Project title	Enhancing synergistic effect for oxidative cross coupling using heterogeneous binuclear [$Cu^{II}Ln^{III}$] catalysts
Project acronym	HBSynCat
Project Code and number	PN-III-P1-1.1-PD-2016-1054, Nr. 29/2018
Contracting Authority	UEFISCDI,
Project Host Institution	University of Bucharest
Run period	02.05.2018-30.04.2020
Total funding	250.000,00 lei

Project Summary

In view of the need to develop new environmentally friendly catalytic materials with tunable properties, the project proposal offers the possibility of developing new heterogeneous catalytic system with enhanced synergistic effect, in order to easy achieve the most demanded catalytic reactions - oxidative cross coupling.

The main objective represents the synthesis of new heterogeneous Schiff-base based binuclear [$Cu^{II}Ln^{III}$] catalysts by immobilization of homogeneous heterobimetallic Cu/La(OTf)$_3$ complex on graphene-based support. Different immobilization approaches will be used to find the most efficient one by correlating catalytic results with methodology of catalytic synthesis. To reach this goal, the project proposal is based on the achievement of the following objectives:

- Synthesis and functionalization of [$Cu^{II}La^{III}$] complex
- Covalent, immobilization of functionalized [$Cu^{II}Ln^{III}$] complex on the graphene. Step by step construction complex on graphene support. Immobilization by anion exchange.
- Characterization of catalytic materials.

Catalysts testing in oxidative cross coupling reactions

The implementation degree of the project:

Phase I/2018 (02.05.2018 - 31.12.2018): ***Synthesis and functionalization of binuclear [$Cu^{II}Ln^{III}$] complexes with compartmental ligands.***

Activity 1.1. Synthesis and functionalization of binuclear homogeneous catalysts [$Cu^{II}Ln^{III}$] with Schiff-base ligands;

Activity 1.2. Functionalization of binuclear [$Cu^{II}Ln^{III}$] complexes;

Summary of the research report (Phase I):

In the first phase of the project, comprised between May 2018 and December 2018, all proposed tasks were achieved. A series of heterobinuclear complexes [$Cu^{II}(L^n)La^{III}$] were synthesized and preliminarily characterized by DRIFT, powder XRD and UV-Vis. The catalytic materials obtained were tested in the oxidative coupling reaction of indole with methyl-vinyl-ketone. The reaction conditions were optimized and the results of the catalytic performance correlated with the method of synthesis of the complexes. The highest achieved yield was 91.4%. The first functionalized and subsequently immobilized complex on graphene oxide was performed by reaction between the hydroxyl group of amine from the Schiff base of the ligand and the epoxide groups on the surface of the graphene oxide.

Phase II/2019 (01.01.2019-31.12.2019): *Immobilization of [$Cu^{II}Ln^{III}$] complex on the graphene.*

Activity 2.1. Covalent immobilization of complex on the graphene;

Activity 2.2. Step by step construction of the complex with compartmental ligand on the graphene surface;

Activity 2.3. Immobilization of complex by anion exchange;

Summary of the research report (Phase II):

In the second phase of the project, comprised between December 2018 and December 2019 different immobilization strategies were applied do obtain heterogeneous catalysts with heterobinuclear complexes [$Cu^{II}(L^n)La^{III}$] supported on graphene oxide (GO). Obtained materials were characterized by DRIFT, powder XRD, TG-DTA, Raman, NMR and UV-Vis. The obtained catalytic materials were tested in the oxidative coupling reactions, best results being obtained for oxidative coupling or Friedel-Crafts alkylation of indole with methyl-vinyl-ketone (MVK). However the step by step protocol to construct the homogeneous complex on the solid support didn’t provide catalytic materials with high activity, at the same time their synthesis and characterization were tedious. The linkers used to attach the complex usually don’t bind selectively on the GO. In this case another three immobilization strategies were developed. The complexes were synthesized together with attached linkers and the immobilization of such prepared functionalized complexes was performed in just one final step. The proposed structures of final catalysts and their simplified representation are presented in figure 1. The corresponding monometallic catalysts were also obtained in order to evaluate the synergistic effect of the two metals.

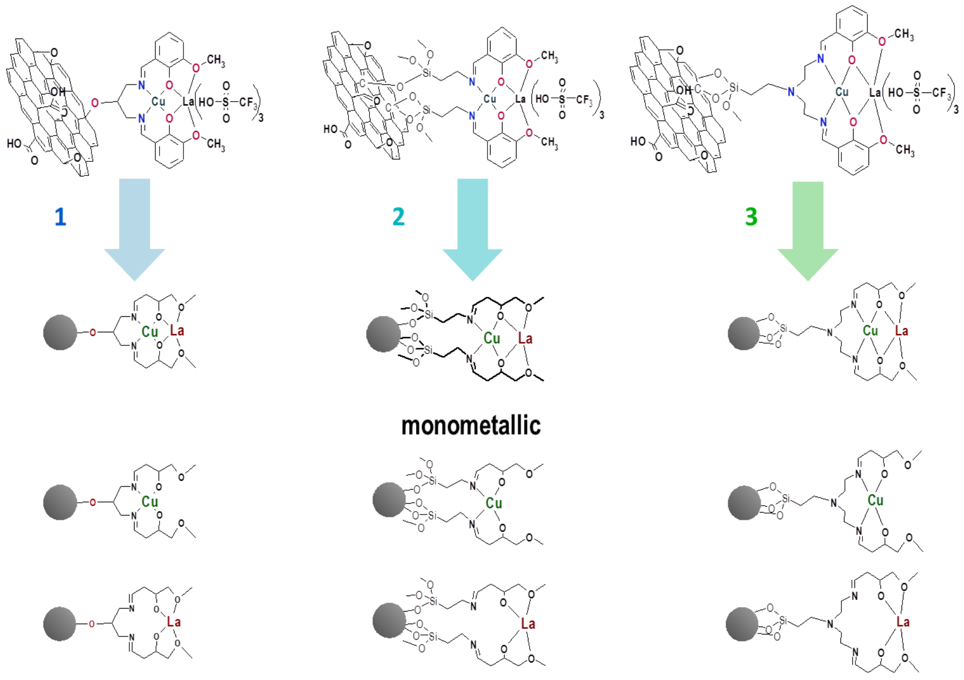
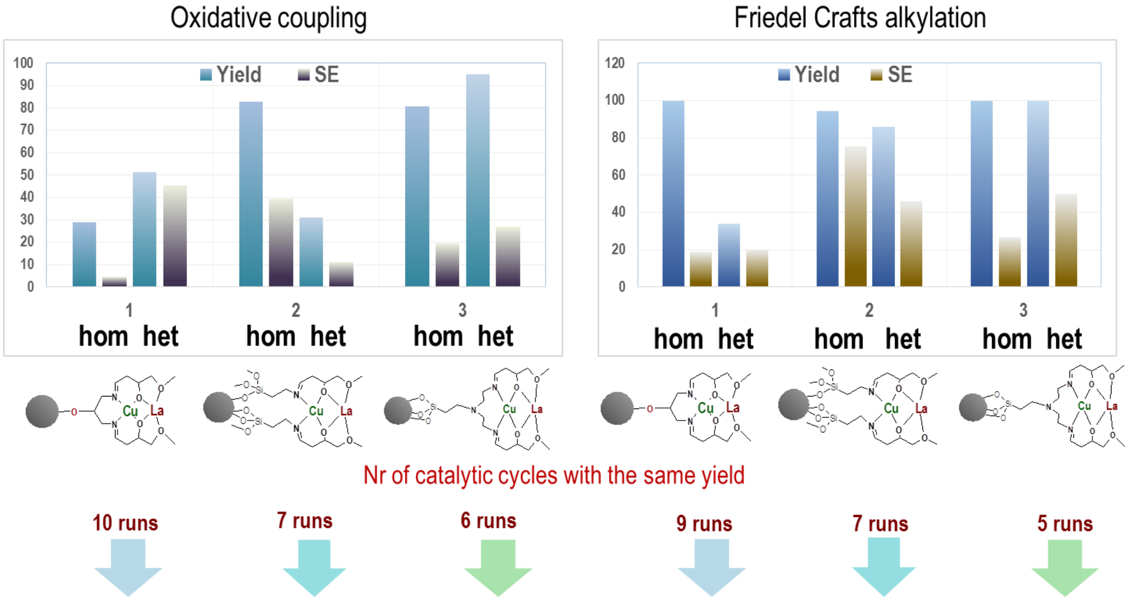


Figure 1: Proposed structure of some of the prepared heterogeneous mono and bi-metallic catalysts and their simplified representation

These materials were used in oxidative coupling and alkylation of indole with MVK to provide 4-(1H-Indol-3-il)butan-2-one as major product. Synergistic effect was calculated as the sum of yields provided by monometallic complexes subtracted from the yield obtained with bimetallic complex.

Comparative catalytic and recycling results for heterogeneous and corresponding homogeneous catalysts are represented in figure 2.



Nr of catalytic cycles with the same yield

10 runs

Increased Activity
and SE / Most stable
Easiest to prepare

7 runs

Lower activity
and SE than
homogeneous

6 runs

Most active
Lower SE
Less stable

9 runs

Less active
Less SE / Most stable
Easiest to prepare

7 runs

High activity
Highest SE

5 runs

Most active
Lower SE
Less stable

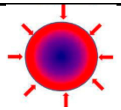
Figure 2: Summary of results for catalytic activity and stability of catalysts

Phase III/2020 (01.01.2020-30.04.2020): ***Optimization of the catalytic system.***

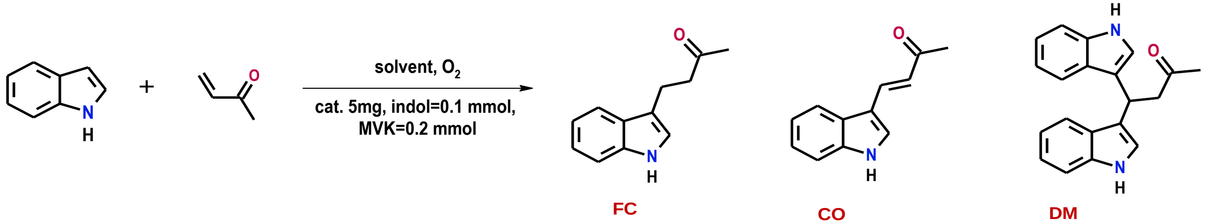
Activity 3.1. Optimization of heterogeneous catalytic system for oxidative cross coupling reaction;

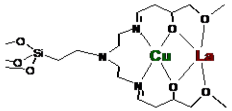
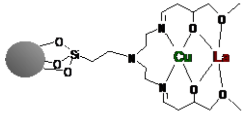
Summary of the research report (Phase II):

In the last phase of the project, comprised between January 2020 and August 2020 (comprising pandemic-related extension period) the synthesis of heterogeneous catalyst and catalytic reaction were optimized. The heterogeneous catalyst 3 (phase II figure 1) was chosen to be optimized due to ease of synthesis and best catalytic test results and best correlation with homogeneous catalyst. The synthesis process was optimized step-by-step starting with Schiff base and finishing with covalent immobilization on graphene oxide (GO). Alternative methods like ball mill (BM) and microwave irradiation (MW) were also used next to classic reflux (RF). The comparative results, based on FTIR, NMR and TGA measurements and corresponding yield are presented in table below.

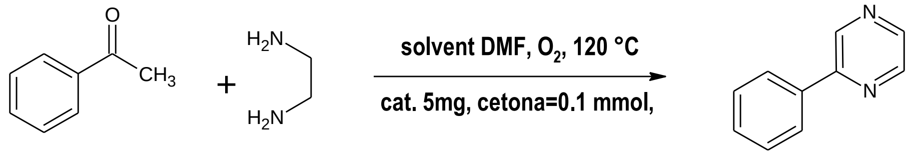
Step	**RF** 	**MW** 	**BM** 
Schiff Base synthesis (EtOH, reflux temperature, washing with Et_2O)	+ Good yield, good product purity	++ Good yield, good product purity, fast synthesis	- Poor yield, laborious separation
Functionalization with 3-chloropropyltrimethoxysilane (DMF, 120ºC, washing with Et_2O)	+- Good yield, long reaction time	++ Good yield, fast synthesis	- Poor yield, laborious separation
Immobilization on GO (EtOH anh., 75ºC)	+ Efficient immobilization	++ Efficient immobilization, fast reaction, 20% more complex immobilized (TGA based)	- Poor immobilization yield, efficient method for GO milling

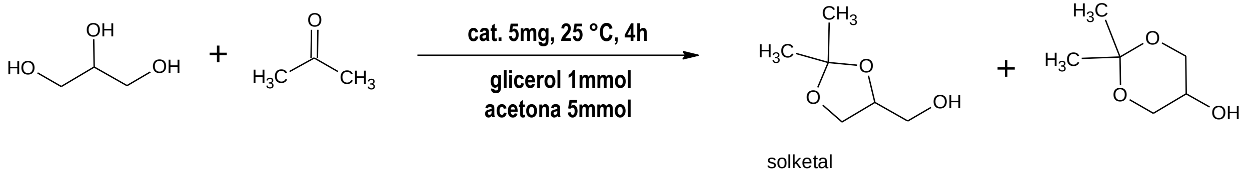
As result, MW is a fast and efficient method for synthesis of homogeneous and heterogeneous complex. Further, the reaction conditions of oxidative coupling of indole were optimized. Best results are presented bellow.



Catalyst	Yield (%) FC	SE (%) FC	Yield (%) CO	SE (%) CO	Yield (%) DM	SE (%) DM	T °C	Solvent
	26	13	11	38	6	78	50	DCM
	19	10	17	41	8	85	50	DCM

Except indole other substrates like chloro- and nitro-indole, pyrrole, furane, thiophene, benzofurane were tested, resulted with lower yields. However the synergistic effect, especially for DM product was proved. Heterogeneous catalyst show similar activity with homogeneous and at least 3 recycles with same activity. Among other tested reaction two gave promising results and are presented below. Direct diamine oxidative coupling with heterogeneous catalyst resulted in 31% conversion and 7% selectivity in pyrazine. Another important reaction is solketal synthesis, that was obtained with heterogeneous catalyst with almost 30% yield at room temperature.





Conclusions*:*

The main target of the project was fulfilled in terms of synthesis of heterogeneous 3d4f bimetallic catalyst applying different immobilization strategies and exploration of the resulted synergistic effect between the two metallic species. The synthesis of the best candidate among the different heterogeneous catalysts was optimized. Obtained heterogeneous catalysts shows higher results in terms of conversion, selectivity and synergistic effect, compared with homogeneous one. Different oxidative couplings and ketalization reactions were screened with promising results.

Dissemination

Papers:

Podolean, I., Zhang, J., Shamzhy, M., Pârvulescu, V.I., Čejka, J. *Solvent-free ketalization of polyols over germanosilicate zeolites: the role of the nature and strength of acid sites*, Green Chem. (2020) (submitted manuscript)

Communications:

1**.** I. Podolean, O. D. Pavel, H.G. Manyar, K. Ralphs, P. Goodrich, S.F.R. Taylor, V.I. Parvulescu, C. Hardacre; The 8th Tokyo Conference on Advanced Catalytic Science and Technology (TOCAT8), YOKOHAMA, Japan, August 5 – 10, 2018 (Poster)

2. I. Podolean, V. I. Parvulescu, M. Andruh; 14th Pannonian International Symposium on Catalysis; Starý Smokovec, Slovak Republic, September 3-7, 2018 (Poster)

3. I. Podolean, V. I. Parvulescu, M. Andruh, *Graphene-immobilized 3d-4f binuclear complexes as non-precious metals catalysts for oxidative coupling*; The 11th International Symposium of the Romanian Catalysis Society (RomCat), Bucharest, Romania, June 5 – 7, 2019 (Poster)

4. I. Podolean, V. I. Parvulescu, M. Andruh, *Transition-metal binuclear complexes as new graphene-supported heterogeneous catalysts*; 8th Asia-Pacific Congress in Catalysis (APCAT), Bangkok, Thailand, August 4 – 7, 2019 (Oral Presentation)