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FEATURE ARTICLE

A new look at the McMurry reaction

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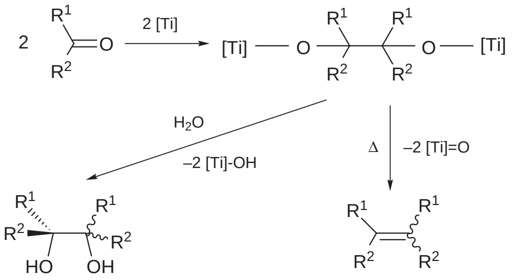
The article emphasizes the contradictory features of the McMurry reaction. The historical view shows how the chemists were firmly convinced of the occurrence of pinacolate intermediates and rejected, in spite of some evidence, the alternative pathway *via* carbenoid species. The McMurry reaction continues to find new important applications but suffers from problems of reproducibility. New practical reagents and simplified methods have been developed but rather complicated systems have been designed for obtaining higher selectivities. Recent investigations confirmed that pinacolates would be the precursors to alkenes but also revealed the possible involvement of carbenoid species, putting forward the dual nature of the mechanism of the McMurry reaction.

The huge interest in the McMurry reaction is expressed by the number of accounts devoted to its synthetic applications and, to a lesser extent, its mechanistic aspects;[1–4] an excellent review by Fürstner and Bogdanovic was published in 1996.[4] In this feature article, we would like to focus on the most recent developments but also recall some older facts, placing this field in a distinct perspective.

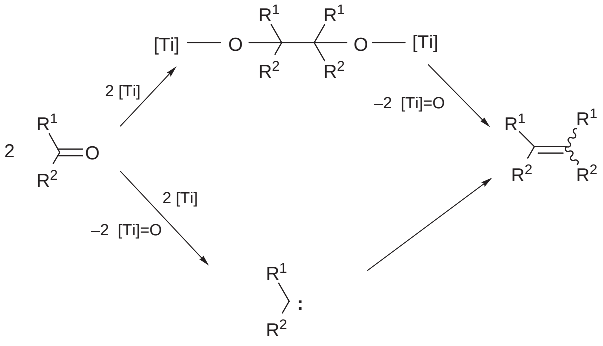
An historical view

The rich and peculiar history of the McMurry reaction will be more easily assessed after recalling the course of some important events which are not necessarily brought together, without confusion, in the chemist's memory.

In 1972, Sharpless *et al.* reported that ketones and aldehydes could be reductively coupled into alkenes by reaction with WCl_6 and RLi reagents.[5] One year after, two groups discovered that low-valent titanium complexes were also efficient in this coupling process. Tyrlik and Wolochowicz, who used the $TiCl_3$–Mg system, suggested that tetramethylethylene was obtained *via* the carbene species Me_2C:, resulting itself from deoxygenation of acetone. On the other hand, Mukaiyama *et al.* proposed that metallopinacols were intermediates in the reductive coupling of aromatic ketones by means of the $TiCl_4$–Zn system; the mechanism shown in Scheme 1 explained how benzaldehyde and acetophenone were selectively transformed into the corresponding pinacols and alkenes when the reaction was performed in THF at low temperature or in refluxing dioxane.[7] The pinacolate intermediates would be formed either by dimerization of ketyl radicals resulting from one electron transfer from the low-valent metal species to the carbonyl and/or, in the case of the more easily reducible and reactive aromatic ketones, by nucleophilic attack of a ketone dianion to the C=O bond. Therefore, at the very beginning in 1973, two mechanisms were envisaged for the reductive coupling of carbonyl molecules (Scheme 2).



Scheme 1 Reductive coupling of ketones *via* a metallopinacol intermediate.



Scheme 2 The two mechanisms proposed in 1973 by Tyrlik and Wolochowicz (bottom) (ref. 6) and by Mukaiyama *et al.* (top) (ref. 7).

In 1974, McMurry and Fleming described a 'new method for the reductive coupling of carbonyls to olefins' with $TiCl_3$ and $LiAlH_4$; they also proposed that pinacolate intermediates were involved in this reaction since pinacols could be isolated as by-products in many cases.[8] The mechanism of Scheme 1 was then rapidly and generally accepted.

Meanwhile, several studies on the reductive coupling of carbonyl compounds to olefins by low-valent molybdenum and tungsten compounds revealed that this reaction involved carbenoid intermediates; the relationship with the alkene metathesis reaction was noted.[9] Such carbene species were detected by Fujiwara *et al.* in 1978,[9] before Bryan and Mayer[10] and Chisholm and co-workers[11,12] isolated in 1990 tungsten oxoalkylidene complexes resulting from reductive cleavage of the ketonic C=O bond. These compounds were found to react further with the ketone to give the olefin at room temperature, presumably *via* a metallaoxetane intermediate, and the mechanism of Scheme 3 could be proposed for the reductive coupling

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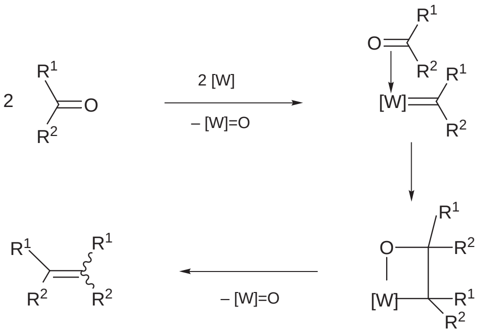
Michel Ephritikhine obtained his PhD in organic chemistry in 1974 at the University of Paris under the supervision of J. Levisalles. His postdoctoral work with M. L. H. Green in Oxford confirmed his interest in organometallic and inorganic chemistry. From 1976 to 1984, he was in the group of H. Felkin in Gif sur Yvette where he studied the chemistry of rhenium polyhydrides and C–H bond activation of alkanes. In 1984, he joined the Commissariat à l'Energie Atomique in Saclay to work on uranium chemistry. He presently holds the position of Research Director in the CNRS.



Scheme 3 Reductive coupling of ketones *via* a carbenoid species.

of carbonyl substrates. It is noteworthy that Chisholm *et al.*[12] and Cotton *et al.*[13] also found that low-valent tungsten compounds could react with ketones to give metallopinacols and demonstrated that these latter species were not the source of alkenes.

Amazingly, the belief in the mechanism of Scheme 1 was so strong that another pathway for the titanium catalyzed reaction did not seem conceivable; Chisholm wrote 'superficially, the (W catalyzed) reaction would seem to provide a molecular model for the McMurry reaction...; however, the mechanisms of the two reactions differ'.[12] We note that the reductive coupling of carbonyls into pinacols and alkenes by means of titanium complexes is now called the McMurry reaction; this is justified by the leading role played by McMurry in establishing the reputation of this reaction in organic chemistry.

Recent applications

It is no longer necessary to demonstrate the remarkable efficiency of low-valent titanium compounds for carbon–carbon bond forming; their use in synthesis has been described in detail in previous reviews and only a brief reminder of the main domains of application will be given here, with recent representative examples shown in Fig. 1.

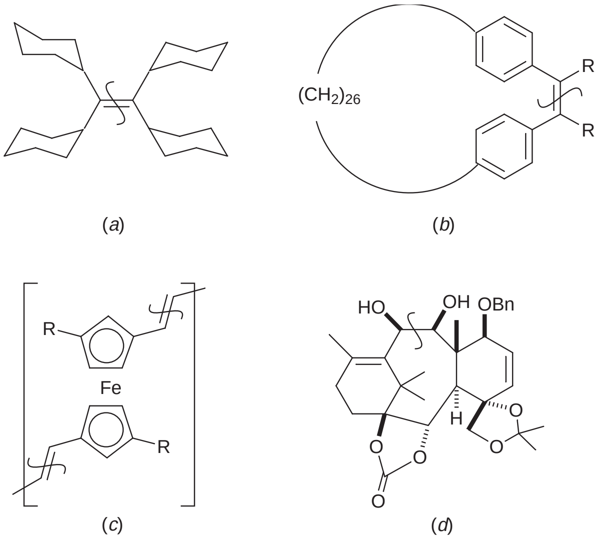
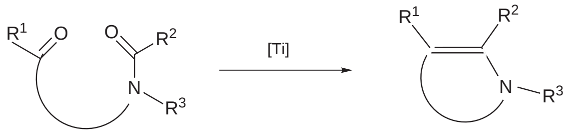


Fig. 1 Examples of compounds obtained by McMurry reactions: (*a*) a strained alkene (ref. 14), (*b*) a macrocycle (ref. 15), (*c*) a polymer (ref. 16) and (*d*) a key intermediate in the synthesis of taxol (ref. 20).

Low-valent titanium compounds served to prepare sterically hindered and/or strained olefins;[14] the driving force of the reaction is the formation of strong titanium–oxygen bonds. Many of these olefins, which exhibit specific physico-chemical properties and have a theoretical interest, could not be prepared by other methods. Also particularly notable is the effectiveness of the McMurry reaction in the synthesis of macrocycles.[15] The exceptional template effect exerted by titanium in intramolecular cyclizations of dicarbonyl molecules allowed the preparation of medium-sized and large rings; the yields are independent of the size of the cycloalkenes. A more recent application of the McMurry reaction was developed in polymer chemistry,[16] with the synthesis of polyvinylene or polypinacol derivatives and the preparation of new monomers with interesting properties.

But above all, it is with its crucial and elegant use in the key steps of numerous syntheses of natural products that the McMurry reaction has known a so great success. After the total synthesis of (+)-compactin and (+)-mevinolin by Clive *et al.*,[17] and the total synthesis of crassin by Dauben *et al.*[18] and McMurry and Dushin,[19] Nicolaou's synthesis of taxol[20] is possibly the most famous synthesis of a natural product which can be prepared with the aid of low-valent titanium compounds.

Very recently, Fürstner and co-workers considerably extended the scope of the conventional McMurry reaction: they found that titanium complexes were valuable auxiliaries for the reductive coupling of acylsilanes[21] and, more notably, the intramolecular cross-coupling reactions of ketones with amides; these substrates were previously reputed unreactive. The chemo- and regio-selective heteroarene synthesis (Scheme 4) represents a new efficient entry to a variety of substituted pyrrole and indole derivatives.[15,22,23]



Scheme 4 Reductive coupling of oxo amide molecules.

However, it is also recognized that the McMurry reaction suffers from serious problems of reproducibility, having a bad reputation as being tricky and highly 'co-worker dependent'. The chemist must be aware of the difficulties they will probably encounter in finding the suitable reagent and experimental conditions.

New reagents, new methods

Problems of reproducibility

McMurry reactions are usually carried out in two consecutive steps: reduction of $\mathrm{TiCl_4}$ or $\mathrm{TiCl_3}$, followed by addition of the carbonyl substrate; this procedure is imperative when the carbonyl compound is not inert towards the reducing agent. Many reducing agents were used: Li, Na, K, $\mathrm{KC_8}$, Mg, Mg(Hg), Zn, Zn(Cu), $\mathrm{LiAlH_4}$. This variety does not reflect the chemist's fantasy, but rather the problematic outcome of the reaction. The nature of the titanium reagent, as well as the solvent, temperature and reaction time, have a strong influence on the eventual formation and stereochemistry of the coupling products, diols (*dl* and *meso*) or alkenes (*Z* or *E*); as outlined by Lenoir,[2] a complete rationale for these results has to be found. In attempts to overcome these problems of reproducibility, McMurry himself proposed, after his discovery of the $\mathrm{TiCl_3}$–$\mathrm{LiAlH_4}$ system (1974),[8] several 'improved procedures' by using the $\mathrm{TiCl_3}$–K, $\mathrm{TiCl_3}$–Li (1976)[24] and then $\mathrm{TiCl_3}$–Zn(Cu) reagents (1978),[25] and finally recommended an 'optimized procedure' with the $\mathrm{TiCl_3(DME)_{1.5}}$–Zn(Cu) combination, which 'gave reproducibly high yields in every case it has been used' (1989).[26] The efficacy of this new procedure was illustrated by the coupling of $\mathrm{Pr^i{}_2CO}$ which afforded $\mathrm{Pr^i{}_2C{=}CPr^i{}_2}$ in 87% yield, instead of 17% by using $\mathrm{TiCl_3}$–$\mathrm{LiAlH_4}$ and 37% by using $\mathrm{TiCl_3}$–Zn(Cu). However, Letcka, a collaborator of McMurry, wrote in 1996, 'McMurry coupling does not always give high yields at the first, or even the second attempt, but with some experience, reproducibly high yields can be attained... We strongly recommend . . . several test couplings on cyclohexanone before venturing a coupling on the more complex material'.[3] Noteworthily, inferior results were attributed to bad experimental conditions—poor quality reagents or solvents, intrusion of air—rather than a lack of control of the mechanistic course of the reaction.

With the aim of obtaining more efficient reactions and better insights into the mechanisms, new low-valent titanium species have been designed in the last few years, and simplified methods have been developed.

Synthesis of alkenes

After the successful use of titanium graphite, especially in indole synthesis, Fürstner and co-workers reported that reduction of $TiCl_3$ with high surface area sodium gave a highly active titanium species supported on Al_2O_3, NaCl or TiO_2. The titanium–alumina species, which is presumably in the +1 oxidation state, was particularly efficient for the preparation of large cycloalkenes.[21]

Barteau and co-workers found that reductive coupling of aldehydes and ketones could also be carried out as a gas–solid process on the surface of reduced titania;[27–30] the reaction could be performed catalytically in the presence of hydrogen. Such reactions are not in need of strong reducing agents and a reduced oxide catalyst would be cheaper and easier to handle than the usual McMurry reagents in liquid–solid slurries. Moreover, the gas–solid reaction represents a potential route for coating of surfaces by conducting polymers, as suggested by the reductive coupling of *p*-benzoquinone.[28]

For the first time, Fürstner and Hupperts showed that commercially available titanium powder could be used as a McMurry reagent, after destruction of the tightly bound oxide layer by chlorosilane during the activation phase.[15] The Ti–R_3SiCl reagent exerted a strong template effect for macrocyclization reactions. In contrast to other systems which were claimed to produce Ti^0, this reagent was ineffective with aliphatic substrates, thus making chemo- and regio-selective coupling possible. The reaction with the Ti–R_3SiCl reagent could be performed either in two steps, by treating the titanium powder with the chlorosilane prior to addition of the substrate, or by heating all the components together.[15] Such a one-pot procedure, which is reliable when the reducing agent is not strong enough to affect the carbonyl group, had been employed by Mukaiyama with the $TiCl_4$–Zn system[7] and was recently reintroduced by Fürstner *et al.*, with the so called 'instant method'.[23] In fact, Bogdanovic and Bolte found that $TiCl_3$ could be reduced by Zn only if its redox potential has been lowered by co-ordination to the carbonyl substrate and therefore, a two step procedure is superfluous.[31] The simple and convenient 'instant' protocol, which is suitable for conventional McMurry couplings, has been applied to the synthesis of strained indoles.[23] Moreover, the reaction was rendered catalytic in titanium when carried out in the presence of a chlorosilane which reconverted the formed titanium oxychloride into $TiCl_3$.[15]

Synthesis of pinacols

Several works were devoted to the search of low-valent titanium compounds which would be suitable for the synthesis of pinacols with high stereoselectivity; these complexes should allow the McMurry reaction to be stopped at the 1,2-diol stage. Corey *et al.*found in 1976 that aromatic and aliphatic ketones and aldehydes could be coupled into the corresponding pinacols by treatment with $TiCl_4$ and Mg(Hg), at 0 °C in THF; reaction of a cyclic ketone with an excess of acetone gave the unsymmetrical diol.[32] Porta and co-workers reported that pinacols were formed with poor stereoselectivity (*dl*/*meso* = 1.3) by coupling of aromatic carbonyl compounds with aqueous $TiCl_4$ in basic media, but with $TiCl_3$ in anhydrous CH_2Cl_2 the pinacolization was highly diastereoselective (*dl*/*meso* > 100).[33]

Most recent studies revealed that such pinacol coupling reactions could be rendered stereoselective and catalytic with the use of additives and/or modified ligands. Banerji succeeded in stopping the reductive dimerization of acetophenone at the pinacol stage by addition of 10 equiv. of pyridine to the $TiCl_3$–Mg system. Also, in the presence of a stoichiometric amount of a mono- or di-hydroxy auxiliary, pinacols were obtained in higher yields and better stereoselectivity (*dl*/*meso* = *ca*. 4–5); among these additives, catechol was the most interesting for total pinacolization of aromatic carbonyl substrates, even under refluxing conditions.[34]

Ephritikhine reported on the first pinacol coupling reactions catalytic in titanium, by using the $TiCl_4$–Li(Hg) system in the presence of $AlCl_3$; a transmetallation reaction of the titanium pinacolate intermediates with $AlCl_3$ regenerated the precatalyst $TiCl_4$ and gave aluminium diolates which were inert towards the reducing agent and not transformed into the alkene.[35]

Catalytic pinacolization of benzaldehyde was achieved by Nelson with 1% $TiCl_3(THF)_3$ in the presence of Zn and Me_3SiCl. This combination was not effective for the coupling reactions of less electrophilic aldehydes and the diastereoselection was very low, but addition of 5 mol% of Bu^tOH led to a more reactive system which catalyzed the pinacolization of aromatic and aliphatic aldehydes and aryl methyl ketones with *dl*/*meso* ratios ranging from 1.5 to 4.8. Moreover, the stereoselectivity of the homocoupling of aryl aldehydes was substantially enhanced (*dl*/*meso* = 6.7 to 10.1) when 30 mol% of 1,3-diethyl-1,3-diphenylurea was added to the $TiCl_3(THF)_3$–Bu^tOH catalyst.[36]

Pinacol coupling can be affected by organotitanium compounds, as demonstrated by Corey *et al.* with the $CpTiCl_3$–$LiAlH_4$ reagent[32] and then by Handa and Inanaga with the Cp_2TiCl_2–Pr^iMgCl system.[37] Such reactions have known a significant improvement in the last few years. Barden and Schwartz reported that $[Cp_2TiCl]_2$ was able to reductively couple aromatic and α,β-unsaturated aldehydes into 1,2-diols in either anhydrous or aqueous media; the diastereoselectivity was high, with *dl*:*meso* ratios greater than 91:9.[38] Pinacol coupling of aromatic aldehydes was catalyzed by 3 mol% of *rac*-ethylenebis(η^5-indenyltitanium) dichloride in the presence of $MgBr_2$, Me_3SiCl and Zn to give the racemic 1,2-diols in good yield and with excellent diastereoselectivity (*dl*:*meso* > 96:4). These results of Gansäuer are encouraging for the investigation of asymmetric induction using enantiomerically pure metallocene catalysts.[39]

The nature of the active species and intermediates in these pinacol coupling reactions, which are performed with the aid of rather complicated systems, is not known. It is generally proposed that the high stereoselectivity of benzaldehyde or acetophenone coupling is due to the dimerization of ketyl radicals oriented in a manner which minimizes steric interactions between the phenyl groups (Fig. 2).

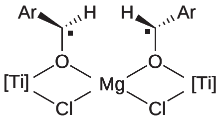


Fig. 2 Proposed intermediate for the diastereoselective coupling of benzaldehyde; [Ti] = Cp_2Ti (ref. 37) or *rac*-ethylenebis(η^5-indenyltitanium) (ref. 39).

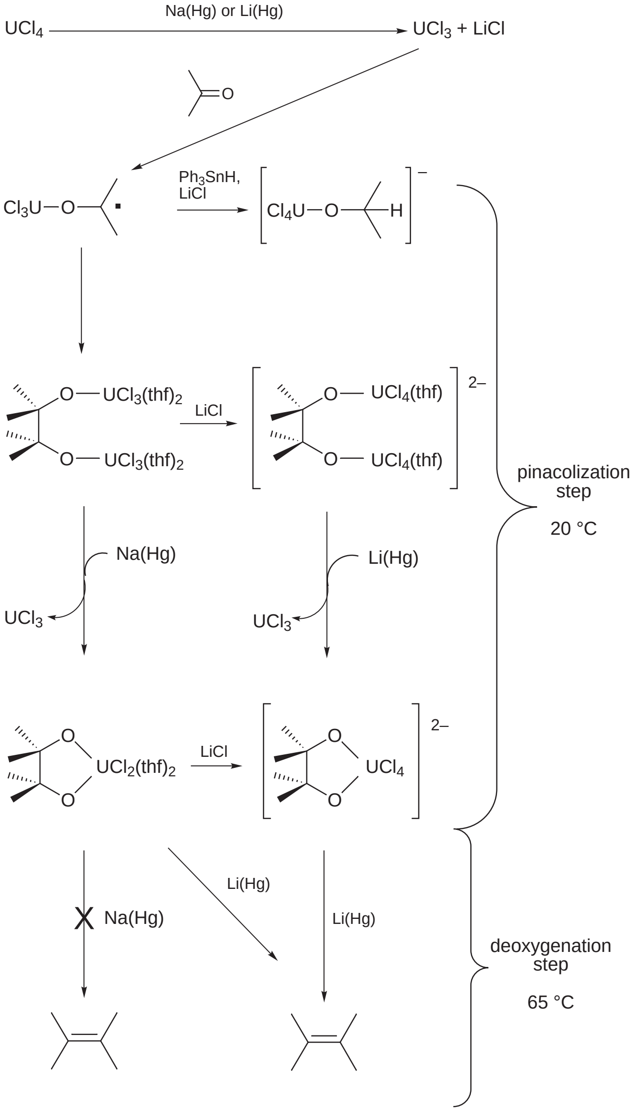
New insights into the mechanism

The nature of the active species

As noted above, there was apparently no doubt about the involvement of pinacolate intermediates in the McMurry reaction and the main questions rather concerned the nature of the active species, and in particular its oxidation state. Despite several indications that Ti^{III} or Ti^{II} compounds could effect the reductive coupling of carbonyl substrates—Corey *et al.* reported in 1976 that $(C_6Me_6)Ti(AlCl_4)_2$ was able to couple acetone and cyclohexanone[32]—it has been long believed that finely divided titanium particles were the active species in McMurry reactions. This assumption was reinforced by the studies of Geise on the $TiCl_3$–M (M = Li, K, Mg) or $TiCl_3$–$LiAlH_4$ systems,[40] but it is now clearly established that the presence of Ti^0 is not a prerequisite for the McMurry reaction.

Barteau found no evidence for the presence of Ti^0 on reduced TiO_2 surfaces active for benzaldehyde coupling; X-ray photoelectron spectroscopy revealed that the active site required for gas–solid reductive coupling is an ensemble of Ti cations in the +1, +2 and +3 oxidation states which collectively effect the four electron reduction.[29]

A decisive contribution to these mechanistic investigations was made by Bogdanovic and Bolte, who identified the nature and mode of action of the active species in some classical McMurry systems.[31] The low-valent titanium species obtained by reduction of $TiCl_3$ with $LiAlH_4$ was shown to be $[HTiCl(THF)_{0.5}]_x$;[41] this titanium hydride reacted with acetophenone to give PhMeC=CMePh and behaved as a strong two electron reductant. In contrast, the $TiCl_2 \cdot LiCl$ reagent proposed by Eisch *et al.*[42] acted as a one electron reductant in the coupling of PhCOMe. Titanium(II) species were also involved in both the ketone→pinacolate and pinacolate→alkene steps of the reductive coupling of acetophenone with the $TiCl_3(DME)$–Zn(Cu) system; the nucleophilic mechanism proposed for this reaction (Scheme 5) was supported by quantum mechanical calculations.[43] These coupling reactions were shown to proceed by two consecutive steps: formation of the pinacolate intermediates which occurred at room temperature, followed by alkene synthesis at reflux temperature. Their progression was determined after analysis of the products obtained by hydrolysis of aliquots, and occurrence of pinacolate intermediates was inferred from formation of 2,3-diphenylbutane-2,3-diol; however, such intermediates were not observed and characterized. In fact, a very few metallopinacols were isolated from reactions of organic carbonyl substrates with $Cp_2Ti(CO)_2$ or $CpTiX_2$ (X = Cl or Br) and no alkene was obtained from these derivatives.[44]

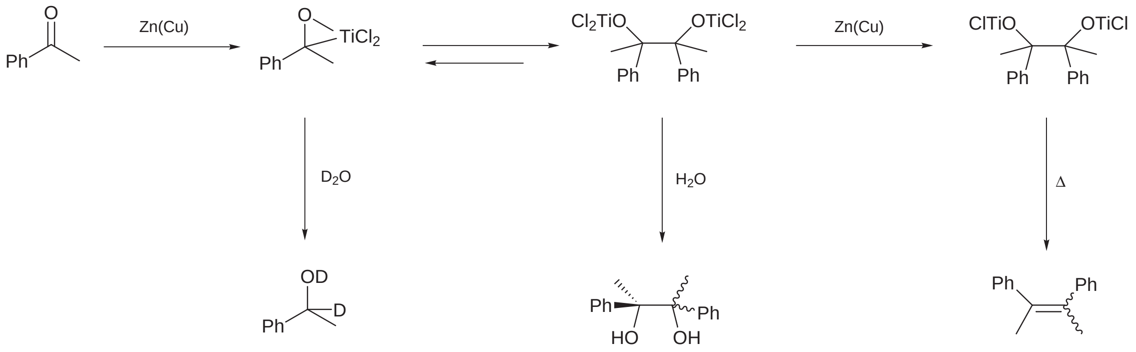


Scheme 6 Metallopinacols isolated from the reductive coupling of acetone with the UCl_4–M(Hg) systems (M = Li or Na).

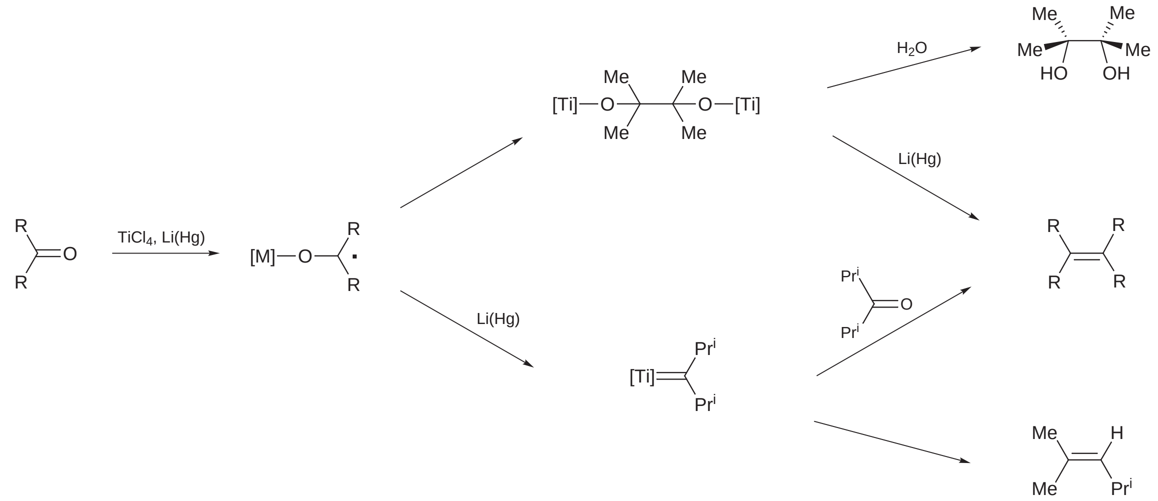
Characterization of the pinacolate intermediates

Ephritikhine considered the reactions of ketones with the UCl_4–M(Hg) and $TiCl_4$–M(Hg) systems (M = Li or Na). Uranium and titanium complexes exhibit strong similarities in structure and reactivity but uranium compounds have some advantages over their titanium counterparts: they can be easily detected by their highly-shifted paramagnetic NMR signals and they often crystallize with less difficulty. Therefore, the chances of isolating and characterizing the intermediates are greater. The active uranium species in the UCl_4–M(Hg) systems were shown to be in the +3 oxidation state; it was demonstrated by electrochemical studies that reduction of UCl_4 into UCl_4^- was rapidly followed by a chloride ion transfer from UCl_4^- to UCl_4, giving UCl_3 and the anionic U^{IV} complexes $U_2Cl_9^-$ and UCl_5^- which were then reduced at lower potentials.[45]

Reaction of benzophenone with UCl_4 and Na(Hg) afforded successively the mono- and bis-benzopinacolates $UCl_2(O_2C_2Ph_4)$ and $U(O_2C_2Ph_4)_2(THF)_2$; the latter was characterized by its X-ray crystal structure. These compounds gave benzopinacol upon hydrolysis and were transformed into tetraphenylethylene after reduction with Na(Hg).[46] Several metallopinacols were isolated from the reaction of acetone with UCl_4 and M(Hg) (Scheme 6); whatever the amalgam used, the first intermediate was the dinuclear complex $(UCl_3L_2)_2$(μ-



Scheme 5 Proposed mechanism for the reductive coupling of benzophenone with the $TiCl_3$–Zn(Cu) system.



Scheme 7 The distinct mechanisms of the reductive coupling of acetone and diisopropyl ketone with the $TiCl_4$–Li(Hg) system.

$OCMe_2CMe_2O$) (L = THF) resulting from dimerization of the ketyl radical $[Cl_3UOCMe_2]^{\cdot}$; the crystal structure of the adduct with L = $OP(NMe_2)_3$ was determined (see front cover). The structure of the metallopinacols and their eventual transformation into $Me_2C{=}CMe_2$ were found to be strongly influenced by the molar ratio of the reactants, the nature of the reducing agent (M = Na or Li) and of the formed salt (NaCl or LiCl).[47]

Problems of reproducibility

The reductive coupling of acetone with the UCl_4–Li(Hg) system raised the problems of reproducibility. The alkene was formed in almost quantitative yield when the reaction was carried out in two consecutive steps: the pinacolization step at 20 °C and the deoxygenation step at 65 °C. However, it was much less easy, without extensive experience of the UCl_4–Li(Hg) system, to produce the alkene in a reproducible manner using a one pot procedure. This discrepancy could be related to side reactions of the different metallopinacols, which could be avoided only by determining the right time for heating the reaction mixture.[48] It was thus pointed out that, in addition to the quality of the reagents, experimental parameters like reaction time and temperature, which are directly connected to the mechanistic control of the reaction, would constitute major sources of non-reproducibility. These parameters cannot always be easily monitored in an heterogeneous medium.

Evidence of carbenoid intermediates

New facts emerged when Me_2CO was replaced with Pr^i_2CO in its reaction with the UCl_4–Li(Hg) or $TiCl_4$–Li(Hg) systems.[49] The only coupling product was then $Pr^i_2C{=}CPr^i_2$ whereas a large amount of 2,4-dimethylpent-2-ene was formed. Control experiments showed that $Pr^i_2C{=}CPr^i_2$ did not result from the deoxygenation of pinacolate intermediates; moreover, it was found that $Cl_3TiOCPr^i_2CPr^i_2OTiCl_3$ was not stable, being readily transformed into a mixture of $TiCl_3$ and Pr^i_2CO. The facile cleavage of the titanium pinacolates and the absence of pinacol in the product mixture indicated that reductive coupling of Pr^i_2CO would not proceed by dimerization of ketyl radicals, whereas formation of 2,4-dimethylpent-2-ene revealed the likely involvement of carbenoid intermediates.

These data put forward the dual nature of the mechanism of these McMurry type reactions (Scheme 7). Contrary to the generally accepted mechanism, metallopinacols are not the only precursors to the alkene; if the ketyl radicals can be effectively coupled into pinacolate intermediates, they can also be reduced and deoxygenated into carbenoid species which provide the alkene after further reaction with the ketone. The course of the reaction, *via* the metallopinacol or the carbenoid intermediates, is largely determined by the steric hindrance of the ketone; the most hindered ketones would follow the carbenoid route because of the difficult coupling of the ketyl radicals, and the reversible cleavage of the pinacolic C–C bond.

Now it seems that some McMurry reactions could be re-examined by considering the possible involvement of carbenoid intermediates. If the formation of 2,4-dimethylpent-2-ene was overlooked in the McMurry reactions of Pr^i_2CO, cyclohexene was detected among the products of the reductive coupling of cyclohexanone with the $TiCl_3$–K system[40] and the alkenes $RCH{=}CH_2$ (R = Me, Ph) were formed during the coupling of acetone and acetophenone on reduced alumina;[30] these alkenes would indicate the occurrence of carbenes as intermediates, even if such species could not be trapped with usual reagents. Also, Barteau observed that during the coupling of PhCOMe on reduced TiO_2 surfaces, the pinacol product was evolved at much higher temperature than $PhCH{=}CH_2$; this result was interpreted by the formation of pinacolate species at protected sites which are difficult to reduce at low temperature,[30] but it is possible that pinacols and alkenes were produced in parallel rather than sequential processes.[50]

Conclusion

The McMurry reaction represents a versatile transformation which is irreplaceable in organic synthesis. However, the huge interest and great success of this reaction conceal some experimental problems which have to be related to the difficulty in understanding the actual mechanism. Significant progress has obviously been made during the last years in the development of new reagents and methods leading to further interesting applications of low-valent titanium complexes, but these investigations also revealed that the course of the McMurry reaction is more complicated than previously assessed. The structure of the intermediates, pinacolate and/or carbenoid species, is strongly dependent on the nature of the carbonyl substrate, the titanium compound, the reducing agent and the by-products. At each stage of the process, the present intermediates can undergo side reactions which would affect the eventual formation of 1,2-diols or alkenes and give rise to problems of reproducibility. Other important aspects of the mechanism, for example the deoxygenation of the pinacolate intermediates and the role of additives in the stereoselectivity, are even more obscure. No doubt these questions will not discourage chemists, but rather incite them to consider the fascinating McMurry reaction with a more critical view.

Acknowledgments

I thank my colleagues and co-workers, whose names appear in the references, for their valuable contributions to this work.

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