Tetrahedron 67 (2011) 689–697

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Exploring the selectivity of the Suzuki–Miyaura cross-coupling reaction in the synthesis of arylnaphthalenes

Carlos F.R.A.C. Lima, José E. Rodriguez-Borges, Luís M.N.B.F. Santos *

Centro de Investigação em Química, Departamento de Química e Bioquímica, Faculdade de Ciências da Universidade do Porto, Rua do Campo Alegre, 687, P-4169-007 Porto, Portugal

ARTICLE INFO

Article history:
Received 11 October 2010
Received in revised form 18 November 2010
Accepted 25 November 2010
Available online 1 December 2010

Keywords:
Suzuki–Miyaura cross-coupling
Selectivity
Arylnaphthalenes
Substituent effect
Nucleophilicity
Aromatic interactions

ABSTRACT

A series of 1-arylnaphthalenes and 1,8-diarylnaphthalenes were synthesized by the Suzuki–Miyaura cross-coupling methodology showing significant differentiation in the yields and selectivity between aryl rings with electron donating (higher yields), and electron withdrawing substituents (lower yields). These results strongly support the relation between the nucleophilicity of the boronate complex and its reactivity, and emphasize the importance of the transmetalation step in the overall efficiency of this cross-coupling reaction. The results obtained with non-symmetric 1,8-diarylnaphthalenes indicate preference for arylation of an already arylated species (the 1-aryl-8-bromonaphthalene intermediate) over mono-arylation of 1,8-dibromonaphthalene. Evidences for the existence of intramolecular Pd···π and aromatic interactions in some Pd(II) complexes were found.

1. Introduction

The Suzuki–Miyaura cross-coupling reaction has received much attention in the past years due to it's versatility in the formation of C–C bonds.[1,2] The reaction is generally green, with good yields and selectivity. The great variety of commercially available boron and halogenated compounds enables the very attractive building-blocks philosophy. In this work, a systematic study on the synthesis of some 1-arylnaphthalenes and structurally symmetric and non-symmetric 1,8-diarylnaphthalenes was carried out (Figs. 1 and 2).

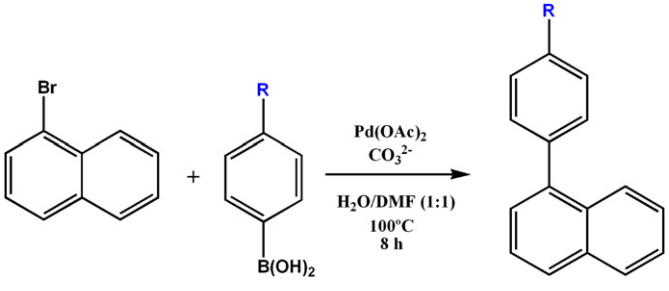

Fig. 1. Suzuki–Miyaura reaction scheme for the synthesis of 1-arylnaphthalenes.

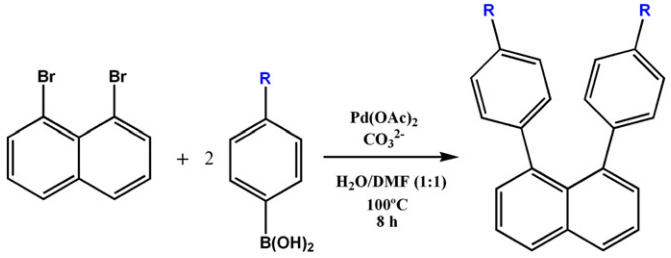

Fig. 2. Suzuki–Miyaura reaction scheme for the synthesis of 1,8-diarylnaphthalenes.

The work of Liu et al.,[3] respecting the synthesis of biaryls and polyaryls, served as a basis for the conditions employed in this study. The general accepted reaction mechanism[2] involves three main steps: an oxidative addition of the halogenated species to the Pd catalyst, followed by a transmetalation step, where the organic group attached to the activated boron species is transferred to the metal, and finally a reductive elimination that yields the coupling product and regenerates the catalyst. In the transmetalation step, the boron species must be activated with a base, in order to increase its nucleophilicity and give a clean reaction.[2,4] Thus, the transmetalation reaction between the Pd catalyst and the organoboron species may be fastened by the increased nucleophilicity of the later.

Fig. 3 depicts the reaction's catalytic cycle for the case of mono-arylation of 1-bromonaphthalene, with the conditions employed in this work. It is important to keep in mind that the role of the base in

* Corresponding author. Tel.: +351 220402536; fax: +351 220402520; e-mail address: lbsantos@fc.up.pt (L.M.N.B.F. Santos).

0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.11.081

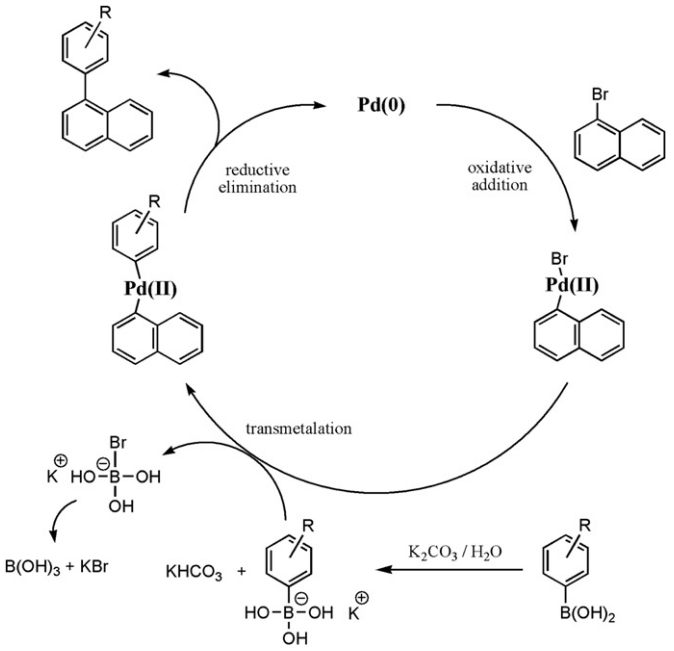

Fig. 3. The Suzuki–Miyaura reaction catalytic cycle adapted to the conditions employed in this work.

this mechanism is not yet fully understood.[2,4] The di-arylation of 1,8-dibromonaphthalene has analogous reaction mechanisms, one for each arylation step. The main objective of this study is to explore the effect of the substituent R in the reaction outcome and use these findings to gain some insights on the mechanistic pathway. Thus, it was imperative to keep all the other reaction variables (stoichiometry, solvent, temperature, reaction time, base, catalyst, and extraction methodology) as constant as possible. In this way the transmetalation step will be the main focus of our attention, since it is expected that the substituents R will not influence the other catalytic steps to any considerable extent. Additionally, the 1,8-diarylnaphthalene system is particularly interesting due to the existence of two equivalent adjacent coupling positions that can be used to explore the effect of intramolecular interactions in the reaction mechanism.

2. Results and discussion

The global results obtained for the Suzuki–Miyaura cross-coupling reaction, concerning the mono- (Fig. 1) and diarylnaphthalenes (Fig. 2) are presented in Table 1, alongside with the substituent Hammett constants, σ_{meta} and σ_{para}, for the groups considered in this work.[5] $\sum\sigma$ is the sum of all the substituents contributions, considered additive for the cases where more than one R group is presented. The Hammett constants are referred to the arylboronic acids. In some cases the presence of the homocoupling product of the boronic acid (Fig. 4) was detected by ^{1}H NMR and by GC (gas chromatography) analysis against a known sample of the compound. This is not surprising since the reactions were carried out in the presence of air, hence with O_2, which is known to induce homocoupling in boronic acids.[6] For example, biphenyl was formed in the synthesis involving phenylboronic acid, and *p*-quaterphenyl was detected in the synthesis were biphen-4-ylboronic acid was used.

2.1. 1-Arylnaphthalenes

Starting from 1-bromonaphthalene the reaction outcome with various *para*-substituted phenylboronic acids was monitored,

Table 1
Reaction yield (%) for the mono-arylation of 1-bromonaphthalene and symmetric di-arylation of 1,8-dibromonaphthalene by the Suzuki–Miyaura cross-coupling, and Hammett constants, σ_{meta} and σ_{para}, as a function of the R group in the phenylboronic acid

R	Yield[a] (%)		σ_{meta}	σ_{para}	$\sum\sigma$
	Mono-	Di-			
4-$N(CH_3)_2$	71	87	—	−0.83	−0.83
3-OCH_3	77	—	0.12	—	0.12
4-OCH_3	85	71	—	−0.27	−0.27
4-Ph	81	55	—	−0.01	−0.01
H	76	60	—	0	0
4-CHO	56	57	—	0.42	0.42
4-COOH	59	—	—	0.45	0.45
4-CN	58	30	—	0.66	0.66
3,4-diOCH_3	75	76	0.12	−0.27	−0.15
3-CHO-4-OCH_3	66	53	0.35	−0.27	0.08
Ar=C_6F_5	no reaction	no reaction	—	—	—

[a] Isolated yield corrected for sample purity.

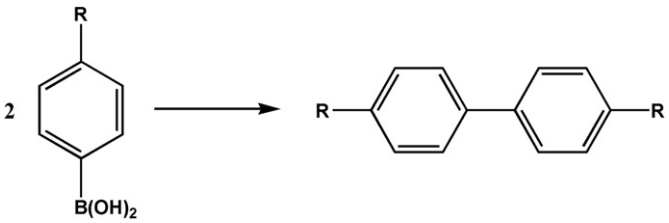

Fig. 4. Homocoupling reaction involving the boronic acid derivatives. The condensation product was identified in some cases.

keeping the reaction conditions essentially constant. Table 1 summarizes these results. As can be seen the % yield of the reaction is larger for electron donating groups (EDG) and lower to electron withdrawing groups (EWG). The R=H compound, 1-phenylnaphthalene, establishes the scale's zero, so EDG's improve the reaction outcome relative to the neutral situation, whereas, EWG's have the opposite effect. This effect is substantially enhanced for the pentafluorophenyl case, where no detectable 1-(pentafluorophenyl)naphthalene was formed. The trend observed in reaction yield with the susbtituent's electron/donor character can in principle be correlated with a Hammett plot. These results are presented in Fig. 5. The % yield of the Suzuki–Miyaura reaction in the experimental conditions adopted in this work clearly have some dependency with substituent electron/donor strength, however this is not the only factor affecting the reaction outcome. Solubility aspects and competing undesirable side reactions may also play a role in defining the trend observed in Fig. 5. For example, in the synthesis of the dimethylamino derivative (the strongest EDG), it was observed that the reaction mixture acquired a green tone, in addition to the custom dark-grey color. During the extractions, the aqueous phase was green, suggesting the formation of a hydrophilic impurity. This is an indication that the % yield of *N*,*N*-dimethyl-4-(naphthalene-1-yl)aniline (R=$N(CH_3)_2$) may be lowered by the presence of a significant side-reaction, what could explain the deviation from the correlation trend. Steric interactions in 1-arylnaphthalenes, relative to the naphthyl–phenyl torsion, prevent a significant conjugation between the aryl and naphthyl moieties. Thus, the 1-arylnaphthalene molecule can roughly be viewed as two independent, non-interacting aromatic groups. Sustain for this statement comes from the ^{1}H NMR spectra of the 1-arylnaphthalenes synthesized in this work. They are very alike in what concerns the naphthalene protons, presenting similar chemical shifts and coupling constants. This fact supports the observation that thermodynamic considerations aren't important for the trend observed in the reaction % yield. By this reasoning we can

argue that kinetic factors play the main role in defining the observed trend. In a mechanistically point of view, a perfect correlation was only to be expected if the influence of the substituent group is in the same way in every steps of the global synthetic process (reaction of interest+side reactions+other physical/chemical features), or is active in one-step and silent in all the others.

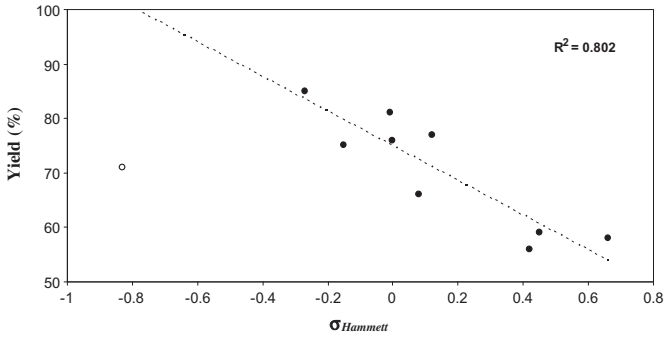

Fig. 5. Isolated reaction yield (%) as a function of ∑σ (Hammett) for the synthesis of 1-arylnaphthalenes by the Suzuki–Miyaura reaction.

dubious; however its addition doesn't disturb the correlation to any significant extent. In 1,8-diarylnaphthalenes the two parallel aryl rings can interact via intramolecular interactions, stabilizing or destabilizing the reaction product.[7–9] Nevertheless, this fact alone should not be responsible for the observed reaction outcomes, and in analogy with the results obtained for 1-arylnaphthalenes, the kinetic factors appear to be the more determinant ones in defining the trends observed in this work so far. As for 1-arylnaphthalenes,

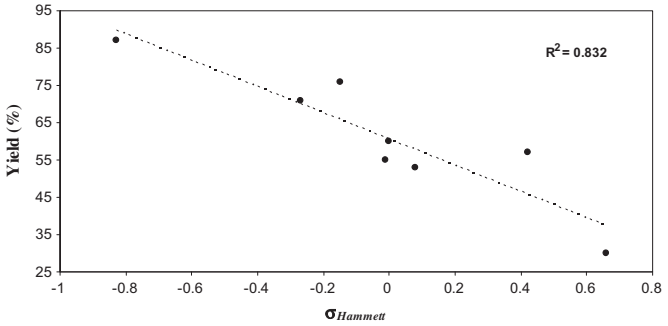

Fig. 6. Isolated reaction yield (%) as a function of ∑σ (Hammett) for the synthesis of 1,8-diarylnaphthalenes by the Suzuki–Miyaura reaction.

The present results and the direct comparison between the outcomes for 3-methoxy (yield (%)=77) and 4-methoxy (yield (%)=85) substituents are a good sign of the importance of conjugation effects in reaction intermediates involving the substituted aryl. These intermediates only participate in the transmetalation and reductive elimination steps. Hence, R can only cause significant kinetic differentiation in these steps, the transmetalation one being the more obvious choice. The starting reagent 1-bromonaphthalene was not detected in any significant amount in all the reactions that were carried out: %(m/m)<1 by GC analysis of the impure products obtained.

2.2. 1,8-Diarylnaphthalenes

As for mono-aryl naphthalenes the same approach was considered for the synthesis of 1,8-diarylnaphthalenes. Table 1 summarizes the experimental results. Clearly, the same dependence of % yield with the substituent identity was found. Correlation with ∑σ (Hammet) constant is statistically relevant, as shown in Fig. 6. Again, we must be aware of the existence of competing side reactions, or other unexpected phenomenon's when analyzing this data. For example, in the case of 1,8-di([1,1′-biphenyl]-4-yl)naphthalene (R=Ph), the synthesis was carried out in a different solvent, toluene/water/EtOH (2:1:1), rather than in DMF/water (1:1). In the last case the yield was only of 40%. The use of a more apolar media increased the yield to 55%. This fact may be associated with solubility issues of reaction intermediates. The difference in reaction solvent makes the inclusion of this case in the Hammet correlation the starting product 1,8-dibromonaphthalene was never detected in considerable amounts; %(m/m) <1 by GC analysis of the impure products obtained. This fact, together with the high yields obtained in the work of Liu et al.[3] using similar reaction conditions, are a strong indication that practically all the brominated reagent reacts completely. Hence, the existence of side reactions should be responsible for not achieving yields (%) near 100%. In this way the presence of EDGs have the effect of increasing the rate of the desired Suzuki–Miyaura coupling reaction relative to the unknown side reactions. One possible important side-reaction may be the homocoupling of the boronic acid, which removes it from the reaction media at a definite rate, competing kinetically with the transmetalation step.

2.3. Non-symmetric 1,8-diarylnaphthalenes

Various approaches were used in order to explore the synthesis of structurally non-symmetric 1,8-diarylnaphthalenes. In these situations three different products can be produced: the two possible symmetric diarylnaphthalenes and the non-symmetric diarylnaphthalene (Fig. 7). The molar fraction of each product was determined by GC. For each symmetric 1,8-diarylnaphthalene the peak area was related to molar concentration by calibrating the signal with solutions of known concentrations. The non-symmetric compound was taken to be the one corresponding to the peak between the two known peaks (intermediate retention time). Our only concern was to access the selectivity of the Suzuki–Miyaura reaction when more than one coupling product is possible. In this

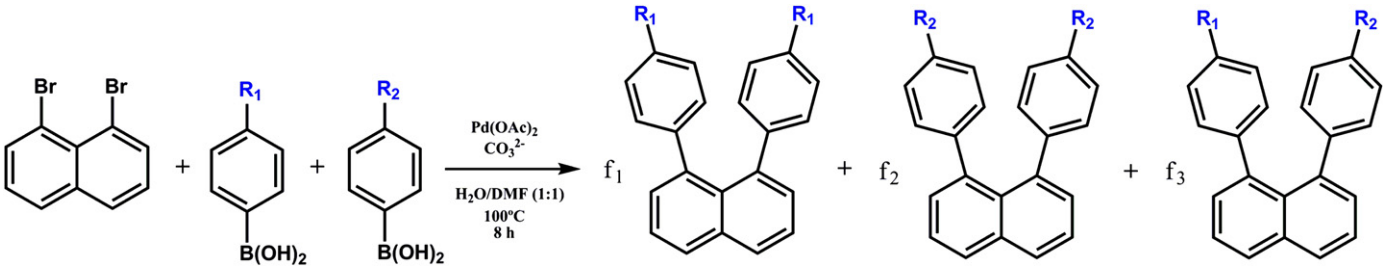

Fig. 7. Suzuki–Miyaura reaction scheme for the synthesis of non-symmetric 1,8-diarylnaphthalenes. The indices f_1, f_2 and f_3 represent the molar fraction of each possible coupling product.

fashion, the final mixture was extracted with ethyl acetate and the organic phase washed, as it was made for all the other synthesis, except for the separation of the different reaction products, which was not carried out. We assume that equal retention times in GC and the success in the preceding synthetic approaches (Sections 2.1. and 2.2.) suffice to prove the product identity. By chromatographic considerations it seems justifiable to ascribe the middle peak to the non-symmetric product.

2.3.1. Effect of addition sequence. First, we began by exploring the effect of addition sequence of the boronic acid on the synthesis of non-symmetric diarylnaphthalenes. These results are presented in Table 2. In entry 1, 1,2 equiv of phenylboronic acid was added first, and after 3 h 3 equiv of biphen-4-ylboronic acid was added. The reaction was allowed to continue at 100 °C for 4 h. In entry 2 the same procedure was employed, but toggling the addition sequence. Entry 3 is the normal case of simultaneous addition. As shown in Table 2, the sequence of addition influences the reaction outcome, clearly favoring the first addition product. Another interesting observation is that the second addition product was formed in very low quantities, even given the fact that the corresponding boronic acid was presented in higher molar equivalents (3 equiv compared to 1.2 equiv). This is a clear indication that thermodynamics alone is not capable of explaining the observed results, and that the reverse reaction occurs in a very small extent. Also, we must conclude that di-arylation of 1,8-dibromonaphthalene is preferred over mono-arylation, or else the non-symmetric product would be formed with higher selectivity.

Table 2
Reaction selectivity (mol %) for the non-symmetric di-arylation of 1,8-dibromonaphthalene by the Suzuki–Miyaura cross-coupling–effect of addition sequence

Entry	Addition sequence	Ratio[a]/mol %
1	1^{st}–H–Ph–$B(OH)_2$ 2^{nd}–Ph–Ph–$B(OH)_2$	Ph–H/Ph–H–81 Ph–Ph/Ph–Ph–1 Ph–H/Ph–Ph–18 Unreacted 1,8-diBr[b]–11
2	1^{st}–Ph–Ph–$B(OH)_2$ 2^{nd}–H–Ph–$B(OH)_2$	Ph–H/Ph–H–11 Ph–Ph/Ph–Ph-74 Ph–H/Ph–Ph–15 Unreacted 1,8-diBr[b]–17
3	Simultaneous	Ph–H/Ph–H–18 Ph–Ph/Ph–Ph–34 Ph–H/Ph–Ph–48 Unreacted 1,8-diBr[b]–1

[a] Measured by GC analysis of the reaction mixture after extraction with AcOEt. Calculated excluding all the other peaks.
[b] mol % of unreacted 1,8-dibromonaphthalene (relative to the three products formed).

A statistical analysis, assuming irreversible reaction steps and the above cited stoichiometry, predicts an outcome of 36% for the symmetric product formed by di-arylation from the first addition of boronic acid, 16% for the symmetric product formed from the second addition, and 48% for the non-symmetric product.

As can be seen in Table 2 the ratio observed is of 81/1/18 for entry 1 and 74/11/15 for entry 2, significantly differing from the statistically unbiased prediction of 36/16/48 (detailed statistical analysis is presented in the Supplementary data). This fact shows a preference for the formation of the symmetric first addition product, indicating the existence of some feature that favors the arylation of an already arylated bromonaphthalene (the 1-aryl-8-bromonaphthalene species) in comparison with 1,8-dibromonaphtalene (Fig. 8). Nonetheless these results should be regarded

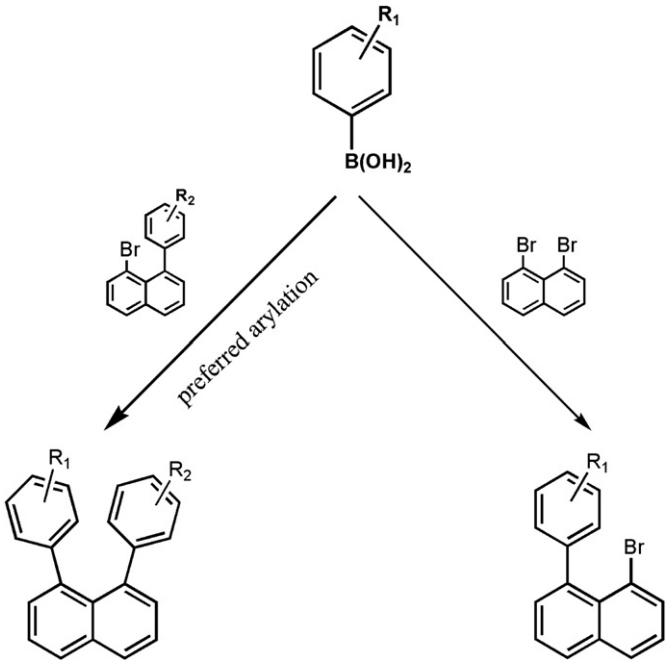

Fig. 8. The results obtained show preferred arylation of the 1-aryl-8-bromonaphthalene species over 1,8-dibromonaphthalene.

with care due to the presence of significant amounts of unreacted 1,8-dibromonaphthalene. This subject will be discussed in more detail in a following section.

2.3.2. Effect of temperature. Second we have studied the effect of temperature on the reaction selectivity. These reactions were carried out in the usual way, changing only the temperature at which the reaction mixture was heated after addition of all the reactants. By a qualitative inspection of Table 3 we can conclude that, in the interval considered, temperature has no meaningful effect on selectivity. Since, in all the cases, the reaction mixture was heated to the desired temperature only after addition of the base, K_2CO_3, we may conclude that the reaction proceeds rapidly at room temperature and the reverse reaction occur in a negligible extent. The mol % of unreacted 1,8-dibromonaphthalene was negligible in all the cases.

Table 3
Reaction selectivity (mol %) for the non-symmetric di-arylation of 1,8-dibromonaphthalene by the Suzuki–Miyaura cross-coupling–effect of temperature

Temperature/°C	Ratio[a]/mol %
25	Ph–H/Ph–H–17 Ph–Ph/Ph–Ph–36 Ph–H/Ph–Ph–47
70	Ph–H/Ph–H–19 Ph–Ph/Ph–Ph–33 Ph–H/Ph–Ph–48
120	Ph–H/Ph–H–18 Ph–Ph/Ph–Ph–33 Ph–H/Ph–Ph–49

[a] Measured by GC analysis of the reaction mixture after extraction with AcOEt. Calculated excluding all the other peaks.

2.3.3. Effect of the substituent R. Third, we have inspected the effect of the substituent R. The results are given on Table 4. All the reactions were carried out by the previously described procedure, and with simultaneous addition of the two boronic acids, in

Table 4
Reaction selectivity (mol %) for the non-symmetric di-arylation of 1,8-dibromonaphthalene by the Suzuki–Miyaura cross-coupling–effect of substituent

R_1/R_2	Ratio[a]/mol %
H/Ph	Ph–H/Ph–H–18
	Ph–Ph/Ph–Ph–34
	Ph–H/Ph–Ph–48
OCH_3/CHO	Ph–OCH_3/Ph–OCH_3–87
	Ph–CHO/Ph–CHO–0
	Ph–OCH_3/Ph–CHO–13
$N(CH_3)_2$/CN	Ph–$N(CH_3)_2$/Ph–$N(CH_3)_2$–89
	Ph–CN/Ph–CN–0
	Ph–$N(CH_3)_2$/Ph–CN–11

[a] Measured by GC analysis of the reaction mixture after extraction with AcOEt. Calculated excluding all the other peaks.

equimolar amounts. These conditions allow for a good competition scenario with respect to arylation. The statistically unbiased outcome is easily demonstrated to be 25/25/50 for $R_1,R_1/R_2,R_2/R_1,R_2$, respectively, as the formation of the non-symmetric product (R_1,R_2) is twice as probable as the formation of each symmetric product (R_1,R_1 and R_2,R_2). In this way, for the case of Ph–H/Ph–Ph, where the distinction between the two substituents in terms of electronic effects are less pronounced, the observed ratio was not very far from the statistical outcome, with, however some preference for the Ph–Ph/Ph–Ph product relative to the Ph–H/Ph–H one. This fact can be related with the weak donor character of the phenyl group, increasing a little the rate of the transmetalation step. For the other two cases the observed outcome is radically different from the expected ratio, with a clearly preference for the formation of the products that correspond to the electron donor substituent, $-OCH_3$ and $-N(CH_3)_2$. This is in agreement with the results obtained so far, supporting the view that the transmetalation step is significantly fastened by the presence of electron donor substituents in the *para*-position of phenylboronic acids.

These results also make less favorable the hypothesis of the distinction to be noted in the reductive elimination step, where the formation of the coupling product from the corresponding complex intermediate would be fastened by the presence of EDGs. This is so, because this step does not impose any selectivity in the reaction, considering that it is relatively fast compared with the total reaction time. If we regard the transmetalation step as independent of the R group, the respective Pd complexes would be populated in a pure statistical ratio and the corresponding products formed at different rates by reductive elimination but in a finite time, reflecting the statistical outcome, which is not the case.

2.4. Mechanistic insights

An ab-inito computational study using the SCS-MP2/cc-pVDZ level of theory[10] was performed in order to provide some support for the experimental results, concerning the observed preference for di-arylation over mono-arylation (Section 2.3.1, see Fig. 8). The results for the gas phase homodesmic schemes, presented in Fig. 9, indicate that the energetic distinction between the two outcomes should be of little importance. In this scheme we picture the two possible reaction pathways for a molecule of 1-phenylnaphthalene, here mimicking the arylboronic acid. This molecule can either arylate 1,8-dibromonaphthalene or the mono-arylated 1-bromo-8-phenylnaphthalene, to yield the respective products of reaction. The relative energies of the two possible arylation products (difference of ca. 2 kJ/mol) do not justify the observed selectivity based on the energetic differentiation. This is an indication that the cyclic mechanism for mono-arylation (yielding 1-bromo-8-phenylnaphthalene) is not thermodynamically significantly distinguished from the cyclic mechanism for di-arylation (yielding 1,8-diphenylnaphthalene). A direct relation between the Suzuki–Miyaura

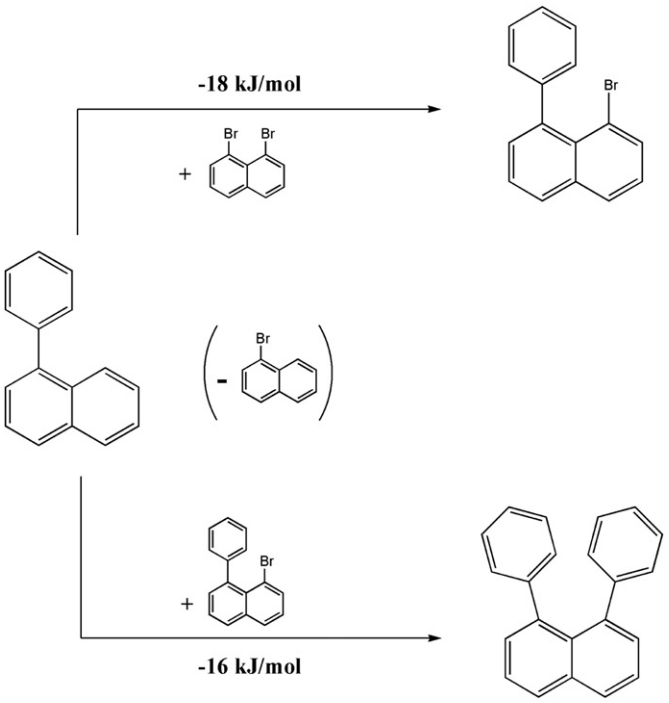

Fig. 9. Homodesmic schemes for the evaluation of the energetic preference for mono- or di-arylation, at the SCS-MP2 level of theory.

overall reaction and the selected homodesmic schemes can be made since the only differences between the two complete cycles (neglecting reaction intermediates) are the brominated reagent and the arylated product. Looking at the reaction mechanism (Fig. 1) the most reasonable explanation for the preference of di-arylation should reside in the oxidative addition step, where the brominted reagent complexes with Pd(0).

The results obtained point to a faster reaction for the addition of the mono-arylated species (1-aryl-8-bromonaphthalene) relative to the addition of the non-arylated species (1,8-dibromonaphthalene), yielding a *trans* Pd(II) complex,[2,11] involving the formation of a metal complex with the aryl ring in close proximity to the Pd atom, versus one with the bromine atom in close contact to the metal center. This indicates that either an attractive Pd···π intramolecular interaction, or a Pd···Br repulsive interaction, or a combination of both, exists and are responsible for the observed reaction selectivity (Fig. 10), by differentiating energetically the respective reaction intermediates and transition states. Another

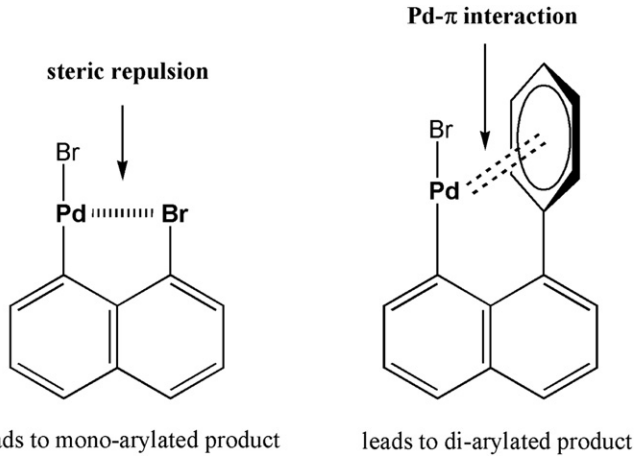

Fig. 10. Schematic representation of the intramolecular interactions that can favor oxidative addition of the mono-arylated naphthalene over 1,8-dibromonaphthalene.

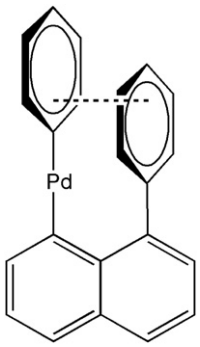

Fig. 11. Schematic representation of the intramolecular aromatic interaction in the *trans* intermediate formed after transmetalation for the mono-arylated species.

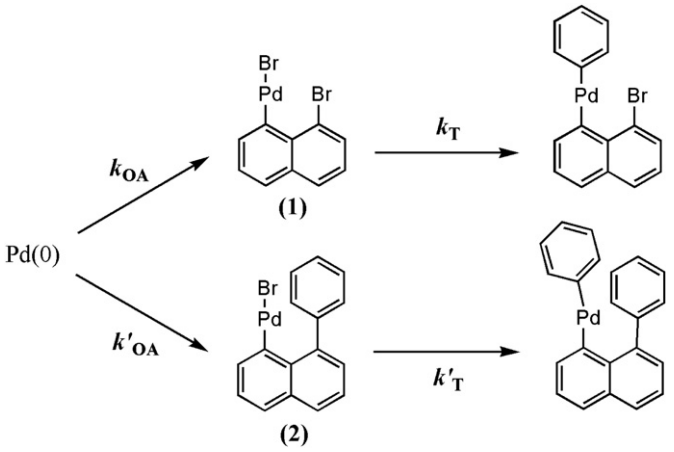

Fig. 12. Schematic representation of the two mechanistic pathways that lead to the formation of the mono- and di-arylated products.

possible explanation may be the existence of an intramolecular aromatic interaction in the *trans* Pd(II) complex[2,11] formed after transmetalation, that is, present only in the mono-arylated species and would increase the rate of this step relative to the one involving the dibromo species. The geometry of the complex permits the phenyl rings to interact in a parallel displaced fashion, as illustrated in Fig. 11. Although the geometric positioning between the two benzene rings is not the ideal alignment for a $\pi\cdots\pi$ interaction (the displacement between the ring centers is too large), it has still associated significant stabilizing interaction energy.[12,13]

However, for this hypothesis to be valid one must assume that the oxidative addition step is reversible to the extent that the equilibrium is rapid enough to ensure a dynamic distribution of Br–Pd(II)–Ar species ready to undergo transmetalation. If this is not so and we assume that no kinetic distinction is made in the oxidative addition step, $k_{OA} \approx k'_{OA}$, then, even if $k_T \neq k'_T$, (**1**) and (**2**) will form in the statistical ratio, and eventually react via transmetalation, yet at different rates (see Fig. 12). Nevertheless, virtually all of them will react and yield the respective products according to the statistical expected outcome.

The irreversibility of the oxidative addition step is a very plausible scenario for aryl halides and Pd,[14,15] making more likely the hypothesis that considers the existence of significant kinetic differentiation in this step, in agreement with the results obtained in this work. However, for explaining the preference for the formation of the Ph–Ph/Ph–Ph product over the Ph–H/Ph–H one, when simultaneous addition of the boronate reagents is considered, as noted in Section 2.3.3 (see Table 4), this hypothesis is more feasible, since in this case differentiation is meaningful in transmetalation. In this case, the formation of the Pd complex presented in Fig. 13 will be favored relative to the other possible complexes, because the two additional aromatic rings enhance the intramolecular aromatic interactions, thus increasing the amount of the Ph–Ph/Ph–Ph product formed.

3. Conclusions

It was found that the nucleophilicity of the boronate species strongly influences the reaction yield and selectivity when the reaction conditions employed in this work are considered. Electron donor substituents in the boronic acid improve the reaction outcome, whereas electron withdrawing substituents show the opposite trend. The effect of addition sequence, temperature and the R group in boronic acid was explored using a competitive arylation methodology. The more consistent conclusions that can be drawn from this study are:

- A preference for the arylation of the 1-aryl-8-bromonaphthalene species over 1,8-dibromonaphthalene was observed, that can be due to specific intramolecular aromatic interactions in some Pd (II) intermediates. Thermodynamic considerations are unable to justify the observed selectivity. The stepwise addition of boronic acids is therefore a bad strategy for the synthesis of non-symmetric 1,8-diarylnaphthalenes by this methodology.

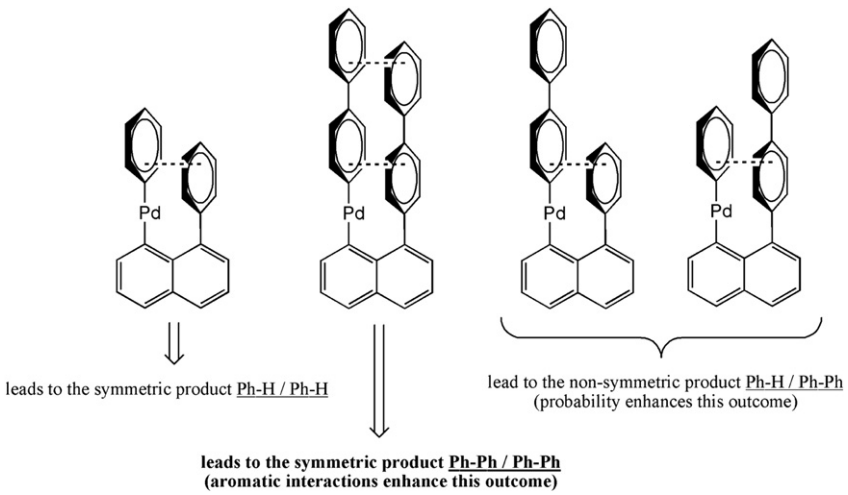

Fig. 13. The four possible *trans* intermediates formed after transmetalation for the Suzuki–Miyaura reaction involving phenylboronic acid (R=H) and biphen-4-ylboronic acid (R=Ph). The observed outcome ratio was of 18/34/48 for Ph–H/Ph–H, Ph–Ph/Ph–Ph, and Ph–H/Ph–Ph, respectively.

- The reaction seems to take place very rapidly at room temperature and the reverse reaction occurs in a negligible extent.
- The reaction mechanism clearly favors the formation of arylnaphthalenes with EDGs, in detriment of arylnaphthalenes with EWGs.

The results obtained in this work are an experimental insight concerning the mechanism of the Suzuki–Miyaura cross-coupling reaction, that represent an experimental support for the current view that increased nucleophilicity of the boronate species increases the rate of the transmetalation step, and contribute to a better overall understanding of this synthetic methodology.

4. Experimental section

4.1. General

1-Bromonaphthalene, 1,8-diaminonaphthalene, all the boronic acids, and $Pd(OAc)_2$ were commercially obtained from Sigma–Aldrich. 1,8-dibromonaphthalene was synthesized as previously described by Kuroda et al.[16,17] Melting points were measured in an IA9200 Melting Point Apparatus. ^1H and ^{13}C NMR spectra were recorded on a *Bruker Avance III 400* spectrometer, equipped with a 5 mm broad band observe (bbo) prove. The spectra were all referenced to TMS. Reaction yields (%) are calculated from the mass of isolated product obtained, corrected for the sample %(m/m) degree of purity, measured by GC analysis, using an HP 4890 apparatus equipped with an HP-5 column, cross-linked, 5% diphenyl and 95% dimethylpolysiloxane. Crystallographic data (excluding structure factors) for some structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication. For each one of those compounds, the CCDC code number is indicated.

4.2. Synthesis of 1-arylnaphthalenes

4.2.1. General synthesis of 1-arylnaphthalenes. A solution of K_2CO_3 (1.4 mol/equiv) in 12 ml of water per 1 mmol of the limiting reactant was added to a solution of 1-bromonaphthalene (1 mol/equiv), arylboronic acid (1.2 mol/equiv) and $Pd(OAc)_2$ (2 mol %) in the same volume of DMF. The resultant mixture was heated at 100 °C for 8 h under stirring. The final solution was allowed to cool to room temperature, and extracted with ethyl acetate. The organic layer was washed with water and aqueous 0.1 M NaOH, dried over anhydrous sodium sulfate and evaporated, yielding the product as impure mono-arylnaphthalene.

4.2.1.1. 1-Phenylnaphthalene. The brown oil obtained (2.73 g, 76%) was distilled under reduced pressure to yield a colorless liquid; ^1H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 7.90–7.81 (3H, m), 7.50–7.39 (9H, m); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 141.8, 141.3, 134.9, 132.7, 131.1, 129.3 (two peaks), 128.7, 128.3, 128.0, 127.1 (two peaks), 126.8, 126.4.

4.2.1.2. 1-([1,1′-Biphenyl]-4-yl)naphthalene. The brown solid obtained (4.91 g, 81%) was washed with boiling MeOH and sublimed under reduced pressure to yield white crystals of the titled compound; ^1H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 7.98 (1H, d, 8-H, J=8.2 Hz), 7.92 (1H, d, 2-H, J=8.0 Hz), 7.87 (1H, d, J=8.1 Hz), 7.73–7.68 (4H, m), 7.59–7.36 (9H, m); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 141.8, 141.0, 140.8, 140.7, 134.8, 132.5, 131.4, 129.8, 129.2, 128.6, 128.3, 128.1, 127.9_2, 127.8_7, 127.0, 126.9, 126.7, 126.3. CCDC 698100.

4.2.1.3. N,N-Dimethyl-4-(naphthalen-1-yl)aniline. The brown solid obtained (0.72 g, 71%) was washed with MeOH and sublimed under reduced pressure to yield white crystals of the titled compound; ^1H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 8.07 (1H, d, 8′-H, J=8.4 Hz), 7.94 (1H, d, 2′-H, J=7.6 Hz), 7.85 (1H, d, J=8.2 Hz), 7.57–7.44 (6H, m), 6.92 (2H, d, 2-H, J=8.7 Hz), 3.08 [6H, s, $N(CH_3)_2$]; ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 150.7, 141.4, 134.9, 132.9, 131.7, 129.7, 129.1, 127.8, 127.7, 127.3, 126.6, 126.5, 126.4, 113.2, 41.6. CCDC 718939.

4.2.1.4. 1-(3-Methoxyphenyl)naphthalene. The brown liquid obtained (0.63 g, 77%) was treated with MeOH, precipitating a white solid that was recrystallized from MeOH and sublimed under reduced pressure to yield white crystals of the titled compound; ^1H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 7.97–7.92 (2H, m, 2-H+8-H), 7.89 (1H, d, J=8.2 Hz), 7.57–7.42 (5H, m), 7.13–7.07 (2H, m), 7.01 (1H, ddd, 2-H, J_1=8.3 Hz, J_2=2.6 Hz, J_3=0.9 Hz), 3.89 (3H, s, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 160.4, 143.1, 141.0, 134.7, 132.5, 130.1, 129.2, 128.6, 127.7, 126.9, 126.7, 126.2, 123.5, 116.5, 113.8, 56.2.

4.2.1.5. 1-(4-Methoxyphenyl)naphthalene. The yellowish solid obtained (2.35 g, 85%) was recrystallized from MeOH and sublimed under reduced pressure to yield white crystals of the titled compound (mp=114.2–114.7 °C); ^1H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 7.92 (1H, d, 8-H, J=8.3 Hz), 7.89 (1H, d, 2-H, J=8.0 Hz), 7.82 (1H, d, J=8.2 Hz), 7.52–7.39 (6H, m), 7.02 (2H, d, 2-H, J=8.6 Hz), 3.88 (3H, s, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 159.9, 140.8, 134.8, 134.1, 132.8, 132.0, 129.2, 128.3, 127.8, 127.0, 126.9, 126.6, 126.3, 114.7, 56.3.

4.2.1.6. 4-(Naphthalen-1-yl)benzaldehyde. The yellowish solid obtained (1.37 g, 56%) was recrystallized from EtOH and sublimed under reduced pressure to yield white crystals of the titled compound (mp=86.5–87.4 °C); ^1H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 10.12 (1H, s, C*H*O), 8.01 (2H, d, 2-H, J=8.1 Hz), 7.94–7.90 (2H, m, 2-H+8-H), 7.83 (1H, d, J=8.7 Hz), 7.67 (2H, d, 3-H, J=8.1 Hz), 7.56–7.42 (4H, m); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 192.9, 148.2, 139.7, 136.2, 134.7, 132.0, 131.7, 130.7, 129.5, 129.4, 127.9, 127.4, 127.0, 126.4, 126.3.

4.2.1.7. 4-(Naphthalen-1-yl)benzoic acid. The white flakes obtained (0.73 g, 59%) were washed with Et_2O and sublimed under reduced pressure to yield white crystals of the titled compound (mp=235.2–236.1 °C); ^1H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 13.04 (1H,br s, COO*H*), 8.11 (2H, d, 2-H, J_1=8.8 Hz), 8.05–7.99 (2H, m, 2-H+8-H), 7.79 (1H, d, J=8.4 Hz), 7.62 (2H, d, 3-H, J=8.4 Hz), 7.60–7.47 (4H, m); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 171.9, 147.4, 139.9, 134.7, 132.1, 131.2, 131.2, 129.4, 129.3, 128.9, 127.9, 127.3, 126.9, 126.5, 126.3. The X-ray structure of this compound was published elsewhere.[18]

4.2.1.8. 4-(Naphthalen-1-yl)benzonitrile. The brown solid obtained (0.45 g, 58%) was recrystallized from MeOH and sublimed under reduced pressure to yield white crystals of the titled compound; ^1H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 7.98–7.92 (2H, m, 2-H+8-H), 7.81 (2H, d, 2-H, J=8.2 Hz), 7.84–7.78 (1H, m), 7.64 (2H, d, 3-H, J=8.2 Hz), 7.61–7.40 (4H, m); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 146.6, 139.1, 134.7, 133.0, 131.9, 131.7, 129.7, 129.5, 127.9, 127.6, 127.1, 126.3, 126.1, 119.8, 112.1.

4.2.1.9. 1-(3,4-Dimethoxyphenyl)naphthalene. The greenish solid obtained (0.77 g, 75%) was recrystallized from MeOH and sublimed under reduced pressure to yield white needles of the titled compound (mp=120.3–121.2 °C); ^1H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 7.94 (1H, d, 8-H, J=8.4 Hz), 7.89 (1H, d, 2-H, J=8.4 Hz), 7.84 (1H, d, J=8.2 Hz), 7.53–7.40 (4H, m), 7.07–6.97 (3H, m), 3.96 (3H, s, OCH_3), 3.89 (3H, s, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 149.6, 149.3, 141.0, 134.8, 134.4, 132.8, 129.2, 128.4, 127.8, 127.0, 126.9, 126.7, 126.3, 123.2, 114.3, 112.0, 56.9, 56.9. CCDC 781816.

4.2.1.10. 2-Methoxy-5-(naphthalen-1-yl)benzaldehyde. The light brown solid obtained (0.94 g, 66%) was recrystallized from MeOH and sublimed under reduced pressure to yield white crystals of the titled compound (mp=92.6–93.9 °C); ^{1}H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 10.59 (1H, s, CHO), 8.01 (1H, d, 6-H, J=2.4 Hz), 7.94 (1H, d, 8′-H, J=7.5 Hz), 7.89 (1H, d, 2′-H, J=8.2 Hz), 7.85 (1H, d, J=8.6 Hz), 7.72 (1H, dd, 4-H, J_1=8.6 Hz, J_2=2.4 Hz), 7.57–7.40 (4H, m), 7.15 (1H, d, 3-H, J=8.6 Hz), 4.05 (3H, s, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 190.7, 162.1, 139.4, 138.3, 134.7, 134.2, 132.4, 130.9, 129.3, 128.8, 128.0, 127.2, 126.8, 126.5, 126.3, 125.6, 112.6, 56.8.

4.3. Synthesis of 1,8-diarylnaphthalenes

4.3.1. General synthesis of 1,8-diarylnaphthalenes. A solution of K_2CO_3 (6 mol/equiv) in 15 ml of water per 1 mmol of the limiting reactant was added to a solution of 1,8-dibromonaphthalene (1 mol/equiv), arylboronic acid (4 mol/equiv), and $Pd(OAc)_2$ (2 mol %) in the same volume of DMF. The resultant mixture was heated at 100 °C for 8 h under stirring. The final solution was allowed to cool to room temperature, and extracted with ethyl acetate. The organic layer was washed with water and aqueous 0.1 M NaOH, dried over anhydrous sodium sulfate and evaporated, yielding the product as impure diarylnaphthalene.

4.3.1.1. 1,8-Diphenylnaphthalene. The yellowish solid obtained (1.10 g, 60%) was recrystallized from AcOEt and sublimed under reduced pressure to yield white crystals of the titled compound (mp=143–145 °C); ^{1}H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 7.98 (2H, dd, 2-H, J_1=8.3 Hz, J_2=1.3 Hz), 7.59 (2H, dd, 3-H, J_1=8.3 Hz, J_2=7.0 Hz), 7.45 (2H, dd, 4-H, J_1=7.0 Hz, J_2=1.3 Hz), 7.03–6.93 (10H, m); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 144.0, 141.4, 136.3, 132.0, 130.7, 130.1, 129.5, 128.0, 126.6, 126.0.

4.3.1.2. 1,8-Di([1,1′-biphenyl]-4-yl)naphthalene. A solution of K_2CO_3 (6 mol/equiv) in a 40 ml solution of water/EtOH (1:1) was added to a solution of 1,8-dibromonaphthalene (1 mol/equiv), arylboronic acid (4 mol/equiv), and $PdCl_2$(dppe) (2 mol %) in 40 ml of toluene. The resultant mixture was heated at 120 °C for 52 h under stirring. The final solution was allowed to cool to room temperature, and the aqueous phase extracted with toluene. The mixed organic layers were washed with water and aqueous 0.1 M NaOH, dried over anhydrous sodium sulfate and evaporated, yielding a greenish solid (0.50 g, 55%) that was recrystallized from cyclohexane, washed with boiling MeOH, and sublimed under reduced pressure to yield white crystals of the titled compound; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 8.02 (2H, dd, 2-H, J_1=8.2 Hz, J_2=1.4 Hz), 7.62 (2H, dd, 3-H, J_1=8.2 Hz, J_2=7.0 Hz), 7.53 (2H, dd, 4-H, J_1=7.0 Hz, J_2=1.4 Hz), 7.36–7.25 (10H, m, Ph), 7.17 (4H, d, 3′-H, J=8.4 Hz), 7.08 (4H, d, 2′-H, J=8.4 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 143.1, 141.9, 141.0, 139.7, 136.3, 131.8, 131.2, 130.4, 129.7, 129.3, 128.1, 127.7, 126.8, 126.1. CCDC 668280.

4.3.1.3. 4,4′-(Naphthalen-1,8-diyl)bis(N,N-dimethylaniline). The yellowish solid obtained (0.58 g, 87%) was recrystallized from AcOEt, washed with boiling MeOH, and sublimed under reduced pressure to yield white crystals of the titled compound; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 7.92 (2H, dd, 2′-H, J_1=8.2 Hz, J_2=1.4 Hz), 7.55 (2H, dd, 3′-H, J_1=8.2 Hz, J_2=7.0 Hz), 7.47 (2H, dd, 4′-H, J_1=7.0 Hz, J_2=1.4 Hz), 6.85 (4H, d, 3-H, J=8.8 Hz), 6.36 (4H, d, 2-H, J=8.8 Hz), 2.88 [12H, s, N(CH_3)$_2$]; ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 149.5, 141.8, 136.5, 133.0, 131.4, 131.3, 130.7, 128.8, 125.9, 112.8, 41.7. CCDC 721267.

4.3.1.4. 1,8-Bis(4-methoxyphenyl)naphthalene. The light brown solid obtained (0.42 g, 71%) was washed with boiling MeOH and sublimed under reduced pressure to yield white crystals of the titled compound; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 7.96 (2H, dd, 2-H, J_1=8.2 Hz, J_2=1.0 Hz), 7.59–7.53 (2H, m, 3-H), 7.44 (2H, dd, 4-H, J_1=7.1 Hz, J_2=1.0 Hz), 6.89 (4H, d, 2′-H, J=8.6 Hz), 6.52 (4H, d, 3′-H, J=8.6 Hz), 3.75 (6H, s, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 158.6, 141.0, 136.7, 136.4, 131.8, 131.6, 130.6, 129.3, 126.0, 113.7, 56.2.

4.3.1.5. 4,4′-(Naphthalen-1,8-diyl)dibenzaldehyde. The yellowish solid obtained (0.35 g, 57%) was washed with MeOH, boiling EtOH and sublimed under reduced pressure to yield white crystals of the titled compound; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 9.82 (2H, s, CHO), 8.05 (2H, d, 2′-H, J=8.3 Hz), 7.64 (2H, dd, 3′-H, J_1=8.3 Hz, J_2=7.1 Hz), 7.47 (4H, d, 2-H, J=8.4 Hz), 7.49–7.45 (2H, 4′-H, m), 7.18 (4H, d, 3-H, J=8.0 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 192.4, 150.2, 139.5, 136.3, 135.0, 132.2, 131.3, 130.5, 129.7, 129.6, 126.4.

4.3.1.6. 4,4′-(Naphthalen-1,8-diyl)dibenzonitrile. The pale grey solid obtained (0.13 g, 30%) was recrystallized from AcOEt, and sublimed under reduced pressure to yield white crystals of the titled compound; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K, TMS) 8.06 (2H, dd, 2′-H, J_1=8.3 Hz, J_2=1.3 Hz), 7.64 (2H, dd, 3′-H, J_1=8.3 Hz, J_2=7.1 Hz), 7.43 (2H, dd, 4′-H, J_1=7.1 Hz, J_2=1.3 Hz), 7.31 (4H, d, 3-H, J=8.4 Hz), 7.12 (4H, d, 2-H, J=8.4 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 148.5, 138.7, 136.3, 132.3, 132.1, 131.3, 130.8, 129.3, 126.5, 119.3, 110.9.

4.3.1.7. 1,8-Bis(3,4-dimethoxyphenyl)naphthalene. The brown oil obtained was treated with MeOH, precipitating a yellow solid (0.64 g, 76%), that was washed with boiling MeOH and sublimed under reduced pressure to yield white crystals of the titled compound (mp=132.1–133.2 °C); ^{1}H NMR (400 MHz, $CDCl_3$, 300 K, TMS), equilibrium of *syn*/*anti* conformers, 7.96 (2H, d, 2-H, J=8.1 Hz), 7.59–7.54 (2H, m, 3-H), 7.46 (2H, d, 4-H, J=6.8 Hz), 6.82–6.32 (6H, m), 3.84, 3.81, 3.75, and 3.70 (12H, s, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 148.2, 141.1, 137.4, 136.4, 131.6, 129.4, 126.0, 122.3, 114.8, 111.9, 111.5, 57.1, 56.5, 56.2. CCDC 769513.

4.3.1.8. 5,5′-(Naphthalen-1,8-diyl)bis(2-methoxybenzaldehyde). The brown solid obtained (0.74 g; 53%) was washed with boiling MeOH and sublimed under reduced pressure to yield white crystals of the titled compound (mp=206.6–207.9 °C); ^{1}H NMR (400 MHz, $CDCl_3$, 300 K, TMS), equilibrium of *syn*/*anti* conformers; *syn* conformer: 10.54 (2H, s, CHO), 8.06 (2H, d, 6-H, J=2.5 Hz), 7.99 (2H, dd, 2′-H, J_1=8.3 Hz, J_2=1.2 Hz), 7.82 (2H, dd, 4-H, J_1=8.8 Hz, J_2=2.5 Hz), 7.57 (2H, dd, 3′-H, J_1=8.3 Hz, J_2=6.8 Hz), 7.40 (2H, dd, 4′-H, J_1=6.8 Hz, J_2=1.2 Hz), 7.10 (2H, d, 3-H, J=8.8 Hz), 4.00 (6H, s, OCH_3); *anti* conformer: 10.32 (2H, s, CHO), 7.99 (2H, dd, 2′-H, J_1=8.3 Hz, J_2=1.2 Hz), 7.57 (2H, dd, 3′-H, J_1=8.3 Hz, J_2=6.8 Hz), 7.40 (2H, dd, 4′-H, J_1=6.8 Hz, J_2=1.2 Hz), 7.34 (2H, d, 6-H, J=2.3 Hz), 7.19 (2H, dd, 4-H, J_1=8.6 Hz, J_2=2.3 Hz), 6.60 (2H, d, 3-H, J=8.6 Hz), 3.85 (6H, s, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$, 300 K) 190.4, 160.9, 139.1, 138.4, 136.6, 136.3, 131.6, 130.5, 130.0, 126.1, 124.2, 111.7, 56.7.

4.4. Synthesis of non-symmetric 1,8-diarylnaphthalenes

4.4.1. First addition: phenylboronic acid. A solution of K_2CO_3 (0.75 mmol, 1.5 mol/equiv) in 10 ml of H_2O was added, at ambient temperature, to a solution of 1,8-dibromonaphthalene (0.50 mmol, 1 mol/equiv), phenylboronic acid (0.60 mmol, 1.2 mol/equiv) and $Pd(OAc)_2$ (2 mol %) in 10 ml of DMF. The resultant mixture was heated at 100 °C under stirring, and after 3 h a solution of biphen-4-ylboronic acid (1.51 mmol, 3 mol/equiv) and $Pd(OAc)_2$ (1 mol %) in 10 ml of DMF, and a solution of K_2CO_3 (1.75 mmol, 3.5 mol/equiv) in 10 ml of H_2O, were added. The reaction was allowed to proceed for 4 h at 100 °C. The final solution was allowed to cool to room temperature, and extracted with ethyl acetate. The organic layer was

washed with water and aqueous 0.1 M NaOH, dried over anhydrous sodium sulfate, and filtered for GC analysis.

4.4.2. First addition: biphen-4-ylboronic acid. A solution of K_2CO_3 (0.77 mmol, 1.5 mol/equiv) in 10 ml of H_2O was added, at ambient temperature, to a solution of 1,8-dibromonaphthalene (0.50 mmol, 1 mol/equiv), biphen-4-ylboronic acid (0.60 mmol, 1.2 mol/equiv) and $Pd(OAc)_2$ (2 mol %) in 10 ml of DMF. The resultant mixture was heated at 100 °C under stirring, and after 3 h a solution of phenylboronic acid (1.50 mmol, 3 mol/equiv) and $Pd(OAc)_2$ (1 mol %) in 10 ml of DMF, and a solution of K_2CO_3 (1.75 mmol, 3.5 mol/equiv) in 10 ml of H_2O, were added. The reaction was allowed to proceed for 4 h at 100 °C. The final solution was allowed to cool to room temperature, and extracted with ethyl acetate. The organic layer was washed with water and aqueous 0.1 M NaOH, dried over anhydrous sodium sulfate, and filtered for GC analysis.

4.4.3. Simultaneous addition. A solution of K_2CO_3 (3.51 mmol, 7 mol/equiv) in 20 ml of H_2O was added, at ambient temperature, to a solution of 1,8-dibromonaphthalene (0.50 mmol, 1 mol/equiv), phenylboronic acid (1.50 mmol, 3 mol/equiv), biphen-4-ylboronic acid (1.50 mmol, 3 mol/equiv), and $Pd(OAc)_2$ (2 mol %) in 20 ml of DMF. The resultant mixture was heated at 100 °C for 8 h under stirring. The final solution was allowed to cool to room temperature, and extracted with ethyl acetate. The organic layer was washed with water and aqueous 0.1 M NaOH, dried over anhydrous sodium sulfate, and filtered for GC analysis.

4.5. Computational details

All theoretical calculations were performed using the Gaussian 03 software package.[19] The full geometry optimizations were performed using the Möller–Plesset perturbation theory with a second order perturbation (MP2) and the correlation consistent basis set cc-pVDZ, using the SCS-MP2 method for evaluation of the electronic energies.[10]

Acknowledgements

Thanks are due to Fundação para a Ciência e Tecnologia (FCT) and Programa Operacional Ciência e Inovação 2010 (POCI 2010) supported by the European Community Fund FEDER for the financial support to Project POCI/QUI/61873/2004. C.F.R.A.C.L. also thanks FCT and the European Social Fund (ESF) under the third Community Support Framework (CSF) for the award of a Ph.D. Research Grant (SRFH/BD/29394/2006).

Supplementary data

Detailed statistical analysis for the mono- and di-arylation of 1,8-dibromonaphthalene. ^1H and ^{13}C NMR spectra for all the synthesized compounds. Detailed computational results. Supplementary data related to this article can be found online version, at doi:10.1016/j.tet.2010.11.081. These data include MOL files and InChIKeys of the most important compounds described in this article.

References and notes

1. Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513.
2. Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
3. Liu, L.; Zhang, Y.; Xin, B. *J. Org. Chem.* **2006**, *71*, 3994.
4. Braga, A. A. C.; Morgon, N. H.; Ujaque, G.; Maseras, F. *J. Am. Chem. Soc.* **2005**, *127*, 9298.
5. Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.
6. Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11.
7. House, H. O.; Koepsell, D. G.; Campbell, W. J. *J. Org. Chem.* **1972**, *37*, 1003.
8. Wolf, C.; Mei, X. *J. Am. Chem. Soc.* **2003**, *125*, 10651.
9. Ibuki, E.; Ozasa, S.; Fujioca, Y.; Mijutoni, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 845.
10. Grimme, S. *J. Chem. Phys.* **2003**, *118*, 9095.
11. Gillie, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4933.
12. Hunter, C. A.; Lawson, K. R.; Perkins, J.; Urch, C. J. *J. Chem. Soc., Perkin Trans. 2* **2001**, 651.
13. Lima, C. F. R. A. C.; Sousa, C. A. D.; Rodriguez-Borges, J. E.; Melo, A.; Gomes, L. R.; Low, J. N.; Santos, L. M. N. B. F. *Phys. Chem. Chem. Phys.* **2010**, *12*, 11228.
14. Stille, J. K.; Lau, K. S. Y. *Acc. Chem. Res.* **1977**, *10*, 434.
15. Fitton, P.; Rick, E. A. *J. Organomet. Chem.* **1971**, *28*, 287.
16. Kuroda, M.; Nakayama, J.; Hoshino, M. *Tetrahedron* **1993**, *49*, 3735.
17. Rees, C. W.; Storr, R. C. *J. Chem. Soc. C* **1969**, 756.
18. Lima, C. F. R. A. C.; Gomes, L. R.; Santos, L. M. N. B. F.; Low, J. N. *Acta Crystallogr.* **2009**, E65, o3037.
19. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Revision C.02*; Gaussian: Pittsburgh, PA, 2004.