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A mechanistic study of the chromium(II)-mediated transformations of trichloromethyl alkyls and carbinols: evidence for carbene, carbyne, and carbenoid intermediates

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Abstract—Using $CrCl_2$ in THF at room temperature, trichloromethyl carbinols and trichloromethylalkanes are readily transformed to the highly reactive α-chlorocarbenes, carbynes and α-chloro-α-chromium(III) vinylidene carbenoids. A mechanistic study is carried out to determine the nature of the intermediates.

As part of our continuing investigation of organochromium methodology, we report herein the mechanistic study of transformations with chromous chloride in THF. Previous studies have identified a chromium vinylidene carbenoid as the penultimate intermediate in the reaction of 1,1,1-trichloroalkanes.[1] The observation of hydride migration led us to postulate new intermediates for the chromium(II)-mediated transformation of these trichloromethyl derivatives. To provide a rationale for this result we propose a carbene and a carbyne as key intermediates.[2]

As a starting point we have assumed that the formation of covalent Cr–alkyl intermediates proceeds initially through the insertion of chromium(II) into a C–Cl bond. Formally, the reduction of one C–Cl bond by Cr(II) involves two consecutive single-electron transfers, thus accounting for 2 equiv of $CrCl_2$.[3] Depending on the electronic environment and the solvation of the chromium(II) salt, reactions pathways may differ. Commercial chromous chloride was previously found to be a mixture of anhydrous $CrCl_2$ and $CrCl_2{\cdot}2H_2O$ so $CrCl_2$ in our reactions is assumed to be solvated by THF and H_2O.[1] Thus we assume a general complex: $CrCl_2{\cdot}n\text{THF}{\cdot}(6\text{-}n)H_2O$ and oligomers.

The results of aromatic, aliphatic, and allylic 1,1,1-trichloroethyl derivatives upon treatment with $CrCl_2$ are summarized in Table 1 (entries 1–6).[4] 1-Chloro-1-alkenes **2**, terminal alkynes **3**, and terminal alkenes **4** are observed as a consequence of competing pathways (Eq. 1). Interestingly, the alkyne was observed without heating of the reaction mixture as described in our previous results.[1]

The formation of chloroolefin **2**, obtained from 1,1,1-trichloroalkane **1**, was previously described to occur via a 1-chloro-1-chromium(III) vinylidene carbenoid intermediate **7** (Scheme 1):[1,5] the unstable 1-chloro-1,1-bischromium(III) alkane carbenoid **6** generated by the reduction of two C–Cl bonds undergoes a syn β-elimination of chromium hydride and gives the known chlorovinylidene carbenoid, which was previously proven to have a nucleophilic character.[1,6]

In presence of water, chloroolefin **2** is formed. As a consequence of the steric requirements of the bis-chromium intermediate **6**, the stereochemistry of chlorovinylidene carbenoid **7** is selectively trans, and (*Z*)-**2** is obtained as the major compound. The formation of 1-chloro-2-d_1-1-alkene **2-d_1** (entries 3 and 5) is consistent with this

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Keywords: Carbene; Carbyne; Chromium; Isotopic labeling; Rearrangement.

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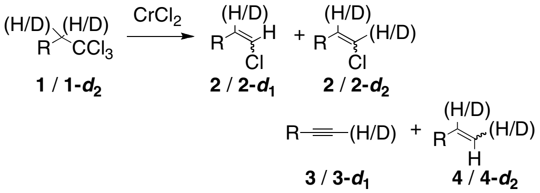
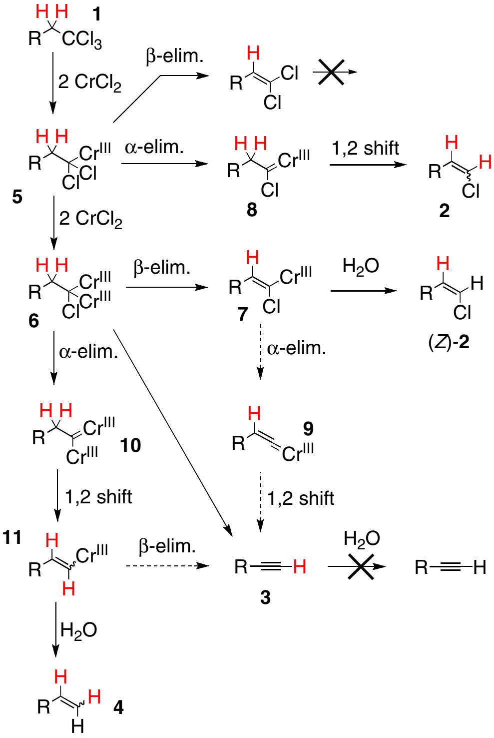
Table 1. Results of the reduction of trichloroalkanes by chromium(II)



(Eq. 1)

Entry	Trichloroalkane	Solvent	Ratio[a] (%)						
	R		2 (*Z*/*E*)	**2-*d*$_1$**	**2-*d*$_2$**	**3**	**3-*d*$_1$**	**4**	**4-*d*$_2$** (*E*/*Z*)
1	Phenyl **1a**	THF	53 (>99:1)			47		<1	
2[b]	4-Biphenyl **1b**	THF	22 (7:1)			75		3	
3	**1b-*d*$_2$**	THF	0	16	4	0	75	0	5
4	Ethyl-benzene **1c**	THF	41 (26:1)			59		<1	
5	**1c-*d*$_2$**	THF	0	22	21	<1	57	0	<1
6	Vinyl-benzene **1d**	THF	95 (20:1)			5		<1	
7[c]	**1a**	THF	55 (13:1)			17		28	
8	**1a**	THF/H_2O (3:1)	88 (50:1)			<1		12	
9	**1b**	THF/H_2O (3:1)	89 (30:1)			4		7	
10	**1b-*d*$_2$**	THF/H_2O (3:1)		89	0	<1	3	0	8 (3:1)
11	**1c**	THF/H_2O (3:1)	92 (40:1)			5		3	
12	**1d**	THF/H_2O (3:1)	94 (60:1)			<1		6	

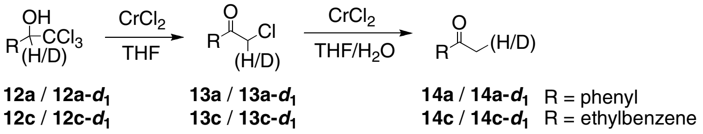
[a] GC analysis of crude material.
[b] GC analysis of the crude material is consistent with isolated yields.
[c] $CrCl_2$ pretreated with an equimolar amount of water.



Scheme 1. Transformation mechanism of trichloroalkanes.

mechanism; however, 1-chloro-1,2-*d*$_2$-1-alkene **2-*d*$_2$** cannot be a result of the chlorovinylidene carbenoid hydrolysis. A second mechanism proceeding through 1,1-dichloro-1-chromium alkane carbenoid **5**, obtained by the reduction of one C–Cl bond, would give, after further α-elimination of $CrCl_3$, α-chlorocarbene **8**. The organochromium species most likely undergoes a rehybridization by placing a positive charge in a p orbital to produce a tight ion pair, and the formation of a chromium(III)–carbene complex is postulated.[7] An intramolecular rearrangement involving a 1,2 migration of hydride then gives 1-chloro-1-alkenes **2**. Alkyne formation appears to proceed through a chlorovinylidene carbenoid. In the absence of an electrophile, the carbenoid species most likely rehybridizes and undergoes α-elimination of $CrCl_3$ to give vinylidene **9**. 1-Alkynes **3** arise from a Fritsch–Buttenberg–Wiechell (FBW) rearrangement.[8] An alternative mechanism postulates the formation of a carbenyl anion equivalent: carbyne **10** obtained through an α-elimination of $CrCl_3$ from 1-chloro-1,1-bis-chromium alkane carbenoid.[2] Subsequent 1,2 migration of hydride affords 1-chromium(III) alkene **11** and syn β-elimination of chromium hydride gives 1-alkyne **3**. Both pathways rationalize the formation of 1-*d*$_1$-1-alkynes **3b-*d*$_1$** and **3c-*d*$_1$** from 1,1,1-trichloro-2,2-*d*$_2$-alkanes **1-*d*$_2$** (entries 3 and 5). Hydrolysis of 1-chromium(III) alkenes affords 1-alkenes and is consistent with the formation of bis-deuterated compound **4-*d*$_2$** from **1-*d*$_2$**. Notably, 1,1-dichloroalkenes do not react with chromium(II) chloride under these reaction conditions, thus excluding them as intermediates in the overall transformation, and no deuterium–hydrogen exchange from terminal alkynes could be observed.[9]

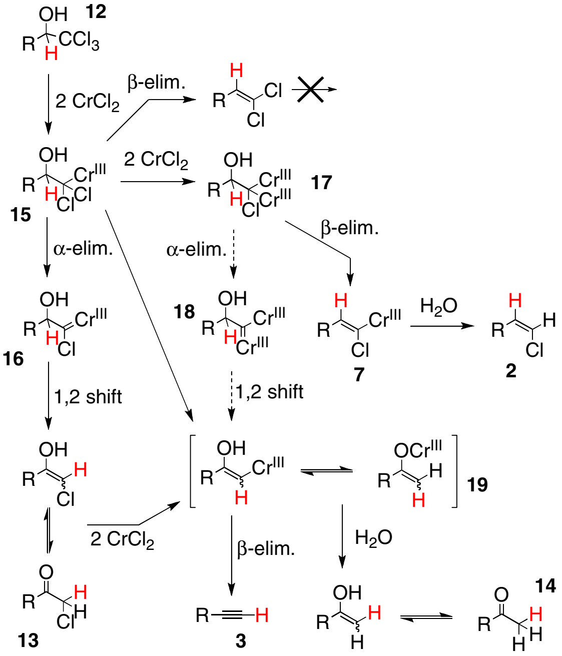
In a THF–water biphasic medium, chloroolefins **2** are also observed (Table 1, entries 8–12). However, the transformation of 1,1,1-trichloro-2,2-*d*$_2$-alkanes **1-*d*$_2$** leads only to mono-deuterated 1-chloro-2-*d*$_1$-1-alkene **2-*d*$_1$** (entry 10). The mechanism through 1-chloro-1,1-bis-chromium(III) alkane carbenoid **6**, which then undergoes a β-elimination, is probably involved (Scheme 2). The formation of alkenes **4** would also involve **6** as an intermediate through an α-elimination. In spite of the heterogeneous medium, water probably



Scheme 2. Reduction of trichloromethylcarbinols.

increases chromous chloride reactivity by solvation and favors the second reduction of a C–Cl bond by Cr(II), thus precluding a rehybridization of 1,1-dichloro-1-chromium alkane carbenoid **5** to α-chlorocarbene **8**.

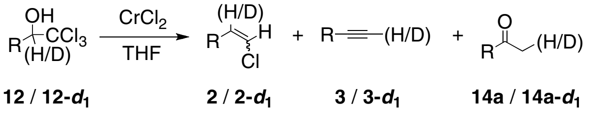
Contrary to what we previously reported,[10] the reduction of trichloromethylcarbinols **12** with $CrCl_2$ in anhydrous conditions gives α-chloromethyl ketones exclusively that can be readily reduced to methyl ketones with $CrCl_2$ in an aqueous medium (Scheme 2). 2,2,2-Trichloro-1-phenylethanol **12a** and 1,1,1-trichloro-4-phenylbutan-2-ol **12c** produce 2-chloroacetophenone **13a** and 1-chloro-4-phenylbutan-2-one **13c**, respectively, with complete conversion, upon treatment in THF with $CrCl_2$ at room temperature.[11] The formation of α-chloromethyl ketones **13** proceeds via an insertion of chromium into a C–Cl bond (Scheme 3). β-Oxy-dichlorocarbenoid species **15** then undergoes an α-elimination of $CrCl_3$ to give β-oxy-α-chlorocarbene **16**. 1,2 Hydride migration converts intermediate **16** into an α-chloroenol in equilibrium with α-chloromethyl ketone **13**. No further reduction occurs in anhydrous conditions, but with the addition of water, the C–Cl bond is reduced by $CrCl_2$ to give methyl ketones **14** in quantitative yield (Scheme 2). The 1,2 hydride migration is consistent with the formation of 2-chloro-2-d_1-methyl-2-ketones **13a-*d*₁** and **13c-*d*₁** from 1,1,1-trichloro-2-d_1-2-alcohols **12a-*d*₁** and **12c-*d*₁**, then converted to 2-d_1-methyl-2-ketones **14a-*d*₁** and **14c-*d*₁** in aqueous conditions.



Scheme 3. Transformation mechanism of trichloromethylcarbinols.

In a THF–water biphasic medium, chloroolefins **2**, terminal alkynes **3**, and methyl ketones **14** are obtained from trichloromethyl carbinols **12** and $CrCl_2$ (Eq. 2);[12] results are summarized in Table 2.[13,14] The formation of 1-chloro-2-d_1-1-alkene **2-*d*₁** from 2,2,2-trichloro-1-d_1-1-phenylethanol **12-*d*₁** does not suggest that a 1,2 hydride migration has taken place, however the formation of by-products **3a-*d*₁** and **14a-*d*₁** does (entry 4). The mechanism of reaction in aqueous conditions is fundamentally different. The presence of water increasing the solubility of $CrCl_2$ in the medium may make a second C–Cl bond reduction faster than the α-elimination. We propose a second C–Cl bond reduction by $CrCl_2$ from the β-oxy-dichlorocarbenoid species **15** (Scheme 3, **15**→**17**), as described for trichloroalkanes reduction, then further syn β-elimination of chromium hydroxide generates the 1-chloro-1-chromium(III) vinylidene

Table 2. Results of the reduction of trichloromethylcarbinols by chromium(II)



(Eq. 2)

Entry	Trichloromethylcarbinols R	Solvent	Ratio[a] (%) 2 (*Z*/*E*)	2-*d*₁	3	3-*d*₁	14	14-*d*₁
1[b]	Phenyl **12a**	THF	15		7		78	
2	Phenyl **12a**	THF/H_2O (3:1)	88 (99:1)		<1		12	
3	**12a**	THF/H_2O (1:1)	87 (99:1)		5		8	
4	**12a-*d*₁**	THF/H_2O (1:1)		94		2		4
5	Ethyl-benzene **12c**	THF/H_2O (3:1)	65 (99:1)		8		27	
6	**12c**	THF/H_2O (1:1)	74 (70:1)		20		6	

[a] GC analysis of crude material.

[b] $CrCl_2$ pretreated with an equimolar amount of water.

carbenoid intermediate **7**, which is quenched with water to lead to chloroolefins **2**. α-Chloromethyl ketone **13** is likely to be reduced under aqueous conditions to give chromium(III)-enolate **19**, which undergoes either a β-elimination to give alkynes **3** or a hydrolysis to generate methyl ketone **14**. Alternatively, enol **19** may be formed through the rehybridization of 1-chloro-1,1-bis-chromium(III) methylcarbinol carbenoid **17** and a subsequent 1,2 hydride migration (**17**→**18**→**19**).

In summary, we have demonstrated that trichloromethyl alkanes and carbinols undergo chromium(II)-mediated transformations to chromium(III)–carbene (**8** and **16**) and –carbyne complexes (**10** and **18**). We do not demonstrate the predominance of a single reaction mechanism to the exclusion of all other alternatives, but competitive mechanisms have been proposed which account for the nature of the observed products: after further transformations, carbenes afford various alkenes (**2** and **4**), alkynes (**3**), and ketones (**13** and **14**).

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.03.150.

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4. Procedure: A suspension of $CrCl_2$ (1.2 mmol, 6 equiv) in oxygen- and water-free THF or in H_2O (1 mL) was added via a syringe to solution of trichloroalkane **1** (0.2 mmol, 1 equiv) in THF (1 mL), under an argon atmosphere at ambient temperature. After 12 h at ambient temperature, the reaction was quenched with 5% HCl and extracted with Et_2O (3×). The combined ethereal extracts were washed with brine, dried over $MgSO_4$, filtered through a small pad of SiO_2, and analyzed by GC–MS.
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10. Trichloromethylcarbinols were described to give 1-chloro-1(*Z*)-alkenes via (*E*)-halovinylidene chromium carbenoids with $CrCl_2$ in anhydrous THF, see: Baati, R.; Barma, D. K.; Falck, J. R.; Mioskowski, C. *Tetrahedron Lett.* **2002**, *43*, 2183.
11. Procedure: A suspension of $CrCl_2$ (1.2 mmol, 6 equiv) in oxygen- and water-free THF (1 mL) was added via a syringe to a solution of trichloromethyl carbinol **12** (0.2 mmol, 1 equiv) in THF (1 mL), under an argon atmosphere at ambient temperature. After 3 h at ambient temperature, an aliquote of the reaction mixture was filtered through a small pad of SiO_2 and GC–MS analysis indicated a complete conversion to α-chloromethyl ketones **13**. H_2O (1 mL) was added to the reaction mixture. After 10 min (for **12a**) or 3 h (for **12c**) at ambient temperature, the reaction was quenched with 5% HCl and extracted with Et_2O (3×). The combined ethereal extracts were washed with brine, dried over $MgSO_4$, filtered through a small pad of SiO_2, and analyzed by GC–MS, which indicated a complete conversion to methylketones **14**. Alternatively a suspension of $CrCl_2$ (0.6 mmol, 3 equiv) in water (1 mL) was added via a syringe at room temperature to a solution of α-chloromethyl ketones **13** (0.2 mmol, 1 equiv) in oxygen-free THF (1 mL), under an argon atmosphere. After 10 min to 3 h at ambient temperature, the reaction was quenched with 5% HCl and extracted with Et_2O (3×). The combined ethereal extracts were washed with brine, dried over $MgSO_4$, filtered through a small pad of SiO_2, and analysis by GC–MS indicated a complete conversion to methyl ketones **14**.
12. Chromium(II) reduction of trichloromethyl carbinols in aqueous DMF was previously described, see: Wolf, R.; Steckhan, E. *J. Chem. Soc., Perkin Trans. 1* **1986**, 733.
13. Procedure: A solution of $CrCl_2$ (1.2 mmol, 6 equiv) in H_2O (1 mL) was added via a syringe at room temperature to a solution of trichloromethylcarbinol **12** (0.2 mmol, 1 equiv) in oxygen-free THF, under an argon atmosphere. After 3 h at ambient temperature, the reaction was quenched with 5% HCl and extracted with Et_2O (3×). The combined ethereal extracts were washed with brine, dried over $MgSO_4$, filtered through a small pad of SiO_2, and analyzed by GC–MS.
14. The 1-chloro-1(*Z*)-alkenes described in Ref. 10 can be obtained from trichloromethylcarbinols and $CrCl_2$ in aqueous conditions. However coupling adducts 2-haloalk-2-(*Z*)-en-1-ols could not be observed in the presence of an aldehyde.