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Article

Lanthanide- and Actinide-Mediated Terminal Alkyne Hydrothiolation for the Catalytic Synthesis of Markovnikov Vinyl Sulfides

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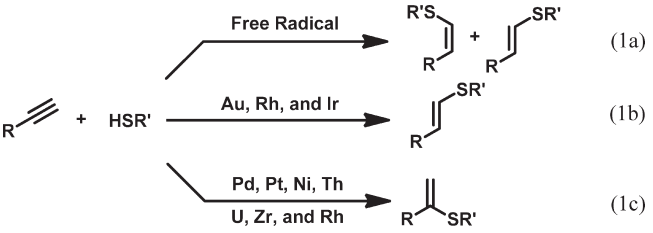
The Markovnikov-selective lanthanide- and actinide-mediated, intermolecular hydrothiolation of terminal alkynes by aliphatic, benzylic and aromatic thiols using $Cp^*_2LnCH(TMS)_2$ ($Cp^* = C_5Me_5$; Ln = La, Sm, Lu), $Ln[N(TMS)_2]_3$ (Ln = La, Nd, Y), $Cp^*_2An(CH_2TMS)_2$, and $Me_2SiCp''_2An(CH_2R)_2$ ($Cp'' = C_5Me_4$; An = Th, R = TMS; An = U, R = Ph) as precatalysts is studied in detail. These transformations are shown to be Markovnikov-selective, with selectivities as high as >99%. Kinetic investigations of the $Cp^*_2SmCH(TMS)_2$-mediated reaction between 1-pentanethiol and 1-hexyne are found to be first-order in catalyst concentration, first-order in alkyne concentration, and zero-order in thiol concentration. Deuterium labeling of the alkyne −C≡C−H position reveals k_H/k_D = 1.40(0.1) and 1.35(0.1) for the organo-Sm- and organo-Th-catalyzed processes, respectively, along with evidence of thiol-mediated protonolytic detachment of the vinylic hydrothiolation product from the Sm center. Mechanistic findings indicate turnover-limiting alkyne insertion into the Sm−SR bond, followed by very rapid, thiol-induced M−C protonolysis to yield Markovnikov vinyl sulfides and regenerate the corresponding M−SR species. Comparisons of different substrates and metal complexes in catalyzing hydrothiolation reveal a strong dependence of hydrothiolation activity on the steric encumbrance in the insertive transition state. Observed deuterium exchange between alkyne −C≡C−H and thiol RS−H in the presence of $Cp^*_2SmCH(TMS)_2$ and $Me_2SiCp''_2Th(CH_2TMS)_2$ argues for a metal−alkynyl ⇌ metal−thiolate equilibrium, favoring the M−SR species under hydrothiolation conditions. A mixture of free radical-derived anti-Markovnikov vinyl sulfides is occasionally observed and can be suppressed by γ-terpinene radical inhibitor addition. Previously reported metal thiolate complex aggregation to form insoluble species is observed and can be delayed kinetically by Cp-based ligation.

Introduction

Sulfur−carbon bonds are a critical constituent of many pharmaceuticals,[1] materials,[2] synthetic reagents,[2b,c,f,3] and natural products,[4] giving impetus to discovering more efficient and selective methods to incorporate sulfur into organic frameworks. The addition of S−H bonds across alkynes is an atom-economical route to a variety of vinyl sulfides. While radical reactions for the formation of S−C bonds have been known to form unselective mixtures of *E* and *Z* vinyl sulfides for decades (eq 1a),[5] only in the past few years has the application of transition metal and f-element catalysts to this transformation (eqs 1b and c)[6] received a surge of attention. Among the



previously reported catalysts exhibiting alkyne hydrothiolation activity are Rh,[6f,g,i,r,u] Ir,[6d] Ni,[6c,k,l,n−p,s] Pd,[6c,k,m,u] Pt,[6k] Au,[6b] Zr,[6a] Th,[6e] and U[6e] (e.g., eqs 2−4).[6a,g,p] While Au, Rh, and Ir catalysts often favor *E* anti-Markovnikov products (e.g., eq 4),[7] Ni, Pd, Pt, and Zr catalysts favor the Markovnikov vinyl sulfides

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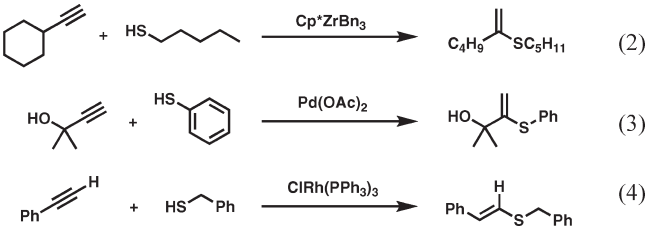
(e.g., eqs 2 and 3). This Markovnikov selectivity observed with the latter catalysts is thought to result from a pathway involving insertion of alkyne into a M−SR bond (see more below).[6a,l]



We previously communicated that organothorium and organouranium complexes[8] are highly selective catalysts for the synthesis of Markovnikov vinyl sulfides.[6e] Interestingly, it was also shown that the occasional formation of anti-Markovnikov products can be suppressed by the addition of a radical inhibitor, implicating a known, nonmetal-centered, radical-mediated side reaction.[5b−f] Among the most notable attractions of these actinide catalysts is their demonstrated ability to accommodate a wide range of thiols. While many late transition metal complexes are competent to mediate this transformation with arylthiols,[6] few have exhibited the same activity with the less reactive aliphatic thiols.[6g,h,m,r,9] Kinetic and mechanistic studies of these organoactinide-mediated transformations led to the proposed insertion/protonolysis sequence of Scheme 1, where the Markovnikov insertion of alkyne into a Th−SR bond is turnover-limiting, followed by a very rapid, thiol-mediated protonolysis of the vinyl sulfide group from the metal to yield vinyl sulfide product and regenerate the catalyst. Examination of organoactinide-mediated hydrothiolation activity as a function of substrate shows that while both steric encumbrance and the electronic structure of the thiols and alkynes influence hydrothiolation activity, thiol steric characteristics dominate. Furthermore, the selectivity of this transformation scales inversely with the ability of a given substrate to initiate and propagate the aforementioned radical side reaction.[5b−f]

Lanthanide complexes[8k,10] are highly active and selective reagents for analogous alkyne hydroamination,[8i,11] hydrophosphination,[11e,12] and hydroalkoxylation[11e,13] processes. However, organolanthanide complexes also exhibit large Ln−SR (Ln = lanthanide) bond enthalpies[14] and are known to form thiolate aggregates,[10e,15] raising concern about whether the insertion of carbon−carbon unsaturations into this type of bond is even possible. In light of the recently

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(7) With the noteable exception of $Tp^*Rh(PPh_3)_2$ (ref 6i).

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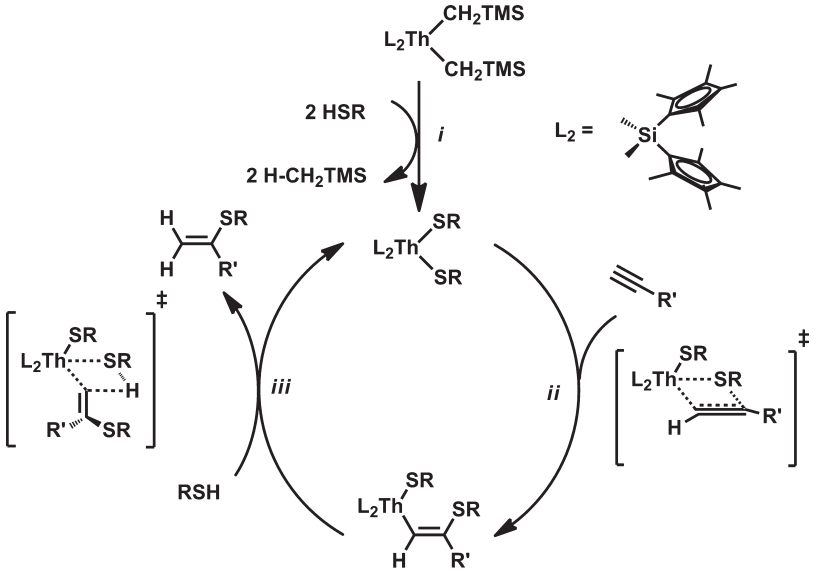
Scheme 1. Proposed Catalytic Cycle for Organothorium-Mediated Alkyne Hydrothiolation[6e]



communicated efficacy of organozirconium and organoactinide complexes in effecting highly Markovnikov-selective alkyne hydrothiolation,[6a,e] the intriguing question arises as to whether and with what efficacy analogous organolanthanide complexes might effect alkyne hydrothiolation.

Bond enthalpy considerations for the unexplored, lanthanide-mediated variant of Scheme 1 (Table 1)[16] predict net exothermicity for thiol addition to alkynes and alkenes mediated by organolanthanide complexes. However, while alkyne insertion into a Sm−SR bond (step ii) is predicted to be exothermic by ca. −12 kcal/mol, alkenes will be more challenging, with insertions predicted to be endothermic by ca. +23 kcal/mol. The final protonolysis process (step iii) is estimated to be highly exothermic for all substrates, reflecting the substantial product C−H and Sm−SR bond enthalpies. Importantly, the exothermicity of alkyne insertion into a Sm−SR bond taken together with the kinetic lability of lanthanide complexes suggests favorable conditions for catalysis,[13b] while the endothermicity of the analogous alkene insertion is expected to be more prohibitive.[17] These predictions parallel reported thermodynamic estimates for organoactinide complexes.[6a,e] Herein we report a detailed study of organolanthanide-mediated alkyne hydrothiolation with scope and mechanistic considerations discussed. We compare and contrast these 4f results with our earlier 5f results.

Table 1. Estimated Δ*H*'s (kcal/mol) for Proposed/Predicted Organothorium- and Organosamarium-Mediated Insertion/Protonolysis Hydrothiolation Cycles (see Scheme *1*)[18]

metal/C−C unsaturation	step ii (insertion)	step iii (protonolysis)
Samarium		
alkene	+23	−43
alkyne	−12	−33
Thorium		
alkene	+12	−32
alkyne	−19	−26

Experimental Section

Materials and Methods. Due to the air- and moisture-sensitivity of the organolanthanide and organoactinide complexes used in this study, all manipulations were carried out in oven-dried, Schlenk-type glassware interfaced to a high-vacuum line (10^{-6} Torr) or in a nitrogen-filled glovebox (< 1 ppm O_2). Argon (Airgas) was further purified by passing through columns of MnO and activated 4 Å Davison molecular sieves immediately before use. Benzene for preparative-scale and THF-d_8 and benzene-d_6 (Cambridge Isotope Laboratories, 99+ atom % D) for NMR-scale reactions and kinetic measurements were stored over Na/K alloy *in vacuo* and vacuum transferred immediately prior to use or were stored in a nitrogen-filled glovebox until use. Pyridine-d_5 was stored over CaH_2 and vacuum transferred prior to use. Thiols and alkynes were purchased from Aldrich, VWR, GFS Chemicals, and Acros; they were distilled and transferred across multiple beds of activated Davison 4 Å molecular sieves as solutions in benzene-d_6 or neat, followed by degassing (10^{-6} Torr) via freeze−pump−thaw methods. Phenylacetylene-*d* (**26-*d***) was

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(16) See Supporting Information for bond enthalpy calculations.

(17) Attempts to insert unactivated olefins into Ln−SR and An−SR bonds have thus far been unsuccessful.

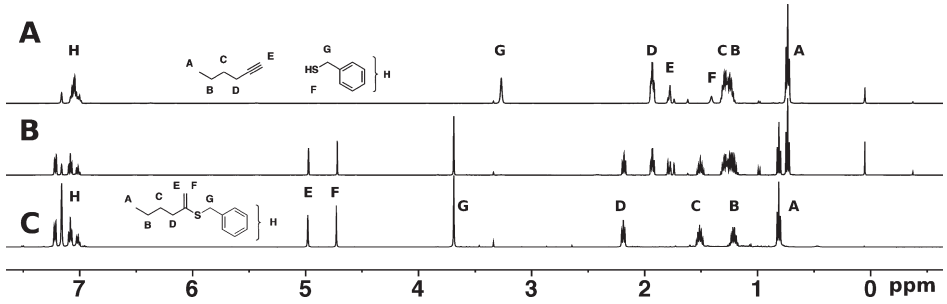


Figure 1. ^{1}H NMR (500 MHz) spectrum of the reaction **6** + **14** → **15** mediated by a $Cp^*_2SmCH(TMS)_2$ (**5**) precatalyst in benzene-d_6 with 3× molar excess of 1-hexyne (A), the completed reaction after 16.0 h in a 120 °C oil bath with 5 mol % catalyst (B), and the isolated product (C).

prepared by literature methods.[6a] All substrates were stored under argon in Teflon-valved glass storage tubes, and conjugated alkynes and thiols were stored at −10 °C until use. The D_2O was purchased from Cambridge Isotope Laboratories (99.9 atom % D) and used as received. The organolanthanide and organoactinide complexes $Ln[N(TMS)_2]_3$ (Ln = La (**1**), Nd (**2**), and Y (**3**)),[19] $Cp^*_2LnCH(TMS)_2$ (Ln = La (**4**), Sm (**5**), Lu (**6**)),[20] $Cp^*_2An(CH_2TMS)_2$ (An = Th (**35**), U (**34**)),[21] and $Me_2SiCp''_2AnL_2$ (An = Th, L = CH_2TMS (**32**);[22] An = U, L = CH_2Ph (**36**)[23]) were prepared as reported in the literature and stored in a nitrogen-filled glovebox until use. Complexes **4**, **5**, **6**, **32**, **34**, **35**, and **36** were stored below 0 °C. The methyltriphenylsilane ^{1}H NMR internal integration standard was purchased from Strem, sublimed twice under high vacuum, and stored in a glovebox. Product NMR spectroscopic data agree with the published literature spectra (see Supporting Information).[6a,e,r,24]

Physical and Analytical Measurements. NMR spectra were recorded on Mercury 400 (400 MHz, ^{1}H; 100 MHz, ^{13}C; 61 MHz, ^{2}H) and Avance III 500 (500 MHz, ^{1}H; 125 MHz, ^{13}C) NMR spectrometers. Chemical shifts (δ) are referenced relative to internal solvent or integration standard resonances and reported relative to Me_4Si. Spectra of air-sensitive reactions and materials were taken in airtight, Teflon-valved J. Young NMR tubes. Samples were heated in silicon oil baths with the temperature controlled by an Ika ETS-D4 probe. GC data for selectivity measurements were collected on a HP6890 GC-MS equipped with a HP5972 detector and an HP-5MS (5% phenylmethylsiloxane, 30 m × 250 μm × 0.25 μm) capillary column.

Typical NMR-Scale Catalytic Reaction. In a glovebox, $Cp^*_2SmCH(TMS)_2$ (**2**, 3.0 mg, 5.2 μmol) and methyltriphenylsilane (8.0 mg, 29.5 μmol) were dissolved in 0.6 mL of benzene-d_6 and added to a J. Young NMR tube. The tube was sealed and interfaced to a high-vacuum line, where 0.2 mL of thiol and 0.2 mL alkyne solutions (both 1.0 M in benzene-d_6; 0.2 mmol; 38 molar excess) were syringed in simultaneously under an argon flush. The reaction mixture was then sealed under argon and placed in a preheated, temperature-controlled oil bath covered with aluminum foil to shield reactions from ambient light.

Kinetic Experiments. The same procedure as described above was followed except that the sample was periodically removed from the oil bath to collect ^{1}H NMR spectra at room temperature. Turnover-frequency (N_t) was determined by the method of initial rate,[25] where a linear regression ($R^2 \geq 0.98$) of data points was taken early in the reaction before the substrates had been appreciably consumed (see Supporting Information). Turnover frequency (N_t) was determined by plotting [product] versus time according to eq 5 and using slope to calculate N_t according to eq 6, where $[catalyst]_0$ = initial concentration of precatalyst and t = time in h. All kinetic experiments in this study were performed at 0.2 M [thiol] and [alkyne] unless otherwise indicated. Samarium kinetics were performed at 2−3 mol % catalyst loading unless otherwise indicated.

$$[\text{product}] = mt \tag{5}$$

$$N_t(\text{h}^{-1}) = \frac{m}{[\text{catalyst}]_0} \tag{6}$$

Conversion and Selectivity Measurements. In the glovebox, $Cp^*_2SmCH(TMS)_2$ (**2**, 5.0 mg, 10 μmol) was dissolved in 0.4 mL of benzene-d_6 and the resulting solution transferred to a J. Young NMR tube. The tube was then sealed and attached to a high-vacuum line, where 0.2 mL of thiol and 0.6 mL of alkyne solutions (both 1.0 M in benzene-d_6; 0.2 mmol; 20 molar excess in thiol) were syringed in under an argon flush. The reaction mixture was then sealed, shaken well, and placed in a temperature-controlled, 120 °C oil bath for 16.0 h. The product selectivity was determined by GC/MS, while conversion was determined by ^{1}H NMR integrations against internal standards or quantitatively liberated catalyst ligands. To purify products, the reaction mixture was eluted through a silica gel plug with ∼10 mL of hexanes or decanted off precipitated catalyst to remove metal. The filtrate was then pumped under vacuum (10^{-3} mTorr) to remove the volatiles and yield pure product.

Larger Scale Procedure. In the glovebox, $Cp^*_2SmCH(TMS)_2$ (**5**, 75 mg, 0.13 mmol) was added to an oven-dried, 20 mL Teflon-valved, glass storage tube dissolved in 1 mL of benzene. On a high-vacuum line, an additional 9 mL of benzene was added by vacuum transfer. The tube was cooled to −78 °C, and 1-hexyne (**7**, 0.90 mL, 7.8 mmol) and benzylmercaptan (**14**, 0.30 mL, 2.6 mmol) were syringed into the tube under an argon flush. The vessel was sealed, thawed, and placed in a preheated 120 °C oil bath for 36.0 h with no stirring.[26] Under ambient conditions, the catalyst was removed by filtering through silica gel, eluting

(18) See Supporting Information for bond enthalpy calculations.
(19) (a) Dash, A. K.; Razavi, A.; Mortreux, A.; Lehmann, C. W.; Carpentier, J.-F. *Organometallics* **2002**, *21*, 3238–3249. (b) Schuetz, S. A.; Day, V. W.; Sommer, R. D.; Rheingold, A. L.; Belot, J. A. *Inorg. Chem.* **2001**, *40*, 5292–5295.
(20) Jeske, G.; Lauke, H.; Mauermann, H.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8111–8118.
(21) Fagan, P. J.; Manriquez, J. M.; Maatta, E. A.; Seyam, A. M.; Marks, T. J. *J. Am. Chem. Soc.* **1981**, *103*, 6650–6667.
(22) Stubbert, B. D.; Stern, C. L.; Marks, T. J. *Organometallics* **2003**, *22*, 4836–4838.
(23) Schnabel, R. C.; Scott, B. L.; Smith, W. H.; Burns, C. J. *J. Organomet. Chem.* **1999**, 14–23.
(24) (a) Silveira, C. C.; Santos, P. C. S.; Mendes, S. R.; Braga, A. L. *J. Organomet. Chem.* **2008**, 3787–3790. (b) Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, L. *Synthesis* **1987**, 1034–1036.
(25) (a) Ansyln, E. V.; Dougherty, D. A. *Modern Physical Organic Chemistry*; University Science Books: Sausalito, CA, 2006. (b) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw-Hill: New York, 1995. (c) Pilling, M. J.; Seakins, P. W. *Reaction Kinetics*; Oxford University Press: New York, 1995.
(26) Similar attempts with stirring show drastically reduced conversion, possibly the result of accelerated catalyst aggregation.

Table 2. Effects of Organolanthanide Ionic Radius on Catalyst Stability and Hydrothiolation Activity for the Hydrothiolation of 1-Hexyne by 1-Pentanethiol

entry	precatalyst complex	ionic radius (Å)[32b]	precipitation delay (h)[a]	N_t (h^{-1})
1	$Cp^*_2LaCH(TMS)_2$ (**4**)	1.160	0.1	—[b]
2	$Cp^*_2SmCH(TMS)_2$ (**5**)	1.079	0.5−6	0.6
3	$Cp^*_2LuCH(TMS)_2$ (**6**)	0.977	> 30	0.03

[a] Time in a sealed tube at 120 °C in benzene-d_6 until precipitate is observed. [b] Unable to measure N_t due to rapid precipitate formation.

with 20 mL of hexanes. The volatiles were then removed under vacuum (10^{-3} mTorr) to yield 97% Markovnikov-pure **15** as a yellow oil (0.22 g, 1.1 mmol, 41% yield). In addition to vinyl sulfide products, 4 mol % alkyne dimer[27] (2-butyloct-1-en-3-yne)[28] is observed.

Results

The principal goal of this study is to examine the scope and selectivity of lanthanide- and actinide-mediated alkyne hydrothiolation and to define the sequence of steps by which these transformations occur. We first report on lanthanide-mediated hydrothiolation processes (e.g., Figure 1) with information on catalyst stability along with substrate scope and selectivity. This is followed by kinetic and mechanistic experiments to elucidate the hydrothiolation pathway and the source of the observed selectivity. Additional actinide results are then presented to gain further insight beyond the previously communicated data.[6e] We conclude with mechanistic discussions: we first compare and contrast lanthanide and actinide catalytic phenomenology and then discuss in what ways these relate to analogous, organozirconium-mediated alkyne hydrothiolation.[6a]

Catalyst Structure and Stability. Upon addition of 20-fold excess RSH (R = pentyl, phenyl, or *tert*-butyl) to $Ln[N(TMS)_2]_3$ complexes (Ln = La (**1**), Nd (**2**), Y (**3**)) in benzene-d_6, a precipitate is immediately observed,[29] similar to those reported in the literature[8k,10d,10e,15d] as resulting from insoluble, oligomeric lanthanide−thiolate complexes.[10e,15b−15e,30] Despite $Ln[N(TMS)_2]_3$ precipitation with excess thiol, trace hydrothiolation activity is nevertheless observed.[31] Literature reports indicate that using sterically hindered thiols[10e,15c] avoids precipitation at lower temperatures; however, we find that bulky thiols delay but do not eliminate precipitate formation under typical hydrothiolation conditions. In an attempt to avoid catalyst precipitation, coordinating solvents[10e,15d] such as THF-d_8 and pyridine-d_5 were also examined; however precipitation and/or low hydrothiolation activity was observed.

Sterically encumbered $Cp^*_2LnCH(TMS)_2$ ($Cp^* = Me_5C_5$, Ln = La (**4**), Sm (**5**), Lu (**6**)) complexes were chosen for the present lanthanide study because of their partial resistance to precipitation in excess thiol at high temperatures. Interestingly, catalyst stability scales inversely with lanthanide ionic radius,[10a,32] with **4** forming a precipitate after heating at 120 °C for 0.1 h, **5** forming an observable precipitate only after 0.5−6 h at 120 °C, and **6** affording only minor precipitation after > 30 h at 120 °C (Table 2). Note that while the Lu species are noticeably more stable than those of Sm and La, they are found to be 20× less active than Sm in catalyzing hydrothiolation under the same reaction conditions.[33] Therefore, complex **5** was chosen for the present lanthanide study, offering a balance between catalytic activity and reasonable stability under hydrothiolation conditions.

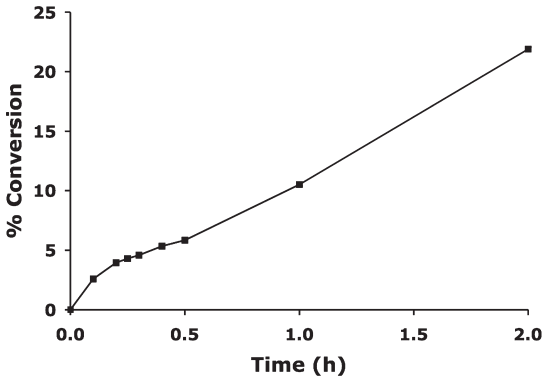


Figure 2. Conversion (%) as a function of time in the hydrothiolation of 1-hexyne by 1-pentanethiol and 5 mol % $Cp^*_2SmCH(TMS)_2$ (**5**) with 17× molar excess alkyne over thiol. Conversion is based on thiol, and the lines are a guide to the eye.

The addition of > 20-fold excess 1-pentanethiol and 1-hexyne to $Cp^*_2SmCH(TMS)_2$ (**5**) in benzene-d_6 results in quantitative formation of $H_2C(TMS)_2$,[34] and approximately 40−60% of the Cp* ligands are rapidly cleaved protonolytically from the metal center at room temperature, on the basis of integration of the free Cp*H signals by ^{1}H NMR spectroscopy. Upon heating in a 120 °C bath, further ligand protonolysis is gradually observed, often culminating in observable precipitate formation after the majority of the Cp* ligands have been detached. Examination of the catalytic reaction progress at 120 °C reveals interesting trends (Figure 2). During the first 0−6 min of reaction, an initial surge in turnover is observed, followed by a stable period of reduced activity. After approximately 0.5 h, a slight increase in activity occurs, typically followed by observable catalyst precipitation. Upon precipitate formation, the hydrothiolation activity falls dramatically. Interestingly, examination of analogous hydrothiolation with $Cp^*_2LuCH(TMS)_2$ (**6**) reveals the same rapid cleavage of half the Cp* ligands from the metal, but in contrast to $Cp^*_2SmCH(TMS)_2$ (**5**), the second ring protonolysis requires > 30 h.[35] The selection and concentration of alkyne used under hydrothiolation conditions also have a significant effect on catalyst stability. In examining a range of alkynes having different steric

(27) Alkyne dimers are not observed in NMR-scale reactions. The presence of the small quantities of dimer early in the preparative scale likely results from **5**-mediated dimerization of 1-hexyne before the benzylmercaptan thaws.

(28) Komeyama, K.; Sasayama, D.; Kawabata, T.; Takehira, K.; Takaki, K. *J. Org. Chem.* **2005**, *70*, 10679–10687.

(29) Precipitate colors vary as a function of lanthanide. See Supporting Information.

(30) (a) Zhang, L.-X.; Zhou, X.-G.; Huang, Z.-E.; Cai, R.-F.; Huang, X.-Y. *Polyhedron* **1999**, *18*, 1533–1537. (b) Mashima, K.; Nakayama, Y.; Shibahara, T.; Fukumoto, H.; Nakamura, A. *Inorg. Chem.* **1996**, *35*, 93–99.

(31) It is unclear if this Markovnikov hydrothiolation activity is the result of the heterogeneous species exhibiting hydrothiolation activity or if it results from traces of homogeneous catalyst still remaining in solution.

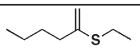
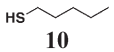
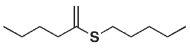
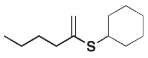
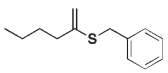
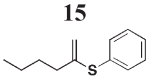
(32) (a) Evans, W. J. *Inorg. Chem.* **2007**, *46*, 3435–3449. (b) Shannon, R. D. *Acta Crystallogr.* **1976**, *A32*, 751–767.

(33) The turnover frequency for complex **1** was unobtainable due to heavy precipitate formation immediately after addition of excess thiol.

(34) The bis(trimethylsilyl)methane 1H resonances appear at δ 0.05 and −0.37 ppm in benzene-d_6.

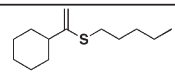
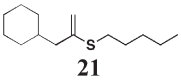
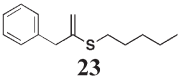
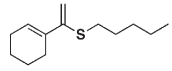
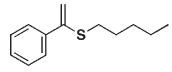
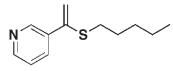
(35) No NMR data on ring cleavage rates for complex **4** were obtainable due to large quantities of precipitation in the NMR tube.

Table 3. $Cp^*_2SmCH(TMS)_2$ (5)-Mediated Intermolecular Hydrothiolation of 1-Hexyne (7)

Entry	Thiol	Product	Selectivity(%)[a]	Conversion(%)[b]
1.	 **8**	 **9**	>99	≥95
2.	 **10**	 **11**	>99	55
3.	 **12**	 **13**	90	11
4.	 **14**	 **15**	>99	92
5.	 **16**	 **17**	91	48

[a] Markovnikov selectivity determined by ^{1}H NMR and GC/MS after 16.0 h at 120 °C with 5 mol % $Cp^*_2SmCH(TMS)_2$ (**5**) and a 3× molar excess of alkyne. [b] Conversions of Markovnikov product determined by ^{1}H NMR with respect to an internal integration standard and are reported with respect to thiol.

Table 4. Catalytic $Cp^*_2SmCH(TMS)_2$ (5)-Mediated Intermolecular Alkyne Hydrothiolation by 1-Pentanethiol (10) as a Function of Alkyne

Entry	Alkyne	Product	Selectivity(%)[a]	Conversion(%)[b]
1.	 **18**	 **19**	88	26
2.	 **20**	 **21**	95	20
3.	 **22**	 **23**	72	55
4.	 **24**	 **25**	40 (77)[c]	48 (56)[c]
5.	 **26**	 **27**	32 (95)[c]	33 (39)[c]
6.	 **28**	 **29**	74	37

[a] Markovnikov selectivity determined by ^{1}H NMR and GC/MS after 16.0 h at 120 °C with 5 mol % $Cp^*_2SmCH(TMS)_2$ (**5**) and a 3× molar excess of alkyne. [b] Conversion of Markovnikov product determined by ^{1}H NMR with respect to an internal integration standard and reported with respect to thiol. [c] Performed with γ-terpinene as a radical inhibitor in a 1:1 molar ratio to alkyne.

characteristics (see below), precipitation was observed more rapidly with α-monosubstituted alkynes and phenylacetylene than with other α-disubstituted alkynes.[36] Additionally, large excesses of alkyne are found to delay precipitate formation.

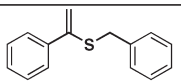
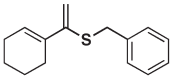
Selectivity and Conversion. To examine substrate scope, a diverse selection of thiols and alkynes with a range of electronic and steric characteristics was examined for conversion and Markovnikov selectivity.[37] Large effects are observed on varying both the steric and electronic characteristics of the thiol. In switching from ethanethiol to 1-pentanethiol (Table 3, entry 1 vs 2), an almost 2× decrease in conversion is observed, while cyclohexylmercaptan (Table 3, entry 3) suffers an even more dramatic fall in conversion. Interestingly, both benzylmercaptan and thiophenol (Table 3, entries 4 and 5) exhibit moderate to high conversions, despite the significant steric encumbrances. In spite of the large variations in conversion, good to excellent selectivities are observed for all thiols examined with 1-hexyne. While all aforementioned hydrothiolation reactions are >90% Markovnikov selective, somewhat lower selectivities are observed with cyclohexylmercaptan and thiophenol.

On varying the alkyne electronic and steric characteristics, dramatic differences in both hydrothiolation selectivity

(36) Images of the resulting precipitates are provided in the Supporting Information.

(37) Unfortunately, due to rapid catalyst precipitation, turnover frequencies could not be accurately measured for most thiols and alkynes, preventing quantitative comparison of substrate hydrothiolation activity.

Table 5. Catalytic $Cp^*_2SmCH(TMS)_2$ (5)-Mediated Intermolecular Alkyne Hydrothiolation by Benzylmercaptan (15)

Entry	Alkyne	Product	Selectivity(%)[a]	Conversion(%)[b]
1.	 **26**	 **30**	76	61
2.	 **24**	 **31**	46	40

[a] Markovnikov selectivity determined by ^{1}H NMR and GC/MS after 16.0 h at 120 °C with 5 mol % $Cp^*_2SmCH(TMS)_2$ (**5**) and a 3× molar excess of alkyne. [b] Conversion of Markovnikov product determined by ^{1}H NMR with respect to an internal integration standard and reported with respect to thiol.

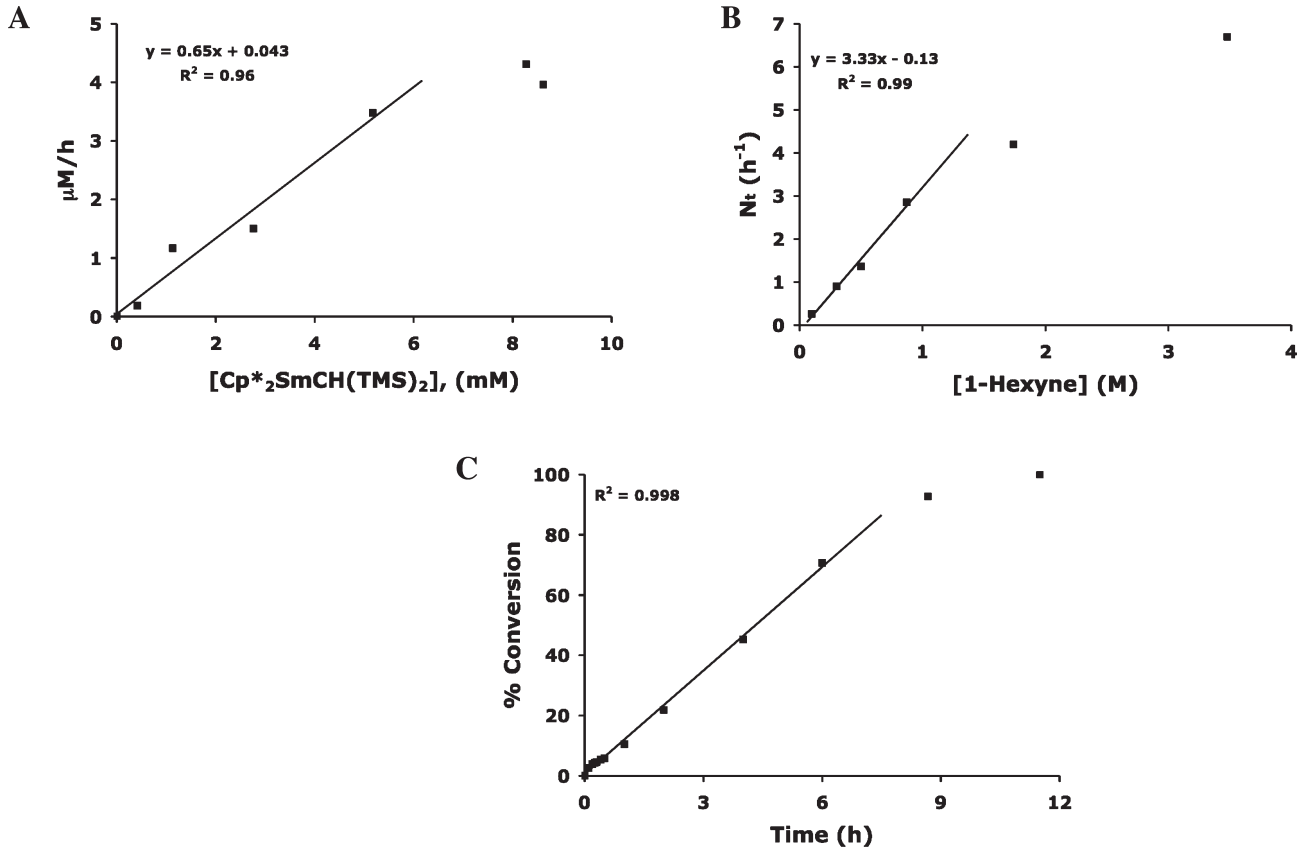


Figure 3. Plot of product formation rate for the reaction **7** + **10** → **11** as a function of [$Cp^*_2SmCH(TMS)_2$ (**5**)] (A) and [1-hexyne (**7**)] (B) with [1-pentanethiol (**10**)] and [1-hexyne (**7**)] = 0.2 M unless otherwise indicated. Plot of hydrothiolation conversion (%) versus time with 17× molar excess 1-hexyne (**7**) over 1-penthanethiol (**10**) exhibits a linear trend (C),[42] indicating a pseudo-zero-order reaction, demonstrating rate independence with respect to [1-penthanethiol (**10**)] except at the highest concentrations, where catalyst precipitation becomes extensive. The lines in plots in panels A, B, and C are least-squares fits.

and conversion are observed. While cyclohexylacetylene (Table 4, entry 1) still affords high selectivity, it yields ca. half the conversion observed for less encumbered 1-hexyne (Table 3, entry 2). Moving the steric bulk from the α- to the β-position gives comparable conversion and only moderately improved selectivity. Introducing aromaticity α and β to the alkyne fragment results in slight to moderately increased conversion efficiency but dramatically depresses the Markovnikov selectivity. The hydrothiolation activity and selectivity of 1-ethynylcylclohexene and phenylacetylene are both rather low. Interestingly, while 3-ethynylpyridine exhibits over 2× the selectivity of phenylacetylene (Table 4, entry 5 vs 6), the conversion is still low.[38]

Adding γ-terpinene as a radical inhibitor[6a,e,l−n] in a 1:1 molar ratio with alkyne effects large decreases in the yields of anti-Markovnikov products for both 1-ethynylcyclohexene and phenylacetylene (Table 5, entries 4 and 5). While this radical inhibitor results in high Markovnikov selectivity for phenylacetylene hydrothiolation, only moderate selectivity is observed in the hydrothiolation of 1-ethynylcyclohexene. Additional catalytic experiments with benzylmercaptan

(38) Additional internal alkyne and terminal α-trisubstituted alkynes were surveyed and displayed little or no activity.

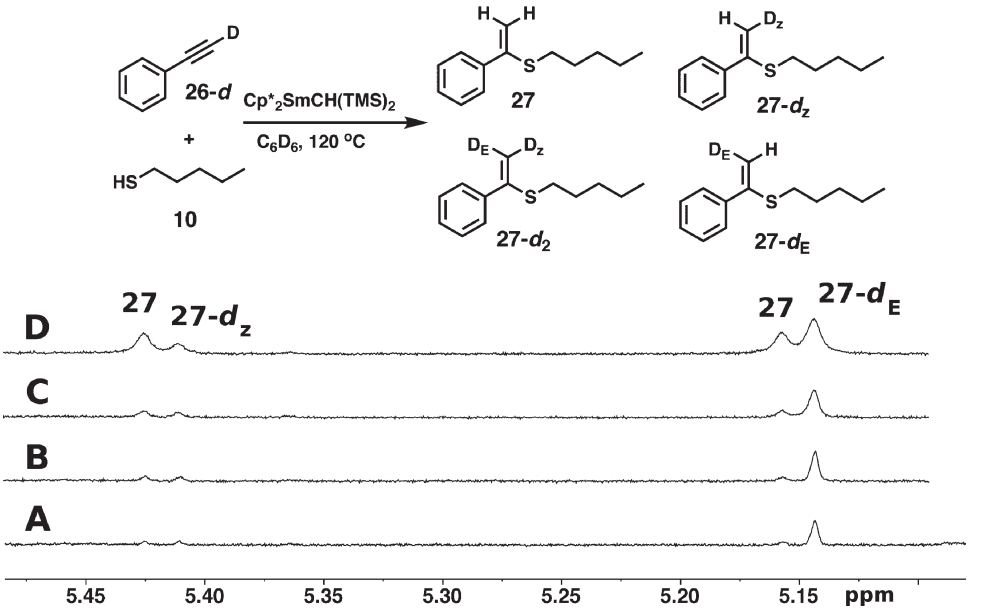


Figure 4. The 2 mol % $Cp^*_2SmCH(TMS)_2$ (**5**)-mediated hydrothiolation of phenylacetylene-*d* (**26-*d***) with 1-penthanethiol (**10**) gives a mixture of Markovnikov product isotopomers. After 0.2 h at 120 °C in benzene-d_6, primarily **27-d_E** is observed. Additional heating for 0.4 h (B), 0.75 h (C), and 2.0 h (D) reveals increasing ratios of **27** and **27-d_Z** products to **27-d_E**. Signal intensities are normalized to an internal integration standard.

(Table 5) reveal increased yields and selectivities versus 1-penthanethiol (Table 3), despite the lower pK_a of benzylmercaptan.[6m,39] Regrettably, selectivity and conversion are not as high as those observed in the hydrothiolation of 1-hexyne by benzylmercaptan (Table 3, entry 4).

Kinetics of Organosamarium- and Organothorium-Mediated Intermolecular Alkyne Hydrothiolation. To develop a better understanding of the reaction pathway, kinetic experiments were performed to understand the effect catalyst and reactant concentrations have on hydrothiolation turnover. Experiments were conducted on the $Cp^*_2SmCH(TMS)_2$ (**5**)-mediated hydrothiolation of 1-hexyne (**7**) by 1-penthanethiol (**10**) in benzene-d_6 at 120 °C. The empirical rate law is derived by examining the turnover frequency (N_t) while systematically varying [catalyst], [alkyne], and [thiol]. By examining [$Cp^*_2SmCH(TMS)_2$] from 0.4 to 8.6 mM, a linear trend is observed for concentrations in the 0.4−5.2 mM range (Figure 3A), indicating a first-order dependence on [catalyst] at lower concentrations,[40] while a fall in activity is observed at higher concentrations. Attempts to explore the reaction at even higher [$Cp^*_2SmCH(TMS)_2$] values, 9−17 mM, resulted in reduced activity and rapid catalyst precipitation from solution. An investigation of the effects of increasing [1-hexyne] from 0.1 to 3.5 M reveals a linear correlation with activity over the [1-hexyne (**7**)] range, 0.1−0.9 M (Figure 3B), indicating initial first-order dependence on [alkyne]. On increasing the alkyne concentration further, a slight reduction in activity is observed, which may be the result of partial alkyne saturation of the metal center and/or alkyne acting as a hydrothiolation inhibitor. Finally, the dependence of N_t on [1-penthanethiol] from 0.01 to 0.2 M at fixed 1-hexyne concentration (i.e., 3.5 M) to force the reaction to pseudo-zero-order[6e,41] shows the reaction to be zero-order with respect to [thiol] (Figure 3C). The fall in rate near the end of the reaction corresponds to the onset of observable catalyst precipitation (Figure 3C). Therefore, the empirical rate law, under standard catalytic conditions with minimal catalyst precipitation, is given by eq 7.

$$\text{rate} = k_{obs}[\text{Sm}]^1[\text{alkyne}]^1[\text{thiol}]^0 \qquad (7)$$

To trace the fate of the PhCC-D (**26-*d***) hydrogens during $Cp^*_2SmCH(TMS)_2$ (**5**)- and $Me_2SiCp''Th(CH_2TMS)_2$ (**32**)-mediated hydrothiolation, deuterium-labeling studies were performed using deuterated phenylacetylene (**26-*d***) and 1-penthanethiol (**10**). Exclusive observation of $H_2C(TMS)_2$ in the ^1H and ^2H NMR evidence thiol-mediated protonolytic activation of the catalyst.[43] By comparing the activity with that of nondeuterated phenylacetylene, apparent KIEs of $k_H/k_D = 1.40(0.1)$ and 1.35(0.1) are observed for catalysts **5** and **32**, respectively. At early reaction times, a single product isotopomer is primarily observed (Figure 4A). However, upon further heating, other known isotopomeric products are observed (Figure 4B−D), along with substantial loss of the phenylacetylene deuterium label. On the basis of ^1H and ^2H NMR spectroscopy, deuterium is observed to scramble from the alkyne terminus to the thiol functionality, as evidenced by a prominent RSD resonance in the ^2H NMR. To determine if the migration is the result of the catalytic cycle, *tert*-butylmercaptan (**33**), phenylacetylene-*d* (**26-*d***), and either complex **5** or **32** were heated in benzene-d_6 at

(39) (a) Bordwell, F. G.; Zhang, X.-M.; Satish, A. V.; Cheng, J. P. *J. Am. Chem. Soc.* **1994**, *116*, 6605–6610. (b) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463. (c) Janousek, B. K.; Reed, K. J.; Brauman, J. I. *J. Am. Chem. Soc.* **1980**, *102*, 3125–3129. (d) Danehy, J. P.; Noel, C. J. *J. Am. Chem. Soc.* **1960**, *82*, 2511–2515. (e) Kreevoy, M. M.; Harper, E. T.; Duvall, R. E.; Wilgus, H. S.; Ditsch, L. T. *J. Am. Chem. Soc.* **1960**, *82*, 4899–4902.

(40) A plot of ln(rate) vs ln([catalyst]) does not give a linear trend, furthur demonstrating that the hydrothiolation reaction is not second-order with respect to [catalyst].

(41) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw-Hill, Inc.: New York, 1995.

(42) Large excesses of alkyne are found to delay precipitate formation.

(43) Because no $DHC(TMS)_2$ is observed, it can be estimated that thiol-mediated protonolysis is >50× faster than analogous alkyne-mediated protonolysis.

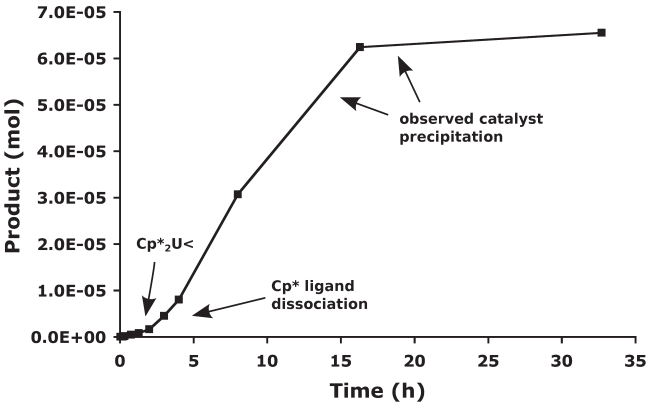


Figure 5. Hydrothiolation of 1-hexyne (**7**) with 1-pentanethiol (**10**) catalyzed by 6 mol % $Cp^*_2U(CH_2TMS)_2$ (**34**) in benzene-d_6 at 120 °C.

120 °C for 0.75 h. Proton NMR integration indicates that 15−30% of the deuterium migrates from the alkyne during this time period despite the fact that no measurable hydrothiolation product is observed.[44] A control experiment without the addition of catalyst results in no detectable deuterium scrambling.[6a]

Organoactinide-Mediated Alkyne Hydrothiolation. The efficacy of $Me_2SiCp''_2Th(CH_2TMS)_2$ (**32**) in alkyne hydrothiolation raises the question of how other Cp-based actinide complexes might perform. In investigating $Cp^*_2U(CH_2TMS)_2$ (**34**)-mediated hydrothiolation, an interesting pattern is observed (Figure 5). During the initial 2 h of turnover, product is formed at a constant rate. After another approximately 2 h, a gradual increase in activity is observed, correlating with the observation of free Cp*H by ^{1}H NMR. After approximately 15 h of reaction, the activity falls dramatically as an observable precipitate is formed. Similar trends are observed with organoactinide complexes **32**, **35**, and **36**.[45]

In examining the importance of organoactinide complex ionic radius[32b] and ligation geometry on hydrothiolation activity,[46] significant effects of steric constraints around the metal center on hydrothiolation activity are observed. Changing the ancillary ligation from Cp^*_2 to $Me_2SiCp''_2$ and the metal ion size from U(IV) to Th(IV) results in a substantial opening of the coordination sphere.[46,47] As steric encumbrance is decreased, hydrothiolation turnover frequency increases (Figure 6). To examine the efficacy of $Cp^*_2Th(CH_2TMS)_2$ (**35**)-mediated hydrothiolation, selectivity and conversion were examined for several thiol + alkyne combinations. While the hydrothiolation of cyclohexylacetylene by 1-pentanethiol (Table 6, entry 1) results in good selectivity, the conversion is relatively low. Similarly, good selectivity is observed in the hydrothiolation of 1-hexyne by benzylmercaptan (Table 6, entry 2), but low conversion is again achieved. Finally, phenylacetylene and thiophenol (Table 6, entry 3) afford both low selectivity and conversion, but the addition of a radical inhibitor substantially increases both selectivity and conversion.

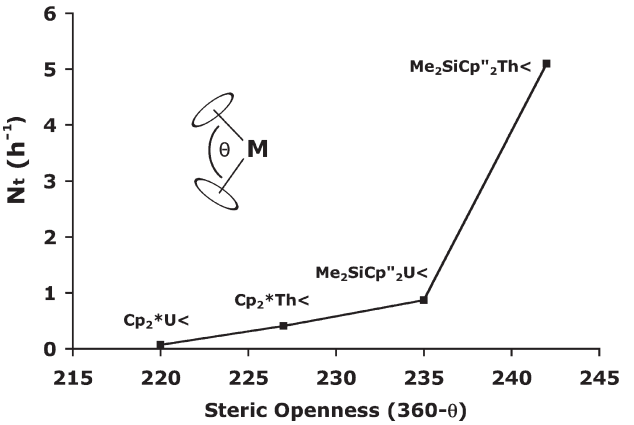


Figure 6. Steric openness[46,47] effects on $Cp^*_2U(CH_2TMS)_2$ (**34**)-, $Cp^*_2Th(CH_2TMS)_2$ (**35**)-, $Me_2SiCp''_2U(Bn)_2$ (Bn = benzyl, **36**)-, and $Me_2SiCp''_2Th(CH_2TMS)_2$ (**32**)-mediated hydrothiolation of 1-hexyne (**7**) by 1-pentanethiol (**10**) in benzene-d_6 at 120 °C.[48]

Discussion

Ancillary Ligand and Metal Effects on Catalyst Stability. Ancillary ligand selection has major consequences for the stability of organolanthanide and organoactinide[6e] complexes in hydrothiolation catalysis. While the addition of excess thiol to $Ln[N(TMS)_2]_3$ precatalysts results in immediate precipitation,[10e] cyclopentadienyl (Cp)-based ligation delays precipitation. This is similar to observations in analogous organozirconium-mediated alkyne hydrothiolation[6a] where $Zr[NMe_2]_4$ undergoes precipitation soon after addition of excess thiol, whereas no precipitate is observed with organozirconium Cp* and CGC (CGC = $Me_2SiCp''NCMe_3$, $Cp'' = C_5Me_4$) complexes. The nonbonded repulsions of the Cp-based ligands likely suppress the formation of insoluble, highly aggregated species.[6e] Likewise, the Cp* and $Me_2SiCp''_2$ ligands must similarly delay the formation of previously reported, insoluble lanthanide[10e,15b−15e] and actinide[49] thiolate aggregates. Nevertheless, at higher $Cp^*_2SmCH(TMS)_2$ concentrations, precipitate formation occurs more rapidly, consistent with a catalyst aggregation model.

In contrast to the behavior of the zirconium Cp*, Cp^*_2, and CGC complexes,[50] addition of excess thiol (typically 20−40× excess) to the present organolanthanide and organoactinide complexes results in immediate to gradual catalyst precipitation. Due to the highly polar nature of f-element−ligand bonding,[51]

(44) The ^{2}H NMR spectrum after further heating shows that the deuterium is migrating to the ^{t}BuSH resonance (1.6 ppm).

(45) Cp ring cleavage for both $Cp^*_2An<$ and $Me_2SiCp''_2An<$ complexes is observed occurring at approximately the same rate. Meanwhile, a comparison of Cp* ring cleavage from complexes **34** and **35** evidences ring cleavage from U at approximately 1/4 the rate observed for Th.

(46) Stubbert, B. D.; Marks, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 4253–4271.

(47) Stubbert, B. D.; Marks, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 6149–6167.

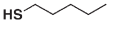
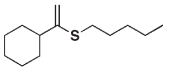
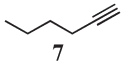
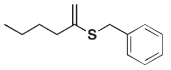
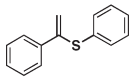
(48) Rate measured as beginning of reaction before signifigant ligand protonolysis.

(49) Roger, M.; Barros, N.; Arliguie, T.; Thuéry, P.; Maron, L.; Ephritikhine, M. *J. Am. Chem. Soc.* **2006**, *128*, 8790–8802.

(50) Cp-based zirconium complexes are not observed to form insoluable aggregates except at extremely high thiol concentrations, exceeding 1 M, and after extended heating. Despite the observed aggregation, no ligand cleavage is observed.

(51) (a) Krogh-Jespersen, K.; Romanelli, M. D.; Melman, J. H.; Emge, T. J.; Brennan, J. G. *Inorg. Chem.* **2009**, *49*, 552–560. (b) Ingram, K. I. M.; Tassell, M. J.; Gaunt, A. J.; Kaltsoyannis, N. *Inorg. Chem.* **2008**, *47*, 7824–7833. (c) Liu, G. K.; Jensen, M. P.; Almond, P. M. *J. Phys. Chem. A* **2006**, *110*, 2081–2088. (d) Guillaumont, D. *J. Phys. Chem.* **2004**, *108*, 6893–6900. (e) Strittmatter, R. J.; Bursten, B. E. *J. Am. Chem. Soc.* **1991**, *113*, 552–559. (f) Nugent, L. J.; Laubereau, P. G.; Werner, G. K.; Vander Sluis, K. L. *J. Organomet. Chem.* **1971**, *27*, 365–372.

Table 6. $Cp^*_2Th(CH_2TMS)_2$-Mediated Intermolecular Alkyne Hydrothiolation of 1-Hexyne by 1-Pentanethiol

Entry	Thiol	Alkyne	Product	Selectivity (%)[a]	Conversion (%)[b]
1.	 **18**	 **10**	 **19**	94	32
2.	 **7**	 **14**	 **15**	90	43
3.	 **26**	 **16**	 **37**	30 (83)[c]	26 (61)[c]

[a] Markovnikov selectivity determined by ^{1}H NMR and GC/MS after 16.0 h in benzene-d_6 at 120 °C with 5 mol % $Cp^*_2Th(CH_2TMS)_2$ and a 3× molar excess of alkyne. [b] Conversion of Markovnikov product determined by ^{1}H NMR with respect to an internal integration standard and reported with respect to thiol. [c] Performed with γ-terpinene as a radical inhibitor in a 1:1 molar ratio to alkyne.

Table 7. Charge and Ionic Radius of Lanthanides, Actinides, and Zirconium[32b]

metal	charge	radius (Å)[a]
La	3+	1.160
Nd	3+	1.109
Th	4+	1.09
Sm	3+	1.079
U	4+	1.05
Y	3+	1.019
Lu	3+	0.977
Zr	4+	0.890

[a] Ionic radius reported for octacoordinate, trivalent lanthanides and nonacoordinate, tetravalent actinides and zirconium.

thiol-mediated Cp* and $Me_2SiCp''_2$ protonolysis occurs rapidly, leaving the metal centers open to aggregation into insoluble, presumably μ-SR species. Greater covalency in actinide versus lanthanide bonding[51d,e] undoubtedly is a factor in the greater resistance of the $Cp^*_2An<$ versus Cp^*_2Ln- complexes to ring cleavage. Consistent with literature reports on related processes,[10e] metal ionic radius[10a,32] also exerts a large influence on catalyst thiolytic stability, with smaller ions exhibiting greater resistance to precipitation despite similar susceptibility to the first Cp* ligand cleavage. This is presumably a result of smaller, more sterically congested coordination spheres resulting in less favorable aggregation and slower protonolysis of the second Cp* ligand. The organoactinide complexes $Cp^*_2Th[CH_2(TMS)]_2$ and $Cp^*_2U[CH_2(TMS)]_2$ exhibit greater protonolytic stability versus $Cp^*_2SmCH(TMS)_2$, even after initial ligand cleavage, likely for similar reasons of metal size and greater charge/radius ratio.

Monitoring the reaction progress for the organolanthanide- and organoactinide-mediated hydrothiolation of 1-hexyne (**7**) by 1-pentanethiol (**10**) reveals interesting reactivity trends with regard to catalyst structure. An initial surge of activity is often observed both at room temperature and at 120 °C with the Sm and Lu catalysts, possibly the result of transitory, less aggregated, catalytic species, whereas no initial phase of heightened activity is observed with the aforementioned organoactinide complexes, likely reflecting the bulky ligation. Upon further heating, regions of invariant rate are observed, with both types of catalyst displaying periods of no obvious change in catalyst structure. Subsequent increases in activity correlate with observed ligand cleavage products, further supporting the hypothesis that reduction in coordination sphere nonbonding repulsions accelerates alkyne hydrothiolation activity. Subsequent declines in activity can be correlated with visible catalyst precipitation and are accompanied by significantly reduced hydrothiolation activity for any aggregated, heterogeneous species.

Ancillary Ligand and Metal Effects on Catalytic Activity. Metal and ancillary ligation exert a pronounced influence on hydrothiolation activity, with decreased nonbonding interactions around the metal invariably enhancing the hydrothiolation activity. In increasing the ionic radius from Lu to Sm (Table 7), a 20-fold increase in initial activity is observed (Table 2, entries 2 and 3), similar to trends observed in analogous lanthanide-mediated alkyne hydroalkoyxlation.[13i,m] A comparison of U and Th (1.05 and 1.09 Å, respectively) catalysts evidences an almost 6× increase in hydrothiolation rate (Figure 6)

In constraining the organoactinide ancillary ligands from Cp^*_2 to $Me_2SiCp''_2$, the opening of the coordination sphere results in a >12× increase in activity (Figure 6), similar to that observed in organoactinide-mediated hydroamination.[46,47] Furthermore, as the cyclopentadienyl ligands in Cp^*_2Sm-, $Cp^*_2An<$, and $Me_2SiCp''_2An<$ (An = U and Th) are removed by protonolysis, an increase in hydrothiolation rate is observed, prior to catalyst precipitation (Figure 5). As a result, the steric properties of the catalytically active species are the dominant factor in dictating the hydrothiolation activity of homogeneous lanthanide and actinide catalysts.

Substrate Scope and Conversion for Intermolecular Alkyne Hydrothiolation. Both the electronic and steric characteristics of the thiol substrates are found to exert a significant influence on hydrothiolation conversion rates, with steric factors exerting a greater influence than electronic factors. The results of organosamarium-mediated hydrothiolation of 1-hexyne (Table 3) indicate that thiol nonbonding repulsions dramatically influence catalytic turnover. This is consistent with turnover frequencies observed in organothorium-mediated[13b] and organozirconium-mediated[6a] alkyne hydrothiolation where the activity dependence on thiol encumbrance is attributed to thiolate ligation. Despite the increased nonbonded repulsions imposed by thiophenol (**16**) and benzylmercaptan (**14**) versus 1-pentanethiol (**10**), moderate-to-high conversions are observed, arguing for a thiol electronic

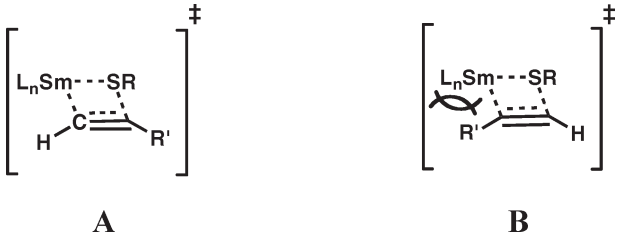


Figure 7. Insertive transition state for the formation of Markovnikov (A) and anti-Markovnikov (B) hydrothiolation products.

effect on hydrothiolation activity. The high activity of benzylmercaptan (**14**), despite the moderate steric encumbrances, indicates an optimization of both steric and electronic factors.

On varying alkyne substituents, both electronic and steric factors are found to influence catalytic activity. Similar to organozirconium-mediated alkyne hydrothiolation,[6a] aliphatic, α-disubstituted alkynes appear to exhibit moderately lower hydrothiolation activity versus similar α-monosubstituted alkynes. In switching to a β-disubstituted alkyne, a similar low conversion is observed. The addition of aromaticity to either the α- or β-position increases the conversion, suggesting electronic effects or possible preorganization effects. While this may stem from a change in the alkyne electronic character, it could also result from the slight reduction in steric encumbrance in phenyl versus cyclohexyl.

Regioselectivity of Intermolecular Terminal Alkyne Hydrothiolation. The observed quantities of anti-Markovnikov hydrothiolation products provide evidence for a known, free radical pathway[5b−f] in kinetic competition with the catalytic pathway. While most thiols afford excellent Markovnikov selectivities, the samarium-mediated hydrothiolations of 1-hexyne (**7**), cyclohexylmercaptan (**12**), and thiophenol (**16**) yield non-negligible quantities of anti-Markovnikov products. While the lower selectivities of the secondary thiols might suggest that nonbonded repulsive effects in the insertive transition state (Scheme 1) could afford anti-Markovnikov products, the congested metal center coordination sphere (Figure 7B) suggests that this is unlikely. More probable is the intrusion of a previously reported, free radical side reaction[5b−f,6a,52,53] in kinetic competition with the metal-centered catalytic pathway. The low conversion/activity using cyclohexylmercaptan (**12**) is consistent with the analogous organothorium-[13b] and organozirconium-mediated hydrothiolation results.[6a] This result argues that the lower Markovnikov selectivity results from the low catalytic activity of cyclohexylmercaptan (**12**) in competition with the free radical process. While thiophenol (**16**) gives moderate conversion to Markovnikov product, a mixture of anti-Markovnikov products is still observed in both the Sm- and Th-mediated hydrothiolation reactions. This likely reflects the weaker RS−H bond[39a,c] more effectively initiating the radical side reactions (eq 8). Variations in hydrothiolation selectivity are also observed as a function of the alkyne substituent, with aryl and nonconjugated substituents affording lower Markovnikov selectivity. These lower selectivities likely arise from an enhanced ability to stabilize free radicals (eqs 9 and 10) via

(52) Silva, M. S.; Lara, R. G.; Marczewski, J. M.; Jacob, R. G.; Lenardão, E. J.; Perin, G. *Tetrahedron Lett.* **2008**, *49*, 1927–1930.

(53) Control experiments performed without catalyst evidence the formation of free radical-derived anti-Markonikov products under reaction conditions presented in this study.

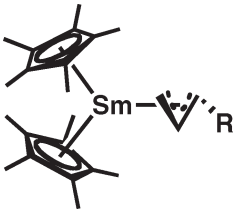


Figure 8. Structure of known Cp^*_2Sm−allyl complexes.[55]

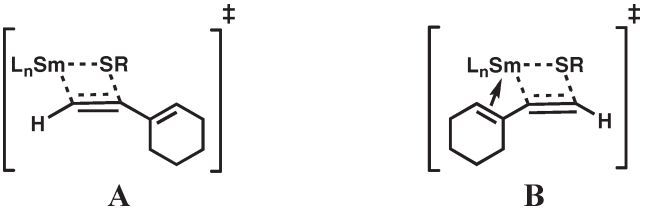
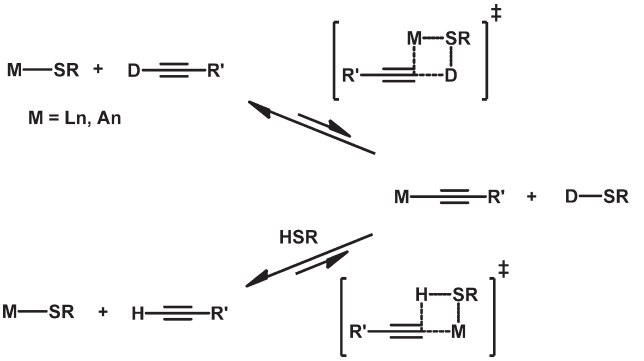
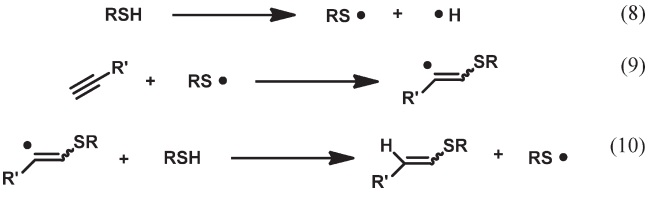


Figure 9. Proposed insertive transition state for the formation of Markovnikov product (A) and a possible, competing transition state for the formation of anti-Markovnikov product (B) with 1-ethynylcyclohexene (**24**).

Scheme 2. Proposed Pathway for the Scrambling of Deuterium between Terminal Alkynes and Thiols



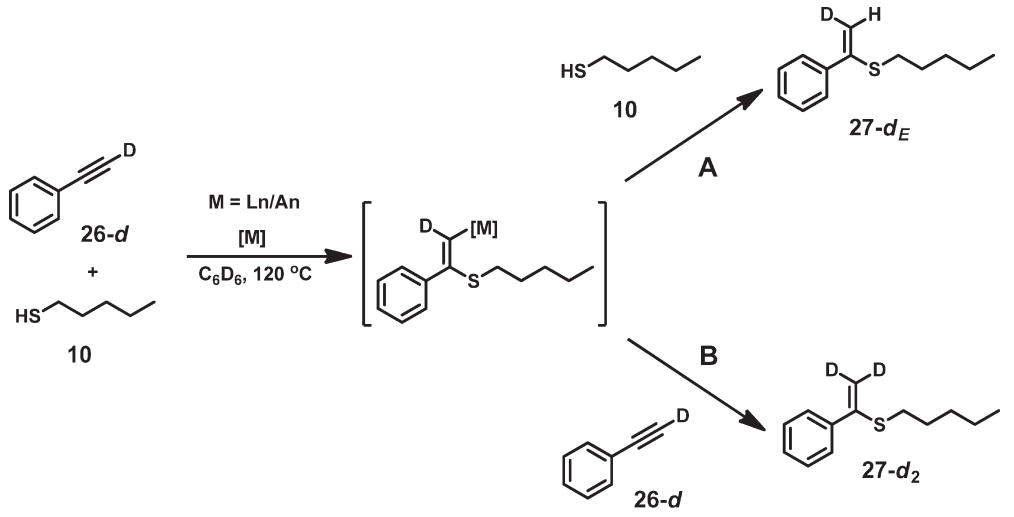
delocalization of the radical through conjugation with the vinyl sulfide.



Further support for the contention that the anti-Markovnikov side product is not primarily the result of a metal-catalyzed process but rather arises from a known radical pathway comes from the effects of radical inhibitors. On introducing γ-terpinene as a radical inhibitor,[54] the yield of anti-Markovnikov products is substantially suppressed, by 3−14×. Despite this modification, the 1-ethynylcyclohexene hydrothiolation (Table 5, entry 4) yields only moderate selectivity, suggesting the possibility that the low selectivity may also reflect the intrinsic selectivity of the catalytic reaction. The deep purple color (see Supporting Information) of the reaction mixture suggests an extended π-interaction: a possible interaction between 1-ethynylcyclohexene (**24**) and

(54) The radical inhibitor is added in a 1:1 molar ratio with alkyne.

Scheme 3. Thiol (A) and Alkyne (B) Protolytic/Deuterolytic Pathways for the Formation of Product Isotopomers



the Sm center similar to that observed in Cp^*_2Sm−allyl complexes (Figure 8).[55] While a favorable interaction between the cyclohexene substituent and the electrophilic metal center in the insertive transition state might be expected to yield *E* anti-Markovnikov product (Figure 9B), the approximately equimolar formation of both *E* and *Z* isomers argues against this pathway. Alternatively, the imperfect selectivity of 1-ethynylcyclohexene could result from a combination of early catalyst deactivation and an alkyne known to be highly active toward radical hydrothiolation.[6a]

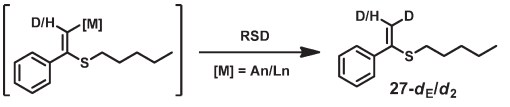
Deuterium Labeling. Isotopic labeling of the alkyne yields insights into the hydrothiolation mechanism. The apparent k_H/k_D = 1.4(0.1) and 1.35(0.1) for the organo-Sm and organo-Th catalysts, respectively, is consistent with a secondary kinetic isotope effect in a turnover-limiting insertion mechanism (Scheme 1) and is similar to that reported for analogous insertion reactions.[56] The observation of **27-*d*$_E$** product early in the reaction is consistent with thiol-mediated protonolysis. As the reaction progresses, increasing quantities of other product isotopomers form, corresponding to redistribution of the alkyne ^{2}H label. The observed ^{2}H exchange between phenylacetylene-*d* (**26-*d***) and ^{t}BuSH (**33**), prior to significant catalytic turnover, as well as negligible ^{2}H migration in the absence of catalyst, strongly supports a metal complex-mediated pathway, independent of the hydrothiolation catalytic cycle.

Hydrogen/deuterium scrambling involving terminal alkynes has been previously observed in analogous organoactinide-mediated hydrothiolation,[13b] lanthanide-mediated hydroalkoxylation,[13i] and organozirconium-mediated hydrothiolation,[6a] as a result of the type of metal−alkynyl/metal−heteroelement equilibration previously reported for organouranium complexes.[8h,i] The known protonolytic reactivity of terminal alkynes[8i,57] with lanthanide− and actinide−heteroelement bonds suggests a pathway such as shown in Scheme 2. Interestingly, the more rapid formation of the product isotopomers in lanthanide- and actinide-mediated hydrothiolation than in zirconium-mediated hydrothiolation is consistent with the more polar bonding and larger ionic radii of lanthanide and actinide complexes, as well as lanthanide and actinide complexes exhibiting a lower protonolytic/deuterolytic barrier.[51e] Bond enthalpy estimates indicate that the protonolytic detachment of alkyne from organo-Th or organo-Sm complexes is ca. −24 and −22 kcal/mol, respectively (eq 11). Due to the Markovnikov selectivity[58] and exothermicity of thiol-mediated protonolysis of metal−alkynyl bonds,[8i,57] the

$$\text{RS-H} + \text{M-C} \equiv \text{CR}' \rightarrow \text{M} - \text{SR} + \text{H-C} \equiv \text{CR}' \quad \text{M} = \text{Th/Sm} \tag{11}$$

metal−alkynyl ⇌ metal−thiolate equilibrium should strongly favor the corresponding thiolates. In the **5-** and **32**-mediated hydrothiolation of phenylacetylene-*d* (**26-*d***) by **10**, the formation of primarily **27-*d*$_E$** further supports the insertion/thiol-mediated protonolysis mechanism (Scheme 3A). The observation of small quantities of **27-*d*$_Z$** and **27** early in the reaction demonstrates the rapid nature of deuterium/proton scrambling between the alkyne and thiol positions.

While alkyne deuterolysis of the M−vinyl product from the lanthanide or actinide center could result in ^{2}H delivery to the *Z* product position (e.g., Scheme 3B), it seems more likely to originate from thiol-mediated deuterolysis of products bound to the metal center (eq 12), because of the RSD detected *in situ* by ^{2}H NMR and REH (E = O and S) protonolysis pathways in analogous organozirconium-mediated hydrothiolation[6a] and lanthanide-mediated hydroalkoxylation processes.[13d,g,i,m]



(12)

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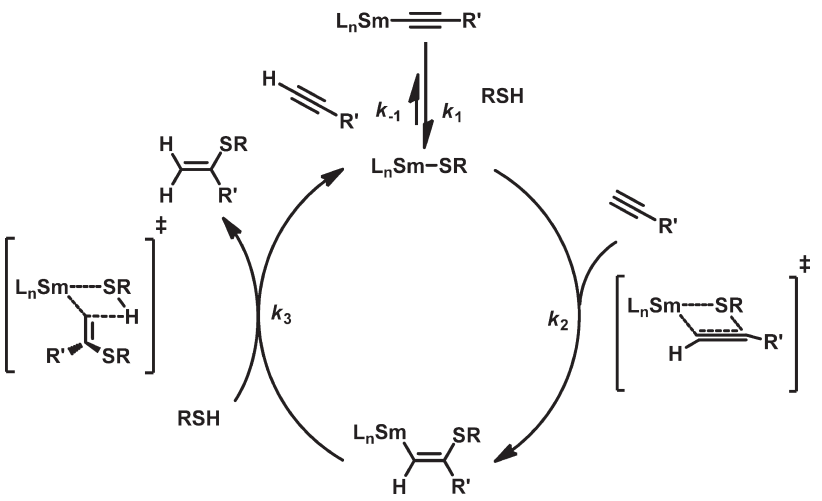
(58) As is discussed earlier, Markovnikov selectivity is suggestive of alkyne insertion into the M−SR bond.

Scheme 4. Proposed Turnover-Limiting Alkyne Insertion (k_2) Pathway for Organosamarium-Mediated Terminal Alkyne Hydrothiolation



Summary

Kinetic and Mechanistic Data for Organolanthanide- and Organoactinide-Mediated Intermolecular Alkyne Hydrothiolation

1. Approximate empirical rate law: rate = k_{obs}[catalyst]^1[alkyne]^1[thiol]^0
2. Markovnikov selectivity
3. Hydrothiolation conversion heavily dependent upon thiol steric encumbrance
4. Alkyne RC≡C−H/D isotopic labeling yields k_H/k_D = 1.40(0.1) and 1.35(0.1) for samarium and thorium, respectively
5. A single product isotopomer is predominant in the early stages of turnover
6. Multiple product isotopomers are produced throughout the reaction
7. Deuterium/hydrogen scrambling between alkyne RC≡C−H/D and thiol RS−H/D is observed
8. Thiol protonolysis of An−/Ln−C products and alkyne release from the metal center is predicted to be highly exothermic
9. Insertion of alkyne into M−SR (M = Sm or Th) bonds is predicted to be exothermic.

The activation of catalyst upon addition of thiol to precursor amides and alkyls is very rapid and quantitative by ^{1}H NMR, consistent with similar observations in organolanthanide-mediated hydroamination[11g] and hydroalkoxylation[13g,i,m] (but not in hydrophosphination).[12b−e] This is indicative of the relatively strong M−SR (M = Ln and An) and H−C bonds. The absence of significant HDC(TMS)$_2$ in the *in situ* ^{1}H and ^{2}H NMR spectra of the deuterium-labeling experiments indicates that thiol protonolysis is significantly more rapid than alkyne protonolysis.

The high Markovnikov selectivity, empirical rate law, deuterium-labeling results, and bond enthalpy considerations are consistent with an insertion/protonolysis pathway for organosamarium-mediated alkyne hydrothiolation. Here alkyne insertion into the L_nSm−SR bond (Scheme 4, k_2) is turnover-limiting and subsequent thiol L_nSm−C protonolysis (Scheme 4, k_3) is rapid (i.e., $k_3 \gg k_2$), with a catalyst metal−thiolate resting state (i.e., $k_1 > k_{-1}$). The invariance of rate with respect to [thiol] under the present experimental conditions indicates very rapid protonolytic cleavage of the L_nSm−vinylic product from the metal after the turnover-limiting step. This is consistent with lanthanide-mediated hydroalkoxylation and organoactinide-mediated hydrothiolation mechanistic patterns but stands in contrast to organozirconium-mediated alkyne hydrothiolation,[6a] where thiol protonolysis of the Zr−vinylic product from the metal center is slow enough to be kinetically relevant. Differences between organozirconium and organo-f-element hydrothiolation likely result from the greater covalency in organozirconium bonding,[51e] affording more sluggish protonolysis. While organoactinide complexes are experimentally more covalent than organolanthanide complexes,[51d] these slight differences are still rather modest and not observable in thiol protonolysis under the present reaction conditions.

Conclusions

Organolanthanide and organoactinide complexes are Markovnikov-selective catalysts for the hydrothiolation of terminal alkynes under homogeneous conditions. Catalyst aggregation is observed but can be ameliorated by using smaller ionic radius metals and sterically encumbering Cp-based ancillary ligation. While anti-Markovnikov products are occasionally observed under reaction conditions, these are often efficiently suppressed by the addition of a radical inhibitor. On the basis of kinetic experiments, deuterium labeling, and other results, an insertion/protonolysis mechanism in which alkyne insertion is turnover-limiting followed by rapid thiol protonolysis is proposed for both lanthanide- and actinide-mediated alkyne hydrothiolation. Comparison of different metal ions, ligation, and substrates reveals that nonbonding repulsions largely dominate hydrothiolation catalytic activity.

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Supporting Information Available: Kinetic data, thermodynamic calculations, NMR spectra, and digital images. This material is available free of charge via the Internet at http://pubs.acs.org.