Aryl Norbornanes and Analogues via Palladium-Catalyzed Hydroarylation with Arenediazonium Tetrafluoroborates

Gabriele Bartoli, Sandro Cacchi,* Giancarlo Fabrizi, Antonella Goggiamani

Dipartimento di Chimica e Tecnologie del Farmaco, Università degli Studi 'La Sapienza', P. le A. Moro 5, 00185 Rome, Italy
Fax +39(06)49912780; E-mail: sandro.cacchi@uniroma1.it

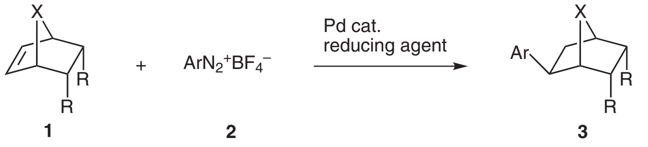
Received 18 June 2008

Abstract: The palladium-catalyzed hydroarylation of arenediazonium tetrafluoroborates with norbornene derivatives and analogues in the presence of $Pd(OAc)_2$ and $i\text{-}Pr_3SiH$ in THF affords hydroarylation products containing the added aryl unit in the *exo* position in good to high yields. The reaction tolerates a variety of useful functional groups and can be performed as a one-pot procedure generating the arenediazonium salt in situ.

Key words: norbornene, palladium, hydroarylation, arenediazonium salts

Because of their higher reactivity, their availability from inexpensive anilines, the utilization of mild conditions, and the absence of added bases in several applications, arenediazonium salts represent an attractive alternative to aryl halides or triflates in palladium-catalyzed reactions.[1] They have been widely utilized in Mizoroki–Heck reactions.[2] Suzuki–Miyaura,[3] and Stille[4] cross-couplings as well as carbonylation reactions,[2a,5] the synthesis of sulfinic acids[6] and boronic esters[7] have also been reported. However, a number of applications still remain a challenging target.[1] Only recently, the first synthetically useful palladium-catalyzed alkyne-based reaction of arenediazonium tetrafluoroborates has been described by us. In particular, we have shown that arenediazonium tetrafluoroborates can be used as aryl partners in the hydroarylation of internal alkynes.[8] Hydroarylation products have been isolated in good to high yields under mild conditions with very high stereoselectivity and, with an asymmetrically disubstituted alkyne such as ethyl phenylpropynoate, the regioselectivity was found to be comparable to that observed with aryl iodides.

On the basis of these results, we decided to study the feasibility of a hydroarylation process involving hindered olefinic systems such as norbornenes and analogues (Scheme 1). Indeed, the hydroarylation of norbornenes with aryl halides and triflates[9,10] has proved to be an effective method for the synthesis of bicyclo[2.2.1]heptanes and related compounds with an aryl substituent in the *exo* position.[11] It has been used in the total synthesis of the potent nonopiate analgesic alkaloid epibatedine,[12] a compound isolated from the skin of the Ecuadorian frog, *Epipedobates tricolor*, as well as in different approaches to its analogues.[12b,13] Enantioselective hydroarylations of norbornene derivatives have also been described.[14] The extension of this chemistry to arenediazonium salts would widen significantly its synthetic scope. Herein we report the results of this study.



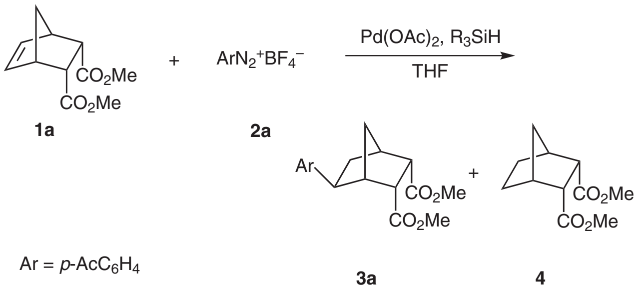
Scheme 1

The reaction of dimethyl bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**1a**, $R = CO_2Me$; $X = CH_2$) and *p*-acetyldiazobenzene tetrafluoroborate (**2a**) was chosen as the model system for our initial investigation of this hydroarylation process. Phosphine-free conditions were selected on the basis of the known detrimental effect of phosphine ligands in many palladium-catalyzed reactions of arenediazonium salts[15] and our results in the hydroarylation of alkynes.[8] Utilization of formate anions as the reducing agent (commonly used in the hydroarylation of norbornene derivatives with aryl iodides or triflates) did not afford the desired hydroaylation product. Apparently, formate anions tend to favor several side processes, including the reduction of the arylpalladium intermediates and the olefinic double bond. For example, no evidence of hydroarylation product formation was obtained using HCOOK and $Pd(OAc)_2$ in THF or DMF at 0 °C to room temperature, acetophenone and **4** being formed in 19–55% and 1–9% yields, respectively. Therefore, we switched to the more selective trialkylsilanes. The influence of several trialkylsilanes on the reaction outcome as well as that of temperature and the excess of arenediazonium salts have been investigated. The results of our screening study are summarized in Table 1.

Under a variety of conditions the reduction product **4**, most probably formed by a palladium-catalyzed reaction, was isolated in significant yields. No evidence of compound **4** formation was obtained when the reaction was carried out omitting the palladium catalyst. Notably, the utilization of Ph_3SiH, which gave the highest yields in the hydroarylation of alkynes, led to the formation of **3a** only in 26% yield[16] (Table 1, entry 5). Compound **4** was isolated as the main product even with Me_2PhSiH, Oct_3SiH, and Et_3SiH (Table 1, entries 6–8). Formation of acetophenone was also observed (Table 1, entries 1, 7–9). Switching to $i\text{-}Pr_3SiH$ yielded **3a** as the main product. However, com-

SYNLETT 2008, No. 16, pp 2508–2512
Advanced online publication: 12.09.2008
DOI: 10.1055/s-2008-1078051; Art ID: G19808ST

Table 1 The Influence of the Trialkylsilane, Temperature, and Excess of Arenediazonium Salt on the Palladium-Catalyzed Hydroarylation of Dimethyl Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**1a**) with *p*-Acetyldiazobenzene Tetrafluoroborate (**2a**)[a]



Entry	Trialkyl-silane	**2a** (equiv)	Temp (°C)	Time (h)	Yield (%)[b] of **3a**	Yield (%)[b] of **4**
1	$i\text{-}Pr_3SiH$	4	0 to 15	1	71[c]	–
2	$i\text{-}Pr_3SiH$	2	0 to 15	0.67	73	20
3	$i\text{-}Pr_3SiH$	2	r.t.	3.5	48[d]	36
4	$i\text{-}Pr_3SiH$	1.1	0 to 15	2	44	34
5	Ph_3SiH	1.2	0 to 15	0.67	26	72
6	Me_2PhSiH	2	0 to 15	0.5	Traces[e]	85
7	Oct_3SiH	2	0 to 15	1.5	17[f,g]	58
8	Et_3SiH	2	0–15	1	–[h]	93

[a] Unless otherwise stated, reactions were carried out under argon on a 0.5 mmol scale using 1 equiv of **1a**, 2 equiv of **2a**, 2 equiv of R_3SiH, 0.05 equiv of $Pd(OAc)_2$ in 4 mL of anhyd THF.

[b] Yields are given for isolated products.

[c] Acetophenone was isolated in 29% yield.

[d] Compound **1a** was recovered in 11% yield.

[e] Acetophenone was isolated in 40% yield.

[f] Acetophenone was isolated in 20% yield.

[g] Compound **1a** was recovered in 14% yield.

[h] Acetophenone was isolated in 35% yield.

Table 2 Palladium-Catalyzed Hydroarylation of Dimethyl Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate **1a** with Arenediazonium Salts **2**[a]

Entry	Arenediazonium salt **2**		Time (h)	Yield (%)[b,c] of **3**	
1	$4\text{-}AcC_6H_4N_2^+BF_4^-$	**2a**	0.67	**3a**	73
2	$4\text{-}MeOC_6H_4N_2^+BF_4^-$	**2b**	3	**3b**	73
3	$2\text{-}MeOC_6H_4N_2^+BF_4^-$	**2c**	2	**3c**	86
4	$4\text{-}ClC_6H_4N_2^+BF_4^-$	**2d**	2	**3d**	78
5	$4\text{-}MeC_6H_4N_2^+BF_4^-$	**2e**	1	**3e**	86
6	$4\text{-}MeO_2CC_6H_4N_2^+BF_4^-$	**2f**	1.5	**3f**	73
7	$4\text{-}O_2NC_6H_4N_2^+BF_4^-$	**2g**	0.5	**3g**	75
8	$4\text{-}NCC_6H_4N_2^+BF_4^-$	**2h**	3	**3h**	85
9	$2,4\text{-}Me_2C_6H_3N_2^+BF_4^-$	**2i**	1.5	**3i**	92
10	$2\text{-}Me\text{-}4\text{-}FC_6H_3N_2^+BF_4^-$	**2j**	3.5	**3j**	56
11	$4\text{-}IC_6H_4N_2^+BF_4^-$	**2k**	20	**3k**	19[d]
12	$PhN_2^+BF_4^-$	**2l**	1.5	**3l**	80
13	$2\text{-}BrC_6H_4N_2^+BF_4^-$	**2m**	7	**3m**	28[e]

[a] Reactions were carried out under argon on a 0.5 mmol scale using 1 equiv of **1a**, 2 equiv of **2**, 2 equiv of $i\text{-}Pr_3SiH$, 0.05 equiv of $Pd(OAc)_2$ in 4 mL of anhyd THF at 0 °C to 15–25 °C.

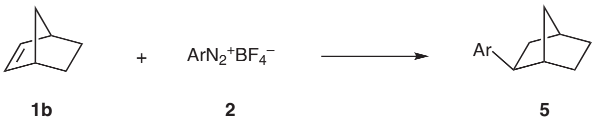
[b] Yields are given for isolated products.

[c] Compound **4** was formed in variable amounts ranging from traces (entries 5, 8, 9) to 35% yield (entries 10 and 13).

[d] The reduction–hydroarylation derivative **7** was isolated in 10% yield.

[e] The reduction–hydroarylation derivative **7** was isolated in 6% yield.

Table 3 Palladium-Catalyzed Hydroarylation of Norbornene **1b** with Arenediazonium Salts **2**[a]



Entry	Arenediazonium salt **2**		Time (h)	Yield (%)[b] of **5**	
1	$4\text{-}AcC_6H_4N_2^+BF_4^-$	**2a**	6	**5a**	94
2	$4\text{-}MeOC_6H_4N_2^+BF_4^-$	**2b**	2.5	**5b**	93
3	$4\text{-}MeO_2CC_6H_4N_2^+BF_4^-$	**2f**	4	**5f**	86
4	$2\text{-}ClC_6H_4N_2^+BF_4^-$	**2n**	5	**5n**	80

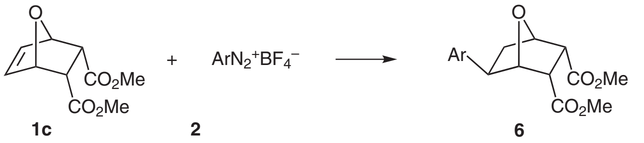
[a] Reactions were carried out under argon on a 0.5 mmol scale using 1 equiv of **1b**, 2 equiv of **2**, 2 equiv of $i\text{-}Pr_3SiH$, 0.05 equiv of $Pd(OAc)_2$ in 4 mL of anhyd THF at 0 °C to 15–25 °C.

[b] Yields are given for isolated products.

pound **4** was still isolated in significant yields under the conditions shown in Table 1, entries 3 and 4. The best result in terms of yield, reaction time, and excess of arenediazonium salt was obtained when the reaction was carried out using 2 equiv of $i\text{-}Pr_3SiH$ and 2 equiv of *p*-acetyldiazobenzene tetrafluoroborate **2a** at 0–15 °C (see experimental section; Table 1, entry 2). Consequently, these conditions were employed when the procedure was extended to include other benzenediazonium salts (Table 2) and bicyclic derivatives such as norbornene (**1b**, R = H, X = CH_2; Table 3) and dimethyl 7-oxa-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**1c**, R = CO_2Me, X = O; Table 4).[17]

Hydroarylation products were isolated in moderate to high yields as single stereoisomers. The *exo* stereochemistry of **3a** was assigned by NOESY experiments.[18] That of the other hydroarylation derivatives was assigned based on this data and all the previous work on this type of chemistry. The reaction tolerates a variety of useful substituents such as chloro, cyano, ester, keto, and nitro groups (frequently, the latter tend to give decomposition products in palladium-catalyzed reactions[15]). Arenediazonium tetrafluoroborates containing *ortho* substituents can also be used (Table 2, entries 3, 9 and 10; Table 3, entry

Table 4 Palladium-Catalyzed Hydroarylation of Dimethyl 7-Oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (**1c**) with Arenediazonium Salts **2**[a]



Entry	Arenediazonium salt **2**		Time (h)	Yield (%)[b] of **6**	
1	4-$CNC_6H_4N_2^+BF_4^-$	**2h**	1.5	**6h**	84
2	4-$ClC_6H_4N_2^+BF_4^-$	**2d**	1.25	**6d**	91
3	3,4,5-$MeOC_6H_2N_2^+BF_4^-$	**2o**	2.25	**6o**	85
4	2-$ClC_6H_4N_2^+BF_4^-$	**2n**	3	**6n**	93

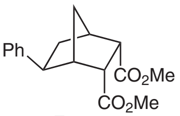
[a] Reactions were carried out under argon on a 0.5 mmol scale using 1 equiv of **1c**, 2 equiv of **2**, 2 equiv of *i*-Pr_3SiH, 0.05 equiv of $Pd(OAc)_2$ in 4 mL of anhyd THF at 0 °C to 15–25 °C.

[b] Yields are given for isolated products.

4; Table 4, entry 4). The low yields observed with iodo and bromo derivatives (Table 2, entries 11 and 13) are most probably due to the competitive oxidative addition of carbon–halogen bonds to Pd(0) species generating arylpalladium intermediates which can undergo several side reactions. Although we have not investigated this point in detail, this notion is strongly supported by the fact that the reaction of *p*-iodo- or *o*-bromodiazobenzene tetrafluoroborate with **1a** affords **7** (Figure 1), very likely formed via reduction of arylpalladium halide intermediates (before and/or after the carbopalladation step). Chloroarenediazonium tetrafluoroborates, however, can be selectively converted into the corresponding chloroaryl derivatives in high yields (Table 2, entry 4; Table 3, entry 4; Table 4, entry 4).

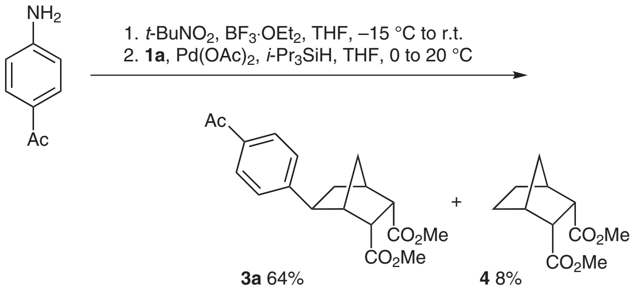
The hydroarylation of norbornene derivatives can be performed generating the diazonium salt in situ.[19,20] This protocol was attempted with *p*-aminoacetophenone and **1a** (Scheme 2). The corresponding hydroarylation product **3a** was isolated in 64% yield along with minor amount of the reduction derivative **4**. The starting norbornene derivative was recovered in 19% yield.

The hydroarylation of norbornadiene was also investigated. However, while an excess of arenediazonium tetrafluoroborate was generally used in the reaction of norbornene derivatives and analogues, with norbornadiene it seems that a 1:3 excess of the hindered olefin is necessary to obtain the desired *exo*-aryl derivative in acceptable yield, at least with our model system (Table 5, entry 3). Increasing further the amount of norbornadiene leads to lower yields, most probably because of the formation of multiple insertion products..



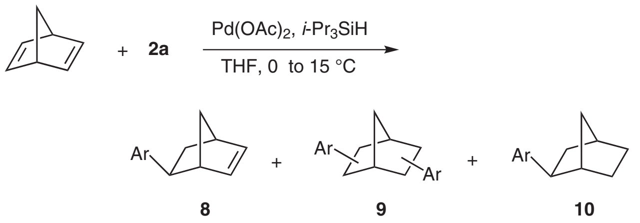
7

Figure 1



Scheme 2

Table 5 Palladium-Catalyzed Reaction of Norbornadiene with *p*-Acetyldiazobenzene Tetrafluoroborate (**2a**)[a]



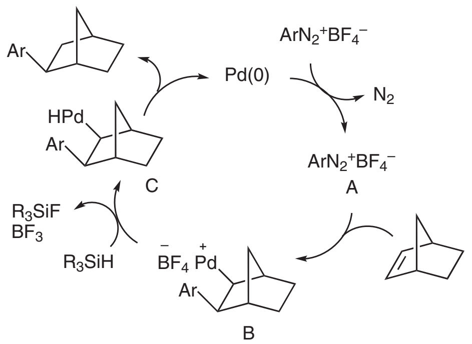
Entry	**2a** (equiv)	Norbornadiene (equiv)	Time (h)	Yield (%)[b] of **8**	Yield (%)[b] of **9**	Yield (%)[b] of **10**
1	2	1	18	traces	38	25
2	1	2	5	20	–	–
3	1	3	5	40	–	–
4	1	5	5	10	–	–

[a] Reactions were carried out under argon on a 0.5 mmol scale using 2 equiv of *i*-Pr_3SiH, 0.05 equiv of $Pd(OAc)_2$ in 4 mL of anhyd THF.

[b] Yields are given for isolated products.

A possible rationale to account for the formation of the hydroarylation products, depicted in Scheme 3 for norbornene, involves (a) a stereoselective addition of the initially formed σ-arylpalladium complex **A** to the carbon–carbon double bond, (b) the reaction of the resultant carbopalladation adduct **B** with trialkylsilane to give the alkylpalladium hydride intermediate **C**, (c) a reductive elimination step which affords the hydroarylation derivative and regenerates the active palladium catalyst. The mechanism based on the cross-coupling of arylpalladium complexes with norbornyltrialkylsilanes formed via a hydrosilylation step appears to be flawed by the fact that alkylfluorosilanes in the presence of fluoride anions are usually required to perform palladium-catalyzed cross-coupling reactions.[21]

In conclusion, we have shown that arenediazonium salts can be efficiently used as aryl donors in the palladium-catalyzed hydroarylation of norbornenes and analogues to give *exo*-arylated derivatives in good to high yields. The



Scheme 3

reaction occurs under mild conditions, tolerates a variety of useful functional groups, and can be performed as a one-pot process generating the arenediazonium salt in situ. Further studies on this chemistry are currently under way.

Acknowledgment

We gratefully acknowledge GlaxoSmithKline for their generous financial support and a fellowship position and Dr. Antonella Carangio and Dr. Alcide Perboni of GlaxoSmithKline for valuable discussions. We are also indebted to MURST and to the University 'La Sapienza'.

References and Notes

(1) For an excellent recent review on the palladium-chemistry of arenediazonium salts, see: Roglans, A.; Pla-Quintana, A.; Moreno-Mañas, M. *Chem. Rev.* **2006**, *106*, 4622.

(2) For some recent selected references, see: (a) Ma, Y.; Song, C.; Chai, Q.; Ma, C.; Andrus, M. B. *Synthesis* **2003**, 2886. (b) Wang, C.; Tan, L.-S.; He, J.-P.; Hu, H.-W.; Xu, J.-H. *Synth. Commun.* **2003**, *33*, 773. (c) Masllorens, J.; Moreno-Manãs, M.; Pla-Quintana, A.; Roglans, A. *Org. Lett.* **2003**, *5*, 1559. (d) Schmidt, B. *Chem. Commun.* **2003**, 1656. (e) Nelson, M. L.; Ismail, M. Y.; McIntyre, L.; Bhatia, B.; Viski, P.; Hawkins, P.; Rennie, G.; Andorsky, D.; Messersmith, D.; Stapleton, K.; Dumornay, J.; Sheahan, P.; Verma, A. K.; Warchol, T.; Levy, S. B. *J. Org. Chem.* **2003**, *68*, 5838. (f) Dai, M.; Liang, B.; Wang, C.; Chen, J.; Yang, Z. *Org. Lett.* **2004**, *6*, 221. (g) Kabalka, G. W.; Dong, G.; Venkataiah, B. *Tetrahedron Lett.* **2004**, *45*, 2775. (h) Xu, L.-H.; Zhang, Y.-Y.; Wang, X.-L.; Chou, J.-Y. *Dyes Pigm.* **2004**, *62*, 283. (i) Sabino, A. A.; Machado, A. H. L.; Correia, C. R. D.; Eberlin, M. N. *Angew. Chem. Int. Ed.* **2004**, *43*, 2514. (j) Sabino, A. A.; Machado, A. H. L.; Correia, C. R. D.; Eberlin, M. N. *Angew. Chem. Int. Ed.* **2004**, *43*, 2514; corrigendum: *Angew. Chem. Int. Ed.* **2004**, *43*, 4389. (k) Masllorens, J.; Bouquillon, S.; Roglans, A.; Hénin, F.; Muzart, J. *J. Organomet. Chem.* **2005**, *690*, 3822. (l) Garcia, A. L. L.; Carpes, M. J. S.; Montes de Oca, A. C. B.; dos Santos, M. A. G.; Santana, C. C.; Correia, C. R. D. *J. Org. Chem.* **2005**, *70*, 1050. (m) Artuso, E.; Barbero, M.; Degani, I.; Dughera, S.; Fochi, R. *Tetrahedron* **2006**, *62*, 3146. (n) Pastre, J. C.; Correia, C. R. D. *Org. Lett.* **2006**, *8*, 1657. (o) Perez, R.; Veronese, D.; Coelho, F.; Antunes, O. A. C. *Tetrahedron Lett.* **2006**, *47*, 1325.

(3) For some recent references, see: (a) Peyroux, E.; Berthiol, F.; Doucet, H.; Santelli, M. *Eur. J. Org. Chem.* **2004**, 1075. (b) Jo, J.; Chi, C.; Höger, S.; Wegner, G.; Yoon, D. Y. *Chem. Eur. J.* **2004**, *10*, 2681. (c) See also: Gallo, V.; Mastrorilli, P.; Nobile, C. F.; Paolillo, R.; Taccardi, N. *Eur. J. Inorg. Chem.* **2005**, 582. (d) Darses, S.; Genet, J. P. *Eur. J. Org. Chem.* **2003**, 4313.

(4) (a) Kikukawa, K.; Kono, K.; Wada, F.; Matsuda, T. *Chem. Lett.* **1982**, 35. (b) Kikukawa, K.; Kono, K.; Wada, F.; Matsuda, T. *J. Org. Chem.* **1983**, *48*, 1333. (c) Kikukawa, K.; Idemoto, T.; Katayama, A.; Kono, K.; Wada, F.; Matsuda, T. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1511. (d) Dughera, S. *Synthesis* **2006**, 1117.

(5) (a) Kikukawa, K.; Kono, K.; Nagira, K.; Wada, F.; Matsuda, T. *Tetrahedron Lett.* **1980**, *21*, 2877. (b) Nagira, K.; Kikukawa, K.; Wada, F.; Matsuda, T. *J. Org. Chem.* **1980**, *45*, 2365. (c) Kikukawa, K.; Kono, K.; Nagira, K.; Wada, F.; Matsuda, T. *J. Org. Chem.* **1981**, *46*, 4413. (d) Sengupta, S.; Sadhukhan, S. K.; Bhattacharyya, S.; Guha, J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 407. (e) Kikukawa, K.; Totoki, T.; Wada, F.; Matsuda, T. *J. Organomet. Chem.* **1984**, *270*, 283. (f) Siegrist, U.; Rapold, T.; Blaser, H.-U. *Org. Process Res. Dev.* **2003**, *7*, 429.

(6) Pelzer, G.; Keim, W. *J. Mol. Catal. A: Chem.* **1999**, *139*, 235.

(7) (a) Willis, D. M.; Strongin, R. M. *Tetrahedron Lett.* **2000**, *41*, 8683. (b) Ma, Y.; Song, C.; Jiang, W.; Xue, G.; Cannon, J. F.; Wang, X.; Andrus, M. B. *Org. Lett.* **2003**, *5*, 4635.

(8) Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Persiani, D. *Org. Lett.* **2008**, *10*, 1597.

(9) (a) Arcadi, A.; Marinelli, F.; Bernocchi, E.; Cacchi, S.; Ortar, G. *J. Organomet. Chem.* **1989**, *368*, 249. (b) Larock, R. C.; Johnson, P. L. *Chem. Commun.* **1989**, 1368.

(10) Mayo, P.; Tam, W. *Tetrahedron* **2002**, *58*, 9527.

(11) Wållberg, A.; Magnusson, G. *Tetrahedron* **2000**, *56*, 8533.

(12) (a) Clayton, S. C.; Regan, A. C. *Tetrahedron Lett.* **1993**, *34*, 7493. (b) Bai, D.; Xu, R.; Chu, G.; Zhu, X. *J. Org. Chem.* **1996**, *61*, 4600.

(13) (a) Kasyan, A.; Wagner, C.; Maier, M. E. *Tetrahedron* **1998**, *54*, 8047. (b) Carroll, F. I.; Brieaddy, L. E.; Navarro, H. A.; Damaj, M. I.; Martin, B. R. *J. Med. Chem.* **2005**, *48*, 7491.

(14) (a) Brunner, H.; Kramler, K. *Synthesis* **1991**, 1121. (b) Sakuraba, S.; Awano, K.; Achiwa, K. *Synlett* **1994**, 291. (c) Sakuraba, S.; Okada, T.; Morimoto, T.; Achiwa, K. *Chem. Pharm. Bull.* **1995**, *43*, 927. (d) Wu, X.-Y.; Xu, H.-D.; Zhoua, Q.-L.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2000**, *11*, 1255. (e) Wu, X.-Y.; Xu, H.-D.; Tang, F.-Y.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2001**, *12*, 2565.

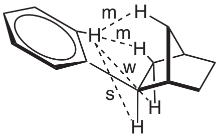
(15) (a) Kikukawa, K.; Nagira, K.; Wada, F.; Matsuda, T. *Tetrahedron* **1981**, *37*, 31. (b) Sengupta, S.; Bhattacharyya, S. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1943.

(16) When **1a** was subjected to the reaction conditions reported in Table 1 (entry 5) omitting Pd(OAc)$_2$ no reduction product **4** was formed suggesting that the reduction of **1a** to **4** proceeds through a palladium-catalyzed process.

(17) **Typical Procedure for the Palladium-Catalyzed Hydroarylation of Norbornene Derivatives with Arenediazonium Tetrafluoroborates – Hydroarylation of 1a with 2a (Table 2, entry 1)**
To a stirred solution of **1a** (105.1 mg, 0.50 mmol) and Pd(OAc)$_2$ (5.6 mg, 0.025 mmol) in anhyd THF (4.0 mL), **2a** (233.8 mg, 1.0 mmol) was added at r.t. under argon. The reaction mixture was cooled in an ice bath. Then, *i*-Pr$_3$SiH (205 μL, 1.0 mmol) was added and the reaction mixture was stirred at 15 °C for 40 min under argon (the reactor was protected from light with aluminum film). After this time, the mixture was diluted with EtOAc, washed with H_2O,

dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel [*n*-hexane–EtOAc, 90:10 (v/v)] to afford 120.8 mg (73% yield) of **3a**, mp 64–66 °C. IR (KBr): 2968, 1735, 1198 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.89$ (d, $J = 8.2$ Hz, 2 H), 7.38 (d, $J = 8.2$ Hz, 2 H), 3.70 (s, 6 H), 3.64 (t, $J = 7.4$ Hz, 1 H), 3.19 (ddd, $J_1 = 11.7$ Hz, $J_2 = 4.5$ Hz, $J_3 = 1.4$ Hz, 1 H), 2.99 (dd, $J_1 = 11.8$ Hz, $J_2 = 3.7$ Hz, 1 H), 2.75–270 (m, 1 H), 2.73–2.58 (m, 1 H), 2.13 (ddd, $J_1 = 11.1$ Hz, $J_2 = 8.8$ Hz, $J_3 = 3.7$ Hz, 1 H), 1.74–1.65 (m, 2 H), 1.42–1.26 (m, 1 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 197.9$, 172.9, 172.6, 151.9, 134.9, 128.5, 127.5, 51.7, 51.5, 47.7, 46.2, 45.9, 41.6, 40.2, 37.5, 33.2, 26.6. MS: *m/z* (relative intensity) = 330 (12) [M^+], 298 (10), 270 (57), 185 (232), 43 (100).

(18) NOESY experiments on **3a**: for selected H–H interactions, see Figure 2.



w: weak; m: medium; s: strong

Figure 2

(19) Doyle, M. P.; Bryker, W. J. *J. Org. Chem.* **1979**, *44*, 1572.

(20) **Palladium-Catalyzed Hydroarylation of 1a with 2a Generated In Situ**
A solution of $BF_3 \cdot OEt_2$ (140 μL, 1.1 mmol) in anhyd THF (1 mL) was cooled at –15 °C and *p*-aminoacetophenone (135.1 mg, 1 mmol) was added. Then, *tert*-butyl nitrite (160 μL, 1.3 mmol) in 1 mL of the same solvent was added dropwise to the rapidly stirred reaction solution over a period of 10 min. Following complete addition, the temperature of the solution was maintained at –15 °C for 10 min and subsequently allowed to warm to 5 °C in an ice-water bath over a period of 20 min. Then, the reaction mixture was warmed to r.t. and stirred at the same temperature till the starting *p*-aminoacetophenone was converted into *p*-acetylbenzenediazonium tetrafluoroborate. The reaction mixture was cooled in an ice bath and **1a** (105.1 mg, 0.50 mmol), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), *i*-Pr_3SiH (205 μL, 1.0 mmol), and of anhyd THF (2 mL) were added. The reaction mixture was allowed to warm to 20 °C and stirred at that temperature for 6 h under argon (the reactor was protected from light with aluminum film). After this time, the mixture was diluted with EtOAc, washed with H_2O, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel [*n*-hexane–EtOAc, 90:10 (v/v)] to afford 106.3 mg (64% yield) of **3a**.

(21) (a) Hatanaka, Y.; Hiyama, T. *Tetrahedron Lett.* **1990**, *31*, 2719. (b) Hatanaka, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1990**, *112*, 7783.