

Carbon-Carbon bond forming reactions of organotransition metal enolate complexes¹

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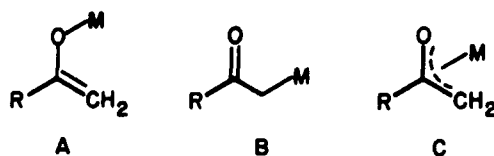
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Abstract - Metal enolates play an important role in stereoselective organic synthesis. Their chemistry is affected profoundly by the metal counterion associated with the enolate fragment. In order to expand the potential of replacing main group with transition metal moieties in such species, methods have been developed for the synthesis of a number of stable, characterizable "late" transition metal η^1 -(C)-enolate complexes having the general structure L_nM-CH_2COR ($M = Mo, W, Re$). The chemistry of these materials (e.g., functional transformations of the organic carbonyl group, transfer of the enolate moiety to organic substrates such as aldehydes and alkynes) has been investigated. The scope and mechanisms of the enolate reactions will be discussed in detail.

The reaction of organic enolates with carbon electrophiles (e.g., alkyl halides, organic carbonyl compounds) gives rise to compounds containing new carbon-carbon bonds; reaction with heteroatom electrophiles results in the formation of oxidized products.² There has been much interest recently in developing methods for carrying out these transformations with high stereoselectivity.³

Historically, most enolate research has focused on salts involving alkali metal anions. More recently, research efforts have been extended to enolates associated with organic cations, main group metals, and transition metals. In the transition metal area, enolates involving the so-called "early" metals (to the left of chromium, molybdenum and tungsten) have seen extensive investigation;⁴ in general these complexes have O-bonded structures A in Scheme 1. This paper describes the synthesis and chemistry of middle- and late transition metal

Scheme 1



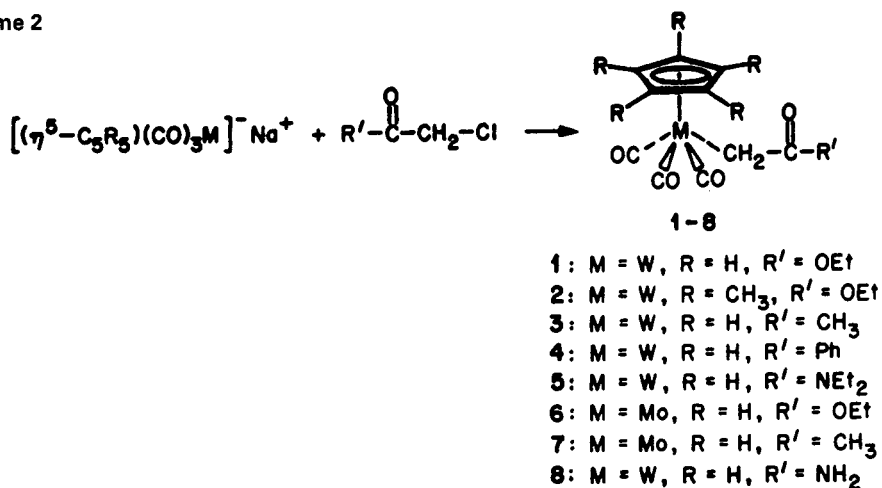
enolates, which have seen less investigation. It was our hope that such species would be more likely to have C-bound structure B, and also to react with both electrophilic and non-electrophilic species (e.g., by insertion rather than nucleophile-electrophile mechanisms).

SYNTHESIS, CHARACTERIZATION AND FUNCTIONAL GROUP TRANSFORMATIONS OF TUNGSTEN AND MOLYBDENUM ENOLATES

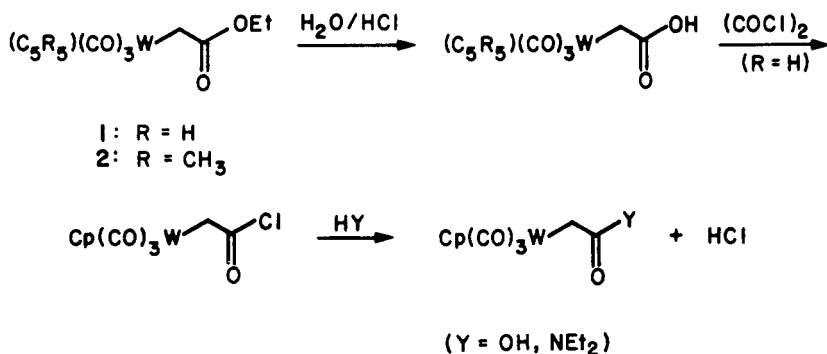
The well-known nucleophilic anionic metal salts⁵ $Na[(\eta^5-C_5R_5)(CO)_3M]$ ($M = Mo, W; R=H, Me$), on treatment with α -chloroketones and esters, provide good yields of enolates 1 - 8, as shown in Scheme 2. These are thermally stable complexes that may be isolated by conventional chromatographic and recrystallization methods; they have been characterized fully by elemental analysis and spectroscopic techniques. Preparation of these materials on a multi-gram scale in a one-pot procedure is possible by treatment of $W(CO)_6$ or $Mo(CO)_6$ with $NaCp$, followed by addition of the α -chlorocarbonyl compound to the resulting metal anion solution.

The stability of the tungsten-carbon bond in tungsten ester enolates, first suggested several years ago by the work of Green and his coworkers⁶, has allowed us to carry out a wide range of transformations on the organic carbonyl group. Thus the reactions shown in Scheme 3 proceed in good yield, and lead to stable tungsten enolates containing ester, amide and even carboxylic acid and acid chloride functionality.

Scheme 2



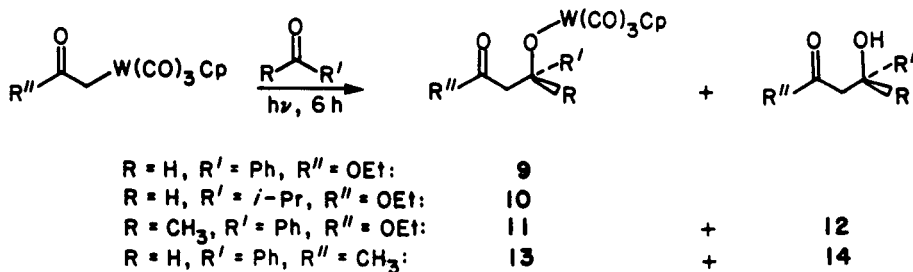
Scheme 3



ALDOL REACTIONS OF TUNGSTEN ENOLATE 1

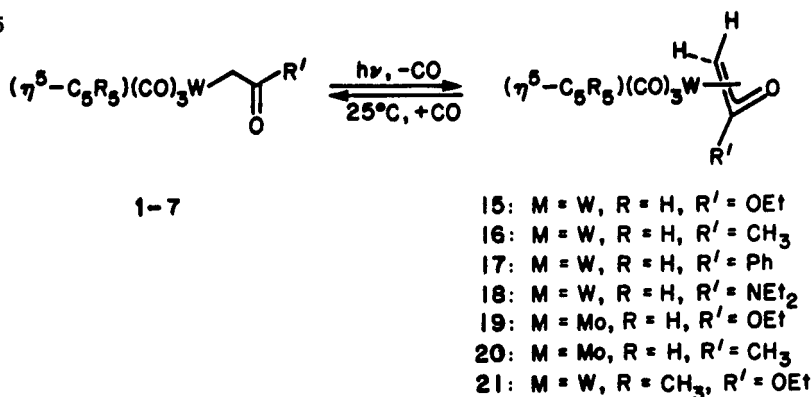
Heating enolate complexes **1-8** with aldehydes in various solvents gives complex mixtures of products. More encouragingly, irradiation of tungsten ester complex **1** in the presence of benzaldehyde led to the formation of clean solutions of a single new product. This material is very sensitive and has resisted isolation. However, it has been characterized extensively by spectroscopic techniques, and these have allowed its identification as the tungsten aldolate complex **9** (Scheme 4). Thus, enolate complex **1** is capable of undergoing aldol-type condensation in good yield. In a reaction analogous to that observed with benzaldehyde, irradiation of **1** with isobutyraldehyde gave solutions containing tungsten aldolate **10** in 87% yield by NMR. Once again, this material was too sensitive to isolate. The corresponding reaction with acetophenone resulted in a mixture of **11** and the free aldol **12** (5:3 ratio) in 78% combined yield (NMR). Similarly, irradiation of tungsten ketone enolate **3** in the presence of benzaldehyde gave a mixture of **13** and **14** (3:1, respectively) by NMR, that accounted for a 60-65% combined yield. All the tungsten aldolates appear to decompose in modest yield to free aldol in solution (although at different rates); this is consistent with a decomposition route involving metal-oxygen bond cleavage followed by hydrogen atom or proton transfer from a second molecule of metal-bound aldolate.

Scheme 4



In order to obtain information about the detailed course of this transformation, the photoreaction was performed in the absence of benzaldehyde. Irradiation of several of the tungsten enolates shown in Scheme 2 resulted in the loss of one equivalent of CO. Spectroscopic monitoring demonstrated that the reaction cleanly generates a new class of complexes, which once again are too sensitive for isolation and full characterization. However, their spectroscopic and chemical properties are consistent with their assignment⁷ as η^3 -oxaallyl complexes (15-21). Using low temperatures and uranium glass filters, the conversion to product is quite good; a side reaction involving tungsten-carbon bond cleavage, leading to the corresponding organic carbonyl compounds (e.g., ethyl acetate in the case of **1**), can be reduced to <5% of the overall process. Alternatively, treatment of **1** with Me_3NO cleanly removes one CO ligand and generates **15** without the use of light.⁸

Scheme 5

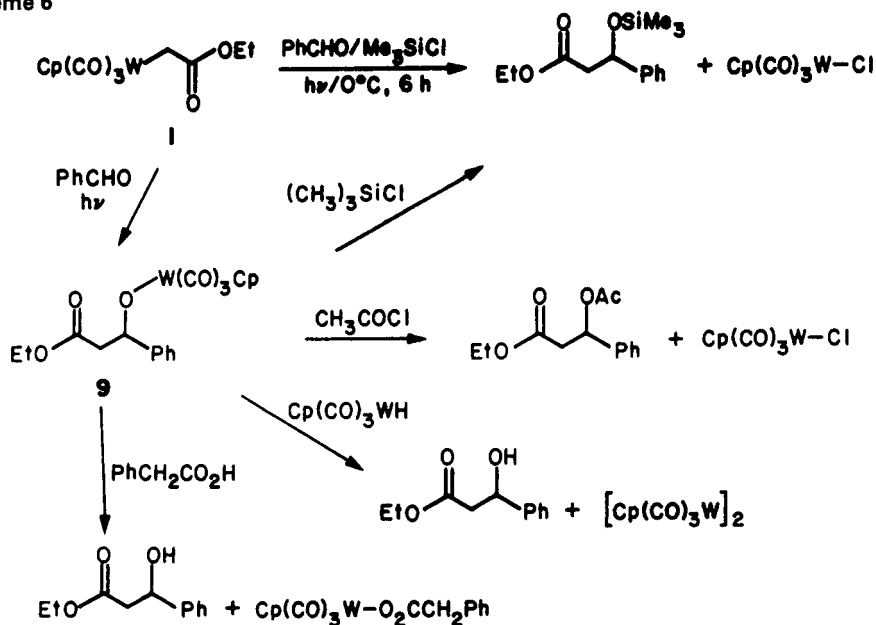


The chemistry of this material clearly supports its structural assignment. For example, treatment of **15** with CO regenerates starting η^1 -enolate **1**, and treatment of solutions of **15** with triphenylphosphine leads initially to the *cis*-phosphine substituted analogue of **1** in 82% isolated yield. R_2N -substituted oxaallyl complex **18** (best prepared by reaction of tungsten amide **5** with Me_3NO in acetonitrile) is substantially more stable than its OEt-substituted relative **15**. This nitrogen-containing complex has been isolated as a crystalline solid, and characterized by X-ray diffraction.

The observations summarized above suggest strongly that the oxaallyl complex **15** is an intermediate in the photo-aldol reaction that occurs between η^1 -enolate complex **1** and aldehydes.

The sensitivity of the tungsten aldolates toward decomposition emphasized the need to remove the metal *in situ* before M-O bond cleavage occurs. Several reagents were found to be effective in accomplishing this; the reactions explored are summarized in Scheme 6. Preliminary NMR experiments indicated that the reactions of acetyl chloride, trimethylsilyl chloride, acetic acid and $\text{Cp}(\text{CO})_3\text{W-H}$ with **9** gave high conversions to the cleavage products shown in Scheme 6 in hours at room temperature. In the reaction with trimethylsilyl chloride, $\text{Cp}(\text{CO})_3\text{W-Cl}$ was recovered in 85% yield, and a mixture of silylated and unsilylated organic aldol product was obtained after chromatography in 47% yield.

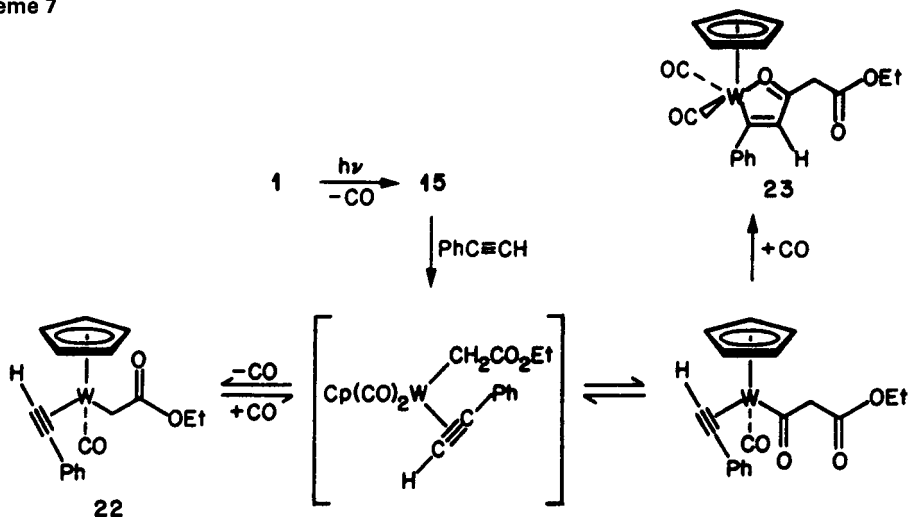
Scheme 6



ALKYNE INSERTION REACTIONS OF TUNGSTEN ENOLATES

In order to examine the reactivity of tungsten enolates with less electrophilic substrates, the reaction of **1** with alkynes was investigated. Insertion of alkynes into conventional metal-carbon bonds has been studied in detail for several alkyl and acyl complexes⁹. Irradiation of a benzene-*d*₆ solution of phenylacetylene and tungsten enolate **1** in a sealed NMR tube leads to two major products: the alkyne-substituted enolate **22** (42%) and the insertion product **23** (42%). The latter complex was crystallized and its structure determined by X-ray diffraction. These reactions closely follow those observed earlier by Alt^{9b} and Davidson^{9c-d}. A proposed mechanism for the overall CO/alkyne insertion process is suggested in Scheme 7.

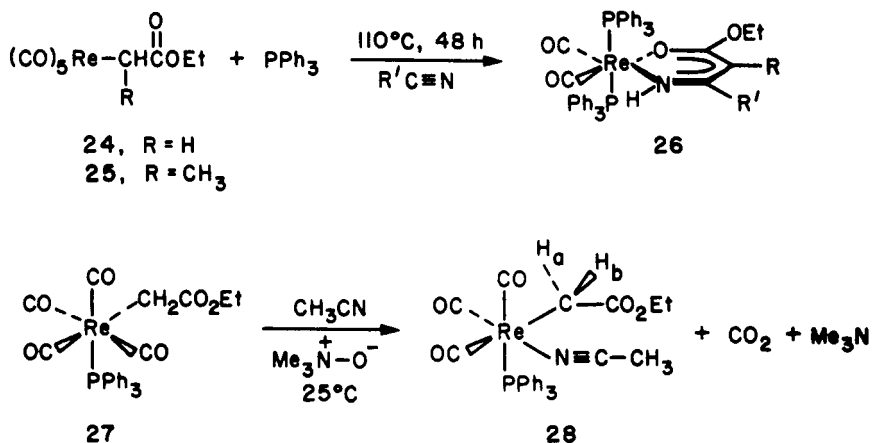
Scheme 7



SYNTHESIS AND CHEMISTRY OF RHENIUM ENOLATES

In analogy to the chemistry of the tungsten and molybdenum systems described above, Na[Re(CO)₅] reacts with organic α -chloro- and α -methanesulfonate compounds to give both primary and secondary octahedral rhenium enolate complexes (e.g., **24** and **25**, Scheme 8). These materials are remarkably stable; for example, solutions of ester enolate **24** can be heated for days in a sealed tube without significant decomposition. However, upon heating **24** at 110 °C with PPh₃ in acetonitrile solution for 48 hours, a new material crystallized from the solution. Its structure, determined by X-ray diffraction, is that of **26** (R = H, R' = CH₃) shown in Scheme 8; thus the reaction producing this material involves condensation of the rhenium-bound enolate fragment with a molecule of acetonitrile. The reaction appears to be general: similar reactions proceed in reasonable yield using the secondary enolate **25** and other organic nitriles (e.g., PhCN, EtCN, *i*PrCN).

Scheme 8

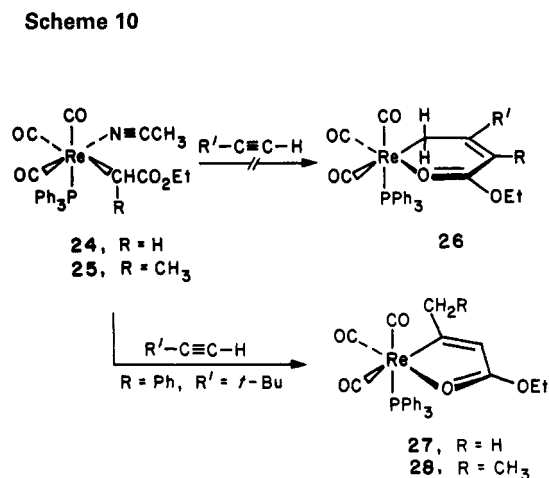
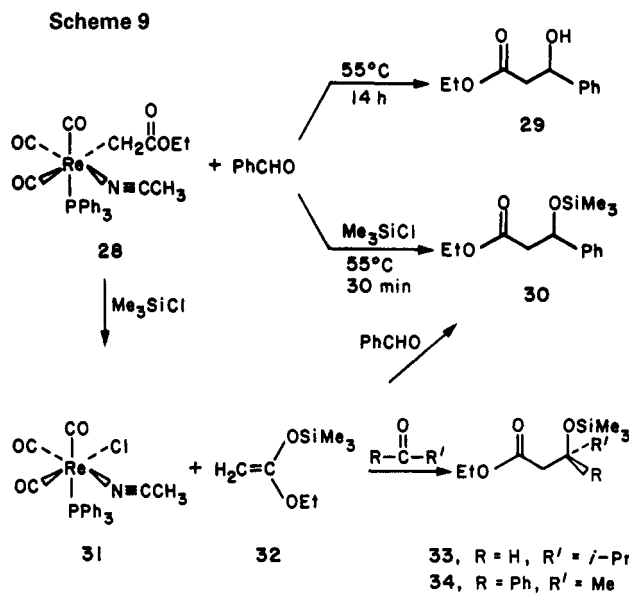


In an effort to make rhenium enolates reactive under milder conditions, we prepared phosphine-substituted enolate complex **27**. Treatment of **27** with Me_3NO caused clean and stereospecific loss of one molecule of CO, and efficient conversion to the acetonitrile- and phosphine-substituted complex **28**. Unlike many acetonitrile complexes, which decompose on attempted isolation, **28** was isolated in pure form in 80% yield. In spite of the ease with which it can be handled, **28** exhibited the hoped-for increase in reactivity toward organic substrates. Thus, heating the material in benzene to only 80 °C caused smooth carbon-carbon bond formation, leading to the mono-phosphine analogue of **26** in 45% yield. This complex was converted to **26** by treatment with one equivalent of PPh_3 at 80 °C.

Replacement of a CO ligand with acetonitrile also allows aldol chemistry to occur. However, the mechanism of the reaction is substantially different from that observed in the tungsten system discussed above. On treatment with benzaldehyde for 14 hours at 55 °C, a modest yield (45% by NMR) of aldol **29**, along with several unidentified rhenium complexes, was formed. Running this reaction in the presence of 1 equivalent of Me_3SiCl provides the silylated aldol **30** in much improved yield (94%). Surprisingly, however, the rate also increases substantially, the process going to completion in just 30 minutes at 55 °C. Thus Me_3SiCl also somehow acts as a promoter for the process.

Monitoring the transformation by NMR spectrometry, or examining the reaction of **28** with Me_3SiCl in the absence of aldehyde, reveals the mechanism of this promotion: the initial step of the reaction involves cleavage of **28** to rhenium chloride **31** and ketene acetal **32**. This is then followed by rapid rhenium-catalyzed reaction of **32** with aldehyde, leading to aldol product. The condensation reaction also occurs when substantially less than one equivalent of rhenium chloride is used (demonstrating that it is catalytic in the metal complex) and it proceeds with other aldehydes and ketones, as shown in Scheme 9.

In our most recent experiments with rhenium acetonitrile complexes, we have found that reactions of the enolate ligand also occur with alkynes. These reactions are not complicated by CO insertion, as they are in the tungsten system. Initially, we surmised that they involved a process analogous to that seen in the acetonitrile/enolate condensation: alkyne insertion into the enolate M-C bond followed by 1,3-hydrogen shift, leading to six-membered rhenacycles **26**. However, further information suggested that the products of the alkyne reactions are instead the five-membered rhenacycles **27** and **28**. Experiments are under way aimed at confirming these structures and elucidating the mechanism of the rhenium enolate/alkyne reaction.



SUMMARY AND CONCLUSIONS

This work has demonstrated that a reasonable range of middle and late-transition metal enolates can be prepared by reaction of nucleophilic metal anions with organic carbonyl compounds having leaving groups, such as chloride and alkylsulfonate, at the α -position. Many of these materials are air-stable and relatively easy to handle; they can be converted to other enolates (some having functional groups incompatible with alkali metal enolates) by chemical transformation of the enolate functionality.

The enolates can be activated toward reaction with organic substrates by photochemical or Me₃NO-induced extrusion of a CO ligand from the metal center. Aldol condensations with aldehydes and ketones have been observed, as well as other carbon-carbon bond-forming reactions involving apparent insertion of CO, nitriles, and alkynes into the metal-carbon bond of the enolate group. Further studies will be aimed at delineating more fully the scope and mechanisms of these reactions, and examining the possibility of utilizing them in stereoselective organic reactions.

Acknowledgements

This work was supported by a grant from the National Institutes of Health (no. GM 35699). We are grateful to Dr. T. Tulip (E. I. DuPont de Nemours and Co.) for helpful discussions for his willingness to disclose data prior to publication.

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