Pergamon

Tetrahedron Letters, Vol. 35, No. 12, pp. 1829-1832, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0186-2

A Convenient Procedure for the Synthesis of Enyne-Allenes

Kung K. Wang* and Zhongguo Wang

Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506.

Abstract: Bromoboration of 1-hexyne with BBr_3 followed by treatment with 2-propanol produced alkenyl boronic ester **3**. Subsequent Pd(0)-catalyzed cross-coupling with acetylenic zinc chlorides and iodination furnished enyne iodides **6**, which were then converted to enyne-allenes **8** by a second Pd(0)-catalyzed reaction with allenic zinc chlorides.

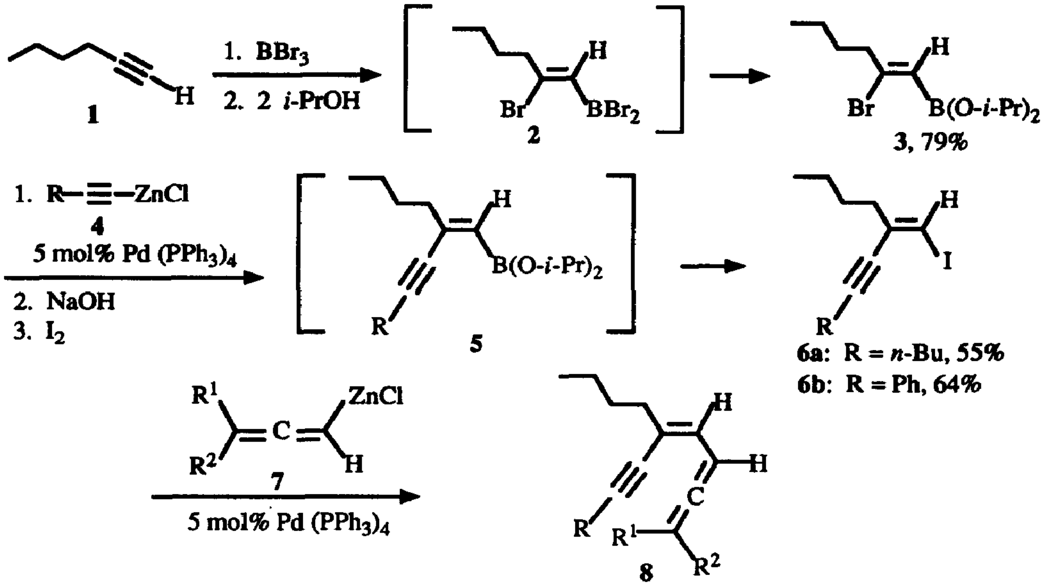
We recently reported a new synthetic route to (*Z*)-1,2,4-heptatrien-6-ynes (enyne-allenes) and the use of these enyne-allenes for synthetic applications through biradical intermediates.[1] The ease of initiating the Myers cyclization reaction under mild thermal conditions to produce the α,3-dehydrotoluene biradicals[2] coupled with the ability to move the radical centers around within the molecule provide opportunities for generating other reactive species for synthetic elaborations. We have since developed an alternative synthetic method for enyne-allenes by bromoboration of a terminal alkyne with BBr_3 followed by consecutive Pd(0)-catalyzed coupling reactions with organozinc chlorides derived from terminal alkynes and allenes. The simplicity of the procedure together with the ready availability of a variety of terminal alkynes and allenes make it possible to synthesize enyne-allenes with diverse chemical structures.

Bromoboration of 1-hexyne (**1**) with BBr_3[3] followed by treatment with 2-propanol[4] furnished alkenylboronic ester **3** in 79% isolated yield (Scheme 1). Conversion of the initially formed alkenyldibromoborane **2** to the chemically more stable **3** allowed the isolation of **3** by distillation. Because bromoboration of terminal alkynes with BBr_3 proceeds with cis addition of the bromine-boron bond to the triple bond, **3** having predominantly the *Z* geometry (*Z*:*E* = 96:4) was obtained. We also observed that **3** appeared to isomerize slowly to produce a substantial amount of the *E* isomer on storage. This isomerization process may be responsible for the presence of about 4% of the *E* isomer in the initially isolated material.

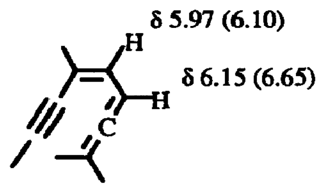
Conversions of **3** to enyne iodides **6** were achieved in a one-pot operation by first using the Pd(0)-catalyzed cross-coupling reaction of **3** with alkynylzinc chlorides **4**,[3,5] prepared by treating the corresponding 1-lithio-1-alkynes with anhydrous zinc chloride, to produce enyne boronic esters **5**. Alkenylboronic esters have been shown to be easily converted to the corresponding alkenyl iodides with retention of configuration by simply treating with iodine.[4,6] Indeed, the transformation was also successful in the cases with **5** to yield **6** (R = *n*-Bu, 55% isolated yield, *Z*:*E* = 96:4; R = Ph, 64% isolated yield, *Z*:*E* = 96:4).

The use of Pd(0) as a catalyst to promote cross-coupling of alkenyl iodides and allenic organometallics to afford conjugated allenenes has been shown to be very efficient under mild reaction temperatures and with retention of configuration of the alkenyl group.[7] The mildness of the reaction condition makes this synthetic protocol especially attractive and suitable for the purpose of producing thermally labile enyne-allenes from **6**. It was gratifying to observe that the Pd(0)-catalyzed cross-coupling between **6** and allenylzinc chlorides **7** proceeded smoothly to furnish the desired enyne-allenes **8** in good isolated yields and with high geometric purity (Table 1). Enyne-allenes **8** were stable enough to allow purification by column chromatography at room temperature. However, cycloaromatization did appear to occur on prolonged storage (approximately 10 days) at 0° C.

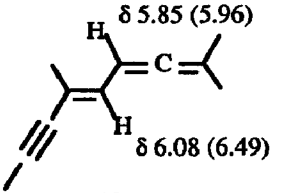
Scheme 1



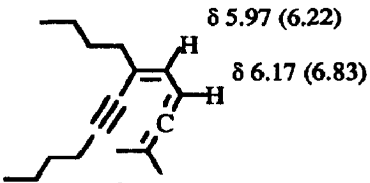
The assignment of the *Z* geometry to the double bond of **8** is based on the comparison of the chemical shifts of the vinylic and allenic hydrogens with those of enyne-allenes reported earlier.[1] For example, the chemical shifts of the vinylic and allenic hydrogens of **8a** in CDCl$_3$ are virtually identical to those of **9**, whereas large discrepancies exist with those of **10**.[1a] On the other hand, minor peaks (4%) at δ 6.09 (vinylic) and 5.89 (allenic), attributed to the minor *E* isomer of **8a**, are in close agreement with those of **10**. It is interesting to note that a much larger difference of chemical shifts was observed between signals of the vinylic and the allenic hydrogens in C$_6$D$_6$ solvent (numbers in parentheses). The double bond geometry of **9** and **10** has been firmly established on the basis of the nuclear Overhauser effect.



9



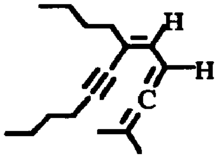
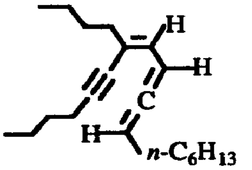
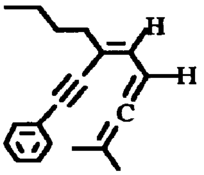
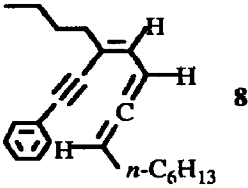
10



8a

The following procedure for the synthesis of **8a** is representative. To a solution of 25.1 g of BBr$_3$ (9.5 mL, 100 mmol) in 50 mL of dry pentane under a nitrogen atmosphere at -78 °C was added dropwise by a syringe 11.5 mL (8.2 g, 100 mmol) of 1-hexyne.[3] After 1 h at -78 °C, the reaction mixture was allowed to warm to room temperature. After an additional 2 h, the reaction mixture was transferred via cannula into a second flask containing a mixture of 50 mL of 2-propanol and 50 mL of pentane at -10 °C.[4] After 30 min at -10 °C, the top layer was separated, and the bottom layer was extracted with cold pentane (3 x 20 mL). The top layer and the pentane extracts were combined and concentrated. The residue was then distilled at reduced pressure (58-60 °C, 0.15 Torr) to afford 22.9 g of **3** (79%, *Z*:*E* = 96:4) as a colorless liquid: IR (neat) 2973, 2933, 2874, 1638, 1466, 1418, 1379, 1321, 1224, 1118, 985, 942, 835, 655 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 5.96 (1 H, s), 4.40 (2 H, septet, *J* = 6.1 Hz), 2.48 (2 H, t, *J* = 7.4 Hz), 1.55 (2 H, quintet, *J* = 7.1 Hz), 1.32 (2 H, sextet, *J* = 7.5 Hz), 1.18 (6 H, d, *J* = 6.0 Hz), 0.91 (3 H, t, *J* = 7.2 Hz); ^{13}C NMR (CDCl$_3$) δ 138.72, 123.4 (very broad, C-B), 66.48, 43.85, 30.17, 24.46, 21.58, 13.79; MS m/e 277, 275 (M$^+$-15 with ^{11}B), 211 (M$^+$-Br), 191,

Table 1. Stereoselective Synthesis of Enyne-Allenes

enyne-allenes	isolated yield[a]	isomer ratio,[b] *Z*:*E*
 **8a**	78%	96:4
 **8b**	68%	96:4
 **8c**	81%	96:4
 **8d**	74%	96:4

[a] The isolated products were characterized by IR, ^{1}H (270 MHz) and ^{13}C (67.9 MHz) NMR,[8] and MS.
[b] Determined by integration of the ^{1}H NMR spectrum.

125, 111, 87. Anal. Calcd for $C_{12}H_{24}BBrO_2$: C, 49.51; H, 8.33. Found: C, 49.14; H, 8.16.

To a 100-mL flask were added 1.45 g of **3** (5.0 mmol), 0.28 g of $Pd(PPh_3)_4$ (0.25 mmol), and 15 mL of dry THF. The resulting mixture was degassed by three cycles of freeze-thaw and kept under a nitrogen atmosphere with stirring for 45 min at room temperature. In a second flask, 1-hexynylzinc chloride was prepared by treating a degassed solution of 0.49 g of 1-hexyne (6.0 mmol) in 5 mL of THF with 2.2 mL of a 2.5 M solution of *n*-butyllithium in hexanes for 5 min followed by the addition of a degassed solution of 0.75 g of anhydrous $ZnCl_2$ (5.5 mmol) in 6 mL of THF. The solution of 1-hexynylzinc chloride was then transferred via cannula to the flask containing **3** at room temperature. After 5 min, the reaction mixture was heated to reflux for 3 h before cooling to 0 °C and was treated sequentially with 7 mL of 6 N NaOH and 3.8 g of I_2 (15 mmol) in 20 mL of Et_2O. After 1 h of stirring at room temperature, excess saturated $Na_2S_2O_3$ was introduced to reduce I_2. An additional 30 mL of Et_2O was added, and the organic layer was then separated. The aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (silica gel / hexane) to furnish 0.80 g of **6a** (55%, *Z*:*E* = 96:4) as a light yellow liquid: IR (neat) 3058, 2958, 2932, 2872, 2220, 1577, 1465, 1429, 1378, 1363, 1327, 1297, 1149, 1104, 929, 765 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.27 (1 H, s), 2.38 (2 H, t, *J* = 6.8 Hz), 2.23 (2 H, dt, *J* = 1.1 and 7.4 Hz), 1.64-1.42 (6 H, m), 1.30 (2 H, sextet, *J* = 7.7 Hz), 0.93 (3 H, t, *J* = 7.2 Hz), 0.89 (3 H, t, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 137.69, 97.45, 81.72, 81.66, 38.94, 30.59, 30.35, 21.93, 21.86, 19.30, 13.80, 13.59; MS m/e 290 (M^+), 248, 233, 205, 163, 127, 121, 107, 105, 93, 91, 79.

To a degassed solution of 0.204 g of 3-methyl-1,2-butadiene (3.0 mmol) in 8 mL of THF at -70 °C was added 1.2 mL of a 2.5 M solution of *n*-butyllithium in hexanes.[9] After 1 h at -60 °C, a degassed solution of 0.422 g of anhydrous zinc chloride (3.1 mmol) in 5 mL of THF was introduced via cannula followed by a degassed mixture containing 0.87 g of **6a** (3.0 mmol) and 0.173 g of $Pd(PPh_3)_4$ (0.15 mmol) in 6 mL of THF. The reaction mixture was then charged with 2 mL of HMPT and allowed to warm to room temperature. After 2 h of stirring, 30 mL of saturated NH_4Cl and 30 mL of pentane were added, and the organic layer was separated. The aqueous layer was extracted with pentane (3 x 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (silica gel / hexane) to give 0.537 g of **8a** (78%, *Z*:*E* = 96:4) as a light yellow liquid: IR (neat) 2958, 2933, 2860, 2220, 1947, 1600, 1466, 1406, 1377, 1362, 1223, 831 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.17 (1 H, d of septet, *J* = 10.8 and 2.8 Hz), 5.97 (1 H, d, *J* = 10.8 Hz), 2.39 (2 H, t, *J* = 6.9 Hz), 2.12 (2 H, t, *J* = 7.4 Hz), 1.72 (6 H, d, *J* = 2.8 Hz), 1.6-1.4 (6 H, m), 1.31 (2 H, sextet, *J* = 7 Hz), 0.93 (3 H, t, *J* = 7 Hz), 0.90 (3 H, t, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 205.80, 130.65, 123.10, 96.77, 96.05, 90.76, 78.83, 37.18, 31.06, 30.69, 22.16, 22.01, 20.47, 19.36, 13.97, 13.64; MS m/e 230 (M$^+$), 215, 188, 173, 159, 145, 131, 117, 91; HRMS calcd for $C_{17}H_{26}$ 230.2028, found 230.2038.

Acknowledgment. The financial support of the National Science Foundation (CHE-9307994) is gratefully acknowledged.

References and Notes

1. (a) Andemichael, Y. W.; Gu, Y. G.; Wang, K. K. *J. Org. Chem.* **1992**, *57*, 794-796. (b) Andemichael, Y. W.; Huang, Y.; Wang, K. K. *J. Org. Chem.* **1993**, *58*, 1651-1652.
2. (a) Myers, A. G.; Kuo, E. Y.; Finney, N. S. *J. Am. Chem. Soc.* **1989**, *111*, 8057-8059. (b) Myers, A. G.; Dragovich, P. S. *J. Am. Chem. Soc.* **1989**, *111*, 9130-9132. (c) Nagata, R.; Yamanaka, H.; Murahashi, E.; Saito, I. *Tetrahedron Lett.* **1990**, *31*, 2907-2910. (d) Nagata, R.; Yamanaka, H.; Okazaki, E.; Saito, I. *Tetrahedron Lett.* **1989**, *30*, 4995-4998.
3. Satoh, Y.; Serizawa, H.; Miyaura, N.; Hara, S.; Suzuki, A. *Tetrahedron Lett.* **1988**, *29*, 1811-1814.
4. Brown, H. C.; Somayaji, V. *Synthesis* **1984**, 919-920.
5. King, A. O.; Okukado, N.; Negishi, E.-i. *J. Chem. Soc., Chem. Commun.* **1977**, 683-684.
6. Brown, H. C.; Hamaoka, T.; Ravindran, N. *J. Am. Chem. Soc.* **1973**, *95*, 5786-5788.
7. Ruitenberg, K.; Kleijn, H.; Meijer, J.; Oostveen, E. A.; Vermeer, P. *J. Organomet. Chem.* **1982**, *224*, 399-405.
8. The ^{1}H and ^{13}C NMR spectra ($CDCl_3$) of **6b**, **8b**, **8c**, and **8d**. **6b**: ^{1}H δ 7.56-7.52 (2 H, m), 7.36-7.32 (3 H, m), 6.47 (1 H, t, *J* = 1 Hz), 2.35 (2 H, dt, *J* = 1 and 6.9 Hz), 1.60 (2 H, quintet, *J* = 7.5 Hz), 1.36 (2 H, sextet, *J* = 7.5 Hz), 0.93 (3 H, t, *J* = 7.3 Hz); ^{13}C δ 137.18, 131.70, 128.61, 128.32, 122.90, 95.48, 90.53, 84.06, 38.61, 30.42, 21.89, 13.83.; **8b**: ^{1}H δ 6.29 (1 H, ddt, *J* = 10.8, 6.2, and 3.0 Hz), 5.98 (1 H, d, *J* = 11.0 Hz), 5.31 (1 H, q, *J* = 6.6 Hz), 2.39 (2 H, t, *J* = 6.8 Hz), 2.13 (2 H, t, *J* = 7.4 Hz), 2.02 (2 H, dq, *J* = 2.8 and 7.1 Hz), 1.6-1.25 (16 H, m), 0.9 (9 H, m); ^{13}C δ 208.02, 129.91, 123.53, 96.97, 92.66, 92.09, 78.80, 37.21, 31.65, 31.04, 30.68, 29.09, 28.81, 28.76, 22.66, 22.12, 22.01, 19.36, 14.10, 13.95, 13.63.; **8c**: ^{1}H δ 7.5-7.4 (2 H, m), 7.32-7.30 (3 H, m), 6.31 (1 H, d of septet, *J* = 10.8 and 2.8 Hz), 6.12 (1 H, dm, *J* = 10.8 and 1 Hz), 2.25 (2 H, t, *J* = 7.5 Hz), 1.75 (6 H, dd, *J* = 2.8 and 0.9 Hz), 1.59 (2 H, quintet, *J* = 7.5 Hz), 1.38 (2 H, sextet, *J* = 7.3 Hz), 0.94 (3 H, t, *J* = 7.1 Hz); ^{13}C δ 206.27, 132.46, 131.42, 128.26, 127.94, 123.71, 122.24, 96.36, 95.72, 90.99, 88.07, 36.78, 30.82, 22.16, 20.42, 20.32, 13.98.; **8d**: ^{1}H δ 7.51-7.47 (2 H, m), 7.37-7.31 (3 H, m), 6.46 (1 H, ddt, *J* = 10.8, 6.2, and 3.0 Hz), 6.16 (1 H, dm, *J* = 10.8 and 1 Hz), 5.40 (1 H, q, *J* = 6.2 Hz), 2.29 (2 H, t, *J* = 7.5 Hz), 2.08 (2 H, dq, *J* = 2.8 and 7.1 Hz), 1.65-1.60 (2 H, m), 1.50-1.30 (10 H, m), 0.97 (3 H, t, *J* = 7.3 Hz), 0.93 (3H, t, *J* = 6.6 Hz); ^{13}C δ 208.45, 131.67, 131.40, 128.25, 127.98, 123.60, 122.61, 95.87, 92.85, 92.31, 87.91, 36.81, 31.64, 30.80, 29.05, 28.75 (2 carbons), 22.65, 22.11, 14.09, 13.95.
9. Clinet, J.-C.; Linstrumelle, G. *Synthesis* **1981**, 875-878.

(*Received in USA* 22 *December* 1993; *accepted* 18 *January* 1994)