ORGANIC
CHEMISTRY
FRONTIERS

Accepted Manuscript

http://rsc.li/frontiers-organic

Journal Name

ARTICLE

A Simple and Practical Catalytic Electron Transfer System Composed of TiCl$_4$ and Metallic Yb: Application in Carbonyl Olefination and Insight into Mechanism

Lili Zhang,[a] Xiaying Yu,[a] Lixin Zhang,[a] Xigeng Zhou*[a,b] and Yanghui Lin*[a]

The McMurry-type olefinations have become a powerful tool in organic synthesis. However, the use of stoichiometric amounts of unmanageable Ti species and the generation of large amount of salts limit their applications on the industrial scale. This paper outlines a simple and practical catalytic electron transfer (ET) system composed of TiCl$_4$ and Yb, which turned out to be effective for homo- and cross-deoxygenative coupling of aldehydes and ketones. Specifically, the method is based upon the strategy that the low valent Ti species abstracts oxygen from carbonyl and delivers them to highly oxophilic Yb in an unprecedented manner. Remarkably, the present process is operationally simple, minimizes the generation of chemical waste, and makes the only by-product Yb$_2$O$_3$ as solid easily removed and utilized; further, the yield improved significantly on that obtained in the stoichiometric version in our system. Our mechanistic data not only provide the direct evidence that Ti(IV) can facilitate the part deoxygenation of pinacol at room temperature, but also demonstrate, for the first time, that for bulky ketones the turnover-limiting step is the Ti-mediated carbonyl coupling rather than the subsequent deoxygenation of the resulting pinacolate intermediates, which are different from the previous observations.

Introduction

The selective construction of C-C double bonds continues to be an important goal in organic synthesis. The McMurry reaction is one of the most broadly utilized methods for the carbonyl olefination as it allows direct formation of crucial C=C bonds and thus reduces the number of steps in synthesis of natural or biologically relevant compounds.[1-3] Despite tremendous advances in this area, most well-established methods require the use of excess titanium reagents and reductants even in the presence of activating reagents[4] and ligands,[5] and involve the stoichiometric production of metal salts (e.g. metal chloride and alkoxide) which are often elusive to remove from the reaction mixture and/or have occasionally adverse effects.[6] Pioneering work reported in 1995 by Fürstner and Hupperts showed that the reductive coupling of aromatic oxoamides to indoles can be performed catalytically in low-valent Ti by using a chlorosilane as the final oxygen trap (Scheme 1).[7] Recently, Barrero and coworkers reported that Cp$_2$TiCl$_2$ could effect the catalytic transformation of benzylic aldehydes to 1,2-diarylethenes in the presence of excess Mn and Me$_3$SiCl.[6] Notably, the introduction of chlorosilanes not only leads yet to the generation of large amounts of metal chlorides, but also probably increases the consumption of reductants due to their potential reaction with chlorosilanes.[8] In view of economical benefit and environmental impact, further improvements in this area are desirable.

One of the most ideal methods for carbonyl reductive-olefination, in our opinion, would be the use of single metal as both the reductant and oxygen-trapper in the presence of a suitable catalyst without the requirement of additives; however, no example of such a reaction has been reported so far.
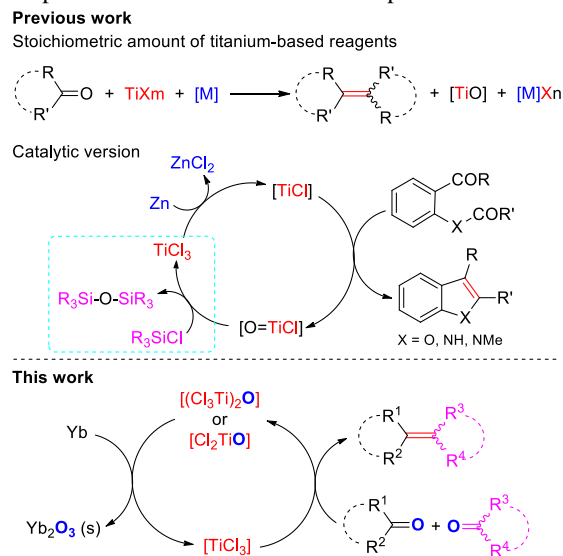
Scheme 1 Comparison of the prior work to the current work.

In addition to the synthetic utility and challenges described above, these carbonyl olefinations also posed an interesting mechanistic question. Although it has been widely accepted that species with low valence states of Ti were required in this reductive process, there is little information concerning the structures and reactivities of the intermediates.[1] The mechanistic subtleties toward reductants, additives, reaction conditions and ancillary ligands in these systems remained yet to be clarified. In particular, the reactivity of reducing agents toward the titanium oxo or oxychloride species resulting from the deoxygenation step remains unexplored. Moreover, the factors that control stereochemistry of products are not well understood yet.[9] Consequently, detailed mechanistic studies involving the reactivity of related Ti species toward the reducing agents and substrates are of great importance in unraveling factors that promote or deter carbonyl olefination. The development of a new strategy for the extrusion of oxygen from the titanium oxo species would permit one to enable design of new reductants and incorporate the stoichiometric reductive carbonyl coupling reaction in some catalytic version.

Synthetic utility of rare earth metals as the reductants is receiving increased attention because of their unique reactivities and inherent advantages over divalent rare earth complexes, such as stability in air, non-toxic, cheaper and more commercial availability, easy manipulation and store, as well as the higher atom efficiency through three-electronic transfer.[8b,10] Disappointingly, the highly kinetic inert and thermodynamic stability of rare earth metals under conventional conditions restrict their applications. Although several methods for activation of rare earth metals have been developed and offer a scaffold for interesting applications in organic synthesis, their application is still relatively limited.[10] Thus, the development of simple and practical electron transfer reagents, especially catalytic systems that can improve the electron-releasing ability of rare earth metals and thus are suitable for selective organic transformations, is required. Although several diversified reductions of ketones and aldehydes with rare earth metals were reported, on the other hand, the olefination product has never been obtained selectively.[11]

Herein, we report a catalytic ET system composed of $TiCl_4$ and Yb and its application in transformation of carbonyls to olefins, in which the Ti(IV) accept electrons from metallic Yb and deliver them to the substrate and the resulting precipitate Yb_2O_3 is easily removed. Some unprecedented mechanistic features are observed under our catalytic conditions. The process exhibits broad scope, simple manipulation, good environmental tolerance and a saving on the metal-containing reagents through the multi-electron reductive effect of metallic Yb and avoidance of additives. Furthermore, the present results represent a convenient way for catalytic activation of commercial rare earth metals as an off-the-shelf reagent.

Results and discussion

Our research is based on the premise that the reducing agent not only provides more than two-electron but also should participate in the oxygen abstraction. To test this premise, we selected rare earth metals as reducing agents. Table 1 summarizes the results of optimization of an $M/TiCl_4$-mediated reductive coupling of benzophenone (**1a**) to tetraphenylethene (**2aa**). In the absence of $TiCl_4$, the reaction did not take place (entry 1). The reaction of **1a** with a mixture of Yb and $TiCl_4$ in molar ratio of 1:1:0.1 at 70 °C for 24 h gave the deoxygenated coupling product **2aa** in 91% yield (entry 2). It was found that

2aa could be obtained in almost quantitative yield when $TiCl_4$ was adjusted to 0.3 equivalences at 70 °C (entry 4). Notably, the reaction can also proceed smoothly at room temperature (entries 5 and 6), which is extremely rare. The loading of one equivalent of $TiCl_4$ gave **2aa** in 95% yield (entry 7), which meant a decrease in the efficiency of transformation when compared to the catalytic version. Unceasingly increasing the amount of Yb would fasten the reaction rate, but did not affect the reaction products (entry 8). Of all solvents tested, THF performed best (entry 4). No desired product was obtained, when the reaction was carried out in non-coordinated solvents such as toluene (entry 10). Examination of different rare earth metals revealed Yb as the best reductant (entries 4, 11, 12). In addition, the use of Fe or Sn in place of the lanthanide metal did not give the desirable product (entries 13 and 14). Based on the stoichiometric ratio of ketone/Yb/$TiCl_4$, the present deoxygenated coupling reaction not only makes full use of the superiority that rare earth metals can provide three reductive electrons, but also makes rare earth metals as a basic oxygen-trapper. Clearly, the present reducing system makes a significant saving on the molar amount of metal-based reagents compared with other reducing systems.[2,4,6,7] To the best of our knowledge, this is the first example that the reductant plays a basic oxygen-trapper in the titanium-based reduction protocol.

Table 1 Optimization of the reaction conditions[a]

| Entry	M (equiv)	TiCl₄ (equiv)	Solvent	Temp (°C)	Isolated yield (%)
1	Yb(1)	0	THF	70	0
2[b]	Yb(1)	0.1	THF	70	91
3	Yb(1)	0.2	THF	70	94
4	Yb(1)	0.3	THF	70	99
5[b]	Yb(1)	0.3	THF	25	74
6[c]	Yb(1)	0.3	THF	25	90
7	Yb(1)	1.0	THF	70	95
8[d]	Yb(2)	0.3	THF	70	99
9	Yb(1)	0.3	DME	70	97
10	Yb(1)	0.3	Toluene	70	0
11	Sm(1)	0.3	THF	70	95
12	Dy(1)	0.3	THF	70	90
13	Fe (1)	0.3	THF	70	0
14	Sn (1)	0.3	THF	70	0

[a] **1a** (1.0 mmol), solvent (8 mL) for 5 h under N_2. [b] Reaction time is 24 h. [c] Reaction time is 72 h. [d] Reaction time is 2 h.

Having established an optimal protocol, we next investigated the generality and the scope of this transformation via variation of ketones and aldehydes. As illustrated in Table 2, the reaction conditions described above are effective for the transformation of a number of ketones and aldehydes, various alkenes can be efficiently synthesized from this reaction in good to excellent yields. In general, the trans-isomer was predominantly obtained when the reaction involved the diastereoselectivity. Aromatic ketones with neutral and electron-donating substituents such as methyl and methoxy groups on the phenyl ring gave the deoxygenated products **2** in nearly quantitative yields (entries 4-6). The presence of electron-withdrawing groups such as chloride in the *para-*

position of benzene rings seems to negatively affect the yields, but the E/Z selectivity remained essentially constant (entries 7-9). Naphthyl methyl ketone (**1j**) worked well under this condition, yielding **2jj** in 88% yield, albeit with low E/Z selectivity (entry 10). Furthermore, 9-fluorenone (**1k**) was also suitable substrate, and the desirable product **2kk** was generated in 89% yield (entry 11). 1-(Furan-2-yl) ethanone and 1-(thiophen-2-yl) ethanone provided the corresponding products in almost quantitative yields too (entries 12 and 13). Gratifyingly, less reactive aliphatic ketone (**1n**) worked smoothly under the optimal reaction conditions, affording **2nn** in 81% yield (entry 14).

Subsequently, utility of various aldehydes was examined. To our delight, various aromatic aldehydes **1o-1s** smoothly underwent the McMurry-type olefination, giving **2oo-2ss** in excellent yields with complete E selectivity (Table 2, entries 15-19). Cinnamaldehyde is clearly compatible with the reaction (Table 2, entry 20).

Table 2 Reductive coupling reaction of ketones and aldehyde[a]

Entry	Substrate	R^1	R^2	Product	E:Z ratio[b]	Isolated yield (%)
1	**1a**	C_6H_5	C_6H_5	**2aa**		99
2	**1b**	C_6H_5	CH_3	**2bb**	94:6	99
3	**1c**	C_6H_5	CH_3CH_2	**2cc**	82:18	98
4	**1d**	4-MeC$_6$H$_4$	CH_3	**2dd**	79:21	99
5	**1e**	4-MeOC$_6$H$_4$	CH_3	**2ee**	78:22	99
6	**1f**	4-MeOC$_6$H$_4$	4-MeOC$_6$H$_4$	**2ff**		99
7	**1g**	4-ClC$_6$H$_4$	4-ClC$_6$H$_4$	**2gg**		90
8	**1h**	3-ClC$_6$H$_4$	CH_3	**2hh**	77:23	96
9[c]	**1i**	$3,4$-Cl$_2$C$_6$H$_3$	CH_3	**2ii**	79:21	90
10	**1j**	1-naphthyl	CH_3	**2jj**	60:40	88
11	**1k**			**2kk**		89
12	**1l**	2-furanyl	CH_3	**2ll**	49:51	98
13	**1m**	2-thiophenyl	CH_3	**2mm**	83:17	97
14[c]	**1n**	PhCH$_2$	PhCH$_2$	**2nn**		81
15	**1o**	C_6H_5	H	**2oo**	100:0	95
16	**1p**	4-ClC$_6$H$_4$	H	**2pp**	100:0	95
17	**1q**	4-MeOC$_6$H$_4$	H	**2qq**	100:0	94
18	**1r**	4-CH$_3$C$_6$H$_4$	H	**2rr**	100:0	98
19	**1s**	2-furanyl	H	**2ss**	100:0	90
20[c]	**1t**	PhCH=CH	H	**2tt**	84:16	86

[a] TiCl$_4$ (0.3 mmol), Yb (1 mmol), carbonyl compound (1 mmol), THF (8 mL) for 5 h at 70 °C under N$_2$. [b] The E/Z ratio measured by ^{1}H NMR. [c] Reaction time is 7 h.

The discovery of reagent systems that allow the selective manipulation of functional groups is crucial for advancements in synthesis. Of particular value are reagent systems that allow functional groups with apparently similar reactivities to be distinguished. Compared to the impressive development of homo-coupling of carbonyl compounds to olefins, the cross-coupling between two different carbonyl compounds has received only scant attention.[2k,6] The major reason may be attributed to the difficulties for controlling required selectivity due to the facile homologous coupling pathways available, in most cases this kind of reactions will generate a roughly statistical mixture of the possible coupling products. Therefore, the use of such reaction in organic synthesis remains a challenge. In seeking to further broaden the scope of this work, we checked the ability of the Yb/TiCl$_4$ reductive system to promote the cross-coupling reaction between different ketones (Table 3). When a variety of diary ketones and one equivalent of aliphatic ketone were submitted to the standard reaction conditions, the desired cross-coupling products were obtained in 83-94% isolated yields. For example, acetone, cyclopentanone and cyclohexanone reacted with one equivalent of benzophenone to give the corresponding cross-coupling products **2au**-**2aw** in 83-87% yields. Aromatic ketones bearing additional functional groups (**1f**, **1g**) led efficiently to the coupling products, which increase the potential of this transformation. The reaction conditions described above are also effective for the cross-coupling of 9-fluorenone (**1k**) with aliphatic ketones, various fulvalenes can be efficiently synthesized from this reaction in excellent yields (**2ku**-**2kw**). Encouraged by the above results, we further envisioned that combination of aldehydes with ketones could subject to the transformation in the current experimental conditions. Treatment of a mixture of aromatic ketone and pivalaldehyde with the Yb/TiCl$_4$ reductive system gave the expected cross-coupling products **2fx**, **2gx** and **2kx** in excellent yields. The cross-coupling of aromatic aldehydes with ketones was also conducted under the same condition, but it gave **2ko** and **2pu** in moderate yields in company with the formation of a small amount of diarylethenes. This protocol proved to be applicable, less efficiently, to the deoxygenative cross-coupling between aromatic aldehyde and aliphatic aldehyde (**2ox**).

Having demonstrated that the lanthanide metals are able to reduce carbonyls to alkenes in the presence of a catalytic amount of TiCl$_4$, we were interested in gaining insight into the reaction mechanism. Initially, we studied the metal-containing components in the reaction mixture when the Ph$_2$CO had been completely consumed. To our delight, the clear solution was concentrated and cooled at –18 °C to give TiCl$_3$(THF)$_3$ (75%), which was confirmed by single crystal X-ray diffraction analysis. The resulting gray precipitate was filtered, washed with hot THF and analyzed by complexometric titration, supporting the selective formation of Yb$_2$O$_3$. In contrast to the observations in reaction of TiCl$_4$ or TiCl$_3$ with other metals, wherein titanium species in zero- or divalent state, such as [Ti(MgCl$_2$)·nTHF][2b, 12], is generally involved as the active reducing species, the reaction of TiCl$_4$ with 1.2 equiv Yb in THF at 70 °C for 1 h gave TiCl$_3$(THF)$_3$ in 82% yield (Scheme 2). Furthermore, we examined the stoichiometric reaction of TiCl$_3$ with Ph$_2$CO and PhCOMe. Only trace amount of olefination product was observed in the reaction of TiCl$_3$ with Ph$_2$CO or PhCOMe even with prolonged heating in THF (70 °C), and the starting materials were recovered unchanged. However, TiCl$_3$ easily abstract the oxygen from 2,3-diphenyloxirane, giving stilbene (**2oo**) in almost quantitative yield (Scheme 3). Significantly, treatment of a 1:2 mixture of TiCl$_3$ and Ph$_2$CO with 1/3 equiv of Yb at room temperature gave a mixture of tetraphenylpinacol and tetraphenylethene in 16.2% and 22.8% electron yields (based on the total number of reductive electrons that

TiCl$_3$ and Yb provide as much as possible), respectively. The product distribution depended on the reaction temperature. Heating the reaction mixture resulted in an increase of the olefin production (Scheme 4). At this point, addition of a further 1 equiv of Yb led to the complete consumption of starting material Ph$_2$CO, tetraphenylethene being the only product formed. Given the facts that Yb is not able to reduce Ti to a valence lower than 3 under mild conditions and that sole Yb does not promote dimerization of Ph$_2$CO in present conditions (Table 1, entry 1), it was reasonable to assume that the ET from Yb to a Ti ketyl is simultaneous to the ET from Ti to another carbonyl in the reductive-coupling process, according to the mechanistic proposal depicted in Scheme 7. The isolation of olefin as the main product from the 3:6:1 reaction of TiCl$_3$, Ph$_2$CO and Yb clearly demonstrates that the coupling step is rate determining and not the subsequent fission of the C-O bonds, which is contrast to the previous observation.[6,9]
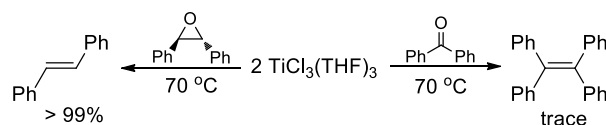
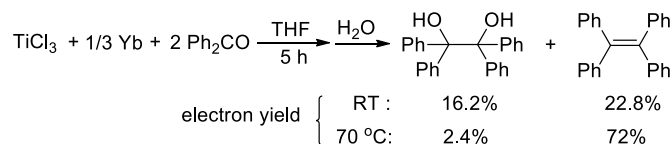**Table 3** Cross-coupling reaction between different carbonyls[a]
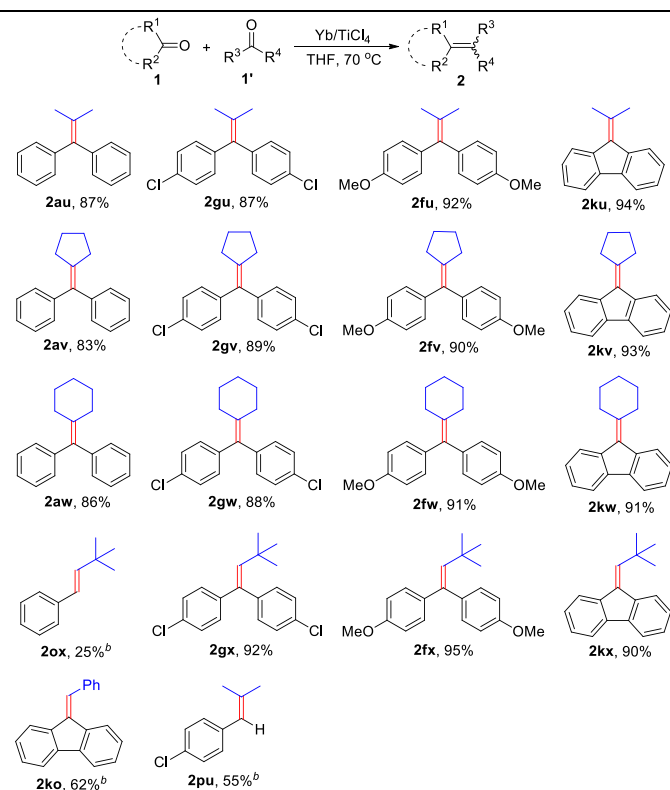
a Reaction conditions: TiCl$_4$ (0.3 mmol), Yb (1 mmol), 0.5 mmol ketone (aldehyde) and 0.5 mmol another carbonyl compound, THF (10 mL) for 5-7 h at 70 °C under N$_2$. *b* homo-coupling by-products, 1,2-diarylethenes, were obtained.
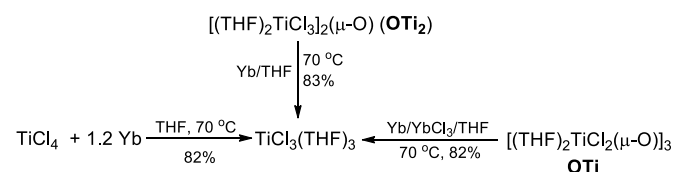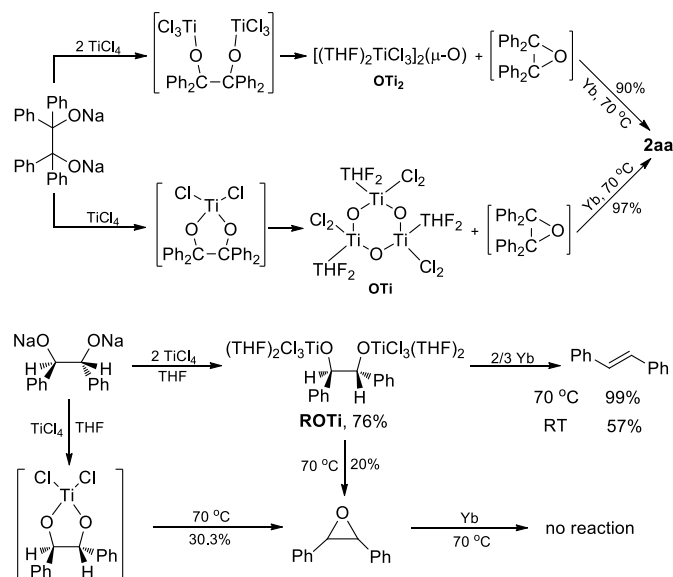

Scheme 2 Formation and regeneration of TiCl$_3$

Scheme 3 Reaction of TiCl$_3$ with epoxide and ketone
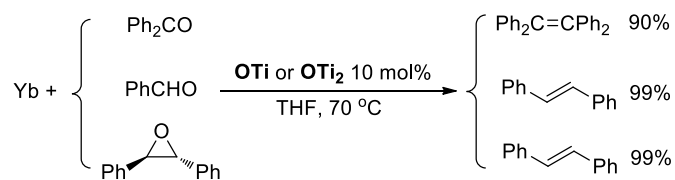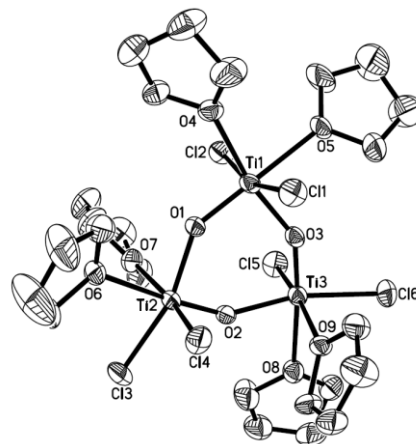

Scheme 4 Examination of rate-determining step

To further assess whether Ti(IV) pinacolates are intermediates in the catalytic olefination reactions, tetraphenylethane-1,2-diol (H$_2$TPL) and 1,2-diphenylethane-1,2-diol (H$_2$DPL) were prepared. Salt-metathesis reactions of TiCl$_4$ with 1 equiv of Na$_2$TPL at room temperature, generated in situ by stirring H$_2$TPL with 2 equiv of NaH as described by Woo,[13] provided [(THF)$_2$TiCl$_2$(μ-O)]$_3$ (**OTi**, Figure 1) in 82% yield, indicating that Ti(IV) tetraphenylpinacolate is unstable. Adding 2/3 equiv of Yb to the above mixture gave tetraphenylethene in 97%. Encouraged by this result, we subsequently treated Na$_2$TPL with 2 equivalent of TiCl$_4$ under the same conditions. A different Ti oxychloride [(THF)$_2$TiCl$_3$]$_2$(μ-O) (**OTi$_2$**)[14] were obtained with high efficiency (83% yield) after 24 h at room temperature. Treatment of Na$_2$TPL with 2 equiv of TiCl$_4$ followed by reacting with 2/3 equiv of Yb gave tetraphenylethene in 90% too (Scheme 5). Interestingly, switching Na$_2$TPL to Na$_2$DPL resulted in the isolation of the expected pinacolate Ti(IV) complex (**ROTi**), which can be partly transformed to **OTi$_2$** and 2,3-diphenyloxirane when heating at 70 °C. This difference between the reactivities of TPL[TiCl$_3$(THF)$_2$]$_2$ and DPL[TiCl$_3$(THF)$_2$]$_2$ is not surprising, since the epoxide elimination should be more facile for larger sterically crowding pinacolate than for the less sterically crowding one. Consistent with this, it was found that the mononuclear Ti pinacolate seems to undergo the epoxide elimination more easily than the dineclear congener **ROTi** under the same conditions. In contrast, no olefination product was observed in reaction of [(Me$_3$Si)$_2$N]$_2$YbCl with H$_2$TPL and subsequent Yb at 70 °C even for 24 hours. These results with pinacol probes support the intermediacy of a Ti(IV) pinacolate, which liberates alkene through a stepwise O-atom-transfer. The stepwise deoxygenation of Ti(IV) pinacolates indicates that the stereochemistry of the resulting alkenes mainly originates from the pinacol coupling of carbonyls.

It is well-known that the low-valent titanium-mediated deoxygenation of pinacols is generally carried out via a successively homolytic cleavage of two C-O bonds, the presence of this first radical would facilitate the second C-O cleavage to lead to the corresponding olefin.[6] As a result, it is very difficult to isolate the epoxide intermediate and control the stereochemistry of the resulting alkenes in such deoxygenation process. Remarkably, a sequential O-atom-transfer pathway became more pronounced under our catalytic conditions, which should explain the excellently completely stereoselective formation of *E*-1,2-diarylethene products.

Scheme 5 Simulating the deoxygenating processes

Scheme 6 Catalytic deoxygenative coupling of carbonyls and epoxide using **OTi** and **OTi$_2$** as a catalyst

Figure 1 ORTEP structure of **OTi**. Thermal ellipsoids set at 30% probability. Hydrogen atoms are omitted for clarity.

Although Ti-promoted pinacolization and deoxygenation coupling of aromatic aldehydes and ketones have been studied extensively, to the best of our knowledge, this is the direct evidence reported to date suggesting that Ti(IV) can facilitate the part deoxygenation of pinacol at room temperature. To gain more information on the mechanism of the catalytic olefination of carbonyls, we conducted catalytic and stoichiometric reactions with isolated **OTi** and **OTi$_2$** complexes. First, we investigated the regeneration of the active titanium species lying on the catalytic reaction (Scheme 2). Reduction of [TiCl$_3$(THF)]$_2$(μ-O) with Yb in THF at 70 °C led smoothly to the regeneration of TiCl$_3$(THF)$_3$. Significantly, reaction of [TiCl$_2$(THF)$_2$(μ-O)]$_3$ with Yb in the presence of YbCl$_3$ in THF at 70 °C for 5 h gave TiCl$_3$(THF)$_3$ too. Second, we performed the catalytic reaction in the presence of **OTi$_2$** or **OTi** (Scheme 6). Indeed, we found that a catalytic amount of **OTi$_2$** or **OTi** (10 mol%) could effect the transformation of Ph$_2$CO to tetraphenylethene in the presence of 1 equiv of Yb at 70 °C. At this moment, Yb$_2$O$_3$, which can be easily removed, was again proven to be the final acceptor of oxygen. Finally, the present **OTi$_2$** or **OTi** catalyst could perform the deoxygenation of 2,3-diphenyloxirane with Yb to give **2oo** in almost quantitative yield.[15] However, in the absence of **OTi$_2$** or **OTi**, the deoxygenation did not take place (Scheme 5). This result is consistent with the intermediacy of [TiCl$_2$(THF)$_2$(μ-O)]$_3$ and [TiCl$_3$(THF)$_2$]$_2$(μ-O) in the catalytic reaction.
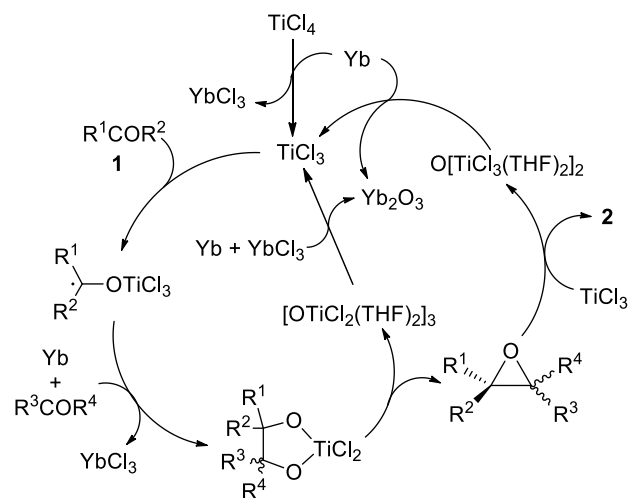
Scheme 7 Possible mechanism for the present catalytic olefination of carbonyls

On the basis of the observations described above and reported previously[6,9], a possible mechanism for the present catalytic olefination of bulky ketones can be proposed as shown in Scheme 7. Reduction of TiCl$_4$ with Yb generates TiCl$_3$, which reacts with ketone to form the Ti ketyl intermediate. The further ET from Yb to the Ti ketyl complex is prerequisite for coupling of the ketyl with another carbonyl.[9] The resulting Ti(IV) pinacolate intermediate undergoes the concerted epoxide elimination to afford **OTi**. TiCl$_3$ abstracts oxygen from epoxide, giving the olefination product **2**. Reduction of the newly formed titanium oxychlorides using Yb leads to the regeneration of TiCl$_3$. A intramolecular oxychloride elimination of Ti(IV) pinacolate followed by a O-atom-transfer from epoxide to Ti(III) species would explains the highly stereoselective formation of the *E*-alkene product **2**. Rare earth metal plays two roles in our system. First, it reduces the Ti(IV) species to generate the active species, that promotes the reductive coupling of carbonyls and cleaves the C–O bond of the epoxide intermediate. Second, rare earth metal accumulates as the final oxygen trap, making the resulting oxide easily removed. Since aromatic ketone would be preferred in the first

carbonyl reduction due to possible formation of a stable ketyl species while for the successive coupling either the Ti centers sensitive to steric factors or the higher reactivity of aliphatic ketyls compared to aromatic ketyls should prefer less sterically demanding aliphatic aldehydes and ketones over bulky aromatic analogues, the present reducing system completely distinguishes between aromatic and aliphatic substrates, and makes the cross-deoxygenative coupling proceed in good to excellent yield. Therefore, the $Yb/TiCl_4$ promoted homo- and cross-coupling of carbonyl compounds to olefins is an ideal addition to the family of the carbonyl olefinations.

Conclusions

In summary, we have demonstrated that Yb in combination with a catalytic amount of $TiCl_4$ can serve as an excellent reductive system for deoxygenative coupling of aldehydes and ketones to olefins. Remarkably, the present process is operationally simple and atom-economical, minimizes the generation of chemical waste, and makes Yb_2O_3 as the only by product easily removed and utilized; further, the yield improved significantly on that obtained in the stoichiometric version in our system. This result showed that in our reaction conditions aromatic ketone-derived ketyl radicals should prefer to attack an aliphatic ketone to give unsymmetrical olefins.

TiCl₃, Ti(IV)-pinacolates and oxychlorides were isolated, characterized, and demonstrated to be potential intermediates for reductive olefination of aldehydes and ketones. Our mechanistic data not only provide the direct evidence that Ti(IV) can facilitate the part deoxygenation of pinacols at room temperature, but also prove, for the first time, that for bulky ketones the turnover-limiting step is the Ti-mediated carbonyl coupling rather than the subsequent deoxygenation of the resulting pinacolate intermediates. Such mechanistic insight would bring to light complications involved in the Ti-mediated McMurry olefination and suggest what might be a general role of pinacolates in organic synthesis. Further studies on other applications of this reducing system in organic synthesis are presently under way in our laboratory.

Acknowledgements

Notes and references

1. (a) J. E. McMurry and L. R. Krepski, *J. Org. Chem.,* 1976, **41**, 3929; (b). J. E. McMurry, *Chem. Rev.,* 1989, **89**, 1513; (c) B. Bogdanovic and A. Bolte, *J. Organomet. Chem.,* 1995, **502**, 109; (d) T. Wirth, *Angew. Chem. Int. Ed.,* 1996, **35**, 61; (e) A. Fürstner and B. Bogdanovic, *Angew. Chem. Int. Ed.,* 1996, **35**, 2442; (f) M. Ephritikhine, *Chem. Commun.,* 1998, 2549; (g) A. Gansäuer and H. Bluhm, *Chem. Rev.,* 2000, **100**, 2771.

2. (a) M. Sato and K. Oshima, *Chem. Lett.,* 1982, 157; (b) R. Dams, M. Malinowski, I. Westdorp and H. Y. Geise, *J. Org. Chem.,* 1982, **47**, 248; (c) S. K. Nayak and A. Banerji, *J. Org. Chem.,* 1991, **56**, 1940; (d) J. Szymoniak, J. Besancon and C. Moïse, *Tetrahedron,* 1992, 48, 3867; (e) T. Eguchi, T. Terachi and K. Kakinuma, *Tetrahedron Lett.,* 1993, **34**, 2175; (f) K. C. Nicolaou, Z. Yang, J. J. Liu, H. Ueno, P. G. Nantermet, R. K. Guy, C. F. Claiborne, J. Renaud, E. A. Couladouros, K. Paulvannan and E. J. Sorensen, *Nature,* 1994, **367**, 630; (g) K. C.

Nicolaou, J. J. Liu, Z. Yang, H. Ueno, E. J. Sorensen, C. F. Claiborne, R. K. Guy, C. K. Hwang, M. Nakada and P. G. Nantermet, *J. Am. Chem. Soc.,* 1995, **117**, 634; (h) A. Fürstner, H. Weintritt and A. Hupperts, *J. Org. Chem.,* 1995, **60**, 6637; (i) K. C. Nicolaou, Z. Yang, J. J. Liu, P. G. Nantermet, C. F. Claiborne, J. Renaud, R. K. Guy and K. Shibayama, *J. Am. Chem. Soc.,* 1995, **117**, 645; (j) A. Fürstner and G. Seidel, *Synthesis,* 1995, 63; (k) D. K. Dutta and D. Konwar, *Tetrahedron Lett.,* 2000, **41**, 6227; (l) T. A. Salama, S. S. Elmorsy and A. G. M. Khalil, *Tetrahedron Lett.,* 2007, **48**, 4395; (m) S. V. Bhilare, N. B. Darvatkar, A. R. Deorukhkar, M. S. Rasalkar and M. M. Salunkhe, *Synth. Commun.,* 2007, **37**, 3111.

3. For applications of McMurry reaction, see: (a) D. R. Moreno, G. Giorgi, C.O. Salas and R. A. Tapia, *Molecules,* 2013, **18**, 14797; (b) Z. Zhao, S. Chen, J. W. Y. Lam, Z. Wang, P. Lu, F. Mahtab, H. H. Y. Sung, I. D. Williams, Y. M. Ma,. H. S. Kwok and B. Z. Tang, *J. Mater. Chem.,* 2011, **21**, 7210; (c) Y. L. Liu, Y. Deng, L. Tang, A. Qin, R. Hu, J. Z. Sun and B. Z. Tang, *J. Am. Chem. Soc.,* 2011, **133**, 660; (d) Y. Xu, L. Chen, Z. Guo, A. Nagai and D. Jiang, *J. Am. Chem. Soc.,* 2011, **133**, 17622; (e) J. Shi, N. Chang, C. Li, J. Mei, C. Deng, X. Luo, Z. Liu, Z. Bo, Y. Q. Dong and B. Z. Tang, *Chem. Commun.,* 2012, **48**, 10675; (f) H. Huang, Z. Chen, R. P. Ortiz, C. Newman, H. Usta, S. Lou, J. Youn, Y. Y. Noh, K. J. Baeg, L. X. Chen, A. Facchetti and T. J. Marks, *J. Am. Chem. Soc.,* 2012, **134**, 10966; (g) S. Lahore, U. Narkhede, L. Merlini and S. Dallavalle, *J. Org. Chem.,* 2013, **78**, 10860.

4. (a) A. Fürstner, *Angew. Chem. Int. Ed.,* 1993, **32**, 164; (b) S. Talukdar, S. K. Nayak and A. Banerji, *J. Org. Chem.,* 1998, **63**, 4925.

5. N. Balu, S. K. Nayak and A. Banerji, *J. Am. Chem. Soc.,* 1996, **118**, 5932.

6. H. R. Diéguez, A. López, V. Domingo, J. F. Arteaga, J. A. Dobado, M. M. Herrador, J. F. Q. Moral and A. F. Barrero, *J. Am. Chem. Soc.,* 2010, **132**, 254.

7. A. Fürstner and A. Hupperts, *J. Am. Chem. Soc.,* 1995, **117**, 4468.

8. (a) Z. Zhu, C. Wang, X. Xiang, C. Pi and X. Zhou, *Chem. Commun.,* 2006, 2066; (b) Z. Zhu, J. Wang, Z. Zhang, X. Xiang and X. Zhou, *Organometallics,* 2007, **26**, 2499; (c) M. Kira, T. Obata, I. Kon, H. Hashimoto, M. Ichinohe, H. Sakurai, S. Kyushin and H. Matsumoto, *Chem. Lett.,* 1998, **11**, 1097.

9. M. Paradas, A. G. Campaña, R. E. Estévez, L. Á. de Cienfuegos, T. Jiménez, R. Robles, J. M. Cuerva and J. E. Oltra *J. Org. Chem.,* 2009, **74**, 3616.

10. (a) T. Imamoto, T. Kusumoto, Y. Hatanaka and M. Yokoyama, *Tetrahedron Lett.,* 1982, **23**, 1353; (b) L. Wang and Y. Zhang, *Tetrahedron,* 1998, **54**, 11129; (c) R. Yanada, N. Negoro, M. Okaniwa and T. Ibuka, *Tetrahedron,* 1999, **55**, 13947; (d) A. Ghatak, F. F. Becker and B. K. Banik, *Tetrahedron Lett.,* 2000, **41**, 3793; (e) S. Talukdar and J. M. Fang, *J. Org. Chem.,* 2001, **66**, 330; (f) W. S. Jin, Y. Makioka, T. Kitamura and Y. Fujiwara, *J. Org. Chem.,* 2001, **66**, 514; (g) T. Nishino, Y. Nishiyama and N. Sonada, *J. Org. Chem.,* 2002, **67**, 966; (h) T. Nishino, M. Okada, T. Kuroki, T. Watanabe, Y. Nishiyama and N. Sonada, *J. Org. Chem.,* 2002, **67**, 8696; (i) H. B. Kagan, *Tetrahedron,* 2003, **59**, 10351; (j) X. Xiang, Q. Shen, J. Wang, Z. Zhu, W. Huang and X. Zhou, *Organometallics,* 2008, **27**, 1959; (k) W. Chen, K. Li, Z. Hu, L. Wang, G. Lai and Z. Li, *Organometallics,* 2011, **30**, 2026.

11. (a) Z. Hou, K. Takamine, Y. Fujiwara and H. Taniguchi, *Chem. Lett.,* 1987, 2061; (b) Z. Hou, K. Takamine, O. Aoki, H. Shiraishi, Y. Fujiwara and H. Taniguchi, *J. Org. Chem.,* 1988, **53**, 6077; (c) Z. Hou, A. Fujita, H. Yamazaki and Y. Wakatsuki, *J. Am. Chem. Soc.,* 1996, **118**, 7843; (d) Z. Hou, A. Fujita, Y.

ARTICLE

Zhang, T. Miyano, H. Yamazaki and Y. Wakatsuki, *J. Am. Chem. Soc.*, 1998, **120**, 754; (e) O. Akiya, T. Hiroki and H. Toshikazu, *Tetrahedron Lett.*, 1999, **40**, 7113; (f) S. Fukuzawa, N. Nakano and T. Saitoh, *Eur. J. Org. Chem.*, 2004, 2863.

12. (a) L. E. Aleandri, B. Bogdanovíc, A. Gaidies, D. J. Jones, S. Liao, A. Michalowicz, J. Rozière, and A. Schott, *J. Organomet. Chem.,* 1993, **459**, 87; (b) L. E. Aleandri, S. Becke, B. Bogdanovíc, D. J. Jones and J. Rozière, *J. Organomet. Chem.,* 1994, **472**, 97; (c) B. Bogdanovíc and A. Bolte, *J. Organomet. Chem.,* 1995, **502**, 109.

13. G. Du and L. K. Woo, *Organometallics*, 2003, **22**, 450.

14. R. Mahrwald, B. Ziemer and S. Troyanov, *Tetrahedron Lett.*, 2001, **42**, 6843.

15. For deoxygenation of epoxide, see: (a) J. E. McMurry, M. G. Silvestri, M. P. Fleming, T. Hoz and M. W. Grayston, *J. Org. Chem.,* 1978, **43**, 3249; (b) L. M. Atagi, D. E. Over, D. R. McAlister and J. M. Mayer, *J. Am. Chem. Soc.*, 1991, **113**, 870; (c) K. G. Moloy, *Inorg. Chem.*, 1988, **27**, 677; (d) T. V. RajanBabu, W. A. Nugent and M. S. Beattie, *J. Am. Chem. Soc.*, 1990, **112**, 6408; (e) T. V. RajanBabu and W. A. Nugent, *J. Am. Chem. Soc.*, 1994, **116**, 986; (f) A. F. Mateos, P. H. Teijón and R. R. González, *Tetrahedron* 2013, **69**, 1611; (g) Y. Li, H. Ji, C. Chen, W. Ma, and J. Zhao, *Angew. Chem. Int. Ed.*, 2013, **52**, 12636.

a Department of Chemistry, Shanghai Key Laboratory of Molecular Catalysis and Innovative Materials, Fudan University, Shanghai 200433, People's Republic of China. E-mail: xgzhou@fudan.edu.cn, lyanghui@fudan.edu.cn.

b State Key Laboratory of Organometallic Chemistry, Shanghai 200032, People's Republic of China

Organic Chemistry Frontiers Accepted Manuscript