7th Portuguese National Meeting of Organic Chemistry

7ENQO

SOCIEDADE PORTUGUESA DE QUÍMICA

Book of abstracts
7ENQO
Sociedade Portuguesa de Química
16th-18th July 2007
Lisboa, Portugal
Email: info7enqo@dq.fct.unl.pt
URL: www.dq.fct.unl.pt/7enqo

Editor:
Sociedade Portuguesa de Química

Editorial Coordinator:
Abel Vieira
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ISBN: 978-989-8124-00-5

SYNTHESIS OF 1,8-DIARYLNAPHTHALENES BY THE SUZUKI CROSS COUPLING REACTION

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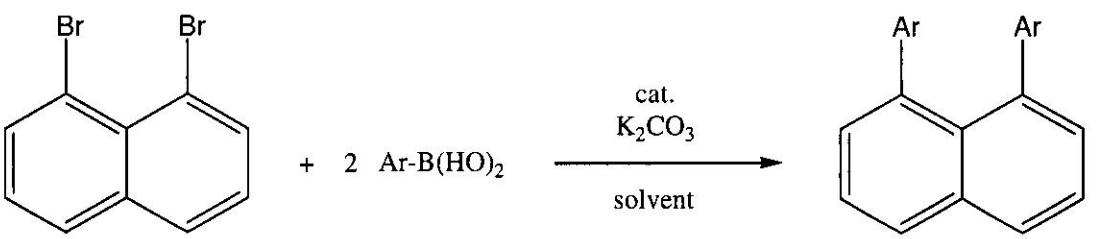
The π-π stacking interaction between adjacent aromatic moieties is a very interesting concept in the fields of chemistry and biochemistry.[1] It's importance in biological systems and crystal packing is known but the nature of this interaction is yet to be completely understood. In the 1,8-diarylnaphthalenes, despite of the steric repulsion, the two parallel aromatic substituents can interact favourably by π-π stacking.[2] Using the experimental values of the standard molar enthalpies of formation on the gaseous phase, $\Delta_f H°(g)$, the magnitude of this interaction can be evaluated. Once these compounds are not commercially available and the synthesis of some of them were never reported in the literature we decided to synthesize them by the Suzuki cross coupling reaction, starting from 1,8-dibromonaphthalene, using a variety of synthetic approaches. The mono-substituted analogues were also synthesized by the same reaction mechanism using 1-bromonaphthalene as the starting aryl halogenated reagent.



cat. = $Pd(OAc)_2$, $PdCl_2(dppe)$
solvent = H_2O/DMF, Toluene/H_2O
Ar = phenyl, biphenyl, thiophene, pyridine

[1] T. Sato, T. Tsuneda and K. Hirao, *J. Chem. Phys.*, 2005, 123, 104307.
[2] Franco Cozzi and Jay S. Siegel, *Pure & Appl. Chem.*, 1995, 67, 683-689.

Acknowledgements: This work was supported by Fundação para a Ciência e Tecnologia (FCT) and the FERDER for the financial support to CIQUP. Carlos F.R.A.C. Lima 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/29394/2007). Thanks are also due to FCT for the financial support to the project POCI/QUI/61873/2004.

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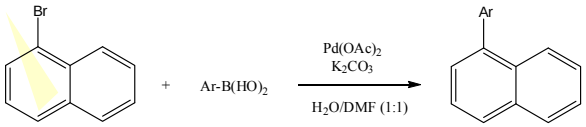
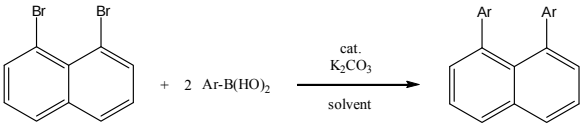
INTRODUCTION

The π-π stacking interaction between adjacent aromatic moieties is a very interesting phenomenon in the fields of chemistry and biochemistry[1]. It's importance in biological systems and crystal packing is known but the nature of this interaction is yet to be completely understood. In the 1,8-diarylnaphthalenes, despite of the steric repulsion, the two parallel aromatic substituents can interact favourably by π-π stacking[2]. Using the experimental values of the standard molar enthalpies of formation on the gaseous phase, $\Delta_f H°(g)$, the magnitude of this interaction can be evaluated. Once these compounds are not commercially available and the synthesis of some of them were never reported in the literature we decided to synthesize them by the Suzuki cross coupling reaction, starting from 1,8-dibromonaphthalene, using a variety of synthetic approaches. The mono-substituted analogues were also synthesized by the same reaction mechanism using 1-bromonaphthalene as the starting aryl halogenated reagent.



Ar = phenyl, biphenyl, thiophene, pyridine, furan, 4-methoxyphenyl

Scheme 1. Suzuki Cross Coupling reaction for the mono-substituted compounds.



cat. = $Pd(OAc)_2$, $PdCl_2(dppe)$
solvent = H_2O/DMF, Toluene/H_2O
Ar = phenyl, biphenyl, thiophene, pyridine, furan, 4-methoxyphenyl

Scheme 2. Suzuki Cross Coupling reaction for the di-substituted compounds.

SYNTHESIS AND PURIFICATION

For the mono-substituted compounds only one methodology was used (Scheme 1). The reactions were carried out at T ≈ 90 ºC for approximately 8 hours.

For the di-substituted analogues some changes in reaction conditions were made, namely in the solvent, temperature, catalyst and reaction time. Nevertheless, in most cases the conditions employed were cat.: $Pd(OAc)_2$, solvent: H_2O/DMF (1:1), T ≈ 100 ºC and t ≈ 8h.

The compounds were purified by recrystallization from ethanol, ethyl acetate or cyclo-hexane and by repeated sublimation under vacuum.

The purity of the compounds was analyzed by gas chromatography and their identity confirmed by ^{1}H-NMR.

DISCUSSION

1) The fair solubility of some substituted naphthalenes in H_2O/DMF was one of the main drawbacks during synthesis. For 1,8-diphenylnaphthalene the yield could be improved changing the solvent for Toluene/H_2O.
2) Higher temperatures seems to improve the reaction yield; the solubility of the compounds increase as well as the energy available for the molecules to overcome considerable steric repulsions in the reaction mechanism due to steric constraints brought about by the adjacent substituents in naphthalene.
3) In some cases the presence of the deboronation product (Ar-H) was detected.
4) The reactions with heterocyclics were not successful. New methodologies will be carried out for these cases.

RESULTS

Table 1 presents the results obtained for the synthesis of the various mono- and di-substituted compounds. The *% yield* is calculated based on the mass obtained of the pure and isolated product.

For the case of 1,8-di(biphenyl-4-il)naphthalene various synthetic methodologies were employed. The results are present in table 2.

Table 1. Reaction conditions for the synthesis of 1,8-di(biphenyl-4-il)naphthalene

Boronic acid	*% yield*	
	Mono-substituted	Di-substituted
Phenylboronic acid	(a)	60
4-Biphenylboronic acid	83	58 *
3-Biphenylboronic acid	(b)	(b) *
4-Methoxyphenylboronic acid	88	60
3-Thiopheneboronic acid	19	traces
3-Furanboronic acid	(c)	traces
3-Pyrideneboronic acid	(c)	traces
Phenethylboronic acid	(c)	traces

* These were the only cases where the catalyst were $PdCl_2(dppe)$ and the solvent Toluene/H_2O.
(a) 1-Phenylnaphthalene is commercially available.
(b) These compounds were not yet isolated due to experimental difficulties but their presence has been confirmed
(c) These compounds were not yet synthesized because this methodology was not satisfactory for the synthesis of the di-substituted analogues.

Table 2. Reaction conditions for the synthesis of 1,8-di(biphenyl-4-il)naphthalene

Synthesis no.	Catalyst	Solvent	T / ºC	t / h	% yield
1	$Pd(OAc)_2$	H_2O/DMF (1:1)	100	6	14
2	$Pd(OAc)_2$	H_2O/DMF (1:1)	25	6	traces
3	$PdCl_2(dppe)$	Toluene/H_2O	115	52	58

REFERENCES

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