Pergamon

Tetrahedron Letters 42 (2001) 203–206

TETRAHEDRON
LETTERS

Silicon-tethered Heck reaction

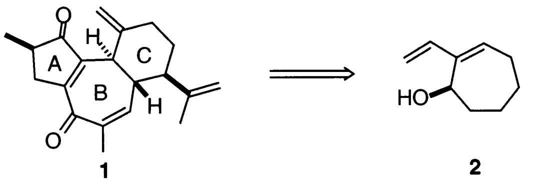
Anand Mayasundari and David G. J. Young*

Department of Chemistry, University of Tennessee, Knoxville, Knoxville, TN 37996, USA

Received 9 August 2000; revised 12 October 2000; accepted 13 October 2000

Abstract—An approach to the synthesis of semicyclic dienes is described. The method employs a silicon-tethered version of the Heck reaction. © 2000 Elsevier Science Ltd. All rights reserved.

Curcusone A (**1**) has attracted interest from the anticancer field due to its ability to enhance hyperthermic oncotherapeutics in the Chinese hamster.[1] As part of a synthetic plan directed towards **1**, **2** was envisioned as a B-ring building block for the tricyclic nucleus (Scheme 1).[2] At the onset of our studies, few approaches to the substitution pattern of **2** had been described, which led to the studies reported here.[3]

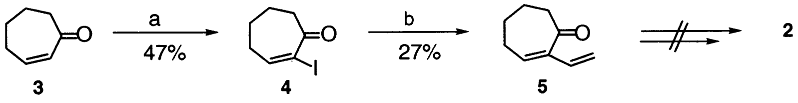


Scheme 1. General synthetic approach to curcusone A.

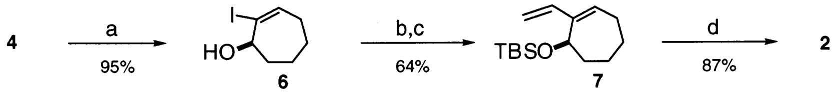
The first approach to **2** involved iodination of **3** to give **4** (Scheme 2).[4] Application of Johnson's modified Stille conditions to **4** afforded **5** in low yield.[5–7] It was expected that 1,2-reduction of **5** would complete our approach to **2**; however, the standard reagents for reduction (lithium aluminum hydride,[8] diisobutylaluminum hydride,[9] and sodium borohydride with or without cerium trichloride[10,11]) failed to produce **2** in meaningful yield.

Luche reduction of **4**, which contains a stronger chelating group at C2, provided **6** in 95% yield (Scheme 3). Attempts to couple **6** with vinyl organometallics were problematic, but **2** could be obtained via the *tert*-butyldimethylsilyl ether derived from **6**.[12]

Due to the toxicity of the reagents in Scheme 3, our attention turned to the silicon-based approach in Scheme 4.[13] The regiochemistry of alkenylation (**8**→**9**



Scheme 2. (a) I_2, Pyr, CCl_4; (b) $Bu_3SnCH{=}CH_2$, $Pd(PhCN)_2Cl_2$, CuI, Ph_3As, NMP.

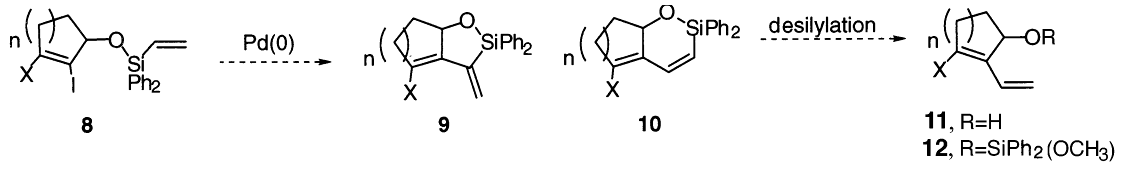


Scheme 3. (a) $NaBH_4$, $CeCl_3{\cdot}7H_2O$; (b) TBSCl, Imid.; (c) $Bu_3SnCH{=}CH_2$, $Pd(PhCN)_2Cl_2$, CuI, Ph_3As, NMP; (d) Bu_4NF.

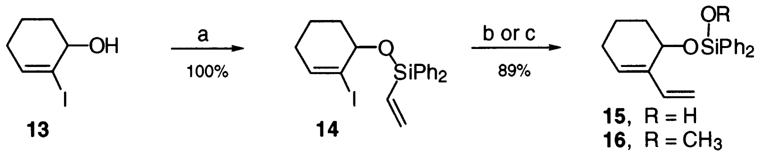
Keywords: vinyl silanes; vinylation; dienes; palladium.

* Corresponding author.

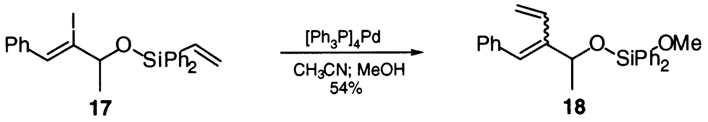
PII: S0040-4039(00)01910-9



Scheme 4.



Scheme 5. (a) $Ph_2(CH_2{=}CH)SiCl$, DMAP; (b) $(Ph_3P)_4Pd$, Et_3N, CH_3CN; H_2O (c) $(Ph_3P)_4Pd$, Et_3N, CH_3CN; CH_3OH.



Scheme 6.

+**10**) was not a concern here since desilylation of either heterocycle was expected to produce **11**.[14,15]

Substrates for the proposed Heck reaction were prepared from the corresponding α-iodocycloalkenols (Scheme 5).[16,17] Treatment of **14** with 10 mol% of tetrakis(triphenylphosphine)palladium(0) produced **15**, which contained the silicon analog of a hemiacetal. Moreover, mixed acetals could be obtained from this reaction by quenching with alcoholic solvents. Methanol, for example, led to the isolation of **16** in good yield. In practice, purification of acetals was easier than hemiacetals, so products were generally isolated as such.

Table 1. Conversion of **14** to **15** in Et_3N, CH_3CN; H_2O

Catalyst	Conditions	% **15**
$Pd(Ph_3P)_4$	12 h, 50	61
$Pd(Ph_3P)_4$	12 h, rt	89
$Pd_2(dba)_3(CHCl_3)$	20 h, rt	39
$Pd(dba)_2$	48 h, 60	30
$Pd(OAc)_2$, Ph_3P	74 h, rt	35

Table 2. Reaction of **8** with $Pd(Ph_3P)_4$, Et_3N, CH_3CN; MeOH

Entry #	Compound	*n*	X	% **12**
1	**8a**	1	H	86
2	**8b**	2	Me	57
3	**8c**	3	H	46

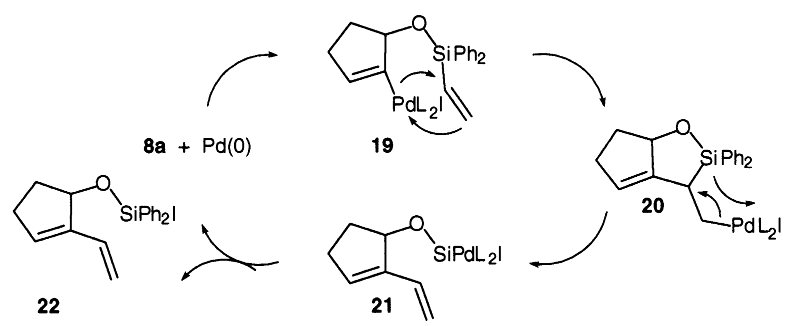
The only acyclic case studied was **17** which produced a 2:1 *E*–*Z* mixture of dienes **18** and suggested the involvement of an unstable vinyl palladate intermediate (Scheme 6).

As shown in Table 1, tetrakis(triphenylphosphine)palladium(0) faired better than palladium acetate or dibenzylideneacetone. Decomposition of starting material occurred at higher temperatures; thus lower temperatures afforded higher yields. The runs in Table 1 employed **14** as the substrate and used a 10 mol% catalyst loading.

Treatment of **8a**–**c** with tetrakis(triphenylphosphine)palladium(0) afforded silylacetals **12a**–**c** (Table 2). The reaction gave good yields of small-ring compounds (entry 1). β-Substitution on the alkene gave lower yields, but was not detrimental (entry 2). The transfer was less efficient in the seven-membered ring case (entry 3).

A hypothetical mechanism is presented in Scheme 7. Oxidative insertion of palladium into **8a** affords **19**. This is followed by insertion of the silylethenyl group into the palladium–alkene bond of **19** to afford **20**. A β-silyl elimination step affords **21**. The catalytic cycle is completed via reductive elimination to produce **22** and regenerate Pd(0).[18]

In summary, a silicon-tethered version of the Heck reaction has been developed. The reaction involves an electrophilic silyl ether intermediate and a β-silyl elimination step. The reaction is useful for alkenylation of five- and six-membered rings, but less efficient for medium rings.[19] Further studies will be reported in due course.[20]



Scheme 7. Proposed catalytic cycle.

Acknowledgements

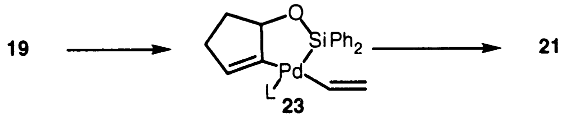
Support provided by the University of Tennessee, Knoxville is gratefully acknowledged.

References

1. Picha, P.; Naengchomnong, W.; Promratanapongse, P.; Kano, E.; Hayashi, S.; Ohtsubo, T.; Zhang, S. W.; Shioura, H.; Kitai, R.; Matsumoto, H.; Kawahara, K.; Puribhat, S.; Phanthumachinda, P. *J. Exp. Clin. Cancer Res.* **1996**, *15*, 2, 177.
2. Naengchomnong, W.; Thebtaranonth, Y.; Wiriyachitra, P.; Okamoto, K. T.; Clardy, J. *Tetrahedron Lett.* **1986**, *27*, 2439–2442.
3. (a) Herz, W.; Rouh-Rong, J. *J. Org. Chem.* **1985**, *50*, 618. (b) Hoye, T. R.; Rother, M. J. *J. Org. Chem.* **1979**, *44*, 458.
4. (a) Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W.; Wovkulich, P. M.; Uskokovic, M. R. *Tetrahedron Lett.* **1992**, *33*, 917. (b) Bovonsombat, P.; Angara, G. J.; McNelis, E. *Tetrahedron Lett.* **1994**, *35*, 6787.
5. Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W. *Tetrahedron Lett.* **1992**, *33*, 919.
6. Negishi, E.; Owczarczyk, Z. R.; Swanson, D. R. *Tetrahedron Lett.* **1991**, *32*, 4453.
7. Farina, V.; Krishnamurthy, V.; Scott, W. *Org. React.* (*NY*) **1997**, *50*, 1.
8. Jackson, W. R.; Zurqiyah, A. *J. Chem. Soc.* **1965**, 5280.
9. Trost, B. M.; Jungheim, L. N. *J. Am. Chem. Soc.* **1980**, *102*, 7910.
10. Johnson, M. R.; Rickborn, B. *J. Org. Chem.* **1970**, *35*, 1041.
11. Germal, A. L.; Luche, J. L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.
12. The Carreno procedure could be used to produce **2**. Carreno, M. C.; Urbano, A.; Di Vitta, C. *J. Org. Chem.* **1998**, *63*, 8320.

$$\mathbf{6} \xrightarrow[\text{(0.01 mol\%) Pd(Ph}_3\text{P)}_4\ 64\%]{\text{(CH}_2\text{=CH)MgBr (2 equiv.)}} \mathbf{2}$$

13. (a) Bols, M.; Skrydstrup, T. *Chem. Rev.* **1995**, 1253. (b) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063.
14. (a) Bols, M.; Skrydstrup, T. *Chem. Rev.* **1995**, *95*, 1253. (b) Hale, M. R.; Hoveyda, A. H. *J. Org. Chem.* **1992**, *57*, 1643. (c) Koot, W.-J.; VanGinkel, R.; Kranenburg, M.; Hiemstra, H.; Louwrier, S.; Moolenaar, M. J.; Speckcamp, W. N. *Tetrahedron Lett.* **1991**, *32*, 401.
15. Karabelas, K.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 4909.
16. Sieburth, S.; Fensterbank, L. *J. Org. Chem.* **1992**, *57*, 5279.
17. Dieck, H. A.; Heck, R. F. *J. Org. Chem.* **1975**, *40*, 1083.
18. It was suggested by a reviewer that oxidative insertion of palladium into the silicon–carbon bond of **19** could produce **23**, which could reductively eliminate to afford **21**.



19. A study on alkenylation of aromatics appeared during the course of these studies, see: Teng, Z.; Keese, R. *Helv. Chim. Acta* **1999**, *82*, 515.
20. Selected spectroscopic data for new compounds: Compound **5**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 6.45 (t, 1H), 6.26 (dd, 1H), 5.32 (d, 1H), 4.99 (d, 1H), 2.51 (m, 2H), 2.32 (m, 2H), 1.65 (m, 4H). For **6**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 6.57 (t, 1H, $J=7.0$ Hz), 4.40 (d, 1H, $J=7.0$ Hz), 2.29–2.15 (m, 1H), 2.03–1.89 (m, 2H), 1.76–1.49 (m, 5H), 0.91 (s, 9H), 0.15 (s, 3H), 0.08 (s, 3H); HRMS (EI) calcd for $C_9H_{16}IOSi$ ($M^+-C_4H_9$) m/z 295.0015, found m/z 295.0024. For **7**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 6.60 (t, 1H, $J=7.1$ Hz), 4.31 (t, 1H, $J=5.1$ Hz), 2.36 (d, 1H, $J=5.0$ Hz), 2.21–1.47 (m, 8H); HRMS (EI) calcd for $C_7H_{11}IO$ (M^+) m/z 237.9855, found m/z 237.9857. Compound **8a**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 7.74–7.71 (m, 4H), 7.49–7.37 (m, 6H), 6.45 (dd, 1H, $J=20.1$, 15.0 Hz), 6.37–6.27 (m, 2H), 5.98 (dd, 1H, $J=20.1$, 3.9 Hz), 4.93–4.88 (m, 1H), 2.54–2.39 (m, 1H), 2.27–2.06 (m, 2H), 1.98–1.52 (m, 1H); HRMS (EI) calcd for $C_{19}H_{19}IOSi$ (M^+) m/z 418.025, found m/z 418.029. For **8b**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 7.76–7.73 (m, 4H), 7.48–7.31 (m, 6H), 6.66 (dd, 1H, $J=20.2$, 14.4 Hz), 6.23 (dd, 1H, $J=14.8$, 3.8 Hz), 5.97 (dd, 1H, $J=20.2$, 3.8 Hz), 4.50 (s, 1H), 2.30–1.96 (m, 2H), 1.91 (s, 3H), 1.83–1.72 (m, 3H), 1.65–1.57 (m, 1H); HRMS (EI) calcd for $C_{21}H_{23}IOSi$ (M^+) m/z 446.0563, found m/z 446.0553. For **8c**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 7.76–7.71 (m, 4H), 7.51–7.32 (m, 6H), 6.70–6.56 (m), 6.34 (dd, 1H, $J=14.8$, 3.9 Hz), 5.98 (dd, 1H, $J=20.1$, 3.9 Hz), 4.63–4.60 (m, 1H), 2.38–2.25 (m, 1H), 2.06–1.94 (m, 1H), 1.81–1.48 (m, 5H); HRMS (EI) calcd for $C_{21}H_{23}IOSi$ (M^+) m/z 446.0563, found m/z 446.0548. For **12a**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 7.74–7.60 (m, 4H), 7.46–7.27

(m, 6H), 6.47 (dd, 1H, $J = 17.6$, 10.9 Hz), 5.91 (s, 1H), 5.39 (d, 1H, $J = 17.6$ Hz), 5.21–5.09 (m, 2H), 3.60 (s, 3H), 2.60–2.48 (m, 1H), 2.37–1.91 (m, 3H); HRMS (EI) calcd for $C_{20}H_{22}O_2Si$ (M$^+$) m/z 322.1389, found m/z 322.1393. For **12b**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.80–7.63 (m, 4H), 7.52–7.24 (m, 6H), 6.40 (dd, 1H, $J = 17.7$, 11.0 Hz), 5.26 (d, 1H, $J = 17.7$ Hz), 5.04 (d, 1H, $J = 11.0$ Hz), 4.69 (t, 1H, $J = 3.0$ Hz), 3.54 (s, 3H), 2.31–1.95 (m, 4H), 1.82 (s, 3H), 1.66–1.44 (m, 2H). For **12c**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.69–7.59 (m, 4H), 7.51–7.28 (m, 6H), 6.22 (dd, 1H, $J = 17.5$, 10.9 Hz), 5.96 (m, 1H), 4.94–4.77 (m, 3H), 3.52 (s, 3H), 2.70–2.58 (m, 1H), 2.33–2.06 (m, 2H, 1.96–1.66 (m, 3H), 1.55–1.34 (m, 2H); HRMS (EI) calcd for $C_{22}H_{26}O_2Si$ (M$^+$) m/z 350.1702, found m/z 350.1711. For **14**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.74–7.70 (m, 4H), 7.48–7.29 (m, 6H), 6.62 (dd, 1H, $J = 20.3$, 14.9 Hz), 6.52 (t, 1H, $J = 3.9$ Hz), 6.32 (dd, 1H, $J = 14.9$, 3.7 Hz), 5.96 (dd, 1H, $J = 20.4$, 3.9 Hz), 4.37 (s, 1H), 2.21–1.74 (m, 5H), 1.64–1.56 (m, 1H). For **15**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.75–7.61 (m, 4H), 7.47–7.28 (m, 6H), 6.29 (dd, 1H, $J = 17.7$, 11.0 Hz), 5.90 (m, 1H), 5.24 (d, 1H, $J = 17.6$ Hz), 4.97 (d, 1H, $J = 11.0$ Hz), 4.73 (t, 1H, $J = 3.0$ Hz), 2.91 (s, 1H), 2.27–1.87 (m, 4H), 1.67–1.50 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 138.1, 137.2, 134.7, 134.2, 132.1, 130.2, 127.8, 127.7, 111.5, 64.5, 31.7, 25.8, 16.8. For **16**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.76–7.61 (m, 4H), 7.52–7.27 (m, 6H), 6.32 (dd, 1H, $J = 17.7$, 11.0 Hz), 5.93 (m, 1H), 5.28 (d, 1H, $J = 17.7$ Hz), 5.00 (d, 1H, $J = 11.0$ Hz), 4.69 (t, 1H, $J = 3.0$ Hz), 3.64 (s, 3H), 2.31–1.95 (m, 4H), 1.66–1.44 (m, 2H); HRMS (EI) calcd for $C_{21}H_{24}O_2Si$ (M$^+$) m/z 336.1546, found m/z 336.1559. For **17**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.68–7.63 (m, 4H), 7.54–7.25 (m, 11H), 6.94 (s, 1H), 6.51 (dd, 1H, $J = 20.1$, 14.8 Hz), 6.28 (dd, 1H, $J = 14.8$, $J = 4.0$ Hz), 5.94 (dd, 1H, $J = 20.1$, 4.0 Hz), 4.35 (q, 1H, $J = 6.0$ Hz), 1.43 (d, 3H, $J = 6.0$ Hz); HRMS (EI) calcd for $C_{24}H_{23}IOSi$ (M$^+$) m/z 482.0563, found m/z 482.0552.