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General facile synthesis of 2,5-diarylheteropentalenes

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Abstract—Palladium-catalyzed cross-coupling reactions of various heteropentalene derivatives were systematically studied. A general three-step synthesis of 2,5-diarylheteropentalenes involving two Suzuki or Negishi couplings and a regiospecific bromination was developed. Nonsymmetrical 2,5-diaryl-furans, thiophenes, pyrroles, 1,3-thiazoles, 1,3-oxazoles, 1,3,4-thiadiazoles, and 1,3,4-oxadiazoles were prepared in 31–67% isolated yield (three steps).

2,5-Diarylheteropentalenes (Fig. 1) represent a common pharmacophore in medicinal chemistry. Numerous examples of these have been reported as inhibitors of selectin,[1a] PDE4,[1b] COX-2,[1c] p38 kinase,[1d–f] platelet aggregation,[1g–i] and 5-lipoxygenase,[1j] estrogen receptor α-selective antagonists,[1k] as well as displaying antifungal,[1l–o] cardiovascular effecting,[1p] antiviral,[1q–s] hypoglycemia regulating,[1t] cytotoxic,[1u] insecticidal,[1v] and CNS depressant[1w,x] activities. Laboratory-scale syntheses of 2,5-diarylheteropenalenes traditionally rely on cyclizations of the corresponding acyclic precursors.[2] Furan, thiophene, and pyrrole analogs are typically prepared from 1,4-diaryl-1,4-butanediones, 1,3,4-oxa- and thiadiazoles from *N*,*N*′-diarylhydrazides, and 1,3-oxa- and thiazoles from/via analogous precursors (Fig. 1, Ret. A). Although the synthesis of heteropentalenes via 1,4-butanediones represents a relatively efficient solution for symmetrical derivatives ($Ar^1 = Ar^2$), it provides less than optimal access to unsymmetrical heteropentalenes ($Ar^1 \neq Ar^2$) due to a lengthy synthesis of their precursors. Both symmetrical and unsymmetrical *N*,*N*′-diarylhydrazides are typically prepared in a straight forward manner, however their cyclization to the relevant heteropentalenes proceeds with a high degree of yield variability.[3] Consequently, when 2,5-diarylheteropentalenes are the subject of a structure–activity relationship (SAR) study, preparation of each compound typically requires a discrete linear multi-step synthetic effort. We present here an alternative general strategy that employs palladium-catalyzed cross-coupling reactions as the key steps and provides access to a wide range of 2,5-diarylheteropentalenes via a uniform route.

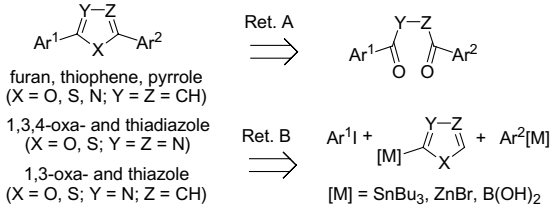

Figure 1. Retrosynthetic disconnections implemented to prepare 2,5-diarylheteropentalenes; Ret. A represents a traditional approach; Ret. B is investigated in this report.

Palladium-catalyzed cross-coupling reactions of various heteropentalene derivatives have been well documented.[4] However, the application of cross-coupling reactions to the synthesis of highly desirable 2,5-diarylheteropentalenes remains largely unexplored[5] and consequently the generality of the substrate scope in question. We propose that once the scope of these reactions is established, it should provide a convergent synthetic route to a variety of heteropentalene derivatives.

We selected thiophene as our model heterocycle and first investigated the formation of 2-arylthiophenes from commercially available starting materials. Optimized Suzuki[4,6] (Table 1, Method A), Stille[4,7] (Method B), and Negishi[4,8] (Method C) couplings of iodobenzene with the corresponding 2-thiophene organometallic reagent provided 2-phenylthiophene in comparable yields of 77%, 84%, and 89%, respectively (Table 1, entries

Keywords: 2,5-Diarylheteropentalenes; Heterocycles; Suzuki; Catalysis; Bromination.
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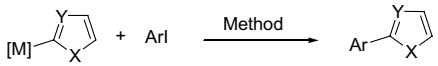
Table 1. Preparation of 2-arylheteropentalenes from aryl iodides and 2-organometallic heterocyclic derivatives via palladium-catalyzed cross-coupling reactions



Entry	Heterocycle		[M]	Ar	Method[a]	Isolated yield (%)
	X	Y				
1	S	CH	$B(OH)_2$	Ph	A	77
2	S	CH	$SnBu_3$	Ph	B	84
3	S	CH	ZnBr	Ph	C	89
4	O	CH	$SnBu_3$	Ph	B	91
5	NMe	CH	$SnBu_3$	Ph	B	82
6	S	N	ZnBr	Ph	C[b]	79
7	S	N	$SnBu_3$	Ph	B	74
8	S	N	$SnBu_3$	4-$MeOC_6H_4$	B	88
9	S	CH	$B(OH)_2$	4-Br-2-MeC_6H_3	A	40[c]
10	S	CH	$SnBu_3$	4-Br-2-MeC_6H_3	B	<10[c]
11	S	CH	ZnBr	4-Br-2-MeC_6H_3	C	90[d]

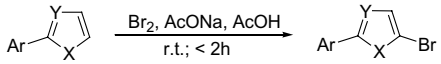
[a] Method A (Suzuki): 10 mol% $Pd(Ph_3P)_4$, Na_2CO_3, H_2O, DMF, 85 °C, 2 h; Method B (Stille): 5 mol% $Pd(Ph_3P)_2Cl_2$, THF, 85 °C, 3 h; Method C (Negishi): 10 mol% $Pd(Ph_3P)_4$, THF, rt 3 h.
[b] Reaction temperature 70 °C, reaction time 12 h.
[c] Yields low due to poor selectivity of aryl iodide versus aryl bromide coupling.
[d] No biscoupled product was observed in the crude reaction.

1–3). The freedom to use any of the coupling methods allows for practical syntheses of these hetropentalenes, for which only a limited number of 2-substituted organometallic reagents is commercially available. Thus, 2-phenylfuran (entry 4) and 2-phenyl-*N*-methylpyrrole (entry 5) were synthesized via Stille coupling, while two examples of 2-aryl-1,3-thiazole derivatives were prepared under both Negishi and/or Stille coupling conditions (entries 6–8). We demonstrated that Negishi conditions provided the best selectivity of the coupling of an aryl iodide in the presence of an aryl bromide (entry 11 vs entries 9–10). Complete chemoselectivity of the Negishi coupling, in spite of a significant steric hindrance of the aryl iodide, implies that such selectivity should be preserved for the synthesis of other substrates, defining the method highly synthetically practical.[9]

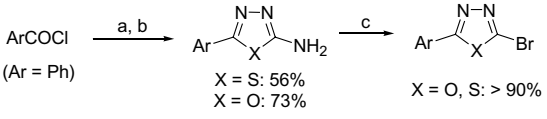
The second step of our proposed synthetic sequence is halogenation of the 5-position of 2-arylheteropentalenes. While bromination and iodination using NBS and NIS as halide sources at elevated temperatures provided a moderate yield for some heterocycles, the most general method proved to be bromination using a solution of bromine in acetic acid buffered with sodium acetate. These conditions were found to be universally effective for the bromination of all investigated heterocycles yet mild enough to be used for even the most sensitive substrates.[10] A variety of 5-bromo-2-arylheteropentalenes were prepared under these conditions with a high level of chemo- and regioselectivity in 58–83% isolated yield (Table 2).[11]

As no organometallic reagents of 1,3,4-oxa- and thiadiazoles are currently commercially available, we present here a practical alternative to the method described in Tables 1 and 2.[12] Condensation of an aroyl chloride with semicarbazide (X = O) or thiosemicarbazide (X = S), was followed by cyclization and conversion of

Table 2. Preparation of 5-bromo-2-arylheteropentalenes via a regioselective bromination



Entry	Heterocycle		Ar	Isolated yield (%)
	X	Y		
1	S	CH	Ph	83
2	O	CH	Ph	77
3	NMe	CH	Ph	58
4	S	N	Ph	67
5	S	N	4-$MeOC_6H_4$	79
6	S	CH	4-Br-2-MeC_6H_3	83



a: $H_2NC(X)NHNH_3^+$, $NaHCO_3$, AcONa, H_2O; b: H_2SO_4, r.t. (X = S), $POCl_3$, toluene, 140 °C (X = O); c: iPentONO_2, $CuBr_2$, MeCN, r.t.

Scheme 1. Preparation of 5-bromo-2-aryl-1,3,4-oxa- and thiadiazoles.

the amines to the desired 5-bromo-2-aryl-1,3,4-oxa- or thiadiazoles in good overall yields (Scheme 1).[13]

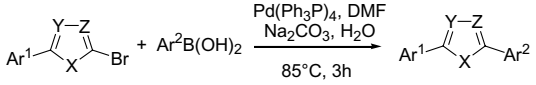
The final step of the 2,5-diarylheteropentalene synthesis is a palladium-catalyzed coupling reaction of 5-bromo-2-arylheteropentalenes with the relevant arylorganometals. A survey of Negishi, Suzuki, and Stille couplings for several heterocycles revealed that all methods were effective for some substrates. The Suzuki protocol stood out as the most general as it proved highly effective for the entire investigated subset of heterocyclic examples. Thiophene derivatives were selected to establish the

generality of the substrate scope for the Suzuki coupling (Table 3). Reaction of 5-bromo-2-arylthiophene with electronically rich (entries 1–4, and 7), neutral (entry 9), as well as electronically deficient (entries 5, 6, and 8) boronic acids proceeded in 59–91% yield. Variation of substitution pattern on the aromatic ring of the boronic acids had no significant influence on the Suzuki coupling; even a sterically hindered *ortho*-substituted aryl bromide was a good substrate for the reaction (compare entries 1–3). The Suzuki coupling was also effective for substrates bearing basic functional groups, including a heterocyclic derivative (entries 7 and 8). A selective Suzuki coupling of the heteroaromatic aryl bromide in the presence of other aromatic aryl bromides was observed (entries 6, 9; ratio of mono/biscoupled product before CC was greater than 7/1 by ^{1}H NMR analysis). Such selectivity is very important as it allows for an immediate use of another palladium-catalyzed coupling reaction for subsequent derivatization. Overall, the Suzuki coupling provided an excellent generality of substrate scope as well as functional group tolerance for thiophene derivatives.[14]

We chose one example of an electron rich (4-$MeOC_6H_4$-$B(OH)_2$) and one example of an electron deficient (4-$CF_3C_6H_4B(OH)_2$) boronic acid to illustrate the scope of our Suzuki methodology for a variety of heterocycles. Examples of 2,5-diaryl-furans (Table 3, entries 10 and 11), *N*-methylpyrroles (entries 12 and 13), 1,3-thiazoles (entries 14–16), 1,3-oxazoles (entries 17 and 18), 1,3,4-thiadiazoles (entries 19 and 20), and 1,3,4-oxadiazoles (entries 21 and 22) were prepared in 63–93% isolated yields following the same Suzuki protocol that was used for thiophene derivatives (entries 1–9). The practicality of our methodology can be highlighted by a pair of 2,5-diaryl-1,3-thiazoles shown in entries 15 and 16, which represent opposite regioisomers of the central heterocycle (compare 5-(4-methoxyphenyl)-2-phenyl-1,3-thiazole, entry 15 vs 2-(4-methoxyphenyl)-5-phenyl-1,3-thiazole, entry 16). Either regioisomer can be synthesized using the same methodology, and even via the same sequence of steps by an a priori choice of aryl iodide and aryl boronic acid. The efficiency of the Suzuki coupling for widely diverse heterocycles and derivatives implies that substrate scope of our methodology as well as functional group tolerance should extend significantly beyond the examples investigated in this report.

In conclusion, we have presented here a general versatile approach to the synthesis of 2,5-diaryl-thiophenes, furans, pyrroles, 1,3-oxa and thiazoles, 1,3,4-oxa and thiadiazoles. Our methodology consists of three steps: (1) a palladium-catalyzed cross-coupling reaction (Table 1), (2) a regio- and chemoselective bromination (Table 2 or Scheme 1), and (3) a Suzuki coupling. More than twenty examples of 2,5-diarylheteropentalenes were prepared in 31–68% overall yield from commercially

Table 3. Preparation of 2,5-diarylheteropentalenes via a general Suzuki coupling approach



Entry	Heterocycle			Ar^1	Ar^2	Isolated yield (%)
	X	Y	Z			
1	S	CH	CH	Ph	4-MeC_6H_4	59
2	S	CH	CH	Ph	3-MeC_6H_4	63
3	S	CH	CH	Ph	2-MeC_6H_4	79
4	S	CH	CH	Ph	4-$MeOC_6H_4$	66
5	S	CH	CH	Ph	4-$CF_3C_6H_4$	71
6	S	CH	CH	Ph	4-BrC_6H_4	54
7	S	CH	CH	Ph	4-$Me_2NC_6H_4$	83
8	S	CH	CH	Ph	3-Pyridyl	91
9	S	CH	CH	4-Br-2-MeC_6H_3	Ph	73[a]
10	O	CH	CH	Ph	4-$MeOC_6H_4$	93
11	O	CH	CH	Ph	4-$CF_3C_6H_4$	85
12	NMe	CH	CH	Ph	4-$MeOC_6H_4$	81
13	NMe	CH	CH	Ph	4-$CF_3C_6H_4$	74
14	S	N	CH	Ph	4-$CF_3C_6H_4$	71
15[b]	S	N	CH	Ph	4-$MeOC_6H_4$	67
16[b]	S	N	CH	4-$MeOC_6H_4$	Ph	74
17[c]	O	N	CH	Ph	4-$MeOC_6H_4$	81
18[c]	O	N	CH	Ph	4-$CF_3C_6H_4$	79
19	S	N	N	Ph	4-$MeOC_6H_4$	91
20	S	N	N	Ph	4-$CF_3C_6H_4$	89
21	O	N	N	Ph	4-$MeOC_6H_4$	85
22	O	N	N	Ph	4-$CF_3C_6H_4$	93

[a] Selectivity of the Suzuki coupling was determined as > 7/1 by NMR analysis before column chromatography purification as a ratio of mono/biscoupled products.

[b] Products in entries 15 and 16 represent opposite regioisomers of the central 1,3-thiazole ring.

[c] 2-Bromo-5-phenyl-1,3-oxazole was prepared according to Kashima, C.; Arao, H. *Synthesis* **1989**, 873.

available materials. We believe that our methodology provides an effective entry to the synthesis of 2,5-diarylheteropentalenes and will serve as a practical basis for thorough SAR analyses as well as other synthetic applications of this class of compounds.

Acknowledgements

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Supplementary data

Supplementary data containing experimental procedures and compound characterizations can be found in the online version, at doi:10.1016/j.tetlet.2004.07.132.

References and notes

1. (a) Slee, D. H.; Romano, S. J.; Yu, J.; Nguyen, T. N.; John, J. K.; Raheja, N. K.; Axe, F. N.; Jones, T. K.; Ripka, W. C. *J. Med. Chem.* **2001**, *44*, 2094; (b) Perrier, H.; Bayly, C.; Laliberte, F.; Huang, Z.; Rasori, R.; Robichaud, A.; Girard, Y.; Macdonald, D. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 323; (c) Carter, J. S.; Kramer, S.; Talley, J. J.; Penning, T.; Collins, P.; Graneto, M. J.; Seibert, K.; Koboldt, C. M.; Masferrer, J.; Zweifel, B. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1167–1171; (d) de Laszlo, S. E.; Hacker, C.; Li, B.; Kim, D.; MacCoss, M.; Mantlo, N.; Pivnichy, J. V.; Colwell, L.; Koch, G. E.; Cascieri, M. A.; Hagmann, W. K. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 641; (e) de Lazslo, S. E.; Visco, D.; Agarwal, L.; Chang, L.; Chin, J.; Croft, G.; Forsyth, A.; Fletcher, D.; Frantz, B.; Hacker, C.; Hanlon, W.; Harper, C.; Kostura, M.; Li, B.; Luell, S.; MacCoss, M.; Mantlo, N.; O'Neill, E. A.; Orevillo, C.; Pang, M.; Parsons, J.; Rolando, A.; Sahly, Y.; Sidler, Y.; Widmer, W. R.; O'Keefe, S. J. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 2689; (f) Gallagher, T. F.; Seibel, G. L.; Kassis, S.; Laydon, J. T.; Blumenthal, M. J.; Lee, J. C.; Lee, D.; Boehm, J. C.; Fier-Thompson, S. M.; Abt, J. W.; Soreson, M. E.; Smietana, J. M.; Hall, R. F.; Garigipati, R. S.; Bender, P. E.; Erhard, K. F.; Krog, A. J.; Hofmann, G. A.; Sheldrake, P. L.; McDonnell, P. C.; Kumar, S.; Young, P. R.; Adams, J. L. *Bioorg. Med. Chem.* **1997**, *5*, 49; (g) Selwood, D. L.; Brummell, D. G.; Glen, R. C.; Goggin, M. C.; Reynolds, K.; Tatlock, M. A.; Wishart, G. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1089; (h) Rehse, K.; Muehler, U. *Arch. Pharm.* **1995**, *328*, 765; (i) Fray, M. J.; Cooper, K.; Parry, M. J.; Richardson, K.; Steele, J. *J. Med. Chem.* **1995**, *38*, 3514; (j) Kerdesky, F. A.; Holms, J. H.; Moore, J. L.; Bell, R. L.; Dyer, R. D. *J. Med. Chem.* **1991**, *34*, 2158; (k) Mortensen, D. S.; Rodriguez, A. L.; Sun, J.; Katzenellenbogen, B. S. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2521; (l) Stephens, C. E.; Tanious, F.; Kim, S.; Wilson, W. D.; Schell, W. A.; Perfect, J. R.; Franzblau, S. G.; Boykin, D. W. *J. Med. Chem.* **2001**, *44*, 1741; (m) Patel, C. L.; Parekh, H. *J. Ind. Chem. Soc.* **1988**, *65*, 606; (n) Pachhamia, V. L.; Parikh, A. R. *J. Ind. Chem. Soc.* **1989**, *64*, 250; (o) Abdel-Rahman, R. M.; El-Gendy, Z.; Fawzy, M. M.; Mahmoud, M. B. *J. Ind. Chem. Soc.* **1991**, *68*, 628; (p) Shukla, S.; Bhalla, M.; Misra, U.; Mukerjee, D.; Saxsena, A. K. *Boll. Chim. Farm.* **1998**, *137*, 229; (q) Almerico, A. M.; Patrizia, D.; Barraja, P.; Dattolo, G.; Mingoia, F. *Farmaco* **1998**, *53*, 33; (r) Zapp, M. L.; Young, D. W.; Kumar, A.; Singh, R.; Boykin, D. W.; Wilson, W. D.; Green, M. R. *Bioorg. Med. Chem.* **1997**, *5*, 1149; (s) Mezentseva, M. V.; Nicolaeva, I. S.; Fomina, A. N.; Akimova, M. I. *Pharm. Chem. J.* **1987**, *21*, 731; (t) Girges, M. M. *Arzneim. Forsch.* **1994**, *44*, 490; (u) Dattolo, G.; Cirrincione, G.; Almerico, A. M.; Aiello, E.; Grimaudo, S. *Farmaco* **1993**, *48*, 191; (v) Idoux, J. P.; Gibbs-Rein, K. S.; Gupton, J. T.; Cunningham, G. N. *J. Chem. Eng. Data* **1988**, *33*, 385; (w) Tandon, S. K.; Doval, D. C.; Shanker, K.; Sinha, J. N. *Pharmazie* **1982**, *37*, 388; (x) Reynaud, P.; El-Youssef, D. C.; Nguyen-Tri-Xuong, E.; Tran, G.; Rinjard, P. *J. Heterocycl. Chem.* **1992**, *29*, 991.
2. For a thorough review on heteropentalene preparations, see: *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vols. 4 and 6.
3. In an unpublished study, we have investigated cyclizations of more than twenty different *N*,*N*′-diarylhydrazides and isolated 2,5-diaryl-1,3,4-thiadiazoles in yields heavily scattered in a range of 5% and 95%. For an experimental procedure used in the study, see: Tschierske, C.; Girdzinuaite, D. *J. Prakt. Chem.* **1991**, *333*, 135.
4. For recent reviews on palladium-catalyzed cross-coupling reactions, including these involving heteropentalenes, see: *Handbook of Organopalladium Chemistry for Organic Synthesis*; (a) Negishi, E., Ed.; Wiley-Interscience: New York, 2002; *Metal-Catalyzed Cross-coupling Reactions*; (b) Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; *Cross-Coupling Reactions: A Practical Guide*; (c) Miyaura, N., Ed.; Topics in Current Chemistry Series 219; Springer-Verlag: New York, 2002; (d) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176, and references cited therein.
5. An exception to this rule is represented by several examples of thiophene derivatives prepared via Stille or Kumada couplings: (a) Cielen, E.; Stobiecka, A.; Tahri, A.; Hoornaerth, G. J.; De Schryver, F. C.; Gallay, J.; Vincent, M.; Boens, N. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1197; (b) Hirayama, D.; Takimiya, K.; Aso, Y.; Otsubo, T.; Hasobe, T.; Yamada, H.; Imahori, H.; Fukuzumi, S.; Sakata, Y. *J. Am. Chem. Soc.* **2002**, *124*, 532; (c) Ankersen, M.; Peschke, B.; Hansen, B. S.; Hansen, T. K. *Bioorg. Chem. Lett.* **1997**, *7*, 1293; (d) Takahashi, K.; Suzuki, T.; Akiyama, K.; Ikegami, Y.; Fukazawa, Y. *J. Am. Chem. Soc.* **1991**, *113*, 4576; (e) Zablocki, J.; Palle, V.; Blackburn, B.; Elzein, E.; Nudelman, G.; Gao, Z.; Li, Z.; Meyer, S.; Bellardinelli, L. *Nucleos. Nucleot.* **2001**, *20*, 343; (f) Minato, A.; Tamao, K.; Suzuki, K.; Kumada, M. *Tetrahedron Lett.* **1980**, *21*, 4017.
6. (a) Suzuki, A. *Acc. Chem. Res.* **1982**, *15*, 178; (b) Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
7. (a) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4992; (b) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.
8. (a) Negishi, E.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821; (b) Negishi, E.; King, A. O.; Okukado, N. *J. Chem. Soc., Chem. Commun.*, **1977**, 683; (c) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340.
9. An alternative approach for the synthesis of 2-phenylthiophene implementing palladium-catalyzed cross-couplings is a reaction of 2-bromothiophene with a corresponding phenylmetallic reagent. Our investigation revealed that Negishi, Stille, and Suzuki couplings were feasible under conditions of Methods A–C described in Table 1. However, the generality of this approach did not extend to some other heterocycles.

10. Bromination of pyrrole derivatives attempted without sodium acetate buffer led to a significant decomposition of starting material.
11. A representative procedure for selective bromination of 2-arylheteropentalenes: To a stirred homogeneous solution of 2-arylheteropentalene (5.0 mmol) and sodium acetate (10 mmol) in acetic acid (25 mL), bromine (5.0 mmol) was added dropwise via syringe at room temperature over 20–30 min (discoloration of reaction mixture was generally observed during bromine addition). The reaction progress was monitored by TLC or LCMS analyses: upon completion, the reaction mixture was combined with 1 M sodium hydroxide (250 mL) and ethyl acetate (250 mL). The organic layer was separated, washed sequentially with 1 M sodium hydroxide (100 mL) and brine (100 mL), and dried over sodium sulfate. The desired product was obtained by column chromatography on silica gel (eluent: hexanes/ethyl acetate).
12. If a given 2-aryl-1,3,4-oxa- or thiadiazole is available, bromination under conditions described in Table 2 represents a viable option: several examples of 2-bromo-1,3,4-oxa- and thiadiazoles were isolated in $\geqslant$75% yield (reaction temperature 50 °C for some derivatives).
13. (a) Hoggarth, E. *J. Chem. Soc. Abstr.* **1949**, 1163; (b) Gehlen, H.; Moeckel, K. *Ann. Chem.* **1962**, *660*, 144.
14. A representative procedure for the Suzuki coupling: 5-bromo-2-arylheteropentalane (1.0 mmol), DMF (20 mL), 1 M aqueous solution of sodium carbonate (5 mL), and boronic acid (1.1 mmol) were combined to form a heterogeneous mixture. This mixture was degassed with a steady stream of argon for 10 min at room temperature. To this mixture, solid $Pd(Ph_3P)_4$ (0.1 mmol) was added and the mixture was degassed with argon for 2 min after which it was heated under argon to 85 °C for 3 h. The reaction mixture was combined with 1 M hydrochloric acid (100 mL) and ethyl acetate (200 mL). The organic layer was separated, washed sequentially with 1 M hydrochloric acid (50 mL) and brine (50 mL), and dried over sodium sulfate. The desired product was obtained by column chromatography on silica gel (eluent: hexanes/ethyl acetate).