silatrane,[13] the Si–C(phenyl) bond of **2** is lengthened in this case by 0.04 Å, to 1.921 (4) Å, and the Si–C(phenyl) bond in (phenylsilatrane)Cr(CO)$_3$[6a] is lengthened by 0.03 Å, to 1.907 (6) Å. The equatorial O–Si bond lengths in **2** (1.654 (3)–1.660 (3) Å, average 1.657 Å) are very close to the values (average 1.656 Å) in (phenylsilatrane)Cr(CO)$_3$.[6a] The C18–C13–C28 bond angle at the ipso carbon of the phenyl ring in **2** is 115.8 (3)°, which is very close to the value for (phenylsilatrane)Cr(CO)$_3$ (116.1 (6)°).[6a] Other numerical parameters for **2** are similar to those for (phenylsilatrane)Cr(CO)$_3$.[6a]

**Acknowledgment.** Financial support from the Korea Science Foundation (Grant No. 90-03-00-18) is gratefully acknowledged.

**Registry No.** 1, 129619-20-1; 2, 138898-80-3; 3a, 138856-08-3; 3b, 138856-09-4; 3c, 138856-10-7; 3f, 138856-11-8; 4a, 138856-12-9; 4b, 138856-13-0; 4c, 138856-14-1; 4d, 138856-15-2; 4e, 138856-16-3; 4f, 138856-17-4; 5a, 138856-18-5; 5b, 138856-19-6; 5c, 138856-20-9; 5d, 138856-21-0; 5e, 138856-22-1; 5f, 138856-23-2; THF, 109-99-9; MeLi, 917-54-4; MeMgBr, 75-16-1; PhLi, 591-51-5; PhMgBr, 100-58-3; NaBH$_4$, 16940-66-2; *t*-BuLi, 594-19-4; LiCMe$_2$CN, 55440-70-5; LiCH$_2$CO$_2$CMe$_3$, 53503-61-0; CH$_2$Cl$_2$, 75-09-2.

**Supplementary Material Available:** Listings of complete interatomic distances and angles, anisotropic thermal parameters, positional and thermal parameters for hydrogen atoms, and torsion angles for non-hydrogen atoms for **2** and text giving experimental details and spectral and analytical data for compounds **3**–**5** (21 pages); a listing of observed and calculated structure factors for **2** (22 pages). Ordering information is given on any current masthead page.

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# Stable Bis($\eta^5$-cyclopentadienyl)zirconacyclopentadiene Complexes

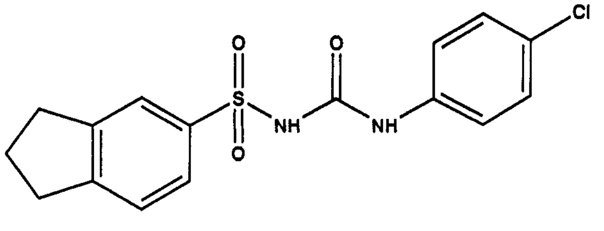
Fariborz Mohamadi* and Michael M. Spees

*Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana 46285*

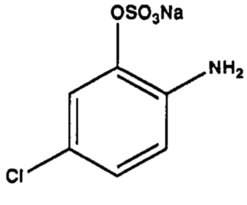
*Received June 10, 1991*

*Summary:* Attempts to synthesize fused bicyclic thiophenes by zirconocene-mediated cyclization of bis(trimethylsilyl) $\alpha,\omega$-diynes led to the isolation of air-stable bis($\eta^5$-cyclopentadienyl)zirconacyclopentadiene complexes when there is a heteroatom (i.e. oxygen or substituted nitrogen) tethered between the acetylenes.

The excellent preclinical antineoplastic properties of a class of diarylsulfonylureas has culminated in clinical development of sulofenur (LY186641).[1] An effort to improve the pharmacological properties of this novel class of oncolytics has resulted in a search for more potent diarylsulfonylureas with decreased levels of circulating sodium 4-chloroaniline *O*-2-sulfate (PCAM1, the metabolite monitored as an indicator of methemoglobinemia).[2] The replacement of the benzenesulfonamide of the diarylsulfonylureas with substituted thiophene-2-sulfonamide has led to the discovery of compounds with increased potency. This paper will summarize the synthesis of fused bicyclic thiophenesulfonylureas with an emphasis on group IV transition-metal-mediated functionalization of bis(trimethylsilyl) $\alpha,\omega$-diynes.[3]

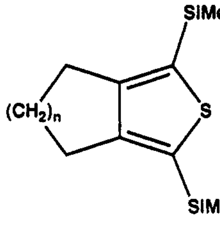


LY186641



PCAM1

The 5,6-dihydro-4*H*-cyclopenta[*b*]thiophene and 4,5,6,7-tetrahydrobenzo[*b*]thiophene were prepared by previously described procedures.[4] The 5,6-dihydro-4*H*-cyclopenta[*c*]thiophene and 4,5,6,7-tetrahydrobenzo[*c*]thiophene were synthesized by the alkylation of the corresponding bis($\eta^5$-cyclopentadienyl)zirconacyclopentadienes with sulfur monochloride[5] followed by tetrabutylammonium fluoride desilylation of **1** and **2**, respectively. Methods for the synthesis of the corresponding *N*-(*p*-chlorophenyl)-*N*′-[(thiaindanyl)sulfonyl]ureas and



**1** n = 1
**2** n = 2

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(1) Howbert, J. J.; Grossman, C. S.; Crowell, T. A.; Rieder, B. J.; Harper, R. W.; Kramer, K. E.; Tao, E. V.; Aikins, J.; Poore, G. A.; Rinzel, S. M.; Grindey, G. B.; Shaw, W. N.; Todd, G. C. *J. Med. Chem.* **1990**, *33*, 2393. Taylor, C. W.; Alberts, D. S.; Ketcham, M. A.; Satterlee, W. G.; Holdworth, M. T.; Plezia, P. M.; Peng, Y.-M.; McCloskey, T. M.; Roe, D. J.; Hamilton, M.; Salmon, S. E. *J. Clin. Oncol.* **1989**, *7*, 1733.

(2) Ehlhardt, W. J. *Drug Metab. Dispos.* **1991**, *19*, 370–375.

(3) Comprehensive review article: Negishi, E.; Takahashi, T. *Synthesis* **1988**, 1–19.

(4) Thiaindanone synthesis: Sam, J.; Thompson, A. C. *J. Pharm. Sci.* **1963**, *52*, 898. Method for reduction of thiaindanone and commercially available 4-keto-4,5,6,7-tetrahydrothianaphthene to produce thiaindan and thianaphthene: MacDowell, D. W. H.; Patrick, T. B.; Frame, B. K.; Ellison, D. L. *J. Org. Chem.* **1967**, *32*, 1226.

(5) For synthesis of main-group heterocycles from bis(cyclopentadienyl)zirconacyclopentadienes see: Buchwald, S. L.; Fang, Q. *J. Org. Chem.* **1989**, *54*, 2793. Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* **1988**, *110*, 2310. Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *Ibid.* **1987**, *109*, 2788.

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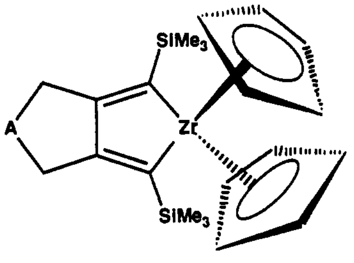
*N*-(*p*-chlorophenyl)-*N*′-[(tetrahydrothianaphthalenyl)sulfonyl]ureas are described in European patent application EP 222,475, May 20, 1987.

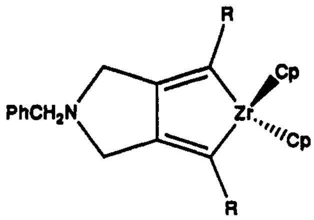
The zirconocene-mediated cyclization[6] of 1,7-bis(trimethylsilyl)-1,6-heptadiyne and 1,8-bis(trimethylsilyl)-1,7-octadiyne, followed by alkylation of the air-sensitive zirconacyclopentadienes[7] with sulfur dichloride provided thiophenes 1 and 2 in 18 and 40% yields. Alkylation of the zirconacyclopentadienes with sulfur monochloride produced thiophenes 1 and 2 in 32 and 40% yields, respectively. In all these reactions the major byproduct was the 1,3-diene arising from protonolysis of the zirconacyclopentadiene.

The placement of an oxygen or nitrogen between the two sites of unsaturation leads to the formation of remarkably stable zirconium-containing complexes.[8] Zirconocene reacts with 1,7-bis(trimethylsilyl)-4-oxahepta-1,6-diyne, 1,7-bis(trimethylsilyl)-4-aza-4-benzylhepta-1,6-diyne, and 1,7-bis(trimethylsilyl)-4-aza-4-(phenylsulfonyl)hepta-1,6-diyne to form zirconacyclopentadienes 3–5 in 37, 63, and 36% yields, respectively, after chromatography on silica gel with ethyl acetate/hexanes.[9] Complex 3, although isolable by chromatography, slowly decomposed upon exposure to air.[10] The sulfonamide-derived complex 5 was air stable for days, but all attempts to crystallize this material for X-ray analysis to elucidate the role of the sulfonamide group in the stabilization of the zirconacyclopentadiene were unsuccessful.



3 A = O
4 A = PhCH$_2$N
5 A = PhSO$_2$NH

All attempts to react complexes 3, 4, or 5 with sulfur monochloride or dichloride resulted in either recovery of starting material or protonolysis of the zirconium-carbon bond to produce 1,3-diene. Iodination of these 2,5-bis(trimethylsilyl)bis($\eta^5$-cyclopentadienyl)zirconacyclopentadienes (3–5) produced only small quantities of the anticipated product.



6 R = tri-*i*-propylsilyl
7 R = diphenyl-*t*-butylsilyl

Compounds 6 and 7 were synthesized to elucidate the role of steric bulk of the silyl protecting groups on the stability of zirconacyclopentadienes. The extent of steric congestion about the zirconium atom in the zirconacyclopentadiene can be modified by altering the size of the alkyl substituents on the silicon since the planarity of the zirconacyclopentadiene places the silyl groups around the coordination sphere of the zirconium.[11] The 2,5-bis(triisopropylsilyl)- (6) and 2,5-bis(diphenyl-*tert*-butylsilyl)zirconacyclopentadienes (7) were isolated in 70 and 62% yields after chromatography in comparison to the chromatographed yield of 63% for 4. Attempts to synthesize and isolate the titanium analogue of 7 using this experimental protocol were unsuccessful.

It is clear that insertion of a heteroatom between the sites of unsaturation of bis(trimethylsilyl) $\alpha,\omega$-diynes produces an electronic stabilization of the zirconocene adduct. The absence of this stabilization in the zirconocene adduct of the *N*-allyl-*N*-propargylbenzylamine substrate reported by Negishi exemplifies the role of the zirconacyclopentadiene versus a zirconacyclopentene.[8] Experiments are underway to obtain X-ray-quality crystals of a zirconacyclopentadiene complex in order to arrive at a better understanding of the structure and bonding of this class of compounds.

## Experimental Section

The $^1$H NMR chemical shifts are reported in ppm downfield from an internal tetramethylsilane standard in the specified deuterated solvent, and the $^{13}$C NMR chemical shifts are referenced to the center of the resonance of CDCl$_3$ (77.0 ppm) or C$_6$D$_6$ (128.0 ppm). Elemental analyses were obtained from the Eli Lilly and Co. microanalysis laboratory. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under nitrogen prior to use. All reactions involving *n*-BuLi were carried out in oven-dried glassware.

**7,7-Bis($\eta^5$-cyclopentadienyl)-6,8-bis(trimethylsilyl)-3-oxa-7-zirconabicyclo[3.3.0]octa-1(8),5(6)-diene (3).** To a solution of bis($\eta^5$-cyclopentadienyl)zirconium(IV) dichloride (0.61 g, 2.1 mmol) in 10 mL of anhydrous THF under nitrogen at −78 °C was added *n*-BuLi (3.2 mL of 1.3 M in hexanes, 4.2 mmol). After stirring at room temperature for 1 h, 1,7-bis(trimethylsilyl)-4-oxahepta-1,6-diyne (0.50 g, 2.1 mmol) was added and the mixture stirred at room temperature for 3 h. The reaction was concentrated in vacuo and purified by flash chromatography using 5% EtOAc/hexanes to provide 0.36 g (37% yield) of a yellow solid. $^1$H NMR (C$_6$D$_6$): $\delta$ 5.55 (s, 10 H), 4.52 (s, 4 H), 0.13 (s, 18 H). $^{13}$C NMR (C$_6$D$_6$): $\delta$ 186.6, 138.5, 125.0, 78.0, 1.2. Anal. Calcd for C$_{22}$H$_{32}$OSi$_2$Zr: C, 57.51; H, 6.96. Found: C, 56.57; H, 7.00. FABMS: (M$^+$) *m/z* 459.

**3-Benzyl-7,7-bis($\eta^5$-cyclopentadienyl)-6,8-bis(trimethylsilyl)-3-aza-7-zirconabicyclo[3.3.0]octa-1(8),5(6)-diene (4).** To a solution of bis($\eta^5$-cyclopentadienyl)zirconium(IV) dichloride (0.89 g, 3.1 mmol) in 10 mL of anhydrous THF under nitrogen at −78 °C was added *n*-BuLi (4.7 mL of 1.3 M in hexanes, 6.1 mmol). After stirring at room temperature for 1 h, 1,7-bis(trimethylsilyl)-4-aza-4-benzylhepta-1,6-diyne (1.0 g, 3.1 mmol) was added and the mixture stirred at room temperature for 2 h. The reaction was concentrated in vacuo and purified by flash chro-

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(6) Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *25*, 2829.

(7) These bis(cyclopentadienyl)zirconacyclopentadienes could not be detected by thin-layer chromatography on silica gel. 7,7-Bis($\eta^5$-cyclopentadienyl)-6,8-bis(trimethylsilyl)-7-zirconabicyclo[3.3.0]octa-1(8),5-(6)-diene has been independently prepared at MIT and is largely unaffected by filtration through a column of alumina III with benzene/pentane: Hsu, D. P.; Buchwald, S. L. Unpublished results.

(8) Titanocene-mediated cyclization of 5-oxanona-2,7-diyne: Nugent, W. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 6422. Zirconocene-mediated cyclization of *N*-propargyl-*N*-allylbenzylamine derivatives: Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *Ibid.* **1989**, *111*, 3336. Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1987**, *28*, 917.

(9) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(10) This complex was characterized in C$_6$D$_6$, since trace quantities of DCl present in CDCl$_3$ led to substantial decomposition.

(11) An alternate method of increasing the steric bulk about the zirconium atom would be to utilize pentamethylcyclopentadiene instead of cyclopentadiene as a ligand.

matography using 15% EtOAc/hexanes to provide 1.0 g (63% yield) of a yellow solid. $^1H$ NMR ($CDCl_3$): δ 7.30 (m, 5 H), 5.87 (s, 10 H), 3.49 (s, 2 H), 3.12 (s, 4 H), 0.15 (s, 18 H). $^{13}C$ NMR ($CDCl_3$): δ 188.9, 138.5, 129.1, 128.2, 127.1, 126.9, 108.6, 64.5, 59.9, 1.1. Anal. Calcd for $C_{29}H_{39}NSi_2Zr$: C, 63.50; H, 7.11; N, 2.55. Found: C, 61.82; H, 7.26; N, 2.13. FABMS: ($M^+$) m/z 548.

**3-(Phenylsulfonyl)-7,7-bis($\eta^5$-cyclopentadienyl)-6,8-bis(trimethylsilyl)-3-aza-7-zirconabicyclo[3.3.0]octa-1(8),5(6)-diene (5).** To a solution of bis($\eta^5$-cyclopentadienyl)zirconium(IV) dichloride (0.77 g, 2.7 mmol) in 35 mL of anhydrous THF under nitrogen at −78 °C was added *n*-BuLi (4.1 mL of 1.3 M in hexanes, 5.3 mmol). After stirring at room temperature for 1 h, 1,7-bis(trimethylsilyl)-4-aza-4-(phenylsulfonyl)hepta-1,6-diyne (1.0 g, 2.7 mmol) was added and the mixture stirred at room temperature for 2 h. The reaction was concentrated in vacuo and purified by flash chromatography using 5% EtOAc/hexanes to provide 0.57 g (36% yield) of a yellow solid. $^1H$ NMR ($CDCl_3$): δ 7.78 (m, 2 H), 7.54 (m, 3 H), 5.82 (s, 10 H), 3.90 (s, 4 H), 0.14 (s, 18 H). $^{13}C$ NMR ($CDCl_3$): δ 193.5, 137.4, 132.8, 129.1, 127.9, 109.5, 109.2, 56.6, 0.8. Anal. Calcd for $C_{28}H_{37}NO_2SSi_2Zr$: C, 56.19; H, 6.18; N, 2.34. Found: C, 55.93; H, 6.20; N, 2.28. FABMS: ($M^+$) *m/z* 598.

**3-Benzyl-7,7-bis($\eta^5$-cyclopentadienyl)-6,8-bis(triisopropylsilyl)-3-aza-7-zirconabicyclo[3.3.0]octa-1(8),5(6)-diene (6).** To a solution of bis($\eta^5$-cyclopentadienyl)zirconium(IV) dichloride (0.15 g, 0.50 mmol) in 15 mL of anhydrous THF under nitrogen at −78 °C was added *n*-BuLi (0.72 mL of 1.4 M in hexanes, 1.0 mmol). After stirring at room temperature for 1 h, 1,7-bis(triisopropylsilyl)-4-aza-4-benzylhepta-1,6-diyne (0.25 g, 0.5 mmol) was added and the mixture stirred at room temperature for 2 h. The reaction was concentrated in vacuo and purified by flash chromatography using 5% EtOAc/hexanes to provide 0.055 g (16% yield)[12] of a yellow solid. $^1H$ NMR ($C_6D_6$): δ 7.34 (d, *J* = 8 Hz, 2 H), 7.16 (dd, *J* = 8, 8 Hz, 2 H), 7.09 (d, *J* = 8 Hz, 1 H), 5.78 (s, 10 H), 3.50 (s, 4 H), 3.23 (s, 2 H), 1.24 (m, 42 H). $^{13}C$ NMR ($C_6D_6$): δ 183.1, 138.6, 123.7, 108.9, 68.6, 59.7, 20.6, 14.4. Anal. Calcd for $C_{41}H_{63}NSi_2Zr$: C, 68.71; H, 8.79; N, 1.95. Found: C, 66.99; H, 8.70; N, 1.94. FABMS: ($M^+ - 1$) *m/z* 715.

**3-Benzyl-7,7-bis($\eta^5$-cyclopentadienyl)-6,8-bis(*tert*-butyldiphenylsilyl)-3-aza-7-zirconabicyclo[3.3.0]octa-1(8),5(6)-diene (7).** To a solution of bis($\eta^5$-cyclopentadienyl)zirconium(IV) dichloride (0.11 g, 0.38 mmol) in 15 mL of anhydrous THF under nitrogen at −78 °C was added *n*-BuLi (0.47 mL of 1.3 M in hexanes, 0.76 mmol). After stirring at room temperature for 1 h, 1,7-bis(*tert*-butyldiphenylsilyl)-4-aza-4-benzylhepta-1,6-diyne (0.25 g, 0.38 mmol) was added and the mixture stirred at room temperature for 2 h. The reaction was concentrated in vacuo and purified by flash chromatography using 5% EtOAc/hexanes to provide 0.25 g (62% yield) of a yellow solid. $^1H$ NMR ($CDCl_3$): δ 7.84 (m, 1 H), 7.62 (m, 5 H), 7.38 (m, 14 H), 7.14 (m, 3 H), 7.02 (m, 2 H), 5.50 (s, 10 H), 3.22 (s, 2 H), 3.12 (s, 4 H), 1.14 (s, 18 H). $^{13}C$ NMR ($CDCl_3$): δ 181.6, 138.4, 138.0, 136.4, 135.6, 129.5, 128.7, 128.6, 128.4, 127.9, 127.7, 127.5, 126.7, 109.4, 69.2, 59.2, 30.37, 27.2, 19.1. Anal. Calcd for $C_{55}H_{59}NSi_2Zr$: C, 74.94; H, 6.74; N, 1.59. Found: C, 75.20; H, 7.00; N, 1.51. FABMS: ($M^+$) *m/z* 880.

**Registry No.** 3, 138856-02-7; 4, 138856-03-8; 5, 138856-04-9; 6, 138856-05-0; 7, 138856-06-1; $Cp_2ZrCl_2$, 1291-32-3; $Me_3SiC{\equiv}CCH_2OCH_2C{\equiv}CSiMe_3$, 18036-67-4; $Me_3SiC{\equiv}CCH_2N(CH_2Ph)CH_2C{\equiv}CSiMe_3$, 138835-25-3; $Me_3SiC{\equiv}CCH_2N(SO_2Ph)CH_2C{\equiv}CSiMe_3$, 138856-01-6; $(i\text{-Pr})_3SiC{\equiv}CCH_2N(CH_2Ph)CH_2C{\equiv}CSi(Pr\text{-}i)_3$, 138835-26-4; $(t\text{-Bu})Ph_2SiC{\equiv}CCH_2N(CH_2Ph)CH_2C{\equiv}CSiPh_2(t\text{-Bu})$, 138835-27-5.

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[12] The yield of this reaction is ~70%, but coelution of an impurity complicates the isolation of pure material.

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# Reaction of $Me_3Al$ with Aza-18-crown-6 (HN18C6): Structure of $Me_2Al[N18C6]AlMe_3$

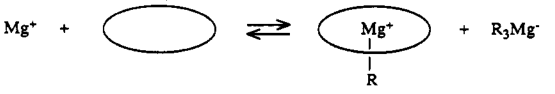
Anthony D. Pajerski,[1a] Thomas P. Cleary,[1b] Masood Parvez,[1a,c] George W. Gokel,*[1d] and Herman G. Richey, Jr.*[1a]

*Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802,*
*Hoffman LaRoche, 340 Kingsland Street, Nutley, New Jersey 07110,*
*and Department of Chemistry, The University of Miami, Coral Gables, Florida 33124*

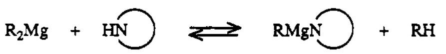
*Received August 21, 1991*

*Summary:* Reaction of $Me_3Al$ and aza-18-crown-6 furnished a solid, $Me_2Al[\overline{N(CH_2CH_2O)_5CH_2CH_2}]AlMe_3$, whose structure was determined by X-ray diffraction. In the crystal structure (monoclinic, $P2_1/m$, $a$ = 9.709 (2) Å, $b$ = 11.697 (3) Å, $c$ = 10.767 (2) Å, $\beta$ = 111.92 (2)°, $Z$ = 2), one Al atom is bonded to two Me groups, the N atom, and the two crown ether O atoms nearest to the N atom; the other Al atom is bonded to three Me groups and the N atom.

Organomagnesium compounds react with appropriate crown ethers and cryptands to form coordinated organomagnesium cations and organomagnesiate anions (e.g., eq 1).[2,3] As part of that study we investigated the use of aza crown ethers.[2,4] Organomagnesium compounds metalate the secondary amine functions of these, of course, as shown in eq 2.[5] We wanted particularly to determine the structures of the species that would be present in such solutions that had been prepared with an *excess* of $R_2Mg$. Defining the structures proved to be complicated, however.



(1)



(2)

Because the results could themselves be interesting and also might help us to understand the solutions prepared from $R_2Mg$, we decided to investigate reactions with aza

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[1] (a) The Pennsylvania State University. (b) Hoffman LaRoche. (c) Present address: Department of Chemistry, The University of Calgary, Calgary, Alberta T2N 1N4, Canada. (d) The University of Miami.

[2] Pajerski, A. D. Ph.D. Dissertation, The Pennsylvania State University, 1990.

[3] Squiller, E. P.; Whittle, R. R.; Richey, H. G., Jr. *J. Am. Chem. Soc.* 1985, *107*, 432. Richey, H. G., Jr.; Kushlan, D. M. *J. Am. Chem. Soc.* 1987, *109*, 2510. Pajerski, A. D.; Parvez, M.; Richey, H. G., Jr. *J. Am. Chem. Soc.* 1988, *110*, 2660. Kushlan, D. M. Ph.D. Dissertation, The Pennsylvania State University, 1987.

[4] Squiller, E. P. Ph.D. Dissertation, The Pennsylvania State University, 1984.

[5] For a review of aluminum amides, including their preparation, see: Lappert, M. F.; Power, P. P.; Sanger, A. R.; Srivsatava, R. C. *Metal and Metalloid Amides*; Ellis Horwood: Chichester, U.K., 1980; Chapter 3.

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