A Combination of Tandem Amine-Exchange/Heterocyclization and Biaryl Coupling Reactions for the Straightforward Preparation of Phenanthro[9,10-*d*]pyrazoles

Roberto Olivera, Raul SanMartin, and Esther Domínguez*

Kimika Organikoa Saila, Zientzi Fakultatea, Euskal Herriko Unibertsitatea, P.O. Box 644, 48080 Bilbao, Spain

qopdopee@lg.ehu.es

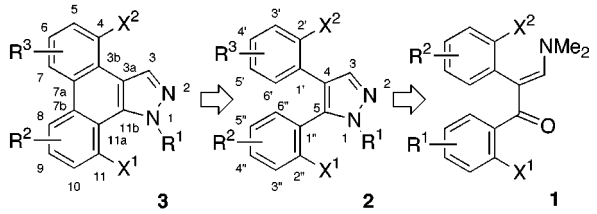
Received April 20, 2000

The tandem amine-exchange/heterocyclization of enaminoketones is successfully applied to the regioselective preparation of a series of new 4,5-diarylpyrazoles by reaction of phenylhydrazine and several 3-*N*,*N*-(dimethylamino)-1,2-diarylpropenones. The comparison of a vast array of biaryl coupling procedures provides general, complementary approaches to new phenanthro[9,10-*d*]-pyrazoles. The most efficient procedures for this final step in the construction of the tetracyclic system are based on a Stille-type tandem stannylation−biaryl coupling of *o*,*o*′-dihalogenated diarylpyrazoles and an hypervalent iodine-mediated nonphenolic oxidative coupling of nonhalogenated precursors.

Introduction

Although scarcely found in nature,[1] pyrazoles are known not only as potent insecticides,[2] herbicides,[3] and monomers for the preparation of electroluminiscent and thermoresistant materials,[4] but also as antitumor, anti-inflamatory, antimicrobial, antipsychotic, or analgesic agents.[5] Thus, due to their wide range of pharmacological and technological applications, pyrazoles have been the focus of much synthetic effort in the past decades.[6] Among the different methodologies for the synthesis of the pyrazole framework, only a few examples of the reaction between hydrazine derivatives and enaminoketones have been reported so far.[7] This protocol provides better regioselectivity compared to (i) the addition of hydrazines to 1,3-dicarbonyl compounds,[8a] (ii) the 1,3-cycloaddition of diazoalkanes to alkynes,[8b,c] or (iii) the addition of hydrazines to α,β-unsaturated carbonyl compounds,[9] but lower yields and limited substitution patterns have been described in most cases.[10]

Once we had demonstrated not only the synthetic potential of the amine-exchange reaction/heterocyclization to prepare heterocycles such as isoxazoles and pyrimidines,[11] but also the viability of the Stille coupling reaction of dihaloarylpyrimidines allowing the access to phenanthro fused pyrimidines,[12] we planned to expand our strategy to the preparation of a new type of pyrazoles, the phenanthro[9,10-*d*]pyrazoles **1**. Toward this end, enaminones **3** were selected as the starting material of



choice to develop an appealing synthetic approach based on the biaryl coupling of diarylpyrazole intermediates **2** as the key step. In this context, it is worthy to remark

* To whom correspondence should be addressed. Tel: 34 94 6012577. Fax: 34 94 4648500.

(1) Eicher, T.; Hauptmann, S. In *The Chemistry of Heterocycles: Structure, Reactivity, Syntheses and Applications*; Thieme-Verlag: New York, 1995; p 184.

(2) (a) Parlok, J. J. *J. Heterocycl. Chem.* **1998**, *35*, 1493−1499. (b) Okada, J.; Itaru, O.; Shuku, W.; Wada, M.; Fukuchi, T.; Yoshiya, K.; Takahashi Y. *ACS Symp. Ser.* **1998**, 168−177.

(3) (a) Frinkelstein, B. L.; Strok, C. J. *J. Pesticide Sci.* **1997**, *50*, 324−328. (b) Schallner, O.; Heinz, K.-H.; Karl, K.-J. Ger. Offen DE, 1997, 19615259; *Chem. Abstr.* **1997**, *127*, 346387.

(4) Valberkel, P. M.; Sherrington, D. C. *Polymer* **1996**, *37*, 1431−1435.

(5) (a) Daidone, G.; Maggio, B.; Plescia, S.; Raffa, D.; Musiu, C.; Milia, C.; Perra, G.; Marongiu, M. E. *Eur. J. Med. Chem.* **1998**, *33*, 375−382. (b) Tsuji, K.; Nakamurana, K.; Konishi, N.; Tojo, T.; Ochi, T.; Scnoh, H.; Masuo, M. *Chem. Pharm. Bull.* **1997**, *45*, 987−995. (c) Nauduri, D.; Reddy, G. *Chem. Pharm. Bull.* **1998**, *46*, 1254−1260. (d) Gajare, A. S.; Bhawsar, S. B.; Shingare, M. S. *Ind. J. Chem.* **1997**, *6*, 321−322. (e) Wise, L. D.; Butler, D. E.; Dewald, H. A.; Lustgarten, D. M.; Pattison, I. C.; Schweiss, D. N.; Coughenour, L. L.; Downs, D. A.; Heffner, T. G.; Pugsley, T. A. *J. Med. Chem.* **1987**, *30*, 1807−1812. (f) Brune, K. *Med. Toxicol. (Suppl. 1)* **1986**, *1*, 1−9.

(6) Elguero, J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Schriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. 3, Chapter 2.1.

(7) Lue, P.; Greenhill, J. V. *Adv. Heterocycl. Chem.* **1997**, *67*, 225−314 and references therein.

(8) (a) Coispeau, G.; Elguero, J. *Bull. Soc. Chim. Fr.* **1970**, *7*, 2717−2736. (b) Behr, L. C.; Fusco, R.; Jarboe, C. H. In *The Chemistry of Heterocyclic Compounds, Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles and Condensed Rings*; Weissberger, A., Ed.; John Wiley & Sons: New York, 1967. (b) Tkagi, K.; Hubert-Habart, M. *J. Heterocycl. Chem.* **1996**, *33*, 1003−1008.

(9) (a) Elnagdi, N. H.; Elgeneie, G. E. H.; Abd-Elaal, F. A. *Heterocycles* **1985**, *23*, 3121−3153. (b) Zelenin, K. N. *Org. Proc. Int.* **1995**, *27*, 521−540.

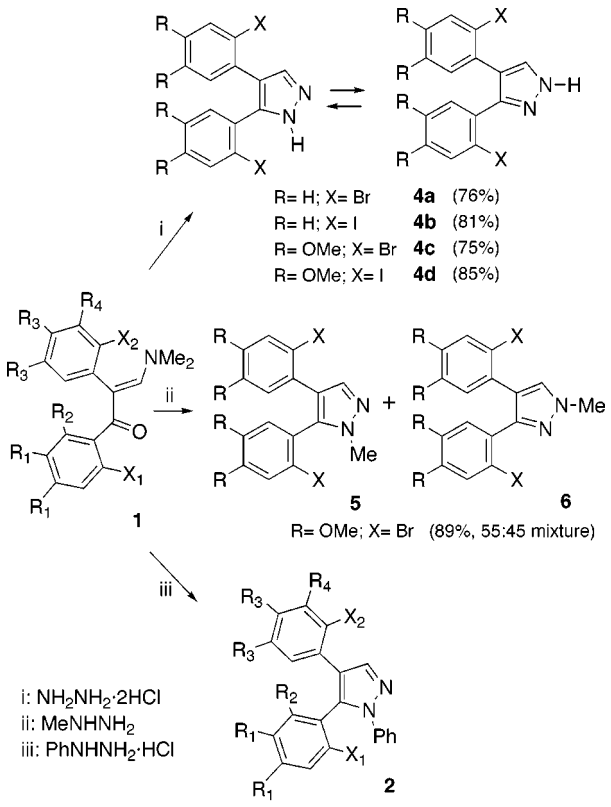
(10) (a) Barluenga, J.; López-Ortiz, J. F.; Tomás, M.; Gotor, V. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1891−1893. (b) Bhardwaj, S.; Jolly, V. S. *Orient. J. Chem.* **1996**, *12*, 185−187. (c) Cacchi, S.; Fabrizi, G.; Caragio, A. *Synlett* **1997**, 959−960. (d) Makino, K.; Kim, H. S.; Kurasawa, Y. *J. Heterocyclic Chem.* **1998**, *35*, 489−497. (e) Kadu, M. V.; Jamode, V. S. *Asian J. Chem.* **1998**, *10*, 480−483.

(11) (a) Domínguez, E.; Ibeas, E.; Martínez de Marigorta, E.; Palacios, J. K.; SanMartin, R. *J. Org. Chem.* **1996**, *61*, 5435−5439. (b) Domínguez, SanMartin, R., Martínez de Marigorta, E.; Olivera, R. *Synlett* **1995**, 955−956.

(12) Olivera, R.; Pascual, S.; Herrero, M.; SanMartin, R.; Domínguez, E. *Tetrahedron Lett.* **1998**, *39*, 7155−7158.

10.1021/jo000609i CCC: $19.00
Published on Web 09/26/2000

Scheme 1



that phenanthro[9,10-*d*]heterocycles, which constitute the core of several natural products such as cryptopleurine, thyloforine or anthofine, exhibit very interesting pharmacological properties related to the planarity of the system and their DNA-chain intercalating ability.[13]

Results and Discussion

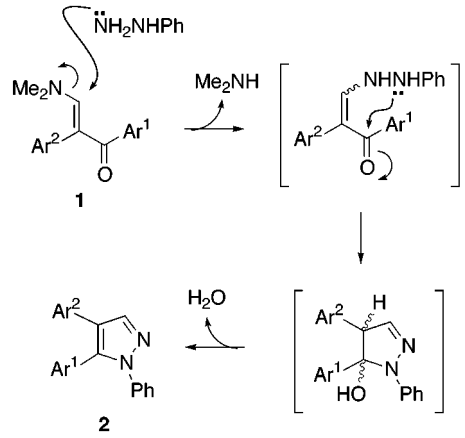
1. Synthesis of 4,5-Diarylpyrazoles. Regarding the construction of diarylpyrazoles **2**, our initial assays on enaminoketones **1a**−**d**[11] using NH_2NH_2·2HCl as the reagent for the amine-exchange/heterocyclization afforded a mixture of pyrazole tautomers **4a**−**d** (Scheme 1).[14] Apart from the observed lack of selectivity of the heterocyclization, we realized that the so-obtained pyrazoles **4** were not compatible with the organometallic species involved in the scheduled cross-coupling reactions due to the acidic H-1 hydrogen.[15] Consequently, we explored the preparation of *N*-methyl pyrazoles such as **5** by reaction of substrate **1c** with NH_2NHMe, but only a mixture of regioisomers **5** and **6** (55:45) was obtained. A similar nucleophilicity of both nitrogens in methyl hydrazine can be proposed as the cause of the null regioselectivity observed in this case. This problem was finally overcome when enaminoketones **1** were reacted with NH_2NHPh, since the corresponding *N*-phenyl-4,5-diarylpyrazoles **2** were obtained as the only isomers (Table 1).[16] A plausible mechanism for the latter transformation, involving an initial amine-exchange process is indicated in Scheme 2.

Table 1. Synthesis of Diarylpyrazoles 2

R^1	R^2	R^3	R^4	X^1	X^2	**2**[a] (%)
H	H	H	H	Br	Br	**2a** (90)
H	H	H	H	I	I	**2b** (71)
OMe	H	OMe	H	Br	Br	**2c** (90)
OMe	H	OMe	H	I	I	**2d** (82)
OMe	H	H	H	Br	Br	**2e** (89)
OMe	H	H	H	I	I	**2f** (91)
H	H	OMe	H	Br	Br	**2g** (88)
H	H	OMe	H	I	I	**2h** (94)
H	H	OMe	H	Br	I	**2i** (79)
H	H	OMe	H	I	Br	**2j** (81)
H	H	OCH_2O[b]	H	Br	Br	**2k** (91)
H	H	H	H	H	H	**2l** (99)
OMe	H	OMe	H	H	H	**2m** (97)
OMe	OMe	OMe	H	H	H	**2n** (95)
OMe	OMe	OMe	OMe	H	H	**2o** (99)

[a] Yield of pure crystallized compound. [b] $R^3 + R^3 = OCH_2O$.

Scheme 2



2. Initial Biaryl Coupling Attempts. The coupling of halogenated pyrazoles **2b** and **2c** was initially attempted by formation of the corresponding alkylstannanes and boronic acids, usual intermediates of Stille and

(13) (a) Chen, K.-X.; Gresh, N.; Pullmann, B. *Nucleic Acid Res.* **1986**, *14*, 9103−9115. (b) Martin, M. A.; del Castillo, B.; Lerner, D. A. *Anal. Chim. Acta* **1988**, *205*, 105−115. (c) Chen, R. X.-F.; Chaudhuri, N. C.; Paris, P. L.; Rumney IV, S.; Kool, E. T. *J. Am. Chem. Soc.* **1996**, *118*, 7671−7678. (d) Kumar, S. *J. Org. Chem.* **1997**, *62*, 8535−8539.

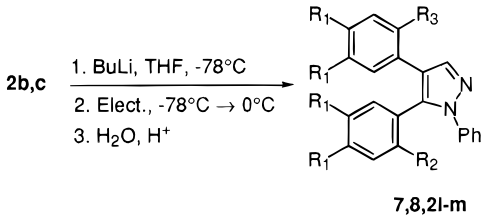
(14) Such 3, 4- or 4,5-disubstituted pyrazoles are always found as a mixture of tautomers. See: Anjaneyulu, A. S. R.; Rani, G. S.; Mallavadhani, U. V.; Murthy, Y. L. N. *Ind. J. Chem.* **1995**, *4*, 277−280 and references therein. In fact, ^{1}H NMR spectra of pyrazoles **4** showed an average signal for H-3(5) at 7.54−7.76 ppm.

(15) The most common organometallic compounds employed in biaryl coupling reactions, are usually synthesized by reaction of an organolithium precursor and a suitable electrophile reagent. The deprotonation of H-1 in pyrazoles by organolithium reagents can promote several side reactions. See: Elguero, J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 5, pp 273−290.

(16) NOE Experiments were employed to confirm this regiochemistry. In fact, NOE effect was observed between H-3 and H-2′(6′) (the ortho hydrogen(s) of the aryl group at C-4) and no NOE could be seen between H-3 and the *N*-Ph hydrogens. In addition, NOE effect was observed between H-3 and H-2″(6″) (the ortho hydrogen(s) of the aryl group at C-5). These experiments were first performed for tetramethoxylated pyrazoles **2c** and **2d** and later extended to the whole series of **2**.

(17) According to the X-ray diffractometry data of a 4,5-diarylisoxazole, both 4- and 5-aryl groups are significantly twisted with respect to the heterocyclic ring (puckering angles are 25° and 59° respectively). See: SanMartin, R.; Olivera, R.; Domínguez, E.; Solans, X.; Urtiaga, M. K.; Font-Bardía, M. *Cryst. Res. Technol.* **1997**, *32*, 1015−1020. In *N*-phenyl-4,5-diarylisoxazoles **2**, the phenyl group should clearly force the other aryl groups to an even more twisted conformation.

Table 2



7,8,2l-m

Elect.= Me_3SnCl, Bu_3SnCl, $B(OMe)_3$, $B(O^iPr)_3$, TMSCl

substrate	R^1	R^2	R^3	product (%)
2b	H	H	I	**7a** (10−21)
2b	H	I	H	**8a** (7−30)
2b	H	H	H	**2l** (9−69)
2c	OMe	H	Br	**7b** (15−77)
2c	OMe	H	H	**2m** (11−88)

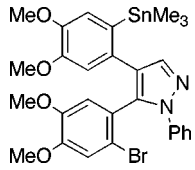
Suzuki biaryl coupling procedures, respectively. However, when derivatives **2b** and **2c** were reacted with BuLi and $B(OR)_3$ or alternatively with BuLi and R_3SnCl under a wide array of conditions, only dehalogenation products **7**−**9** were obtained (Table 2). It can be proposed that an unusually stable aggregation state of the so-formed organometallic species could avoid the attack of bulky electrophiles.[18] Similar results were obtained by the use of the methodologies reported by Ziegler[19a] and Lipshutz.[19b]

The desired intramolecular cyclization was achieved when the procedure developed by Lemaire et al. for the preparation of symmetrical biaryls[20] was applied to diarylpyrazoles **2b**−**d**, as the conditions used ($Pd(OAc)_2$, Bu_4NBr, K_2CO_3, DMF) provided low yields (12−22%) of the target tetracycles **3a**,**b**, but only from diiodo derivatives **2b** and **2d**.

3. Ullmann Coupling Assays. As shown in Table 3, the Ullmann reaction of diaryl derivatives **2b**−**d** was attempted under a wide range of experimental conditions.[21] It is worth pointing out the good results obtained by the system $(CuOTf)_2$·PhH, DMF[20f] (entries 4−6) under relatively mild conditions. However, it was only applicable to substrates bearing *o*,*o*-diiodo substituents, since the bromo analogues provided the already mentioned dehalogenation products **7** and **9**. The use of activated copper in different solvents (entries 7−12, 15, 16, and 18−21)[21a−f] afforded moderate yields of the target phenanthropyrazoles **3a**,**b**, but much harsher reaction conditions were required. In comparison with the previous cross-coupling procedures assayed, the Ullmann reaction constituted a useful methodology for the access to phenanthro[9,10-*d*]pyrazoles **3**, but a need for a more general, efficient methodology still remained.

4. Intramolecular Stille-Type Coupling. A useful way to generate arylstannanes involves the palladium-catalyzed reaction between aryl halides and ditin derivatives such as Me_6Sn_2 and $^nBu_6Sn_2$.[22] We tried the latter protocol on substrate **2c** using $Pd(PPh_3)_4$ as catalyst and several solvents (1,4-dioxane, DMF, NMP, toluene) with the following results: A mixture of products **7b** and **2m** was obtained in all cases, and depending on the conditions applied arylstannane **9** was also isolated in moderate yields. Nevertheless, the most important feature was the isolation of coupled phenanthropyrazole **3b** when Me_6Sn_2 was used.[23] In fact, this evidence together with the result obtained from the control test carried out in the absence of Me_6Sn_2 as reagent (Table 4, entry 19), discounts the possibility of a biaryl coupling reaction mediated by a direct intramolecular palladation.

This result encouraged us to improve the tandem stannylation/biaryl coupling by means of exploring different palladium catalyst−ligand systems. As shown in Table 4, both $Pd(PPh_3)_4$ and $PdCl_2(PPh_3)_2$ (entries 3, 4, and 13) were effective to promote the coupling reaction. The use of bidentate ligands (entries 5−7) or ligands of poor electron-donating ability (entries 8−11) did not improve the yield or the kinetic of the reaction, affording mainly the dehalogenation products. The employment of ligands such as benzonitrile or acetonitrile (entries 14 and15) were incompatible with the applied reaction conditions. In fact, palladium black was deposited during the first moments after the beginning of the reaction. The addition of common additives or cocatalysts in the Stille reaction (entries 2, 9, 11, and 12) did not appreciably affect the kinetic of the reaction. Finally, the pyrazole **2c** did not undergo the coupling reaction to an appreciable extent when palladium "naked" (entries 16 and 17) or nickel catalysts (entries 18) were applied.



Both $Pd(PPh_3)_4$ and $PdCl_2(PPh_3)_2$ proved to be efficient catalysts for the above-described transformation, al-

(18) (a) Winkler, H. J. S.; Winkler, H. *J. Am. Chem. Soc.* **1966**, *88*, 969−974. (b) Bailey, W. F.; Patricia, J. J. *J. Organomet. Chem.* **1988**, *352*, 1−46. Several experiments were carried out in order to effect the insertion of electrophiles $B(OR)_3$ and R_3SnCl, including the addition of metal-complexing agents such as TMEDA and crown ethers (18-crown-6), the use of ^{t}BuLi or activated magnesium. Along with the negative results obtained from the latter assays, it was observed that even Me_3SiCl did not react with the organometallic species involved, and only small electrophiles such as H^+ or D^+ could be inserted in the stable organolithium or organomagnesium species (the addition of H_2O or D_2O could be carried out after 10 h without observed any changes in the yields showed in Table 2). Only when trying Negishi coupling conditions (1. BuLi, THF, −78 °C.; 2. $ZnCl_2$, −78 °C → rt; 3. $Pd(PPh_3)_4$, rt → reflux) a white suspension was observed after treating with $ZnCl_2$, thus indicating the formation of the corresponding organozinc intermediate. However, on adding the palladium catalyst the reaction mixture turned to a coagulated gel which was impossible to be worked up or analyzed.

(19) (a) Ziegler, F. E.; Chliwner, I.; Fowler, K. W.; Kanfer, S. J.; Kuo, S. J.; Sinha, N. D. *J. Am. Chem. Soc.* **1980**, *102*, 790−798. (b) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 138−590. Both methodologies are based on the generation and coupling of arylorganocuprates. We tried two different Cu(I) systems, CuI·PEt_3 and $CuCN-O_2$, after performing the lithium−halogen exchange at −78 °C, and in both cases only single and double dehalogenation products **7** and **2l**−**m** were isolated.

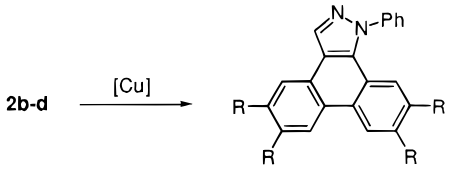
(20) Hassan, J.; Penalva, V.; Lavenot, L.; Gozzi, C.; Lemaire, M. *Tetrahedron* **1998**, *54*, 13793−13804.

(21) (a) Suzuki, H.; Enya, T.; Hisamatsu, Y. *Synthesis* **1997**, 1273−1276. (b) Meyers, A. I.; Mackennon, M. J. *Tetrahedron Lett.* **1995**, *36*, 5864−5872. (c) Copper(I) 2-thipophenecarboxylate has been reported to promote the biaryl Ullmann reaction in extremely mild conditions. See: Zhang, S.; Zhang, D.; Liebeskind, L. S. *J. Org. Chem.* **1997**, *62*, 2312−2313. (d) Horner, L.; Weber K.-H. *Chem. Ber.* **1967**, *100*, 2842−2853. (e) Newman, M. S.; Cella, J. A. *J. Org. Chem.* **1974**, *39*, 2084−2087. (f) Ziegler, F. E.; Schwartz, J. A. *J. Org. Chem.* **1978**, *43*, 985−991.

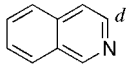
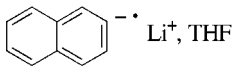
(22) (a) Azarian, D.; Dua, S. S.; Eaborn, C.; Walton, D. R. M. *J. Organomet. Chem.* **1976**, *117*, C55−C57. (b) Mitchell, T. N. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F.; Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; pp 189−190 and references therein.

(23) The use of $^nBu_6Sn_2$ as the stannylating agent led to mixtures of dehalogenation products. This observation could be aduced to the lower reactivity or to steric interactions of $^nBu_6Sn_2$ compared to Me_6Sn_2 during the transmetalation steps. See: Azizian, H.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1981**, *215*, 49−58.

Table 3. Summary of the Ullmann Reaction Assays Performed on Pyrazoles 2b−d



R= H **3a**
R= OMe **3b**

entry	2	reaction conditions	T^a (°C)	t (h)	**3**[a] (%)	dehalog. products[a] (%)	conv[b] (%)
1	**2b**	Cu, $Pd(PPh_3)_4$ (5 mol %), DMSO	100	77		**7a**−**2l** (62)	66
2	**2c**			77		**7b**−**2m** (69)	79
3	**2d**			77		**7c**−**2m** (76)	95
4	**2b**	$(CuOTf)_2$·PhH, DMF	100	34	**3a** (86) *77*	**7a**−**2l** (14)	100
5	**2c**		100	89	**3b** 6	**7b**−**2m** (46)	52
6	**2d**		130	38	**3b** (68) *56*	**7c**−**2m** (19)	90
7	**2b**	Cu[c], DMF[d]	220	31	**3a** (73) *68*	**7a**−**2l** (12)	85
8	**2b**		190	39	**3a** 76	**7a**−**2l** (16)	92
9	**2c**	Cu[c], DMF[d]	220	72		**7b**−**2m** (41)	52
10	**2d**		220	33	**3b** 32	**7c**−**2m** (22)	56
11	**2b**	CuTC[e], NMP	170	89		**7a**−**2l** (14)	15
12	**2c**			72			
13	**2b**	Cu_2O, DMF	190	56		**7a**−**2l** (17)	29
14	**2c**			72			
15	**2b**	Cu , Py	190	22	**3a** 64	**7a**−**2l** (21)	100
16	**2c**			72			
17	**2b**	Cu, 	260	10		**7a**−**2l** (55)	100
18	**2b**	Cu, NMP	195	48	**3a** (79)	**7a**−**2l** (15)	94
19	**2d**			77	**3d** (51)	**7c**−**2m** (29)	100
20	**2b**	Cu, $PhNO_2$[d]	175	41	**3a** (81)	**7a**−**2l** (19)	100
21	**2d**			49	**3d** (72)	**7c**−**2m** (26)	100
22	**2b**	CuI•PEt_3,  Li^+, THF	−78 → rt → 100	7		**7a**−**2l** (85)	100
23	**2d**			7		**7c**−**2m** (78)	88

[a] GCMS yields. Isolated yields are indicated in italics. [b] Conversion. [c] Activated copper, which was prepared by treatment of copper bronze with EDTA·Na_2 and dried over P_2O_5 at 0.1 mmHg. In the other cases, commercially available copper bronze was used. [d] Complementary assays were carried out sonicating the reaction mixture at 4−65 °C, affording in all cases only unreacted starting material. [e] CuTC: Copper(I) 2-thiophenecarboxylate.

though the latter system provided an easier purification due to the absence of byproducts. The procedure included the use of a heavy-wall pressure tube as the reaction flask, since very poor yields of phenanthro derivative **3b** were obtained by simple refluxing. As shown in Table 5, the application of the so-optimized conditions to *o*,*o*-dihalogenated pyrazoles **2a**−**k** provided tetracycles **3a**−**e** in good yields. From an examination of these results it may be proposed that the extended degree of conjugation of the final tetracyclic product probably compensates the steric constraint at the transmetalation step of such a Stille-type process.[24] A proposal for the mechanism based on previous reports regarding Stille coupling reactions is displayed in Scheme 3.

It should be pointed out that the target coupling products **3a**−**e** were obtained with similar yields from diiodo, dibromo, or even mixed iodobromo precursors **2a**−**k**, and that no significant change was observed when using methoxylated substrates, even though they are generally reported to undergo a slower transmetalation step, due to the electron-donating nature of the OMe group.[25]

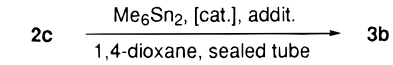
5. Biaryl Coupling Mediated by Pinacol Borane and Bis(pinacolate)diboron Reagents. In a fashion similar to the intermolecular Stille−Kelly reaction, Miyaura et al. have reported a sequential generation of arylboronates/biaryl coupling by reaction of aryl halides and bis(pinacolate)diboron.[26] To improve previous results, diarylpyrazoles **2b**−**d** were reacted with the latter diboron reagent using different conditions. A mixture of the aryl boronates **10** and **11** was detected from diiodo derivatives **2b** and **2d**, when the reaction was performed in a sealed tube using $PdCl_2(PPh_3)_2$ and NaOAc as the catalyst−base system (method A), whereas dibromopyrazole **2c** provided complex mixtures under the same conditions. The coupling of boronates **10** and **11** was

(24) Very few examples of such an intramolecular coupling via tandem or domino processes have been reported to date. See: (a) Kelly, T. R.; Li, Q.; Bushan, V. *Tetrahedron Lett.* **1990**, *31*, 161−164. (b) Grigg, R.; Teasdale, A.; Sridharan, V. *Tetrahedron Lett.* **1991**, *32*, 3859−3862. (c) Kelly, T. R.; Xu, W.; Ma, Z.; Li, Q.; Bushan, V. *J. Am. Chem. Soc.* **1993**, *115*, 5843−5844. (d) Beddoes, R. L.; Cheeseright, T.; Wang, J.; Quayle, P. *Tetrahedron Lett.* **1995**, *36*, 283−286. (e) This Stille-type reaction has been recently called "Stille-Kelly reaction". See: Fukuyama, Y.; Yaso, K.; Nakamura, K.; Kodama, M. *Tetrahedron Lett.* **1999**, *40*, 105−108.

(25) (a) Saá, J. M.; Martorell, G.; García-Raso, A. *J. Org. Chem.* **1992**, *57*, 678−685. (b) González, J. J.; García, N.; Gómez-Lor, B.; Echavarren, A. M. *J. Org. Chem.* **1997**, *62*, 1286−1291.

(26) (a) Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508−7510. Several variants of this procedure using the Miyaura's reagent can be found in: (b) Giroux, A.; Han, Y.; Prasit, P. *Tetrahedron Lett.*, **1997**, *38*, 3841−3844. (c) Zembower, D. E.; Zhang, H. *J. Org. Chem.* **1998**, *63*, 9300−9305. (d) Firooznia, F.; Gude, C.; Chan, K.; Marcopulos, N.; Satoh, Y. *Tetrahedron Lett.* **1999**, *40*, 213-216.

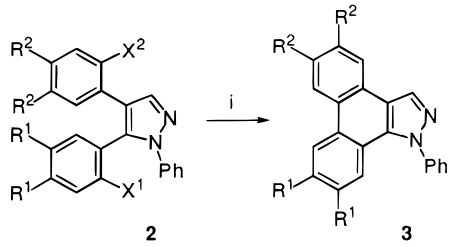
Table 4. Results from the Stannylation/Biaryl CouplingAssays Performed on Pyrazole 2b



					yield[d] (%)			
entry	catalyst system[a–c]	additive	*T* (°C)	*t* (h)	**2m**	**7b**	**9**	**3b**
1	$Pd(PPh_3)_4$		105	39	13	14	61	11
2	$Pd(PPh_3)_4$ [4,5 mol %] (1:4)	LiCl	140	74	14	18	0	70
3	$Pd(PPh_3)_4$ [6 mol %]		140	76	12	5	5	78
4	Pd_2dba_3/PPh_3 (1:4)		140	60	18	7	0	71
5	Pd_2dba_3/dppf (1:4)		140	96	19	25	0	*9* (61)[e]
6	Pd_2dba_3/(R)-(+)-BINAP (1:4)		140	96	8	6	0	*0* (15)[e]
7	$PdCl_2$ (dppe)		140	84	39	9	0	*5* (55)[e]
8	$Pd_2dba_3/AsPh_3$ (1:4)		100 → 140	96	19	4	0	0 (24)[e]
9	$Pd_2dba_3/AsPh_3$ (1:4:4)	CuI	100 → 140	92	12	8	0	0 (21)[e]
10	Pd_2dba_3/TPF (1:4)		100 → 140	78	27	7	0	0 (39)[e]
11	Pd_2dba_3/TPF(1:4:4)	CuI	100 → 140	75	21	9	0	0 (31)[e]
12	$Pd(PPh_3)_4$ (1:4) [7 mol %]	CuI	140	66	16	8	0	71
13	$PdCl_2(PPh_3)_2$ [4 mol %]		140	71	5	0	0	75
14	$PdCl_2(CH_3CN)_2$		140	72				*f*
15	$PdCl_2(PhCN)_2$		140	72				*f*
16	Pd_2dba_3 [1:4]	LiCl	140	88				*f*
17	Pd−C		140	72				*f*
18	$NiCl_2(PPh_3)_2$, Zn, PPh_3		80 → 120	72	16	10	0	0 (42)[e]
19			140	72				*f*

[a] Reactions were generally carried out using a 5 mol % amount of the catalyst; otherwise, the proportion is indicated in brackets. [b] The Pd:Ligand:Additive ratio is indicated in parentheses. [c] BINAP: 2,2′-bis(diphenylphosphino)-1.1′-binaphthyl. dppf: 1,1′-Bis(diphenylphosphino)ferrocene. dppe: 1,2-Bis(diphenylphosphino)ethane. TFP: tri-2-furylphosphine. [d] Isolated yield. GCMS yields are indicated in italics. [e] The conversion was complete except for the cases indicated in parentheses. [f] Unreacted starting material was recovered.

Table 5. Phenanthropyrazoles 3 Prepared



2 **3**

i: Me_6Sn_2, $PdCl_2(PPh_3)_2$ (5 mol%), 1,4-dioxane, 140°C, sealed tube

substrate	R^1	R^2	X^1	X^2	product[a] (%)
2a	H	H	Br	Br	**3a** (88)
2b	H	H	I	I	**3a** (80)
2c	OMe	OMe	Br	Br	**3b** (78)
2d	OMe	OMe	I	I	**3b** (40)
2e	OMe	H	Br	Br	**3c** (80)
2f	OMe	H	I	I	**3c** (74)
2g	H	OMe	Br	Br	**3d** (81)
2h	H	OMe	I	I	**3d** (77)
2i	H	OMe	Br	I	**3d** (59)
2j	H	OMe	I	Br	**3d** (40)
2k	H	OCH_2O[b]	Br	Br	**3e** (79)

[a] Yield of pure crystallized compound. [b] $R^2 + R^2 = OCH_2O$.

effected in situ by addition of potassium phosphate, affording tetracycles **3a**,**b** in 41−60% yield.[27]

As an alternative to generate aryl boronates **10** and **11**, pyrazoles **2b**−**d** were reacted with pinacolborane[28] and Et_3N in the presence of $PdCl_2(PPh_3)_2$ (method B), and only inseparable mixtures of pinacolboronates **10**−**12** were observed.[29] It was necessary again the use of a stronger base (K_3PO_4) to attain the coupling of intermediates **10** and **11**, but the yields were moderate (33−45%) due to the presence of the *o*,*o*-diboronate **12** in the reaction mixture (Scheme 4).

Although valuable and environmentally safer methodologies for the coupling of dihaloarylpyrazoles, the above-described boron-based procedures showed some disadvantages compared to the previously developed Stille-type reaction, since the yields were considerably lower and significant differences in the reactivity of dibromo and diiodo precursors were observed.

6. Nonphenolic Oxidative Coupling Mediated by PIFA. Finally, once the biaryl coupling of dihalogenated derivatives **2a**−**k** was achieved, an alternative approach to the phenanthro[9,10-*d*]pyrazole system based on the oxidative coupling of nonhalogenated pyrazoles **2l**−**o** was carried out. Such oxidative coupling reactions, formerly developed for phenols[30] and later extended to phenol ethers and other oxygenated, electron-rich arenes,[31] are effected by anodic oxidation [32] or by using several oxidants, mostly heavy metal reagents.[33] In comparison with photochemical approaches, oxidative coupling is reported to show no serious limitations concerning substitution patterns,[34] and as no halogenated precursors are

(27) The use of a weak base such as NaOAc proved to be essential for the synthesis of pinacolboronates **11** and **12** as reported by Miyaura et al. (See ref 25a). In one attempt of carrying out the reaction in a tandem process, the addition of K_3PO_4 instead NaOAc did not succeed, affording an intractable mixture of products.

(28) Murata, M.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **1997**, 6451−6459. Tucker, C. H.; Davidson, J.; Knochel, P. Pinacolborane was prepared according to the procedure reported in *J. Org. Chem.* **1992**, *57*, 3482−3485.

(29) The analysis of the ^1H NMR and ^{13}C NMR spectra of different chromatograpic fractions indicated the existence of pinacol derivatives, as concluded by observation of singlet signals in the range of 1.19−1.27 and 23.2−25.1 ppm, respectively. Likewise, peaks corresponding to the molecular ions of boronates **10**−**12** were registered (*m*/*z*: 548 for **10a**−**11a**, 668 for **10b**−**11b**, 620 and 622 for **10c**−**11c**, 548 for **12a** and 668 for **12b**). In the case of the pinacolboronates **10** and **11**, the peaks corresponding to the fragmentation by dehalogenation were also detected and of remarkable intensity (44−76%).

(30) Taylor, W. I.; Battersby, A. B. In *Oxidative coupling of phenols*; Arnold: London, 1967.

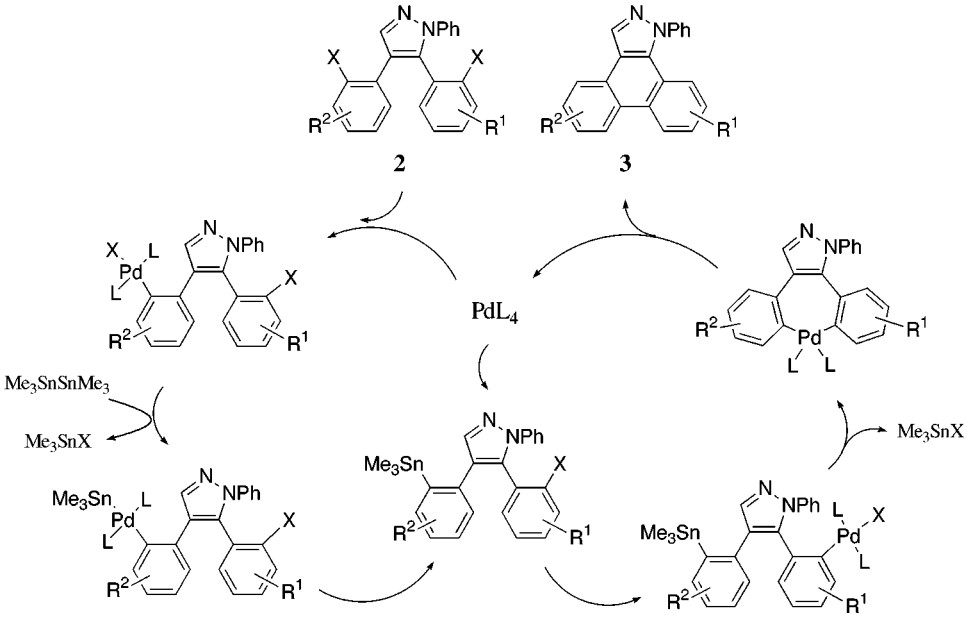
(31) Whiting, A. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Exeter, 1991; vol. 3, pp 659−703.

(32) Chapuzet, J.-M.; Simonet, J. *Tetrahedron* **1991**, *47*, 791−798.

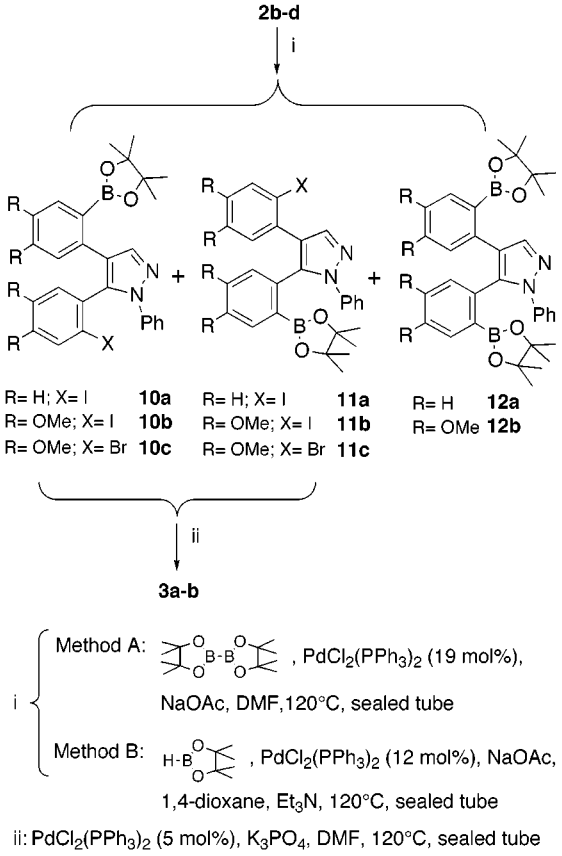
(33) Kumar, S.; Manickam, M. *Chem. Commun.* **1997**, 1615−1616.

(34) Mallory, F. B.; Mallory, C. W. *Org. React.* **1984**, *30*, 1−456.

Scheme 3

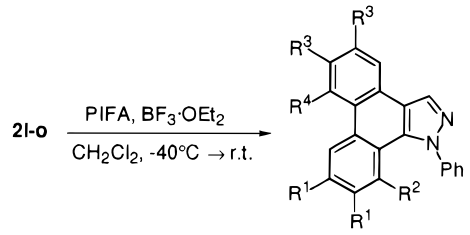


Scheme 4



required, it may constitute a valid alternative to Ullmann, Suzuki, or Stille cross-coupling methodologies. A recent communication on the oxidative coupling of isoxazoles and pyrimidines has presented the system PhI(OCOCF$_3$)−BF$_3$·OEt$_2$ as an efficient and nontoxic oxidant which avoids the formation of electrophilic metalation byproducts.[35] Thus, nonhalogenated diarylpyrazoles **2l**−**o** were submitted to the latter conditions, providing regioselectively the corresponding tetracycles **3a**, **3b**, and **3f** with the results summarized in Table 6. In addition, phenanthro[9,10-*d*]pyrazole **3a** was unexpectedly obtained in a low but significant yield from the nonmethoxylated substrate **2l**. It can be proposed that the pyrazole ring could promote a slight stabilization of the aromatic radical cation intermediate, otherwise very unstable due to the lack of electron-donating groups. Under the same conditions the polymethoxylated pyrazole **2o** provided a complex mixture, a result that could be rationalized if steric factors are considered.

Table 6



substrate	R^1	R^2	R^3	R^4	product[a] (%)
2l	H	H	H	H	**3a** (16)
2m	OMe	H	OMe	H	**3b** (86)
2n	OMe	OMe	OMe	H	**3f** (55)
2o	OMe	OMe	OMe	OMe	

[a] Yield of pure crystallized compound.

To sum up, an expeditious approach to the phenanthro[9,10-*d*]pyrazole system is presented, featuring as the key steps the tandem amine-exchange/heterocyclization of diaryl enaminoketones with phenylhydrazine, and the biaryl coupling of the so-obtained 4,5-diarylpyrazoles. A complete comparative study of the applicability of the main cross-coupling methodologies to the *o*,*o*-dihalogenated pyrazoles was carried out, resulting that the Stille-Kelly reaction based on a tandem stannylation/biaryl coupling, derivatives constitutes a general, convenient procedure for the target transformation. In addition, the tetracycles **3** can be also synthesized by oxidative nonphenolic coupling of nonhalogenated diarylpyrazoles mediated by phenyliodine bis(trifluroacetate) (PIFA).

(35) Olivera, R.; SanMartin, R.; Pascual, S.; Herrero, M.; Domínguez, E. *Tetrahedron Lett.* **1999**, *40*, 3479−3480.

Experimental Section

General Methods. For general experimental details, see ref 11a.

Synthesis of Diarylpyrazoles. 3(5),4-Bis(2-bromophenyl)pyrazole (4a). Typical Procedure. Hydrazine dihydrochloride (98%, 0.146 g, 1.368 mmol) was added to a solution of enaminoketone **1a** (0.509 g, 1.244 mmol) and ground Na_2CO_3 (99%, 88.6 mg, 0.83 mmol) in MeOH (13 mL) and H_2O (26 mL) under stirring at room temperature. The resulting mixture was acidified with glacial acetic acid (0.49 mL) to pH∼4 and refluxed for 6 h. After cooling, the mixture was parcially (1/2) evaporated in vacuo, and H_2O (50 mL) was added. This aqueous solution was extracted with CH_2Cl_2 (5 × 25 mL) and the combined organic layers were washed with brine (1 × 10 mL) and H_2O (1 × 10 mL). The organic layers were dried over anhydrous sodium sulfate, evaporated under reduced pressure and the resulting yellow residue was purified by chromatography using 5% EtOAc/CH_2Cl_2 as eluent. Pyrazole **4a** (0.393 g, 76%) was obtained as a yellow oil: R_f 0.25 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 7.02−7.28 (6H, m), 7.54−7.66 (2H, m), 7.73 (1H, s); ^{13}C NMR ($CDCl_3$) δ 119.9, 123.5, 123.9, 127.0, 127.2, 128.4, 129.9, 131.9, 132.2, 132.8, 133.0, 133.1, 133.8, 149.4; FTIR (neat film, cm^{-1}): 3413, 1584; EIMS (*m*/*z*) 380 (M + 2, 9), 378 (M$^+$, 18), 376 (M − 2, 9), 218 (M − 2Br, 100). Anal. Calcd for $C_{15}H_{10}Br_2N_2$: C, 47.65; H, 2.67; N, 7.41. Found: C, 47.49; H, 2.77; N, 7.58.

By use of the same procedure the following compounds were prepared:

3(5),4-Bis(2-iodophenyl)pyrazole (4b): 81%; yellow oil; R_f 0.27 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 6.73−7.32 (6H, m), 7.54 (1H, s) 7.76−7.88 (2H, m); ^{13}C NMR ($CDCl_3$) δ 99.1, 100.8, 122.5, 127.8, 128.5, 129.9, 131.3, 131.8, 133.7, 136.5, 136.7, 139.3, 147.4; FTIR (neat film, cm^{-1}):3413, 1584; EIMS (*m*/*z*) 472 (M$^+$, 42), 218 (M − 2I, 100). Anal. Calcd for $C_{15}H_{10}I_2N_2$: C, 38.16; H, 2.14; N, 5.93. Found: C, 38.01; H, 2.06; N, 5.83.

3(5),4-Bis(2-bromo-4,5-dimethoxyphenyl)pyrazole (4c): 75%; white powder; mp 159−160 °C (Et_2O); R_f 0.28 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.57 (3H, s), 3.67 (3H, s), 3.84 (3H, s), 3.85 (3H, s), 6.56 (1H, s), 6.75 (1H, s), 6.95 (1H, s), 7.02 (1H, s), 7.76 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.7, 55.9, 56.0, 113.8, 113.9, 114.2, 114.3, 115.3, 115.4, 119.8, 124.5, 125.8, 134.2, 144.8, 147.8, 147.9, 148.3, 149.4; FTIR (neat film, cm^{-1}) 3335, 1604; EIMS (*m*/*z*) 500 (M + 2, 5), 498 (M$^+$, 19), 496 (M − 2, 3). Anal. Calcd for $C_{19}H_{18}Br_2N_2O_4$: C, 45.81; H, 3.64; N, 5.62. Found: C, 45.88; H, 3.77; N, 5.56.

3(5),4-Bis(4,5-dimethoxy-2-iodophenyl)pyrazole (4d): 85%; yellow powder; mp 197−198 °C (hexane); R_f 0.24 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.62 (3H, s), 3.69 (3H, s), 3.84 (3H, s), 3.86 (3H, s), 6.63 (1H, s), 6.76 (1H, s), 7.19 (1H, s), 7.24 (1H, s), 7.75 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.7, 55.9, 56.0, 87.5, 88.8, 114.2, 114.3, 121.3, 121.4, 124.3, 128.9, 130.2, 134.1, 147.1, 148.2, 148.4, 148.7, 149.4; FTIR (neat film, cm^{-1}): 3335, 1598; EIMS (*m*/*z*) 465 (M − I, 5), 338 (M − 2I, 100). Anal. Calcd for $C_{19}H_{18}I_2N_2O_4$: C, 38.54; H, 3.06; N, 4.73. Found: C, 38.39; H, 3.17; N, 4.89.

The same procedure on enaminoketone **1c**, substituting the reagent NH_2NH_2·2HCl for $MeNHNH_2$ provided the following products:

4,5-Bis(2-bromo-4,5-dimethoxyphenyl)-1-methylpyrazole (5): 49%; colorless oil, R_f 0.48 (60% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.62 (3H, s), 3.74 (6H, s), 3.84 (3H, s), 3.89 (3H, s), 6.60 (1H, s), 6.69 (1H, s), 7.01 (1H, s), 7.08 (1H, s), 7.73 (1H, s); ^{13}C NMR ($CDCl_3$) δ 37.1, 55.7, 56.0, 56.1, 56.2, 113.9, 114.3, 114.5, 115.2, 115.3, 120.9, 123.1, 125.9, 138.7, 140.0, 147.7, 148.3, 150.2; FTIR (neat film, cm^{-1}): 1600; EIMS (*m*/*z*) 514 (M + 2, 16), 512 (M$^+$, 33), 510 (M − 2, 16), 352 (M − 2Br, 100). Anal. Calcd for $C_{20}H_{20}Br_2N_2O_4$: C, 46.90; H, 3.94; N, 5.47. Found: C, 46.78; H, 3.89; N, 5.55.

3,4-Bis(2-bromo-4,5-dimethoxyphenyl)-1-methylpyrazole (6): 40%; colorless oil; R_f 0.53 (60% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.51 (3H, s), 3.78 (3H, s), 3.84 (6H, s), 4.01 (3H, s), 6.52 (1H, s), 6.89 (1H, s), 6.98 (1H, s), 7.02 (1H. s), 7.67 (1H, s); ^{13}C NMR ($CDCl_3$) δ 39.2, 55.6, 56.0, 56.16, 113.4, 114.1, 114.4, 115.4, 115.5, 120.2, 125.9, 126.8, 130.6, 148.1, 148.2, 149.4; FTIR (neat film, cm^{-1}): 1605; EIMS (*m*/*z*) 514 (M + 2, 8), 512 (M$^+$, 15), 510 (M − 2, 7), 352 (M − 2Br, 100). Anal. Calcd for $C_{20}H_{20}Br_2N_2O_4$: C, 46.90; H, 3.94; N, 5.47. Found: C, 46.95; H, 3.86; N, 5.41.

Synthesis of 4,5-Diaryl-1-phenylpyrazoles 2. 4,5-Bis-(2-bromophenyl)-1-phenylpyrazole (2a). Typical Procedure. Phenylhydrazine hydrochloride (99%, 1,566 g, 10.7 mmol) was added to a solution of enaminoketone **1a** (3,654 g, 8.9 mmol) and ground Na_2CO_3 (99%, 0,538 g, 5,02 mmol) in MeOH (89 mL) and H_2O (178 mL) under stirring at room temperature. The resulting mixture was acidified with glacial acetic acid (3.51 mL) to pH ∼4 and heated at 135 °C overnight. After cooling, the suspension was filtered, and the filtrate was partially (1/3) evaporated in vacuo. This aqueous solution was extracted with CH_2Cl_2 (5 × 25 mL), and the organic layer was washed with brine (1 × 10 mL) and H_2O (1 × 10 mL), dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was mixed with the filtrand previously obtained and triturated with a mixture of 75% MeOH/H_2O to afford pyrazole **2a** (4.12 g, 90%) as a white powder: 124−125 °C (MeOH/H_2O); R_f 0.40 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 7.30−7.01 (11H, m), 7.48 (1H, dd, J = 7.9, 1.7 Hz), 7.60 (1H, dd, J = 7.8, 1.2 Hz), 7.96 (1H, s); ^{13}C NMR ($CDCl_3$) δ 122.7, 124.0, 124.3, 124.9, 126.9, 127.3, 128.6, 128.7, 130.4, 131.9, 132.8, 133.0, 133.3, 139.1, 139.9, 140.7; FTIR (neat film, cm^{-1}): 1596; EIMS (*m*/*z*) 456 (M + 2, 46), 454 (M$^+$, 92), 452 (M + 2, 46), 375 (M − ^{79}Br, 61), 373 (M − ^{81}Br, 59), 293 (100). Anal. Calcd for $C_{21}H_{14}Br_2N_2$: C, 55.54; H, 3.11; N, 6.17. Found: C, 55.39; H, 3.06; N, 6.29.

By use of the same procedure the following compounds were prepared:

4,5-Bis(2-iodophenyl)-1-phenylpyrazole (2b) was purified by flash column chromatography using 30% EtOAc/hexane as eluent and obtained as an amber oil: 71%; R_f 0.50 (10% hexane/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 6.90 (1H, ddd, J = 7.7, 7.4, 1.7 Hz), 6.91 (1H, ddd, J = 7.8, 7.7, 1.5 Hz), 7.00−7.01 (2H, m), 7.05 (1H, dd, J = 7.7, 1.8 Hz), 7.13 (1H, dd, J = 7.3, 1.2 Hz), 7.33−7.22 (5H, m), 7.74 (1H, d, J = 7.9, 1.4 Hz), 7.89 (1H, dd, J = 7.9, 1.2 Hz), 7.95 (1H, s); ^{13}C NMR ($CDCl_3$) δ 100.7, 100.8, 124.2, 125.5, 127.1, 127.7, 128.6, 128.7, 130.3, 131.3, 132.5, 135.4, 137.2, 139.4, 139.9, 140.7, 141.6; FTIR (neat film, cm^{-1}) 1596; EIMS (*m*/*z*) 548 (M$^+$, 62), 421 (M − I, 42), 294 (M − 2I, 71), 293 (100). Anal. Calcd for $C_{21}H_{14}I_2N_2$: C, 46.01; H, 2.57; N, 5.11. Found: C, 46.19; H, 2.66; N, 5.01.

4,5-Bis(2-bromo-4,5-dimethoxyphenyl)-1-phenylpyrazole (2c): 90%; white powder; mp 165−166 °C (MeOH/H_2O); R_f 0.49 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.59 (3H, s), 3.65 (3H, s), 3.82 (3H, s), 3.84 (3H, s), 6.58 (1H, s), 6.69 (1H, s), 6.93 (1H, s), 7.04 (1H, s), 7.23−7.35 (5H, m), 7.91 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.6, 56.0, 114.0, 114.4, 114.7, 115.2, 115.2, 115.4, 122.7, 123.3, 123.7, 125.4, 127.0, 128.6, 139.1, 139.9, 140.4, 147.7, 148.2, 148.4, 149.9; FTIR (neat film, cm^{-1}): 1599; EIMS (*m*/*z*) 495 (M + 2, 6), 493 (M$^+$, 6), 414 (M − ^{79}Br, 100). Anal. Calcd for $C_{25}H_{22}Br_2N_2O_4$: C, 52.29; H, 3.86; N,. 4.88. Found: C, 52.38; H, 3.88; N, 4.81.

4,5-Bis(4,5-dimethoxy-2-iodophenyl)-1-phenylpyrazole (2d): 82%; white powder; mp 149−150 °C (MeOH/H_2O); R_f 0.41 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.63 (3H, s), 3.72 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 6.56 (1H, s), 6.80 (1H, s), 7.12 (1H, s), 7.24−7.35 (7H, m), 7.88 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.7, 56.0, 88.6, 89.3, 114.2, 114.7, 121.1, 123.8, 125.7, 126.9, 127.8, 128.7, 130.0, 140.0, 140.4, 141.7, 148.6, 149.1, 149.8; FTIR (neat film, cm^{-1}) 1596; EIMS (*m*/*z*) 541 (5), 414 (M − I, 100). Anal. Calcd for $C_{25}H_{22}I_2N_2O_4$: C, 44.93; H, 3.32; N, 4.19. Found: C, 45.11; H, 3.21; N, 4.30.

5-(2-Bromo-4,5-dimethoxyphenyl)-4-(2-bromophenyl)-1-phenylpyrazole (2e): 89%; white powder; mp 140−142 °C (MeOH/H_2O); R_f 0.43 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.64 (3H, s), 3.83 (3H, s), 6.67 (1H, s), 6.92 (1H, s), 7.04−7.18 (4H, m), 7.27−7.34 (5H, m), 7.60 (1H, dd, J = 7.1, 1.2 Hz), 7.92 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.8, 114.5, 115.2, 122.7, 122.8, 123.8, 124.2, 126.9, 127.0, 128.7, 131.9, 132.7, 133.4, 139.0, 139.9, 140.5, 147.9, 149.7; FTIR (neat film, cm^{-1}) 1597; EIMS (*m*/*z*) 516 (M + 2, 22), 514 (M$^+$, 42), 512 (M − 2, 22),

435 (M − ^{79}Br, 100), 433 (M − ^{81}Br, 100). Anal. Calcd for $C_{23}H_{18}Br_2N_2O_2$: C, 53.72; H, 3.53; N, 5.45. Found: C, 53.70; H, 3.51; N, 5.61.

5-(4,5-Dimethoxy-2-iodophenyl)-4-(2-iodophenyl)1-phenylpyrazole (2f) (91%) was purified by flash column chromatography using 30% EtOAc/hexane as eluent and obtained as an colorless oil: R_f 0.34 (60% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.69 (3H, s), 3.82 (3H, s), 6.78 (1H, s), 6.92 (1H, ddd, J = 7.5, 7.1, 1.8 Hz), 7.09 (1H, dd, J = 7.5, 1.6 Hz), 7.11 (1H, s), 7.21 (1H, ddd, J = 7.9, 7.1, 1.2 Hz), 7.25−7.37 (5H, m), 7.84 (1H, s), 7.90 (1H, dd, J = 7.9, 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 55.8, 56.1, 89.0, 101.0, 114.6, 121.2, 123.8, 125.5, 126.9, 127.2, 127.8, 128.6, 128.8, 131.4, 137.4, 139.1, 139.8, 140.3, 141.3, 148.7, 149.4; FTIR (neat film, cm^{-1}): 1598; EIMS (*m*/*z*) 608 (M$^+$, 27), 481 (M − I, 100), 354 (M − 2I, 60). Anal. Calcd for $C_{23}H_{18}I_2N_2O_2$: C, 45.42; H, 2.98; N, 4.60. Found: C, 45.41; H, 2.88; N, 4.37.

4-(2-Bromo-4,5-dimethoxyphenyl)-5-(2-bromophenyl)-1-phenylpyrazole (2g: 88%; white powder; mp 130−131 °C (MeOH/H_2O); R_f 0.48 (50% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.50 (3H, s), 3.85 (3H, s), 6.50 (1H, s), 7.05 (1H, s), 7.19−7.33 (8H, m), 7.52 (1H, dd, J = 7.5, 1.2 Hz), 7.99 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.2, 55.6, 113.5, 114.0, 115.2, 122.3, 123.6, 124.7, 126.8, 127.1, 128.3, 130.2, 131.4, 132.6, 138.7, 139.5, 140.4, 147.3, 148.0; FTIR (neat film, cm^{-1}) 1597; EIMS (*m*/*z*) 516 (M + 2, 23), 514 (M$^+$, 56), 512 (M − 2, 26), 354 (M − 2Br, 100). Anal. Calcd for $C_{23}H_{18}Br_2N_2O_2$: C, 53.72; H, 3.53; N, 5.45. Found: C, 53.80; H, 3.56; N, 5.39.

4-(4,5-Dimethoxy-2-iodophenyl)-5-(2-iodophenyl)-1-phenylpyrazole (2h: 94%; white powder; mp 185−186 °C (MeOH/H_2O); R_f 0.44 (50% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.52 (3H, s), 3.84 (3H, s), 6.53 (1H, s), 6.98−7.04 (1H, m), 7.28−7.33 (8H, m), 7.78 (1H, dd, J = 7.5, 1.6 Hz), 7.98 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.8, 55.9, 88.1, 100.9, 113.9, 121.3, 124.0, 125.2, 127.0, 128.1, 128.6, 129.4, 130.3, 132.4, 137.2, 139.8, 140.7, 141.7, 148.2, 148.4; FTIR (neat film, cm^{-1}): 1597; EIMS (*m*/*z*) 608 (M$^+$, 58), 354 (M − 2I, 11). Anal. Calcd for $C_{23}H_{18}I_2N_2O_2$: C, 45.44; H, 2.98; N, 4.60. Found: C, 45.39; H, 3.06; N, 4.56.

5-(2-Bromophenyl)-4-(4,5-dimethoxy-2-iodophenyl)-1-phenylpyrazole (2i): 79%; white powder; mp 155−157 °C (MeOH/H_2O); R_f 0.32 (20% hexane/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.54 (3H, s), 3.83 (3H, s), 6.55 (1H, s), 7.16−7.33 (9H, m), 7.50 (1H, dd, J = 7.2, 1.4 Hz), 7.95 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.4, 55.8, 88.0, 113.8, 121.2, 123.7, 125.6, 126.9, 127.2, 128.5, 129.5, 130.4, 131.6, 138.9, 139.7, 140.5, 148.2, 148.4; FTIR (neat film, cm^{-1}) 1597; EIMS (*m*/*z*) 562 (M + 1, 16), 561 (M$^+$, 63), 560 (M − 1, 63), 436 (15), 434 (M − I, 14), 355 (33), 354 (M − I − Br, 100). Anal. Calcd for $C_{23}H_{18}BrIN_2O_2$: C, 49.22; H, 3.23; N, 4.99. Found: C, 49.29; H, 3.21; N, 5.01.

4-(2-Bromo-4,5-dimethoxyphenyl)-5-(2-iodophenyl)-1-phenylpyrazole (2j): 81%; white powder; mp 138−140 °C (MeOH/H_2O); R_f 0.42 (20% hexane/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.50 (3H, s), 3.85 (3H, s), 6.47 (1H, s), 7.01 (1H, ddd, J = 8.0, 8.0, 2.1 Hz), 7.04 (1H, s), 7.23−7.33 (8H, m), 7.79 (1H, dd, J = 7.9, 1.3 Hz), 8.01 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.5, 55.9, 100.9, 113.8, 114.2, 115.4, 122.1, 124.1, 124.9, 127.0, 128.6, 130.3, 132.4, 135.8, 139.3. 139.7, 140.7, 141.7, 147.5, 148.2; FTIR (neat film, cm^{-1}): 1596; EIMS (*m*/*z*) 562 (M + 1, 59), 560 (M − 1, 59), 436 (22), 355 (27), 354 (M − I − Br, 100). Anal. Calcd for $C_{23}H_{18}BrIN_2O_2$: C, 49.22; H, 3.23; N, 4.99. Found: C, 49.37; H, 3.19; N, 5.18.

4-(5-Bromo-1,3-benzodioxol-6-yl)-5-(2-bromophenyl)-1-phenylpyrazole (2k): 91%; white powder; mp 143−144 °C (MeOH/H_2O); R_f 0.42 (50% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 5.92 (2H, s), 6.54 (1H, s), 7.04 (1H, s), 7.29−7.50 (8H, m), 7.52, (1H, dd, J = 7.5, 1.9 Hz), 7.87 (1H, s); ^{13}C NMR ($CDCl_3$) δ 101.6, 111.3, 112.7, 115.0, 122.7, 124.0, 124.8, 126.3, 127.1, 127.3, 128.7, 130.5, 131.4, 132.7, 133.0, 139.0, 139.9, 140.8, 146.8, 147.5; FTIR (neat film, cm^{-1}): 1586; EIMS (*m*/*z*) 500 (M + 2, 18), 498 (M$^+$, 34), 496 (M − 1, 18), 338 (M − 2Br, 100). Anal. Calcd for $C_{22}H_{14}Br_2N_2O_2$: C, 53.04; H, 2.83; N, 5.62. Found: C, 53.19; H, 2.80; N, 5.51.

1,4,5-Triphenylpyrazole (2l): 99%; white powder; mp 197−198 °C (MeOH); R_f 0.28 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 6.56−7.32 (15H, m), 7.93 (1H, s); ^{13}C NMR ($CDCl_3$) δ 122,4, 125.2, 126.4, 127.2, 128.0, 128.4, 128.6, 128.7, 130.2, 130.4, 132.8, 139.2, 139.7, 139.9; FTIR (neat film, cm^{-1}) 1590; EIMS (*m*/*z*) 296 (M$^+$, 100). Anal. Calcd for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 84.97; H, 5.32; N, 9.71.

4,5-Bis(3,4-dimethoxyphenyl)-1-phenylpyrazole (2m): 97%; white powder; mp 146−147 °C (MeOH); R_f 0.24 (4% EtOAc/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.56 (3H, s), 3.66 (3H, s), 3.86 (6H, s), 6.60 (1H, d, J = 1.5 Hz), 6.73−6.80 (4H, m), 7.22−7.33 (6H, m), 7.86 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.6, 55.7, 111.0, 111.1, 111.2, 113.2, 120.2, 121.8, 122.5, 123.2, 125.1, 125.6, 127.2, 128.7, 138.6, 139.4, 140.0, 147.6, 148.6, 148.7, 148.9; FTIR (neat film, cm^{-1}) 1597; EIMS (*m*/*z*) 416 (M$^+$, 100). Anal. Calcd for $C_{25}H_{24}N_2O_4$: C, 72.10; H, 5.81; N, 6.73. Found: C, 71.89; H, 5.89; N, 6.80.

4-(3,4-Dimethoxyphenyl)-1-phenyl-5-(2,3,4-trimethoxyphenyl)pyrazole (2n): 95%; white powder; mp 132−133 °C (MeOH); R_f 0.66 (EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.37 (3H, s), 3.64 (3H, s), 3.72 (3H, s), 3.86 (6H, s), 6.63 (1H, d, J = 8.7 Hz), 6.69 (1H, d, J = 1.5 Hz), 6.78 (1H, d, J = 8.3 Hz), 6.86 (1H, d, J = 8.3 Hz), 7.21−7.33 (6H, m), 7.93 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.3, 55.7, 55.9, 60.1, 60.7, 107.0. 110,4, 111.0, 116.9, 119.4, 122.5, 123.9, 125.7, 126.6, 128.5, 135.4, 138.8, 140.3, 142.1, 147.3, 148.4, 152.0, 154.6; FTIR (neat film, cm^{-1}) 1600; EIMS (*m*/*z*) 446 (M$^+$, 100). Anal. Calcd for $C_{26}H_{26}N_2O_5$: C, 69.94; H, 5.87; N, 6.27. Found: C, 70.06; H, 5.82; N, 6.34.

1-Phenyl-5-(2,3,4-trimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl)pyrazole (2o): 99%; white powder; mp 157−158 °C (MeOH); R_f 0.60 (EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.38 (3H, s), 3.67 (6H, s), 3.72 (3H, s), 3.82 (3H, s), 3.87 (3H, s), 6.45 (2H, s), 6.65 (1H, d, J = 8.3 Hz), 6.88 (1H, d, J = 8.3 Hz), 7.22−7.34 (5H, m), 7.95 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.2, 55.4, 59.7, 60.2, 60.4, 103.6, 106.6, 116.5,122.1, 123.6, 126.1, 128.0, 135.1, 135.8, 138.8, 139.8, 141.7, 151.6, 152.5, 154.2; FTIR (neat film, cm^{-1}) 1598; EIMS (*m*/*z*) 476 (M$^+$, 100). Anal. Calcd for $C_{27}H_{28}N_2O_6$: C, 68.05; H, 5.92; N, 5,88. Found: C, 68.21; H. 5.84; N, 5.80.

Attempts at Synthesis of Arylboronic Acids or Aryltrimethylstannanes by the Corresponding Organolithium Derivatives. Typical Procedure. A solution of pyrazole **2c** (0.6 g, 1.044 mmol) in dry THF (105 mL) at −78 °C was treated with *n*-BuLi (1.32 mL, 1.30 M solution in hexane, 1.72 mmol) under Ar. This mixture was stirred at the same temperature for 35 min. A solution of $B(OMe)_3$ (tridistilled from Na) (0.54 mL, 4.70 mmol) in dry THF (1 mL) was added slowly, during which time the solution changed color from pale yellow to dark orange. The resulting mixture was stirred for 2 h at −78 °C, allowed to reach room temperature, and poured onto a HCl 5% solution (80 mL) and stirred for 15 min. Brine (5 mL) was added, and the aqueous layer was separated and extracted with Et_2O (5 × 25 mL). The combined organic layers were washed with H_2O (1 × 50 mL) and brine (1 × 50 mL) and dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography using 6% EtOAc/CH_2Cl_2 as eluent affording the following products:

4-(2-Bromo-4,5-dimethoxyphenyl)-5-(3,4-dimethoxyphenyl)-1-phenylpyrazole (7b): 0.398 g, 77%; white powder; mp 154−156 °C (MeOH); R_f 0.45 (6% EtOAc/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.49 (3H, s), 3.60 (3H, s), 3.82 (3H, s), 3.87 (3H, s), 6.50 (1H, d, J = 1.8 Hz), 6.59 (1H, dd, J = 8.2, 1.9 Hz), 6.60 (1H, s), 6.69 (1H, d, J = 8.3 Hz), 7.07 (1H, s), 7.29−7.33 (5H, m), 7.84 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.6, 55.7, 55.8, 56.1, 110.8, 113.0, 114.6, 114.9, 115.4, 121.3, 122.0, 122.7, 123.8, 125.1, 126.0, 127.2, 128.7, 140.0, 140.8, 147.9, 148.4, 148.6, 148.8; FTIR (neat film, cm^{-1}) 1598; EIMS (*m*/*z*) 496 (M + 1, 24), 494 (M − 1, 25), 415 (M − Br, 100). Anal. Calcd for $C_{25}H_{23}BrN_2O_4$: C, 60.62; H, 4.68; N, 5.65. Found: C, 60.81; H, 4.69; N, 5.34.

4,5-Bis(3,4-dimethoxyphenyl)-1-phenylpyrazole (2m) (11%) was also obtained as a green oil.

The same procedure on pyrazole **2b** provided the 1,4,5-triphenylpyrazole **2l** (9%) as an amber oil and the corresponding monodehalogenated products **4-(2-iodophenyl)-1,5-diphenylpyrazole (7a)** and **5-(2-iodophenyl)-1,4-diphen-**

ylpyrazole (8a), which were purified by column chromatography on alumina using 5% EtOAc/hexane as eluent. The exact assignation of the structures is not possible on the basis of spectrometric data. The major product (30%) was obtained as an amber oil: R_f 0.26 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 6.92 (1H, d, J = 7.7, 1.5 Hz), 6.99 (1H, d, J = 6.6, 1.7 Hz), 7.09 (1H, d, J = 7.6, 1.5 Hz), 7.13−7.27 (10H, m), 7.82 (1H, s), 7.88 (1H, d, J = 7.9 Hz); ^{13}C NMR ($CDCl_3$) δ 101.3, 125.1, 125.3, 127.0, 127.2, 127.9, 128.2, 128.3, 128.4, 128.8, 129.7, 130.0, 131.7, 138.1, 139.2, 140.0, 140.8; FTIR (neat film, cm^{-1}): 1595; EIMS (*m*/*z*) 422 (M$^+$, 96), 295 (M − I, 100). Anal. Calcd for $C_{21}H_{15}IN_2$: C, 59.73; H, 3.58; N, 6.63. Found: C, 59.94; H, 3.69; N, 6.59. The minor product (21%) was isolated as a yellow oil: R_f 0.26 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 7.00 (1H, ddd, J = 7.9, 7.9, 1.7 Hz), 7.09−7.28 (12H, m), 7.77 (1H, d, J = 7.8 Hz), 7.92 (1H, s); ^{13}C NMR ($CDCl_3$) δ 98.6. 125.5, 126.6. 127.4, 127.9, 128.6, 131.1. 131.9, 138.8. 139.2, 139.6, 140.6; FTIR (neat film, cm^{-1}) 1595 (C=N); EIMS (*m*/*z*) 422 (M$^+$, 100), 295 (M − I, 85). Anal. Calcd for $C_{21}H_{15}IN_2$: C, 59.73; H, 3.58; N, 6.63. Found: C, 60.14; H, 3.22; N, 6.79.

The variation of the reaction conditions (temperature (−100 °C → −40 °C), stoichiometry of the organolithium reagent (1.1−2.3 equiv), nature of the organolithium (^{n}BuLi, ^{t}BuLi) and of the electrophile reagents ((B(OMe)$_3$, B(O^{i}Pr)$_3$, TMSCl, Me_3SnCl)) led to the obtention of the former products in different yields ranged in Table 2.

Synthesis of Phenanthro[9,10-*d*]pyrazoles via Ullmann Biaryl Coupling Reaction. A selection of the most advantageous Ullmann biaryl coupling procedures assayed (Table 3) are described below.

Procedure 1. A suspension of diarylpyrazole **2b** (0.06 g, 0.11 mmol) and $(CuOTf)_2$·PhH (90%, 0.218 g, 0.39 mmol) in degassed DMF (5 mL) was stirred at 100 °C under Ar for 39 h. The mixture was allowed to reach room temperature, poured into H_2O (50 mL) and extracted with EtOAc (3 × 10 mL). The organic layers were dried over anhydrous sodium sulfate and evaporated in vacuo. The residue was purified by flash column chromatography using 20% EtOAc/hexane as eluent, providing 1-phenylphenanthro[9,10-*d*]pyrazole **(3a)** (0.035 g, 77%) as a colorless oil.

The same procedure on diarylpyrazole **2d** provided 1-phenyl-5,6,9,10-tetramethoxyphenanthro[9,10-*d*]pyrazole **(3b)** (56%) as a yellow oil.

Procedure 2. A suspension of diarylpyrazole **2b** (0.09 g, 0.157 mmol) and copper bronze (99%, 0.039 g, 0.63 mmol) in dry nitrobenzene (9 mL) was heated in a heavy-wall pressure tube at 175 °C under Ar for 41 h. The mixture was allowed to reach room temperature and filtered. It was diluted with $CHCl_2$ (30 mL) and washed with NH_4OH (3 × 3 mL). The organic extract was dried over anhydrous sodium sulfate and filtered off, and the solvent was evaporated under pressure (1 mmHg. 90 °C). The residue was analyzed by GC/MS showing the presence of 1-phenylphenanthro[9,10-*d*]pyrazole **3a** in a 81% yield.

The same procedure was applied on diarylpyrazole **2d**, and the GC/MS analysis of the residue indicated the formation of 1-phenyl-5,6,9,10-tetramethoxyphenanthro[9,10-*d*]pyrazole **3b** (56%) in a 77% yield.

Synthesis of Arylstannane (9). 5-(2-Bromo-4,5-dimethoxyphenyl)-4-(4,5-dimethoxy-2-trimethylstannylphenyl)-1-phenylpyrazole (9). A heavy wall-pressure tube was charged with pyrazole **2c** (0.151 g, 0.261 mmol), Pd(PPh$_3$)$_4$ (99%, 15,2 mg, 13 μmol) and degassed 1,4-dioxane (1 mL) under Ar. A solution of Me_6Sn_2 (0.425 g, 1.30 mmol) in degassed 1,4-dioxane (1.6 mL) was added to resulting suspension, and after flushing with Ar at room temperature for 15 min and closing the tube, the mixture was heated at 105 °C in an autoclave for 4 h. After cooling, the resulting black suspension was centrifugated and the deposited black palladium was washed with CH_2Cl_2. The combined organic solvents were washed with saturated KF solution. The organic layer was dried over anhydrous Na_2SO_4 and filtered off, and the solvent was evaporated in vacuo. The resulting residue was purified by flash column chromatography using 40% EtOAc/hexane as eluent providing stannane **9** (0.104 g, 61%) as a colorless oil: R_f 0.55 (60% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 0.11 (satel. Sn, ^2J (^{119}Sn-^{1}H) 29 Hz), 0.22 (9H, s), 0.33 (satel. ^2J (^{117}Sn-^{1}H) 27 Hz), 3.60 (3H, s), 3.62 (3H, s), 3.84 (3H, s), 3.89 (3H, s), 6.56 (1H, s), 6.65 (1H, s), 6.96 (1H, s), 6.97 (1H, s), 7.27−7.34 (5H, m), 7.74 (1H, s); ^{13}C NMR ($CDCl_3$) δ −7.42, 55.4, 55.8, 56.0, 56.1, 113.4, 114.7, 115.9, 118.3, 123.6, 123.9, 126.6, 127.2, 128.8, 132.9, 133.4, 138.8, 139.9, 140.1, 147.4, 148.2, 148.7, 150.0; FTIR (neat film, cm^{-1}): 1596; EIMS (*m*/*z*) 645 (26), 643 (14), 641 (15), 640 (14), 419 (10), 415 (37), 414 (87), 399 (48), 383 (11), 371 (25), 356 (21), 355 (24), 341 (14), 339 (10), 327 (12), 320 (100), 318 (95). Anal. Calcd for $C_{28}H_{31}BrN_2O_4Sn$: C, 51.10; H, 4.75; N, 4.26. Found: C, 51.29; H, 4.86; N, 4.34.

Synthesis of Phenanthro[9,10-*d*]pyrazoles via Stannylation/Biaryl Coupling. 1-Phenylphenanthro[9,10-*d*]pyrazole (3a). Typical Procedure. A heavy wall-pressure tube was charged with diarylpyrazole **2a** (207 mg, 0.456 mmol), $PdCl_2(PPh_3)_2$ (16.0 mg, 22.8 μmol), and degassed 1,4-dioxane (1.8 mL) under Ar. A solution of Me_6Sn_2 (225 mg, 0.684 mmol) in degassed 1,4-dioxane (0.8 mL) was added to resulting suspension, and after flushing with Ar at room temperature for 15 min and closing the tube, the mixture was heated at 140 °C in an autoclave for 40 h. After cooling, the resulting black suspension was centrifuged, and the deposited black palladium was abundantly washed with CH_2Cl_2. The combined organic solvents were washed with saturated KF solution. The organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated in vacuo. The resulting residue was purified by crystallization from hexane/EtOAc 50% to afford phenanthropyrazole **(3a)** (119 mg, 88%) as a white powder: mp 181−182 °C (EtOAc); R_f 0.47 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 7.34 (1H, ddd, J = 7.9, 7.9, 1.5 Hz), 7.56−7.90 (9H, m), 8.28 (1H, dd, J = 7.9, 1.5 Hz), 8.58 (1H, s), 8.64 (1H, dd, J = 7.9, 1.5 Hz), 8.70 (1H, dd, J = 8.0, 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 119.1, 121.6, 122.8, 123.4, 124.0, 125.3, 126.3, 127.1, 127.6, 127.8, 127.9, 129.1, 129.5, 134.1, 135.1, 141.8; FTIR (neat film, cm^{-1}) 1596; EIMS (*m*/*z*) 294 (M$^+$, 100). Anal. Calcd for $C_{21}H_{14}N_2$: C, 85.69; H, 4.79; N, 9.52. Found: C, 85.46; H, 4.69; N, 9.85.

The same procedure on pyrazole **2c** provided **1-phenyl-5,6,9,10-tetramethoxyphenanthro[9,10-*d*]pyrazole (3b)** (78%) as a yellow powder: mp 181−182 °C (EtOAc); R_f 0.47 (40% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.48 (3H, s), 4.09 (3H, s), 4.12 (6H, s), 6.97 (1H, s), 7.58−7.67 (6H, m), 7.81 (1H, s), 7.83 (1H, s), 8.49 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.0, 55.9, 56.0, 56.2, 104.1, 104.7, 114.8, 118.1, 120.6, 121.2, 125.1, 127.8, 129.1, 129.4, 133.4, 134.6, 141.7, 147.7, 147.9, 148.7, 149.4; FTIR (neat film, cm^{-1}) 1596; EIMS (*m*/*z*) 414 (M$^+$, 100). Anal. Calcd for $C_{25}H_{22}N_2O_4$: C, 72.45; H, 5.35; N, 6.76. Found: C, 72.39; H, 5.41; N, 6.81.

The same procedure on pyrazole **2e** provided **9,10-dimethoxy-1-phenylphenanthro[9,10-*d*]pyrazole (3c)** (80%) as a white powder, mp 155−157 °C (80% hexane/EtOAc); *Rf* 0.28 (60% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.48 (3H, s), 4.03 (3H, s), 6.96 (1H, s), 7.55−7.67 (7H, m), 8.03 (1H, s), 8.28 (1H, dd, J = 8.3, 2.0 Hz), 8.49 (1H, dd, J = 8.0, 1.2 Hz), 8.56 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.0, 55.9, 104.1, 105.0, 115.8, 118.2, 122.9, 123.5, 125.1, 126.0, 126.7, 127.4, 127.8, 129.2, 129.4, 134.1, 135.1, 141.7, 148.2, 148.4; FTIR (neat film, cm^{-1}): 1596; EIMS (*m*/*z*, %) 355 (M$^+$, 28), 354 (100). Anal. Calcd for $C_{23}H_{18}N_2O_2$: C, 77.95; H, 5.12; N, 7.90. Found: C, 77.84; H, 5.29; N, 8.19.

The same procedure on pyrazole **2g** provided **5,6-dimethoxy-1-phenylphenanthro[9,10-*d*]pyrazole (3d)** (81%) as a white powder: mp 199−201 °C (MeOH); *Rf* 0.32 (50% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 4.13 (6H, s), 7.27 (1H, d, J = 8.0 Hz), 7.55−7.63 (8H, m), 7.99 (1H, s), 8.50 (1H, s), 8.54 (1H, d, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 56.0, 104.0, 104.9, 111.1, 119.0, 120.7, 121.2, 121.6, 122.9, 123.4, 125.3, 126.5, 127.1, 129.0, 129.5, 133.5, 134.6, 141.8, 148.0, 149.9; FTIR (neat film, cm^{-1}): 1597; EIMS (*m*/*z*) 354 (M$^+$, 100). Anal. Calcd for $C_{23}H_{18}N_2O_2$: C, 77.95; H, 5.12; N, 7.90. Found: C, 78.02; H, 5.21; N, 7.94.

The same procedure on pyrazole **2g** provided **1-phenyl[1,3]-dioxolo[2,3-*d*]phenanthro[9,10-*d*]pyrazole (3e)** (79%) as a yellow powder: mp 209−210 °C (MeOH); R_f 0.35 (50% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 6.13 (2H, s), 7.30 (1H, d, J = 7.1 Hz), 7.53−7.62 (8H, m), 8.00 (1H, s), 8.46 (1H, s), 8.50

(1H, d, $J = 7.1$ Hz); ^{13}C NMR ($CDCl_3$) δ 101.3, 101.7, 102.3, 119.4, 120.7, 122.6, 122.8, 123.1, 123.6, 125.5, 126.6, 127.1, 129.0, 129.5, 130.8. 133.7. 134.6. 141.8, 147.0, 148.2; FTIR (neat film, cm^{-1}): 1596; EIMS (*m*/*z*) 338 (M^+, 100). Anal. Calcd for $C_{22}H_{14}N_2O_2$: C, 78.09; H, 4.17; N, 8.28. Found: C, 78.27; H, 4.07; N, 8.41.

Assays of Biaryl Coupling Using Bis(pinacolato)-diboron. 1-Phenylphenanthro[9,10-*d*]pyrazole (3a). Typical Procedure. A heavy wall-pressure tube was charged with diarylpyrazole **2b** (0.25 g, 0.46 mmol), $PdCl_2(PPh_3)_2$ (61.5 mg, 87.6 μmol), bis(pinacolato)diboron (0.128 g, 0.51 mmol), NaOAc (0.253 g, 1.38 mmol), and degassed DMF (2 mL) and purged with Ar at room temperature for 15 min. After closing the tube, the mixture was heated at 120 °C in an autoclave for 17 h until TLC showed the completion of the reaction. After cooling, the resulting black suspension was centrifugated and the deposited black palladium was removed. The reaction mixture was degassed again, and anhydrous K_3PO_4 (0.376 g, 2.3 mmol) and $PdCl_2(PPh_3)_2$ (16.5 mg, 23.5 μmol) were added. After closing the tube, the resulting mixture was heated at 120 °C in an autoclave for 55 h. After cooling, the resulting black suspension was centrifugated and the deposited black palladium was abundantly washed with dichlromethane. The combined organic solvents were washed with saturated NH_4Cl solution (2 × 10 mL), dried over anhydrous sodium sulfate and filtered off. The solvent was evaporated under pressure (1 mmHg, 90 °C). The resulting residue was purified by flash column chromatography using 20% EtOAc/hexane as eluent providing 1-phenylphenanthro[9,10-*d*]pyrazole **3a** (0.081 g, 60%) as a white powder.

The same procedure on diarylpyrazole **2d** afforded 1-phenyl-5,6,9,10-tetramethoxyphenanthro[9,10-*d*]pyrazole **3b** (41%) as a yellow oil.

Assays of Biaryl Coupling Using Pinacolborane. 1-Phenylphenanthro[9,10-*d*]pyrazole (3a). Typical Procedure. A heavy wall-pressure tube was charged with diarylpyrazole **2b** (0.156 g, 0.29 mmol), $PdCl_2(PPh_3)_2$ (24.4 mg, 34.8, μmol), anhydrous Et_3N (0.12 mL, 0.87 mmol), and degassed 1,4-dioxane (5 mL). Pinacolborane (50 μL of a stock solution prepared as previously reported,[27] 0.50 mmol) was added dropwise, and the mixture was purged with Ar at room temperature for 15 min. After closing the tube, the mixture was heated at 120 °C in an autoclave for 6 h. After cooling, the resulting black suspension was centrifugated and the deposited black palladium was removed. The reaction mixture was diluted with H_2O (40 mL) and extracted with Et_2O (5 × 5 mL). The organic layer was dried over anhydrous sodium sulfate, filtered off and the solvent was evaporated in vacuo. The residue was dried under pressure (1 mmHg) at room temperature over P_2O_5 for 6 h. It was transferred into a heavy-wall presure tube and disolved in degassed DMF (1.25 mL). A mixture K_3PO_4 (0.235 g, 1.43 mmol) and $PdCl_2(PPh_3)_2$ (10.2 mg, 14.5 μmol) were added, and after closing the tube, the resulting mixture was heated at 120 °C in an autoclave for 55 h until TLC showed the completion of the reaction. After cooling, the resulting black suspension was centrifugated and the deposited black palladium was abundantly washed with CH_2Cl_2. The combined organic solvents were washed with saturated NH_4Cl solution (2 × 10 mL), dried over anhydrous sodium sulfate, and filtered off. The solvent was evaporated under pressure (1 mmHg, 90 °C) and the resulting residue was purified by flash column chromatography using 20% EtOAc/hexane as eluent, providing 1-phenylphenanthro[9,10-*d*]pyrazole **3a** (0,037 g, 45%) as a colorless oil.

The same procedure on diarylpyrazole **2c** afforded 1-phenyl-5,6,9,10-tetramethoxyphenanthro[9,10-*d*]pyrazole **3b** (41%) as a yellow oil.

The same procedure on diarylpyrazole **2d** afforded 1-phenyl-5,6,9,10-tetramethoxyphenanthro[9,10-*d*]pyrazole **3b** (33%) as a yellow oil.

Synthesis of Phenanthro[9,10-*d*]pyrazoles via Oxidative Coupling Reaction. 5,6,9,10,11-Pentamethoxy-1-phenylphenanthro[9,10-*d*]pyrazole (3f). Typical Procedure. A solution of PIFA (0.137 g, 0.31 mmol) in dry CH_2Cl_2 (1 mL) was added to a stirred solution of diarylpyrazole **2n** (0.125 g, 0.28 mmol) in dry CH_2Cl_2 (7 mL) at −40 °C under Ar. After the addition of $BF_3{\cdot}OEt_2$ (35.6 μL, 0.32 mmol), the resulting brown solution was stirred for 15 min at −40 °C, allowed to warm at room temperature and absorbed on silica gel (0.725 g). Purification by flash column chromatography using 50% hexane/EtOAc as eluent provided phenanthropyrazole **3f** as a yellow powder (0.068 g, 55%): mp 188−190 °C (MeOH); R_f 0.52 (30% hexane/EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.29 (3H, s), 3.81 (3H, s), 4.11 (9H, s), 7.30−7.36 (1H, m), 7.40−7.42 (4H, m), 7.57 (1H, s), 7.66 (1H, s), 7.80 (1H, s), 8.52 (1H, s); ^{13}C NMR ($CDCl_3$) δ 56.0, 56.1, 56.2, 60.0, 61.2, 100.2, 104.0, 105.0, 111.0, 119.7, 121.3, 123.2, 126.7, 127.9, 128.6, 134.0, 134.4, 141.0, 145.1, 148.1, 148.6, 150.0, 153.0; FTIR (neat film, cm^{-1}):1597; EIMS (*m*/*z*) 444 (M^+, 100). Anal. Calcd for $C_{26}H_{24}N_2O_5$: C, 70.26; H, 5.44; N, 6.30. Found: C, 70.21; H, 5.42; N, 6.39.

The same procedure on diarylpyrazole **2l** afforded 1-phenylphenanthro[9,10-*d*]pyrazole **3a** (16%) as a colorless oil.

The same procedure on diarylpyrazole **2m** afforded 1-phenyl-5,6,9,10-tetramethoxyphenanthro[9,10-*d*]pyrazole **3b** (86%)-as a white powder.

Acknowledgment. This research was supported by the University of the Basque Country (Project UPV 170.310G37/98), the Ministry of Education and Culture (PB97-0600) and the Basque Government (GV170.310-G0053/96). R.O. thanks the Basque Government for a predoctoral scholarship.

JO000609I