Pergamon

TETRAHEDRON

Tetrahedron 56 (2000) 4907–4915

A Novel Use of the Anions of Fischer-type Carbene Complexes as Alkenyl Metallic Species

Kohei Fuchibe[a] and Nobuharu Iwasawa[b,*]

[a]*Department of Chemistry, Graduate School of Science, the University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan*
[b]*Department of Chemistry, Tokyo Institute of Technology, 2-12-1 O-okayama, Meguro-ku, Tokyo 152-8551, Japan*

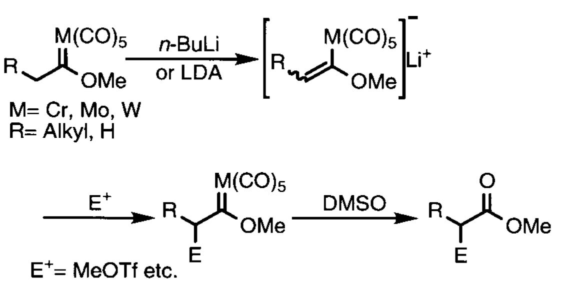
Received 6 December 1999; accepted 18 January 2000

Abstract—The anions generated by deprotonation of Fischer-type carbene complexes or by 1,4-addition of lithium enolates to α,β-unsaturated complexes are found to act as alkenyl metallic species on iodine oxidation. Various α-methoxy-α,β-unsaturated esters are formed by the treatment of such anions with iodine in the presence of methanol and silver trifluoromethanesulfonate. In addition, alkylcerium reagents are found to undergo 1,4-addition to α,β-unsaturated carbene complexes with high efficiency. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

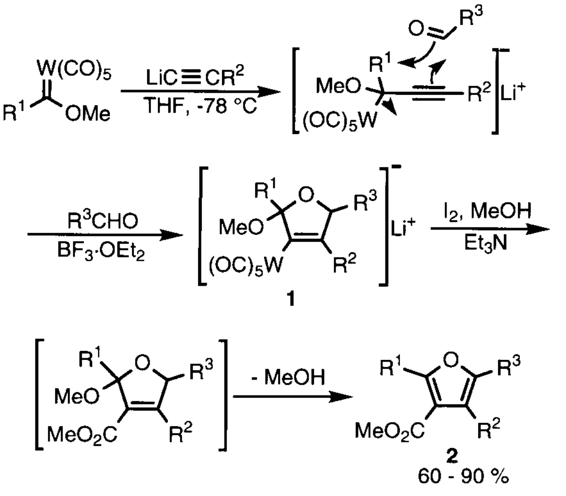
Since their first synthesis by E. O. Fischer and A. Maasböl,[1] Fischer-type carbene complexes have attracted the attention of many organic chemists due to their unique reactivity.[2] Cyclopropanation,[2e] and ketene-generating reactions[2f] are well-known, and many natural products have been synthesized[2a,d] by the benzannulation reaction originally reported by Dötz et al.[2g]

In Fischer-type carbene complexes, the pentacarbonylmetal moiety serves as a strong electron-withdrawing group, making the α-proton of the carbene carbon highly acidic.[3] For example, deprotonation of alkyl carbene complexes with bases such as *n*-BuLi and LDA generates anionic species, which react with various electrophiles such as aldehydes or alkyl trifluoromethanesulfonates to give α-substituted carbene complexes.[4] As carbene complexes can be converted to the corresponding esters by oxidation with DMSO,[5a] ceric diammonium nitrate,[5b] etc., the complexes are often utilized as ester-equivalents (Eq. (1)).[6]



(1)

We have recently reported a useful method for the synthesis of substituted furans, pyrroles, butenolides and other five-membered heterocyclic compounds utilizing the anionic propargyl metallic species generated by the addition of alkynyllithiums to Fischer-type carbene complexes (Eq. (2)).[7] In this reaction, 1,2-migration of the pentacarbonyltungsten moiety occurs on reaction of the anionic propargyl metallic species with electrophiles such as aldehydes, giving alkenyltungsten species **1**. These alkenyltungsten species **1** can be oxidized with iodine to give ultimately the carboxylated products **2** via elimination of methanol.[8] We expected that the anions derived from Fischer-type carbene complexes on treatment with bases could also be employed as alkenyl metallic species on iodine-oxidation, as they have a similar structure to the alkenyltungsten species **1**. In this paper, a successful realization of this approach is described;[9] that is, the methoxycarbonylation of anions of Fischer-type carbene complexes on iodine-oxidation.



(2)

Keywords: Fischer-type carbene complexes; lithium enolates; iodine oxidation; methoxycarbonylation; alkylcerium reagents.

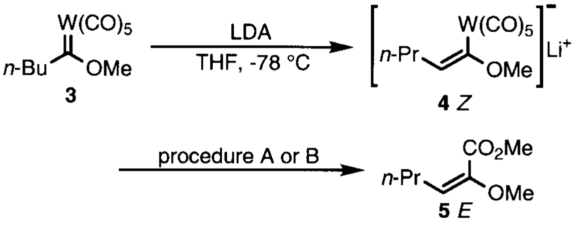
* Corresponding author. Tel.: +81-3-5734-2746; fax: +81-3-5734-2746; e-mail: niwasawa@chem.titech.ac.jp

PII: S0040-4020(00)00205-2

Results and Discussions

Preparation of α-methoxy-α,β-unsaturated esters by the iodine-oxidation of anionic species generated on deprotonation of Fischer-type carbene complexes

We first examined the iodine-oxidation of the anionic species generated by deprotonation of Fischer-type carbene complexes with lithium diisopropylamide (LDA).[10] When the anionic species **4**, generated by deprotonation of butyl carbene complex **3** with LDA, was treated sequentially with triethylamine, iodine and a large excess of methanol at −78°C, the desired α-methoxy-α,β-unsaturated ester **5** was obtained in 21% yield as a single, *E* isomer (Eq. (3), procedure A).[11] The stereochemistry of the product indicates that the stereochemistry of the anionic species **4** was *Z*, assuming that carbonyl insertion occurs with retention of geometry. Various reaction conditions were examined, the greatest improvement in yield of the ester **5**, to 70%, occurring when methanol was added before treatment with triethylamine and iodine (Eq. (3), procedure B).[12]



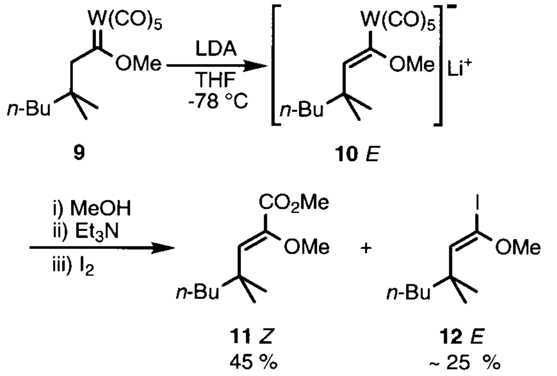
(3)

procedure A: i) Et_3N ii) I_2 iii) MeOH 21 %
B: i) MeOH ii) Et_3N iii) I_2 70 %

The probable reaction mechanism is as follows: treatment of the anionic species **4** with iodine gives hepta-coordinated unstable intermediate **6**. The intermediate **6** is converted to acyl metallic species **7** via migration of the alkenyl moiety to the carbonyl carbon. Then nucleophilic addition of methanol, either directly to the acyl metallic species **7**, or to the acyl iodide **8** produced by reductive elimination from **7**, yields the α-methoxy-α,β-unsaturated ester **5** (Scheme 1).

As already mentioned, to obtain the ester **5** in good yield it is important to add methanol before oxidation with iodine. It is likely that the acyl metallic species **7** is unstable, and must be captured by methanol before it decomposes.

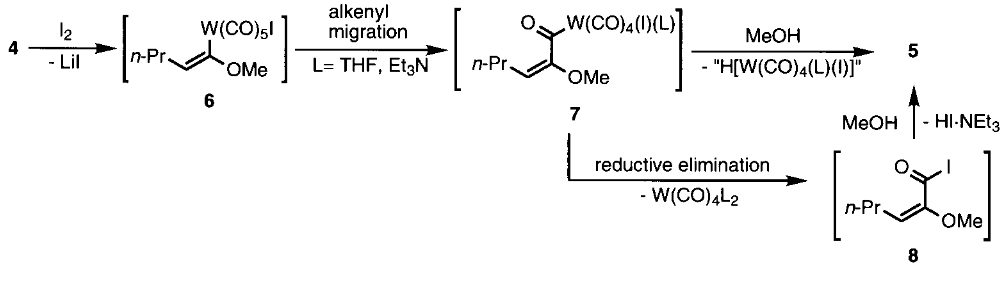
Next, the reaction with 2,2-dimethylhexyl carbene complex **9** was examined. When **9** was treated under conditions similar to those used for the butyl carbene complex **3**, the desired ester **11** was obtained in 45% yield as a single, *Z* isomer,[13] accompanied by alkenyl iodide **12** in about 25% yield as a single, *E* isomer.[14] The stereochemistry of the products indicates that the stereochemistry of the alkenyl metallic species **10** was *E*, opposite to that of the alkenyl metallic species **4** (Eq. (4)). Apparently, the bulkiness of the β-carbon has a significant effect on the stereochemistry of the alkenyl metallic species and its reactivity.



(4)

The difference in geometry of the products can be explained as follows. In the case of the butyl carbene complex **3**, deprotonation occurs via the *syn* conformation in order to minimize the steric repulsion between the propyl group and LDA, resulting in formation of *Z*-alkenyltungsten species **4**. On the other hand, in the case of the 2,2-dimethylhexyl carbene complex **9**, deprotonation occurs via the *anti* conformation, because the steric repulsion between the bulky 2,2-dimethylhexyl group and pentacarbonyltungsten moiety becomes more severe, and hence *E*-alkenyltungsten species **10** is formed selectively (Fig. 1).

As already mentioned, the difference in geometry of the alkenyltungsten species has a significant effect on product distribution. In the case of intermediate **6**, it is assumed that steric repulsion between the propyl group and the tungsten moiety accelerates migration of the alkenyl moiety, giving acyl metallic species **7** selectively. On the other hand, in the case of intermediate **13**, there is less steric repulsion between the olefinic hydrogen and the tungsten moiety, and reductive elimination to alkenyl iodide **12** proceeds competitively (Eq. (5)).



Scheme 1.

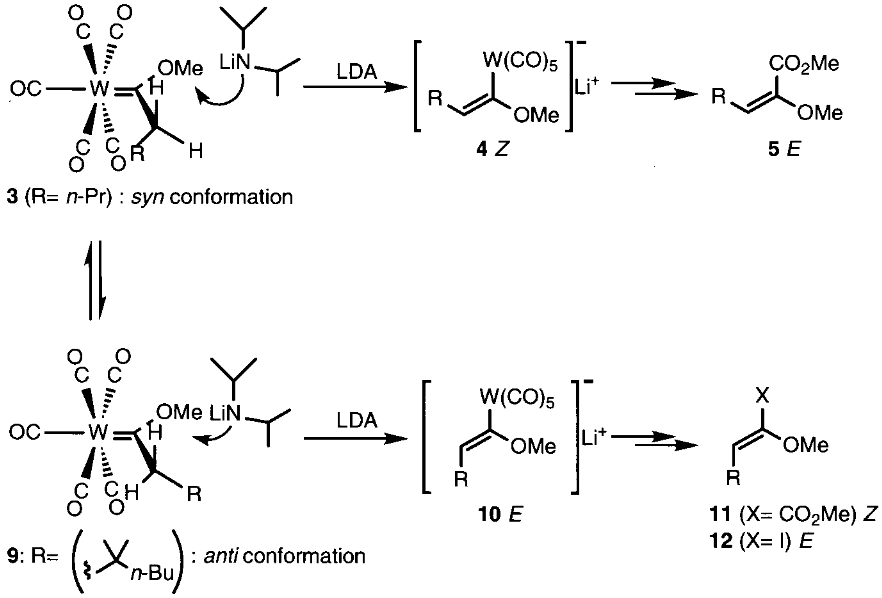
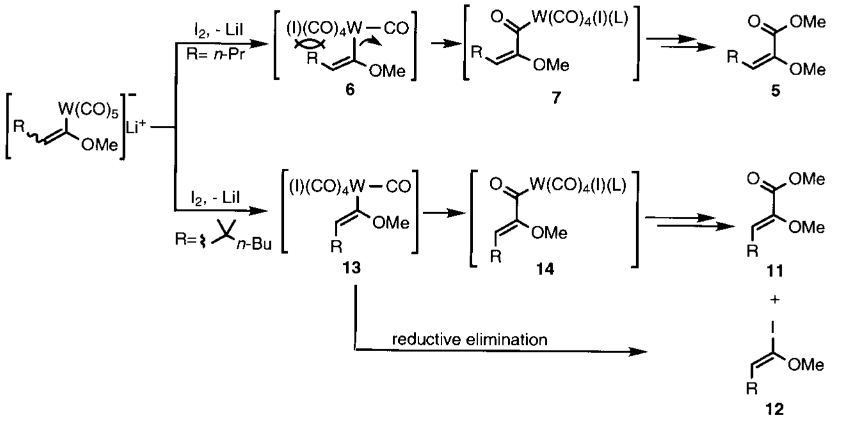
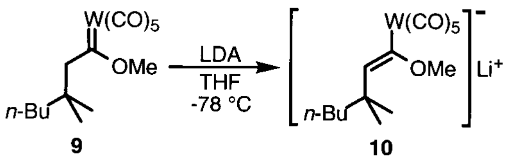


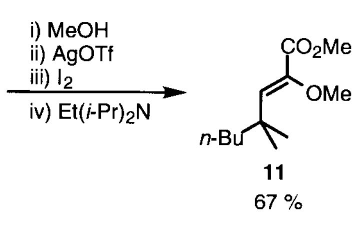
Figure 1.



(5)

In order to suppress formation of the alkenyl iodide **12**, we examined further the reaction conditions. Reactions under a CO atmosphere and at different oxidation temperature (−40°C and −120°C) both failed to suppress the formation of the iodide **12**. Next we tried to remove the iodide from the intermediate **13** as its silver salt. After the addition of methanol to a THF solution of the alkenyl metallic species **10**, a THF solution of silver trifluoromethanesulfonate (silver triflate, AgOTf) was added, followed by the addition of iodine and ethyl(diisopropyl)amine (Eq. (6)). Using this procedure, formation of iodide **12** was completely suppressed, and the desired ester **11** was obtained in 67% yield.



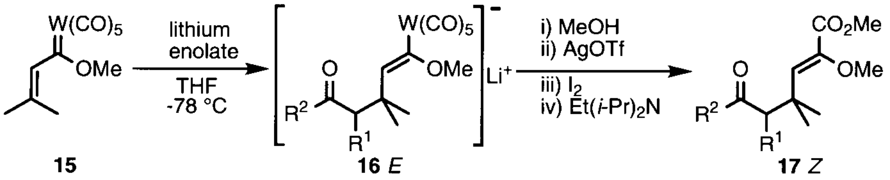


(6)

Iodine-oxidation of the alkenyl metallic species generated by 1,4-addition of lithium enolates to α,β-unsaturated carbene complexes

It is widely known that a similar kind of alkenyl metallic species is generated on 1,4-addition of lithium enolates to α,β-unsaturated carbene complexes.[15] We next examined the iodine-oxidation of these alkenyl metallic species in the expectation that α-methoxy-α,β-unsaturated esters possessing carbonyl functionality would be obtained.

Table 1. Formation of α-methoxy-α,β-unsaturated esters employing isobutenyl carbene complex **15**



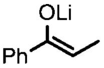
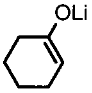
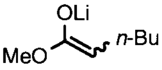
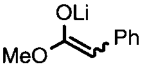
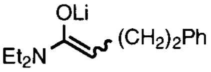
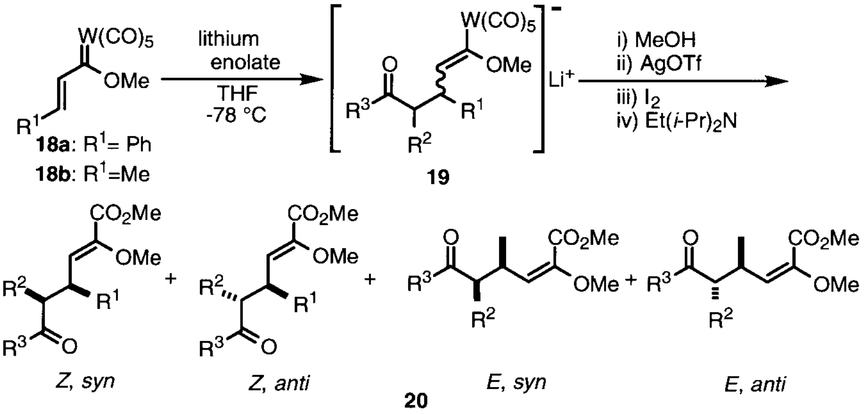
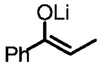
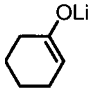
Lithium enolate (R^1, R^2)		Product	Yield (%)
	(R^1=Me R^2=Ph)	**17a**	79
	(R^1, R^2)=–(CH_2)$_4$–	**17b**	75
	(R^1=n-Bu R^2=OMe)	**17c**	65
	(R^1=Ph R^2=OMe)	**17d**	62
	(R^1=(CH_2)$_2$Ph R^2=NEt_2)	**17e**	43

Table 2. Formation of α-methoxy-α,β-unsaturated esters employing β-mono-substituted carbene complexes **18**



R^1	Lithium enolate		Product	Yield (%)	Isomer ratio Z, syn/Z, anti/E, syn/E, anti
Ph		(R^2= Me R^3= Ph)	**20a**	79	50:28:22:trace
Me			**20b**	45	80:9:9::2
Ph		(R^2, R^3= -(CH_2)$_4$-)	**20c**	59	81:6:13:trace
Me			**20d**	88	54:16:30:trace

Isobutenyl carbene complex **15** was treated with various lithium enolates derived from ketones, esters, and an amide in THF at −78°C, and the resulting alkenyl metallic species **16** was oxidized with iodine in the presence of methanol, silver triflate, and ethyl(diisopropyl)amine. As shown in Table 1, the reaction proceeded as expected, and various functionalized α-methoxy-α,β-unsaturated esters **17** were obtained in good yields as single, *Z* isomers.[16,17]

Reactions employing β-mono-substituted carbene complexes **18** also gave good yields of the products as summarized in Table 2. In this case, however, the products were obtained as mixtures of the four possible *E*/*Z*[18] and *syn*/*anti* isomers.[15a,b]

In the case of isobutenyl carbene complex **15**, the complex assumes the *s-trans* conformation to avoid the steric repulsion between the methyl group (R^1 in Fig. 2) and metal

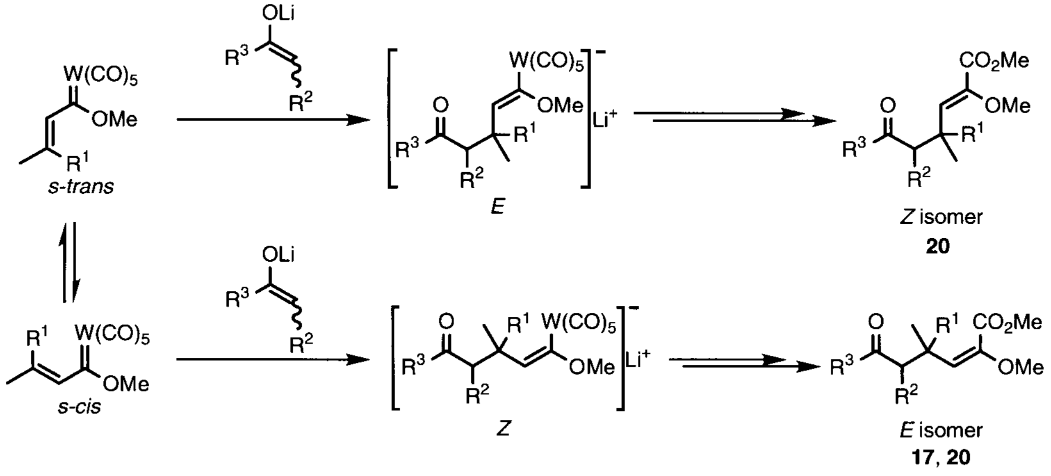


Figure 2.

moiety. 1,4-Addition proceeds via the *s-trans* conformation, and an *E*-alkenyltungsten species is generated, giving the products as single, *Z* isomers. On the other hand, in the case of *trans*-propenyl or *trans*-styryl carbene complex **18**, the steric repulsion between hydrogen (R^1 in Fig. 2) and the metal moiety is relatively small. As a result, 1,4-addition proceeds both via the *s-trans* and the *s-cis* conformation, and the products are obtained as a mixture of *E*/*Z* isomers (Fig. 2).

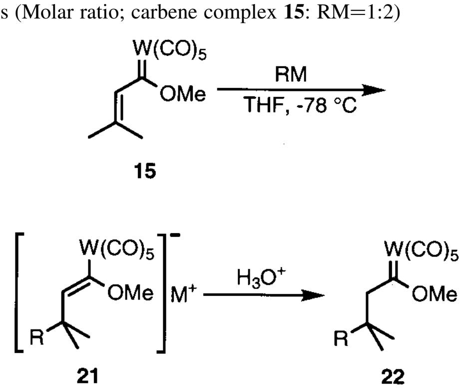
The *syn*/*anti* selectivity of the 1,4-addition of lithium enolates to α,β-unsaturated carbene complexes has been described by E. Nakamura[15a] and W.D. Wulff,[15b] previously. According to their results, it is expected that the *syn* isomers are obtained as the major products irrespective of the *s-cis* and *s-trans* conformation. Although the metal center is different (Cr vs W), we currently assign the major product for both the *E* and *Z* isomers to be *syn*.

1,4-Addition of alkylcerium reagents to α,β-unsaturated carbene complexes and iodine-oxidation of the resulting alkenyl metallic species

As described above, α-methoxy-α,β-unsaturated esters possessing carbonyl functionalities were obtained by iodine-oxidation of the alkenyl metallic species generated on 1,4-addition of lithium enolates to α,β-unsaturated carbene complexes. If we could employ other alkyl metallic reagents, this methodology would become a more general method for constructing α-methoxy-α,β-unsaturated esters. However, as yet there is no good method for the 1,4-addition of alkyl metallic species to α,β-unsaturated carbene complexes.[19]

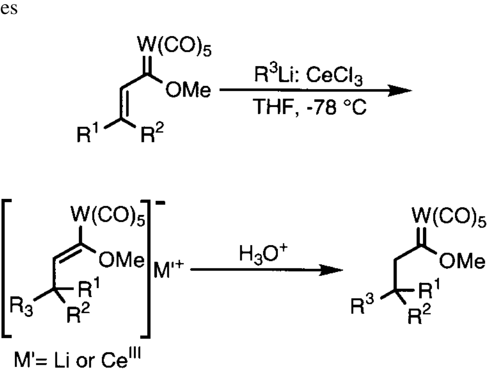
The reaction of several typical, alkyl metallic species with isobutenyl carbene complex **15** was examined. As shown in Table 3, when butyllithium, lithium dibutylcuprate or diethylzinc was employed, the desired 1,4-adduct **22** was not obtained (entries 1, 2 and 3). When butylmagnesium bromide was employed, **22** was obtained but in low yield (entry 4). Further investigation revealed that butylcerium reagent, easily prepared from butyllithium and anhydrous cerium chloride(III),[20] undergoes almost quantitative 1,4-addition (entry 5).

Table 3. 1,4-Additon of alkyl metallic species to α,β-unsaturated carbene complexes (Molar ratio; carbene complex **15**: RM=1:2)



Entry	RM	Yield (%)
1	*n*-BuLi	Complex mixture
2	*n*-Bu_2CuLi	Complex mixture
3	Et_2Zn	No reaction
4	*n*-BuMgBr	13
5	*n*-BuLi/$CeCl_3$	98

Table 4. 1,4-Addition of alkylcerium reagents to α,β-unsaturated carbene complexes

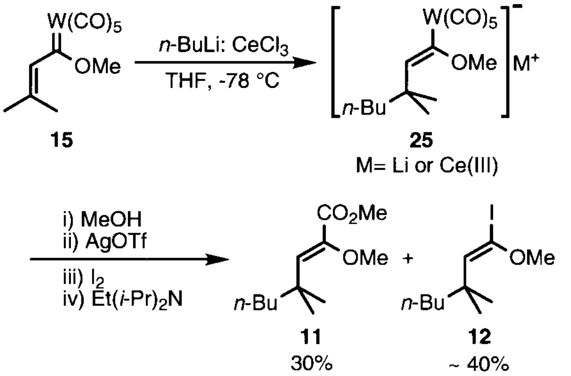


Entry	R^1	R^2	R^3Li	Yield (%)
1	Me	Me	*n*-BuLi	98
2	Me	Me	*s*-BuLi	93
3	Me	H	*n*-BuLi	94
4	Ph	H	*n*-BuLi	81
5	Me	Me	*t*-BuLi	10[a]

[a] 12% of the starting carbene complex was recovered.

The generality of the 1,4-addition of alkylcerium reagents was investigated, as summarized in Table 4. *s*-Butylcerium reagent gave a satisfactory result (entry 2). Also in the case of β-mono-substituted carbene complexes, the reaction proceeded successfully (entries 3 and 4). However, in the case of *t*-butylcerium reagent, the yield decreased to only 10% (entry 5).

Iodine-oxidation of the addition intermediate **25** derived from isobutenyl carbene complex **15** and butylcerium reagent gave the ester **11** and the iodide **12** in 30% and about 40% yield, respectively (Eq. (7)). In this case, formation of the alkenyl iodide **12** was not suppressed, even in the presence of silver triflate, because the silver cation was captured by chloride derived from cerium(III) chloride.



(7)

Conclusion

The anionic species generated by deprotonation of Fischer-type carbene complexes or by 1,4-addition of lithium enolates to α,β-unsaturated complexes are shown to behave as alkenyl metallic species on iodine-oxidation. Treatment of the anionic species with iodine in the presence of methanol and silver triflate gives various α-methoxy-α,β-unsaturated esters in good yields. Alkylcerium reagents are also found to undergo smooth 1,4-addition to α,β-unsaturated complexes.

Experimental

General information

All the reactions were carried out under an argon atmosphere. All the materials were used after purification by distillation or recrystallization. NMR spectra were recorded on a Bruker AM500 (FT, 500 MHz, ^{1}H; 125 MHz, ^{13}C), Bruker DRX500 (FT, 500 MHz, ^{1}H; 125 MHz, ^{13}C) or JEOL AL270 (FT, 270 MHz, ^{1}H; 68 MHz, ^{13}C) instrument. Chemical shifts (δ) for ^{1}H (δ=7.24 ppm) and ^{13}C (δ=77.0 ppm) are referenced to internal solvent resonances. High-resolution mass spectrometry (HRMS) was conducted with 70 eV electron impact ionization. Carbene complexes **3**, **15** and **18** were synthesized according to the literature.[21]

Iodine-oxidation of anionic species generated by deprotonation of Fischer-type carbene complexes

Methyl (*E*)-2-methoxy-2-hexenoate (5). To a THF solution (1.0 ml) of LDA, prepared from diisopropylamine (42 mg, 0.42 mmol) and 0.27 ml of a hexane solution of butyllithium (1.54 M, 0.42 mmol), was added a THF solution (1.5 ml) of butyl carbene complex **3** (148 mg, 0.35 mmol) at −78°C. The resulting solution was treated in succession with 0.30 ml of methanol, 0.50 ml of triethylamine and a THF solution (3.0 ml) of iodine (418 mg, 1.6 mmol). The mixture was stirred for 5 min at −78°C, then the reaction was quenched with pH=7 phosphate buffer and the mixture was treated with saturated aqueous sodium thiosulfate to remove excess iodine. The products were extracted with ethyl acetate (four times) and the combined extracts were dried over anhydrous sodium sulfate. Purification by preparative TLC (hexane/ethyl acetate=4:1) gave 39 mg (70%) of **5**. ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.92 (3H, t, *J*=7.5 Hz), 1.44 (2H, sextet, *J*=7.5 Hz), 2.43 (2H, q, *J*=7.5 Hz), 3.58 (3H, s), 3.79 (3H, s), 5.20 (1H, t, *J*=7.5 Hz); ^{13}C NMR (125 MHz, CDCl$_3$) δ 13.7, 23.4, 28.6, 51.8, 55.6, 115.1, 145.5, 164.0; IR (neat) 2960, 1730, 1227, 1163 cm^{-1}.

Methyl (*Z*)-2-methoxy-4,4-dimethyl-2-octenoate (11). To a THF solution (1.5 ml) of LDA, prepared from diisopropylamine (40 mg, 0.40 mmol) and 0.26 ml of a hexane solution of butyllithium (1.54 M, 0.40 mmol), was added a THF solution (1.5 ml) of butyl carbene complex **9** (160 mg, 0.33 mmol) at −78°C. The resulting solution was treated with 0.30 ml of methanol, a THF solution (2.0 ml) of silver triflate (488 mg, 1.9 mmol), a THF solution (3.0 ml) of iodine (418 mg, 1.6 mmol) and 0.50 ml of ethyl(diisopropyl)amine. The mixture was stirred for 5 min at −78°C, then the reaction was quenched with pH=7 phosphate buffer and the mixture was treated with saturated aqueous sodium thiosulfate to remove excess iodine. The products were extracted with ethyl acetate (four times) and the combined extracts were dried over anhydrous sodium sulfate. Purification by preparative TLC (hexane/ethyl acetate=4:1) gave 47 mg (67%) of **11**. ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.87 (3H, t, *J*=7.1 Hz), 1.12 (6H, s), 1.15–1.30 (4H, m), 1.37–1.41 (2H, m), 3.60 (3H, s), 3.75 (3H, s), 6.07 (1H, s); ^{13}C NMR (125 MHz, CDCl$_3$) δ 14.0, 23.4, 27.2, 27.7, 35.7, 43.0, 51.8, 59.4, 136.2, 145.0, 164.9; IR (neat) 1730, 1261, 1107, 800 cm^{-1}; HRMS Found: *m/z* 214.1546, Calcd for C$_{12}$H$_{22}$O$_3$: 214.1568.

Iodine-oxidation of alkenyl metallic species generated by 1,4-addition of lithium enolates to α,β-unsaturated carbene complexes

A typical procedure is described for the preparation of **17b** from isobutenyl carbene complex **15** and lithium enolate of cyclohexanone.

Methyl (*Z*)-2-methoxy-4-methyl-4-(2-oxocyclohexyl)-2-pentenoate (17b). To a THF solution (1.5 ml) of LDA, prepared from diisopropylamine (52 mg, 0.52 mmol) and 0.34 ml of a hexane solution of butyllithium (1.54 M, 0.52 mmol), was added a THF solution (1.0 ml) of cyclohexanone (42 mg, 0.43 mmol) at −78°C. The mixture was stirred for 10 min at −78°C, then a THF solution (1.5 ml) of isobutenyl carbene complex **15** (153 mg, 0.36 mmol) was added at −78°C. After an additional 20 min stirring, the resulting solution was treated in succession with 3.0 ml of methanol, a THF solution (2.0 ml) of silver triflate (146 mg, 0.57 mmol), a THF solution (1.5 ml) of iodine (145 mg, 0.57 mmol) and 0.50 ml of ethyl(diisopropyl)amine. The mixture was stirred for 5 min at −78°C, then the reaction was quenched with pH=7 phosphate buffer and was treated with saturated aqueous sodium thiosulfate to remove excess iodine. The products were extracted with ethyl acetate (four times) and the combined extracts were dried over anhydrous sodium sulfate. Purification by preparative TLC (hexane/ethyl acetate=4:1) gave 67 mg (75%) of **17b**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17 (3H, s), 1.18 (3H, s), 1.45 (1H, dq, *J*=5.0, 13.0 Hz), 1.54–1.67 (2H, m), 1.84–1.91 (1H, m), 1.98–2.07 (1H, m), 2.09–2.15 (1H, m), 2.22–2.29 (2H, m), 2.70 (1H, dd, *J*=5.0, 12.5 Hz), 3.58 (3H, s), 3.70 (3H, s), 6.27 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.6, 25.7, 25.9, 28.2, 29.5, 36.3, 43.6, 51.7, 59.1, 59.4, 136.5, 143.7, 164.6, 211.2; IR (neat) 2943, 1714, 1641, 1448, 1101 cm^{-1}; HRMS Found: *m*/*z* 254.1535, Calcd for $C_{14}H_{22}O_4$: 254.1518.

Methyl (*Z*)-2-methoxy-4,4,5-trimethyl-6-oxo-6-phenyl-2-hexenoate (17a). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16 (3H, d, *J*=6.8 Hz), 1.21 (3H, s), 1.22 (3H, s), 3.61 (3H, s), 3.70 (3H, s), 3.80 (1H, q, *J*=6.8 Hz), 6.27 (1H, s), 7.41 (2H, t, *J*=7.7 Hz), 7.51 (1H, t, *J*=6.9 Hz), 7.92 (2H, d, *J*=7.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 25.4, 25.9, 38.4, 47.5, 51.9, 59.3, 128.2, 128.5, 132.7, 134.1, 138.2, 145.0, 164.4, 204.0; IR (neat) 2970, 1724, 1678, 1643, 1265, 1105 cm^{-1}; HRMS Found: *m*/*z* 290.1493, Calcd for $C_{17}H_{22}O_4$: 290.1518.

Methyl (*Z*)-2-methoxy-5-methoxycarbonyl-4,4-dimethyl-2-nonenoate (17c). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (3H, t, *J*=7.3 Hz), 1.176 (3H, s), 1.182 (3H, s), 1.10–1.18 (2H, m), 1.20–1.35 (2H, m), 1.38–1.44 (1H, m), 1.60–1.70 (1H, m), 2.45 (1H, d, *J*=13.0 Hz), 3.61 (3H, s), 3.63 (3H, s), 3.75 (3H, s), 6.17 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 22.6, 24.9, 26.1, 28.0, 30.6, 37.9, 51.1, 52.0, 55.4, 59.4, 133.1, 145.5, 164.6, 175.3; IR (neat) 2953, 1732, 1645, 1437, 1267 cm^{-1}; HRMS Found:*m*/*z* 286.1794, Calcd for $C_{15}H_{26}O_5$: 286.1780.

Dimethyl (*Z*)-2-methoxy-4,4-dimethyl-5-phenyl-2-hexenedioate (17d). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (3H, s), 1.23 (3H, s), 3.54 (3H, s), 3.61 (3H, s), 3.75 (3H, s), 3.82 (1H, s), 6.29 (1H, s), 7.24–7.36 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.4, 26.2, 39.0, 51.6, 52.0, 59.3, 60.0, 127.4, 128.0, 130.0, 132.7, 135.4, 145.3, 164.5, 172.9; IR (neat) 2951, 1732, 1722, 1261, 704 cm^{-1}; HRMS Found: *m*/*z* 275.1273, Calcd for $C_{16}H_{19}O_4$ (−MeO): 275.1283.

Methyl (*Z*)-5-(*N*,*N*-diethylcarbamoyl)-2-methoxy-4,4-dimethyl-7-phenyl-2-heptenoate (17e). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.11 (3H, t, *J*=7.0 Hz), 1.16 (3H, t, *J*=7.0 Hz), 1.21 (3H, s), 1.23 (3H, s), 1.67–1.73 (1H, m), 2.12–2.20 (1H, m), 2.33–2.39 (1H, m), 2.50–2.56 (1H, m), 2.90 (1H, dd, *J*=2.8, 11.2 Hz), 3.18–3.27 (2H, m), 3.52–3.63 (2H, m), 3.61 (3H, s), 3.74 (3H, s), 6.27 (1H, s) 7.12–7.15 (3H, m), 7.22–7.25 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.8, 14.6, 25.4, 25.7, 31.4, 34.7, 38.7, 40.1, 42.1, 48.1, 51.9, 59.2, 125.8, 128.3, 134.8, 141.9, 144.9, 164.5, 172.9; IR (neat) 2978, 1728, 1635, 1263, 702 cm^{-1}; HRMS Found: *m*/*z* 375.2432, Calcd for $C_{22}H_{33}NO_4$: 375.2410.

Methyl 2-methoxy-5-methyl-6-oxo-4,6-diphenyl-2-hexenoate (20a). The product was obtained as a mixture of four isomers. See the text for the assignment of their structure. The ratio was determined by integration of the distinguishable peaks, which are shown for the minor isomers. The ratio of the isomers is (***Z***, ***syn***)/(***Z***, ***anti***)/(***E***, ***syn***)/(***E***, ***anti***)=50:28:22:trace. ^{1}H NMR (500 MHz, $CDCl_3$) (***Z***, ***syn***) δ 1.04 (3H, d, *J*=7.0 Hz), 3.60 (3H, s), 3.63 (3H, s), 3.89–3.97 (1H, m), 4.27 (1H, t, *J*=10.0 Hz), 6.36 (1H, d, *J*=10.0 Hz); (***Z***, ***anti***) δ 3.61 (3H, s), 3.75 (3H, s), 6.43 (1H, d, *J*=11.0 Hz); (***E***, ***syn***) δ 3.32 (3H, s), 3.81 (3H, s), 5.30 (1H, d, *J*=10.5 Hz); (***E***, ***anti***) δ 3.62 (3H, s), 3.73 (3H, s), 5.34 (1H, d, *J*=11.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.6, 16.4, 16.5, 16.6, 44.3, 44.5, 45.1, 45.45, 45.52, 46.8, 46.9, 51.7, 51.8, 52.0, 52.1, 55.2, 55.6, 59.7, 59.9, 113.6, 114.4, 125.0, 126.4, 126.6, 126.9, 127.7, 127.8, 128.0, 128.1, 128.2, 128.3, 128.5, 128.6, 128.65, 128.74, 132.7, 133.0, 136.7, 136.8, 137.7, 137.8, 141.0, 141.7, 142.5, 145.4, 145.7, 146.3, 163.4, 164.1, 202.6, 202.7, 203.5; IR (neat) 1726, 1684, 1645, 970, 702 cm^{-1}; HRMS Found: *m*/*z* 338.1530, Calcd for $C_{16}H_{20}O_4$: 338.1518.

Methyl 2-methoxy-4,5-dimethyl-6-oxo-6-phenyl-2-hexenoate (20b). The product was obtained as a mixture of four isomers. See the text for the assignment of their structure. The ratio was determined by integration of the distinguishable peaks, which are shown for the minor isomers. The ratio of the isomers is (***Z***, ***syn***)/(***Z***, ***anti***)/(***E***, ***syn***)/(***E***, ***anti***)=80:9:9:2. ^{1}H NMR (500 MHz, $CDCl_3$) δ (***Z***, ***syn***) 0.96 (3H, d, *J*=7.0 Hz), 1.15 (3H, d, *J*=7.0 Hz), 3.15–3.22 (2H, m), 3.67 (3H, s), 3.71 (3H, s), 7.44 (2H, t, *J*=7.5 Hz), 7.52 (1H, t, *J*=7.5 Hz), 7.96 (2H, d, *J*=7.5 Hz); (***Z***, ***anti***) 3.56 (3H, s), 3.75 (3H, s), 6.08 (1H, d, *J*=10.5 Hz); (***E***, ***syn***) 3.44 (3H, s), 3.77 (3H, s), 5.08 (1H, d, *J*=9.6 Hz); (***E***, ***anti***) 4.91 (1H, d, *J*=10.5); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.9, 13.4, 15.9, 32.8, 33.6, 44.9, 45.7, 51.9, 52.1, 55.4, 59.9, 117.0, 128.2, 128.3, 128.4, 128.57, 128.62, 128.7, 131.8, 132.8, 132.9, 136.5, 145.2, 164.1, 202.8; IR (neat) 2933, 1722, 1680, 1450, 1240 cm^{-1}; HRMS Found:*m*/*z* 276.1375, Calcd for $C_{16}H_{20}O_4$: 276.1362.

Methyl 4-(2-oxocyclohexyl)-2-methoxy-4-phenyl-2-butenoate (20c). The product was obtained as a mixture of four isomers. See the text for the assignment of their structure. The ratio was determined by integration of the distinguishable peaks, which are shown for the minor isomers. The ratio of the isomers is (***Z***, ***syn***)/(***Z***, ***anti***)/(***E***, ***syn***)/(***E***, ***anti***)=81:6:13:trace. ^{1}H NMR (500 MHz, $CDCl_3$) (***Z***, ***syn***) δ 1.32–1.40 (1H, m), 1.52–1.58 (1H, m), 1.70–1.80 (3H, m), 1.88–1.96 (1H, m), 2.28–2.35 (1H, m), 2.39–2.48 (1H, m), 2.74–2.82 (1H, m), 3.60 (3H, s), 3.69 (3H, s), 4.19 (1H, t, *J*=9.9 Hz), 6.37 (1H, d, *J*=9.9 Hz), 7.15–7.20 (2H, m), 7.22–7.30 (3H, m); (***Z***, ***anti***) δ 6.30 (1H, d, *J*=10.6 Hz); (***E***, ***syn***) δ 3.54 (3H, s), 3.78 (3H, s), 5.35 (1H, d, *J*=10.3 Hz); (***E***, ***anti***) δ 5.30 (d, *J*=11.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.5, 23.9, 28.0, 28.2, 30.8, 31.8, 41.0, 41.5, 41.8, 42.1, 51.8, 52.0, 55.6, 55.9, 57.1, 59.5, 115.8, 126.6, 126.8, 128.3, 128.67, 128.73, 129.5, 141.2, 142.4, 145.18, 145.21, 163.8, 164.1, 211.8, 212.9; IR (neat) 2931, 1720, 1448, 1435, 1225 cm^{-1}; HRMS Found: *m*/*z* 302.1505, Calcd for $C_{18}H_{22}O_4$: 302.1518.

Methyl 4-(2-oxocyclohexyl)-2-methoxy-2-pentenoate (20d). The product was obtained as a mixture of four isomers. See the text for the assignment of their structure. The ratio was determined by integration of the distinguishable peaks, which are shown for the minor isomers. The ratio of the isomers is (***Z***, ***syn***)/(***Z***, ***anti***)/(***E***, ***syn***)/(***E***, ***anti***)=54:16:30:trace. ^1H NMR (500 MHz, $CDCl_3$) (***Z***, ***syn***) δ 1.03 (3H, d, *J*=7.0 Hz), 1.50–1.70 (4H, m), 1.80–2.10 (2H, m), 2.25–2.40 (2H, m), 3.09–3.18 (1H, m), 3.64 (3H, s), 3.73 (3H, s), 6.19 (1H, d, *J*=10.0 Hz); (***Z***, ***anti***) δ 3.65 (3H, s), 3.75 (3H, s), 6.04 (1H, d, *J*=10.4 Hz); (***E***, ***syn***) δ 3.53 (3H, s), 3.77 (3H, s), 5.15 (1H, d, *J*=10.3 Hz); (***E***, ***anti***) δ 3.56 (3H, s), 3.79 (3H, s), 5.04 (1H, d, *J*=10.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.0, 18.8, 19.0, 23.8, 24.6, 27.6, 28.0, 29.88, 29.93, 30.1, 30.5, 31.2, 31.8, 41.8, 41.9, 42.1, 51.9, 55.2, 55.5, 56.5, 56.8, 59.8, 117.8, 118.3, 144.9, 163.8, 212.4; IR (neat) 2937, 1724, 1709, 1448, 1437, 1234 cm^{-1}; HRMS Found: *m*/*z* 240.1372, Calcd for $C_{13}H_{20}O_4$: 240.1362.

1,4-Addition of alkylcerium reagents to α,β-unsaturated carbene complexes

A typical procedure is described for the preparation of **9**.

Pentacarbonyl(1-methoxy-3,3-dimethylheptylidene)-tungsten(0) (9). To a THF slurry (5.0 ml) of anhydrous cerium trichloride (520 mg as heptahydrate), prepared according to the literature,[20] was added 0.50 ml of a hexane solution of butyllithium (1.64 M, 0.82 mmol) at −78°C. After 10 min at −78°C, a THF solution (1.0 ml) of carbene complex **15** (183 mg, 0.43 mmol) was added and the mixture was stirred for 15 min. The reaction was quenched with pH=7 phosphate buffer and the product was extracted with ethyl acetate (four times). The combined extracts were dried over sodium sulfate, and purified by preparative TLC (hexane/ethyl acetate=12:1) to give 202 mg (98%) of **9**. ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (3H, t, *J*=7.2 Hz), 0.95 (6H, s), 1.13–1.21 (2H, m), 1.23–1.30 (4H, m), 3.20 (2H, s), 4.62 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 23.4, 26.6, 28.3, 37.5, 43.4, 70.3, 74.9, 197.6, 203.4, 342.3; IR (neat) 2956, 2069, 1917, 1456, 1250 cm^{-1}; HRMS Found: *m*/*z* 480.0744, Calcd for $C_{15}H_{20}O_6{}^{184}W$: 480.0769.

Pentacarbonyl(1-methoxy-3,3,4-trimethylhexylidene)-tungsten(0). ^1H NMR (500 MHz, $CDCl_3$) δ 0.81 (3H, d, *J*=6.8 Hz), 0.88–0.91 (3H, m), 0.93 (6H, s), 1.15–1.22 (1H, m), 1.49–1.55 (1H, m), 3.21 (1H, d, *J*=15.0 Hz), 3.28 (1H, d, *J*=15.0 Hz), 4.62 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.2, 13.4, 24.0, 25.4, 25.6, 40.6, 45.4, 70.4, 73.6, 197.5, 203.4, 342.9; IR (neat) 2970, 2069, 1917, 1450, 1257 cm^{-1}; HRMS Found: *m*/*z* 480.0783, Calcd for $C_{15}H_{20}O_6{}^{184}W$: 480.0769.

Pentacarbonyl(1-methoxy-3,3,4,4-tetramethylpentylidene)tungsten(0). ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (9H, s), 0.95 (6H, s), 3.30 (2H, s), 4.63 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.9, 25.4, 37.2, 42.6, 70.4, 70.8, 197.6, 203.4, 344.9; IR (neat) 2067, 1911, 1589, 1450, 1259 cm^{-1}; HRMS Found: *m*/*z* 480.0762, Calcd for $C_{15}H_{20}O_6{}^{184}W$: 480.0769.

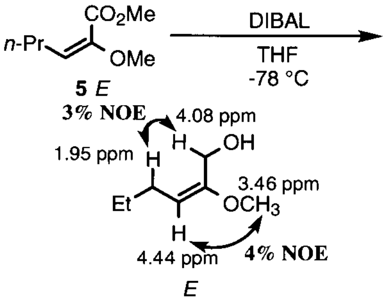
Pentacarbonyl(1-methoxy-3-methylheptylidene)tungsten(0). ^1H NMR (500 MHz, $CDCl_3$) δ 0.80–0.90 (6H, m), 1.12–1.34 (6H, m), 2.00–2.15 (2H, m), 3.06–3.12 (2H, m), 4.61 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 19.9, 22.7, 29.3, 32.3, 36.9, 70.4, 72.3, 197.4, 203.4, 339.4; IR (neat) 2960, 2065, 1960, 1455, 1255, 595 cm^{-1}; HRMS Found: *m*/*z* 466.0609, Calcd for $C_{14}H_{18}O_6{}^{184}W$: 466.0613.

Pentacarbonyl(1-methoxy-3-phenylheptylidene)tungsten(0). ^1H NMR (500 MHz, $CDCl_3$) δ 0.81 (6H, s), 1.00–1.18 (2H, m), 1.18–1.35 (2H, m), 1.49–1.66 (2H, m), 3.10–3.18 (1H, m), 3.45 (1H, dd, *J*=8.0, 14.5 Hz), 3.51 (1H, dd, *J*=7.0, 15.0 Hz), 4.52 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 22.4, 29.6, 35.8, 43.7, 70.1, 71.9, 126.3, 127.4, 128.4, 143.9, 197.2, 203.1, 336.7; IR (neat) 2931, 2069, 1920, 1450, 1265 cm^{-1}; HRMS Found: *m*/*z* 528.0743, Calcd for $C_{19}H_{20}O_6{}^{184}W$: 528.0769.

References

1. Fischer, E. O.; Maasböl, A. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 580.
2. For review, see: (a) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587. (b) Brown, F. J. *Prog. Inorg. Chem.* **1980**, *27*, 1. (c) Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Flemming, I., Eds.; Pergamon: New York, 1991; Vol. 5, p 1065. (d) 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. (e) Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: New York, 1995; Vol. 12, p 387. (f) Hegedus, L. S. *Tetrahedron*, **1997**, *53*, 4105. (g) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 644.
3. For example, the *p*Ka of the methyl carbene complex of chromium (R=H in Eq. (1)) is 8 (in THF) and 12 (in water). See: Casey, C. P.; Anderson, R. L. *J. Am. Chem. Soc.* **1974**, *96*, 1230; Gandler, J. R.; Bernasconi, C. F.; Sun, W. *Organometallics* **1989**, *8*, 2282.
4. For alkylation, see: Xu, Y.-C.; Wulff, W. D. *J. Org. Chem.* **1987**, *52*, 3263. For aldol-type addition, see: Wulff, W. D.; Gilbertson, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 503; Aumann, R.; Heinen, H. *Chem. Ber.* **1987**, *120*, 537.
5. (a) For example, see: Chan, K. S.; Yeung, M. L.; Chan, W.-K.; Wang, R.-J.; Mak, T. C. W. *J. Org. Chem.* **1995**, *60*, 1741. (b) Casey, C. P.; Brunsvold, W. R. *J. Organomet. Chem.* **1975**, *102*, 175.
6. For example, see: Wulff, W. D.; Yang, D.C. *J. Am. Chem. Soc.* **1983**, *105*, 6726.
7. Iwasawa, N.; Maeyama, K.; Saitou, M. *J. Am. Chem. Soc.* **1997**, *119*, 1486.
8. Iwasawa, N.; Ochiai, T.; Maeyama, K. *J. Org. Chem.* **1998**, *63*, 3164. See also: Iwasawa, N.; Ochiai, T.; Maeyama, K. *Organometallics* **1997**, *16*, 5137.
9. Iwasawa, N.; Fuchibe, K. *Chem. Lett.* **1998**, 1149.
10. When butyllithium was employed as base, it partly underwent nucleophilic addition to the carbene carbon to yield 5-nonanone in about 40% yield after iodine-oxidation.
11. The stereochemistry of the double bond of the unsaturated

ester **5** was determined by the measurement of differential NOE of the allylic alcohol obtained by DIBAL reduction of **5**.



12. It should be noted that the anionic species **4** is not protonated by methanol under these conditions.

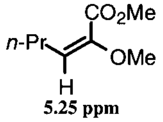
13. The stereochemistry of the ester **11** was determined by the same procedure as for **5**.[11]

14. This iodide **12** was unstable and its stereochemistry was determined immediately after separation by preparative TLC. The stereochemistry of alkenyl iodide **12** was determined by the coupling constant (6.9 Hz) between the vicinal olefinic protons of the alkenyl ether prepared by lithiation and protonation of **12**.

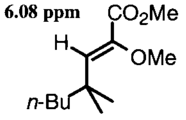
15. (a) Nakamura, E.; Tanaka, K.; Fujimura, T.; Aoki, S.; Willard, P. G. *J. Am. Chem. Soc.* **1993**, *115*, 9015. (b) Shi, Y.; Wulff, W. D. *J. Org. Chem.* **1994**, *59*, 5122. (c) Casey, C. P.; Brunsvold, W. R. *Inorg. Chem.* **1977**, *16*, 391.

16. The stereochemistry of the ester **17d** was determined by the same procedure as for **5**.[11]

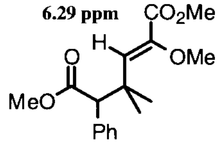
17. The stereochemistries of the other products in Table 1 were all assigned to be *Z* from the chemical shifts of the olefinic protons which were all distributed between 6.17–6.29 ppm. These values are close to that of **11** (6.08 ppm, established to have *Z* configuration), and far from the value of **5** (5.25 ppm, established to have *E* configuration).



5 *E*



11 *Z*



17d *Z*

18. The stereochemistries of the double bond were determined in a similar manner to the cases of isobutenyl carbene complex **15**. All the products consist of 4 isomers. Two of them have olefinic protons between 4.91–5.39 ppm, and the others are distributed between 6.04–6.43 ppm. The former are assigned to have *E* configuration, and the latter to have *Z* configuration.

19. There are several specific examples of the 1,4-addition of organolithium reagents to α,β-unsaturated carbene complexes, see: Barluenga, J.; Trabanco, A. A.; Flórez, J.; García-Granda, S.; Martín, E. *J. Am. Chem. Soc.* **1996**, *118*, 13099; Barluenga, J.; Montserrat, J. M.; García-Granda, S.; Martín, E. *Chem. Eur. J.* **1995**, *1*, 236, and references are cited therein.

20. Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392.

21. Carbene complexes **3**, **15** and **18** were synthesized by the reaction of the corresponding alkyl or alkenyllithiums with W(CO)$_6$, followed by methylation using methyl triflate. See: Wulff, W. D.; Bauta, W. E.; Kaesler, R. W.; Lankford, P. J.; Miller, R. A.; Murray, C. K.; Yang, D. C. *J. Am. Chem. Soc.* **1990**, *112*, 3642.