution was dried over Na₂SO₄. After removal of the solvents, chromatographic purification of the residue on silica gel (5% ethyl acetate in hexane) gave the pure bicyclic ketones **7**.

Method B. To 50 mL of a 0.02 M THF solution of the alkenyl Fischer carbene complex **1** or **2** at 0 °C was added 180 mg (1.3 mmol) of the enamine **3a**. The mixture was stirred at 0 °C for 6 h. Then, 1 mL of trifluoroacetic acid and 10 mL of water were subsequently added. The solution was allowed to reach room temperature and stirred for an additional 2 h. The mixture was extracted with methylene dichloride (3 × 30 mL) and the organic layer washed with 20 mL of a saturated solution of sodium hydrogen carbonate and 20 mL of water. The resulting solution was dried over Na₂SO₄. After removal of the solvents, chromatographic purification of the residue on silica gel (5% ethyl acetate in hexane) gave the pure bicyclic ketones **7**.

Data for Compound (±)-7a. Yield: 87%. Colorless oil. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.7−1.9 (m, 2H), 1.9−2.0 (m, 2H), 2.55 (m, 1H), 2.65 (m, 1H), 4.4 (m, 1H), 5.7 (ddd, 1H, J = 1.2, 2.3, 9.3 Hz), 6.05 (ddd, 1H, J = 2.7, 7.0, 9.4 Hz), 6.15 (m, 1H), 6.35 (m, 1H), 7.4 (m, 1H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 19.8 (CH$_2$), 28.6 (CH$_2$), 44.6 (CH), 46.9 (CH), 49.5 (CH), 107.0 (CH), 110.0 (CH), 125.1 (CH), 133.7 (CH), 141.8 (CH), 153.8 (C), 215.1 (C). HRMS (m/z): calcd for C$_{12}$H$_{12}$O$_2$ 188.0837, found 188.0827. Anal. Calcd for C$_{12}$H$_{12}$O$_2$: C, 76.57; H, 6.42. Found: C, 76.45; H, 6.33.

Data for Compound (±)-7c. Yield: 91%. White solid. Mp: 110−111 °C. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.6−1.9 (m, 2H), 1.9−2.1 (m, 2H), 2.45 (m, 1H), 2.55 (m, 1H), 3.8 (s, 3H), 4.4 (m, 1H), 5.7 (br d, 1H, J = 9.9 Hz), 6.1 (ddd, 1H, J = 2.5, 7.2, 9.5 Hz), 6.9 (d, 2H, J = 8.6 Hz), 7.1 (d, 2H, J = 8.6 Hz). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 18.9 (CH$_2$), 28.6 (CH$_2$), 44.4 (CH), 50.1 (CH), 54.3 (CH$_3$), 55.0 (CH), 113.8 (2 CH), 128.1 (CH), 129.0 (2 CH), 132.6 (C), 133.5 (CH), 158.4 (C), 215.9 (C); HRMS (m/z): calcd for C$_{15}$H$_{16}$O$_2$ 228.1150, found 228.1144. Anal. Calcd for C$_{15}$H$_{16}$O$_2$: C, 78.92; H, 7.06. Found: C, 78.56; H, 7.14.

Synthesis of Bicyclo[3.3.1]non-2-en-9-ones 8. A 200 mg (1.3 mmol) sample of the cyclohexanone pyrrolidine enamine **4a** was added to a solution of 1 mmol of the alkenyl Fischer carbene complex **1** or **2** in 50 mL of THF at 0 °C. The mixture was stirred at 0 °C for 12 h. Then, 390 μL (5 mmol) of trifluoroacetic acid and 10 mL of water were subsequently added and, the solution was allowed to reach room temperature and stirred for an additional 2 h. The resulting mixture was extracted with methylene dichloride (3 × 30 mL) and the organic layer washed with 20 mL of a saturated solution of sodium hydrogen carbonate and 20 mL of water and finally dried over Na$_2$SO$_4$. The solvents were removed, and subsequent chromatographic purification of the residue on silica gel (5% ethyl acetate in hexane) yielded the pure bicyclic ketones **8**.

Data for Compound (±)-endo-8a. Yield: 67%. White solid. Mp: 49−50 °C. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.3 (m, 1H), 1.4−1.65 (m, 2H), 1.8−2.0 (m, 3H), 2.8 (m, 1H), 2.95 (m, 1H), 4.15 (m, 1H), 5.8 (ddd, 1H, J = 2.9, 5.9, 9.9), 6.05 (dd, 1H, J = 2.3, 9.9 Hz), 6.2 (m, 1H), 6.35 (m, 1H), 7.35 (m, 1H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 16.9 (CH$_2$), 31.4 (CH$_2$), 32.5 (CH$_2$), 44.2 (CH), 47.4 (CH), 49.6 (CH), 106.8 (CH), 110.0 (CH), 128.5 (CH), 129.4 (CH), 141.7 (CH), 154.0 (C), 214.7 (C); HRMS (m/z): calcd for C$_{13}$H$_{14}$O$_2$ 202.0994, found 202.0992. Anal. Calcd for C$_{13}$H$_{14}$O$_2$: C, 77.20; H, 6.98. Found: C, 77.42; H, 6.80.

Data for Compound (±)-exo-8a. Yield: 13%. Colorless oil. ^{1}H NMR (CDCl$_3$, 200 MHz): δ 1.5−1.7 (m, 2H), 1.8−2.2 (m, 4H), 2.7 (m, 1H), 2.9 (m, 1H), 3.95 (m, 1H), 5.75 (m, 1H), 5.95 (m, 1H), 6.05 (m, 1H), 6.25 (m, 1H), 7.3 (m, 1H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 17.0 (CH$_2$), 32.6 (CH$_2$), 36.0 (CH$_2$), 47.3 (CH), 47.4 (CH), 41.0 (CH), 105.2 (CH), 110.2 (CH), 128.5 (CH), 129.8 (CH), 141.7 (CH), 155.3 (C), 214.8 (C). HRMS (m/z): calcd for C$_{13}$H$_{14}$O$_2$ 202.0994, found 202.1002. Anal. Calcd for C$_{13}$H$_{14}$O$_2$: C, 77.20; H, 6.98. Found: C, 77.45; H, 7.09.

Synthesis of Optically Active Ketones 7. To a solution of 1 mmol of the alkenyl Fischer carbene complex **2** in 50 mL of THF at −20 °C was added 180 mg (1.3 mmol) of cyclopentanone methoxymethyl-pyrrolidine enamine **3b**. After 6.5 h of stirring at −20 °C, 390 μL (5 mmol) of trifluoroacetic acid was added, the resulting mixture was stirred for 0.5 h, 10 mL of water was added, and the mixture was allowed to react for an additional 2 h at room temperature. Then the mixture was extracted with methylene dichloride (3 × 30 mL) and the organic layer washed with 20 mL of a saturated solution of sodium hydrogen carbonate and 20 mL of water and dried over Na$_2$SO$_4$. After removal of the solvents, chromatographic purification of the residue on silica gel (5% ethyl acetate in hexane) gave the optically active ketones **7**.

Data for Compound (+)-7a. Yield: 85%. [α]^{20}$_D$ = +2.8 (c 0.8, CH$_2$Cl$_2$). For spectroscopic data, see those for (±)-**7a**. The enantiomeric ratio was determined by HPLC (Chiracel OB-H column, 250 × 4.6 mm; 0.8 mL/min; hexane/2-propanol, 50:1): retention times 13.6 (6%) and 14.9 (94%) min.

Data for Compound (+)-7c. Yield: 90%. [α]^{20}$_D$ = +81 (c 0.1, CH$_2$Cl$_2$). For spectroscopic data, see those for (±)-**7c**. The enantiomeric ratio was determined by HPLC (Chiracel OJ column, 250 × 4.6 mm; 0.8 mL/min; hexane/2-propanol, 50:1): retention times 39.8 (3.5%) and 44.7 (96.5%) min.

Synthesis of Optically Active Ketones 8. To 50 mL of a 0.02 M solution (in the appropriate solvent) of the alkenyl Fischer carbene complex **2** was added 1.3 mmol of the enamine **4b,c**. After the mixture was stirred at low temperature, 390 μL (5 mmol) of trifluoroacetic acid and 10 mL of water were subsequently added. The solution was allowed to reach room temperature and stirred for an additional 2 h. The mixture was extracted with methylene dichloride (3 × 30 mL) and the organic layer washed with 20 mL of a saturated solution of sodium bicarbonate and 20 mL of water. The resulting solution was dried over Na$_2$SO$_4$, and the solvents were removed. Purification of the residue by chromatography on silica gel (5% ethyl acetate in hexane) gave the optically active bicyclic ketones **8**.

Data for Compound (−)-endo-8a. Solvent: CH$_2$Cl$_2$. Temperature: −50 °C. Reaction time: 7 days. Yield: 52%. [α]^{20}$_D$ = −17.6 (c 0.23, CH$_2$Cl$_2$). For spectroscopic data, see the those for (±)-endo-**8a**. The enantiomeric ratio was determined by HPLC (Chiracel OJ column, 250 × 4.6 mm; 0.8 mL/min; hexane/2-propanol, 200:1): retention times 15.8 (1%) and 18.2 (99%) min.

Data for Compound (−)-exo-8a. Solvent: THF. Temperature: −20 °C. Reaction time: 72 h. endo:exo ratio 1:2. For spectroscopic data, see those of (±)-exo-**8a**. The enantiomeric ratio was determined by HPLC (Chiracel OJ column, 250 × 4.6 mm; 0.8 mL/min; hexane/2-propanol, 200:1): retention times 20.2 (99%) and 22.3 (1%) min.

Reaction of Pentacarbonyl[1-pentenyl(methoxy)carbene]tungsten (2d) with Cyclopentanone Pyrrolidine Enamine 3a. Synthesis of Enol Ether 9. To a solution of carbene complex (1 mmol) in THF (50 mL) was added at 0 °C 178 mg (1.3 mmol) of cyclopentanone pyrrolidine enamine **3a**. The reaction was stirred at 25 °C for 2 h. Then, 1 mL of trifluoroacetic acid and 10 mL of water were added. The mixture was extracted with methylene dichloride (3 × 30 mL) and the organic layer washed with water (2 × 20 mL). The resulting solution was dried over Na$_2$SO$_4$. After removal of the solvents, chromatographic purification of the residue on silica gel (5% ethyl acetate in hexane) gave the pure enol ether **9**.

^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.5 (d, 3H, J = 1.32 Hz), 1.5−1.9 (m, 2H), 1.9−2.4 (m, 7H), 3.5 (s, 3H), 5.85 (m, 1H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 17.1 (CH$_3$), 20.5 (CH$_2$), 28.9 (CH$_2$), 29.0 (CH$_2$), 38.1 (CH$_2$), 47.2 (CH), 59.1 (CH$_3$), 111.6 (C), 143.0 (CH), 219.5 (C). HRMS (m/z): calcd for C$_{10}$H$_{16}$O$_2$ 168.1150, found 168.1154. Anal. Calcd for C$_{10}$H$_{16}$O$_2$: C, 71.39; H, 9.59. Found: C, 71.57; H, 9.64.

Reaction of Nonstabilized Carbene Complex 10 with Bases. Synthesis of Complexes 12. A 1 mmol sample of racemic complex **6** was cooled to −80 °C and then suspended in CH$_2$Cl$_2$ (25 mL), and 290 μL (1.6 mmol) of trimethylsilyl triflate was added at this temperature. After 30 min the reaction mixture became a dark red solution. A 291 μL (2 mmol) sample of enamine **3a** was added to form a deep yellow solution which was allowed to reach room temperature. The solvents were evaporated, and the yellow solid crude product was dissolved in the minimum of methylene dichloride (1.5 mL). Cooling the solution at −20 °C for 14 h afforded yellow crystals, which were filtered and washed with cold CH$_2$Cl$_2$. Other common bases such as triethylamine, pyridine, etc. are suitable, but they do not allow isolation of the metalate. In turn, they are used to the in situ reaction better than enamine.

Data for Compound 12a. Yield: 65%. Yellow solid. Mp: 160−162 °C dec. ^{1}H NMR (CD$_2$Cl$_2$, 300 MHz): δ 1.6−1.8 (m, 2H), 1.8−2.0 (m, 1H), 2.0−2.2 (m, 1H), 2.2−2.5 (m, 4H), 3.1 (br s, 1H), 3.8 (br s, 1H), 3.9−4.2 (m, 4H), 4.8 (m, 1H), 5.3 (m, 1H), 7.2−7.5 (m, 5H).

^{13}C NMR (CD$_2$Cl$_2$, 75 MHz): δ 22.1 (CH$_2$), 25.0 (CH$_2$), 25.1 (CH$_2$), 30.0 (CH$_2$), 48.5 (CH), 52.4 (CH$_2$), 53.9 (CH$_2$), 62.1 (CH), 66.9 (CH), 127.4 (CH), 128.7 (2 CH), 128.8 (2 CH), 134.2 (CH), 141.1 (C), 169.7 (C), 199.5 (C), 203.3 (4 C), 206.9 (C). FAB-HRMS (*m/z*): calcd for C$_{23}$H$_{22}$NO$_5$^{184}W 576.1007, found 576.1003. Anal. Calcd for C$_{23}$H$_{21}$-NO$_5$W: C, 48.02; H, 3.68; N, 2.43. Found: C, 47.96; H, 3.59; N, 2.35.

Synthesis of Deuterated Derivatives Bicyclo[3.2.1]oc-2-en-8-ones 7-*d*. To a solution of complex **12** (1 mmol) in THF (10 mL) at room temperature were subsequently added 1 mL of deuterated water and 0.15 mL (2 mmol) of deuterated trifluoroacetic acid. After 15 min the mixture was extracted with methylene dichloride (3 × 10 mL), and the combined organic layers were washed with 20 mL of a 5% solution of sodium hydrogen carbonate and 20 mL of water. The resulting solution was dried over sodium sulfate and filtered. After removal of the solvents, chromatographic purification of the residue on silica gel (5% ethyl acetate in hexane) gave the pure bicyclic ketones **7-*d*.**

Data for Compound 7a-*d*. Yield: 91%. Colorless oil. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.6–18 (m, 2H), 1.9–2.1 (m, 2H), 2.5 (m, 1H), 2.6 (m, 1H), 4.4 (s, 1H), 5.7 (s, 1H), 7.1–7.5 (m, 5H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 19.0 (CH$_2$), 28.6 (CH$_2$), 44.5 (CH), 49.8 (CH), 55.0 (CH), 126.8 (CH), 127.7 (CH), 128.1 (2 CH), 128.4 (2 CH), 133.6 (CD, t, J = 28.1 Hz), 140.5 (C), 215.9 (C). HRMS (*m/z*): calcd for C$_{14}$H$_{13}$DO 199.1107, found 199.1100. Anal. Calcd for C$_{14}$H$_{13}$DO: C, 84.38; H, 7.59. Found: C, 84.28; H, 7.68.

Methoxycarbonylation of Complexes 12. Synthesis of Ketones 13. Method A. To a solution of complex **12** (1 mmol) in THF (40 mL) at −80 °C were subsequently added 1 mL of methanol, 1.5 mL of triethylamine, and 1 g of iodine in THF (4 mL). After 15 min at this temperature the reaction was quenched with 50 mL of 5% Na$_2$S$_2$O$_3$ solution. The solution was allowed to reach room temperature and extracted with methylene dichloride (3 × 30 mL). The combined organic layers were washed with water and dried over sodium sulfate. After removal of the solvents, chromatographic purification on silica gel (5% ethyl acetate in hexane) gave the pure bicyclic ketones **13**.

Method B. To 50 mL of a 0.02 M THF solution of the alkenyl Fischer carbene complex **1** or **2** at 0 °C was added 180 mg (1.3 mmol) of the enamine **3a**. The mixture was stirred at 0 °C for 6 h. Then, 361 μL (2 mmol) of trimethylsilyl triflate was added at −80 °C. After 30 min at this temperature, 418 μL (3 mmol) of triethylamine was added. The dark red solution became yellow, and 1 mL of methanol, 1.5 mL of triethylamine, and 1 g of iodine in THF (4 mL) were subsequently added. After 15 min at this temperature the reaction was quenched with 50 mL of 5% Na$_2$S$_2$O$_3$ solution. The solution was allowed to reach room temperature and extracted with methylene dichloride (3 × 40 mL). The combined organic layers were washed with water and dried over sodium sulfate. After removal of the solvents, chromatographic purification on silica gel (5% ethyl acetate in hexane) gave the pure bicyclic ketones **13**.

Data for Compound 13a. Yield: 61% (method A, from complex **12b**), 55% (method B, from alkenyl Fischer carbene complex **1b** or **2b**). Colorless oil. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.6–1.8 (m, 2H), 2.0–2.2 (m, 2H), 2.5 (m, 1H), 3.2 (m, 1H), 3.7 (s, 3H), 4.5 (m, 1H), 7.0 (m, 1H), 7.1–7.5 (m, 5H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 19.2 (CH$_2$), 28.7 (CH$_2$), 43.6 (CH), 49.0 (CH), 52.2 (CH$_3$), 53.0 (CH), 127.3 (CH), 128.2 (2 CH), 128.7 (2 CH), 137.2 (C), 138.2 (CH), 139.1 (C), 165.0 (C), 214.3 (C). HRMS (*m/z*): calcd for C$_{16}$H$_{16}$O$_3$ 256.1099, found 256.1100. Anal. Calcd. for C$_{16}$H$_{16}$O$_3$: C, 74.98; H, 6.29. Found: C, 74.89; H, 6.36.

Nonstabilized Carbene Complex 10 Oxidation. Formation of Diketones 14. A 1 mmol sample of racemic complex **6** was cooled to −80 °C and then suspended in CH$_2$Cl$_2$ (25 mL), and 290 μL (1.6 mmol) of trimethylsilyl triflate was added at this temperature. After 30 min at −80 °C, 0.448 g (2 mmol) of 3-chloroperbenzoic acid (77%) was added. After 5 min the reaction was quenched with 50 mL of 5% Na$_2$S$_2$O$_3$ solution. The reaction was allowed to reach room temperature. The mixture was extracted with diethyl ether (3 × 40 mL), and the combined

organic layers were washed with water. Filtration and solvent removal afford the crude reaction product, which contains diketone **14** and 3-chlorobenzoic acid. Basic extraction or chromatographic purification affords mixtures of retro-Claisen-type products from diketone **14**, and then nonanalytically pure samples were obtained. The signals belong to **14b** in the NMR reaction crude product analysis.

Data for Compound 14b. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 2.0–2.1 (m, 3H), 2.2 (m, 1H), 2.7 (m, 1H), 2.9–3.0 (m, 2H), 3.2–3.4 (m, 2H), 6.1 (m, 1H), 6.3 (m, 1H), 7.4 (m, 1H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 18.1 (CH$_2$), 23.2 (CH$_2$), 34.6 (CH), 37.6 (CH$_2$), 48.3 (CH), 63.6 (CH), 106.6 (CH), 110.2 (CH), 142.5 (CH), 152.7 (C), 203.9 (C), 207.5 (C).

Synthesis of Methoxycarbonylcycloheptanones 15. The crude product of 1 mmol formation of **14** is placed into a flask and dissolved in 10 mL of methanoic acid (50% v/v). The mixture was stirred and heated at 80 °C for 1 h. After the mixture was cooled at room temperature, the methanoic acid was evaporated and the crude product diluted with water and extracted with diethyl ether (4 × 40 mL). The combined organic layers were washed with water and filtered. To the filtrate was added 10 mL of a 0.3 M solution of diazomethane in ether. (The diazomethane excess was destroyed with 0.3 mL of acetic acid.) Removal of solvents at reduced pressure and column chromatography (20% ethyl acetate in hexane) afforded the cycloheptanones **15**.

Data for Compound (±)-15a. Yield: 64%. White solid. Mp: 96–98 °C. ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.7 (m, 1H), 1.9 (m, 1H), 2.1 (m, 1H), 2.2 (m, 1H), 2.6 (m, 3H), 2.9 (dt, 1H, J = 2.80, 10.85 Hz), 3.1 (m, 2H), 3.4 (s, 3H), 7.1–7.4 (m, 5H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 22.0 (CH$_2$), 31.9 (CH$_2$), 43.2 (CH$_2$), 44.4 (CH), 49.5 (CH$_2$), 51.4 (CH$_3$), 54.8 (CH), 126.9 (3 CH), 128.5 (2 CH), 143.4 (C), 174.5 (C), 211.9 (C). FAB-HRMS (M + 1) (*m/z*): calcd for C$_{15}$H$_{19}$O$_3$ 247.1334, found 247.1325. Anal. Calcd for C$_{15}$H$_{18}$O$_3$: C, 73.15; H, 7.37. Found: C, 73.19; H, 7.32.

Synthesis of Optically Active Cycloheptanones 15. To 50 mL of a 0.02 M THF solution of the alkenyl Fischer carbene complex **2a**–**c** at −20 °C was added 0.235 mg (1.3 mmol) of the enamine **3b**. The mixture was stirred at this temperature for 6 h. Then, 0.448 g (2 mmol) of 3-chloroperbenzoic acid was added. After 5 min, 40 mL of a 5% Na$_2$S$_2$O$_3$ solution and 10 mL of methanoic acid were subsequently added. The reaction was stirred at 80 °C for 1 h. Volatiles was removed, and the mixture was extracted with diethyl ether (4 × 40 mL). The combined organic layers were washed with water and filtered. To the filtrate was added 20 mL of a 0.3 M solution of diazomethane in ether. (The diazomethane excess was destroyed with 0.3 mL of acetic acid.) Removal of solvents at reduced pressure and column chromatography on silica gel (20% ethyl acetate in hexane) afforded the optically active cycloheptanones **15**.

Data for Compound (+)-15a. Yield: 51%. [α]$^{20}_D$ = +61.0 (*c* 0.92, CH$_2$Cl$_2$). For spectroscopic data, see those of (±)-**15a**. The enantiomeric ratio was determined by HPLC (chiracel OB-H column, 250 × 4.6 mm; 0.8 mL/min; hexane/ethanol, 99:1): retention times 24.9 (3.5%) and 30.7 (96.5%) min.

Formation of Simple Nonstabilized Carbene Complexes 17. To a solution of carbene complex **16** (1 mmol) in THF (25 mL) was added 1.6 mmol of the appropriate alkyllitium (methyllithium as a complex with lithium bromide, 1.5 M in ether, or butyllithium, 1.6 M solution in hexanes). The bright yellow mixture was cooled to −80 °C, and then 361 μL (2 mmol) of freshly distilled trimethylsilyl triflate was added. The color change to dark brown was due to the new carbene formed "in situ".

Synthesis of Alkenes 18. The THF solution of carbene **17** formed as above was allowed to reach room temperature. Solvent removal and chromatographic purification on silica gel (5% ethyl acetate in hexane) afforded the well-known styrene (**18a**) (67% yield) and 1-phenyl-1-pentene (**18b**) (61% yield).

Synthesis of Ketones 19. To the THF solution of **17** at −80 °C was added 0.285 g (3 mmol) of pyridine *N*-oxide. After 30 min the

reaction was quenched with 50 mL of a 5% solution of $Na_2S_2O_3$. After being warmed to room temperature, the mixture was extracted with methylene chloride (3 × 30 mL), and the combined organic layers were washed with water. Filtration and chromatographic purification (5% ethyl acetate in hexane) afforded the pure ketones acetophenone (**19a**) and valerophenone (**19b**) in 45% and 40% yields, respectively.

Synthesis of Methyl 2-Phenylalk-2-enoates 20. To the THF solution of carbene **17** at −80 °C was added 418 μL (3 mmol) of triethylamine. Then, 1 mL of methanol, 1.5 mL of triethylamine, and 1 g of iodine in THF (4 mL) were subsequently added. After 15 min at this temperature the reaction was quenched with 50 mL of 5% $Na_2S_2O_3$ solution. The solution was allowed to reach room temperature and extracted with methylene dichloride (3 × 40 mL). The combined organic layers were washed with water and dried over sodium sulfate. After removal of the solvents, chromatographic purification on silica gel (5% ethyl acetate in hexane) gave the pure alkenoates **20**.

Yield: 74%. Colorless oil. ^1H NMR (CDCl$_3$, 300 MHz): 3.8 (s, 3H), 5.9 (s, 1H), 6.4 (s, 1H), 7.3−7.5 (m, 5H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 52.1 (CH$_3$), 126.8 (CH$_2$), 128.0 (2 CH), 128.1 (CH), 128.2 (2 CH), 136.6 (C), 141.1 (C), 167.1 (C). HRMS (m/z): calcd for C$_{10}$H$_{10}$O$_2$ 162.0681, found 162.0685. Anal. Calcd for C$_{10}$H$_{10}$O$_2$: C, 74.06; H, 6.21. Found: C, 74.11; H, 6.12.

Data for Compound (Z)-20b (Major). Yield: 70%. Colorless oil. ^1H NMR (CDCl$_3$, 300 MHz): 1.0 (t, 3H, J = 7.4 Hz), 1.5−1.6 (m, 2H), 2.4 (c, 2H, J = 7.5 Hz), 3.8 (s, 3H), 6.2 (t, 1H, J = 7.5 Hz), 7.3−7.5 (m, 5H). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 13.7 (CH$_3$), 22.5 (CH$_2$), 32.0 (CH$_2$), 51.6 (CH$_3$), 127.2 (2 CH), 127.4 (CH), 128.2 (2 CH), 134.4 (C), 138.0 (C), 140.6 (CH), 168.6 (C). HRMS (m/z): calcd

for C$_{13}$H$_{16}$O$_2$ 204.1150, found 204.1142. Anal. Calcd for C$_{13}$H$_{16}$O$_2$: C, 76.44; H, 7.90. Found: C, 76.50; H, 7.83.

Synthesis of Alkenylmetalates 21. To the THF solution of carbene **17** was added 10 mL of a deoxygenated 1 M NaOH solution which contains 0.5 g of tetraethylammonium bromide. When the mixture reached room temperature, THF was removed at reduced pressure until an orange solid was formed. The water was decanted and the solid washed with degassed water (2 × 10 mL) and diethyl ether (2 × 10 mL).

Yield: 32%. Yellow solid. Mp: 95−98 °C dec. ^1H NMR (CD$_2$Cl$_2$, 300 MHz): 1.2−1.4 (m, 12H), 2.9−3.1 (c, 8H, J = 7.4 Hz), 5.5 (d, 1H, J = 5.8 Hz), 5.9 (d, 1H, J = 5.8 Hz), 6.9−7.2 (m, 5H). ^{13}C NMR (CD$_2$Cl$_2$, 75 MHz): δ 7.7 (4 CH$_3$), 52.9 (4 CH$_2$), 122.4 (CH), 125.1 (CH$_2$), 125.3 (2 CH), 127.0 (2 CH), 163.9 (C), 174.2 (C), 204.6 (4 C), 209.0 (C). Anal. Calcd for C$_{17}$H$_{27}$NO$_5$W: C, 40.10; H, 5.34; N, 2.75. Found: C, 39.95; H, 5.26, N 2.65.

Supporting Information Available: Characterization data for **5b,f**, **6b,d**, **7b,d**, **8b**, **12b,c**, **7b**-*d*, **13b**, **15b,c**, (+)-**22**, (−)-**23**, and (+)-**24** and HPLC data for racemic **7** and **8** and enantioenriched **7** and **8** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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