Synthesis of α-Methoxy-α,β-unsaturated Esters by Iodine-oxidation of the Anions of Fischer-type Carbene Complexes

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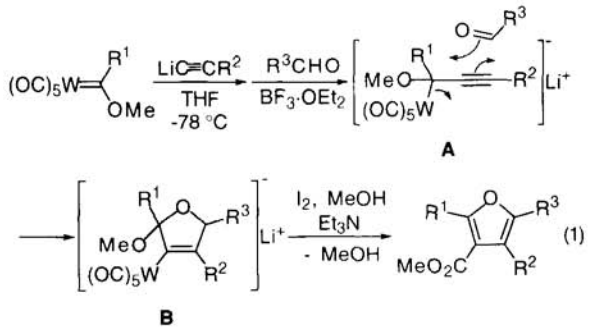
α-Methoxy vinyl tungsten species, generated by the deprotonation reaction of Fischer-type carbene complexes or by the Michael addition of lithium enolates to α,β-unsaturated carbene complexes, were found to give α-methoxy-α,β-unsaturated esters in good yields by iodine-oxidation in the presence of silver triflate.

Recently, Fischer-type carbene complexes have attracted much interest as useful reagents for organic synthesis.[1] One of the most extensively studied is the use of Fischer-type carbene complexes as ester-equivalents.[2] For example, α-proton of the carbene carbon is highly acidic and the deprotonated anionic species react with various electrophiles to give α-substituted carbene complexes, which can be further oxidized to the corresponding esters in good yields.[3]

In previous papers,[4] we have reported that vinyl tungsten species **B** were produced via 1,2-migration of pentacarbonyltungsten moiety when propargyl tungsten species **A**, generated by the addition of alkynyllithiums to Fischer-type carbene complexes, were reacted with electrophiles such as aldehydes. These vinyl tungsten species **B** were further oxidized with iodine to give methoxycarbonylated products in good yields (Eq. 1). In this communication, we would like to report that the anions, which were generated by the deprotonation reaction of Fischer-type carbene complexes or by the Michael addition of lithium enolates to α,β-unsaturated carbene complexes, could be employed for carbon-carbon bond formation as vinylmetallic species[5] on iodine-oxidation.[6]



We first examined iodine-oxidation of the anion produced by the deprotonation reaction of a Fischer-type carbene complex. Pentacarbonyl(1-methoxypentylidene)tungsten(0) **1** was treated with lithium diisopropylamide at -78 °C and the produced anionic species was treated with iodine in the presence of triethylamine followed by addition of methanol under argon atmosphere. Reductive work-up with aqueous sodium thiosulfate gave desired α-methoxy-α,β-unsaturated ester **2**[7] in 21% yield (Table 1). Examination of the reaction conditions revealed that the order of the addition of the reagents was crucial for the optimal yield of **2** and that **2** was obtained in 70% yield by adding methanol before the treatment with iodine. It is noteworthy that methanol does not protonate the anionic species.

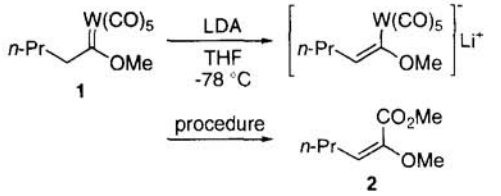
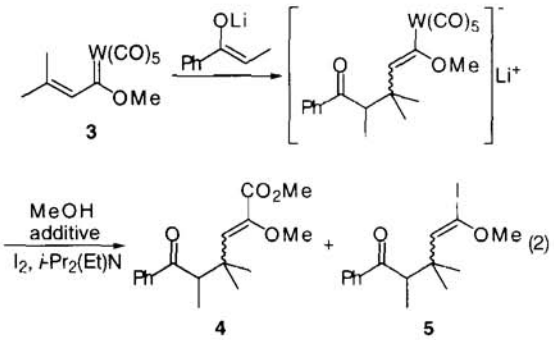


Table 1. Iodine-oxidation of the vinyl tungsten species produced by the deprotonation reaction of **1**

procedure	yield/ %
i) I_2, Et_3N ii) MeOH	21
i)MeOH ii) I_2, Et_3N	70

Next, we examined iodine-oxidation of the same kind of vinyl tungsten species produced by the Michael addition of lithium enolates to α,β-unsaturated carbene complexes.[8] After the lithium enolate derived from propiophenone was added to pentacarbonyl(1-methoxyisopentenylidene)tungsten(0) **3**, the produced anionic species was oxidized by the same procedure as described above. However, the desired α-methoxy-α,β-unsaturated ester **4**[9] was obtained in low yield and iodide **5**[9] was obtained as a major product. Further examination of the reaction conditions revealed that when silver triflate was added before the treatment with iodine we could obtain the desired unsaturated ester **4** in 79% yield as shown in Eq. 2.



additive	yield of **4**/ %	yield of **5**/ %
none	12	35
AgOTf	79	0

Finally, we examined the generality of this reaction. As shown in Table 2, various lithium enolates and Fischer-type carbene complexes could be employed for this reaction and α-methoxy-α,β-unsaturated esters were obtained in good yields. In particular, enolates derived from esters or an amide could also be employed and the corresponding dicarboxyl compounds were obtained in good yields.

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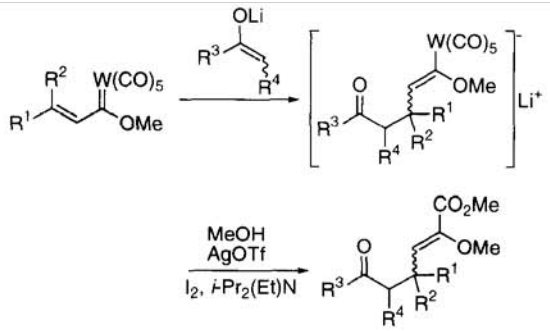

Table 2. Iodine-oxidation of the vinyl tungsten species produced by the Michael addition of lithium enolates to α,β-unsaturated carbene complexes[a]

R^1	R^2	R^3	R^4	yield/ %
Me	Me	Ph	Me	79[b]
Me	Me	-$(CH_2)_4$-		75[b]
Me	Me	OMe	Ph	62[b]
Me	Me	OMe	*n*-Bu	65[b]
Me	Me	NEt_2	$(CH_2)_2Ph$	43[b]
Me	H	-$(CH_2)_4$-		88[c]
Ph	H	Ph	Me	79[d]
Ph	H	-$(CH_2)_4$-		59[e]

[a]Molar ratio; carbene complex : enolate : AgOTf : iodine = 1 : 1.3 : 1.7 : 1.6. Methanol and diisopropylethylamine were used in large excess. [b]The product was obtained as a single isomer. Geometry of the double bond was not determined. [c]The product was obtained as a mixture of three major isomers in a ratio of 10: 6: 3. [d]The product was obtained as a mixture of three major isomers in a ratio of 16: 9: 7. [e]Two major isomers were obtained in 41% and 18% yield, respectively. Both products contained a trace amount of other isomers.

A typical procedure is described for the addition of lithium enolate of cyclohexanone to pentacarbonyl(1-methoxy-2-butenylidene)tungsten(0), followed by the iodine-oxidation: To a THF solution (1 ml) of LDA, prepared from diisopropylamine (29 mg, 0.29 mmol) and butyllithium (1.54 M hexane solution, 0.19 ml, 0.29 mmol), was added a THF solution (1.5 ml) of cyclohexanone (30 mg, 0.31 mmol) at -78 °C. To the mixture was added a THF solution (1.5 ml) of pentacarbonyl(1-methoxy-2-butenylidene)tungsten(0) (95 mg, 0.23 mmol) and the mixture was further stirred for 20 min at -78 °C. Then methanol (3 ml), a THF solution (2 ml) of AgOTf (101 mg, 0.39 mmol), a THF solution (2 ml) of iodine (95 mg, 0.37 mmol), and a THF solution (0.5 ml) of diisopropylethylamine (359 mg, 2.8 mmol) was successively added to the mixture. After the mixture was stirred for 5 min at -78 °C, the reaction was quenched with saturated $Na_2S_2O_3$ solution and the organic materials were extracted with ethyl acetate three times. The combined extracts were dried over Na_2SO_4 and then evaporated to give a residue, which was purified by silica-gel TLC (Hexane : ethyl acetate = 2 : 1) to give an isomeric mixture of products (49 mg, 88% yield).

In summary, the anionic tungsten species, generated by the deprotonation reaction of Fischer-type carbene complexes or by the Michael addition of lithium enolates to α,β-unsaturated carbene complexes could be used as vinyl tungsten species and gave α-methoxy-α,β-unsaturated esters in good yields by iodine-oxidation.

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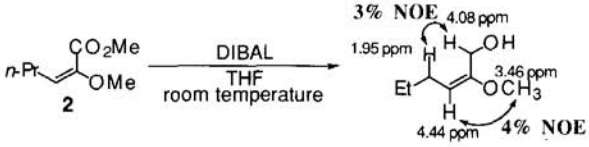
7 **2** was obtained as a single isomer. The geometry of the double bond of **2** was determined to be *E* by the measurement of the differential NOE of the reduced allylic alcohol.



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9 **4** and **5** were obtained as single isomers, respectively. The geometries of these compounds were not determined.