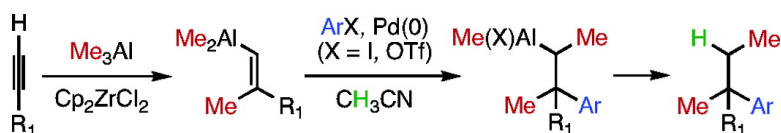


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Palladium-Catalyzed Carbon–Carbon Bond-Forming 1,2-Ligand Migration of Organoalanes

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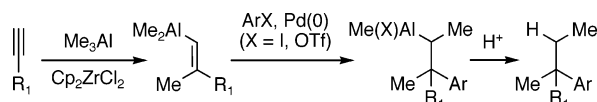
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1,2-Alkyl migration reactions are common in organoboron, organocopper, and organozinc chemistry and represent powerful methods for forming multiple carbon–carbon bonds and generating structural complexity in a single synthetic operation.¹ Scarce examples of this type of migratory insertion have been described for organoalanes, and catalytic strategies remain unexplored.²

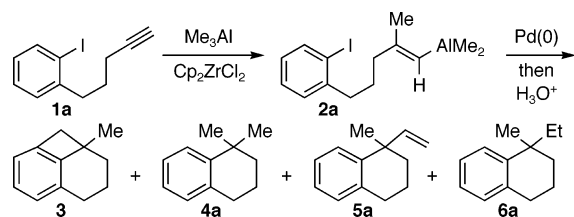
We report herein that (*E*)-2,2-disubstituted-1-alkenyldimethylalanes participate in 1,2-alkyl migration from aluminum to carbon with concomitant arylation at the 2-position when reacted intramolecularly with aryl halides and triflates in the presence of a Pd(0) catalyst to furnish ethyl methyl-substituted benzylic quaternary carbon centers. From terminal alkynes, a total of three new C–C single bonds are made, and two of the three alkyl groups on Me₃Al are transferred to the substrate on vicinal carbons (Scheme 1).³

Scheme 1



E-Vinylalane **2a**, prepared from alkyne **1a** following Negishi's alkyne methylalumination protocol,⁴ was initially subjected to Pd(PPh₃)₄ in toluene at 85 °C. Four major cyclic compounds were generated in a 6:24:12:58 ratio and a 31% combined yield and were identified as tricycle **3** and bicycles **4a**, **5a**, and **6a** (Scheme 2).^{5,6} The incorporation of additional methylene and methyl groups, presumably from the alane moiety, to provide **5a** and **6a**, respectively, induced us to explore that unprecedented catalytic C–C bond-forming transformation.

Scheme 2



Synthetically useful yields of **5a** and **6a** would be obtained by preventing formation of both **4a** and thermally unstable tricycle **3**. 2,6-Disubstituted aryl triflates and iodide **1b–k** were prepared and subjected to the two-step, one-pot procedure. Alkyne methylaluminations provided the key alkenylalanes that were isolated by removal of the volatiles and used without further purification.⁷ For the subsequent step, CH₃CN was found to be the optimal solvent, giving good yields of the ligand transfer product. When **1c** was treated with Pd(PPh₃)₄ (25 mol %) for 22 h at 100 °C, crude ¹H NMR analysis showed a 9:1 mixture of 1-ethyl-1,7-dimethylindan (**6c**) and 1,7-dimethyl-1-vinylindan (**5c**), in addition to the uncyclized and desulfonylated uncyclized products. A 42% combined

yield of **5c** and **6c** was obtained.⁸ Complete conversion was attained with Pd[P(*p*-MeOPh)₃]₂Cl₂ (10 mol %), reduced in situ by Et₃N in the presence of P(*p*-MeOPh)₃ (20 mol %). This catalyst provided superior results in terms of yields and reproducibility.⁹ To circumvent the formation of vinyl byproduct **5c**, Lewis basic additives were investigated. After an extensive survey of amines, it was found that 6 equivalents of DABCO cleanly led to **6c** in 67% yield from **1c** and that the formation of **5c** was entirely suppressed (Table 1, entry 2).

Table 1. Scope of the Pd-Catalyzed 1,2-Ligand Transfer Reaction

Entry	Substrate	R	X	n	Product	Yield ^b (%)
1	1b	H	OTf	1	6b	6
2	1c	Me	OTf	1	6c	67
3	1d	<i>i</i> -Pr	OTf	1	6d	54
4	1e	<i>i</i> -Pr	OTf	2	6e	35
5	1f	Me ₃ Si	OTf	1	6f	53
6	1g	MeO	OTf	1	6g	53
7	1h	MeO	I	1	6g	40
8	1i	MeS	OTf	1	6h	63
9	1j			1	6i	63
10	1k			2	6j	35 ^c

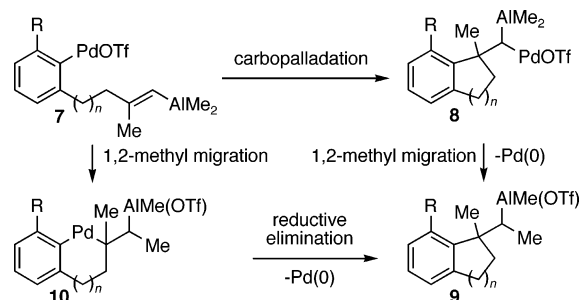
^a See the Supporting Information for details. ^b Compounds **6b–g**, **6i**, and **6j** were contaminated with <6% of the *gem*-dimethyl byproduct. Bicycle **6h** contained 19% of the *gem*-dimethyl byproduct. ^c Using Pd(PPh₃)₄ (25 mol %) in PhMe at 100 °C.

Having established a high-yielding protocol, we set out to define the scope of the methodology (Table 1). As expected, aryl triflate **1b** afforded a low yield of **6b**. Sterically demanding substrate **1d** required higher temperatures and longer reaction times to give bicycle **6d** (entry 3), while DABCO greatly reduced the formation of *gem*-dimethyl byproduct **4d**.¹⁰ Alternatively, TMS substrate **1f** smoothly reacted in 24 h at 100 °C (entry 5). Heteroatom-containing substrates **1g–i** were tolerated (entries 6–8), but aryl iodide **1h** provided a lower yield of **6g** compared to that of triflate **1g**, and thioether **1i** necessitated harsher conditions than **1g**. In contrast to **1d** and **1j**, substrates **1e** and **1k** were resilient to the cyclization reaction and resulted in the formation of the corresponding desulfonylated uncyclized byproducts in equimolar amounts (entries 4 and 10).

Two mechanistic proposals accounting for the formation of products **6** are outlined in Scheme 3. Starting from **2**, formation of **7** by oxidative insertion of Pd(0) into the aryltriflate (or iodide) is

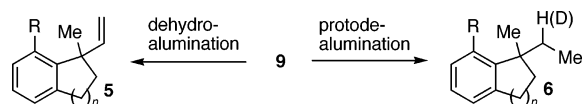
the initial step in both pathways. Alkenylalane carbopalladation generates dimetallic¹¹ species **8** that undergoes 1,2-methyl migration from aluminum to carbon with concomitant regeneration of Pd(0), leading to **9**. Alternatively, 1,2-migration of the methyl group from aluminum to carbon triggered by electrophilic palladium-triflate **7** forms palladacycle **10** that reductively eliminates to **9**.^{12,13} 5-*exo-trig*-Carbopalladation is faster than the analogous 6-*exo-trig* reaction,¹⁴ and formation of seven-membered ring palladacycle is slower than that of six-membered.¹⁵ Thus, competition between ring closure and alkenylalane cross-coupling, leading to oligomerization, may explain the lower yields obtained for **6e** and **6j**. Yield enhancement for 2,6-disubstituted aryltriflates and isolation of **3** support the carbopalladation pathway.

Scheme 3



In the absence of Lewis basic additives, intermediate **9** dehydroaluminated partially to byproduct **5** (Scheme 4).¹⁶ DABCO played a dual role in this transformation by complexing with the aluminum center: it facilitated 1,2-methyl migration, while suppressing dehydroalumination of **9** (Scheme 3).

Scheme 4



Deuteriolysis of **9g** was unsuccessful in CH₃CN and suggested premature protodealumination (Scheme 4).¹⁷ When alanes **2g** or **2h** were reacted in CD₃CN, deuterium incorporation at the C-1 position of the ethyl group confirmed the intermediacy of **9g** and the solvent as proton source in the protodealumination step. From alane **2g**, 74–95% deuterium incorporation was determined by integration of the ¹H NMR spectrum, and 70% to >95% from alane **2h**. Similarly, the cyclization of alane **2j** in CD₃CN yielded *d*₁-**6i**, with 70–80% deuterium incorporation at the C-1 position of the ethyl group. Furthermore, replacing CH₃CN by benzene in the Pd-catalyzed step allowed for deuteriolysis of the C–Al bond of intermediate **9i** with 10% DCl in D₂O to furnish tricyclic *d*₁-**6i**, for which a 39% deuterium incorporation at the C1-position of the ethyl group was determined.

In summary, we demonstrated that Pd(0) catalyzes the 1,2-ligand migration of 2,2-disubstituted-1-alkenyldimethylalanes from aluminum to carbon with concomitant intramolecular arylation at the

2-position to furnish benzylic all-carbon quaternary centers. Further results of our studies on this reaction will be reported in due course.

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Supporting Information Available: Experimental procedures and NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>. See any current masthead page for ordering information and Web access instructions.

References

- (a) Marek, I. *Tetrahedron* **2002**, *58*, 9463–9475. (b) Kocienski, P. in *Organic Synthesis via Organometallics*; Enders, D., Gais, H.-J., Keim, W., Eds.; Vieweg: Wiesbaden, 1993; pp 203–223.
- (a) Alexakis, A.; Hanaizi, J.; Jachiet, D.; Normant, J.-F.; Toupet, L. *Tetrahedron Lett.* **1990**, *31*, 1271–1274. (b) Miller, J. A. *J. Org. Chem.* **1989**, *54*, 998–1000. (c) Negishi, E.; Akiyoshi, K. *J. Am. Chem. Soc.* **1988**, *110*, 646–647. (d) Hoberg, H. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 513–514.
- Diethylation of α -imino esters by Et₂AlCl: Niwa, Y.; Shimizu, M. *J. Am. Chem. Soc.* **2003**, *125*, 3720–3721.
- (a) Negishi, E.; Van Horn, D. E.; Yoshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639–6647. (b) Van Horn, D. E.; Negishi, E. *J. Am. Chem. Soc.* **1978**, *100*, 2252–2254.
- Tricyclic **3** decomposed on standing. Retention time, MS fragmentation pattern, and ¹H NMR spectra were compared with authentic samples.
- A plausible mechanism for the formation of **3** is a Pd-carbenoid 1,4-insertion into the arene C–H bond. For other mechanisms, see: Hennessy, E. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 12084–12085.
- The yields were unaffected by the presence of Cp₂ZrCl₂, and its removal by precipitation was omitted for operational simplicity: Negishi, E.; Boardman L. D. *Tetrahedron Lett.* **1982**, *23*, 3327–3330.
- The structure of 1,7-dimethyl-1-vinylindan (**5c**) was indirectly determined by hydrogenation of the unseparable mixture to yield exclusively **6c**.
- Qadir, M.; Möchel, T.; Hii, K. K. *Tetrahedron* **2000**, *56*, 7975–7979.
- Lau, S. Y. W.; Andersen, N. G.; Keay, B. A. *Org. Lett.* **2001**, *2*, 181–184.
- (a) Fillion, E.; Taylor, N. J. *J. Am. Chem. Soc.* **2003**, *125*, 12700–12701. (b) For a review on sp³-gem-dimetallics: Marek, I.; Normant, J.-F. *Chem. Rev.* **1996**, *96*, 3241–3267.
- Alkyl 1,2-migration from boron to carbon triggered by Pd(II) complex: (a) Ishikura, M.; Hiromi, K. *Tetrahedron* **2002**, *58*, 9827–9838. (b) Ishikura, M.; Terashima, M.; Okamura, K.; Date, T. *Chem. Commun.* **1991**, 1219–1221.
- Alkenylalanes as π -nucleophiles: (a) Negishi, E.; Boardman, L. D.; Sawada, H.; Bagheri, V.; Stoll, A. T.; Tour, J. M.; Rand, C. L. *J. Am. Chem. Soc.* **1988**, *110*, 5383–5396 and references therein. ArPd(II)OTf as electrophiles: (b) Aoki, S.; Fujimura, T.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1988**, *110*, 3296–3298. For a discussion on the electrophilicity of ArPd(II) complexes: (c) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009–3066.
- Link, J. T. *Org. React.* **2002**, *60*, 157–534.
- Tietze, L. F.; Schimpf, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1089–1091.
- Dehydroalumination at elevated temperature has been reported: Eisch, J. J.; Fichter, K. C. *J. Organomet. Chem.* **1983**, *250*, 63–81.
- Eisch, J. J.; Manfre, R. J.; Komar, D. A. *J. Organomet. Chem.* **1978**, *159*, C13–C19.

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