Final report on project entitled
"Investigation of catalytic transformations in biomass-based solvents"

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1. Introduction

The gradual replacement of fossil resources with renewables is one of the most pressing challenges in the development of sustainable chemical industry.[1] Biomass or biomass-based wastes have been identified as global alternative resources.[2] The research activity on biomass conversion identified the so-called platform chemicals including levulinic acid (LA) and γ-valerolactone (GVL),[3, 4] which could either replace the currently used fossil-based chemicals or serve as renewable feedstock for their production[4, 5] even in solvent applications.[6]

The solvents are intrinsic part of many chemical reactions and the "solvent friendly chemical thinking" has evolved due to many advantages in laboratory operations including the simple regulation of temperatures, moderation of exothermic reactions, dissolution of solids to get molecules in a common phase, facilitation of mixing, *etc*.[7] Consequently, the chemical industry utilizes enormous amounts of solvents, which certainly contribute to the release of millions of tons of organic compounds in the EU27 annually[8] resulting in serious environmental concerns and causing significant economic issues. Accordingly, the replacement of conventional, fossil-based organic solvents with green alternatives having low vapor pressure even at high temperature, low or no toxicity, low flammability and limited negative impacts on the environment is a crucial part in the development of greener and cleaner chemical technologies.[9]

Thus, the main objective of my proposal was to demonstrate that GVL and its ionic liquid derivatives (GVLILs) could be a key component of environmentally benign and renewable reaction media for catalysis by selected catalytic transformations. The proof of concept is depicted on Fig. 1.

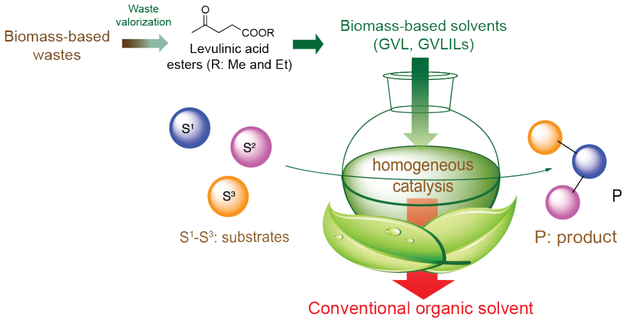


Fig. 1 Application of GVL as a biomass-based solvent

According to the proof of concept, the research activity was focused on continuous production of GVL from levulinic acid esters such as methyl- and ethyl levulinate, as well as the application of GVL and GVL-ILs as a reaction media for selected homogeneous transition metal-catalyzed reactions such as carbonylation and cross-coupling reactions.

The environmental sustainability assessment of biomass-based chemical industry in Visegrád Countries having comparable chemical production to each other's capacities was performed as an extension of the project. In addition, the determination of vapor-liquid equilibria of GVL–toluene, GVL–acetone, GVL–ethyl acetate, GVL–tetrahydrofuran, and GVL-2-methyltetradydrofuran as model solvents mixture was also completed.

2. Results

2.1 Environmental sustainability assessment of a biomass-based chemical industry in the Visegrád countries

First, as an extension of the original proposal, the environmental sustainability of biomass-based chemical industry was assessed for Visegrad-countries: Czech Republic, Hungary, Poland, and Slovakia having comparable chemical production capacities. The production of basic chemicals i.e. ethylene, propylene, toluene, xylenes, styrene, and benzene from bioethanol was evaluated by using three ethanol equivalent-based sustainability metrics, namely the sustainability value of resource replacement, the sustainability value of the fate of waste, and sustainability indicator.[10]

It was revealed that the current bioethanol production in each country – in spite of the continuous increase in ethanol production – cannot cover the feedstock needs of the chemical industry, and the sustainability value of resource replacement determines the low value of the sustainability indicator. The same chemical technology can be used in Czech Republic, Hungary, Poland and Slovakia – therefore – the sustainability values of the fate of waste of the selected chemicals are the same, thus the environmental sustainability almost completely depends on bioethanol production. The low values of SV_{rep} in each country could be increased when second-generation bioethanol would be added to the primary resources. It should be noted that although cellulosic ethanol production has been started in the V4-countries its volume is one order of magnitude lower than starch-based first-generation bioethanol (see further details on cellulosic ethanol provided by the European Technology and Innovation Platform (Cellulosic Ethanol 2020). The study enlightened dual conclusions: (i) basic chemicals can be produced on bioethanol basis and the chemical industry may be switched to biomass basis instead of fossil fuels (ii) the current bioethanol production is far below the industrial requirements and its volume has to be increased by one order of magnitude. The sustainability indices of basic chemicals for Visegrád courtiers are presented in Fig. 2.

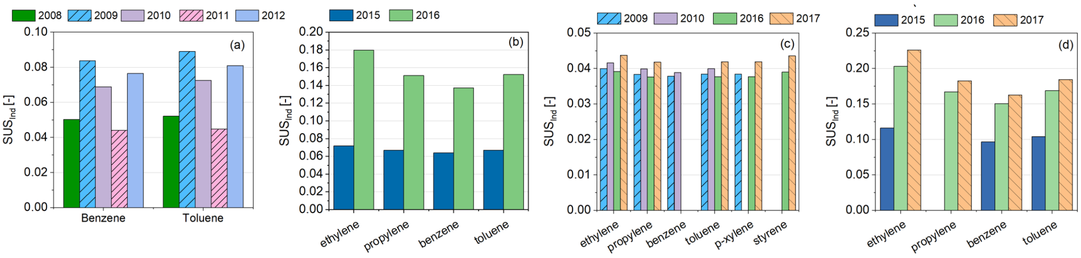


Fig. 2 Sustainability indices of basic chemicals in (a) Czech Republic (b) Hungary, (c) Poland, (d) Slovakia

The conclusion of the study has additionally verified that biomass-based chemicals should be utilized in the areas of chemical industry that have significantly less feedstock needs such as solvent applications.

2.2 Continuous synthesis of γ-valerolactone

The efficient conversion of various lignocellulosic wastes to levulinic acid and even its esters and subsequently to GVL even under continuous conditions could open an economically viable process to produce this biomass-based solvents. Although, several studies were focused on the conversion of LA to GVL, only a few reports were published on the continuous GVL production of levulinic acid esters. Accordingly, we investigated the continuous synthesis of GVL from methyl- and ethyl-levulinate (Ml and EL) by the use of H-Cube® continuous flow hydrogenation system focusing on the effect of the catalyst (Ru/C or Pd/C), the total system pressure (50–100 bar), the flow rate (0.2–2.5 mL/min), the solvent, and the presence of water soluble trisulfonated triphenylphoshine (TPPTS, 0–1.5 × 10^{-2} M) on the productivity ($mol_{GVL} \times g_{metal}^{-1} \times h^{-1}$) of GVL.

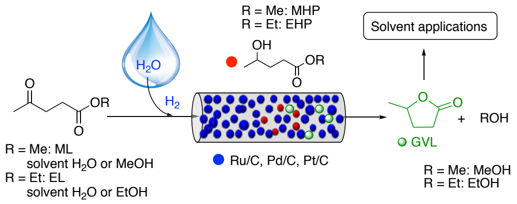


Fig. 3 Continuous production of GVL from levulinic acid esters using H-Cube® system

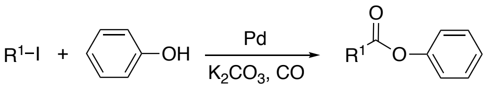
It was proven that the H-Cube® equipped with 5% Ru/C CatCart® is suitable for reduction of ML and EL. While excellent conversion rates (> 99.9%) of both esters could be achieved in water as well as MeOH and EtOH for ML and EL, respectively, the selectivities of GVL formation were primarily affected by the solvent used. In water, 100% conversion and ca. 50% selectivity that represent ca. 0.45 $\text{mol}_{\text{GVL}} \times \text{g}_{\text{metal}}^{-1} \times \text{h}^{-1}$ towards GVL, were obtained under 100 bar of total system pressure. The application of alcohols as solvent, which maintained high conversion rates up to 1 mL min^{-1} flow rate, resulted in lower productivities (< 0.2 $\text{mol}_{\text{GVL}} \times \text{g}_{\text{metal}}^{-1} \times \text{h}^{-1}$) of GVL. Therefore, from a synthesis point of view, the corresponding 4-hydroxyvalerate esters could be obtained even in higher reaction rate. The addition of TPPTS allowed reduction of the system pressure and resulted in the higher selectivity towards GVL.

2.3 Application of γ-valerolactone as a solvent for homogeneous catalysis

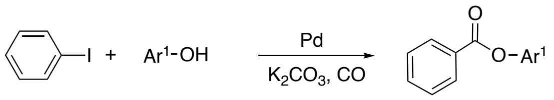
2.3.1 Alkoxy- and aryloxycarbonylations of iodoaromatic compounds.

Since the discovery of hydroformylation and the Reppe carbonylation,[11] the transition metal-catalyzed carbonylation reactions, providing a facile method for the introduction of C=O functionality to various skeletons, have gained tremendous importance in numerous fields of synthetic chemistry.[12] Among these reactions, the transformation of aryl halides with alcohols O–nucleophiles provide a direct route towards the synthesis of aromatic esters that have been widely used as building blocks for synthesis of biologically active compounds[13] including anti-inflammatory and antiseptic pharmaceuticals,[14, 15] etc. Because of their importance, the Pd-catalyzed conversion of iodobenzene as model substrate and its para-substituted derivatives to corresponding esters were investigated in detail. The comparison of various solvents to eliminate the fossil-based ones (toluene, DMSO, DMF), the effect of base (Et_3N, K_2CO_3, Na_2CO_3), the electronic properties of substituents of both iodoaromatic and O-nucleophile substrates, the CO pressure (1–14 bar), and reaction temperature (80–100 °C) on the catalytic efficiency were investigated. The alkoxycarbonylation reactions in the presence of different C_1–C_4 alcohols were also monitored.

It was definitely demonstrated that fossil-based solvents and Et_3N as toxic and volatile base were successfully replaced with GVL as non-volatile solvent and K_2CO_3 as also non-volatile base in the alkoxy- and aryloxycarbonylation of aryl iodides using phosphine-free Pd catalysts system without any decrease in the efficiency of the catalytic system under conditions as follows: catalyst precursor: $Pd(OAc)_2$ (0.25 mol%), 0.5 mmol iodobenzene (or its derivatives), 0.625 mmol of phenol or its substituted form, 2.5 equiv. of K_2CO_3, p_{CO} = 7 bar, 2.5 mL GVL as a solvent, T = 100 °C, t = 3 h.



Scheme 1. Phenoxycarbonylation of iodo-aromatic compounds. R^1 on $C_6H_4R^1$–I: H, 2-Me, 3-Me, 4-Me, 4-OCH$_3$, 4-tBu, 4-Cl, 4-F, 4-Br, 3-Br, 4-OCF$_3$, 4-COCH$_3$,



Scheme 2. Phenoxycarbonylation of iodobenzene. Ar^1 on $C_6H_4R^1$–OH: H, 4-Me, 4-OCH$_3$, 4-iPr, 4-CHO, 4-OPh, 4-Br, 4-F, 4-CF$_3$, 4-COOEt, 4-COOH

For the phenoxycarbonylation of iodoaromatic substances (Scheme 2.) depending on the substituents the conversion rates varied between 60–99.9%. It appeared that aryl iodides bearing substituents with strongly positive electronic parameters (σ+) on the phenyl ring (typically electron withdrawing groups in para position) facilitate the rate of the reaction. The TONs were found to be 156–396. Thus, possibly the rate of the crucial oxidative addition step of R–I is increased by the increased polarization of the C–I bond. It was shown that the presence of different substituents of phenols at para position, strongly affected the reaction efficiency, as well. However, both $+\sigma_p$ and $-\sigma_p$ substituents on the aromatic ring of phenol significantly enhanced the reaction rate compared to unsubstituted phenol. The TONs were found to be 0–352, no conversion for 4-COOH substituted phenol was detected.

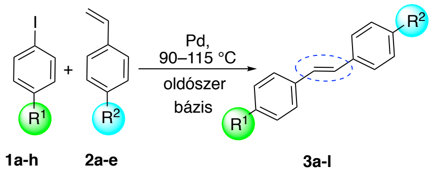
The GVL-based carbonylation protocol was further explored for the alkoxycarbonylation of aryl iodides with aliphatic alcohols to form the corresponding esters. By comparing n-octane, DMF, DMSO, and GVL, the latter medium exhibited the highest conversion rate for methoxycarbonylation of iodobenzene as model transformation. As mentioned above with phenol, the effect of aryl substituents of aryl iodide was also studied on the yield and rate, by using numerous aryl iodides bearing various electron donating or withdrawing functional groups with MeOH under the standard applied conditions. For a comparison, the aryl-substituted aryl iodides were also reacted with methanol and aryl iodide was also alkoxycarbonylated using several different lower alcohols. From the observed correlations between the electronic parameters of the aromatic substituents and the rates, furthermore, excluding the expectedly very fast CO-insertion, it appeared that the rate determining step is the oxidative addition of Ar–I to Pd^0, provided that sufficient amounts of nucleophiles present for the ester formation.

2.3.2 Heck-coupling reactions

The catalytic cross-coupling reactions have emerged as one of the most powerful tools for the creative construction of both carbon-carbon and carbon-heteroatom bonds, especially in multistep synthesis of biologically active compounds.[16–18] Among these reactions, the Heck coupling between an aryl halide and an sp^2 carbon atom represents a facile protocol to access fine chemicals[19] including complex structures of active pharmaceutical ingredients, for example, Montelukast (Merck, antiasthma agent),[20] Rilpivirine (Johnson & Johnson, anti-AIDS),[21] and Eletriptan (Pfizer, anti-migraine).[22]

Because of industrial importance of Heck reaction, catalytic, kinetic, and computational studies were performed to demonstrate the elimination of common organic solvents and application of GVL as a green solvent. The efficiency of the catalytic system was compared by the use of DMF as a fossil-based and GVL as a biomass-based media involving a detail kinetic study.

It was successfully shown that GVL can be utilized as a biomass originated, renewable aprotic dipolar reaction medium for homogeneous Pd-catalyzed Heck coupling reaction. The reaction shows remarkable tolerance for the moisture content of reaction mixture and gives good efficiency for Pd(II) catalyst precursors such as $PdCl_2$, $Pd(OAc)_2$, and $Pd(PPh_3)_4$. In addition, the catalyst system shows excellent functional group tolerance. It was revealed that the electron withdrawing para substituents of iodoaromatic substances (Scheme 3.) accelerate the activity of corresponding species. An opposite tendency was shown for styrene derivatives.



R^1: H (**a**), Me (**b**), OMe (**c**), F (**d**), Cl (**e**), OCF_3 (**f**), $COOCH_3$ (**g**) NO_2 (**h**)
R^2: H (**a**), OMe (**b**), Cl (**c**), CF_3 (**d**), $OCOCH_3$ (**e**)

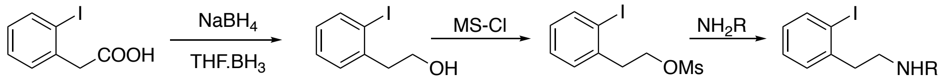
Scheme 3. Heck coupling reactions of substituted iodobenzene (**1a–h**) and styrene (**2a–f**) derivatives

A simplified kinetic model was found to model the transformation, which can be represented by excellent fitting of calculated concentration of corresponding species on the experimentally determined points. The $\Delta H^{\ddagger}_{app}$ = 103.0 kJ·mol^{-1} for the apparent overall activation enthalpy of the reaction in GVL and the $\Delta H^{\ddagger}_{app}$ =

103.7 kJ·mol^{-1} in case of DMF were determined. Similarly, almost same of $\Delta S^{\ddagger}_{app} = +139.7$ J·mol^{-1}·K^{-1} was calculated for the apparent overall activation entropy of the reaction in presence of GVL, and $\Delta S^{\ddagger}_{app} = +138.1$ J·mol^{-1}·K^{-1} in presence of DMF. According to our best knowledge, no comparative kinetically determined thermodynamic parameters were reported on a conventional – biomass-based solvent pair. Consequently, it was first revelaed that the solvent switch has no effect on the overall activation energy of the reaction, and therefore, presumably for the reaction mechanism, as well. The computational study confirmed the experimentally observed trends regarding the effect of electron donation and withdrawing substituents of iodobenzene and styrene as follows: the electron-donating substituents accelerates the reaction rate for iodobenzene and oppositely decreases the reactivity for styrene derivatives. By the use of experimental and computational data a detail mechanism was proposed for the ligand-free Heck coupling reaction involving key intermediates and transition states.

2.3.3 Intramolecular aminocarbonylation

It was proposed that various 1-oxo-3,4-dihydroisoquinoline derivatives cold be synthesized *via* intramolecular aminocarbonylation of 2-(2-iodophenyl)-*N*-alklyethan-1-amine. A series of amine precursors were successfully synthesized according to the Scheme 4. The 3-(2-iodophenyl)acetic acid was first converted to the corresponding alcohol, followed by its reaction with mesyl-chloride to form 2-iodophenethyl methanesulfonate. The series of 2-(2-iodophenyl)-*N*-alklyethan-1-amines was prepared by reaction of the 2-iodophenethyl methanesulfonate with corresponding amines.[23]



Scheme 4. Synthesis of 2-(2-iodophenyl)-*N*-alklyethan-1-amine. R: hexyl, octyl, benzyl, cyclohexyl.

Although, four amines have already been synthesized with average yield of 60%, their conversion to corresponding 2-alkyl-3,4-dihydroisoquinolin-1(2*H*)-one has not been finalized yet. Due to the limited access of the laboratory caused by pandemic regulations including close of laboratories for the University, this part of the project is still in progress.

2.4 Application of γ-valerolactone-based ionic liquids for homogeneous cross coupling reactions

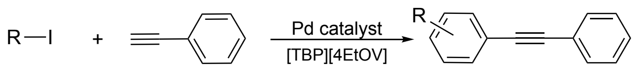
2.4.1 Sonogashira coupling

From the series of Pd-assisted C–C bond formation, the Sonogashira coupling reaction has been identified as a viable synthetic method for the preparation of various alkenyl- and aryl-acetylenes[24,25] having great importance in organic synthetic schemes of pharmaceutical industry.

It was demonstrated that a γ-valerolactone-based ionic liquid, tetrabutylphosphonium 4-ethoxyvalerate ([TBP][4EtOV]) can be utilized as an alternative solvent for Pd-catalyzed Sonogashira coupling reactions of aryl iodides and functionalized acetylenes under mild and even Cu- and base-free conditions.

In the study, different ionic liquids were compared by the view of reaction efficiency, as well as the effect of catalyst precursor ($PdCl_2(PPh_3)_2$, PdCl2, $Pd_2(DBA)_3$, $Pd(PPh_3)_4$, $Pd(OAc)_2$), the moisture content (0.05–5 wt%) were investigated at following conditions: 0.8 mL ionic liquid, 0.5 mol% Pd source, 0.75 mmol phenylacetylene, 0.5 mmol iodoaromatic compound, T = 55 °C, t = 3 h.

While negligible reaction rate was observed in conventional [BMIM]$^{+}$ and [EMIM]$^{+}$ –based ILs complete conversion was detected in [TBP][4EtOV] in the presence of Et_3N. It should be noted that same efficiency was detected by the elimination of base from the reaction mixture. The moisture content had no effect on the product formation up to 5 wt%. The substituent's effect was systematically investigated in the presence of both electron donating and withdrawing substituents on para position of iodoaromatic substrate (Scheme 5). Additionally, various iodoaromatic compounds such as iodotiophene and iodopyridines were converted to corresponding acetylenes. Twenty-two cross-coupling products were isolated with good to excellent yields (72–99%) depending on the substrate's structure, and purity with > 98%.



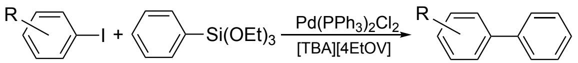
1a-n **2a** **3a-l**

Scheme 5. Sonogashira coupling reactions of substituted iodobenzene (**1a–h**) and styrene (**2a–f**) derivatives. R on R–C_6H_4–I: H, 2-Me, 4-Me, 4-OCH_3, 4-F, 4-Cl, 4-Br.

It is important to note that efficiency of carbonylative Sonogashira coupling were unexpectedly low in GVL. When iodobenzene and phenylacetylene was reacted in GVL using 1 mol% Pd under 20 bar CO at 120 °C for 1 h, less that 45 % conversion was detected. In comparison in THF or toluene solvents higher than 98% conversion was observed. The selectivity towards carbonylative coupling was also moderate (66%) in comparison with THF (99%).

2.4.2 Hiyama coupling

Since the efficiency of carbonlylative Sonogashira couplings were moderate or even low in both GVL and GVLIls, our investigations were focused further to Hiyama-coupling reaction, which is an excellent protocol for the synthesis of symmetrically and non-symmetrically substituted biaryl structures. According to previous experimental plans, a comparison of different ionic liquids ($[BMIM]^+[X]^-$, where $[X]^-$: $[PF_6]^-$, $[BF_4]^-$, $[OctSulf]^-$, etc.) was performed and the effects of the catalyst precursor ($PdCl_2(PPh_3)_2$, $PdCl_2$, $Pd_2(DBA)_3$, $Pd(DBA)_2$, $Pd(COD)Cl_2$, $Pd(OAc)_2$), and the moisture content of the reaction mixture on the activity of the catalyst system were investigated. The functional group tolerance was also studied, resulting in fifteen cross-coupling products (**3a–o**) with isolated yields of 45–72% and excellent purity (>98%) by applying standard Hiyama conditions as follows: 0.5 mL [TBP][4EtOV], 0.5 mmol iodoaromatic compounds, 0.75 mmol triethoxyphenylsilane, 1.5 eq TBAF, T = 130 °C, t = 24 h (Scheme 6.). It should be noted that no Hammet-sigma (σ_p) correlation can be established for *para*-substituted species. Both electron-donating groups *i.e.*, methyl, *tert*-butyl, methoxy and electron-withdrawing groups *i.e.*, chloro, fluoro or trifluoromethoxy were tolerated on the aryl iodide. No significant differences of the isolated yields were observed.



1a-o **2a** **3a-o**

Scheme 6. Heck coupling reactions of substituted iodobenzene (**1a–o**) and styrene (**3a–o**) derivatives. R on R–C_6H_4–I: H, 2-Me, 3-Me, 4-Me, 4-tBu, 4-Ph, 4-OCH_3, 4-Cl, 4-OCF_3, 4-F, 4-COPh.

2.4.3 Intramolecular Ullmann coupling

According to the section 2.3.3., a series of 2-(2-iodophenyl)-*N*-alklyethan-1-amines were successfully synthesized and characterized. However, due to the pandemic regulations for the University, this part of the project has not been finalized yet.[23]

2.5 Synthesis of functionalized steroids

The objective of the project, the functionalization of steroids has been started and the 17-iodoandrost-16-ene was successfully synthesized with purity > 98%. An analytical protocol was developed for the identification of corresponding products of its subsequent carbonylation reactions in the presence of N-nucleophiles. The preliminary experiments established that the 0.5 mmol of 17-iodoandrost-16-ene could be converted to the correspondiong carboxamides by the use uf tert-butylamine in 5 mL GVL and in the presence of 2.5 mol% Pd, 0.5 mL Et_3N, under 1–10 bar of CO at 50 °C. The conversion was over 90%. The reactions were further extended by the use of various amines as follows:, furfuryl amine, 3-aminopyridine, (*S*)-a-methyl-benzyl amine, morpholine, L-alanin methylester hydrochloride, L-proline methyester hydrochloride, diethyl amine, glycine methylester hydrochloride. With exception of morpholine (38%), the conversion varied between 60–98% depending on the structure of N-nucleophiles. The isolation and purification of the product is still in progress.[23]

2.6 Vapor–Liquid (VLE) studies on GVL-containing solvent mixtures

Since the utilization of GVL as a solvent has received increasing interests, we also focused on the separation issues of GVL with selected commonly used fossil-based solvents. A vapor-liquid equilibrium still was used for the determination of VLE data for GVL-containing mixtures as follows: GVL–acetone, GVL–ethyl-acetate, GVL–toluene, GVL–THF, and GVL–2-methyltetrahydrofurane.

No azeotrope mixture formation was observed for each binary mixture in the complete concentration range; therefore, these compounds can easily be separated from GVL via simple distillation. The binary interaction parameters (BIPs) for Wilson, NRTL, and UNIQUAC activity coefficient models were determined for selected mixtures allowing subsequent modeling, which is in progress, if their separations in distillation units.

3. Conclusion

The environmental sustainability assessment of biomass-based chemical industry in Visegrád Countries showed that the replacement of fossil-based basic chemicals such as ethylene, propylene, toluene, xylenes, styrene, and benzene was limited by the fact that the current bioethanol production is far below the industrial requirements.

The investigation of industrially important catalytic transformation established that the application of GVL as a non-fossil-based solvent was successfully extended for several homogeneous transition-metal catalyzed reactions i.e. phenoxycarbonylation, alkoxycarbonylation, Heck-coupling reaction. The extension of the application of GVL-based ionic liquid, tetrabutylammonium 4-ethoxyvalerate was also shown by its novel application for Pd-catalyzed Sonogashira and Hiyama-type reactions. It is important to note, that the base as auxiliary substances, could be eliminated from the Sonogashira reaction.

The vapor-liquid equilibria studies of the GVL-containing solvent mixtures revealed that GVL can be separated from acetone, ethyl-acetate, tetrahydrofurane, and 2-methyltetrahydrofurane by distillation, and no azeotrope formation could be considered for these mixtures in complete concentration range.

4. Notes

The extension of the project frame to August 31, 2021, which could further support the finalization of the opened task of the project and establish the possibility to publish additional papers with the financial support of NKFIH is greatly appreciated. However, due to the COVID-19 issue, the unexpected regulations such as visits and work of students and colleagues in the laboratory limited the finalization of all the tasks of the project. These parts will be finalized as soon as possible.

5. Publications

Scientific papers: Total 11, Sum of IF 35.091 Journal Ranks: 2 Q1/D1, Q1: 4, Q2 5

1. Tukacs, J. M.; Sylvester, Á.; Kmecz, I.; Jones, R. V.; Óvári, M.; Mika, L. T. Continuous Flow Hydrogenation of Methyl and Ethyl Levulinate: An Alternative Route to γ-Valerolactone Production. *Royal Society Open Science* **2019**, *6* (5), 182233–182239. https://doi.org/10.1098/rsos.182233. IF: 2.647. Q1/D1
2. Cséfalvay, E.; Hajas, T.; Mika, L. T. Environmental Sustainability Assessment of a Biomass-Based Chemical Industry in the Visegrad Countries: Czech Republic, Hungary, Poland, and Slovakia. *Chem Pap* **2020**, *74* (9), 3067–3076. https://doi.org/10.1007/s11696-020-01172-8. IF: 2.097. Q2
3. Orha, L.; Tukacs, J. M.; Kollár, L.; Mika, L. T. Palladium-Catalyzed Sonogashira Coupling Reactions in γ-Valerolactone-Based Ionic Liquids. *Beilstein J. Org. Chem.* **2019**, *15* (1), 2907–2913. https://doi.org/10.3762/bjoc.15.284. IF: 2.097. Q2
4. Orha, L.; Papp, Á.; Tukacs, J. M.; Kollár, L.; Mika, L. T. Tetrabutylphosphonium 4-Ethoxyvalerate as a Biomass-Originated Media for Homogeneous Palladium-Catalyzed Hiyama Coupling Reactions. *Chem Pap* **2020**, *74* (12), 4593–4598. https://doi.org/10.1007/s11696-020-01287-y. IF: 2.097. Q2
5. Tukacs, J. M.; Marton, B.; Albert, E.; Tóth, I.; Mika, L. T. Palladium-Catalyzed Aryloxy- and Alkoxycarbonylation of Aromatic Iodides in γ-Valerolactone as Bio-Based Solvent. *J Organomet Chem* **2020**, *923*, 121407. https://doi.org/10.1016/j.jorganchem.2020.121407. IF: 2.369. Q2
6. Fodor, D.; Kégl, T.; Tukacs, J. M.; Horváth, A. K.; Mika, L. T. Homogeneous Pd-Catalyzed Heck Coupling in γ-Valerolactone as a Green Reaction Medium: A Catalytic, Kinetic, and Computational Study. *Acs Sustain Chem Eng* **2020**, *8* (26), 9926–9936. https://doi.org/10.1021/acssuschemeng.0c03523. IF: 8.198. Q1/D1
7. Havasi, D.; Farkas, D.; Mika, L. T. Isobaric Vapor–Liquid Equilibria of Binary Mixtures of γ-Valerolactone + Acetone and Ethyl Acetate. *J. Chem. Eng. Data.* **2020**, *65* (2), 419–425. https://doi.org/10.1021/acs.jced.9b00379. IF: 2.694. Q1
8. Al-Lami, M.; Havasi, D.; Koczka, K.; Mika, L. T. Isobaric Vapor–Liquid Equilibria for Binary Mixtures of Gamma-Valerolactone + Toluene. *J. Chem. Eng. Data* **2020**, *66* (1), 568–574. https://doi.org/10.1021/acs.jced.0c00791. IF: 2.694. Q1
9. Al-Lami, M.; Havasi, D.; Batha, B.; Pusztai, É.; Mika, L. T. Isobaric Vapor–Liquid Equilibria for Binary Mixtures of Biomass-Derived γ-Valerolactone + Tetrahydrofuran and 2-Methyltetrahydrofuran. *J. Chem. Eng. Data* **2020**, *65* (6), 3063–3071. https://doi.org/10.1021/acs.jced.0c00084. IF: 2.694. Q1
10. Mika, L. T.; Horváth, I. T. Homogeneous Transition Metal Catalyzed Conversion of Levulinic Acid to Gamma-Valerolactone. *Adv. Inorg. Chem.* **2021**, *77*, 1–25. https://doi.org/10.1016/bs.adioch.2021.02.004. IF: 2.568, Q2
11. Kégl, T. R.; Mika, L. T.; Kégl, T. 27 Years of Catalytic Carbonylative Coupling Reactions in Hungary (1994–2021). *Molecules* **2022**, *27* (2), 460. https://doi.org/10.3390/molecules27020460. IF: 4.411, Q1

Conference presentations

1. <u>Mika, L. T.</u> Role of Homogeneous Catalysis in Biomass Conversion, ABCP2021 Conference, Hong Kong, May 11–12, **2021** (Invited lecture, online conference).
2. <u>Mika, L. T.</u>; Kégl, T. Tukacs, J. M. Fodor, D.; Horváth, A. K. Homogeneous Pd-catalyzed Heck coupling in γ-valerolactone as a green reaction medium. 47th

International Conference of the SSCHE online, May 18, Bratislava, Slovakia, **2021** (online conference).

3. Mika, L. T. γ-Valerolactone as a renewable solvent for catalysis, Austrian Chemistry Days 2019, Linz, Austria, September 24–27, **2019**.
4. Mika, L. T.; Sylveszter, A.; Tukacs, J. M. Kmecz, I. Continuous flow hydrogenation of methyl - and ethyl levulinate: an alternative route to gamma-valerolactone production. 46th International Conference of the SSCHE online, May 20–23, Tatranské Matliare, Slovakia, **2019**.

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