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Reactions of Alkenyl Fischer Carbene Complexes with Ketene Acetals: Formation of Alkynes

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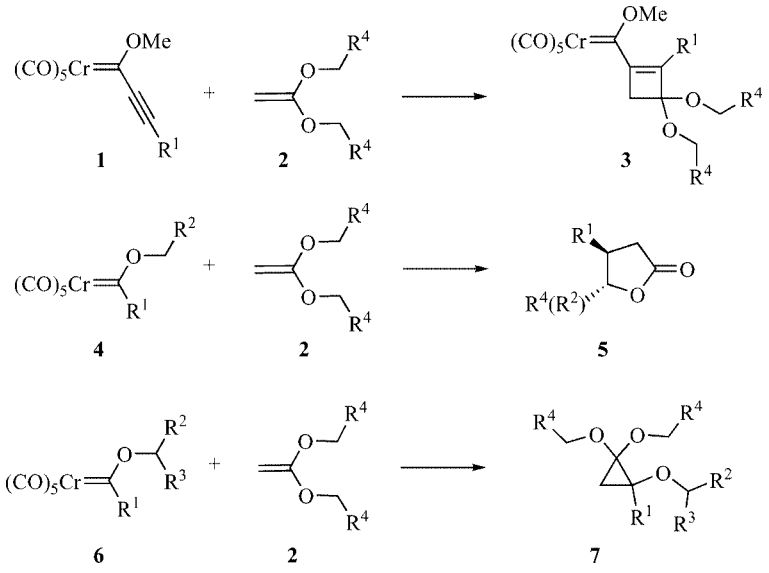
Alkenyl Fischer carbene complexes with an isopropoxy group on the carbene carbon will react with ketene acetals by 1,4-addition to give a zwitterionic intermediate, which undergoes subsequent internal isopropoxide transfer to generate a vinylidene complex. Either a hydrogen or phenyl group on the vinylidene carbon will undergo a formal 1,2-migration to give 4-pentynoate esters after hydrolysis of the intermediate orthoester.

Introduction

There are three known reactions types resulting from the interaction of a Fischer carbene complex with a ketene acetal. Alkynyl carbene complexes will react with ketene acetals by a [2+2] cycloaddition that gives rise to cyclobutenyl carbene complexes of the type **3** (Scheme 1).[1,2] These cyclobutenyl complexes have proved synthetically valuable due to their unique reactivity.[1,2] A second reaction involves a formal insertion of the ketene acetal into the carbon–oxygen bond of the carbene carbon to give a non-stabilized Fischer carbene complex (such as **13** in Scheme 2) which subsequently undergoes an internal C–H insertion to give the butyrolactone **5**.[3,4] Finally, just recently conditions have been found which will lead to the formal [2+1] cycloaddition of the carbene ligand and the ketene acetal to give cyclopropanone acetals **7**.[5] While the cyclopropanation of alkenes with Fischer carbene complexes has been known for thirty-six years,[6,7] this is the first example of cyclopropane formation with a ketene acetal.



Scheme 1.

The mechanism that has been proposed to account for the formation of the butyrolactone **5** and the cyclopro panone acetal **7** is shown in Scheme 2.[3] Nucleophilic addition of the ketene acetal to the carbene carbon would give

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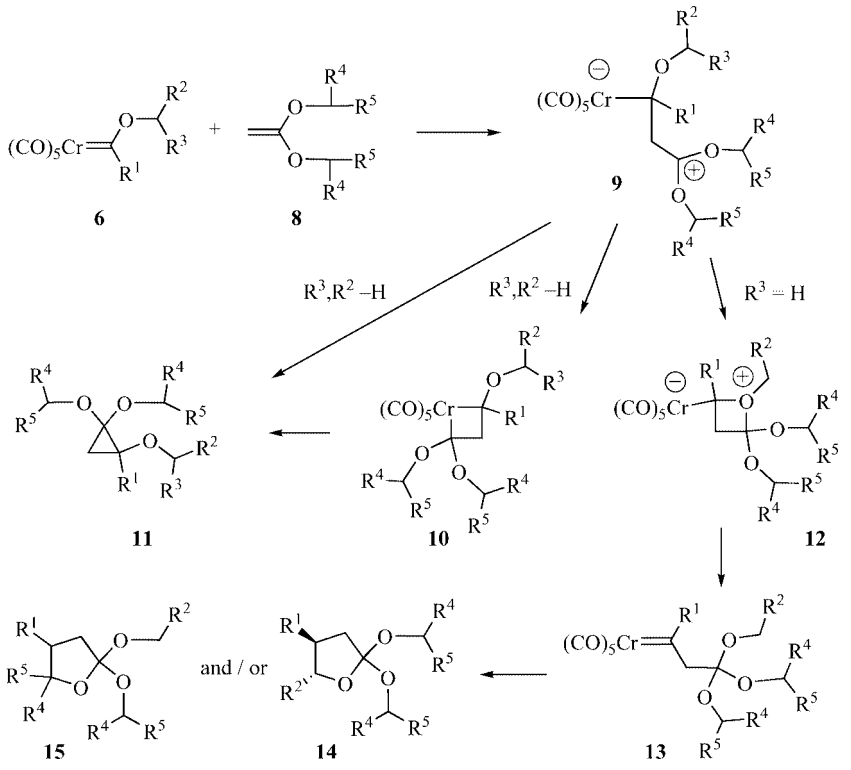


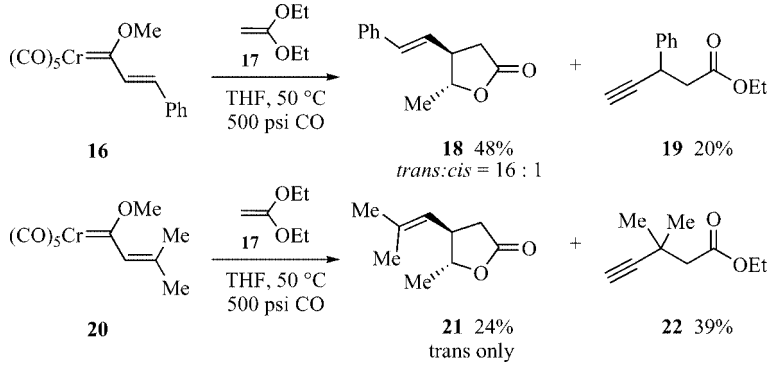
Scheme 2.

the zwitterion **9**. If the substituent on the oxygen attached to the carbene carbon is not too large, then the carbocation in **9** can bridge to the oxygen forming the four-membered ring oxonium ion **12**. Fragmentation with charge recombination leads to the formation of the non-heteroatom stabilized carbene complex **13** which is not isolable but rather suffers an intramolecular C–H insertion with preference for a methine over methylene hydrogen. The cyclopropanone acetal **11** is formed if the oxygen on the carbene carbon bears a hindered carbon group (R^3, $R^2 \neq H$), which slows down the interaction between this oxygen and the carbocationic center in the zwitterionic intermediate **9**. The formation of **11** could presumably happen either by direct carbon–carbon bond formation by backside interaction of the carbocation with the chromium–carbon bond or by an initial formation of the chromacyclobutanone **10** and then reductive elimination.

Results and Discussion

In an attempt to extend the butyrolactone synthesis to alkenyl carbene complexes we examined the reactions of the carbene complexes **16** and **20** with diethylketene acetal. The reactions were carried out with 2.5 equiv. of ketene acetal at 0.05 M in carbene complex in THF at 50 °C for 24 h under 500 psi of carbon monoxide in a Paar reactor. While each reaction did give some of the expected butyrolactone product, a second product was observed in each case and they were identified as the ethyl 4-pentynoates **19** and **22** (Scheme 3).

Apparently, the butyrolactone and pentynoate products result from a competition between 1,2- and 1,4-addition of the ketene acetal to the carbene complex. As indicated in Scheme 4, 1, 2-addition would lead to the zwitterion **24** which should proceed to the butyrolactone product via a

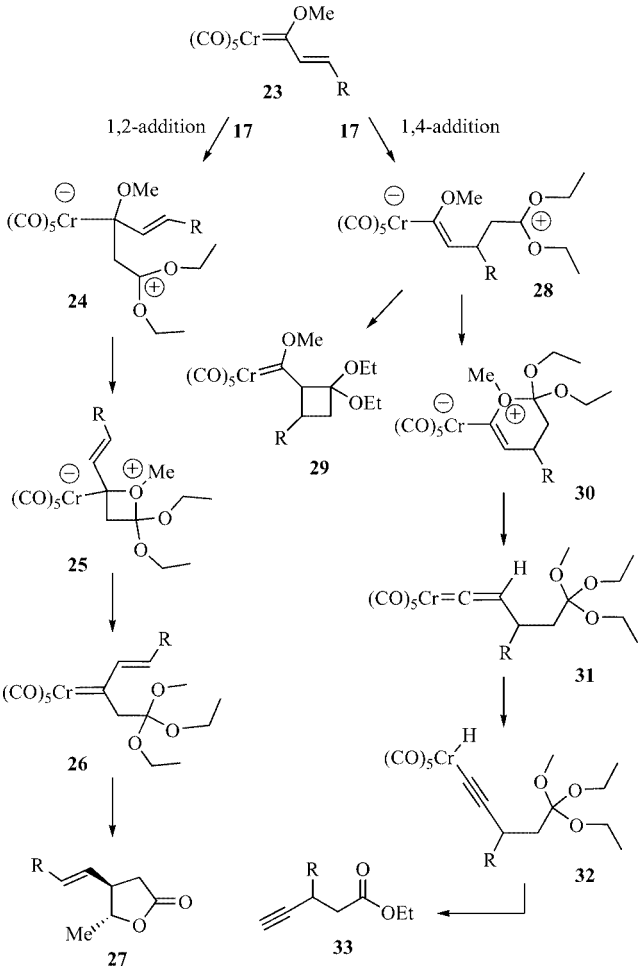


Scheme 3.

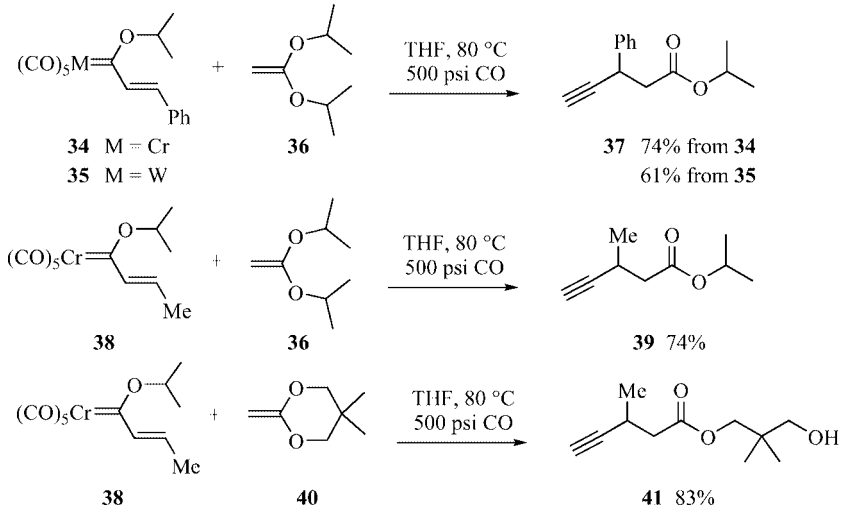
pathway analogous to that for alkyl and aryl carbene complexes (Scheme 2). On the other hand, 1,4-addition leads to the zwitterion **28**, which upon closure to the oxonium ion **30** and fragmentation gives rise to the vinylidene carbene complex **31**. The formation of the alkyne **33** can then be accounted for by a 1,3-shift of a hydrogen to give the alkynyl chromium hydride **32** followed by reductive elimination. This could also involve a 1,2-hydrogen shift (see Scheme 7).

Considering the mechanistic analysis outlined in Scheme 4, it appeared that the distribution between 1,4- and 1,2-addition products could be regulated by controlling the steric bulk of the oxygen substituent on the carbene complex **23**. If the methoxy group on complex **23** were replaced by a larger alkoxy group, it would be expected that the proportion of the 1,4-addition product should increase. What is not so easy to foretell, is whether the increased flux through the zwitterions **28** would in fact lead to increased proportions of the pentynoate product **33**. As was the case for the reaction of alkyl and aryl complexes (Scheme 2), an increase in the size of the alkoxy group on the carbene carbon disfavored the formation of the bridged oxonium ion **12** and instead lead to the formation of the cyclopropanone acetal **11**. Thus, it is certainly possible that a large alkoxy substituent in zwitterion **28** may result in "*C*-alkylation" of the chromium enolate to give the cyclobutenyl carbene complex **29** which would in effect be non-concerted [2+2] cycloaddition.

With these expectations in mind, the reaction of the isopropoxy carbene complex **34** (Scheme 5) was carried out with the bis(isopropoxy) ketene acetal **36** to find that the 1,2-addition product was completely shut down. In contrast to the reaction of the analogous methoxy complex **16**, this reaction gave only the pentynoate **37** in 74% yield as the only product. The bis(isopropoxy) ketene acetal **36** was used instead of the diethyl ketene acetal **17** to prevent the formation of a mixture of ethyl and isopropyl esters. The same yield of the pentynoate **39** was observed from the reaction of the *trans*-propenyl complex **38**. The tungsten complex **35** gave a slightly lower yield of **37** than did the chromium complex **34**. An increased yield of the pentynoate was observed when the cyclic ketene acetal **40** was employed. The butyrolactone product **27** (Scheme 4) was not observed in



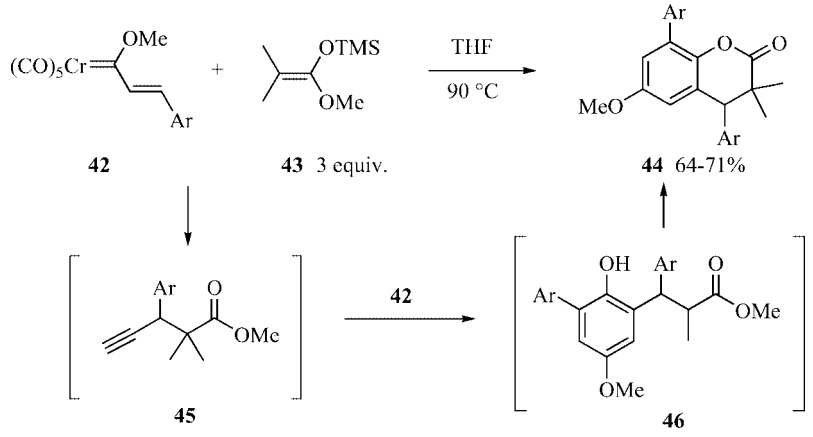
Scheme 4.



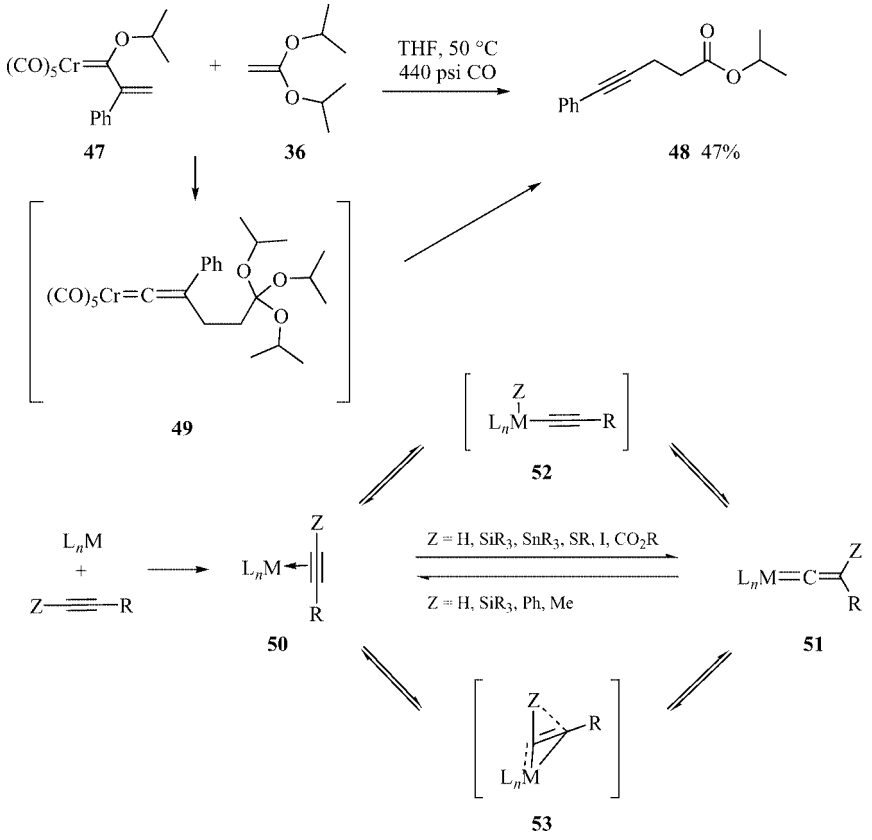
Scheme 5.

these reactions indicating that the presence of the isopropoxy group on the carbene carbon is sufficient to prevent 1,2-addition. No evidence for the cyclobutyl carbene complex **29** was observed indicating that the carbonium ion **28** prefers to form the oxonium ion **30** rather than form a carbon–carbon bond to give **29**.

A related observation has recently been made by Barluenga and co-workers.[8] They found that the reaction of alkenyl carbene complexes of the type **42** (Scheme 6) with β,β-disubstituted ketene acetals give the dihydrocoumarins **44** in good chemical yield. This product results from two sequential reactions. The first reaction involves the formation of the pentynoate **45** via a preferential 1,4-addition of the ketene acetal to complex **42** and then a subsequent benzannulation of the alkyne **45** with the carbene complex **42** to give the phenol **46**, which upon internal ester formation gives rise to the dihydrocoumarins **44**.[9] Evidence for this two-step process was taken from the fact that the intermediate alkyne product could be isolated if the reaction was performed at room temperature. Apparently the reason that the type of sequential process is not observed in the present work is because all of the reactions were carried out under 500 psi of CO. The first and rate-limiting step in the benzannulation reaction has been determined to be a loss



Scheme 6.



Scheme 7.

of CO from the carbene complex to form a 16 e⁻ intermediate which is prevented in the presence of a high pressure of CO.[10] Indeed, when either the reaction of the chromium or tungsten complexes **34** or **35** with the ketene acetal **36** were carried out under one atmosphere of argon a complex mixture of products was observed with none of the alkyne **37** present in the crude reaction mixture.

In a final experiment, we examined the reaction of the α-phenyl-substituted carbene complex **47** (Scheme 7) with the ketene acetal **36** because, according to the mechanism shown in Scheme 4, the formation of the vinylidene intermediate **49** would be expected. Because the migration of the hydrogen to give a terminal alkyne is not possible in **49**, the question to be probed was whether the vinylidene would suffer attack by a second equivalent of the ketene acetal. We were thus surprised to find that this reaction gave the pentynoate **48** in 47% yield, which resulted from a migration of the phenyl group to produce the alkyne function. Consultation of the literature reveals that there is one known example of a vinylidene complex of the type **51** (M = Fe) that undergoes migration of a phenyl group to give a coordinated alkyne complex **50**.[11] The interconversion of vinylidene complexes and alkyne complexes is a well-known process for a variety of metals including the group VI metals and is often reversible and has been most thoroughly documented with terminal alkynes (Z = H).[12] This process is most often employed in the forward direction as a method of preparing vinylidene complexes from terminal alkynes.[12,13] However, the reverse process has been investigated to some extent as a method for the preparation of alkynes.[14] Other than terminal alkynes (Z = H), the formation of vinylidene complexes has been observed with alkynes where Z is trialkylsilyl,[15] trialkyltin,[16] thioethers,[17] iodide[18] and an ester.[19]

The reverse direction involving the formation of alkynes has been largely reported for the synthesis of terminal alkynes but a few examples have been reported for Z = trialkylsilyl and one report describes the migration of methyl and phenyl.[11] Interestingly, the migration of phenyl is faster than that of methyl. The mechanism of the migration can either involve a direct 1,2-migration of the Z group via structure **53** or an initial oxidative addition to give the alkynyl hydride **52** and then a 1,3-shift of the Z group.[20] The most common pathway involves the direct 1,2-shift mechanism, but for certain electron-rich metal complexes the alkynyl hydride pathway is operative.

Conclusions

The change in the oxygen heteroatom substituent of an alkenyl Fischer carbene complex from methoxy to isopropoxy is sufficient to switch the mode of attack of a ketene acetal from 1,2-addition to 1,4-addition. The product resulting from 1,4-addition to an isopropoxy alkenyl complex of either chromium or tungsten is an isopropyl 4-pentynoate. This is proposed to occur through a zwitterionic intermediate, which prefers to undergo an internal isopropoxide migration to a carbocation rather than ring closure to a cyclobutyl carbene complex. The isopropoxide transfer leads to the formation of a non-stabilized vinylidene complex, which undergoes rearrangement to an acetylene. This rearrangement can involve the 1,2-shift of either a hydrogen or a phenyl group. Subsequent reaction of the alkyne product with an additional equivalent of carbene complex to give a phenol product is prevented by the CO atmosphere employed in the reaction.

Supporting Information (see also the footnote on the first page of this article): General procedures for the preparation of the carbene complexes and for their reactions with ketene acetals and of spectroscopic data for new compounds.

Acknowledgments

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