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Synthesis Methods

Chromium–Carbyne Complexes: Intermediates for Organic Synthesis**

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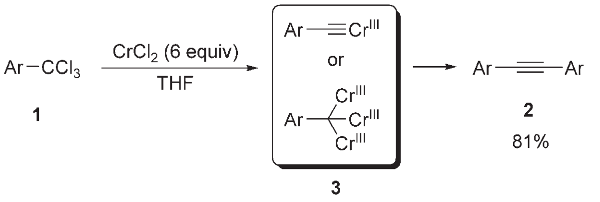
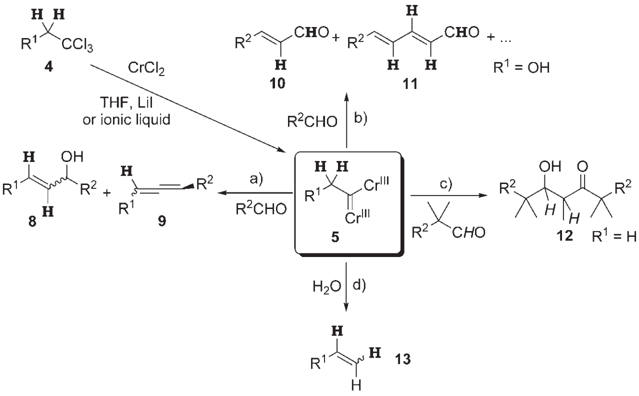
Since the first reference to carbenes in the literature by Buchner and Curtius in 1885,[1] they have become some of the most prominent and well-studied intermediates in organic and organometallic chemistry.[2] Carbenes are characterized by a divalent carbon and six electrons in their valence shell. In the free state, or in metal complexes, they are usually highly reactive, and amongst all of the transient intermediates in chemistry, carbenes have received special interest because of their unique reactivity and versatility in organic transformations. Carbynes, by analogy, are presumed to be just as intriguing and synthetically useful, but have remained, for the most part, little studied as intermediates. It took almost one hundred years until the first report by Fischer et al. of a monovalent carbon species with only five valence electrons (known as a carbyne or alkylidyne).[3] Despite the many developments in metal–carbyne complexes, such species remain an intriguing and little studied class of chemical intermediates. While reagents having a metal–carbon triple bond are well represented amongst alkyne metathesis catalysts,[4] very few other alkylidyne species have been well studied or shown to be intermediates in organic transformations.[5] Consequently, both practical and theoretical interest in the synthesis and transformations of carbynes remain high.[6]

During our investigations into organochromium chemistry,[7] we discovered that treatment of 1,1,1-trichloromethylaryl reagents **1** with chromium(II) chloride in THF induces a rapid, high yield dimerization that affords diaryl acetylenes **2** [Eq. (1)]. This result can be rationalized on the basis of the coupling of two arylidyne moieties, either a (η^1-arylidyne)chromium or a (μ^3-arylidyne)trichromium complex (**3**).[8,9]



(1)

In light of this we began a more detailed investigation and developed a valuable synthetic route to chromium–alkylidyne intermediates from *gem*-trichloroethyl derivatives based upon a substrate and a medium effect, in this case with a combination of chromium(II) chloride and lithium iodide or with chromium(II) chloride alone in an ionic liquid. We report herein the first reactions of *gem*-trichloroethyl derivatives **4** with various electrophiles through carbyne complexes **5** (Scheme 1). Carbynes are usually reported as having a negatively charged carbyne carbon, but the frequently observed nucleophilic additions to carbynes are interpreted as frontier orbital controlled reactions.[10] In addition to the anticipated reactions, we describe a novel carbanion character associated with the nascent chromium–carbyne complexes, as revealed by their reactions with various electrophiles.



Scheme 1. Reactions of chromium–alkylidyne complexes.

The chromium–alkylidyne complex **5** is shown in Scheme 1 as a (μ^2-alkylidyne)dichromium complex to suggest the carbenyl anion type reactivity of the intermediate species. Nevertheless, its exact structure could not be determined and this complex could also be a (η^1-alkylidyne)chromium complex (**6**) or a (μ^3-alkylidyne)trichromium complex (**7**; Scheme 2). These chromium–carbyne complexes are easily prepared from chlorinated substrates **5** upon treatment with $CrCl_2$ and LiI[11] in THF at room temperature or with $CrCl_2$ in an ionic liquid. The mechanism of formation appears to

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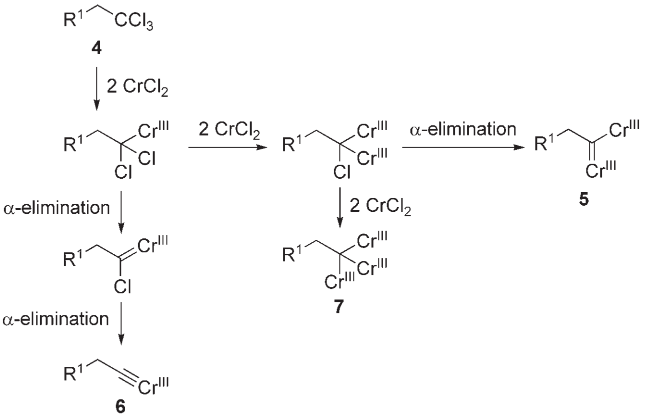
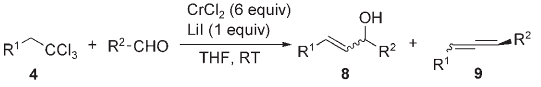


Scheme 2. Proposed chromium–alkylidyne complexes **5**, **6**, and **7** obtained from *gem*-trichloroalkane **4**.

involve the reduction of one of the C–Cl bonds (Scheme 2). Reduction of a second C–Cl bond and rehybridization of the 1-chloro-1,1-bis(chromio)alkane carbenoid results in a polynuclear complex with a bridging alkylidyne ligand (**5**).[12] Rehybridization of the 1,1-dichloro-1-chromioalkane carbenoid can also lead to a chromium complex containing a metal–carbon triple bond (**6**).[13] The reduction of all C–Cl bonds should give the tris(chromio)carbyne complex **7**.[14] The role of lithium iodide and the ionic liquid is not clear but we propose a Lewis acid effect or a nucleophilic catalysis that can inhibit the stabilizing donation from the lone electron pair of the chlorine bonded to the carbenoid or to the carbene carbon and induce the rehybridizations,[15,16] thus precluding the formation of a chromium–vinylidene carbenoid.[7]

The nucleophilic character of these chromium–alkylidyne complexes is evidenced by their reactions with aldehydes and water. Previous work has shown that carbyne formation depends critically on the substituents,[12a,17] and various adducts were observed here depending upon the substitution pattern. In the presence of aldehydes, for example, allylic alcohols **8** and allenes **9** were isolated (Scheme 1, reaction a and Table 1), and α,β-unsaturated aldehydes **10** and **11** were obtained from 2-hydroxyethylidynes and aldehydes (Scheme 1, reaction b and Table 2). β-Hydroxy ketones **12** were obtained from ethylidynes and neopentanal derivatives, (Scheme 1, reaction c and Table 3), and alkylidynes afford terminal alkenes **13** in 90% yield in the presence of water (Scheme 1, reaction d and Table 4).

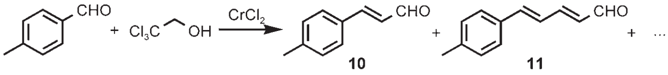
Table 1: Reaction of alkylidynes with aldehydes.



Entry	R^1	R^2	Yield[a] 8	9
1	phenyl	*p*-tolyl	45% $Z/E = 80{:}20$[b]	41%
2	biphenyl	*tert*-butyl	65% $Z/E = 50{:}50$[b]	7%
3	hydrocinnamyl	*tert*-butyl	44% $Z/E = 64{:}36$[b]	–[c]

[a] Yield of isolated product. [b] Ratio determined by ^1H NMR spectroscopy and/or GC. [c] Not isolated.

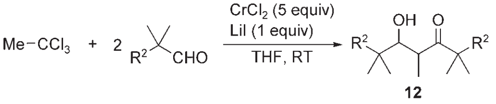
Table 2: Reaction of alkylidynes with 2,2,2-trichloroethanol.

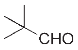
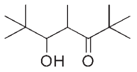
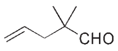
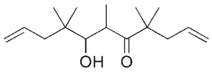


Entry	Solvent (additive)	Conditions	Yield[a] 10	11
1	THF (LiI)	65 °C, 3 h	38%	12%
2	EtOAc (LiI)	70 °C, 3 h	70%	15%
3	[bmim]Br	65 °C, 15 h	18%	< 2%[b]
4	[bmim]I	90 °C, 15 h	31%	10%

[a] Yield determined from the ^1H NMR spectrum of the isolated mixture of α,β-unsaturated aldehydes. [b] Not detected in the ^1H NMR spectrum.

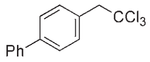
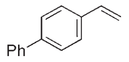
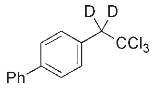
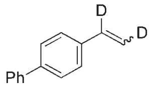
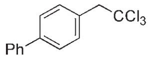
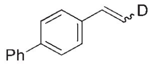
Table 3: β-Hydroxy ketone formation.



Entry	Aldehyde	Adduct	Yield[a]
1			78% *erythro/threo* = 84:16[b]
2			58% *erythro/threo* = 90:10[b]

[a] Yield of isolated product. [b] Ratio determined by ^1H NMR spectroscopy.

Table 4: Reduction of *gem*-trichloromethyl compounds through 1,2-hydride migration.

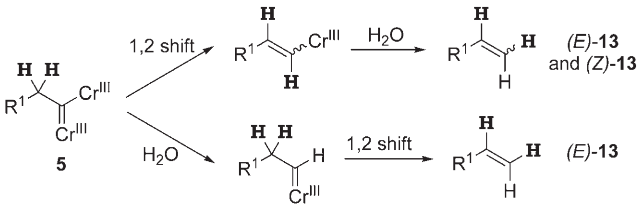
Entry	Conditions	Trichloromethyl reagent	Adduct
1	LiI, H_2O		
2	LiI, H_2O		 E/Z = 70:30[a]
3	LiI, D_2O		 E/Z = 60:40[a]

[a] Ratio determined by ^1H and ^2H NMR spectroscopy.

We propose the following mechanisms, which are based on the nucleophilicity of chromium–alkylidyne intermediates and the known reactivities of carbenes, to rationalize the formation of the observed adducts:

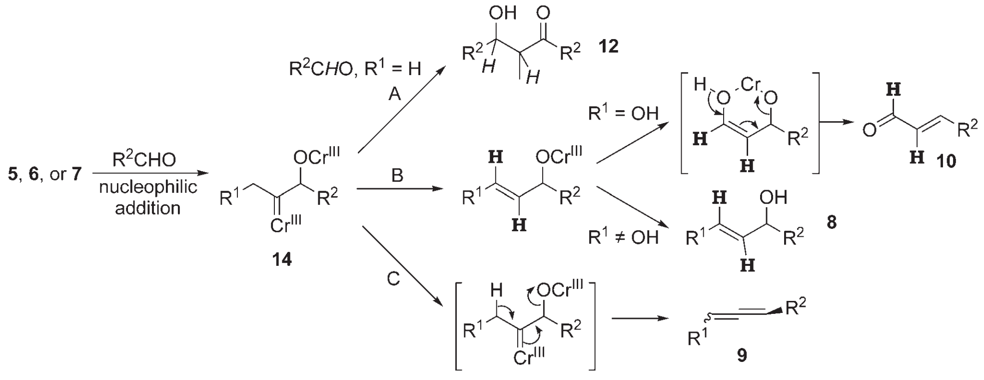
1) Hydrolysis: The formation of terminal alkenes involves protonation and 1,2-hydride migration of the corresponding carbynes. Addition of D_2O to an anhydrous solution containing $CrCl_2$ and LiI leads to the formation of the 1-(1-D)alkene (Table 4, entry 3), and reduction of the deuterium-labeled 1,1,1-trichloro-(2,2-D_2)ethyl substrate gives a complete

migration of the deuterium atom to yield the 1-(1,2-D_2)alkene (Table 4, entry 2). 1,1-Dichloroalkenes do not react under these reaction conditions, therefore they can be excluded as intermediates in the overall transformation. Previous work have demonstrated that intramolecular 1,2-suprafacial migration of a hydride in carbene complexes affords *Z* isomers selectively due to steric repulsions between the hexacoordinate chromium center and the R^1 group.[12b] In contrast, 1,2-hydride migration in carbyne complexes should afford both isomers, which means that the formation of an isotopically labeled terminal alkene as a mixture of *E* and *Z* isomers implies that first pathway is involved to some degree (Scheme 3).



Scheme 3. Proposed mechanisms for the formation of **13**.

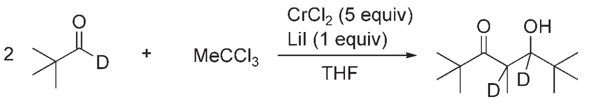
2) Nucleophilic Addition: Nucleophilic addition of the chromium–alkylidyne complexes to a carbonyl affords β-chromium(III) alkoxide carbene species **14** that can undergo insertion into a C–H bond, either intermolecularly (into an aldehydic C–H bond, Scheme 4, path A) or intramolecularly (1,2-hydride migration, Scheme 4, path B).[18] In addition, a concerted deprotonation and β-elimination of metal oxide moiety converts the carbene intermediates **14** into allenes **9** (Scheme 4, path C).[19] Alternatively, the mechanism of formation of allylic alcohol **5** may proceed by a reverse stepwise process, in other words 1,2-hydride migration and addition to an electrophile.



Scheme 4. Proposed mechanisms for the reaction of alkylidynes with electrophiles. Path A: intermolecular insertion into a C–H bond. Path B: intramolecular insertion into a C–H bond. Path C: five-centered cyclic elimination.

When the carbyne carbon substituent (R^1) is a hydroxy group a six-membered transition state elimination selectively affords *E* vinylic aldehydes **10** and **11** and derivatives thereof (Scheme 4). The aldehydes obtained are electrophiles that can react further with the reactive species to give a series of vinylic aldehydes (Table 2).[20] Interestingly, this result could be reproduced with $CrCl_2$ in 1-butyl-3-methylimidazolium bromide ([bmim]Br) and 1-butyl-3-methylimidazolium iodide ([bmim]I).

With neopentanal derivatives, insertion of carbenes **14** into the aldehydic C–H bond gives β-hydroxy ketones **12**. Insertion into the C–H bond was confirmed by performing the reaction with deuterium-labeled pivaldehyde [Eq. (2)]. β-Hydroxy ketones may also arise from insertion of the alkylidyne species into the C–H bond of aldehydes and subsequent addition of chromium(III) enolates to these aldehydes. However, this mechanism, which has been reported to be totally *erythro*-selective,[21] cannot be the only one involved as we obtained diastereomeric mixtures of β-hydroxy ketones upon treatment with $CrCl_2$/LiI.



(2)

In summary, we have observed that some trichloromethyl derivatives, upon reduction with $CrCl_2$, can exhibit an interesting and specific reactivity that can be related to a new kind of intermediate species, namely a chromium–alkylidyne complex. The results reported above indicate that the carbyne and electrophile substitution patterns influence the reaction mechanism to selectively afford alkynes, alkenes, β-hydroxy ketones, aldehydes, allylic alcohols, and allenes, which can subsequently be applied for the construction of a wide variety of carbon skeletons. Finally, the study reported herein will open up a new field of reactions that proceed through versatile carbyne intermediates. Further studies are underway in our laboratories to evaluate the functional group compatibility.

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Keywords: carbenes · carbynes · chromium · isotopic labeling · rearrangements

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[18] Reduction of a deuterium-labeled substrate with $CrCl_2$/LiI gave complete migration of the deuterium label.

[19] Treatment of allylic alcohols with $CrCl_2$/$CrCl_3$/LiI conditions did not lead to allenes, which is consistent with a different mechanism for the formation of allenes.

[20] 1,2-Hydride migration was confirmed by treatment with deuterium-labeled 2,2,2-trichloro-(1,1-D_2)ethanol, which gave di- and monodeuterated vinylic aldehydes in a 2:1 ratio (the latter adduct formation probably involves an enolization equilibrium).

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