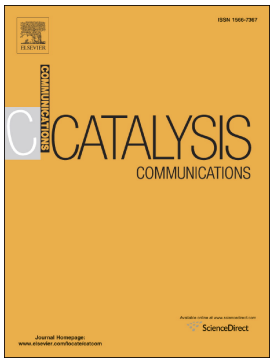

Reactivity of 5-aminopyrazoles bearing a cyclopropyl group at C3-position in palladium-catalyzed direct C4-arylation

Ameni Sidhom, Jean-Francois Soulé, Henri Doucet, Fatma Allouche

PII: S1566-7367(18)30252-8
DOI: doi:10.1016/j.catcom.2018.07.008
Reference: CATCOM 5448

To appear in: *Catalysis Communications*

Received date: 2 June 2018
Revised date: 5 July 2018
Accepted date: 7 July 2018

Please cite this article as: Ameni Sidhom, Jean-Francois Soulé, Henri Doucet, Fatma Allouche , Reactivity of 5-aminopyrazoles bearing a cyclopropyl group at C3-position in palladium-catalyzed direct C4-arylation. Catcom (2018), doi:10.1016/j.catcom.2018.07.008

Reactivity of 5-aminopyrazoles bearing a cyclopropyl group at C3-position in palladium-catalyzed direct C4-arylation

Ameni Sidhom,[a,b] Jean-Francois Soulé,[b]* Henri Doucet,[b]* Fatma Allouche[a]

[a] *Laboratoire de Chimie Médicinale et Environnementale, Institut Supérieur de Biotechnologie, Route de la Soukra km 4, 3038 Sfax, Tunisie.*

[b] *Univ Rennes, CNRS, ISCR-UMR 6226, F-35000 Rennes, France. E-mail: jean-francois-soule@univ-rennes1.fr, henri.doucet@univ-rennes1.fr*

Abstract— Pyrazole derivatives bearing a cyclopropyl group at C3-position and an amino substituent at C5 were successfully employed in palladium-catalyzed direct arylations. These couplings were performed using air-stable $PdCl(C_3H_5)$(dppb) catalyst associated to KOAc as inexpensive base, and afforded regioselectively the C4-arylated pyrazoles without decomposition of the cyclopropyl unit and formation of amination products. A wide variety of functional groups on the aryl bromide including electron-withdrawing and electron-donating ones such as nitrile, nitro, propionyl, ester, trifluoromethyl, chloro, fluoro or methoxy was tolerated. Moreover, from 5-aminopyrazoles bearing *N*-2'-bromoaryl or 2'-bromobenzenesulfonamide substituent on the amino group, intramolecular Pd-catalyzed direct arylations allowed the formation of tricyclic compounds by formation of 5- or 6-membered rings.

Keywords: palladium, C-H bond functionalization, pyrazoles, cyclopropyl, aryl bromides

1. Introduction

Pyrazoles derivatives bearing a cyclopropyl unit are of considerable interest for pharmaceutical chemists due to their biological activities. Several molecules containing a cyclopropylpyrazole moiety such as compounds **I-IV** exhibit properties against some cancers; and some of them such as **III** and **IV** are under *in vivo* and *in vitro* investigation in the field of insulin-like growth factor and IGF-1 receptor which play an important role in cancer [1,2]. Therefore, the development of simple and reliable methods for the synthesis of 3-cyclopropylpyrazol derivatives, especially using commercially available 3-cyclopropylpyrazoles is highly desirable.