Pergamon

Tetrahedron Letters 40 (1999) 6871–6874

TETRAHEDRON
LETTERS

Reductions of aryl perfluorosulfonates with dimethylamine·borane ($Me_2NH \cdot BH_3$) catalyzed by Pd(0): an operationally simple, inexpensive, and general protocol

Bruce H. Lipshutz,* D. J. Buzard and Randall W. Vivian

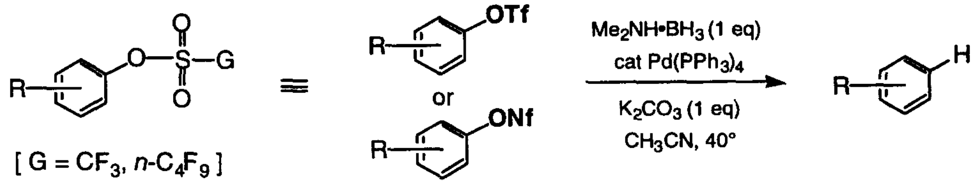
Department of Chemistry, University of California, Santa Barbara, CA 93106, USA

Received 1 June 1999; revised 23 June 1999; accepted 24 June 1999

Abstract

Treatment of aryl nonaflates or triflates in CH_3CN in the presence of one equivalent of $Me_2NH \cdot BH_3$ and K_2CO_3 leads via Pd(0) catalysis to high yields of reduced arenes. © 1999 Elsevier Science Ltd. All rights reserved.

The seemingly simple task of replacing a hydroxy group on an aryl ring with hydrogen has engendered a noticeable flurry of activity in the synthetic community over the past decade.[1] There are, of course, good reasons for such directed efforts, an appreciation for which can be quickly gleaned from recent reports in complex molecule total synthesis which rely on this type of transformation (e.g., vancomycin aglycon,[2a] gelsamine alkaloids,[2b] angelicin,[2c] etc.). As none of these has emerged as the method of choice, we were attracted to the potential of amine–boranes to serve in this capacity, under the influence of palladium(0) catalysis. These reagents of main group origin, having just recently been reviewed,[3] are available in several combinations of an amine and borane which allow for considerable fine-tuning of physical as well as reducing properties. Ideally, the species of choice should be readily available, soluble in most commonly used organic solvents, compatible with most functional groups, inexpensive, and yet effective in stoichiometric amounts. We now report that $Me_2NH \cdot BH_3$ is an especially mild reagent for effecting reductions of aryl perfluorosulfonates to arenes.



Among the numerous amine–boranes which are commercially available,[4] $Me_2NH \cdot BH_3$ was selected for several reasons: (1) it is an easily handled, stable white solid; (2) it has a low molecular weight; (3) it

---

* Corresponding author. Tel: 805-893-2521; fax: 805-893-8265; e-mail: lipshutz@chem.ucsb.edu

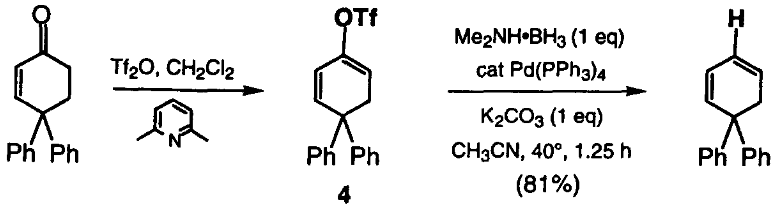
PII: S0040-4039(99)01255-1

is very soluble in polar as well as non-polar solvents; (4) it is unaffected by the presence of moisture in a reaction mixture, but is quickly hydrolyzed under acidic conditions; (5) it is completely lost upon reaction workup, and therefore does not complicate TLC or NMR analyses and requires no chromatographic separation; (6) it is readily converted to its more active *N*-metalated form.

Several examples attesting to the quality of this combination of reagents are illustrated in Table 1. In all cases but one, only one equivalent of $Me_2NH \cdot BH_3$, along with the heterogeneous base K_2CO_3, is needed. For many reactions, conducted at 40°C in CH_3CN at 0.30 M, times in the order of a few hours are sufficient for complete consumption of educt. Notably, several functional groups present in these substrates are unaffected, including an isolated olefin, e.g., **1** (entry **C**). When **1** is treated under otherwise identical conditions in the absence of K_2CO_3, hydroboration occurs readily (within 1.5 h) rather than nonaflate reduction, strongly implicating the kaliated form of the amine borane[5] as the source of hydride being provided to a likely Pd(II) intermediate. The presumed potassium aminoborohydride generated in situ was selected rather than the more reactive lithiated analog, the latter known to be less tolerant of functionality susceptible to hydride addition.[6] Utilizing the morpholine analog as reductant, albeit a more costly reagent (entry **E**), a similar yield and identical reactivity pattern were noted. An aryl bromide does not offer competition for a nonaflate with both groups present in the same molecule (entry **F**). Hindered substrate **2** (entry **I**) required additional reagent (2 equiv.) and far longer at reflux to reach completion, although the reduction did eventually give the desired product in high yield. Reduction of an L-tyrosine triflate **3** (entry **J**) was successful without compromising amido ester stereopurity.[7] As nonaflation proceeds[8] normally via the preformed phenoxide (NaH), which under these conditions epimerizes the α-site, the triflate was required in this case. Triflation involves less basic conditions which are readily tolerated (Tf_2O, 2,6-lutidine, rt), and yet the reactivity patterns of these sulfonates are similar to those of the nonaflates (entry **H**).

Control experiments documented the catalysis by Pd(0), with $Pd(PPh_3)_4$ affording the smoothest reactions. Alternative sources of Pd(0), such as Pd/C and $Pd_2(dba)_3$, or presumed in situ generation from $Pd(OAc)_2$, were either less efficient (as with $Pd_2(dba)_3$) or completely ineffective. Likewise, attempts to substitute Ni(0) employing $NiCl_2 \cdot dppe$ were fruitless even at higher reaction temperatures. Replacement of palladium with copper in the form of CuOTf, with hopes that CuH might be formed and effect the reduction, led to no reaction. Replacement of a nonaflate by phosphate showed no consumption of starting material.[9]

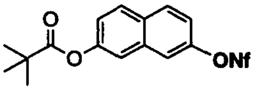
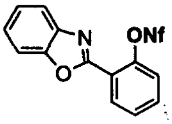
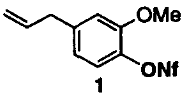
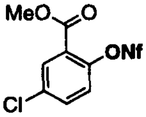
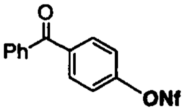
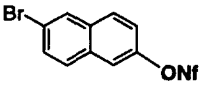
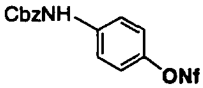
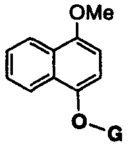
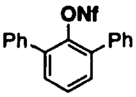
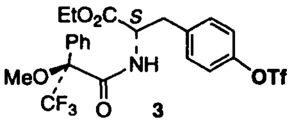
One example of the reduction of a vinyl triflate[10] (**4**) was studied (Eq. 1). Treatment of **4** under our standard conditions smoothly delivered the expected dienic product in good yield (81%).



(1)

In summary, a method[11] has been developed for the clean reduction of perfluorosulfonates to arenes using $Me_2NH \cdot BH_3$ via catalysis by Pd(0). The virtues of this reagent combination are manifold and offer confidence that this mild procedure will be found applicable to many sequences where functional group compatibility and reagent cost may be critical issues.

Table 1
Pd(0)-catalyzed reductions of aryl perfluorosulfonates with $Me_2NH \cdot BH_3/K_2CO_3$[a]

Entry	Sulfonate	Temp (° C)	Time (h)	Yield (%)[b]
A		40°	4.5	**86**
B		40°	3.5	**93**
C	 **1**	75°	6.0	**86**
D		40°	9	**91**
E		40°	3.5[c]	**96**
F		40°	5	**84**
G		70°	3	**77**
H		[G = **Nf**] 60°	5	**94**
		[G = **Tf**] 60°	6	**86**
I	 **2**	reflux	32[d]	**95**
J	 **3**	60°	10	**71**

---

[a] New products of reduction were fully characterized by IR, NMR, MS, and HRMS data; spectra of known products agreed with literature data. [b] Isolated, chromatographically purified materials. [c] Morpholine•borane was used. [d] Two equivalents of amine•borane and K_2CO_3 were used .

Acknowledgements

Financial support for our programs provided by the NSF (CHE 9734813) is warmly acknowledged with thanks.

References

1. Katsuki, H.; Datta, P. K.; Hayakawa, H.; Suenaga, H. *Synthesis* **1995**, 138. Saa, J. M.; Dopico, M.; Martorell, G.; Garcia-Raso, A. *J. Org. Chem.* **1990**, *55*, 991.
2. (a) Evans, D. A.; Wood, M. R.; Trotter, B. W.; Richardson, T. I.; Barrow, J. C.; Katz, J. L. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2700. (b) Takayama, H.; Kitajima, M.; Sakai, S. *Heterocycles* **1990**, *30*, 325. (c) Peterson, G. A.; Kunng, F.; McCallum, J. S.; Wulff, W. D. *Tetrahedron Lett.* **1987**, *28*, 1381.
3. Carboni, B.; Monnier, L. *Tetrahedron* **1999**, *55*, 1197.
4. Lane, C. F. *Aldrichimica Acta* **1973**, *6*, 51.
5. Premixing $Me_2NH\cdot BH_3$ with K_2CO_3 for one hour in acetonitrile is recommended for substrates (entries **C** and **J**) that contain functionality susceptible to hydroboration or epimerization under basic conditions.
6. For a comparison of various reductions employing sodium and lithium aminoborohydrides, see: Hutchins, R. O.; Learn, K.; El-Telbany, F.; Stercho, Y. P. *J. Org. Chem.* **1984**, *49*, 2438. Fisher, G. B.; Fuller, J. C.; Harrison, J.; Alvarez, S. G.; Burkhardt, E. R.; Goralski, C. T.; Singaram, B. *J. Org. Chem.* **1994**, *59*, 6378.
7. The nonracemic reduced product in entry **J** was compared with its racemate; no dectectable epimerization was observed by ^{19}F, ^{1}H, and ^{13}C analyses.
8. Subramanian, L. R.; Bentz, H.; Hanack, M. *Synthesis* **1973**, 293.
9. Nan, Y.; Yang, Z. *Tetrahedron Lett.* **1999**, *40*, 3321.
10. Dupre, B.; Meyers, A. I. *J. Org. Chem.* **1991**, *56*, 3197. Polniaszek, R. P.; Dillard, L. W. *J. Org. Chem.* **1992**, *57*, 4103. Cacchi, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1984**, *25*, 4821.
11. Typical procedure (Table 1, entry B): Borane•dimethylamine complex (59 mg, 1.0 mmol), arylsulfonate (493 mg, 1.0 mmol), $Pd(PPh_3)_4$ (58 mg, 0.05 mmol, 5 mol%), and K_2CO_3 (138 mg, 1.0 mmol) were weighed into an oven dried 10 mL round bottomed flask equipped with stir bar and septa and purged with argon. Acetonitrile (3.5 mL, distilled from CaH_2) was added via syringe and the reaction was allowed to stir for 10 min and then warmed to 40°C. The reaction was monitored by TLC and GC, and was judged complete after 3.5 h. The solution was cooled to rt and then poured into a separatory funnel containing 10 mL of H_2O and 10 mL of diethyl ether. The organics were separated and the aqueous layer was extracted two additional times with 10 mL of diethyl ether. The organic extracts were dried over anhydrous Na_2SO_4, filtered, and the solvents removed in vacuo. The crude material was adsorbed onto silica gel and purified by column chromatography on silica gel (5% diethyl ether in pet ether) to give 182 mg (93%) of the reduced product.