Direct, high-yielding, one-step synthesis of *vic*-diols from aryl alkynes

P. Veeraraghavan Ramachandran *, Michael P. Drolet

Herbert C. Brown Center for Borane Research, Department of Chemistry, Purdue University, 560 Oval Drive, West Lafayette, IN 47907-2084, USA

ABSTRACT

An unprecedented, high yielding, direct, one-step synthesis of *vic*-diols from alkynes has been developed *via* metal-free, open-to-air dihydroboration with ammonia borane. The electronics of the alkyne and the reaction stoichiometry are critical for obtaining optimal yields of the 1,2-diol.

© 2018 Published by Elsevier Ltd.

Hydroboration, discovered six decades ago, has become a mainstay in organic syntheses.[1] Despite involving pyrophoric reagents requiring strictly anhydrous conditions, some with short shelf lives, it has found myriad industrial-scale applications for the preparation of valuable intermediates and target molecules. In addition to the common borane reagents, borane-dimethyl sulfide (BMS, **1**) and borane-tetrahydrofuran (BTHF, **2**), several mono- and di-substituted alkyl-, alkoxy-, and haloboranes have been developed for hydroboration.[1] While the uncatalyzed addition of B-H bonds to alkenes is common, the corresponding reaction of alkynes has been restricted,[2] mostly to those involving terminal alkynes with hindered dialkylboranes.[1,3]

Ideally, the two unsaturations in alkynes can result in as many hydroborations providing bi-functionalized molecules. On this basis, the laboratories of Brown,[4] Hassner,[5] and Pasto[6] independently examined the hydroboration of alkynes with gaseous diborane or **2**. With hex-1-yne and -3-yne as substrates, Brown and Zweifel concluded that the hydroboration/oxidation of internal aliphatic alkynes resulted in ketones, whereas those of terminal alkynes formed hexan-1-ol *via* geminal diboro intermediates. Altering the oxidation conditions, they achieved 54% yield of the corresponding aldehyde and small amounts (10–12%) of the 1,2-diol.[4,7] Subsequently, Brown developed the hydroboration of terminal alkynes with dialkylboranes for aldehyde synthesis, which has become a classic textbook reaction. Hassner, on the other hand, examined the hydroboration/oxidation of only an aromatic internal alkyne, diphenylacetylene (**4a**), with a large excess of diborane
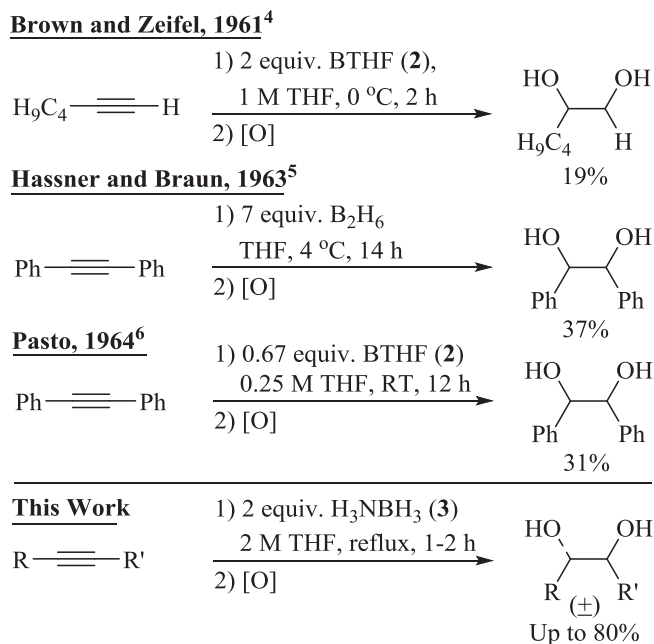
bubbled through tetrahydrofuran (THF), and reported the formation of mixtures of hydrobenzoin (**6a**) and 1,2-diphenylethanol (**7a**) in low yields.[5,8] Pasto carried out deuterium labeling studies and confirmed that terminal alkynes predominantly produce 1°-ols and internal aromatic alkynes give roughly equal amounts of ketone and 1,2-diols, in low yields.[6] All of these studies were limited in the scope of substrates and conditions, providing low amounts of vicinal diols.

Since these initial reports, there has been little effort[9,10] to examine the dihydroboration of alkynes in detail to provide broad conclusions. As part of our program on amine-borane chemistry,[11] we recently reported the first open-flask, non-dissociative hydroboration of alkenes with ammonia borane (AB, **3**).[12] To expand the utility of air and moisture stable **3** as a hydroborating agent, alkynes were included as substrates to possibly achieve the direct synthesis of valuable vicinal diols in high yields.[13] The fruitful results of this study follow (Scheme 1).

The project was initiated with the hydroboration of a representative internal alkyne, diphenylacetylene (**4a**) with 0.33 equiv **3**, in THF at room temperature. ^{11}B NMR spectroscopic analysis of an aliquot of the reaction mixture revealed no progress after 1 h. Gradual increase of the temperature, followed by analysis showed that reaction occurred only at reflux, when after 1 h, the ^{11}B NMR spectrum revealed the consumption of **3** and the presence of several overlapping peaks centered at δ −5 ppm. This suggested the formation of polymeric[4] alkylborane-ammonia complexes, attempted separation of which failed. Nevertheless, purification of an identical reaction after alkaline H_2O_2 oxidation afforded 57% deoxybenzoin (**5a**) and 11% (±)-hydrobenzoin (**6a**), along with 19% of recovered **4a**. The recovery of a large amount of **4a**

---

* Corresponding author.
  E-mail address: chandran@purdue.edu (P.V. Ramachandran).

Brown and Zeifel, 1961[4]

1) 2 equiv. BTHF (**2**),
   1 M THF, 0 °C, 2 h
2) [O]

19%

Hassner and Braun, 1963[5]

1) 7 equiv. B_2H_6
   THF, 4 °C, 14 h
2) [O]

37%

Pasto, 1964[6]

1) 0.67 equiv. BTHF (**2**)
   0.25 M THF, RT, 12 h
2) [O]

31%

This Work

1) 2 equiv. H_3NBH_3 (**3**)
   2 M THF, reflux, 1-2 h
2) [O]

(±)

Up to 80%

Scheme 1. Hydroboration/oxidation of alkynes.

prompted the examination of the effect of stoichiometry on the reaction outcome (Table 1).

Increasing the equivalents of **3** to 0.5 resulted in an increased yield of the ketone **5a** (70%) and diol **6a** (15%), with very little recovery of **4a**. Hydroboration-oxidation with one equivalent of **3** for 5 h yielded a drastically different product distribution of 18% **5a** and 62% **6a**, with negligible recovery of **4a**. Prolonging the reaction had no effect on the outcome. Isolation of significantly larger quantity of the vicinal diol than previously reported encouraged further increases in **3** to achieve maximum yield. We hypothesized that an excess of **3** may be required for full saturation of the triple bond since the vinylborane-ammonia complex from the first hydroboration might be a slower hydroborating reagent than **3** due to steric hindrance. Utilizing 2 equiv of **3**, gratifyingly, resulted in an improved yield of **6a** (76%, Table 1, Entry 5), supporting our assumption. Further increase of **3** to 3 equiv improved the yield,

modestly, to 83% (Entry 6), while incurring an unacceptable loss to atom economy. In all cases, only minimal (3–4% of the isolated diol) meso-hydrobenzoin was detected. Thus, 2 equiv of **3** was chosen as optimal for further standardization.

Reactions were also performed in several other etheric solvents, such as 1,2-dimethoxyethane, 2-methyltetrahydrofuran, diisopropyl ether, and dioxane, with no improvement in yield.[14] The effect of the reagent concentration in THF was gauged and 2 M was deemed best, providing **6a** in 79% yield. The presence of excess reagent made it difficult to determine the time required for completion by ^{11}B NMR spectroscopy. Accordingly, **3** and **4a** were heated at reflux in THF for 1 h and worked up. Gratifyingly, the product distributions remained the same (Table 1, Entry 7) as with the reaction performed for 22 h (Entry 5). This optimal condition, 2 equiv **3** in refluxing THF at 2 M for 1 h, was then applied to other alkynes, focusing initially on aryl alkynes (Table 2).

The steric and electronic environment on either side of the alkyne was varied, proceeding from doubly aromatic-substituted alkyne **4a** to singly substituted phenylacetylene (**4b**) to a mixed aryl alkyl substituted 1-phenylprop-1-yne (**4c**). The corresponding products **6b** and **6c** were isolated in 75% and 76% yields, respectively (Table 2, entries 2–3), with only the racemic anti-diol detected for **6c**.[14] Electron-deficient 4-fluorophenylacetylene (**4d**) and 4-(trifluoromethyl)phenylacetylene (**4e**) were subjected to hydroboration with **3** and diols **6d** and **6e** were isolated in 78% yield each (Table 2, entries 4–5).

Adding a methyl substituent at the ortho- (**4f**), meta- (**4g**), and para- (**4h**) positions of phenylacetylene provided the diols **6f–h** in 71%, 70%, and 68% yields, respectively (Table 2, entries 6–8). This effect of the electron-donating group was even more apparent for 4-methoxyphenylacetylene (**4i**), with the isolation of only 54% of **6i** (Table 2, Entry 9). We expected that even electron-rich aliphatic alkynes would behave in a similar manner to **4i**.[15] Indeed, when a terminal aliphatic alkyne dec-1-yne (**4j**) was submitted to these conditions (Table 2, Entry 10), only 36% of diol **6j** was isolated with 48% of decan-1-ol (**7j**) as the major product. This points to preferential geminal dihydroboration for electron-rich alkynes as reported previously.[4,6] Similarly, dec-5-yne (**4k**) resulted in low yields (53%) of the racemic, anti- (±)-5,6-decanediol (**6k**).

The generality of the preference for vicinal dihydroboration, as seen with **3**, was explored by treating **4a** with other common hydroborating reagents (Table 3).

Table 1
Stoichiometry-controlled product distribution.
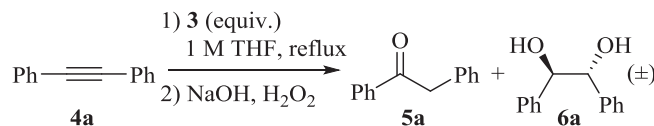
Entry	**3** (equiv.)[a]	Time[b] (h)	Recovery **4a** (%)[c]	Yield **5a** (%)[c]	Yield **6a** (%)[c]
1	0.33	1	19	57	11
2	0.5	3	3	70	15
3	1	5	4	18	62
4	1	22	3	22	64
5	2	22	3	7	76
6	3	28	3	6	83
7	2	1	3	6	78

[a] Concentration with respect to **4a**.
[b] Time required for complete consumption of **3** by hydroboration or thermal decomposition as determined by ^{11}B NMR spectroscopy.
[c] Isolated yield.