Tetrahedron 69 (2013) 5737–5743

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Easily assembled, modular *N*,*O*-chelating ligands for Ta(V) complexation: a comparative study of ligand effects in hydroaminoalkylation with *N*-methylaniline and 4-methoxy-*N*-methylaniline

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ARTICLE INFO

Article history:
Received 23 March 2013
Received in revised form 13 April 2013
Accepted 15 April 2013
Available online 18 April 2013

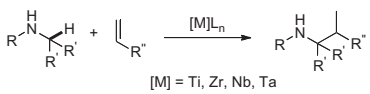
Keywords:
Hydroaminoalkylation
Tantalum
Amidate-like ligands
Heteroatom
C(sp^3)–O bond cleavage

ABSTRACT

The influence of structurally related *N*,*O*-chelating ligands with additional heteroatoms (N, O, P, S) on the reactivity of in situ generated tantalum complexes for the hydroaminoalkylation of amines has been explored. Reactivity was probed by evaluating the catalytic ability of these *N*,*O*-chelating systems with *N*-methylaniline and 4-methoxy-*N*-methylaniline substrates. Enhanced reactivity is observed with amide proligands bearing an *ortho*-methoxyphenyl group on the nitrogen. 4-Methoxy-*N*-methylaniline is found to be more prone to undergo C–H functionalization via hydroaminoalkylation than *N*-methylaniline. The use of the related substrate 2-methoxy-*N*-methylaniline is not tolerated, and instead C(sp^3)–O bond cleavage was observed.

1. Introduction

Amine moieties are prevalent in biologically active compounds,[1] and the development of efficient and selective methods to synthesize substituted amines is an important area of research. Catalytic preparative routes toward amine building blocks are attractive, as byproducts are reduced by means of step and atom economies.[2,3] Methodologies that do not require the use of protecting groups are also desirable for the synthesis of reactive amine intermediates that can be readily substituted. To this end, an attractive approach is early transition metal catalyzed hydroaminoalkylation, a 100% atom economic C–H alkylation reaction occurring at the α-position of an unprotected amine (Scheme 1).[4]



Scheme 1. Hydroaminoalkylation of alkenes with unprotected secondary amines.

While initial investigations into this transformation were reported in the early 1980s,[5] further developments have only been reported recently.[6,7] A series of Ta(V) systems have been reported for intermolecular hydroaminoalkylation and collectively this work has shown that slight modifications of the ancillary ligands dramatically impacts the reactivity of these catalytic systems.[7] These advances in ligand design have resulted in improved reaction conditions, enhanced substrate scope, and enantioselective variants of this transformation.[6,7] However, detailed investigations into ligand features that promote enhanced catalyst activity have not been extensively explored.

Previously, our group showed that *N*,*O*-chelating amidate ligands for tantalum hydroaminoalkylation catalysis results in the preparation of complexes that show good reactivity with a broad range of substrates.[7c] By using the electron-withdrawing properties of these ligands to advantage, the electrophilicity of the metal center can be enhanced to access improved reactivity profiles.[8] Another advantage that may be critical to the improved reactivity of these *N*,*O*-chelates with tight bite-angles is the availability of different potential coordination modes (Scheme 2). Access to κ^1 binding modes could allow for release of steric crowding about the

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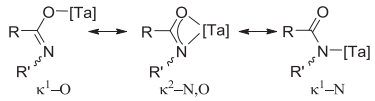
0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.04.070

metal center, while creating an open-coordination site for reagent binding.



Scheme 2. Different binding modes of *N,O*-chelating ligands.

To further explore the ability of related *N,O*-chelating ligands to support highly reactive hydroaminoalkylation catalyst systems we decided to investigate the impact of modifications to the successful ligand framework of previously reported **L-0** (Fig. 1).[7c] These investigations included altering the ligand backbone with the incorporation of additional heteroatoms (N, O, P, S) as well as altering the ligand substituent pattern (Fig. 1). The design, synthesis, and influence of these proligands on Ta(V) catalyzed hydroaminoalkylation are reported through a comparative study of the reaction of 1-octene with *N*-methylaniline and 4-methoxy-*N*-methylaniline.

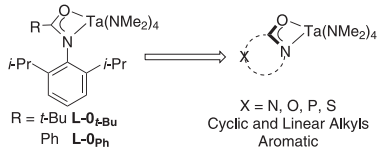


Fig. 1. New *N,O*-heteroatom containing-chelating Ta(V) complexes.

2. Results and discussion

2.1. Ligand design and synthesis

Four classes of *N,O*-chelating proligands have been designed for investigation (Fig. 2). We first envisioned modification of the electronic properties of the reactive complex by incorporating an electron-withdrawing group at the nitrogen (**A**) of the ligand framework while keeping the *tert*-butyl moiety consistent to **HL-0**$_{t\text{-Bu}}$. Introduction of heteroatoms directly linked to the carbonyl moiety (**B**) have also been examined to vary the electronic properties of the ligand. Finally, the addition of a pendent neutral donor heteroatom has been incorporated into the ligand framework in an effort to modify steric and electronic properties through the access of alternative coordination geometries. For this purpose, two systems have been explored; one with an extra donor on the nitrogen substituent (**C**) and another with the donor atom incorporated into the carbonyl backbone (**D**).

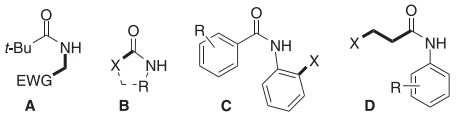
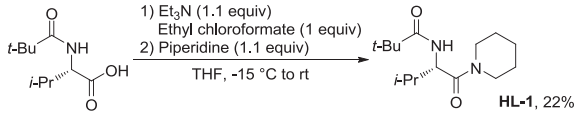


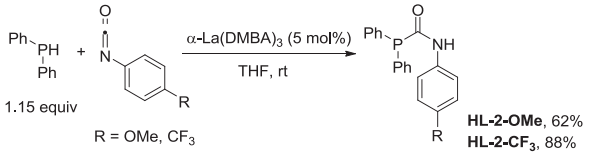
Fig. 2. Proligand motifs reported herein.

Our investigations began with the synthesis of a chiral linear proligand of type **A**, by taking advantage of naturally occurring amino acids. Proligand **HL-1** is prepared from L-valine (Scheme 3) via the known pivaloyl protected amino acid.[9] The treatment of *N*-*t*-Bu-Val-COOH with ethyl chloroformate and piperidine furnishes **HL-1** in 22% recrystallized yield.



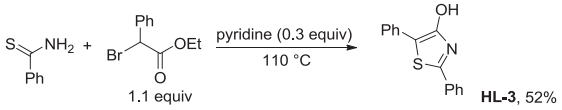
Scheme 3. Synthesis of **HL-1**.

In order to examine type **B** ligands we targeted phosphine-carboxamide **HL-2**, which can be easily obtained in a one-step procedure (Scheme 4).[10] To isolate and compare the effect of this heteroatom addition to the backbone to **L-0** for hydroaminoalkylation, the aryl group on the nitrogen has been maintained.



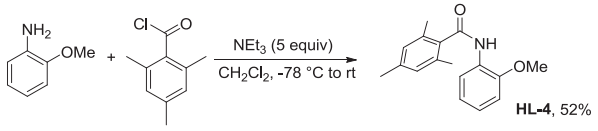
Scheme 4. Synthesis of **HL-2**.

Another related type **B** proligand that has been explored contains a heteroaromatic structure (Scheme 5). The proligand **HL-3** with a 4-hydroxy-1,3-thiazole backbone and a phenyl group adjacent to the carbonyl and the nitrogen has been synthesized in 52% yield in a single step from commercially available starting materials.[11]



Scheme 5. Synthesis of **HL-3**.

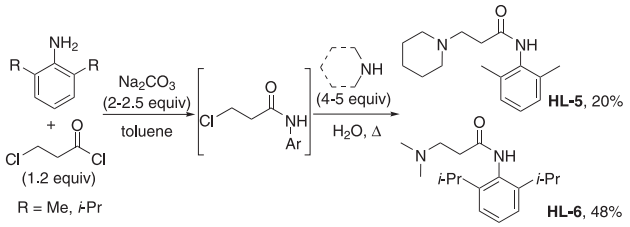
For proligands of type **C**, an *ortho*-methoxy group has been chosen as a potential additional donor. The amide proligand **HL-4** has been prepared in 52% recrystallized yield from a straightforward amidation reaction with 2-methoxyaniline and 2,4,6-trimethylbenzoylchloride (Scheme 6).



Scheme 6. Synthesis of **HL-4**.

The synthesis of ligand **D**, with a donor on the carbonyl moiety has been realized through a one-pot, two-step sequence: amidation reaction of aniline with 3-chloropropanoyl chloride, followed by nucleophilic displacement of Cl with a secondary amine (Scheme 7). Two ligands of varying steric bulk on the aryl ring have been prepared by this method (**HL-5** and **HL-6**). These ligands also have varied steric bulk on the pendant amine moiety. Here, the two carbon tether length provides flexibility to allow for coordination to the metal center.

In light of the recent work from both Doye[6g] and ourselves[12] regarding the advantageous use of the κ^2-*N,N*-chelating amino-



Scheme 7. Synthesis of type **D** proligands: **HL-5** and **HL-6**.

pyridinate ligands in group 4 metal catalyzed hydroaminoalkylation and hydroamination reactions, we present our evaluation of a bulky aminopyridinate ligand. The proligand **HL-7**, is anticipated to maintain a similar asymmetric coordination mode to **HL-0** *t*-Bu,[7c] although significantly enhanced steric bulk has been incorporated into this proligand than is accessible with *N*,*O*-chelating ligands (Fig. 3).[13]

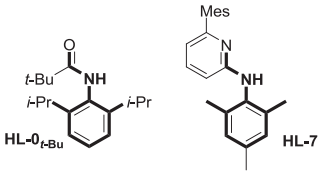
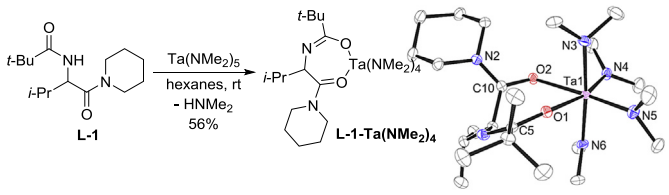


Fig. 3. Design of **HL-7**.

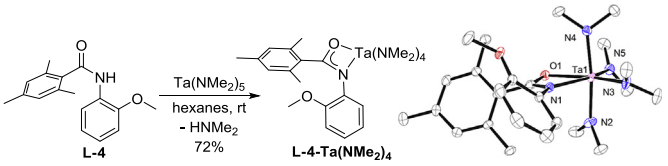
2.2. Catalyst preparation and performance

The synthesis of the Ta(V) complexes has been achieved by the protonolysis reaction of $Ta(NMe_2)_5$ with the proligand in a 1:1 ratio at room temperature (Schemes 8–10). Using this route, crystalline samples of complexes **L-1-Ta(NMe$_2$)$_4$**, **L-4-Ta(NMe$_2$)$_4$**, and **L-7-Ta(NMe$_2$)$_4$** have been isolated and fully characterized. Unfortunately, the combination of proligands **HL-2**, **HL-3**, **HL-5** or **HL-6** did not afford comparable crystalline complexes and thus these systems were not isolated before use in catalytic investigations (vide infra). The complex **L-1-Ta(NMe$_2$)$_4$** was obtained as yellow crystals by recrystallization from hexanes in 56% yield, and its solid-state molecular structure was obtained by X-ray diffraction (Scheme 8).[14] This complex exhibits a pseudo-octahedral geometry with **L-1** bound to the metal center through the two oxygen atoms of the ligand, highlighting the oxophilicity of this early-transition metal. The secondary amide component of the ligand shows an imide alkoxide binding mode to the metal center [C5–O1 1.326(2) Å, C5–N1 1.282(2) Å, Ta–O1 2.043(1) Å], while the other oxygen atom of the tertiary amide component binds as a neutral donor [C10–O2 1.262(2) Å, C10–N2 1.335(2) Å, Ta–O2 2.283(1) Å].

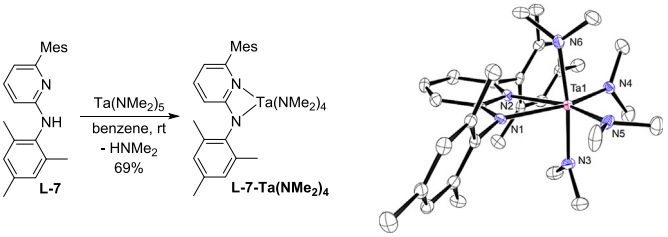
The synthesis of **L-4-Ta(NMe$_2$)$_4$** proceeds to generate a yellow-orange solid after removal of volatiles under reduced pressure. Recrystallization from hexanes afforded yellow crystals suitable for



Scheme 8. Synthesis of **L-1-Ta(NMe$_2$)$_4$** and ORTEP representation of the molecular structure (ellipsoids drawn at 50% probability, hydrogen atoms are omitted). Selected bond lengths (Å) : Ta–O1 2.043(1), Ta–O2 2.283(1), Ta–N3 2.051(2), Ta–N4 1.996(2), Ta–N5 1.996(2), Ta–N6 2.047(2), C5–O1 1.326(2), C5–N1 1.282(2), C10–O2 1.262(2), C10–N2 1.335(2).



Scheme 9. Synthesis of **L-4-Ta(NMe$_2$)$_4$** and ORTEP representation of the molecular structure (ellipsoids drawn at 50% probability, hydrogen atoms are omitted). Selected bond lengths (Å) and angles (°):Ta–O1 2.148(2), Ta–N1 2.351(2), Ta–N2 2.040(3), Ta–N3 1.981(3), Ta–N4 2.037(3), Ta–N5 1.998(3), N1-Ta–O1 57.70(8).



Scheme 10. Synthesis of **L-7-Ta(NMe$_2$)$_4$** and ORTEP representation of the molecular structure (ellipsoids drawn at 50% probability, hydrogen atoms are omitted). Selected bond lengths (Å) : Ta–N1 2.300(3), Ta–N2 2.320(4), Ta–N3 2.039(4), Ta–N4 2.003(4), Ta–N5 1.975(4), Ta–N6 2.082(4).

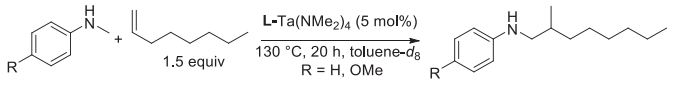
analysis by X-ray diffraction in 72% yield (Scheme 9).[15] The solid-state molecular structure of the complex is consistent with the solution phase NMR data, indicating formation of a monomeric species with the amidate ligand bound in a κ^2 fashion to the metal center. The *ortho*-methoxy group of the ligand is situated away from the metal center and is not acting as a neutral donor in the solid state.

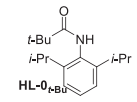
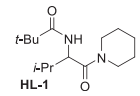
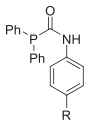
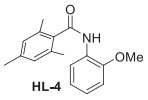
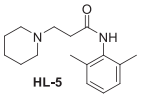
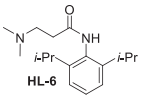
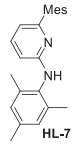
The analogous protonolysis route has been used to prepare the aminopyridinate complex **L-7-Ta(NMe$_2$)$_4$** (Scheme 10).[16] After recrystallization from a toluene/hexanes solution at −35 °C, the complex is obtained as golden-brown crystals in 69% yield. In contrast to other aminopyridinate supported tantalum complexes,[17] the solid-state molecular structure of the complex shows a symmetric *N*,*N*-binding mode, evident by the near equidistant Ta–N bond lengths [Ta–N1 2.300(3) Å, Ta–N2 2.320(4) Å].

A comparison of the axial Ta–dimethylamido bond lengths in these three solid-state molecular structures shows negligible differences in Ta–N bond lengths, indicating limited steric differences between the *N*,*O*- or *N*,*N*-chelating ligands. However, for both *N*,*O* **L-1-Ta(NMe$_2$)$_4$** and **L-4-Ta(NMe$_2$)$_4$** the equatorial dimethylamido ligands show similar bond lengths (approximately 1.98–1.99 Å), while **L-7-Ta(NMe$_2$)$_4$** shows two distinct equatorial dimethylamido ligand bond lengths to tantalum [Ta–N4 2.003(4) Å, Ta–N5 1.975(4) Å].

Most importantly, the influence of ligands **L-1**–**L-7** has been evaluated for Ta(V) catalyzed hydroaminoalkylation through a comparative study of the reactivity of 1-octene with *N*-methylaniline and 4-methoxy-*N*-methylaniline as amine substrates (Table 1). This study provides key information on the ligand parameters that influence catalytic activity.[18] As a point of reference, the homoleptic $Ta(NMe_2)_5$ has been evaluated for both substrates and poor reactivity is observed in 20 h at 130 °C (entry 1). This is in agreement with Hartwig's earlier work, which required higher reaction temperatures to achieve full conversion.[7a] For the homoleptic complex a slight increase in reactivity is observed when 4-methoxy-*N*-methylaniline is used as the amine substrate. The introduction of parent amide proligand **HL-0$_{t\text{-Bu}}$**[7c] resulted in a dramatic increase in the hydroaminoalkylation reactivity (entry 2), with a marked improvement on conversion again when 4-methoxy-*N*-methylaniline is used (87%). The reaction has been repeated at a lower temperature to see whether the reactivity could

Table 1
Screening of proligands and comparison of *N*-methylaniline versus 4-methoxy-*N*-methylaniline[a]



Entry	Ligand	R=H	R=OMe
1[b]	NMe_2	7%	13%
2[b]	 HL-0$_{t\text{-Bu}}$	33%	87% (19%)[d]
3[b]	 HL-1	2%	5%
4[c]	 HL-2-OMe	—[e]	40% (43%)[f]
5[c]	HL-2-CF$_3$	4%[f]	5%[f]
6[c]	 HL-3	29%	61%
7[b]	 HL-4	>98%[c] (51%)[c,d] (50%)[b,d]	>98%[c] (60%)[c,d] (55%)[b,d]
8[c]	 HL-5	42%	40%
9[c]	 HL-6	53%	50%
10[b]	 HL-7	0%	0%

[a] Reaction conversion determined by ^{1}H NMR spectroscopy.
[b] Isolated complex.
[c] In situ prepared complexes.
[d] 110 °C.
[e] Reaction not performed.
[f] 10 mol %.

be sustained. At 110 °C, the reaction is feasible, but the conversion within 20 h is significantly lowered. The complex **L-1-Ta(NMe$_2$)$_4$** with the type **A** ligand is not a good catalyst system for hydroaminoalkylation, and negligible conversion is observed in 20 h (entry 3). Here the six-membered *O*,*O*-chelating motif dramatically impacts reactivity at the metal center.

Evaluation of the type **B** proligands indicates that use of the aromatic **HL-3** proligand incorporating the thiazole backbone results in much more favorable hydroaminoalkylation reactivity than the phosphinecarboxamide ligands **HL-2** (entries 4–6). The use of **HL-2-OMe** did not afford improved reactivity and increasing the catalyst loading to 10 mol % did not help to reach a better conversion (entry 4). Once more however, 4-methoxy-*N*-methylaniline was shown to be a better substrate. It is noteworthy that the use of the more electron-withdrawing proligand **HL-2-CF$_3$** results in a system with negligible reactivity even with 10 mol % catalyst loading (entry 5).

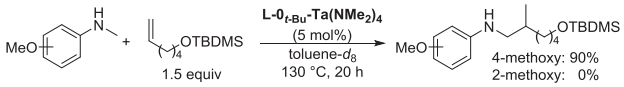
The complex **L-4-Ta(NMe$_2$)$_4$** with the type **C** ligand incorporating a pendant donor on the *N*-substituent is shown to be particularly promising as it results in full conversions in situ with both of the substrates within 20 h (entry 7). Although the solid state structure shows no interaction with the extra *ortho*-methoxy substituent in solid state (Scheme 9) it is possible that under the reaction conditions (solution phase, high temperature) more flexibility in coordination modes are realized, thereby enhancing reactivity. Good reactivity can even be achieved at lower reaction temperatures (110 °C) and once more 4-methoxy-*N*-methylaniline is the more reactive substrate with a conversion of 60% at this lower temperature. The comparison of reactivity of the isolated complex **L-4-Ta(NMe$_2$)$_4$** and in situ reaction at 110 °C shows, indeed, the same reactivity and confirms that the presence of dimethylamine generated upon ligand substitution does not significantly affect the reaction (entry 7).

Type **D** proligands with an extra donor on the side arm of the carbonyl moiety show similar reactivity that is not dramatically impacted by the different steric bulk of the *N*-substituents (entries 8 and 9). However, unlike most other types of proligands in this study, attempts to prepare discrete complexes utilizing these proligands have been unsuccessful, and the role of the extra donor in terms of metal coordination remains unclear.

Lastly, the use of **L-7-Ta(NMe$_2$)$_4$** was completely unsuccessful, with no reactivity observed for either of the amine substrates (entry 10). This is in sharp contrast to the recently disclosed Ti(IV) aminopyridinate-catalyzed hydroaminoalkylation report from Doye.[6g] In Doye's example, a less sterically demanding aminopyridinate was used at a higher catalyst loading, a higher reaction temperature, and for longer reaction times to give a mixture of linear and branched hydroaminoalkylation products.

In summary, the results in Table 1 show that hydroaminoalkylation with *N*,*O*-chelated Ta complexes is an efficient way to construct branched secondary amines via hydroaminoalkylation. Importantly, products bearing a 4-methoxyphenyl (PMP) protecting group on nitrogen, can be deprotected to realize the preparation of selectively substituted primary amines. However, due to the quite harsh conditions required for the oxidative cleavage of the 4-methoxyphenyl group,[19] we wanted to consider 2-methoxy-*N*-methylaniline as an alternative hydroaminoalkylation substrate. Snapper and Hoveyda have shown that milder deprotection conditions are effective for the generation of primary amines with this protecting group.[20]

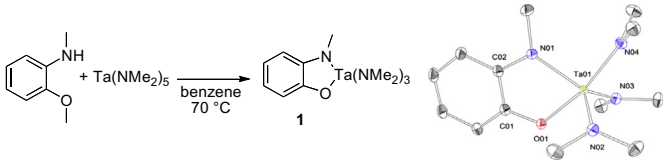
To further explore alkene substrate scope, an alkene bearing a *tert*-butyldimethylsilyl protected alcohol has also been tested (Scheme 11). In the presence of 5 mol % of **HL-0$_{t\text{-Bu}}$** and 5 mol % Ta(NMe$_2$)$_5$, 4-methoxy-*N*-methylaniline is well tolerated to give the predicted product in high conversion (90%).[7c] However, 2-methoxy-*N*-methylaniline is incompatible with this catalyst system, and instead a color change of the reaction mixture from yellow to deep red is noted along with the observation of *N*-(2,6-diisopropylphenyl)pivalamide as the free proligand, as evidenced by the diagnostic chemical shift for the doublet corresponding to the *i*-Pr groups of the free ligand (1.2 ppm).



Scheme 11. Evaluation of 2- and 4-methoxy-*N*-methylaniline.

In order to determine the impact of this substrate, the stoichiometric protonolysis reaction of Ta(NMe$_2$)$_5$ with 2-methoxy-*N*-

methylaniline was performed (Scheme 12). When the two compounds are heated to 70 °C for 18 h, a complex mixture of products are observed by ^{1}H NMR spectroscopy, from which complex **1** could be isolated as a crystalline solid in modest yield.[21] Notably, this dianionic ligand is formed upon cleavage of the O–Me bond to generate a new *N*,*O*-chelated Ta complex with a five-membered metallacycle, which contrasts with our most successful catalyst systems disclosed thus far with four-membered metallacycles. This selective C(sp^3)–O bond cleavage reactivity is, to the best of our knowledge, unknown for Ta amido complexes, however related examples have been realized using niobium and tantalum pentahalides.[22,23] Disappointingly, a crystalline sample of **1** shows no catalytic activity when evaluated using the same reaction conditions as described in Table 1.



Scheme 12. Reaction between 2-methoxy-*N*-methylaniline and Ta(NMe$_2$)$_5$ and ORTEP representation of the molecular structure (ellipsoids drawn at 50% probability, hydrogen atoms are omitted). Selected bond lengths (Å): Ta–O1 2.032(2), Ta–N1 2.063(2), Ta–N2 1.961(2), Ta–N3 1.975(3), Ta–N4 2.014(2), O1–C1 1.348(3), N1–C2 1.404(4).

3. Summary and conclusion

The influence of eight related *N*,*O*-chelating ligands, one of which was found to bind as *O*,*O*-ligand, and one *N*,*N*-chelating ligand on Ta(V) catalyzed hydroaminoalkylation has been studied through the assessment of the reactivity of *N*-methylaniline and 4-methoxy *N*-methylaniline with 1-octene. The use of proligand **HL-4**, an aromatic amide bearing an *ortho*-methoxyphenyl group on nitrogen, enables a notable improvement of the reaction conditions over the previously reported **HL-0**$_{t\text{-}\mathbf{Bu}}$. The 4-methoxy-*N*-methylaniline substrate has been shown to promote enhanced hydroaminoalkylation over *N*-methylaniline with this class of catalysts, presumably due to the enhanced nucleophilicity of this amine to promote protonolysis. Protonolysis has been proposed to be the turnover limiting step in BINOLate chelated Ta(V) catalyzed hydroaminoalkylation.[7g] Generally, the incorporation of heteroatoms into the ligand set did not promote improved reactivity and ligands that can adopt chelating modes that are less strained than the four-membered *N*,*O*-metallacycles, such as five- and seven-membered metallacycles do not yield favorable catalytic results. These results suggest that systems that have ligand hemi-lability are favorable for accessing improved reactivity profiles. Notably, the use of the related 2-methoxy-*N*-methylaniline cannot be tolerated as a hydroaminoalkylation substrate and an unexpected C(sp^3)–O bond cleavage has been observed to yield a new Ta(V) complex. In conclusion, hemi-labile *N*,*O*-chelated Ta metallacyclic complexes show promise as easily modified ligand backbones to support catalytically active complexes. The incorporation of a potentially labile donor atom on the *N*-substituent shows improved reactivity and provides a basis for ongoing ligand development efforts.

4. Experimental section

4.1. Synthesis and techniques

All preparative scale reactions were conducted using oven dried (160 °C) glassware with magnetic stirring using Schlenk-line techniques or a glove box under an atmosphere of dry nitrogen. Experiments on the NMR tube scale were carried out in Teflon cap sealed NMR tubes (5 mm). Toluene, benzene, hexanes, and pentane were purified by passage over an activated aluminum oxide column and degassed prior to use. Benzene-d_6 and toluene-d_8 were dried over 4 Å molecular sieves and degassed by 3 freeze-pump-thaw cycles. Solvents for chromatography were used as received from commercial sources. Silica gel F60: 40–63 μm (230–400 mesh) was purchased from Silicycle. TLC were run on silica gel coated aluminum plates Merck 60 F_{254} and revealed with UV at 254 nm and by dipping in aqueous potassium permanganate solution.

4.2. Reagents and materials

Commercial amines and olefins were distilled under reduced pressure from CaH_2 and degassed by 3 freeze-pump-thaw cycles or sublimed in the case of solids. Ta(NMe$_2$)$_5$ was purchased from Strem and used as received. Commercially available reagents were used as received unless indicated otherwise.

4.3. Characterization

NMR spectra were recorded on Bruker Avance 300, Bruker Avance 400 MHz, and Bruker Avance 600 MHz instruments. The samples were measured as solutions in the indicated solvent at ambient temperature in non-spinning mode unless mentioned otherwise. To specify the signal multiplicity, the following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, and m=multiplet; br indicates a broad resonance and app indicates apparent multiplicity. Chemical shifts δ are reported in parts per million (ppm) and calibrated against the residual solvent signal. Coupling constants *J* are given in Hertz (Hz). Low resolution mass spectra (EI-MS and ESI-MS), high resolution mass-spectra (HRMS), and elemental analyses (EA) were measured by the mass spectrometry and microanalysis service at University of British Columbia. Mass spectra were measured on a Kratos MS-50. Fragment signals are given in mass per charge number (*m*/*z*). Elemental analyses were performed on a Carlo Erba Elemental Analyzer EA 1108. The content of the specified element is expressed in percent (%).

4.4. Proligands

Proligands **HL-0**$_{t\text{-}\mathbf{Bu}}$,[7c] **HL-2-OMe**,[10] **HL-2-CF$_3$**,[10] **HL-3**,[11] and **HL-7**[23] were synthesized following reported procedures.

4.4.1. ***HL-1****: N-(3-methyl-1-oxo-1-(piperidin-1-yl)butan-2-yl)pivalamide.* To a solution of Piv-Val-COOH[9] (2.0 g, 10 mmol) and triethylamine (1.53 mL, 11 mmol) in dry THF (35 mL) at −15 °C were successively added dropwise ethyl chloroformate (0.96 mL, 10 mmol) and piperidine (1.09 mL, 11 mmol). After one night at room temperature, the volatiles were removed under reduced pressure and the residual yellow oil diluted in EtOAc (20 mL), washed with 0.5 M aqueous $NaHCO_3$, 1 M aqueous HCl, brine, and dried over $MgSO_4$. Removal of the volatiles under reduced pressure yielded a white powder recrystallized from hexanes/EtOAc (9:1) at −10 °C to give **HL-1** as a white crystalline solid in 22% yield (0.59 g). Mp: 114 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.84 (d, *J*=6.9 Hz, 3H), 0.94 (d, *J*=6.8 Hz, 3H), 1.21 (s, 9H), 1.48–1.68 (m, 6H), 1.91–2.03 (m, 1H), 3.43–3.50 (m, 2H), 3.50–3.63 (m, 2H), 4.85 (dd, *J*=8.58, 5.12 Hz, 1H), 6.54 (d, *J*=8.06 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.0, 19.9, 24.4, 25.6, 26.4, 27.5, 31.7, 38.8, 43.1, 46.7, 52.7, 170.0, 178.2. MS (CI): *m*/*z*=269 (M+H)$^+$. EA calcd for $C_{15}H_{28}N_2O_2$: C, 67.13; N, 10.44; H, 10.52; found: C, 67.01; N, 10.20; H, 10.52.

4.4.2. ***HL-3****: 2,5-diphenylthiazol-4-ol (Adapted from literature).*[24] A mixture of thiobenzamide (1.37 g, 10.0 mmol), ethyl α-bromop-

henylacetate (1.93 mL, 11.0 mmol), and pyridine (0.243 mL, 3.00 mmol) was stirred under nitrogen at 110 °C for 3 h. The resulting solidified yellow mixture was diluted with EtOH (15 mL) and stirred at room temperature for 30 min. The crude product was filtered, and recrystallized from EtOH–DMF to give yellow needles in 52% (1.32 g). Mp 199.9 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.21 (t, J=7.4 Hz, 1H), 7.39 (t, J=7.8 Hz, 2H), 7.54–7.36 (m, 3H), 7.72 (d, J=7.4 Hz, 2H), 7.89 (dd, J=8.0, 1.7 Hz, 2H), 11.6 (br s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 107.5, 125.2, 125.9, 126.1, 128.8, 129.3, 130.2, 131.8, 132.9, 158.4, 159.6. HRMS (EI) calcd for $C_{15}H_{11}NOS$: m/z 253.05614 (M^+); found: m/z 253.05631 (M^+). EA calcd for $C_{15}H_{11}NOS$: C, 71.12; H, 4.38; N, 5.53; found: C, 71.05; H, 4.34; N, 5.34.

4.4.3. ***HL-4****: N-(2-methoxyphenyl)-2,4,6-trimethylbenzamide.* 2-Methoxyaniline (0.34 mL, 3 mmol) was added to dichloromethane (100 mL) in a round bottom flask equipped with a stir bar. After addition of triethylamine (2.1 mL, 15 mmol), the mixture was cooled to −78 °C and 2,4,6-trimethylbenzylchloride (0.5 mL, 3 mmol) added dropwise. The reaction was left to warm to room temperature, stirred overnight and then quenched with saturated aqueous $NaHCO_3$, extracted with dichloromethane (3×20 mL), and dried over $MgSO_4$. After filtration, and removal of volatiles under reduced pressure, a pinkish solid was obtained, which upon recrystallization from dichloromethane/hexane, afforded **HL-4** as a white solid in 52% yield (0.42 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.40 (s, 6H), 3.86 (s, 3H), 6.87–6.96 (m, 3H), 6.99–7.18 (m, 2H), 7.95 (br s, 1H), 8.62 (dd, J=7.9, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 21.0, 55.5, 109.9, 119.9, 121.0, 123.9, 127.5, 128.3, 134.4, 135.3, 138.7, 148.0, 168.4. HRMS (EI) calcd for $C_{17}H_{19}NO_2$: m/z 269.14158 (M^+); found: m/z 269.14142 (M^+).

4.4.4. ***HL-5****: N-(2,6-dimethylphenyl)-3-(piperidin-1-yl)propanamide (Adapted from literature).*[25,26] 3-Chloropropanoic acid (2.35 g, 21.7 mmol) was dissolved in toluene in a round bottom Schlenk flask equipped with a condenser and a stir bar. Thionyl chloride (15.7 mL, 216.6 mmol) was added through the top of the condenser and the solution heated to reflux for 1.5 h. The reaction mixture was cooled to room temperature and the excess thionyl chloride and toluene were removed under reduced pressure. Dry toluene (100 mL) and Na_2CO_3 (4.59 g, 43.3 mmol) was then added to the crude product followed by 2,6-dimethylaniline (2.23 mL, 18.1 mmol) added dropwise over 15 min resulting in a bright yellow solution. After addition the reaction mixture was left to stir for 1 h at room temperature. The mixture was then diluted with water (50 mL), piperidine (8.6 mL, 86.7 mmol) added and the reaction mixture was refluxed for 8 h. After cooling to room temperature the organic layer was collected and washed with water (3×50 mL). The organic layer was then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography (MeOH/DCM 1:99 to 5:95) and recrystallization from hot hexanes afforded **HL-5** in 20% yield (0.95 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45–1.57 (m, 2H), 1.59–1.64 (m, 4H), 2.25 (s, 6H), 2.42–2.64 (m, 6H), 2.70–2.74 (m, 2H), 7.09 (s, 3H), 10.30 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 24.2, 25.9, 32.0, 53.8, 54.9, 126.6, 128.0, 134.7, 134.8, 170.9. HRMS (EI) calcd for $C_{16}H_{24}N_2O$: m/z 260.18886 (M^+); found: m/z 260.18904 (M^+).

4.4.5. ***HL-6****: N-(2,6-diisopropylphenyl)-3-(dimethylamino)propanamide (Adapted from literature).*[25,26] 3-Chloropropanoic acid (2.546 g, 23.46 mmol) was dissolved in toluene in a round bottom Schlenk flask equipped with a condenser and a stir bar. Thionyl chloride (5.1 mL, 70.38 mmol) was added through the top of the condenser and the solution heated to reflux for 2 h. The reaction mixture was cooled to room temperature and the excess thionyl chloride and toluene were removed under reduced pressure. Dry toluene (80 mL) and Na_2CO_3 (4.14 g, 39.1 mmol) was added followed by 2,6-diisopropylaniline (3.69 mL, 19.55 mmol) added dropwise over 30 min. After addition the reaction mixture was left to stir for 1 h at room temperature and then diluted with water (50 mL). After addition of Na_2CO_3 (8.29 g, 78.20 mmol) and Me_2NH_2Cl (6.38 g, 78.20 mmol) the reaction mixture was heated to reflux overnight. After cooling to room temperature the organic layer was collected and washed with water (3×50 mL). The organic layer was then dried over $MgSO_4$, filtered, and the solvent removed under reduced pressure. The resulting solid was rinsed repeatedly with hexanes until a white powder was obtained. Recrystallization from hot hexanes afforded **HL-6** in 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12–1.42 (m, 12H), 2.44 (s, 6H), 2.64–2.71 (m, 2H), 2.77–2.83 (m, 2H), 3.16 (dt, J=13.8, 6.8 Hz, 2H), 7.25 (s, 2H), 7.32–7.38 (m, 1H), 10.30 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6, 28.8, 32.7, 44.5, 55.3, 123.3, 127.7, 132.0, 145.6, 171.7. HRMS (EI) calcd for $C_{17}H_{28}N_2O$: m/z 276.22016 (M^+); found: m/z 276.22009 (M^+).

4.5. Complexes

4.5.1. ***L-1-Ta(NMe$_2$)$_4$****: (Z)-(2,2-dimethyl-1-((3-methyl-1-oxo-1-(piperidin-1-yl)butan-2-yl)imino)propoxy)tetrakis(dimethylamido)tantalum.* **HL-1** (36.1 g, 0.135 mmol) and $Ta(NMe_2)_5$ (54.0 mg, 0.135 mmol) in hexanes (3 mL) were stirred overnight at room temperature. Removal of volatiles under reduced pressure and crystallization at −30 °C from hexanes afforded **L-1-Ta(NMe$_2$)$_4$** in 56% yield (47.3 mg). ^{1}H NMR (600 MHz, C_6D_6): δ 0.96 (d, J=6.8 Hz, 3H), 0.99–1.05 (m, 1H), 1.05–1.15 (m, 3H), 1.15–1.22 (m, 1H), 1.22–1.29 (m, 1H), 1.25 (d, J=6.4 Hz, 3H), 1.49 (s, 9H), 1.97–2.15 (m, 1H), 2.84 (br s, 2H), 3.53 (br s, 24H), 3.77 (d, J=11.5 Hz, 1H), 3.89 (br s, 2H). ^{13}C NMR (150 MHz, C_6D_6) δ 20.1, 21.8, 24.6, 25.8, 25.8, 25.9, 30.1, 31.6, 39.2, 45.2, 47.5, 47.6, 69.5, 175.1, 178.5. MS (EI): m/z=580 (M^+−NMe_2). EA calcd for $C_{23}H_{51}N_6O_2Ta$: C, 44.22; N, 13.45; H, 8.23; found: C, 44.00; N, 13.31; H, 8.22. Characterized by X-ray crystallography.

4.5.2. ***L-4-Ta(NMe$_2$)$_4$****: mono(N-(2-methoxyphenyl)-2,4,6-trimethylbenzamidate) tetrakis(dimethylamido)tantalum.* **HL-4** (0.135 g, 0.5 mmol) and $Ta(NMe_2)_5$ (0.200 g, 0.5 mmol) in hexanes were stirred overnight at room temperature. Removal of volatiles under reduced pressure afforded a yellow powder, which after recrystallization from hexanes yielded **L-4-Ta(NMe$_2$)$_4$** in 72% yield (225 mg) as yellow crystals. ^{1}H NMR (400 MHz, C_6D_6) δ 1.98 (s, 3H), 2.43 (s, 6H), 3.10 (s, 3H), 3.56 (s, 24H), 6.34–6.41 (m, 1H), 6.57 (s, 2H), 6.72–6.82 (m, 2H), 7.06–7.22 (m, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ 21.3 (CH_3), 21.4 (CH_3), 47.4 (CH_3), 54.6 (CH_3), 111.9 (CH), 120.8 (CH), 125.3 (CH), 126.5 (CH), 129.0 (CH), 134.8 (C), 135.4 (C), 135.7 (C), 138.2 (C), 153.0 (C), 177.3 (C). MS (EI): m/z=581 (M^+-NMe_2). EA calcd for $C_{25}H_5N_2O_2Ta$: C, 48.00; N, 11.19; H, 6.77; found: C, 48.02; N, 10.93; H, 7.01. Characterized by X-ray crystallography.

4.5.3. ***L-7-Ta(NMe$_2$)$_4$****: mono(N,6-Dimesityl-2-aminopyridinatetetrakis-(dimethylamido)tantalum.* **HL-7** (0.33 g, 1.00 mmol) and $Ta(NMe_2)_5$ (0.40 g, 1.00 mmol) in benzene (3 mL) were stirred at room temperature for 24 h. The volatiles were removed under vacuum, and the resulting solid was recrystallized from toluene/hexanes (3:1) at −35 °C to give the complex as golden-brown crystals (0.477 g, 69%). ^{1}H NMR (400 MHz, C_6D_6): δ 2.18 (s, 3H), 2.27 (s, 6H), 2.28 (s, 3H), 2.41 (s, 6H), 3.32 (s, 24H), 5.68 (dd, J=8.7, 0.8 Hz, 1H), 5.85 (dd, J=6.9, 0.7 Hz, 1H), 6.82 (s, 2H), 6.87 (dd, J=8.6, 6.9 Hz, 1H), 6.98 (s, 2H). ^{13}C NMR (100 MHz, C_6D_6): δ 19.8, 21.3, 21.4, 21.8, 48.0, 107.9, 110.0, 128.7, 130.2, 133.2, 134.8, 137.0, 137.4, 138.3, 138.6, 143.7, 156.8, 167.0. MS (EI): m/z=642 (M^+-NMe_2). EA calcd for $C_{31}H_{49}N_6Ta$: C, 54.22; H, 7.19; N, 12.24;

found: C, 54.53; H, 7.09; N, 11.84. Characterized by X-ray crystallography.

4.6. General procedure for catalysis experiments

4.6.1. Starting from isolated complexes. In a J. Young NMR tube was added a solution of the corresponding *N*-methylaniline (0.5 mmol) and 1-octene (112 μL, 0.75 mmol) in 0.30 g of toluene-d_8. A solution of the complex (5 mol %, 0.025 mmol) in 0.30 g of toluene-d_8 was then added and the mixture warmed to 130 °C. In all cases, conversion was determined by ^{1}H NMR spectroscopy after 20 h.

4.6.2. Starting from in situ generated complexes. To a solution of the $Ta(NMe_2)_5$ (0.025 mmol) in toluene-d_8 (0.30 g) was added the corresponding proligand (0.025 mmol) at room temperature. After 15 min, the mixture was transferred to a solution of the corresponding *N*-methylaniline (0.5 mmol) and 1-octene (112 μL, 0.75 mmol) in 0.30 g of toluene-d_8 in a J. Young NMR tube. The mixture warmed to 130 °C. In all cases, conversion was determined by ^{1}H NMR spectroscopy after 20 h.

4.7. Synthesis of 1

To a solution of the $Ta(NMe_2)_5$ (129 mg, 0.32 mmol) in benzene-d_6 (0.60 g) was added 2-methoxy-*N*-methylaniline (44 mg, 0.32 mmol). After 4 h at room temperature, the mixture was transferred onto a J. Young NMR tube and warmed to 70 °C for 16 h and the crude mixture analyzed by ^{1}H NMR. Slow evaporation of the volatiles enabled the isolation of **1** as red crystals. ^{1}H NMR (300 MHz, C_6D_6): δ 1.28 (s, 18H), 2.15 (s, 3H), 6.70 (d, J=7.5 Hz, 1H), 6.96 (dd, J=7.5, 7.4 Hz, 1H), 7.07 (dd, J=7.6, 7.4 Hz, 1H), 7.20 (d, J=7.4 Hz, 1H). MS (EI): m/z=434 (M^+). Characterized by X-ray crystallography.

Acknowledgements

The authors thank Mr. Jacky C.-H. Yim for assistance with X-ray crystallography and NSERC and Boehringer Ingelheim (Canada) Ltd for financial support of this work. P.R.P. and E.C. thank NSERC for postgraduate scholarships. R.L.W. thanks the Government of Canada for a Commonwealth Postdoctoral Fellowship. A.C.B. and J.A.R.S. acknowledge the Donors of the American Chemical Society Petroleum Research Fund for partial support of this research. This research was undertaken, in part, thanks to funding from the Canada Research Chairs program.

Supplementary data

These data include NMR spectra and details of X-ray crystallographic data. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.04.070.

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