

ORGANONICKEL PHOSPHINE COMPLEXES AS CATALYSTS IN CROSS-COUPLING OF 2-CHLORO-5-(TRIFLUOROMETHYL)PYRIDINE WITH (2,4-DIFLUOROPHENYL)BORONIC ACID

*Ivanytsya M. O.*<sup>1,3,4</sup>, Kolotilov S. V.<sup>3</sup>, Ryabukhin S. V.<sup>1,4</sup>, Volochnyuk D. M.<sup>1,2,4</sup>

<sup>1</sup>Enamine Ltd, Kyiv, Ukraine

<sup>2</sup>Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kyiv, Ukraine

<sup>3</sup>L. V. Piszarshevskii Institute of Physical Chemistry of the National Academy of Sciences of Ukraine, Kyiv, Ukraine

<sup>4</sup>National Taras Shevchenko University of Kyiv, Kyiv, Ukraine

ivanytsya.mykyta@gmail.com

Arylnickel phosphine complexes have been studied for more than a decade as a substitute for palladium catalysts for cross-coupling reactions because of the considerable cost of platinum-group metals. Simple replacement of palladium by nickel in catalytic systems often leads to a decrease in catalytic activity, therefore optimization of the reaction conditions and selection of appropriate ligands is required. The decrease of activity in the dppf-containing precatalyst when replacing Pd on Ni in the cross-coupling reaction of alpha-pyridyl halides with boronic acids is especially noticeable due to deactivation of the nickel catalyst **1** during the reaction [1,2]. This obstacle has not been overcome yet.

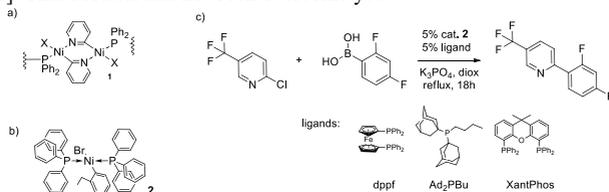


Fig. 1. a) dimer causing deactivation of Ni-dppf catalyst; b) presumable structure of Ni(PPh<sub>3</sub>)<sub>2</sub>(EtPh)Br; c) cross-coupling reaction of 2-chloro-5-(trifluoromethyl)pyridine with (2,4-difluorophenyl)boronic acid

We hypothesized that the dimer **1** (Fig. 1a) could be destabilized if dppf was replaced either with a ligand with a larger conical angle (Ad<sub>2</sub>PBU) or with a bidentate ligand where the cis conformation of phosphine residues is more firmly anchored in the ligand structure itself (XantPhos), which, in turn, would stabilize bidentate ligand binding to nickel and prevent coordination of an "extra" nitrogen atom.

To test this hypothesis, the Ni(PPh<sub>3</sub>)<sub>2</sub>(EtPh)Br (**2**) complex was obtained and characterized by NMR. This compound served as a metal precursor in the reaction of 2-chloro-5-(trifluoromethyl)pyridine with (2,4-difluorophenyl)boronic acid (Fig. 1c), this reaction was chosen since the reaction product is an important ligand for iridium photocatalysts. It was found that the highest product yield (68 %) was obtained when Ad<sub>2</sub>PBU was added to the reaction mixture, while the addition of bidentate phosphines led to a drop in the product yield, which was especially noticeable in the case of dppf (45 %). It was found that increasing the reaction time did not lead to increase of the product yield, as well as addition of small amounts of water also had no effect on the catalytic activity of the nickel complexes.

Thus, the use of highly donor monodentate phosphine ligands with large cone angle allows to increase the efficiency of nickel-containing catalytic systems in the cross-coupling of 2-chloro-5-(trifluoromethyl)pyridine with (2,4-difluorophenyl)boronic acid.

1. M.J. West, A.J.B. Organic & Biomolecular Chemistry, **2019**, 17.20: 5055-5059

2. A.K Cooper, M.E. Greaves, W. Donohoe, P.M. Burton, T.O. Ronson, A.R. Kennedy, D.J. Nelson. *Chemical science*, **2021**, 12.42: 14074-14082.