Use of new supported palladium heterogeneous catalysts in the production of key intermediates for the synthesis of "sartans"via the Suzuki reaction

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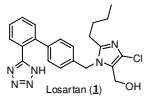
INTRODUCTION

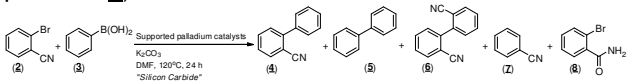
Angiotensin II receptor antagonists are widely used in the treatment of hypertension, heart diseases, heart attack, and bladder diseases (e.g. Losartan-Cozaar®, **1**).[1]



The "sartans" contain characteristic *ortho* functionalized biaryl moiety in their structure that can be synthetized by palladium mediated cross-coupling.[1] In this context, we use new supported palladium heterogeneous catalysts for the production biaryl intermediate via Suzuki reactions.

RESULTS AND DISCUSSION

In the inicial studies, the supported palladium heterogeneous catalysts Pd-Ru/CeO_2-TiO_2; Pd-Ru/Nb_2O_5-TiO_2; Pd-Ru/La_2O_3-TiO_2; Pd-Ru/La_2O_3-Nb_2O_5; Pd-Ru/TiO_2; Pd-Ru/Nb_2O_5; Pd-Ru/La_2O_3; Pd-Cu/γAl_2O_3, and Pd/Nb_2O_5 previously characterized by TG/DTA, BET, XRD and XRF were tested for the Suzuki reaction between 2-bromobenzonitrile (**2**) and phenylboronic acid (**3**) with K_2CO_3 as base in DMF at 120°C for 24 h on the silica carbide plate (Scheme 1). The catalyst supported on niobium(V) oxide presents the best performance with excellent conversion (>99%) and selectivity (>99%) to the desired cross-coupling product, **4**).



Scheme 1. Suzuki reaction between 2-bromobenzonitrile (**2**) and phenylboronic acid (**3**)

In a second set of experiments, we decided to evaluate at the same reaction profile under microwave irradiation conditions and results are summarized in the Table 1.

Table 1. Influence of solvent, reaction time and catalyst load under microwave irradiation on the Suzuki reaction.

Entry	Solvent	Reaction Time	Catalyst Load	Conv.[(a)]	Select.[(a)]
1	DMF	10	10%	>99%	73%
2	DMF	20	10%	>99%	78%
3	DMF	30	10%	>99%	88%
4	EtOH/H_2O 50%	30	10%	>99%	>99%
5	EtOH/H_2O 50%	30	5%	>99%	>99%
6	EtOH/H_2O 50%	30	1%	>99%	>99% (>99%)[b]
7	EtOH/H_2O 50%	30	0.5%	>99%	88%

General conditions: 2-bromobenzonitrile (1 mmol); phenylboronic (1,2 mmol); K_2CO_3 (1,2 mmol); Pd/Nb_2O_5; Solvent (2 mL)
[a]Conversion and selectivity to the cross-coupling product **4** was determined by GC-MS. [b]Isolated yield determined by NMR ^1H and NMR ^{13}C

As can be seem, the reaction assisted by microwave in EtOH/H_2O 50% mixture in only 30 min afforded higher selectivity for cross coupling product, **4** (Table 1; Entries 4-6).

CONCLUSION

The use of palladium supported in niobium(V) oxide presented high efficiency in terms of yield and selectivity in the synthesis of important biaryl building block via Suzuki reaction.

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REFERENCES

[1]Veverka, M.; Putala, M.; Brath, H.; Zuppancic, S. US Patent 7,868,180 Jan 11, **2011**.