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Understanding the competitive dehydroalkoxylation and dehydrogenation of ethers with Ti–C multiple bonds†

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The divergent reactivity of a transient titanium neopentylidyne, (PNP)Ti≡C^{t}Bu (**A**) (PNP = *N*[2-P^{i}Pr$_2$-4-methylphenyl]$_2^-$), that exhibits competing dehydrogenation and dehydroalkoxylation reaction pathways in the presence of acyclic ethers (Et$_2$O, ^{n}Pr$_2$O, ^{n}Bu$_2$O, ^{t}BuOMe, ^{t}BuOEt, ^{i}Pr$_2$O) is presented. Although dehydrogenation takes place also in long-chain linear ethers, dehydroalkoxylation is disfavoured and takes place preferentially or even exclusively in the case of branched ethers. In all cases, dehydrogenation occurs at the terminal position of the aliphatic chain. Kinetics analyses performed using the alkylidene-alkyl precursor, (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu), show pseudo first-order decay rates on titanium ($k_{avg} = 6.2 \pm 0.3 \times 10^{-5}$ s^{-1}, at 29.5 ± 0.1 °C, overall), regardless of the substrate or reaction pathway that ensues. Also, no significant kinetic isotope effect ($k_H/k_D \sim 1.1$) was found between the activations of Et$_2$O and Et$_2$O-d$_{10}$, in accord with dehydrogenation (C–H activation and abstraction) not being the slowest steps, but also consistent with formation of the transient alkylidyne **A** being rate-determining. An overall decay rate of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) with a $t_{1/2}$ = 3.2 ± 0.4 h, across all ethers, confirms formation of **A** being a common intermediate. Isolated alkylidene-alkoxides, (PNP)Ti=CH^{t}Bu(OR) (R = Me, Et, ^{n}Pr, ^{n}Bu, ^{i}Pr, ^{t}Bu) formed from dehydroalkoxylation reactions were also independently prepared by salt metatheses, and extensive NMR characterization of these products is provided. Finally, combining theory and experiment we discuss how each reaction pathway can be altered and how the binding event of ethers plays a critical role in the outcome of the reaction.

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Introduction

The ether functional group is ubiquitous in industry, being readily produced on massive scales either by acid-catalyzed dehydration of alcohols (alkoxy-de-hydroxylation; the preferred method for linear, symmetric ethers), or by reaction of alkyl halides with alkali-metal alkoxides (the Williamson-ether synthesis).[1] Commonplace in chemistry, acyclic ethers are essentially inert substrates comparable to alkanes.[2] This feature explains their ready availability and use as solvents, yet confers them little importance for chemical transformations. Given our interest in C–H activation of alkanes, it is possible to conceive that the same organometallic compounds that cleave C–H bonds of alkanes can equally be useful in the presence of ethers, in order to exploit their reactivity. However, unlike alkanes, ethers might show divergent reactivity due to the oxygen lone pair of electrons being a better donor than a C–H bond. A promising alternative could be the direct conversion of ethers to ether-substituted α-olefins *via* transfer dehydrogenation; an attractive transformation given the potential that these unsaturated products exhibit as monomers in polymerization reactions.[3] Unfortunately, α,β-dehydrogenation of ethers is a rare phenomenon[4–7] when compared to α,α′-dehydrogenation of ethers[8,9] or α,β-dehydrogenation of alkanes,[10,11] and therefore, this process constitutes a new paradigm in chemical transformation: ether-substituted α-olefins sometimes being challenging compounds to synthesize. Another important transformation of ethers is their cracking[12] or dehydroalkoxylation to α-olefins.[13]

Templeton and co-workers reported an example of transfer dehydrogenation of Et$_2$O and THF by a transient (nacnac)Pt(CH$_3$) (nacnac$^-$ = [PhNC(CH$_3$)]$_2$CH) complex, using *tert*-butyl ethylene as a hydrogen acceptor.[7] Bergman and Grubbs have also reported iridium based systems that can dehydrogenate Et$_2$O to the vinyl ether adduct.[5,6] To our knowledge, examples of early transition metal complexes that can dehydrogenate ethers have not been

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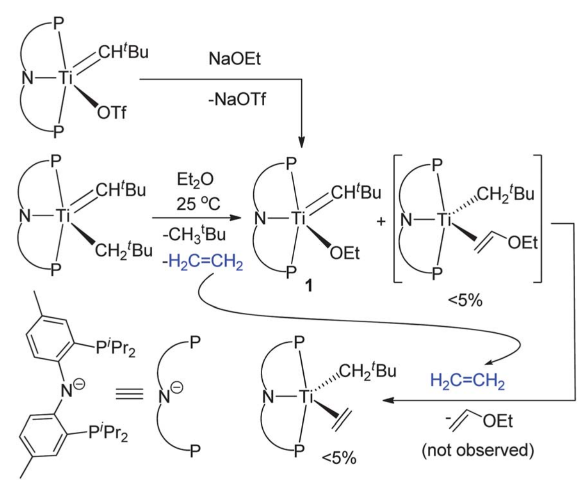
reported and developing a system that could convert ethers to α-olefins having an ether moiety would be attractive, especially if one could understand the mechanism for this conversion and selectivity behind C–H *versus* C–O activation. In this work we report competitive transformations in ethers promoted by a transient titanium neopentylidyne, (PNP)Ti≡C^{t}Bu (**A**) (PNP = N[2-P^{i}Pr$_2$-4-methylphenyl]$_2$$^-$)[14] and establish that ethers can be dehydroalkoxylated as well as selectively dehydrogenated at the terminal position, in close resemblance to what happens with linear alkanes;[15] the extent and preference of one route over the other being dependent on the chain length of the aliphatic ether and its degree of ramification. Experimental and theoretical studies were performed to understand the nature of these competitive pathways which share common intermediates and in this light, predict how each pathway can be favored or disfavored.

Results and discussion

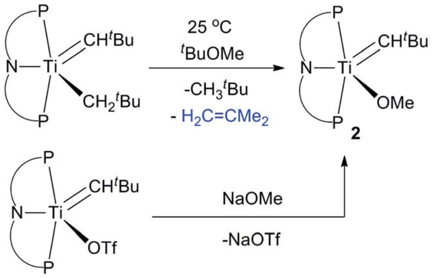
Dehydroalkoxylation of ethers by a titanium neopentylidyne

Dissolving (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) in neat Et$_2$O (room temperature) over 12 h results in clean (>90%) formation of the neopentylidene-ethoxide (PNP)Ti=CH^{t}Bu(OEt) (**1**), accompanied by concomitant evolution of ethene and CH$_3$^{t}Bu (Scheme 1).[16]

Examination of the reaction mixture by ^{1}H and ^{31}P{^{1}H} NMR spectroscopy also revealed formation of an additional titanium-based product in minor yield (≤5%), which we identified to be the ethene complex, (PNP)Ti(η^2-H$_2$C=CH$_2$)(CH$_2$^{t}Bu), by spectroscopic comparison with an authentic sample prepared independently from (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) and ethane or by salt metathesis of (PNP)Ti=CH^{t}Bu(OTf) with LiCH$_2$CH$_3$ (Scheme 1).[15] Compound **1** was characterized spectroscopically by ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectroscopy, along with other multidimensional techniques (COSY, dqCOSY, HSQC, DEPT),[16] and was independently prepared (albeit marred with ~4 to 6% content of the free ligand (PNP)H, by ^{31}P{^{1}H} NMR) from (PNP)Ti=CH^{t}Bu(OTf) and NaOEt, in THF (Scheme 1). Vacuum transfer of the volatiles from neat Et$_2$O activation permitted definite identification of free ethene formed in the mixture, using a combination of spectroscopic techniques (^{1}H NMR spectroscopy and GC-MS). Unfortunately, we cannot conclusively state by these techniques whether another organic product, (CH$_2$=CHOEt), was also present given the low quantity of (PNP)Ti(η^2-H$_2$C=CH$_2$)(CH$_2$^{t}Bu) that was produced, as well as the reactive nature of this vinyl ether. Regardless, formation of the organometallic adduct with ethene suggests that a competitive pathway takes place in the reaction: dehydrogenation of Et$_2$O to a vinyl ether adduct, (PNP)Ti(η^2-H$_2$C=CHOEt)(CH$_2$^{t}Bu), which then likely undergoes exchange with ethene to form (PNP)Ti(η^2-H$_2$C=CH$_2$)(CH$_2$^{t}Bu) and free CH$_2$=CHOEt (Scheme 1).

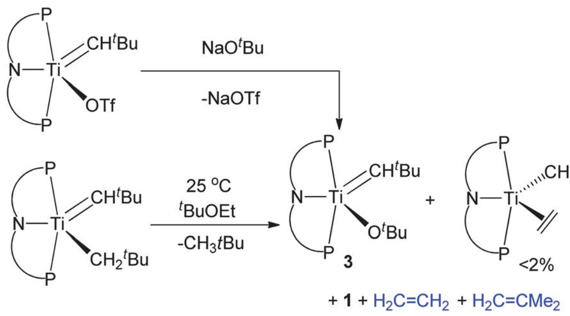


Scheme 1 Dehydroalkoxylation and dehydrogenation reactions involving (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) and Et$_2$O.



Scheme 2 Dehydroalkoxylation and dehydrogenation reactions involving (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) and ^{t}BuOMe.

When (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) is treated with ^{t}BuOMe, the neopentylidene-alkoxide derivative (PNP)Ti=CH^{t}Bu(OMe) (**2**) is the only titanium complex formed, along with isobutene and CH$_3$^{t}Bu (Scheme 2). Analogous to **1**, complex **2** can be similarly prepared from (PNP)Ti=CH^{t}Bu(OTf) and NaOMe (although contaminated with some free ligand (PNP)H, as gauged by ^{31}P{^{1}H} NMR spectroscopy, Scheme 2). Compounds **1** and **2** possess similar NMR spectroscopic signatures: the alkylidene hydrogen at ~11 ppm ($^1J_{CH}$ ~ 98 Hz) and alkoxide resonances around 4.5 ppm (4.7 and 4.5 ppm for **1**, 4.4 ppm for **2**; Table S2†)[16] in the ^{1}H NMR spectra. To probe for selectivity of the dehydroalkoxylation reaction, complex (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) was also treated with ^{t}BuOEt. Examination of the mixture revealed almost a 1 : 1 ratio of **1** and (PNP)Ti=CH^{t}Bu(O^{t}Bu) (**3**), in addition to the β-elimination products ethene and isobutene (Scheme 3). No vinyl ether could be detected by ^{1}H NMR spectroscopy although formation of (PNP)Ti(η^2-H$_2$C=CH$_2$)(CH$_2$^{t}Bu)[15] is also observed but in very low yields (<2% based on ^{31}P{^{1}H}



Scheme 3 Dehydroalkoxylation and dehydrogenation reactions involving (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) and ^{t}BuOEt.

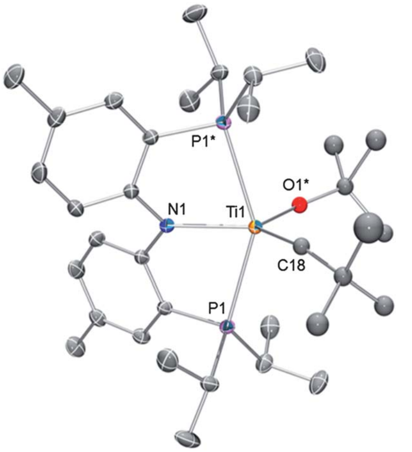


Fig. 1 Solid state molecular structure of [(PNP)Ti=CH^{t}Bu(O^{t}Bu)] (**3**) with 50% probability ellipsoids. Asterisks denote symmetry generated atoms.

Table 1 Summarized kinetic data for aliphatic ether activations as well as some hydrocarbons

Entry	Substrate	T_{avg} (°C)	Conv. (%)	$k_{avg} \times 10^{-5}$ (s^{-1})	$\sigma \times 10^{-5}$	$t_{1/2}$[c] (h)
1	^{t}BuOMe	29.4	90	5.8	0.2	3.3
2[a]	Et_2O	29.6	97	7.0	0.2	2.7
3[a]	Et_2O-d_{10}	29.2	91	6.4	0.2	3.0
4	$^nPr_2O$	29.5	83	5.9	0.5	3.3
5	$^nBu_2O$	29.6	85	5.0	0.0	3.9
6	^{t}BuOEt	29.6	96	7.5	0.1	2.6
7	$^iPr_2O$	29.6	95	6.0	0.5	3.2
8	^{t}BuOMe:Et_2O	29.5	92	5.7	0.5	3.4
9[b]	C_6D_6	27.0	88	6.5	0.4	3.0
10	Pentane	29.7	90	6.0	0.5	3.2
11	Cyclohexane	29.6	89	4.97	0.02	3.9

[a] KIE = $k_H/k_D = 1.1(0)$. Reactions were performed by duplicate runs; σ indicates the normal error (standard deviation). [b] Ref. 13. [c] $t_{1/2} = \ln(2)/k_{avg}$.

NMR spectroscopy). Complex **3** has been fully characterized including a single crystal structural study (Fig. 1), and samples have been compared spectroscopically to independently prepared material from (PNP)Ti=CH^{t}Bu(OTf) and NaO^{t}Bu (Scheme 3).[16] In the solid state, unfortunately, the *tert*-butoxide and neopentylidene ligands of **3** exhibit positional disorder in the asymmetric unit that results in the overlap of the two groups and their *tert*-butyl moieties. The Ti–O1 and Ti–C18 bond lengths are therefore not reported due to this occupancy disorder. Regardless, the solid state structure of **3** clearly confirms formation of an alkylidene-alkoxide titanium derivative from the dehydroalkoxylation of ^{t}BuOEt.

A separate competition experiment using equimolar amounts of Et_2O and ^{t}BuOMe in the presence of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) also showed simultaneous formation of **1** and **2**, with approximately the same minor amount of (PNP)Ti(η^2-H_2C=CH_2)(CH$_2$^{t}Bu) being formed. Vacuum transfer of volatiles confirmed the presence of ethene and isobutene based on ^{1}H NMR spectroscopy.[16]

To probe the mechanism of formation of the olefin and the titanium alkoxide complex, we conducted kinetic measurements as well as an isotopic labeling study using Et_2O-d_{10}. It was found that formation of **1–3** from (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) follows pseudo first order decay with similar rates ($k_{avg} = 7.0 \pm 0.2$, 5.8 ± 0.2 and $7.5 \pm 0.1 \times 10^{-5}$ s^{-1} at 29.5 ± 0.1 °C; duplicate runs) respectively, which is comparable to the reported rate of decay of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) in C_6D_6 ($k_{avg} = 6.5 \pm 0.4 \times 10^{-5}$ s^{-1}) at 27 °C, in pentane ($k_{avg} = 6.0 \pm 0.5 \times 10^{-5}$ s^{-1}), and in cyclohexane ($k_{avg} = 4.97 \pm 0.02 \times 10^{-5}$ s^{-1}) at 29.6 °C (Table 1).[14] In addition, conducting the reaction of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) in Et_2O-d_{10} at 29.2 °C did not change the overall rate of the reaction ($k_{avg} = 6.4 \pm 0.2 \times 10^{-5}$ s^{-1}; KIE = $1.099 \pm 0.004 \sim 1.1$, duplicate runs), thus implying that activation of ether (*e.g.*, C–H activation) is not the rate determining step and without significant secondary isotope effects. These results in addition to the similar rates for pseudo-first order decay suggest that α-hydrogen abstraction, to give the transient alkylidyne intermediate **A** from its precursor (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu), is most likely the overall rate-determining step. Detailed kinetic studies arguing for the formation of transient **A** have been previously reported.[14] Table 1 summarizes our kinetic data involving various ethers. Measurements in C_6D_6 ($k_{avg} = 6.5 \pm 0.4 \times 10^{-5}$ s^{-1}, at 27 °C),[14] pentane ($k_{avg} = 6.0 \pm 0.5 \times 10^{-5}$ s^{-1}, at 29.7 °C) and cyclohexane ($k_{avg} = 4.97 \pm 0.02 \times 10^{-5}$ s^{-1}, at 29.6 °C)[16] are also included for comparison purposes.

Based on the measured rates, we propose a reaction mechanism for dehydroalkoxylation that differs from prior studies involving low-valent Zr(II) complexes known to undergo C–O bond cleavage of the ether group.[13,17,18] For Et_2O at least, we propose that (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) undergoes α-hydrogen abstraction to form **A**, followed by 1,2-CH bond addition of the distal group on the ether (Fig. 2, initial step of the blue pathway)

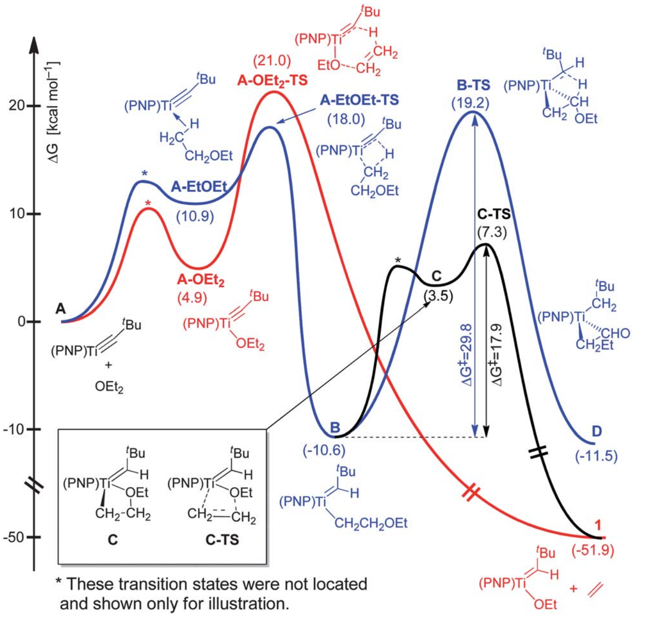
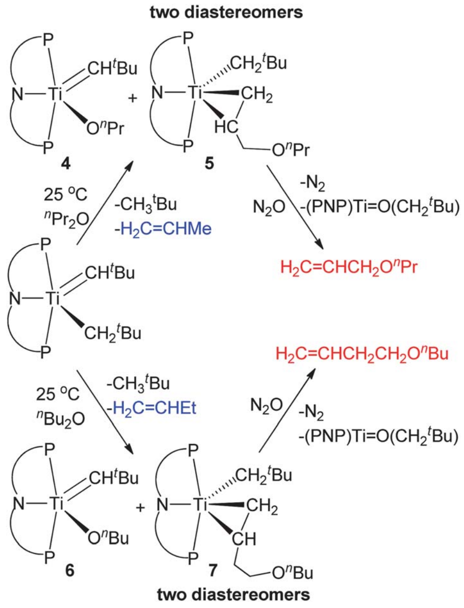


Fig. 2 Computed reaction coordinates for the competing dehydrogenation and dehydroalkoxylation of Et_2O using intermediate **A** as the starting point. All energies are indicated with only one decimal.[20]

to yield an intermediate such as (PNP)Ti=CH^{t}Bu(CH$_2$R) (R = CH$_2$OEt; see intermediate **B** in Fig. 2). The latter rapidly undergoes β-alkoxide elimination to furnish compound **1** and the corresponding olefin (black path in Fig. 2). A more general mechanism that applies to all the ethers (branched or linear) involves competing coordination of the ether functionality to **A**, followed by concerted cleavage of a distal C–H and a C–O bond to form the respective alkoxide and a terminal olefin (red curve in Fig. 2). In addition, the presence of small amounts of (PNP)Ti(η^2-H$_2$C=CH$_2$)(CH$_2{}^t$Bu) from experiments involving Et$_2$O or ^{t}BuOEt activations indicates that a separate, competitive dehydrogenation mechanism akin to that of alkanes by **A** (*e.g.*, ethane, pentane or hexane)[15] is also operative for linear ethers (final step of the blue path). The absence of vinyl ether type complexes (namely, (PNP)Ti(η^2-H$_2$C=CHOR)(CH$_2{}^t$Bu); R = Et, ^{t}Bu) in the solution suggests that products of this transformation must undergo facile exchange with ethylene to yield the titanium–ethene adduct **1** and free ether-substituted α-olefins. Detailed discussion of these reaction pathways is shown in Fig. 2 and will be further addressed in this paper.

Evidence of competing dehydrogenation and dehydroalkoxylation pathways

To further examine if dehydrogenation was an operative mode in the aforementioned reactions and whether an olefin adduct could be clearly identified, we explored the reactivity of (PNP)Ti=CH^{t}Bu(CH$_2{}^t$Bu) with longer-chain linear ethers such as ^{n}Pr$_2$O and ^{n}Bu$_2$O. Activation of the terminal C–H bond of these substrates would place the ether functionality further away from the metal site (Scheme 4) and, thus, β-alkoxide elimination *through the black trace shown in* Fig. 2 should not interfere with the dehydrogenation process. Accordingly, treatment of (PNP)Ti=CH^{t}Bu(CH$_2{}^t$Bu) with any of these two ethers resulted in formation *of critical amounts of both dehydrogenation and dehydroalkoxylation products advocating that as the chain of ether becomes longer, formation of the former products becomes more prominent.* As a result, the reaction of ^{n}Pr$_2$O and ^{n}Bu$_2$O with (PNP)Ti=CH^{t}Bu(CH$_2{}^t$Bu) result in the formation of α-olefins, propene and 1-butene, along with the alkoxides, (PNP)Ti=CH^{t}Bu(O^{n}Pr) (**4**) and (PNP)Ti=CH^{t}Bu(O^{n}Bu) (**6**), as well as the dehydrogenated alkene products, (PNP)Ti(CH$_2{}^t$Bu)(η^2-H$_2$C=CHCH$_2$O^{n}Pr) (**5**) and (PNP)Ti(CH$_2{}^t$Bu)(η^2-H$_2$C=CHCH$_2$CH$_2$O^{n}Bu) (**7**), respectively (Scheme 4).



Scheme 4 Dehydroalkoxylation and dehydrogenation of ^{n}Pr$_2$O and ^{n}Bu$_2$O by complex (PNP)Ti=CH^{t}Bu(CH$_2{}^t$Bu).

In the case of ^{n}Pr$_2$O, compounds **4** and **5** were formed in a 1 : 1 ratio while activation of ^{n}Bu$_2$O resulted in **6** and **7** in a 1 : 2 ratio as implied by ^{31}P{^{1}H} NMR spectroscopy. Additional minor unidentifiable products were also formed over time in the latter mixture with consumption of the olefin adducts, indicative of their low stability. Overall however, the experiments show that increasing the chain length of the ether favors dehydrogenation over dehydroalkoxylation. Worth noting, complexes **4** and **6** show similar spectroscopic features to the alkoxide derivatives **1–3** and can be prepared independently and cleanly from salt metathesis reaction of (PNP)Ti=CH^{t}Bu(OTf) with the corresponding sodium alkoxide (NaO^{n}Pr or NaO^{n}Bu).[16]

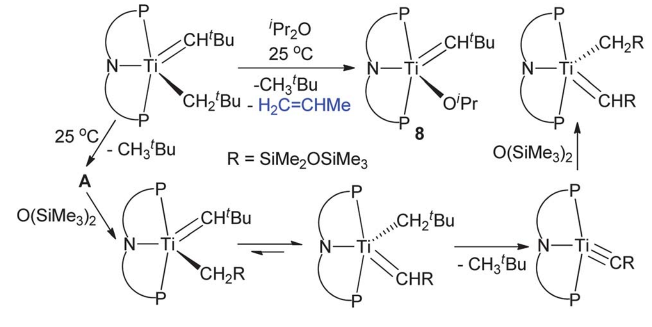
The olefin adducts **5** and **7** exist as a mixture of diastereomers (Scheme 4). This feature is not unexpected since the analogous α-olefin adducts (PNP)Ti(CH$_2{}^t$Bu)(η^2-H$_2$C=CHR) (R = ^{n}Pr or ^{n}Bu), which are formed from the dehydrogenation of pentane and hexane by (PNP)Ti=CH^{t}Bu(CH$_2{}^t$Bu), exist as a mixtures of diastereomers each with their corresponding pair of enantiomers due to the C_2 symmetry of the PNP backbone and one stereogenic olefinic carbon.[15]

Although complexes **4** and **6** display similar ^{1}H and ^{31}P{^{1}H} NMR spectroscopic features to **1–3** (Table S2†),[16] complexes **5** and **7** are novel olefin adducts of titanium that contain a pendant ether arm. The latter makes spectroscopic elucidation less trivial, especially due to the presence of diastereomers. Additional peak overlap in the ^{1}H NMR spectra rising from the mixture of dehydrogenation and dehydroalkoxylation products also complicates assignment. Regardless, ^{31}P{^{1}H} NMR spectroscopy is critical for the assignment of these compounds: the phosphorus resonances and the magnitude of the $^2J_{PP}$ of the PNP backbones in the components of the mixtures being an extremely useful tool for their characterization. Typically, the $^2J_{PP}$ for titanium-alkoxides is in the order of 48 Hz (Table S2†),[16] whereas those of the α-olefin-adducts (produced either from ether or alkane activation) ranges from ~22 to 27 Hz.[15]

To conclusively establish the formation of such olefins, we resorted to treatment with N$_2$O since oxidation of alkene adducts derived from alkanes is known to cleanly produce the metastable complex (PNP)Ti=O(CH$_2{}^t$Bu)[15] with concomitant release of the olefin. Independently, N$_2$O does not react with the Ti(IV) alkylidene-alkoxide side-products **4** or **6**. Indeed, treatment of a mixture of **4–5** or **6–7** resulted in the immediate and exclusive consumption of **5** and **7**. The titanium-alkoxides remained unreacted in presence of N$_2$O as expected and vacuum transfer of the volatiles revealed the existence of the α-olefins 3-propoxy-1-propene and 4-butoxy-1-butene respectively, based on a combination of GC-MS and ^{1}H NMR spectroscopies

(Scheme 4).[15] We were however, unable to unambiguously detect (PNP)Ti=O(CH$_2$^{t}Bu) due to its known thermal instability.[14] Exposure of **4–5** or **6–7** to ethene was also attempted with the idea of promoting olefin exchange, since (PNP)Ti(H$_2$C=CH$_2$)(CH$_2$^{t}Bu) is known to be one of the most stable olefin derivatives[15] and prior observations with Et$_2$O and ^{t}BuOEt showed this product to form by exchange of the ether-substituted α-olefin in (PNP)Ti(η^2-H$_2$C=CHOEt)(CH$_2$^{t}Bu) (Scheme 1, *vide supra*). Indeed, formation of (PNP)Ti(η^2-H$_2$C=CH$_2$)(CH$_2$^{t}Bu) was detected in both mixtures after exposure to ethene (~1 atm),[16] although the reactions are complicated by formation of other side products, presumably given the reactive nature of the ether substituted α-olefins. In context, our results validate that it is possible for a complex with formula, (PNP)Ti(η^2-H$_2$C=CH(CH$_2$)$_n$OR)(CH$_2$^{t}Bu) ($n = 0, 1, 2$; R = Et, ^{n}Pr, ^{n}Bu) to undergo exchange with ethene in order to release the ether substituted α-olefin. Unfortunately, we have yet to develop an independent synthesis of **5** or **7** in order to fully characterize these species spectroscopically.

Monitoring the decay of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) in ^{n}Pr$_2$O and ^{n}Bu$_2$O by ^{31}P NMR spectroscopy at ~29 °C reveals the following average rate constants, k_{avg}: $5.9 \pm 0.5 \times 10^{-5}$ and $5.0 \pm 0.0 \times 10^{-5}$ s^{-1} at 29.5 °C (Table 1), again suggestive of formation of **A** being overall rate-determining.[16] As a result, the development of **4–5** and **6–7** from (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) and the ethers ^{n}Pr$_2$O and ^{n}Bu$_2$O respectively, must involve competing routes for C–O and C–H bond activations leading into dehydroalkoxylation and dehydrogenation *via the common intermediate* **A**. The latter is a recurrent theme for long alkanes or as in this case, long-chain linear ethers. Also, since **4–5** or **6–7** do not interconvert under normal conditions or with mild heating (65 °C),[16] these results validate the conclusion that the products originate from two independent routes stemming from the same intermediate. To further explore this idea, we treated (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) with a sterically hindered ether such as ^{i}Pr$_2$O, since dehydrogenation was predicted to be disfavored due to the steric hindrance of the isopropyl groups. Indeed, when (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) was treated with ^{i}Pr$_2$O, only (PNP)Ti=CH^{t}Bu(O^{i}Pr) (**8**) and propene (^{1}H NMR) were formed, therefore suggesting the dehydrogenation pathway to be completely shut down (Scheme 5). The rate of decay of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) in ^{i}Pr$_2$O at 29.6 °C ($k_{avg} = 6.0 \pm 0.5 \times 10^{-5}$ s^{-1}) is comparable with all the previous ones for different ethers and even alkanes (Table 1), thus confirming that dehydroalkoxylation is definitely dependent on the formation of **A**.



Scheme 5 Reactivity of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) with ^{i}Pr$_2$O and O(SiMe$_3$)$_2$.

It is worth noting that unlike ^{i}Pr$_2$O, when a weakly donating ether lacking β-hydrogens such as O(SiMe$_3$)$_2$ is used, C–H activation steps involving α-hydrogen abstractions, tautomerization, α-hydrogen abstraction, and 1,2-CH bond addition overrule the dehydroalkoxylation giving rise to the degenerate alkylidene alkyl, (PNP)Ti=CHSiMe$_2$OSiMe$_3$(CH$_2$SiMe$_2$OSiMe$_3$) along with two equiv. of CH$_3$^{t}Bu (Scheme 5).[14] In context, one possible explanation for this result is that a binding event in addition to the presence of accessible, internal C–H bonds, are both critical for the β-alkoxide elimination pathway to take place.

Computational evidence for competing dehydrogenation and dehydroalkoxylation pathways

To gain insight into the mechanisms leading to β-alkoxide elimination and dehydrogenation in the aforementioned reactions we examined several pathways for the transformations of Et$_2$O and ^{n}Pr$_2$O using DFT calculations.[16] Fig. 2 depicts the three most plausible mechanistic scenarios for the competing dehydrogenation and dehydroalkoxylation of Et$_2$O and in Fig. 3, we present the three most likely reaction coordinates involving a longer ether chain such as ^{n}Pr$_2$O.[16]

The dehydrogenation of Et$_2$O (blue trace) follows a mechanism analogous to that of ethane to ethene:[15] intermediate **A** and free ether first form a σ-complex (**A-EtOEt**), followed by the 1,2-addition of the terminal C–H bond across the reactive Ti≡C linkage (**A-EtOEt-TS**). The latter gives rise to the alkyl-neopentylidene intermediate (**B**),[19] which finally allows the formation of the dehydrogenated vinyl ether adduct (PNP)Ti(η^2-H$_2$C≡CHOEt)(CH$_2$^{t}Bu) (**D**) through a concerted metal mediated β-hydrogen migration step (**B-TS**). The latter step is associated with a relatively high barrier of 29.8 kcal mol^{-1}.

The generic dehydroalkoxylation pathway in Fig. 2 (red trace) also begins with an adduct involving the alkylidyne **A**. However, in this adduct the ether binds to the titanium center with its

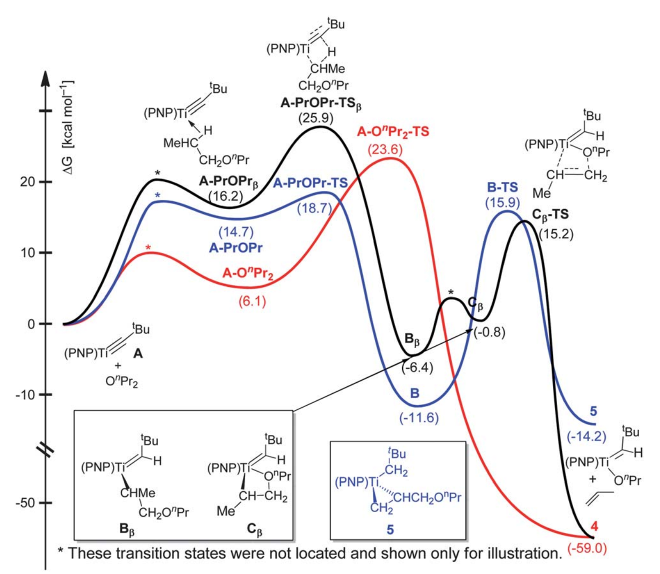


Fig. 3 Computed reaction profiles for the competing dehydrogenation and dehydroalkoxylation of ^{n}Pr$_2$O using intermediate **A** as the starting point. All energies are indicated with only one decimal.[20]

oxygen (**A-OEt$_2$**). A β-hydrogen transfer from the ethyl moiety to the neopentylidyne ligand concomitant with a concerted C–O bond breaking yields product **1** and free ethene, traversing the transition state (**A-OEt$_2$-TS**) with a relative free energy in solution of 21.0 kcal mol^{-1}. Apart from the latter pathway having a lower barrier with respect to dehydrogenation, the product of dehydroalkoxylation, compound **1** is significantly more thermodynamically stable than the dehydrogenated product **D** by nearly 40 kcal mol^{-1}.

In the cases when the alkyl chain of the reacting ether contains two carbons, that is R = Et, ^{i}Pr or ^{t}Bu, these two pathways are accompanied by a third possible side-reaction (black trace in Fig. 2) that also leads to **1** and free ethene. From the C–H activated intermediate **B**, the putative quasi-octahedral intermediate **C** can also be formed by a simple chelation of the ether moiety. Structure **C** is a prerequisite for the simultaneous breaking of the O–C and Ti–C bonds, by which ethene is extruded from the complex and **1** is formed. Since the latter pathway involves only two moderate barriers of about 18 kcal mol^{-1}, one for the C–H bond activation and one for the ethene extrusion step, this pathway provides the energetically most advantageous channel for the transformation of ethers in the case of R = Et, ^{i}Pr or ^{t}Bu. In addition, Fig. 2 illustrates why dehydrogenation is not competitive when ethers with short alkyl chain are involved in the activation: the barriers corresponding to **C-TS** and **B-TS** differ by 12 kcal mol^{-1}, with the former being lower, thereby favoring formation of **1** over **D** in line with our experimental results.[20]

Note that generation of **1** from **B**, *i.e.* the black pathway shown in Fig. 2, *is not operative when the alkyl chain of the ether is longer than two carbons*. In these cases traversing **C-TS** would result in the formation of a high-energy radical species, where the terminal carbon holds the unpaired electrons (Schemes S1 and S2†).[16] Thus dehydrogenation and dehydroalkoxylation become more equally competitive for ethers with longer alkyl chains mostly because the stepwise mechanism leading to **1**, shown in black trace, is the least energetically accessible for ^{n}Pr$_2$O because it costs a penalty of 25.9 kcal mol^{-1} for 1,2-CH addition to take place at the β-position of the ether as indicated by **A-PrOPr-TS$_β$** (Fig. 3). When compared to Fig. 2, the barrier corresponding to the O-bound ether, **A-OEt$_2$-TS**, is slightly higher (**A-O^{n}Pr$_2$-TS**, red trace), whereas the barrier of **B-TS** becomes lower in energy (15.9 kcal mol^{-1}) with longer alkyl chains. In other words, the red and blue traces shown in Fig. 3 become more competitive according to our calculations.[20] Maximal barriers of 23.6 and 27.5 kcal mol^{-1} were calculated for the dehydroalkoxylation and dehydrogenation of ^{n}Pr$_2$O, respectively, which is in good agreement at least qualitatively (within computational error) with the experimental observations that **4** and **5** are formed in almost equal amounts. Also noteworthy is the similarity in the transition state energies involving the O-bound ether and the β-1,2-CH bond addition of the ether across the alkylidyne linkage ($\Delta\Delta G^‡ = 2.3$ kcal mol^{-1}), which suggest that either pathway is viable to propose in the dehydroalkoxylation/dehydrogenation of linear ethers.[20]

Lastly, we examined whether the vinyl ether complex **D**, which we propose is formed in very small quantities in the reaction of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) with Et$_2$O, could undergo exchange with ethene. Our findings by DFT suggest that compound **D** can undergo exchange with ethene *via* a dissociative process involving an $S = 1$ system (PNP)Ti(CH$_2$^{t}Bu). Notably, it was also found that the ethene adduct (PNP)Ti(η^2-H$_2$C=CH$_2$)(CH$_2$^{t}Bu) is −9.6 kcal mol^{-1} lower in energy than **D** (Fig. S67†).[16] Therefore, ethene exchange in **D** as well as in the ether substituted olefin complex **5** and **7** should be all thermodynamically favorable steps.

Conclusions

In conclusion, we have shown a new mechanistic scenario for the dehydroalkoxylation and dehydrogenation of ethers. By studying a series of linear and branched ethers we concluded the following: (i) the alkylidyne functionality in **A** binds ethers and preferentially activates the O–CH$_2$C*H*$_2$R hydrogen as opposed to the more exposed OMe group,[21] (ii) binding of the ether to **A** *via* its oxygen most likely initiates the dehydroalkoxylation pathway, (iii) for short chain ethers dehydroalkoxylation can also occur after one of the terminal C–H bonds was split by the Ti≡C^{t}Bu functionality, (iv) the longer the linear ether chain the more unfavourable the dehydroalkoxylation becomes, whereas the process described in (ii) becomes non-operative, and (v) α-hydrogen migration is the last alternative to other pathways and it is only favoured if the substrate has no β-hydrogens or no available binding sites.[22]

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19 Attempts to observe formation of intermediate **B** in solution were attempted unsuccessfully. Follow-up of all neat ether activation reactions by ^{1}H and ^{31}P NMR spectroscopy, showed only consumption of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) with concomitant formation of the dehydroalkoxylation or dehydrogenation products (see ESI†).

20 DFT methods might be significantly overestimating some of these barriers due to several reasons including tunneling effects. In addition, since solvent molecules are activated, there might be an overestimate of kinetic entropy loss upon association when applying statistical thermodynamics on the gas phase reaction.

21 We cannot refute the possibility of the MeO group being reversibly activated, since treatment of (PNP)Ti=CH^{t}Bu(CH$_2$^{t}Bu) with Me$_2$O results in a myriad of products none of which can be isolated in pure form. A computed barrier of 20.7 kcal mol^{-1} indicates that the activation of the C–H bond of methyl group in a molecule such as $CH_3OCH_2CH_3$ is indeed likely. However such barrier is ~3 kcal mol^{-1} higher than activation of the C–H bond of ethyl group. In addition, no β-alkoxide elimination or β-H abstraction is possible after the OMe is activated.

22 1,2-CO bond addition is observed with (PNP)Ti≡C^{t}Bu and $CH_3OC_6F_5$. See ref. 14.