Suzuki Reactions with B-Allyl-9-Borabicyclo[3.3.1]nonane (B-Allyl-9-BBN)

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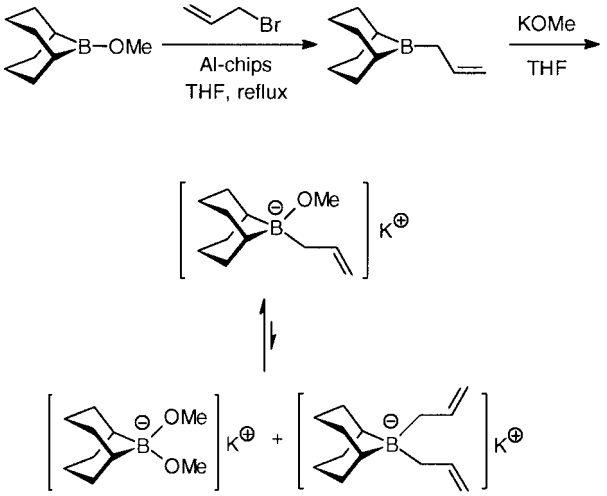
Abstract: The mixture of borate complexes formed on treatment of B-allyl-9-BBN with KOMe readily undergoes Suzuki reactions in the presence of catalytic amounts of Pd(0) complexes, thus transferring their allyl moiety to aryl bromides, -iodides or -triflates.

The palladium catalyzed cross coupling of aryl halides, triflates or diazonium salts with various organoboron derivatives in the presence of a base became one of the most popular methods for C-C-bond formations in recent years.[1,2] Generally referred to as Suzuki reactions, these transformations exhibit an unrivaled compatibility with functional groups in both reaction partners and represent environmentally benign processes with considerable appeal for the preparation of pharmacologically active compounds and the production of fine chemicals.[3]

In order to widen the scope of Suzuki-type reactions, we have recently described a complementary protocol employing 9-MeO-9-BBN as a "shuttle" that allows to transfer *i.a.* methyl-, $TMSCH_2$- and alkynyl groups which are beyond the scope of the traditional set-up.[4,5] As a further extension, we now report the first general procedure for the transfer of allyl groups under Suzuki conditions.

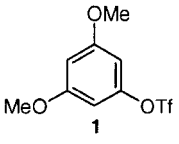
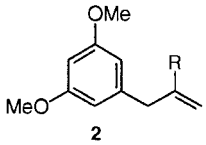
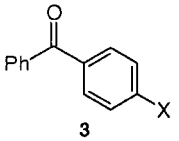
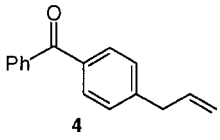
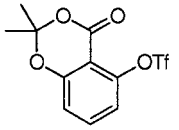
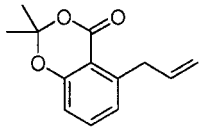
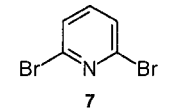
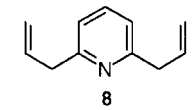
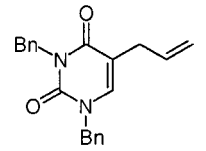
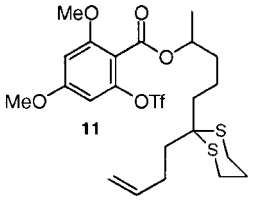
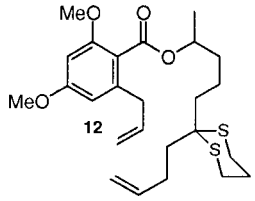
Palladium-catalyzed cross coupling reactions of allylboron derivatives are essentially unknown. In a close survey of the literature we found only a brief mentioning of reactions of tricrotylboron in the presence of aq. NaOH and $Pd(PPh_3)_4$ cat.[6] and a preliminary report on the use of allyl(dimethoxy)borane.[7] The latter, however, is rather limited in scope since only aryl iodides were found to be suitable substrates while bromides afforded the cross coupling products in poor yield. Having in mind our previous experiences that various types of organic residues can be transferred from the 9-BBN template to an aryl-PdX species,[4] we investigated whether B-allyl-9-BBN may be useful in this context.



Scheme 1

B-Allyl-9-BBN can be prepared on a mole scale from allyl bromide and B-methoxy-9-BBN in the presence of aluminum chips.[8] Addition of 1 equiv. KOMe[9] to a solution of this compound in THF leads to a mixture of borate complexes as can be deduced from the ^{11}B NMR spectrum. K[(MeO)(allyl)BBN] (δ = -1.5 ppm) is the major component of this mixture, but some ligand scrambling leading to the formation of minor amounts of K[$(MeO)_2$BBN] (δ = 4.5 ppm) and K[$(allyl)_2$BBN] (δ = -15.6 ppm) cannot be avoided (Scheme 1).

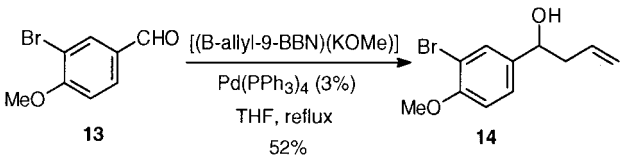
Table. Suzuki-Type Allylation Reactions Employing B-Allyl-9-BBN [a]

Nr.	Substrate	Product	Yield (%)[b]
1			85 (R = H)[c]
2	**1**	**2**	75 (R = Me)
3			86 (X = OTf)[d]
4	**3**	**4**	77 (X = Br)[d]
5			81[e]
	5	**6**	
6			66
	7	**8**	
7			68
	9	**10**	
8			86[f]
	11	**12**	

[a] Aryl halide (triflate) (1 eq.), [(B-allyl-9-BBN)·(KOMe)] (1.2 eq.), $PdCl_2$(dppf) (3 mol%), THF, reflux, 0.5-1 h; [b] Isolated yields of analytically pure compounds. [c] Contains 13% (GC) of the 1-propenyl isomer; [d] Contains ≤ 5% (GC) of the 1-propenyl isomer; [e] Employing $Pd(PPh_3)_4$ (3 mol%) instead of $PdCl_2$(dppf); [f] refers to material which is ≥ 93% by GC and NMR prepared as described in ref. 12; for the results obtained in Stille coupling reactions *cf.* Text

Reaction of an aryl halide or triflate with this mixture of borate complexes in the presence of 3 mol% of either $PdCl_2$(dppf) or $Pd(PPh_3)_4$ in refluxing THF afforded the desired cross coupling

products in good to excellent yields. The results are compiled in the Table. As can be deduced from these experiments, electron rich and electron poor substrates react with similar ease and several functional groups turned out to be compatible. This includes ethers, esters, aromatic ketones, thioketals and heterocyclic motives. Aldehydes, however, are not tolerated as evident from Scheme 2.



Scheme 2

Several practical aspects of this new allylation procedure are worth mentioning. Although B-allyl-9-BBN is a very sensitive compound,[8] solutions of the borate complexes formed on addition of KOMe are fairly easy to handle. They can be bottled and stored for extended periods of time without loss of activity. The palladium catalyzed cross coupling reactions usually proceed to completion in 30-60 min and only a slight excess of the borate is required (≈ 1.2 equiv.). The conversion is roughly indicated by the precipitation of the KX salts and can be quantitatively monitored by ^{11}B NMR of aliquots of the crude mixtures. Aryl bromides, iodides and triflates were found to react with comparable ease. Since B-allyl-9-BBN can be easily prepared in multigram amounts,[8] this new protocol is particularly suitable for large scale preparations. As can be seen from entry 2, substituted allyl groups can also be transferred in this way.

This new Suzuki type allylation reaction favorably compares to the well known Stille coupling employing allyltributyl (or trimethyl) stannane.[10,11] Thus, compound **12** was prepared on a multigram scale in 86% in only 0.5 h reaction time by means of this new method,[12] whereas the Stille coupling afforded the desired compound in significantly lower yield only after extended periods of time [allyltributylstannane (1.4 equiv.), $Pd_2(dba)_3$ (3 mol%), tris(2-furyl)-phosphine (12 mol%), LiCl (3 equiv.), NMP, 40 °C, 48 h, 41%; 60 °C, 24 h, 60%]. Moreover, the purification of the product is easy in the boron based protocol whereas the removal of the noxious tin residues formed in the latter case may be tedious. These features make the new Suzuki-type protocol for the transfer of allyl groups attractive for further applications to organic synthesis.

References and Notes

(1) Review: Miyaura, N.; Suzuki, A. *Chem. Rev*. **1995**, *95*, 2457.

(2) For some recent developments see: (a) Darses, S.; Genêt, J.-P.; Brayer, J.-L.; Demoute, J.-P. *Tetrahedron Lett.* **1997**, 4393. (b) Giroux, A.; Han, Y.; Prasit, P. *Tetrahedron Lett.* **1997**, 3841. (c) Indolese, A. F. *Tetrahedron Lett.* **1997**, 3513. (d) Sengupta, S.; Bhattacharyya, S. *J. Org. Chem*. **1997**, *62*, 3405. (e) Andersen, N. G.; Maddaford, S. P.; Keay, B. A. *J. Org. Chem*. **1996**, *61*, 9556. (f) Hildebrand, J. P.; Marsden, S. P. *Synlett* **1996**, 893. (g) Reetz, M. T.; Breinbauer, R.; Wanninger, K. *Tetrahedron Lett.* **1996**, 4499. (h) Saito, S.; Sakai, M.; Miyaura, N. *Tetrahedron Lett.* **1996**, 2993. (i) Beller, M.; Fischer, H.; Herrmann, W. A.; Öfele, K.; Broßmer, C. *Angew. Chem.* **1995**, *107*, 1992 and lit. cited.

(3) *Applied Homogeneous Catalysis with Organometallic Compounds* (Cornils, B.; Herrmann, W. A., Eds.), VCH, Weinheim, **1996**, Vol. 2.

(4) (a) Fürstner, A.; Seidel, G. *Tetrahedron* **1995**, *51*, 11165. (b) For a similar concept see: Soderquist, J. E.; Matos, K.; Rane, A.; Ramos, J. *Tetrahedron Lett.* **1995**, 2401.

(5) For other applications of the Suzuki reaction from our laboratory see: (a) Fürstner, A.; Seidel, G. *J. Org. Chem*. **1997**, *62*, 2332. (b) Fürstner, A.; Konetzki, I. *Tetrahedron* **1996**, *52*, 15071. (c) Fürstner, A.; Nikolakis, K. *Liebigs Ann*. **1996**, 2107. (d) Fürstner, A.; Seidel, G.; Gabor, B.; Kopiske, C.; Krüger, C.; Mynott, R. *Tetrahedron* **1995**, *51*, 8875.

(6) Cited as unpublished results in ref.[1], p. 2476.

(7) Kalinin, V. N.; Denisov, F. S.; Bubnov, Y. N. *Mendeleev Commun*. **1996**, 206.

(8) (a) Kramer, G. W.; Brown, H. C. *J. Organomet. Chem*. **1977**, *132*, 9. (b) For a review see: Yamamoto, Y. in *Encyclopedia of Reagents for Organic Synthesis* (Paquette, L. A., Ed.), Wiley, New York, **1995**, 90.

(9) It is important to use exactly 1.0 equiv. of KOMe per mole of B-allyl-9-BBN; an excess of the base may cause allyl → 1-propenyl isomerisations under the reaction conditions.

(10) (a) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc*. **1987**, *109*, 5478. (b) Farina, V.; Krishnan, B. *J. Am. Chem. Soc*. **1991**, *113*, 9585. (c) For a timely and comprehensive review see: Farina, V.; Krishnamurthy, V.; Scott, W. J. *Org. React*. **1997**, *50*, 1.

(11) For a leading reference on transition metal catalyzed reactions using other allylmetal reagents see: Hayashi, T.; Konishi, M.; Yokata, K-I.; Kumada, M. *J. Organomet. Chem*. **1985**, *285*, 359 and lit. cited.

(12) ***Representative Procedure***: To a solution of B-allyl-9-BBN (1.35 g, 8.3 mmol) in THF (120 mL) is added KOMe (582 mg, 8.3 mmol) and the mixture is stirred for 10 min until a clear solution is formed. Triflate **11** (3.98 g, 6.9 mmol) and $PdCl_2$(dppf) (171 mg, 3 mol%) are introduced and the mixture is refluxed under Ar for 30 min. After that time the ^{11}B NMR of an aliquot shows a single peak at δ = 56.6 ppm (external standard: BF_3•Et_2O). For work-up the volatiles are removed *in vacuo*, the residue is suspended in CH_2Cl_2 (120 mL) and the undissolved salts are filtered off over a short pad of silica. Evaporation of the solvent and drying of the residue at 10^{-2} torr affords **12** (purity by NMR and GC ≥ 93%, rest: cyclooctanone) as a colorless syrup (2.97g, 86%). An analytically pure sample is obtained by flash chromatography using hexane/Et_2O (20/1) as the eluent. IR (cm^{-1}): 3077, 2940, 2840, 1719, 1689, 1639, 1605, 1456, 1423, 1379, 1327, 1271, 1208, 1160, 1096, 1047, 995, 912, 833, 734, 622.- ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.33 (s, 2H), 5.92 (ddt, 1H, *J* = 16.4, 10.5, 6.4 Hz), 5.82 (ddt, 1H, *J* = 17.0, 10.4, 6.6 Hz), 5.18 (sext., 1H, *J* = 6.2 Hz), 5.07 (dq, 1H, *J* = 17.2, 1.6 Hz), 5.06 (dq, 1H, *J* = 10.1, 1.4 Hz), 5.04 (dq, 1H, *J* = 17.1, 1.6 Hz), 4.96 (dq, 1H, *J* = 10.2, 1.4 Hz), 3.80 (s, 3H), 3.79 (s, 3H), 3.37 (dd, 2H, *J* = 6.6, 1.3 Hz), 2.80 (m, 4H), 2.20 (m, 2H), 1.86-1.99 (m, 6H), 1.49-1.76 (m, 4H), 1.34 (d, 3H, *J* = 6.3 Hz).- ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.7, 161.3, 156.1, 139.8, 137.9, 136.3, 117.1, 116.4, 114.9, 105.8, 96.7, 71.5, 55.9, 55.3, 53.0, 38.4, 37.7, 37.5, 36.1, 28.6, 26.0, 25.4, 20.2, 20.1.- MS (EI, rel. intensity): 464 (14, [M^+]), 243 (50), 223 (30), 207 (12), 206 (14), 205 (100), 204 (26), 187 (19), 177 (14), 173 (45), 168 (16), 167 (76), 145 (15), 135 (25), 125 (14), 107 (14), 93 (13), 55 (11), 41 (12).- HR-MS ($C_{25}H_{36}O_4S_2$): *calcd*. 464.20551; *found* 464.20384.