Pergamon

Tetrahedron Letters 40 (1999) 1451–1454

TETRAHEDRON LETTERS

Cyclization/Hydrosilylation of Functionalized 1,7-Dienes to Form Substituted Six-Membered Carbocycles.

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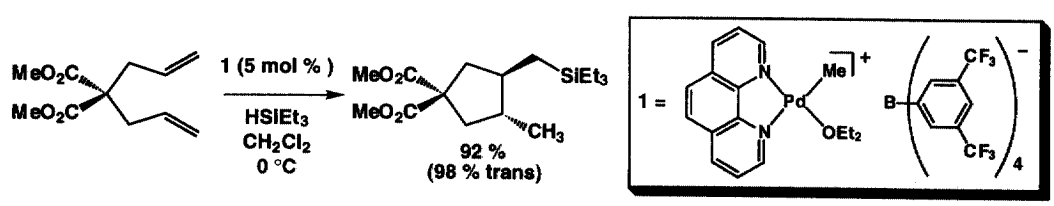
Received 11 December 1998; revised 21 December 1998; accepted 22 December 1998

Abstract: The cationic palladium complex (phen)Pd(Me)$(OEt_2)^+$ BAr_4^- [phen = 1,10-phenanthroline; Ar = 3,5-$C_6H_3(CF_3)_2$] catalyzed the cyclization/hydrosilylation of functionalized 1,7-dienes to form silylated cyclohexanes in good yield and with moderate to good trans-selectivity.

Keywords: catalysis, cyclization, dienes, palladium

We recently reported that the cationic Pd(II) complex (phen)PdMe$(OEt_2)^+$ BAr_4^- [phen = 1,10-phenanthroline; Ar = 3,5-$C_6H_3(CF_3)_2$] (**1**) in CH_2Cl_2 serves as an effective catalyst for the cyclization/hydrosilylation of 1,6-dienes to form silylated cyclopentane derivatives (Scheme 1).[1-3] The potential of this protocol stems from its high reactivity, good functional group compatibility, low air- and moisture-sensitivity, and high trans-selectivity of ring closure. Because six-membered carbocycles represent the most common ring size found in naturally occurring compounds, we hoped to apply our cyclization/hydrosilylation protocol to the synthesis of silylated cyclohexane derivatives. Unfortunately, our initial attempts to cyclize 1,7-dienes employing **1** met with limited success. However, our recent discovery that 1,2-dichloroethane (DCE) is a superior solvent to methylene chloride for both the Pd-catalyzed cyclization/hydrosilylation of 1,6-dienes[4] and the cyclization of alkenylsilanes[5] has led to the development of an effective protocol for the cyclization of 1,7-dienes to form silylated cyclohexanes. Here we report our initial results in this area.



Scheme 1

0040-4039/99/$ - see front matter
PII: S0040-4039(99)00022-2

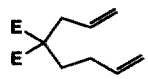
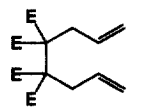
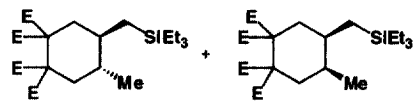
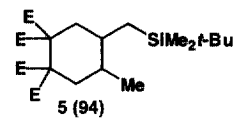
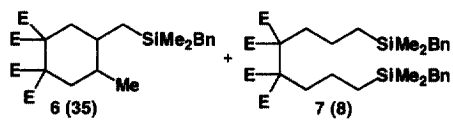
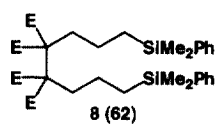
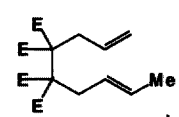
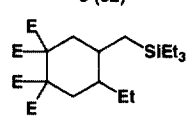
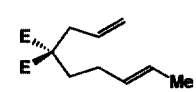
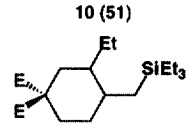
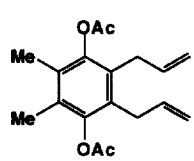
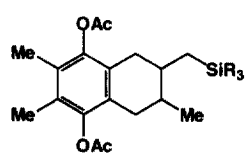
We began our study employing dimethyl-4,4-dicarboxy-1,7-octadiene (**2**). Treatment of **2** with triethylsilane and **1** (5 mol %) led to rapid and complete consumption of starting material, but formed an intractable mixture of mono-silylated products in 71 % combined yield (Table 1, entry 1). We reasoned that the lack of selectivity arose, at least in part, from indiscriminate attack of the Pd–Si intermediate on either olefin of the diene.[1] In an effort to circumvent this problem, we employed the symmetric tetracarboxylate derivative **3**. Reaction of **3** with triethylsilane and **1** (5 mol %) was complete within 5 min at room temperature with formation of a 22:1 mixture of trans:cis silylated cyclohexanes **4** (entry 2). Evaporation of solvent and flash chromatography of the residue gave *trans*-**4** in 93% and *cis*-**4** in 3% yield.[6] Diene **3** also reacted with dimethyl-*t*-butylsilane to give carbocycle **5** in good yield and with good diastereoselectivity (entry 3). However, reaction of **3** with dimethylbenzylsilane led to formation of both carbocycle **6** and disilylated-uncyclized product **7** (entry 4), while reaction of **3** with dimethylphenylsilane led to exclusive formation of the disilylated product **8** (entry 5).

The cyclization/hydrosilylation protocol tolerated substitution at the terminal olefinic carbon atom. For example, reaction of triethylsilane with substituted tetracarboxylate derivative **9** in the presence of **1** (10 %) formed carbocycle **10** in 51 % yield as a single isomer by NMR spectroscopy (entry 6). The substituted dicarboxylate derivative **11** also reacted with triethylsilane in the presence of **1** (5 %) to form carbocycle **12** in 68 % yield as a 1.6:1 mixture of trans:cis isomers (entry 7). We have also applied this protocol to the formation of fused bicyclic compounds employing acylated 2,3-diallyl-4,5-dimethylhydroquinone derivative **13**. For example, treatment of **13** with triethylsilane in the presence of **1** (5 mol %) led to the isolation of the corresponding fused bicycle **14** in 64 % yield as a 6:1 mixture of trans:cis diastereomers (entry 8). Higher catalyst loading (10 %) led to dramatic improvement in the yield (99 %) as well as slight improvement in diastereoselectivity (8:1) (entry 9). Diene **13** also reacted with dimethylphenylsilane, dimethylbenzylsilane, and dimethyl-*t*-butylsilane to form bicycles **15** - **17**, respectively, in fair to good yield and with good trans selectivity (entries 10-12).

In summary, we have shown that **1** in DCE solvent serves as an effective catalyst system for the cyclization/hydrosilylation of selected 1,7-dienes to form silylated cyclohexanes. However, formation of six-membered rings employing **1** is clearly less favorable than is the formation of five-membered carbocycles. For example, cyclization of 1,7-dienes was typically slower, required higher catalyst loading, and gave lower trans-selectivity than did the cyclization of 1,6-dienes. In addition, cyclization of 1,7-dienes with sterically hindered silanes or cyclization of substituted dienes tended to form silylated-uncyclized products in addition to the desired carbocycles. This behavior is not surprising as palladium complexes are typically more effective for the formation of five-membered rings than for the corresponding six-membered rings.[7] We are currently working towards the development of more active catalysts for the cyclization/hydrosilylation of 1,7-dienes.

Acknowledgments. R.W. thanks the Camille and Henry Dreyfus Foundation for a New Faculty Award. Additional funding was provided by the Petroleum Research Fund.

Table 1. Cyclization/hydrosilylation of 1,7-dienes catalyzed by **1** in 1,2-dichloroethane at 25 °C.

Entry	Diene	Silane	Silylated product(s) (% isolated yield)[a]	% Pd	Time	trans:cis ratio[b]
1	 2 (E = CO_2Me)	$HSiEt_3$	mono-silylated products (71)	5	30 min	—
2	 3 (E = CO_2Et)	$HSiEt_3$	 *trans*-4 (93) + *cis*-4 (3)	5	15 min	22:1
3		$HSiMe_2t$-Bu	 5 (94)	5	3 h	>25:1[c]
4		$HSiMe_2Bn$	 6 (35) + 7 (8)	5	45 min	>25:1[c]
5		$HSiMe_2Ph$	 8 (62)	5	2 h	—
6	 9 (E = CO_2Et)[d]	$HSiEt_3$	 10 (51)	10	90 min	>25:1[c]
7	 11 (E = CO_2Me)[d]		 12 (68)	5	2 h	1.6:1
8	 13	$HSiEt_3$	 14 (64)	5	30 min	6:1
9			14 (99)	10	20 min	8:1
10		$HSiMe_2Ph$	15 (93)	10	1 h	12:1
11		$HSiMe_2Bn$	16 (40)	10	15 min	20:1
12		$HSiMe_2t$-Bu	17 (35)	10	2 h	20:1

[a]Yields refer to material of >95 % purity as determined by ^1H NMR and GC analysis. All new compounds characterized by ^1H and ^{13}C NMR spectroscopy, IR spectroscopy, combustion analysis, and/or HRMS. [b]cis-trans Ratio of the carbocyclic product determined by capillary GC or HPLC analysis of the crude reaction mixture. [c]Determined by ^1H and ^{13}C NMR analysis. [d]4:1 Mixture of trans:cis isomers.

References and Notes

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6) Synthesis and NMR data for *cis*-**4** and *trans*-**4**: Diene **3** (100 mg, 0.25 mmol) and triethylsilane (350 mg, 3.01 mmol) were added sequentially via syringe to a solution of **1** (0.013 mmol) [generated in situ from (phen)$PdMe_2$ (4 mg, 0.013 mmol) and $HBAr_4^- \cdot (Et_2O)_2$ (13 mg, 0.013 mmol)][8] in DCE (10 mL) at 0° C and then stirred for 10 minutes at room temperature. The resulting brown solution was concentrated under vacuum and the residue was chromatographed (SiO_2, 9:1 hexane:EtOAc) to give *trans*-**4** (120 mg, 93%) and *cis*-**4** (4 mg, 3 %) as colorless oils. *trans*-**4**: ^1H NMR: δ 4.23-4.10 (m, 8 H), 2.26 (dd, J = 4.1, 14.2 Hz, 1 H), 2.15 (dd, J = 4.1, 14.3 Hz, 1 H), 2.07 (dd, J = 12.1, 14.0 Hz, 1 H), 1.97 (dd, J = 12.1, 14.2 Hz, 1 H), 1.22 (t, J = 6.2 Hz, 12 H), 0.898 (t, J = 7.9 Hz, 9 H), 0.896 (d, J = 6.27 Hz, 3 H), 0.50 (q, J = 7.9 Hz, 6 H), 0.22 (dd, J = 10.5, 14.96 Hz, 1 H), 1.50-1.35 (m, 2 H), one $SiC\underline{H}_2CH_3$ proton obscured. $^{13}C\{^1H\}$ NMR: δ 170.8, 169.5, 169.4, 65.8, 61.5, 61.4, 61.2, 61.1, 59.5, 58.7, 37.4, 37.2, 35.2, 34.9, 19.8, 15.7, 15.2, 13.8, 13.73, 13.72, 7.3, 3.9. *cis*-**4**: ^1H NMR: 4.22-4.09 (m, 8 H), 2.08-1.93 (m, 4 H), 1.50-1.35 (m, 2 H), 1.24 (t, J = 7.2 Hz, 12 H), 0.90 (d, J = 6.3 Hz, 3 H), 0.89 (t, J = 8.0 Hz, 9 H), 0.46 (q, J = 8.0 Hz, 6 H), $SiC\underline{H}_2CH_3$ protons obscured.

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