Organolanthanide-Catalyzed Cyclization/Silylation of Nitrogen-Containing Enynes

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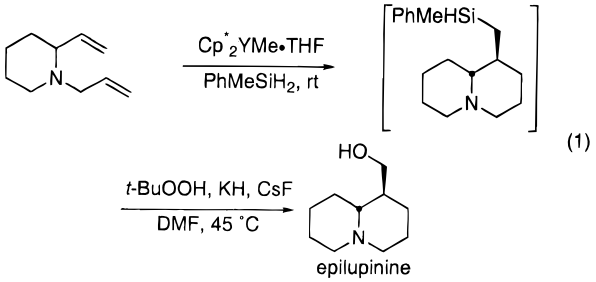
Cyclization/silylation reactions of nitrogen-containing enynes catalyzed by the complexes Cp^*_2LnMe·THF (Ln = Y, Lu) were investigated. Utilizing standard conditions previously developed for carbocyclic systems, the Cp^*_2YMe·THF complex suffered from poor reactivity at room temperature with nitrogen α to the alkyne. This was overcome in the current studies either by slow catalyst addition or by using the smaller lutetium catalyst Cp^*_2LuMe·THF. The use of Cp^*_2LuMe·THF allowed the preparation of various nitrogen-containing ring systems in excellent yields with good to excellent diastereoselectivities at room temperature. The results of this study highlight the ability to tune the reactivity of an organolanthanide complex by changing the metal center.

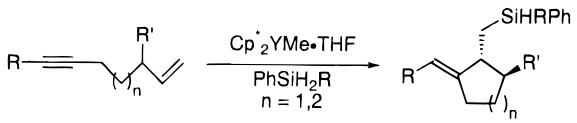
Introduction

Organolanthanide complexes have been used as catalysts for the cyclization/silylation of dienes,[1] enynes,[2] and dienynes.[3] These catalysts produce remarkable stereoselectivities in the aforementioned reactions as a result of the steric environment about the metal center.[1] The organolanthanide catalyst Cp^*_2YMe·THF (**1**, Cp* = C_5Me_5) has been used in the cyclization/silylation of a nitrogen-containing diene to provide the quinolizidine natural product epilupinine (eq 1).[1d] This transformation proceeded with excellent diastereoselectivity and provided an organosilane that was oxidized to the alcohol in good yield.[1d,4]

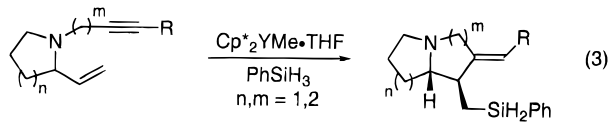


(1)

Enyne cyclizations have also been shown to provide excellent yields of carbocyclic organosilane products with very high diastereoselectivities (eq 2).[2] As part of an ongoing investigation of metallocene catalyzed reactions, we sought to expand the scope of the cyclization/silylation method to include nitrogen-containing enynes, thereby providing access to a variety of heterocyclic compounds (eq 3).

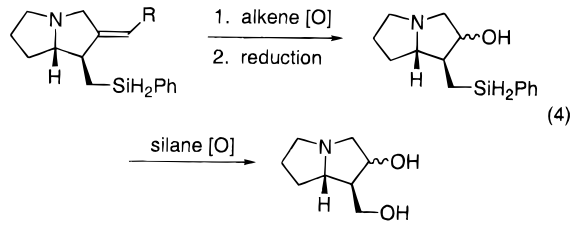


(2)



(3)

Numerous naturally occurring pyrrolizidines[5] and quinolizidines[6] possess the same core structure as the products displayed in eq 3. Oxidation of the resulting exomethylene-containing organosilane and reduction of the resulting ketone could potentially provide access to such targets (eq 4). Chiral, nonracemic pyrrolizidines



(4)

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† University of Pennsylvania.

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(1) (a) Molander, G. A. *Chemtracts* **1998**, *11*, 237, and references therein. (b) Molander, G. A.; Dowdy, E. D.; Schumann, H. *J. Org. Chem.* **1998**, *63*, 3386. (c) Molander, G. A.; Nichols, P. J.; Noll, B. C. *J. Org. Chem.* **1998**, *63*, 2292. (d) Molander, G. A.; Nichols, P. J. *J. Org. Chem.* **1996**, *61*, 6040. (e) Molander, G. A.; Nichols, P. J. *J. Am. Chem. Soc.* **1995**, *117*, 4415. (f) Onozawa, S.; Sakakura, T.; Tanaka, M. *Tetrahedron Lett.* **1994**, *35*, 8177. (g) Molander, G. A.; Dowdy, E. D. In *Topics In Organometallic Chemistry*. Kobayashi, S., Ed.; Springer-Verlag: New York, 1999; Vol. 2, pp 120−154. (h) Fu, P.-F.; Brard, L.; Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1995**, *117*, 7157.

(2) Molander, G. A.; Retsch, W. H. *J. Am. Chem. Soc.* **1997**, *119*, 8817.

(3) Retsch, W. H. Ph.D. Thesis, University of Colorado at Boulder, 1997.

(4) (a) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1996**, *61*, 6044. For other oxidation protocols, see: (b) Molander, G. A.; Corrette, C. P. *Organometallics* **1998**, *17*, 5504. (c) Fleming, I.; Winter, S. B. D. *Tetrahedron Lett.* **1993**, *34*, 7287. (d) Bergens, S. H.; Noheda, P.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1992**, *114*, 2121. (e) Tamao, K.; Ishida, N. *J. Organomet. Chem.* **1984**, *269*, C37.

(5) Mattocks, A. R. *Chemistry and Toxicology of Pyrrolizidine Alkaloids*; Academic Press: New York, 1986; and references therein.

(6) (a) Hua, D. H.; Miao, S. W.; Bravo, A. A.; Takemoto, D. J. *Synthesis* **1991**, 970, and references therein. (b) Veen, G.; Greinwald, R.; Witte, L.; Wray, V.; Czygan, F.-C. *Phytochemistry* **1991**, *30*, 1891.

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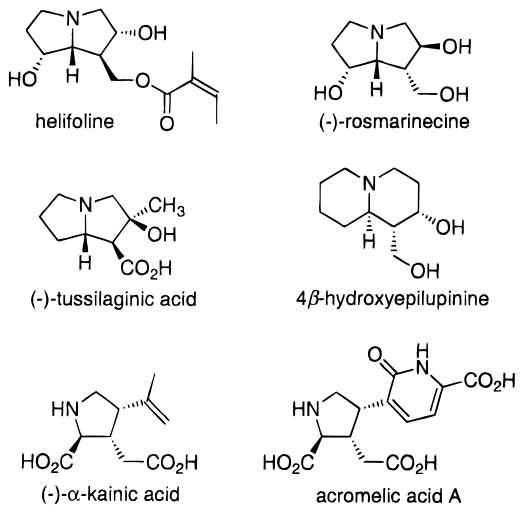


Figure 1. Representative pyrrolizidines, quinolizidine, and pyrrolidine alkaloids potentially accessible by a nitrogen-containing enyne cyclization/silylation strategy.

such as the necine alkaloids (Figure 1)[7] might be prepared stereoselectively from substrates derived from commercially available (*S*)-prolinol utilizing the metallocene catalyzed process. The necine alkaloids are well-known for their hepatotoxic and/or carcinogenic properties in animals and man.[5] The quinolizidine 4*β*-hydroxyepilupinine[6] and pyrrolidine-based natural products[8] such as (−)-α-kainic acid or acromelic acid A represent other examples of target structures that might be accessed by a nitrogen-containing enyne cyclization/silylation approach.

Results and Discussion

Formation of Five-Membered Rings. Initial examination of the enyne cyclization/silylation strategy involved formation of five-membered rings with pyrrolidine, piperidine, and perhydroazepine ring systems (substrates **3**, **5**, and **7**, Table 1). The choice of a proper catalyst is always critical to the success of metallocene-catalyzed cyclization/silylation reactions, because each class of catalysts displays specific reactivity and selectivity patterns. The choice to begin the current studies with Cp^*_2YMe·THF (**1**) was based upon practical considerations. Thus, this catalyst is readily available in quantity by a straightforward synthetic transformation. Although one might assume that the Lewis basic THF present in this complex would compete with the olefin substrate and lower the rate of reaction, in fact, quite the opposite is true. Thus, the single THF of solvation appears to catalyze the hydrometalation reaction in the same manner that Lewis bases catalyze the hydroboration of olefins with 9-BBN.[9] For example, we have previously demonstrated that a complex lacking a THF of association, Cp_2*YCH(TMS)$_2$, is orders of magnitude less reactive than **1** in hydrosilylation reactions with terminal alkenes.[10] Addition of 1 molar equiv of THF per equivalent of Cp^*_2YCH(TMS)$_2$ restores catalytic activity to the level of the methyl complex. Apparently, THF also depresses the rate of *σ*-bond metathesis relative to olefin insertion,[11] with important ramifications for the cyclization/silylation process. In the event, reactions of enyne **3** with Cp^*_2YMe·THF (**1**) proceeded at 50 °C over 24−48 h to provide a mixture of at least five different products. By NMR, the major product was determined to be **4**. However, the organosilane could not be isolated cleanly by flash chromatography using either silica gel or alumina, apparently because of decomposition as evidenced by 2D TLC.

Because the cyclization/silylation reaction appeared to proceed efficiently, we attempted a cyclization reaction with enyne **5** (entry 2, Table 1). This reaction proceeded at 50 °C with **1** to provide a product that was amenable to flash chromatography. The desired product **6** was isolated in 82% yield with complete selectivity for the diastereomer shown.[12]

The observed stereochemistry has ample precedent in organolanthanide-catalyzed cyclization reactions and can be explained by a preference for the chairlike transition structure shown in Figure 2.[1,2,13] This transition structure minimizes the strain between the ligand array about the metal center and the piperidine ring system. The cyclohexane ring of the developing exomethylene unit in this conformation can adopt an orientation that minimizes its strain with the piperidine ring. The boat conformation brings a pentamethylcyclopentadienyl ligand into close proximity of the piperidine ring system.

Extension of the series to the perhydroazepine enyne **7** was also successful, providing **8** in 82% yield in a reaction taking place over a period of 48 h (entry 4, Table 1). A deterioration in diastereoselectivity was observed for the cyclization of **7**. This may be the result of the more fluxional character of the seven-membered ring system. The seven-membered ring may also exacerbate steric interactions associated with the cyclohexyl group in the favored chairlike transition structure as described above (see Figure 2).

Although cyclizations of carbocyclic skeleta investigated previously proceeded to form five-membered rings at room temperature in several hours with 5 mol % or less catalyst loading, reactions with heterosubstituted substrates **3**, **5**, and **7** slowed over time and required both large catalyst loadings and heating to proceed in a reasonable amount of time. The primary difficulty encountered with these enynes was thought to be the result of the interaction between the propargylic nitrogen atom and the metal center of the catalyst. One can envision the formation of a four-membered ring chelate via binding between the nitrogen and yttrium atoms of the

(7) Representative syntheses and isolations: (a) Ha, D.-C.; Ahn, J.-B.; Kwon, Y.-E. *Bull. Kor. Chem. Soc.* **1998**, *19*, 514. (b) Denmark, S. E.; Thorarensen, A.; Middleton, D. S. *J. Org. Chem.* **1995**, *60*, 3574. (c) Kueger, H.; Benn, M. *Heterocycles* **1983**, *20*, 1331. (d) Ito, H.; Ikeuchi, Y.; Taguchi, T.; Hanzawa, Y.; Shiro, M. *J. Am. Chem. Soc.* **1994**, *116*, 5469. (e) Pabreiter, C. M. *Phytochemistry* **1992**, *31*, 4135. (f) Tatsuta, K.; Takahashi, H.; Amemiya, Y.; Kinoshita, M. *J. Am. Chem. Soc.* **1983**, *105*, 4096. (g) Yamada, K.; Tatematsu, H.; Unno, R.; Hirata, Y.; Hirono, I. *J. Org. Chem.* **1978**, 29, 4543.

(8) (a) Campbell, A. D.; Raynham, T. M.; Taylor, R. J. K. *J. Chem. Soc., Chem. Commun.* **1999**, 245. (b) Chevliakov, M. V.; Montgomery, J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3144.

(9) Wang, K. K.; Brown, H. C. *J. Am. Chem. Soc.* **1982**, *104*, 7148.

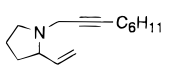
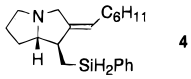
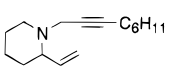
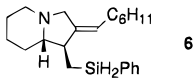
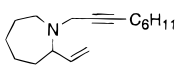
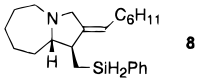
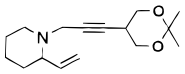
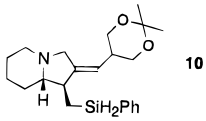
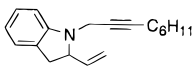
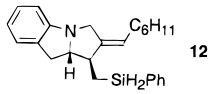
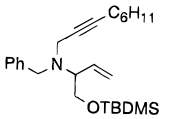
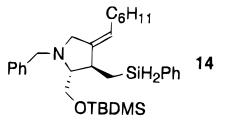
(10) Nichols, P. J. Ph.D. Thesis, University of Colorado at Boulder, 1997.

(11) Haar, C. M.; Stern, C. L.; Marks, T. J. *Organometallics* **1996**.

(12) The relative stereochemistry depicted for the bicyclic products was inferred from that determined by NOE difference spectroscopy for **16**.

(13) (a) Gagné, M. R.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 275. (b) Giardello, M. A.; Conticello, V. P.; Brard, L.; Gagné, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **1994**, *116*, 10241. (c) Arredondo, V. M.; Tian, S.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1999**, *121*, 3633.

Table 1. Cyclization/Silylation of Enynes To Afford Five-Membered Nitrogen Heterocycles

entry	substrate	catalyst	conditions	product	% isoltd yield (ds) [a]
	 **3**			 **4**	
1		6% **2**	rt, 24 h [b]		43%
	 **5**			 **6**	
2		8% **1**	50 °C, 24 h		82% (>50:1)
3		6% **2**	rt, 6 h [b]		92% (>50:1)
	 **7**			 **8**	
4		6% **1**	50 °C, 48 h		82% (8:1)
5		10% **1**	rt, 44 h [b]		64% (6.8:1)
	 **9**			 **10**	
6		10% **1**	70 °C, 3 h		70% (>50:1)
7		10% **1**	rt, 54 h [b]		64% (>50:1)
8		5% **2**	rt, 24 h		78% (>50:1)
	 **11**			 **12**	
9		10% **1**	90 °C, 24 h		34%
10		10% **2**	rt, 5 d [b]		43% (15:1)
	 **13**			 **14**	
11		10% **1**	70 °C, 40 h		58% (>50:1)
12		14% **1**	rt, 21 h [b]		84% (>50:1)
13		10% **2**	rt, 24 h		90% (>50:1)

[a] The diastereoselectivity was determined by GC analysis on the crude reaction mixture. [b] The catalyst was added in portions.

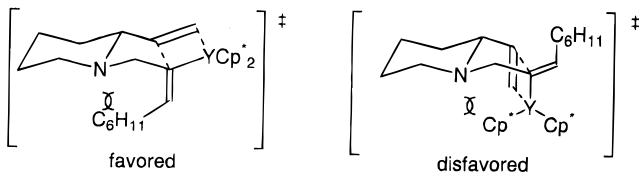


Figure 2. Proposed transition structures for the cyclization of **5**.

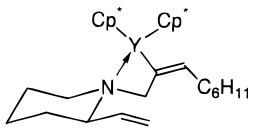


Figure 3. Proposed structure for nitrogen−yttrium binding interaction.

hydrometalated alkyne intermediate (Figure 3). This is a reasonable explanation as this is the orientation associated with β-elimination processes that are well-documented reactions in organometallic systems. Additionally, four-membered ring nitrogen-containing chelates have been observed and isolated in lanthanide metallocene systems.[14] Over time, the hydride catalyst can become further deactivated by hydride-bridged dimerization or redistribution reactions, incrementally slowing the process even further.[1a]

As a means to overcome the latter problem, a cyclization/silylation reaction of enyne **7** with silane and 10 mol % of **1** was investigated in greater detail (entry 5, Table 1). This time, the catalyst was added in several portions over the course of 36 h at room temperature in order to ensure that active catalyst was always present in the reaction mixture. After stirring the reaction a total of 44 h, the reaction was found to be complete, providing the azabicycle **8** in 64% yield with reasonable diastereoselectivity (6.8:1).

Another set of reactions aimed at overcoming the complexation phenomenon was performed with enyne **9**. The branched dioxane regiodirecting group was utilized in these studies. The protected diol provided a handle for further functionalization of the resulting indolizidine

(14) Obora, Y.; Ohta, T.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1997**, *119*, 3745.

10, thereby underscoring the versatility of the synthetic method. When 10 mol % of **1** was used as the catalyst, the reaction was complete in 3 h when heated to 70 °C (entry 6, Table 1). The product was isolated in 70% yield and the reaction proceeded with excellent diastereoselectivity (>50:1) as in the analogous cyclohexyl-directed system (Table 1, entries 2 and 3).[12] The addition of 10 mol % of **1** in portions at room temperature provided the desired product in 64% isolated yield but the reaction time was very long (entry 7, Table 1). This prompted the use of $Cp^*_2LuMe{\cdot}THF$ (**2**) which, with the smaller, more sterically crowded metal incorporated into the complex, was expected to reduce the ability of the Lewis acidic metal to participate in the binding mode depicted in Figure 3.[15] We were pleased to see that 5 mol % of **2** added in one portion provided **10** in good yield in 24 h at room temperature (entry 8, Table 1).

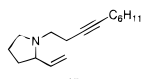
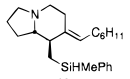
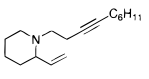
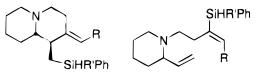
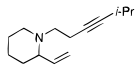
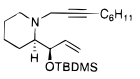
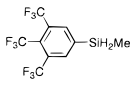
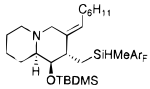
The cyclization/silylation reactions with **3** and **5** were reexamined and improved by applying the results obtained with **9**. The lutetium complex **2** was used and added slowly to the reaction mixture (entries 1 and 3, Table 1). This resulted in reactions that proceeded at room temperature. The pyrrolizidine product **4** was isolated by Kugelrohr distillation in fair yield (entry 1, Table 1).[16] The result for the cyclization of enyne **5** demonstrated the dramatic effect of combining the lutetium complex with slow catalyst addition. The desired azabicyclic organosilane **6** was isolated in 92% yield after only 6 h at room temperature (entry 3, Table 1).

An aromatic system was examined for compatibility with the enyne cyclization-silylation protocol. When enyne **11** was exposed to **1** the reaction did not proceed at lower temperatures (50−70 °C). If the reaction was heated to 90 °C, the enyne was consumed to provide a poor yield of the desired product in low purity (entry 9, Table 1). If the smaller lutetium catalyst **2** was employed and added over several days, a modest yield of the organosilane **12** could be isolated as a 15:1 mixture of diastereomers (entry 10, Table 1).

The acyclic enyne **13** was successfully employed in the cyclization/silylation protocol. Results were similar to those previously obtained for the cyclization of **9**. The use of yttrium complex **1** required heating and long reaction times, providing a fair yield of the substituted pyrrolidine **14** (entry 11, Table 1). When **1** was added slowly the reaction proceeded at room temperature in half the time with a substantial increase in isolated yield (entry 12). Finally, the use of lutetium complex **2** further increased the yield with a similar reaction time at room temperature (entry 13). In all cases, the reactions were completely selective for the diastereomer **14** via a chairlike transition structure.[17]

Formation of Six-Membered Rings. Having successfully applied the cyclization/silylation method to the formation of five-membered nitrogen heterocycles, a protocol was sought to extend the method to six-membered rings. If the problems associated with the enynes used for five-membered ring formation were indeed the result of the propargylic nitrogen atom, then the enynes to be utilized for six-membered rings heterocyclic ring synthesis might minimize this effect. The binding mode in the alkenylmetallic intermediate would require a five-membered ring chelate of the nitrogen and metal atoms. Because of the relatively long metal−carbon bonding distance, five-membered chelates might be less favorably formed.

Table 2. Cyclization/Silylation of Enynes with Catalyst 1 To Afford Six-Membered Nitrogen Heterocycles

entry	substrate	silane	product(s)	% isoltd yield
1	 **15**	$PhMeSiH_2$	 **16**	100%
2	 **17a**	$PhMeSiH_2$	 **18** **19** (R = C_6H_{11}, R' = Me; **18a**)	94%
3		$PhSiH_3$	(R = C_6H_{11}, R' = H; **18c**)	40%[a]
4	 **17b**	$PhMeSiH_2$	(R = *i*-Pr, R' = Me; **18b**)	100%
5	 **20**		 **21**	61%

[a] 35% of **19** (R = C_6H_{11}, R′ = H) was also isolated.

The enynes **15** and **17** were cyclized with 5−10 mol % of **1** and $PhSiH_2Me$ at 50 °C (Table 2). The need to use $PhSiH_2Me$ and to heat the reaction mixtures in six-membered ring-forming reactions of enynes has been demonstrated previously in carbocyclic systems.[1c,2] Thus, the transformation of each of these substrates provided very high yields of the desired azabicyclic organosilanes with short reaction times (entries 1, 2, and 4, Table 2). The products were obtained as a mixture of diastereomers (by GC analysis) as a result of the added stereocenter at silicon.

The stereochemistry observed in the formation of six-membered rings has precedent in previous studies.[1−3] However, because of the stereocenter at silicon, the level of diastereoselectivity achieved in the cyclizations was often difficult to judge. Unfortunately, oxidation of the organosilane products to remove the stereocenter at silicon and more accurately evaluate the diastereoselectivity of the reaction failed.[18] As a practical solution to the problem we chose to perform a cyclization/silylation reaction **17** with phenylsilane (Table 2, entry 3). This reaction produced two types of products, **18** and **19**, that have been previously observed in analogous carbocyclic systems.[2] The generation of the uncyclized, hydrosilylated product results from premature trapping of the hydrometalated alkyne with the less hindered silane.[2] From this study it was determined that a single isomer was

(15) The ionic radii of Lu^{3+} and Y^{3+} are 98 pm and 102 pm, respectively. Shannon, R. D. *Acta Crystallogr.* **1976**, *A32*, 751.

(16) The isolated product was found to be only 75% pure by GC analysis. See the Experimental Section.

(17) The relative stereochemistry was determined by NOE difference spectroscopy.

(18) Oxidation reactions with all of the azabicyclic products prepared in this study were attempted and failed to provide the desired alcohols upon purification. The problems associated with the oxidation of a similar system have been previously encountered. See ref 1d.

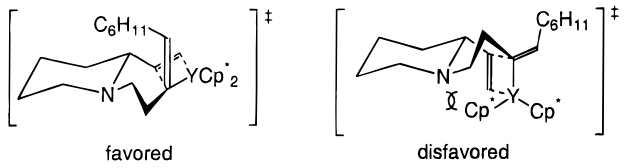


Figure 4. Proposed transition structures for the cyclization of **17**.

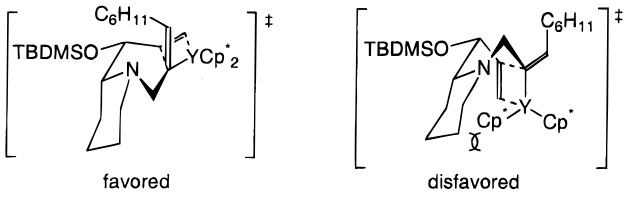


Figure 5. Proposed transition structures for the cyclization of **20**.

generated via a chairlike transition structure (Figure 4). The boatlike transition structure represents a high energy conformation for cyclization, and thus the diastereomer of **18** that would be derived from this transition structure is not observed.

The preparation of a quinolizidine structure with a shift in the positions of the exomethylene and silylmethyl units is possible by the cyclization/silylation of **20**. Enyne **20** could be cyclized at 120 °C to provide **21** in 61% isolated yield (Table 2, entry 5). Attempted cyclization reactions of the diastereomer of **20** failed. The need for the elevated temperatures presumably results from a combination of a slower six-membered ring cyclization and complexation with the nitrogen atom located at the propargylic position in the intermediate alkenylmetallic. The fluoroarylsilane 3,4,5-(trifluorophenyl)methylsilane trapping agent was used in anticipation of a difficult silane oxidation of the resulting azabicyclic organosilane. Even with this more easily oxidized silane, transformation to the corresponding alcohol failed employing several standard reaction conditions.[4]

The stereochemistry of **20** depicted in Table 2 results from transformation through the transition structure shown in Figure 5 with the chairlike conformation and pseudoequatorial positioning of the protected alcohol being favored. The steric interaction between the ligand array of the yttrium complex and the piperidine ring system should be significant in a boatlike transition structure. Figure 5 also suggests a reason for the failure of the diastereomer of **20** to provide the cyclized product: the silyl-protected alcohol would be in a pseudoaxial orientation, creating a severe steric interaction between the cyclohexyl group and the protected alcohol in the chairlike transition structure. The boatlike structure remains prohibited by strain between the ligand array and piperidine ring system.

Conclusions

The organolanthanide-catalyzed enyne cyclization/silylation strategy has been expanded to include nitrogen-containing enynes. Problems encountered with the incorporation of a nitrogen atom at the propargylic position in an enyne could be overcome in some cases with the slow addition of an yttrium-based catalyst. Alternatively, a lutetium complex that was postulated to minimize Lewis acid-Lewis base interactions for steric reasons in the key intermediate could be employed, providing azabicyclic compounds in good to excellent yields with high diastereoselectivities. This work adds to the growing number of examples highlighting the flexibility of group 3 and lanthanide metallocene catalysis in that the "tuning" of the reactivity of a given complex can be achieved by simply changing the metal center.[1a,g,19] One present limitation is the inability to obtain a good yield of alcohols from the oxidation of the organosilane products. Further efforts to develop a completely reliable protocol for this transformation must be developed.

Experimental Section

Materials and Methods. All NMR spectra were recorded on a 300 or 500 MHz spectrometer. All catalytic experiments were performed in a nitrogen-filled Vacuum Atmospheres glovebox or in a sealed reaction vessel initially prepared in the glovebox. The organolanthanide complexes **1** and **2** were prepared according to literature procedures.[20] Cyclohexane and benzene-d_6 used in catalytic reactions were distilled from sodium/benzophenone ketyl and stored in the glovebox. Phenylsilane (Aldrich) and phenylmethylsilane (Gelest) used in catalytic reactions were freeze-pump-thaw-degassed as received and stored in the glovebox. All products synthesized were found to be >95% pure by capillary GC analysis unless otherwise indicated.

(1*R,2*E*,8*S**)-2-(Cyclohexylmethylene)-1-(phenylsilyl)-methylhexahydropyrrolizidine (4). (Representative Procedure for the Cyclization−Silylation of an Enyne with Organolanthanide Catalysts).** In the glovebox, **2** (14 mg, 6.0 mol %) was dissolved in cyclohexane (1.0 mL). To this solution were added **3** (100 mg, 0.46 mmol) and phenylsilane (60 mg, 0.55 mmol). The reaction was stirred at room temperature for 24 h. The reaction was filtered through a small plug of silica to remove the catalyst and concentrated by rotary evaporation. Purification by flash chromatography (silica gel or alumina) resulted in decomposition in previous experiments; thus, the crude product was purified by Kugelrohr distillation. This provided the title compound as 75% pure material by GC analysis in 43% yield: ot 170−180 °C/0.1 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.33 (t, J = 4.0 Hz, 2H); IR (neat) 2134.1 cm^{-1}; HRMS calcd for $C_{21}H_{30}NSi$ (M − H$^+$) 324.2148, found 324.2139; LRMS (EI) *m*/*z* 325 (55), 242 (100).

(1*R,2*E*,9*S**)-2-(Cyclohexylmethylene)-1-(phenylsilyl)-methyloctahydroindolizidine (6)** was prepared according to the general procedure given for **4**. After 6 h at room temperature, the reaction was stopped. Workup and purification by flash chromatography and Kugelrohr distillation provided the title compound in 92% yield: ot 160−175 °C/0.1 mmHg; R_f 0.35 (2:1 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55−7.53 (m, 2H), 7.38−7.31 (m, 3H), 5.06 (dq, J = 2.2, 9.3 Hz, 1H), 4.32 (m, 2H), 3.69 (d, J = 13.3 Hz, 1H), 3.04 (d, J = 10.9 Hz, 1H), 2.77 (dt, J = 13.3, 2.8 Hz, 1H), 2.44−2.42 (m, 1H), 2.03−1.90 (m, 2H), 1.84 (d, J = 8.3 Hz, 1H), 1.77−1.76 (m, 1H), 1.73−1.53 (m, 8H), 1.27−1.07 (m, 7H), 1.05−0.92 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.16, 133.19, 129.45, 127.95, 126.83, 70.23, 56.89, 53.03, 45.01, 38.78, 32.97, 32.82, 29.70, 26.10, 25.99, 25.49, 24.17, 11.23; IR (neat) 2135.8 cm^{-1}; HRMS calcd for $C_{22}H_{32}NSi$ (M − H$^+$) 338.2304, found 338.2292; LRMS (EI) *m*/*z* 338 (8), 256 (17), 232 (46), 84 (100). Anal. Calcd for $C_{22}H_{33}NSi$: C, 77.81; H, 9.79. Found: C, 78.15; H, 10.10.

(1*R,2*E*,11*S**)-2-(Cyclohexylmethylene)-1-(phenylsilyl)-methyloctahydropyrrolo[1,2-*a*]azepine (8)** was prepared according to the general procedure given for **4** with **1** in a sealed tube initially prepared in the glovebox. After 48 h at

(19) See, for example: Molander, G. A.; Dowdy, E. D.; Noll, B. C. *Organometallics* **1998**, *17*, 3754.

(20) den Haan, K. H.; de Boer, J. L.; Teuben, J. H.; Smeets, W. J.; Spek, A. L. *J. Organomet. Chem*. **1987**, *327*, 31.

50 °C, the reaction was stopped. Workup and purification by flash chromatography provided the title compound in 82% yield: R_f 0.20 (2:1 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60−7.58 (m, 2H), 7.43−7.36 (m, 3H), 5.05 (dd, J = 2.4, 9.3 Hz, 1H), 4.36 (t, J = 4.2 Hz, 2H), 3.78 (d, J = 13.7 Hz, 1H), 3.09−3.04 (m, 1H), 3.01−2.97 (m, 1H), 2.53−2.51 (m, 1H), 2.29−2.24 (m, 1H), 2.15−2.11 (m, 1H), 2.02−1.94 (m, 1H), 1.92−1.86 (m, 1H), 1.81−1.56 (m, 9H), 1.51−1.41 (m, 2H), 1.32−1.14 (m, 6H), 1.09−1.00 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.34, 135.19, 133.37, 129.43, 127.95, 126.40, 72.25, 59.12, 56.27, 47.15, 38.67, 33.00, 32.88, 27.15, 26.49, 26.12, 25.60, 24.85, 12.64; HRMS calcd for $C_{23}H_{34}NSi$ (M − H$^+$) 352.2461, found 352.2440; LRMS (EI) *m*/*z* 270 (53), 246 (29), 98 (100). Anal. Calcd for $C_{23}H_{35}NSi$: C, 78.12; H, 9.98. Found: C, 77.59; H, 10.33.

(1*R,2*E*,9*S**)-2-(2,2-Dimethyl-1,3-dioxan-5-ylmethylene)-1-(phenylsilyl)methyloctahydroindolizidine (10)** was prepared according to the general procedure given for **4**. After 24 h at room temperature, the reaction was stopped. Workup and purification by flash chromatography provided the title compound in 78% yield: R_f 0.50 (3:1 ethyl acetate/methanol); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54−7.52 (m, 2H), 7.40−7.32 (m, 3H), 4.86 (d, J = 8.1 Hz, 1H), 4.33−4.29 (m, 2H), 3.74−3.68 (m, 2H), 3.67−3.63 (m, 1H), 3.58−3.52 (m, 2H), 3.08−2.98 (m, 1H), 2.78 (d, J = 13.3 Hz, 1H), 2.61−2.53 (m, 1H), 2.60−2.40 (m, 1H), 2.42 (br s, 1H), 1.89−1.83 (m, 1H), 1.82−1.67 (m, 2H), 1.66−1.47 (m, 2H), 1.41 (s, 3H), 1.37 (s, 3H), 1.29−1.09 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.16, 129.67, 128.06, 115.95, 109.61, 97.38, 70.21, 63.81, 63.69, 56.96, 52.90, 45.45, 36.34, 29.69, 28.63, 25.40, 24.06, 19.28, 11.15; IR (neat) 2136.4 cm^{-1}; HRMS calcd for $C_{22}H_{32}NO_2Si$ (M − H$^+$) 370.2202, found 370.2190; LRMS (EI) *m*/*z* 356 (25), 264 (32), 84 (100). Anal. Calcd for $C_{22}H_{33}NO_2Si$: C, 71.11; H, 8.95. Found: C, 71.38; H, 9.23.

(1*R,2*E*,3*S**)-2-(Cyclohexylmethylene)-1-(phenylsilyl)-methyl-2,3,9,9a-tetrahydro-1*H*-pyrrolo[1,2-*a*]indole (12)** was prepared according to the general procedure given for **4** except that 10% of **2** was added in four portions daily. After 5 d at room temperature, the reaction was stopped. Workup and purification by flash chromatography provided the title compound in 43% yield: R_f 0.15 (10:1 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59−7.57 (m, 2H), 7.41−7.32 (m, 3H), 7.10−7.05 (m, 2H), 6.73 (t, J = 17.4 Hz, 1H), 6.58 (d, J = 7.9 Hz, 1H), 5.08−5.05 (m, 1H), 4.44−4.38 (m, 2H), 4.06 (d, J = 15.1 Hz, 1H), 3.85 (d, J = 15.1 Hz, 1H), 3.63 (t, J = 9.1 Hz, 1H), 3.15−3.10 (m, 1H), 2.97 (d, J = 15.9 Hz, 1H), 2.37−2.30 (m, 1H), 2.06−1.99 (m, 1H), 1.72−1.62 (m, 4H), 1.55−1.52 (m, 1H), 1.32−1.24 (m, 4H), 1.19−0.95 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.59, 135.23, 135.14, 132.49, 129.71, 129.02, 128.09, 127.55, 126.94, 125.06, 119.16, 110.10, 71.57, 53.73, 43.54, 38.38, 33.30, 33.04, 32.90, 26.02, 25.96, 25.89, 10.68; IR (neat) 2135.4 cm^{-1}; HRMS calcd for $C_{25}H_{31}NSi$ 373.2226, found 373.2239; LRMS (EI) *m*/*z* 265 (5), 290 (1), 373 (3). Anal. Calcd for $C_{25}H_{31}NSi$: C, 80.37; H, 8.36. Found: C, 80.60; H, 8.75.

(2*R, 3*S**, 4*E*)-1-Benzyl-2-(*tert*-butyldimethylsiloxy)-methyl-3-(phenylsilyl)methyl-4-cyclohexylmethylenepyrrolidine (14)** was prepared according to the general procedure given for **4**. After 24 h at room temperature, the reaction was stopped. Workup and purification by flash chromatography provided the title compound in 90% yield: R_f 0.10 (10:1 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56−7.54 (m, 2H), 7.38−7.29 (m, 7H), 7.25−7.22 (m, 1H), 5.02 (dd, J = 1.8, 9.1 Hz, 1H), 4.36−4.30 (m, 2H), 4.20 (d, J = 13.3 Hz, 1H), 3.76−3.72 (m, 1H), 3.65−3.62 (m, 1H), 3.48 (dd, J = 1.6, 13.7 Hz, 1H), 3.42 (d, J = 13.3 Hz, 1H), 2.94−2.91 (m, 1H), 2.67−2.64 (m, 1H), 2.62−2.59 (m, 1H), 1.88−1.80 (m, 1H), 1.64−1.51 (m, 5H), 1.35−1.26 (m, 2H), 1.22−1.09 (m, 3H), 1.08−0.91 (m, 2H), 0.87 (s, 9H), 0.03 (d, J = 4.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.18, 139.78, 135.25, 133.30, 129.40, 128.69, 128.19, 127.93, 127.19, 126.72, 71.48, 65.77, 59.23, 55.73, 43.09, 38.49, 32.98, 32.88, 26.07, 25.97, 25.88, 25.81, 18.29, 14.97, −5.41; IR (neat) 2136.4 cm^{-1}; HRMS calcd for $C_{32}H_{48}NOSi_2$ (M − H$^+$) 518.3274, found 518.3244; LRMS (EI) *m*/*z* 74 (100), 266 (70), 91 (76). Anal. Calcd for $C_{32}H_{49}NOSi_2$: C, 73.93; H, 9.50. Found: C, 73.51; H, 9.82.

(8*R,7*E*,9*S**)-7-(Cyclohexylmethylene)-8-(phenylmethylsilyl)methyloctahydroindolizidine (16)** was prepared according to the general procedure given for **4** with **1** and $PhMeSiH_2$ except that the reaction was heated to 50 °C in a sealed tube. After 4 h at 50 °C, no starting enyne could be detected by GC analysis and the reaction was stopped. Workup and purification by flash chromatography and Kugelrohr distillation provided the title compound in 100% yield: ot 115−125 °C/0.1 mmHg; R_f 0.21 (3:1 ethyl acetate/methanol); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53−7.48 (m, 2H), 7.36−7.28 (m, 3H), 5.04 (d, J = 8.7 Hz, 0.43H), 4.98 (d, J = 8.7 Hz, 0.57H), 4.46−4.43 (m, 0.43H), 4.42−4.39 (m, 0.57H), 3.12−3.01 (m, 2H), 2.62−2.56 (m, 1H), 2.24−2.15 (m, 1H), 2.14−1.85 (m, 5H), 1.83−1.74 (m, 1H), 1.73−1.51 (m, 6H), 1.46−1.37 (m, 1H), 1.31−1.19 (m, 2H), 1.18−0.86 (m, 6H), 0.32 (d, J = 3.8 Hz, 1.7H), 0.28 (d, J = 3.8 Hz, 1.3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.40, 136.89, 134.29, 134.23, 129.12, 129.11, 128.31, 127.85, 127.82, 72.53, 54.16, 54.13, 53.20, 44.70, 44.61, 36.68, 34.08, 33.52, 33.50, 29.97, 29.18, 26.08, 20.97, 12.88, 12.55, −4.32, −5.05; IR (neat) 3067.5, 2126.2 cm^{-1}; HRMS calcd for $C_{23}H_{35}NSi$ 353.2539, found 353.2533; LRMS (EI) *m*/*z* 353 (17), 270 (64), 232 (100), 121 (96). Anal. Calcd for $C_{23}H_{35}NSi$: C, 78.12; H, 9.98. Found: C, 77.15; H, 10.26.

(1*R,2*E*,10*S**)-2-(Cyclohexylmethylene)-1-(phenylmethylsilyl)methyloctahydroquinolizidine (18a)** was prepared according to the general procedure given for **4** with **1** and $PhMeSiH_2$ except that the reaction was heated to 50 °C in a sealed tube. After 19 h at 50 °C, no starting enyne could be detected by GC analysis and the reaction was stopped. Workup and purification by flash chromatography provided the title compound in 94% yield: R_f 0.25 (1:2 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53−7.47 (m, 2H), 7.36−7.28 (m, 3H), 5.02 (d, J = 8.7 Hz, 0.39H), 4.95 (d, J = 8.7 Hz, 0.61H), 4.43−4.41 (m, 0.39H), 4.40−4.37 (m, 0.61H), 2.90−2.85 (m, 1H), 2.83−2.79 (m, 1H), 2.55−2.47 (m, 1H), 2.24−1.83 (m, 6H), 1.75−1.51 (m, 9H), 1.30−0.97 (m, 9H), 0.31 (d, J = 3.8 Hz, 1.2H), 0.26 (d, J = 3.8 Hz, 1.8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.61, 137.19, 137.02, 134.29, 134.24, 129.05, 127.81, 127.78, 127.56, 127.50, 69.60, 69.53, 56.90, 56.32, 56.26, 44.97, 44.80, 36.50, 33.40, 33.97, 33.66, 33.63, 30.22, 30.03, 29.38, 29.26, 26.10, 24.95, 24.79, 24.65, 24.55, 12.24, 11.77, −4.23, −5.05; IR (neat) 2127.3 cm^{-1}; HRMS calcd for $C_{24}H_{37}NSi$ 367.2695, found 367.2712; LRMS (EI) *m*/*z* 367 (11), 284 (48), 246 (100).

(1*R,2*E*,10*S**)-2-(Isopropylmethylene)-1-(phenylmethylsilyl)methyloctahydroquinolizidine (18b)** was prepared according to the general procedure given for **4** with **1** and $PhMeSiH_2$ except that the reaction was heated to 50 °C in a sealed tube. After 6 h at 50 °C, no starting enyne could be detected by GC analysis and the reaction was stopped. Workup and purification by flash chromatography provided the title compound in 100% yield: (1.3 to 1 ds): R_f 0.19 (3:1 ethyl acetate/methanol); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53−7.47 (m, 2H), 7.36−7.28 (m, 3H), 5.01 (d, J = 8.1 Hz, 0.43H), 4.94 (d, J = 8.9 Hz, 0.57H), 4.43−4.41 (m, 0.43H), 4.40−4.37 (m, 0.57H), 2.96−2.84 (m, 2H), 2.57−2.47 (m, 2H), 2.16−1.98 (m, 4H), 1.84 (d, J = 9.3 Hz, 1H), 1.78−1.68 (m, 2H), 1.66−1.48 (m, 2H), 1.30−1.14 (m, 2H), 1.13−0.98 (m, 2H), 0.94−0.86 (m, 6H), 0.31 (d, J = 3.8 Hz, 1.7H), 0.27 (d, J = 3.8 Hz, 1.3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.45, 136.92, 136.12, 134.30, 134.24, 129.45, 129.09, 127.82, 127.79, 69.38, 56.49, 56.11, 56.03, 44.82, 44.61, 29.81, 29.63, 28.80, 28.65, 26.66, 26.62, 24.48, 24.37, 23.75, 23.72, 23.39, 23.36, 23.31, 12.43, 11.98, −4.30, −5.05; IR (neat) 2128.7 cm^{-1}; HRMS calcd for $C_{21}H_{32}NSi$ (M − H$^+$) 326.2304, found 326.2365; LRMS (EI) *m*/*z* 312 (10), 284 (46), 206 (100). Anal. Calcd for $C_{21}H_{33}NSi$: C, 77.00; H, 10.15. Found: C, 76.75; H, 10.50.

(1*R,2*E*,10*S**)-2-(Cyclohexylmethylene)-1-(phenylsilyl)methyloctahydroquinolizidine (18c)** was prepared according to the general procedure given for **4** with **1** and $PhSiH_3$ except that the reaction was heated to 50 °C in a sealed tube. After 17 h at 50 °C, no starting enyne could be detected by GC analysis and the reaction was stopped. Workup and

purification by flash chromatography provided the title compound in 40% yield. The use of phenylsilane resulted in the isolation of **19** in 35% yield. Data for **18c**: R_f 0.22 (1:2 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54−7.52 (m, 2H), 7.37−7.30 (m, 3H), 5.00 (d, J = 8.5 Hz, 1H), 4.34−4.28 (m, 2H), 2.89−2.87 (m, 1H), 2.82−2.80 (m, 1H), 2.54−2.51 (m, 1H), 2.23−2.17 (m, 1H), 2.09−2.01 (m, 4H), 1.90−1.80 (m, 1H), 1.74−1.50 (m, 9H), 1.30−1.00 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.76, 135.16, 133.40, 129.38, 127.92, 127.66, 69.16, 57.05, 56.27, 45.17, 36.49, 33.96, 33.59, 30.22, 29.26, 26.08, 26.07, 26.04, 24.95, 24.53, 8.98; IR (neat) 2136.9 cm^{-1}; HRMS calcd for $C_{23}H_{35}NSi$ 353.2539, found 353.2534; LRMS (EI) *m*/*z* 353 (10), 270 (46), 246 (100). Anal. Calcd for $C_{23}H_{35}NSi$: C, 78.12; H, 9.98. Found: C, 77.36; H, 10.12. Partial data for **19**: R_f 0.76 (1:2 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59−7.48 (m, 2H), 7.38−7.29 (m, 3H), 5.84 (d, J = 9.3 Hz, 1H), 5.73−5.65 (m, 1H), 5.08 (dd, J = 1.8, 17.3 Hz, 1H), 4.97 (dd, J = 1.8, 10.1 Hz, 1H), 4.48 (s, 2H), 2.86−2.81 (m, 1H), 2.61−2.55 (m, 1H), 2.38−2.31 (m, 2H), 2.30−2.20 (m, 2H), 2.05 (dt, J = 3.0, 11.5 Hz, 1H), 1.70−1.44 (m, 9H), 1.40−1.32 (m, 1H), 1.29−1.20 (m, 4H), 1.19−1.04 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.13, 141.74, 135.54, 132.65, 129.45, 129.08, 127.87, 115.28, 65.81, 55.28, 32.88, 33.61, 32.90, 32.87, 26.20, 25.96, 25.91, 25.84, 25.81, 23.85.

(1*R,2*R**,3*E*,10*R**)-3-(Cyclohexylmethylene)-2-[(3,4,5-trifluorophenyl)methylsilyl]methyl-1-(*tert*-butyldimethylsiloxy)octahydroquinolizidine (21)** was prepared according to the general procedure given for **4** with **1** and (3,4,5-trifluorophenyl)methylsilane except that the reaction was heated to 120 °C in a sealed tube (POTENTIAL HAZARD!). After 24 h at 120 °C, no starting enyne could be detected by GC analysis and the reaction was stopped. Workup and purification by flash chromatography (twice) provided the title compound in 61% yield (94% pure by GC analysis): R_f 0.35 (5:1 hexanes/ethyl acetate + 1% Et_3N); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13−7.09 (m, 2H), 5.06 (br s, 1H), 4.54−4.49 (m, 1H), 3.56 (br s, 1H), 3.09 (br s, 1H), 2.94 (br s, 1H), 2.42 (br s, 1H), 2.26 (br s, 1H), 2.07−2.02 (m, 3H), 1.78−1.46 (m, 10H), 1.34−0.89 (m, 17H), 0.39−0.34 (m, 3H), 0.16−0.05 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.08−150.06 (dm, J = 254 Hz), 141.76−139.26 (dm, J = 254 Hz), 135.28−135.02 (m), 134.16−134.02 (m), 129.43−129.02 (m), 117.37 (dd, J = 4.3, 13.9 Hz), 79.67, 68.86, 56.92, 56.49, 44.62, 44.53, 44.49, 36.55, 33.92, 33.46, 33.07, 29.69, 26.55, 26.12, 26.04, 25.85, 25.42, 24.07, 19.37, 19.35, 14.79, 14.67, 14.18, −1.93, −2.08, −2.18, −2.21, −2.29, −2.35; IR (neat) 2131.9 cm^{-1}; HRMS calcd for $C_{30}H_{48}F_3NOSi_2$ 551.3227, found 551.3207; LRMS (EI) *m*/*z* 551 (18), 468 (29), 206 (100).

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