

Green Chemistry

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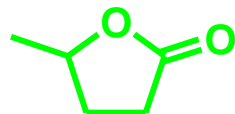
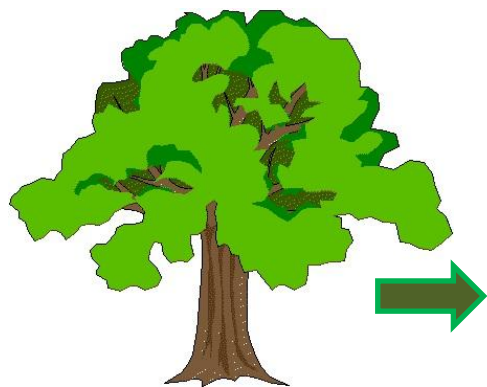


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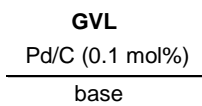
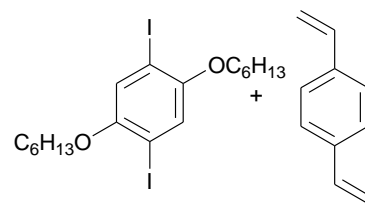
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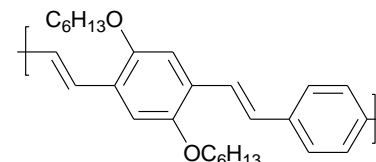


(GVL)

bio-based chemical to
replace toxic dipolar
aprotic media



HECK COUPLING



low Pd-content

ARTICLE

Biomass-derived safe medium to replace toxic dipolar solvents and access cleaner Heck coupling reactions[†]

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γ -Valerolactone (GVL) is an excellent reaction medium, derived from biomasses, which can replace classic dipolar aprotic media such as DMF or NMP. In this contribution, we have investigated the use of GVL in the palladium-catalyzed Heck reaction and have accessed the clean synthesis of several small molecules. Furthermore, we optimized a GVL-based protocol to synthesize a poly(phenylenevinylene) (PPV) derivative in high yields and purity, and with very low Pd-content. Finally, we demonstrated that GVL is superior to conventional dipolar media in terms of controlling palladium impurities, which may influence the performance of certain optoelectronic devices such as organic solar cells and field-effect transistors.

Introduction

Major challenges in Environmental Science relates to the evaluation and monitoring of the impact of chemical production. Thus, academic and industrial efforts are directed to the identification of novel routes towards the use of renewable raw materials and energy sources to maximize sustainability.¹ Striking examples are given by the social challenges highlighted by the 2011 European Association for Chemical and Molecular Sciences (*EuChemS*) roadmap,² where it has been clearly highlighted the importance of designing new efficient protocols for key synthetic methodologies employing catalysts based on exhaustible precious metals, such as palladium (Pd)-catalyzed cross-coupling reactions. These synthetic methodologies have become fundamental for accessing several complex molecules including drugs, semiconducting materials for opto-electronic applications, and agrochemicals.^{2,3} Particularly, improved protocols for coupling reactions are required aiming at minimizing the waste volumes^{4,5} by using, for instance, recoverable/recycling catalysts, which minimize metal and reagent consumption.

The use of green alternative reaction media is also of key relevance, since organic solvents account for more than the 80% of the waste production of a process. Cross-coupling reactions are commonly carried out in dipolar aprotic solvents such as dimethylformamide (DMF), *N*-methylpyrrolidin-2-one (NMP), *N,N*-dimethylacetamide (DMA) thanks to their ability to solubilise several chemicals and promote a large number of reactions. However, they have significant environmental and safety issues due to their toxicity and problematic waste disposal originating from the aqueous/organic mixtures used in reaction work-up procedures. Such wastes are typically incinerated with consequent emission of toxic NO_x.⁶ Indeed,

DMF, NMP and DMA are among the first six chemicals of highest concern,⁷ and suitable replacements are therefore required.^{6,8-10} Furthermore during the coupling reactions, dipolar aprotic solvents coordinate the catalytically active metal (e.g., Pd) causing its dissolution.¹¹⁻¹⁵ Although this phenomenon (so-called leaching) may lead to an enhanced catalytic activity, the final product is often metal contaminated which is not desirable.¹¹⁻¹⁵ For instance, regulatory basis applies to the limit for palladium residues into drug chemicals, which must be kept at a very low level (<5 ppm).^{12,13} Moreover, it has been found that metal contamination of organic semiconductors may negatively affect their performance.^{11,14,15}

Nowadays, the most recommended polar aprotic solvent is acetonitrile (MeCN)¹⁶ which is actually a relatively poor alternative medium because of large volatility and toxicity.¹⁷ In the search for safer organic solvents a special attention is directed towards bio-based solvents derived from biomass,^{18,19} since they hold the promise of low-cost, safety, biodegradability, and reduced toxicity. To this front, some of us have contributed to the development of synthetic protocols employing eco-compatible reaction media,²⁰ solvent free conditions (SolFC),²¹ and supported organocatalysts,²² demonstrating that significant improvements in both chemical efficiency and process sustainability can be obtained. Thus, in this context, we directed our attention to the use of biomass-derived γ -valerolactone (GVL)^{18b,23-26} as sustainable cross-coupling reaction medium. GVL²⁷ is attractive because its polarity is comparable to that of classical polar aprotic solvents,^{28,29} and exhibits high boiling point, high viscosity and a generally good stability to acidic and basic environments. Particularly, continuing our efforts for the sustainable and large scale synthesis of organic semiconductors,³⁰ we here explore

for the first time the use of GVL as a reaction medium³¹ in the Heck-Mizoroki coupling reaction aiming this material class.³² This reaction is widely employed to access several active pharmaceutical ingredients (API), materials and fine chemicals,^{33,34} and it is typically performed in DMF, NMP, DMA, or MeCN.³³ Importantly to the scope of this study, a major issue in Heck-Mizoroki coupling is related to the gradual leaching of the catalytically active palladium³⁵ into the final product. Although purification methods to remove palladium from API^{12,35,36} and from conjugated organic polymers³⁷ are commonly used and have been reported, they are time/solvent-consuming and create a large amount of (contaminated) waste.

As a model of an organic semiconductor synthesized via the Heck-Mizoroki coupling, we employed a poly(*p*-phenylene)vinylene (PPV) derivative, specifically poly(2,5-dihexylphenylenedivinylene-*alt*-1,4-phenylenevinylene) **1** (Figure 1). Furthermore the PPV family remains of prime importance for several opto-electronic applications including transistors, photovoltaic, and (bio)chemical sensor devices.³⁸

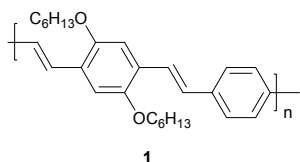


Figure 1. Poly(2,5-dihexylphenylenedivinylene-*alt*-1,4-phenylenevinylene)

Our results demonstrate that GVL is an excellent medium to synthesize very pure PPVs in high yields and in a more sustainable way. It will be seen that GVL is superior to conventional dipolar NMP in terms of control of palladium impurities in PPV **1**, and that it has influence on the material optoelectronic properties. These results are rationalized by the lower complexing ability of GVL in the Heck-Mizoroki cross-coupling procedure.

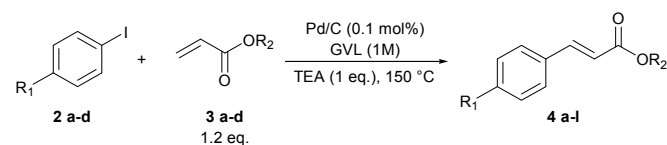
Results and discussion

In the following sections we first investigate whether GVL can be a solvent for the Heck-Mizoroki reactions by testing several protocol conditions and substrates, second we compare vis-à-vis the properties of GVL with other polar aprotic solvents for a specific reaction, and next selected conditions were applied to the synthesis of PPV **1**. Finally, we report the properties of PPV derivative and the corresponding performance in two organic opto-electronic devices

Substrate scope and E-factor optimization

To verify the applicability of GLV as reaction medium for the preparation of PPVs, we investigated first the Heck-Mizoroki coupling using iodobenzenes **2** and acrylic esters/acids **3** (Table 1) or styrenes **4** (Table 2) as models of monofunctional reagents. Furthermore, we decided to carry out these reactions by employing a supported catalyst. Indeed, heterogeneous palladium catalysts are one of the most useful tools to avoid the

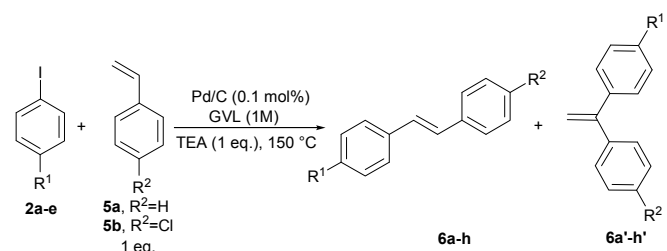
Table 1. Synthesis of cinnamate esters and acids **4a-l**



Entry	R ¹	R ²	t (h)	Yield (%)	Product	E-factor
1	-H	-Me	1	82 %	4a	25
2	-OCH ₃	-Me	2	82 %	4b	21
3	-OCH ₃	-Et	2	90 %	4c	18
4	-COCH ₃	-Me	1.5	87 %	4d	19
5	-COCH ₃	-Et	1.5	85 %	4e	18
6	-NO ₂	-Me	1	84 %	4f	19
7	-NO ₂	-Et	1	86 %	4g	18
8	-NO ₂	- <i>n</i> Bu	1	82 %	4h	16
9 ^a	-H	-H	1	84 %	4i^b	27
10 ^a	-OCH ₃	-H	2	80 %	4j	24
11 ^a	-COCH ₃	-H	1.5	85 %	4k	21
12 ^a	-NO ₂	-H	1	83 %	4l	21

^a 1.5 eq. of acrylic acid was used. ^b this reaction has been also performed in 10, 20 and 40% GVL/water mixtures obtaining identical results.

Table 2. Synthesis of stilbenes **6a-h**



Entry	R ¹	R ²	t (h)	Yield (%) (6a/6a')	Product	E-factor
1	-H	-H	2	83 (94/6)	6a	22
2	-OCH ₃	-H	2.5	82 (95/5)	6b	18
3	-COCH ₃	-H	1.5	86 (99/1)	6c	16
4	-NO ₂	-H	1.5	84 (99/1)	6d	17
5	-Me	-H	2.5	83 (94/6)	6e	20
6	-H	-Cl	2	90 (92/8)	6f	16
7	-OCH ₃	-Cl	2.5	90 (90/10)	6g	14
8	-COCH ₃	-Cl	1.5	85 (97/3)	6h	14

We were pleased to find that using a low loading of Pd/C (0.1 mol%), only 1 equivalent of triethylamine (TEA), instead

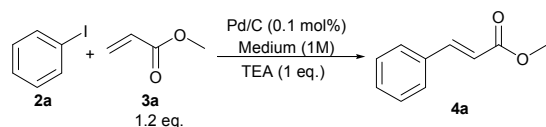
leaching of palladium into the product.³⁹ In particular, we focused on the cheap, ligand-free palladium on activated charcoal (Pd/C), which has shown great potential in several Heck-Mizoroki reactions.^{40, 41} of over-stoichiometric amounts that are routinely employed, and high reactant concentrations (1M) at 150 °C, a good reactivity of the substrates **2** in the reaction with alkenyl derivatives **3** or **4** was achieved. Thus, in short times (1-2 h) several types of cinnamate esters (**4a-h**), cinnamate acids (**4i-l**) (Table 1) and stilbenes (**6a-h**) (Table 2) were synthesized in good yields (80-90%). It should be noticed that the use of 10, 20, or 40% GVL/water mixtures gave the same results. Therefore, the use of only GVL was preferred. In the reaction of **2a-e** with **5a-b**, the formation of gem-substituted regioisomer **6'a-h** was detected in traces,^{40a,b} particularly when unsubstituted/electron-donating substituted iodobenzenes were used as substrates.

Next, to reduce the reactions' environmental burden, we focused our attention on the work-up procedure optimization. The Pd/C catalyst was removed by a simple filtration of the reaction mixture. Notably, the pure product could be conveniently isolated by direct precipitation from minimal amount of water, due to the high solubility in this medium of both GVL and triethylammonium iodide byproduct.

To monitor the amount of waste produced by the process we calculated E-Factor,⁴² which is defined by the ratio between the kg of waste produced per kg of the desired product. For our reactions, we found that the optimized work-up protocol is very efficient for waste reduction. Indeed, the E-factors range from 14 to 27 (Tables 1 and 2), and are significantly smaller than those for conventional extraction work-up,^{38c} where an average of ~ 63 was obtained, thereby achieving a reduction of waste by 60% (see ESI for detailed work-up procedures and E-Factor calculation).

Leaching of the palladium catalyst

To investigate the palladium leaching issue in details when employing GVL as the reaction medium and in comparison with conventional dipolar aprotic media, we focused on the Heck-Mizoroki reaction between iodobenzene (**2a**) and methyl acrylate (**3a**) (Scheme 1). Thus, the model substrates showed a high reactivity in DMF and NMP (Table 3, entries 1 and 2), whereas other dipolar aprotic solvents, dimethyl sulfoxide (DMSO), MeCN and water respectively, gave modest conversions (Table 3, entries 3-5). Similarly, a water/DMF mixture resulted in a conversion of **2a** to **4a** as high as ~30% (Table 3, entry 6). GVL gave complete conversion at 130 °C but in bit longer reaction time compare to DMF and NMP (Table 3, entry 7)



Scheme 1. Synthetic protocol to **4a**.

Table 3. Screening of solvents for Heck-Mizoroki reaction between **2a** and **3a**

Entry	T (°C)	t(h)	Medium	Conversion (%)
1	130	0.5	DMF	100
2	130	0.5	NMP	100
3	130	24	DMSO	75
4	70	24	CH ₃ CN	36
5	100	24	H ₂ O	33
6	100	24	H ₂ O/DMF (4/1)	29
7	130	2	GVL	100

Next, we investigated the leaching of palladium in the solvent enabling the best reaction performance, and compared it to what observed in GVL (Table 4).

Previous works showed that the palladium leaching was also influenced by the temperature,⁴⁰ so we also carried out this model reaction at different temperatures in the selected media. Our results indicate that with GVL the leaching of palladium diminished with the increasing temperature. Indeed, inductively coupled plasma-atomic emission spectrometric (ICP-AES) measurements revealed a constant decrease of leached palladium from 8.9 ppm for the reaction carried out at 130 °C (Table 4, entry 1), down to 3.9 ppm when heating at 200 °C (Table 4, entry 4).

Table 4. Data for palladium leaching for Heck-Mizoroki coupling between **2a** and **3a**

Entry	Medium	T (°C)	t (h)	Pd content in 4a (ppm)
1	GVL	130	2	8.9
2	GVL	150	1	7.7
3	GVL	180	0.5	6.3
4	GVL	200	0.33	3.9
5	NMP	150	0.17	835
6	NMP	200	0.08	279
7	DMF	150	0.17	50
8	GVL ^a	200	1	3.27

^a the reaction is performed using **1b/5a** substrates to give **6b**

By employing NMP and DMF as reaction media, we found a much higher product contamination, reflecting a significant palladium leaching. Particularly, **4a** through NMP contained 835 ppm and 279 ppm of palladium level for reaction occurring at 150 °C and 200 °C, respectively (Table 4, entries 5 and 6), which also confirmed the trend with temperature, whereas when DMF was used, the Pd level was found to be 50 ppm (150 °C) (Table 4, entry 7). Moreover, we demonstrated that with GVL the leaching of palladium was not substrate-

dependent. since comparable metal content was detected in product **6b** when prepared under the same conditions (200°C) as those for the synthesis of **4a** (Table 4, entry 8).

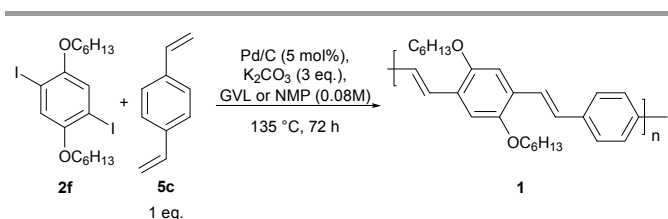
All these findings confirm that GVL is the optimal medium to limit the leaching of palladium into the product. Thus, GVL is not only a safer and cleaner reaction medium but it enables the formation of cleaner products thereby avoiding the need for further costly and tedious purification steps.

Heck-Mizoroki coupling copolymerization reaction

In light of these encouraging results, we aimed at the preparation of poly(2,5-dihexylphenylenedivinylene-alt-1,4-phenylenedivinylene) **1** (Figure 1, Scheme 2). To this end, the Heck-Mizoroki polymerization between 2,5-dihexyl-1,4-diodobenzene (**1f**) and 1,4-divinylbenzene (**4c**) (Table 5) (1:1 co-monomer molar ratio, 0.08 M concentration) was performed employing Pd/C as the catalyst (5 mol%), K₂CO₃ as the base (3 eq.), and GVL as reaction medium (135°C, 72h). These conditions were found to lead to polymer **6** with M_n= 8.14 kDa and PDI of ~2 (Table 5) in 72% yields. Under similar conditions but using NMP polymer **6** was achieved with a higher molecular weight (M_n= 16.43 kDa, PDI= ~2, Table 5) and a similar yields (70%). All polymer samples were purified through multiple Soxhlet extractions with acetone, hexane, and chloroform

However, the solvent type had a notable effect on the Pd residue in the polymer. Indeed, it was found that polymer **6** prepared employing NMP contained a Pd level of 860 ppm whereas when using GVL the Pd level was reduced by two orders of magnitude (6 ppm), as accessed by atomic absorption spectroscopy (Table 5). Most importantly, this was achieved without any purification step. The lower complexing ability of GVL towards palladium relative to that of NMP during the Heck polymerization, may account for a different catalyst activity, thereby resulting in lower molecular weight polymer chains, as well as for the negligible Pd impurity content.

Finally, the UV-Vis absorption spectrum of polymer **1** as a thin film synthesized with GVL is nearly identical to that of polymer prepared *via* Heck-Mizoroki cross-coupling in NMP (Figure S1 ESI), with absorption maxima (λ_{max}) located at 344 and 464 nm. The slightly stronger absorbance up to ~ 450 nm for the NMP sample may be due to the greater molecular weight as this is known to promote interchain stacking and red-shift the optical absorption.⁴³



Scheme 2. Synthesis of the PPV-based polymer **1**

Table 5. PPV derivatives properties synthesized with the indicated solvents.

Entry	medium	M _n (kDa)	M _w (kDa)	PDI	Pd (ppm)
1	GVL	8.14	16.27	1.99	6
2	NMP	16.43	36.98	1.99	860

Photovoltaic and transistor device performance

To demonstrate that GVL-based protocols can afford device-quality semiconductors and access the effect of the metal impurity on the device performance, bulk heterojunction (BHJ) solar cells and field-effect transistors were fabricated using different **1** samples. The BHJ devices used here have the following architecture: ITO/PEDOT:PSS/PPV:PC₆₁BM/LiF/Al. The photoactive layer was spin-coated from chlorobenzene (7 mg/mL, 1:1 = 1:PC₆₁BM). Typical current-voltage (J-V) characteristics of the devices fabricated with PPV derivative samples under white light illumination (AM1.5G, 100 mW/cm²) are shown in Figure S2 in ESI.

A representative BHJ cell based on polymer **1** via GVL featured J_{sc}= 2.4 mA/cm², V_{oc}= 0.92 V, and FF= 33.7 %, leading to a PCE= 0.73% (Table 6, entry 1). These performance are typical for PPV derivatives.³⁸ On the other hand, devices based on polymer **1** through NMP exhibited better performance characterized by a V_{oc} of 0.91 V, J_{sc}= 3.8 mA/cm² and FF= 36.1%, giving a power conversion efficiency of 1.26 % (Table 6, entry 2). To discriminate the influence of the polymer molecular weight from that of the metal content on the device performance⁴⁴, we prepared BHJ solar cells from polymer **1** through GVL with the addition of Pd using Pd(PPh₃)₄ to reach the contamination level of the polymer from the NMP-based protocol (~ 800 ppm). Notably, both the relevant parameters J_{sc}=1.6 mA/cm² and V_{oc}= 0.75 V obtained using artificially contaminated polymer **1** through GVL in the BHJ active layer were lower (PCE= 0.39%, Table 6, entry 3) than those from devices employing the clean counterpart (Table 6, entry 2). Thus, it is clear that the presence of palladium metal contaminant has a major adverse effect in the device performance, causing a ~ 40% reduction in efficiency.

The detrimental effect of palladium impurities on J_{sc} parameter can also be observed from the EQE spectra (Figure S3 in ESI) which show a large increase in current generation over the entire wavelength range for BHJ cell based on polymer **1** through GVL compared to those using the artificially Pd-contaminated counterpart.

Next, to investigate the influence of Pd impurities on in-plane charge-transport efficiency, also a critical parameter for organic photovoltaics,⁴⁵ in bottom-gate top-contact field-effect transistors (FETs) were also fabricated with films of polymer **1** spin-coated on Si/SiO₂ substrates (6 mg/ml in chlorobenzene). The Si/SiO₂ substrates were used without dielectric surface treatment. Vacuum deposited gold source/drain electrodes completed the OFET structure.

The transfer and output characteristics of transistors fabricated from polymer **1** samples are shown in Figure S4 and S5 of the ESI. The derived field effect transistor mobilities are modest, although consistent with those reported in the literature

for PPV derivatives,³⁸ with a maximum value of $1.21 \times 10^{-3} \text{ cm}^2/\text{Vs}$ ($I_{\text{on}}/I_{\text{off}} = 2 \times 10^2$) for devices based on the polymer prepared employing NMP as the solvent (Table 6, entry 1). For the batch achieved using NMP, a slightly lower FET mobility was achieved, however, the $I_{\text{on}}/I_{\text{off}}$ is larger. Considering the modest performance, the statistical FET transport characteristics is comparable. Furthermore, no significant effects of the palladium impurities on FET charge carrier mobility is observed (Table 6, entries 1 and 3). These results are in agreement with some general observations where OPV performance are more affected by metal impurities than FET charge transport.⁴⁶

Table 6. Opto-electronic performance for the indicated PPV samples.^a

Entry	Medium	J_{sc} (mAcm^{-2})	V_{oc} (V)	FF (%)	PCE (%)	$\mu \times 10^{-3}$ (cm^2/Vs)	$I_{\text{on}}/I_{\text{off}}$
1	GVL	2.4	0.92	33.7	0.73	1.01	1500
2	NMP	3.8	0.91	36.1	1.26	1.21	200
3	GVL ^b	1.6	0.75	33.8	0.39	0.90	1400

^a Average of ~ 5 devices. ^b Pd(PPh₃)₄ was added to achieve ~ 800 ppm of Pd.

Experimental

Materials synthesis

The reagents 2,5-bis(hexyloxy)-1,4-diiodobenzene⁴⁷ and 1,4-divinylbenzene⁴⁸ were synthesized according to published procedures. All starting organic reagents and solvents were purchased from Aldrich, and used without further purification, unless otherwise noted. Tetrahydrofuran was distilled from sodium/benzophenone.

General procedure for Heck-Mirozoki reaction and E-Factor calculation (precipitation work-up)

In a screw capped vial equipped with a magnetic stirrer Pd/C 10 wt% (2.1 mg, 0.002 mmol, 0.1 mol%), GVL (2 mL), iodobenzene (**1a**) (416 mg, 0.228 mmol, 2 mmol), triethylamine (202 mg, 0.279 mmol, 2 mmol) and methyl acrylate (**2a**) (207 mg, 0.216 mmol, 2.4 mmol) were consecutively added and the resulting mixture was left under stirring at 150 °C. After 1 hour the catalyst was filtered off, 3 mL of water were added and the mixture was cooled down to 0 °C, then the precipitate was filtered off and washed with 1 mL of cold water. Ultimately the obtained solid was dried on high vacuum. In this way **3a** was obtained as a pale yellow solid (266 mg, 82% yield).⁴⁹

$$\text{E-Factor} = (4000 (\text{H}_2\text{O}) + 2100 (\text{GVL}) + 416 + 202 + 207 + 2.1 - 266) / 266 = 25$$

General procedure for Heck-Mirozoki reaction and E-Factor calculation (extraction work-up)

In a screw capped vial equipped with a magnetic stirrer Pd/C 10 wt% (2.1 mg, 0.002 mmol, 0.1 mol%), GVL (2 mL), iodobenzene (**1a**) (416 mg, 0.228 mmol, 2 mmol), triethylamine (202 mg, 0.279 mmol, 2 mmol) and methyl acrylate (**2a**) (207 mg, 0.216 mmol, 2.4 mmol) were consecutively added and the

resulting mixture was left under stirring at 150 °C. After 1 hour the catalyst was filtered off, 6 mL of cyclopentyl methyl ether were added and the organic phase was washed with water (3x3 mL). Then the organic phase was dried under vacuum. In this way **3a** was obtained as a pale yellow solid (266 mg, 82% yield).

$$\text{E-Factor} = (9000 (\text{H}_2\text{O}) + 2100 (\text{GVL}) + 5160 (\text{cyclopentyl methyl ether}) + 416 + 202 + 207 + 2.1 - 266) / 266 = 63$$

Poly(2,5-bis(hexyloxy)phenylenedivinylene-alt-1,4-

phenylenevinylene) **1**. 1,4-Divinylbenzene (0.5 mmol, 0.065 g), 2,5-bis(hexyloxy)-1,4-diiodobenzene (0.5 mmol, 0.265 g), potassium carbonate (1.5 mmol, 0.208 g), Pd/C (10 wt%, 5 mol%, 0.026 g) and GVL (6 mL) were placed in a 25 mL round bottom flask equipped with a magnetic stirrer and closed with rubber septum. The mixture was degassed with N₂ for 15 minutes, then heated at 135 °C for 72 hours. Chloroform was added and the mixture was filtered over Celite to remove the catalyst. After evaporation of chloroform under reduced pressure, the polymer was precipitated in methanol. The crude polymer (0.100 g) was washed on Soxhlet apparatus using in sequence acetone, hexane and chloroform.

Physical characterization.

NMR spectra were recorded on a Bruker DRX-ADVANCE 400 MHz (¹H at 400 MHz and ¹³C at 100.6 MHz) spectrometer in CDCl₃ using TMS as the internal standard.

The molecular weights of the polymer samples were determined on an Agilent 1100 series HPLC, equipped with Phenomenex Phenogel columns and polystyrene (M_p 400-2'000'000) was used as calibration standard.

The amount of residual palladium in the polymer samples was determined by ICP-AES (Inductively Coupled Plasma – Atomic Emission Spectrometry). The samples (~25 mg) were dissolved in *aqua regia* at r.t., diluted to 5 mL with deionized water, filtrated and subjected to analysis.

UV-visible spectroscopy was performed on a Varian Cary 5000 UV-vis-NIR spectrophotometer.

Organic field effect transistors (OFETs) were fabricated on p+-Si/SiO₂ (300 nm thermal oxide). Top contact gold (500 Å) were deposited by evaporating gold (pressure < 10⁻⁵ Torr); channel dimensions were 100 μm (L) by 1.0 mm (W). The capacitance of the insulator is 10.5 nF/cm² for 300 nm SiO₂. Device measurements were carried out at room temperature in a customized probe station under nitrogen. OFET characterizations were performed with a Keithley 6430 subfemtoamp (drain) and a Keithley 2400 (gate) source meter, operated by a locally written Labview program.

OPV characterization was performed on a Spectra-Nova Class A Solar Simulator with AM1.5G light (100 mW/cm²) from a Xe arc lamp. The light source was calibrated with a NREL-certified Si diode equipped with a KG3 filter to bring spectral mismatch to unity. Current *versus* potential (J-V) measurements were recorded with a Keithley 2400 digital source meter. Power conversion efficiencies were calculated

from the following equation: $PCE = (J_{sc}V_{oc}FF)/P_0$, where J_{sc} (mA/cm^2) is the short circuit current, V_{oc} (V) the open circuit voltage, FF the fill factor, and P_0 the power of incident light source (mW/cm^2).

External quantum efficiency (EQE) was measured using an Oriel model QE-PV-SI (Newport instruments) equipped with a NIST (National Institute of Standards and Technology)-certified Si-diode and a Merlin lock-in amplifier and optical chopper. Monochromatic light was generated from a 300 W Xe arc lamp.

Conclusions

In conclusion, in this contribution we have showed that GVL is an excellent reaction medium, derived from biomasses, which can replace classic dipolar aprotic media such as DMF or NMP. The palladium-catalyzed Heck reaction has been investigated as a representative and widely important process for achieving chemicals used in several applied fields. A specific attention in this study has been devoted to the critical issue of palladium leaching, which commonly occurs in Heck reactions, leading to a high metal impurity content in the final products for both small and macro-molecules.

We have used GVL for the clean preparation of several small molecules (**4a-l**, and **6a-h**) and also for the synthesis of a very pure PPV semiconductor (**1**) in high yields and with a very low Pd-content. We have proved that GVL is superior to conventional dipolar media in terms of controlling palladium impurities. These results are rationalized by the lower complexing ability of GVL in the Heck-Mirozoki cross-coupling procedure. Furthermore, OPV and FET data demonstrate that device-quality PPV **1** can be achieved without extensive purification processes complementing recent synthetic efforts to semiconducting materials without the use of toxic Sn metal.^{30c,50} These results are extremely encouraging and prove that GVL, as a biomass derived solvent, is a promising medium and its use in strategic processes may significantly reduce the environmental impact and energy cost of the chemical industry.

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Notes

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References

- 1 A.J. Ragauskas, C. K. Williams, B. H. Davison, G. Britovsek, J. Cairney, C. A. Eckert, W. J. Frederik Jr., J. P. Hallet, D. J. Leak, C. L. Liotta, J. R. Mielenz, R. Murphy, R. Templer and T. Tschaplinski, *Science*, 2006, **311**, 484-489.
- 2 European Association for Chemical and Molecular Sciences EuCheMS, *Chemistry-Developing solutions in a changing world*, 2011.
- 3 D. J. Burke and D.J. Lipomi, *Energy Env. Sci.* 2013, **6**, 2053-2066.
- 4 (a) C. Capello, U. Fischer and K. Hungerbühler, *Green Chem.*, 2007, **9**, 927-934; (b) C. Seyler, C. Capello, S. Hellweg, C. Bruder, D. Bayne, A. Huwiler and K. Hungerbühler, *Ind. Eng. Chem. Res.*, 2006, **45**, 7700-7709; (c) C. Jiménez-González, A. D. Curzons, D.J.C. Constable and V. L. Cunningham, *Int. J. Life Cycle Assess.*, 2004, **9**, 114-121.
- 5 (a) E. S. Beach, Z. Cui and P. T. Anastas, *Energy Environ. Sci.*, 2009, **2**, 1038-1049; (b) A. D. Curzons, D. J. C. Constable, D. N. Mortimera and V. L. Cunningham, *Green Chem.*, 2001, **3**, 1-6.
- 6 D. J. C. Constable, P. J. Dunn, J. D. Hayler, G. R. Humphrey, J. L. Leazer, Jr., R. J. Linderman, K. Lorenz, J. Manley, B. A. Pearlman, A. Wells, A. Zaksh and T. Y. Zhang, *Green Chem.*, 2007, **9**, 411-420.
- 7 D. J. C. Constable, C. Jiménez-González and R. K. Henderson, *Org. Process Res. Dev.*, 2007, **11**, 133-137.
- 8 R. K. Henderson, C. Jiménez-González, D. J. C. Constable, S. R. Alston, G. G. A. Inglis, G. Fisher, J. Sherwood, S. P. Binks and A. D. Curzons, *Green Chem.*, 2011, **13**, 854-862.
- 9 C. Jiménez-González, P. Poechlauer, Q. B. Broxterman, B.-S. Yang, D. am Ende, J. Baird, C. Bertsch, R. E. Hannah, P. Dell'Orco, H. Noorman, S. Yee, R. Reintjens, A. Wells, V. Massonneau and J. Manley, *Org. Process Res. Dev.*, 2011, **15**, 900-911.
- 10 (a) T. Laird, *Org. Process Res. Dev.*, 2012, **16**, 1-2; (b) G. M. Kemeling, *ChemSusChem*, 2012, **5**, 2291 - 2292.
- 11 M. P. Nikiforov, B. Lai, W. Chen, S. Chen, R. D. Schaller, J. Strzalka, J. Maserb and S. B. Darling, *Energy Environ. Sci.*, 2013, **6**, 1513-1520.
- 12 C. E. Garrett and K. Prasad, *Adv. Synth. Catal.*, 2004, **346**, 889-900.
- 13 Note for Guidance on Specification Limits for Residues of Metal Catalysts, The European Agency for the Evaluation of Medicinal Products, Evaluation of Medicines for Human Use; London, 17 December 2002; <http://www.emea.eu.int>.
- 14 For a recent example see: J. Kuwabara, T. Yasuda, S. J. Choi, W. Lu, K. Yamazaki, S. Kagaya, L. Han and T. Kanbara, *Adv. Funct. Mater.*, 2014, **24**, 3226-3233.
- 15 (a) A. Saeki, M. Tsuji and S. Seki, *Adv. Energy Mater.*, 2011, **1**, 661-669; (b) P. A. Troshin, D. K. Susarova, Y. L. Moskvina, I. E. Kuznetsov, S. A. Ponomarenko, E. N. Myshkovskaya, K. A. Zakharcheva, A. A. Balakai, S. D. Babenko and V. F. Razumov, *Adv. Funct. Mater.*, 2010, **20**, 4351-4357.
- 16 M. C. Bryan, B. Dillon, L. G. Hamann, G. J. Hughes, M. E. Kopach, E. A. Peterson, M. Pourashraf, I. Raheem, P. Richardson, D. Richter and H. F. Sneddon, *J. Med. Chem.*, 2013, **56**, 6007-6021.
- 17 K. Alfonsi, J. Colberg, P. J. Dunn, T. Fevig, S. Jennings, T. A. Johnson, H. P. Kleine, C. Knight, M. A. Nagy, D. A. Perry and M. Stefaniak, *Green Chem.*, 2008, **10**, 31-36.
- 18 (a) Y. Gu and F. Jérôme, *Chem. Soc. Rev.*, 2013, **42**, 9550-9570; (b) I. T. Horváth, *Green Chem.*, 2008, **10**, 1024-1028.
- 19 (a) C. O. Tuck, E. Pérez, I. T. Horváth, R. A. Sheldon and M. Poliakov, *Science*, 2012, **337**, 695-699; (b) J. C. Serrano-Ruiz, R. Luque and A. Sepúlveda-Escribano, *Chem. Soc. Rev.*, 2011, **40**, 5266-5281; (c) D. R. Dodds and R. A. Gross, *Science* 2007, **318**,

- 1250–1251; (d) A. Corma, S. Iborra and A. Velty, *Chem. Rev.*, 2007, **107**, 2411–2502.
- 20 (a) T. Angelini, D. Lanari, R. Maggi, F. Pizzo, G. Sartori and L. Vaccaro, *Adv. Synth. Catal.* 2012, **354**, 908–916; (b) D. Lanari, O. Piematti, F. Pizzo and L. Vaccaro, *Synthesis* 2012, **44**, 2181–2184; (c) S. Bonollo, D. Lanari, F. Pizzo and L. Vaccaro, *Org. Lett.* 2011, **13**, 2150–2152; (d) S. Bonollo, D. Lanari and L. Vaccaro, *Eur. J. Org. Chem.* 2011, 2587–2598.
- 21 (a) D. Lanari, R. Ballini, A. Palmieri, F. Pizzo and L. Vaccaro, *Eur. J. Org. Chem.* 2011, 2874–2884; (b) F. Fringuelli, D. Lanari, F. Pizzo and L. Vaccaro, *Green Chem.* 2010, **12**, 1301–1305; (c) A. Zvagulis, S. Bonollo, D. Lanari, F. Pizzo and L. Vaccaro, *Adv. Synth. Catal.* 2010, **352**, 2489–2496.
- 22 (a) M. Alonzi, M. P. Bracciale, A. Broggi, D. Lanari, A. Marrocchi, M. L. Santarelli and L. Vaccaro, *J. Catal.* 2014, **309**, 260–267; (b) S. Bonollo, D. Lanari, J. M. Longo and L. Vaccaro, *Green Chem.* 2012, **14**, 164–169; (c) S. Bonollo, D. Lanari, T. Angelini, F. Pizzo, A. Marrocchi and L. Vaccaro, *J. Catal.* 2012, **285**, 216–222.
- 23 (a) E. I. Gürbüz, J. M. R. Gallo, D. M. Alonso, S. G. Wettstein, W. Y. Lim and J. A. Dumesic, *Angew. Chem. Int. Ed.*, 2013, **52**, 1270 – 1274; (b) L. Deng, J. Li, D.-M. Lai, Y. Fu and Q.-X. Guo, *Angew. Chem. Int. Ed.*, 2009, **48**, 6529 – 6532.
- 24 (a) D. M. Alonso, J. M. R. Gallo, M. A. Mellmer, S. G. Wettstein and J. A. Dumesic, *Catal. Sci. Technol.*, 2013, **3**, 927 – 931; (b) P. Azadi, R. Carrasquillo-Flores, Y. J. Pagán-Torres, E. I. Gürbüz, R. Farnood and J. A. Dumesic, *Green Chem.*, 2012, **14**, 1573–1576; (c) Z. Yan, L. Lin and S. Liu, *Energy & Fuels*, 2009, **23**, 3853–3858.
- 25 (a) D. M. Alonso, S. G. Wettstein, J. Q. Bond, T. W. Root and J. A. Dumesic, *ChemSusChem*, 2011, **4**, 1078 – 1081; (b) J. Q. Bond, D. M. Alonso, D. Wang, R. M. West and J. A. Dumesic, *Science*, 2010, **327**, 1110 – 1114; (c) D. M. Alonso, J. Q. Bond and J. A. Dumesic, *Green Chem.*, 2010, **12**, 1493–1513; (d) I. T. Horváth, H. Mehdî, V. Fábos, L. Boda and L. T. Mika, *Green Chem.*, 2008, **10**, 238–242.
- 26 (a) D. M. Alonso, S. G. Wettstein and J. A. Dumesic, *Green Chem.*, 2013, **15**, 584–595; (b) J.-P. Lange, J. Z. Vestering and R. J. Haan, *Chem. Commun.*, 2007, 3488–3490.
- 27 GVL dielectric constant at 25 °C is 36.47; S. Aparicio and R. Alcalde, *Phys. Chem. Chem. Phys.*, 2009, **11**, 6455–6467.
- 28 Dielectric constant (25 °C) for: Acetonitrile= 37.5, DMF= 36.7, NMP= 32.0, DMA= 37.8. Vogel's Textbook of Practical Organic Chemistry, 4th edition, Longman, London and New York, 1978.
- 29 P. G. Jessop, *Green Chem.*, 2011, **13**, 1391–1398.
- 30 (a) E. Bartollini, M. Seri, S. Tortorella, A. Facchetti, T. J. Marks, A. Marrocchi and L. Vaccaro, *RSC Adv.* 2013, **3**, 9288–9295; (b) M. Alonzi, D. Lanari, A. Marrocchi, C. Petrucci and L. Vaccaro, *RSC Adv.* 2013, **3**, 23909–23923; (c) A. Facchetti, L. Vaccaro and A. Marrocchi, *Angew. Chem. Int. Ed.* 2012, **51**, 3520–3523.
- 31 (a) J. M. R. Gallo, D. M. Alonso, M. A. Mellmer and J. A. Dumesic, *Green Chem.* 2013, **15**, 85; (b) Z.-Q. Duan and F. Hu, *Green Chem.*, 2012, **14**, 1581–1583; (c) S. G. Wettstein, D. M. Alonso, Y. Chong and J. A. Dumesic, *Energy Environ. Sci.*, 2012, **5**, 8199–8203; (d) L. Qi and I. T. Horváth, *ACS Catal.*, 2012, **2**, 2247–2249; (e) D. M. Alonso, J. Q. Bond, J. C. Serrano-Ruiz and J. A. Dumesic, *Green Chem.* 2010, **12**, 992.
- 32 (a) Y.-J. Cheng, S.-H. Yang and C.-S. Hsu, *Chem. Rev.*, 2009, **109**, 5868–5923; (b) A. C. Grimsdale, K. L. Chan, R. E. Martin, P. G. Jokisz and A. B. Holmes, *Chem. Rev.*, 2009, **109**, 897–1091, (c) S. Günes, H. Neugebauer and N. S. Sariciftci, *Chem. Rev.*, 2007, **107**, 1324–1338.
- 33 (a) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215–1292; (b) J. Le Bras and J. Muzart, *Chem. Rev.*, 2011, **111**, 1170–1214; (c) L. Yin and J. Liebscher, *Chem. Rev.* 2007, **107**, 133–173; (d) V. Farina, *Adv. Synth. Catal.*, 2004, **346**, 1553–1582; (e) C. Amatore and A. Jutand, *Acc. Chem. Res.*, 2000, **33**, 314–321.
- 34 (a) Y. Lim, Y.-S. Park, Y. Kang, D. Y. Jang, J. H. Kim, J.-J. Kim, A. Sellinger and D. Y. Yoon, *J. Am. Chem. Soc.*, 2011, **133**, 1375–1382; (b) C. Torborga and M. Beller, *Adv. Synth. Catal.*, 2009, **351**, 3027–3043; (c) Y. Lee, Y. Liang and L. Yu, *Synlett*, 2006, 2879–2893.
- 35 (a) D. Barbaras, J. Brozio, I. Johannsen and T. Allmendinger, *Org. Process Res. Dev.*, 2009, **13**, 1068–1079; (b) M. J. Girgis, L. E. Kuczynski, S. M. Berberena, C. A. Boyd, P. L. Kubinski, M. L. Scherholz, D. E. Drinkwater, X. Shen, S. Babiak and B. G. Lefebvre, *Org. Process Res. Dev.*, 2008, **12**, 1209–1217.
- 36 (a) C. J. Welch, J. Albaneze-Walker, W. R. Leonard, M. Biba, J. DaSilva, D. Henderson, B. Laing, D. J. Mathre, S. Spencer, X. Bu and T. Wang, *Org. Process Res. Dev.*, 2005, **9**, 198–205; (b) V. W. Rosso, D. A. Lust, P. J. Bernot, J. A. Grosso, S. P. Modi, A. Rusowicz, T. C. Sedergran, J. H. Simpson, S. K. Srivastava, M. J. Humora and N. G. Anderson, *Org. Process Res. Dev.*, 1997, **1**, 311–314.
- 37 (a) K. T. Nielsen, H. Spanggaard and F. C. Krebs, *Macromolecules*, 2005, **38**, 1180–1189; (b) K. T. Nielsen, K. Bechgaard and F. C. Krebs, *Macromolecules*, 2005, **38**, 658–659; (c) K. T. Nielsen, K. Bechgaard and F. C. Krebs, *Synthesis*, 2006, 1639–1644.
- 38 (a) C. Wang, H. Dong, W. Hu, Y. Liu and D. Zhu, *Chem. Rev.* 2011, **112**, 2208 – 2267; (b) A. J. Heeger, *Chem. Soc. Rev.* 2010, **39**, 2354–2371; (c) A. C. Grimsdale and A. B. Holmes in T. A. Skotheim and J.R. Reynolds (Eds), *Handbook of Conducting Polymers* (3rd Edition), 2007.
- 39 M. Pagliaro, V. Pandarus, R. Ciriminna, F. Béland, and P. D. Carà, *ChemCatChem*, 2012, **4**, 432–445.
- 40 (a) R. G. Heidenreich, J.G.E. Krauter, J. Pietsch and K. Köhler, *J. of Mol. Cat. A: Chem.*, 2002, **183**, 499–509; (b) K. Köhler, R.G. Heidenreich, J.G.E. Krauter and J. Pietsch, *Chem. Eur. J.*, 2002, **8**, 622–631; (c) F. Zhao, B. M. Bhanage, M. Shirai, and Masahiko Arai, *Chem. Eur. J.*, 2000, **6**, 843–848.
- 41 S.-Y. Liu, H.-Y. Li, M.-M. Shi, H. Jiang, X.-L. Hu, W.-Q. Li, L. Fu and H.-Z. Chen, *Macromolecules*, 2012, **45**, 9004–9009.
- 42 R. A. Sheldon, *Chem. Commun.*, 2008, 3352–3365.
- 43 R.J. Kline and M.D. McGehee, *Macromolecules* 2005, **38**, 3312–3319.
- 44 C. J. Brabec, M. Heeney, I. McCulloch and J. Nelson, *Chem. Soc. Rev.* 2011, **40**, 1185–1199.
- 45 (a) G. Y. Sang, Y. P. Zou, Y. F. Li, *J. Phys. Chem. C*, 2008, **112**, 12058–12064; (b) M. Morana, P. Koers, C. Waldauf, M. Koppe, D. Muehlbacher, P. Denk, M. Scharber, D. Waller and C. Brabec, *Adv. Funct. Mater.*, 2007, **17**, 3274–3283.
- 46 (a) Sonar, P.; Grimsdale, A. C.; Heeney, M.; Shkunov, M.; McCulloch, I.; Muellen, K, *Synthetic Metals* 2007, **157**(21), 872–875. (b) Bjoerklund, N.; Lill, J.-O.; Rajander, J.; Oesterbacka, R.; Tierney, S.; Heeney, M.; McCulloch, I.; Coelle, M. *Organic Electronics* 2009, **10**, 215–221. (c) Nikiforov, M. P.; Lai, B.; Chen, W.; Chen, S.; Schaller, R. D.; Strzalk, J.; Maserb, J.; Darling, S. B. *Energy Environ. Sci.*, 2013, **6**, 1513–1520. (d) P. A. Troshin, D. K. Susarova, Y. L. Moskvina, I. E. Kuznetsov, S. A. Ponomarenko, E. N. Myshkovskaya, K. A. Zacharcheva, A. A. Balakai, S. D. Babenko and V. F. Razumov, *Adv. Funct. Mater.*, 2010, **20**, 4351–4357. (e) W. L. Leong, G. C. Welch, L. G. Kaake, C. J. Takacs, Y. Sun, G. C. Bazan and A. J. Heeger, *Chem. Sci.*, 2012, **3**, 2103–2109. (f) A. Saeki, M. Tsuji and S. Seki, *Adv. Energy Mater.*, 2011, **1**, 661–669.
- 47 P. Singh, U. Saha and T. H. Goswami, *Synth. Met.* 2012, **162**, 1240–1254.
- 48 T. Ohishi, T. Masukawa, S. Fujii, A. Yokoyama and T. Yokozawa, *Macromolecules*, 2010, **43**, 3206–3214.
- 49 Z. Zhang, Z. Zha, C. Gan, C. Pan, Y. Zhou, Z. Wang and M.M. Zhou, *J. Org. Chem.* 2006, **71**, 4339–4342.
- 49 (a) Senkovskyy, V.; Tkachov, R.; Komber, H.; Sommer, M.; Heuken, M.; Voit, B.; Huck, W. T. S.; Kataev, V.; Petr, A.; Kiriy, A. *J. Am. Chem. Soc.* 2011, **131**, 19966. (b) Senkovskyy, V.; Tkachov, R.; Komber, H.; John, A.; Sommer, J.-U.; Kiriy, A. *Macromolecules* 2012, **5**, 7770. (c) Tkachov, R.; Karpov, Y.; Senkovskyy, V.; Raguzin, I.; Zessin, J.; Lederer, A.; Stamm, M.; Voit, B.; Beryozkina, Te.; Bakulev, V.; Facchetti, A.; Kiriy, A. *Macromolecules* 2014, **47**(12), 3845–3851.