

Article

A Recyclable Palladium-Catalyzed Synthesis of 2-Methylene-2,3-Dihydrobenzofuran-3-ols by Cycloisomerization of 2-(1-Hydroxyprop-2-ynyl)phenols in Ionic Liquids

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Abstract: A recyclable palladium-catalyzed synthesis of 2-methylene-2,3-dihydrobenzofuran-3-ols **2** by heterocyclization of 2-(1-hydroxyprop-2-ynyl)phenols **1** in an ionic liquid medium (BmimBF₄) is presented. The process takes place under relatively mild conditions (100 °C, 5 h) in the presence of catalytic amounts (2 mol %) of PdI₂ in conjunction with KI (5 equiv with respect to PdI₂) and an organic base, such as morpholine (1 equiv with respect to **1**), to give **2** in high yields (70%–86%). The PdI₂-KI catalytic system could be recycled up to six times without appreciable loss of activity. Moreover, products **2** could be easily converted in a one-pot fashion into 2-hydroxymethylbenzofurans **3** (52%–71%, based on **1**) and 2-methoxymethylbenzofurans **4** (52%–80%, based on **1**) by acid-catalyzed allylic isomerization or allylic nucleophilic substitution.

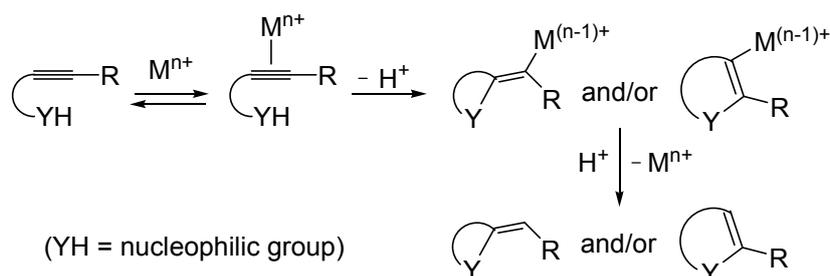
Keywords: benzofurans; cycloisomerization; dihydrobenzofurans; ionic liquids; palladium; recyclable synthesis

1. Introduction

Metal-catalyzed heterocyclization reactions are a powerful methodology for the direct synthesis of substituted heterocyclic derivatives starting from readily available substrates [1–11]. The process

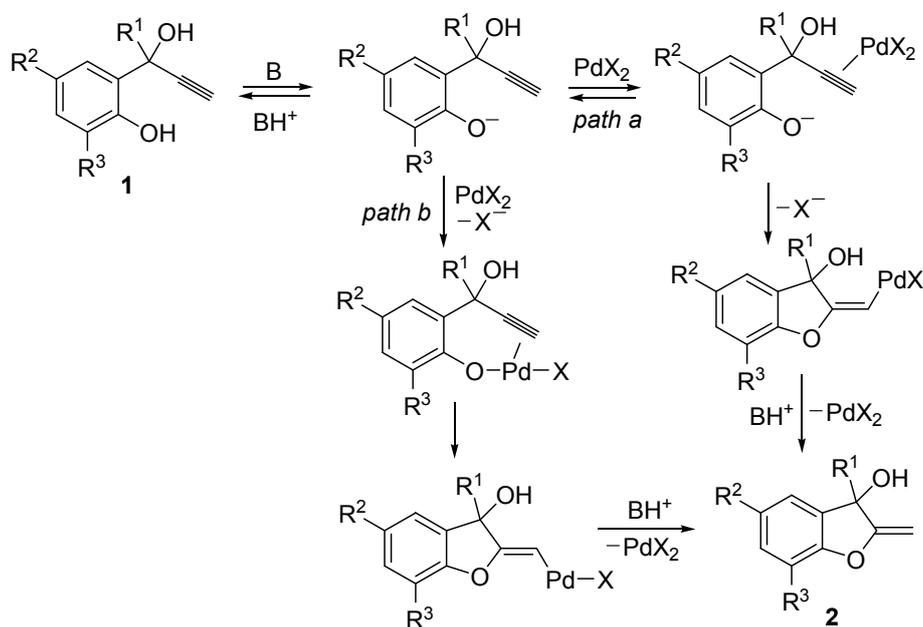
occurs through the activation of an unsaturated bond by coordination to the metal center, followed by *endo* or *exo* intramolecular attack by the nucleophilic group (YH) and protonolysis or vice versa (Scheme 1—the case of a functionalized alkyne is shown). In particular, we have reported several metal-catalyzed heterocyclizations of acetylenes, bearing a nucleophilic group in a suitable position for cyclization, which have proved valuable for the preparation of a variety of important heterocycles, including furans, pyrroles, thiophenes, and benzothiophenes [12–20].

Scheme 1. Metal-catalyzed heterocyclization of acetylenes bearing a suitably placed nucleophilic group leading to heterocycles through activation of the triple bond by the metal species followed by intramolecular nucleophilic attack and protonolysis.



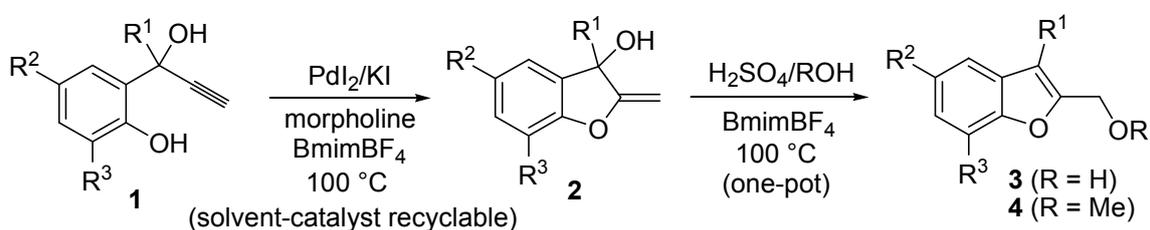
Recently, we have reported a novel approach to the synthesis of 2-methylene-2,3-dihydrobenzofuran-3-ols **2** by Pd-catalyzed heterocyclization of 2-(1-hydroxyprop-2-ynyl)phenols **1**, carried out in MeOH in the presence of PdX₂ as catalyst in conjunction with KX (X = Cl, I) and morpholine as the base, necessary for substrate deprotonation [18]. Either 5-*exo-dig* intramolecular attack to coordinated triple bond (path *a*) or triple bond insertion into the Pd-O bond of a phenoxypalladium intermediate (path *b*) may take place, according to Scheme 2 [18].

Scheme 2. Formation of 2-methylene-2,3-dihydrobenzofuran-3-ols **2** by Pd-catalyzed heterocyclization of 2-(1-hydroxyprop-2-ynyl)phenols **1** in the presence of morpholine as the base (B) in MeOH as the solvent [18].



We have now found that this process can also be conveniently performed in an ionic liquid (IL), such as 3-butyl-1-methyl-imidazolium tetrafluoroborate (BmimBF₄) as the solvent, and that by using this unconventional medium [21–31], it is possible to recycle the catalytic system several times without appreciable loss of activity (Scheme 3). We have also found that, in BmimBF₄, methylenedihydrobenzofuranols **2** can be readily converted into 2-hydroxymethylbenzofurans **3** or 2-methoxymethylbenzofurans **4** by acid-catalyzed allylic isomerization or allylic nucleophilic substitution in a one-pot fashion. The recyclability of metal catalysts has acquired an increasing importance in the modern organic synthesis, as testified by recent publications in this field [32–41].

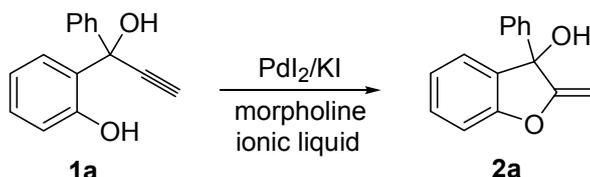
Scheme 3. Recyclable Pd-catalyzed synthesis of 2-methylene-2,3-dihydrobenzofuran-3-ols **2** in BmimBF₄, and their one-pot conversion into 2-hydroxymethylbenzofurans **3** or 2-methoxymethylbenzofurans **4**.



2. Results and Discussion

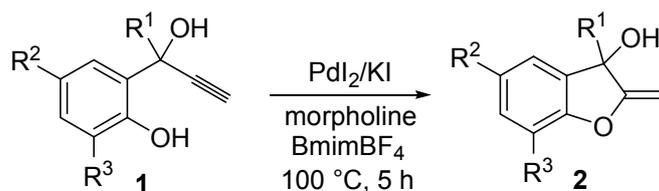
2-(1-Hydroxy-1-phenylprop-2-ynyl)phenol (**1a**) was chosen as the model substrate for testing the reactivity of 2-(1-hydroxyprop-2-ynyl)phenols in ionic liquids. The reaction of **1a**, carried out in BmimBF₄ as the solvent at 70 °C for 5 h, in the presence of 2 mol % of PdI₂ in conjunction with KI (5 equiv with respect to PdI₂) and morpholine (1 equiv. with respect to **1a**), led to the formation of 2-methylene-3-phenyl-2,3-dihydrobenzofuran-3-ol (**2a**) in 60% isolated yield at 80% substrate conversion (Table 1, entry 1). This initial result clearly confirmed the feasibility of the process in an ionic liquid as the reaction medium. Substrate conversion reached 100% either after 8 h at the same temperature (with a **2a** yield of 82%, Table 1, entry 2) or after 5 h at 100 °C (with a **2a** yield of 86%, Table 1, entry 3). The reaction also worked well with 1 mol % of catalyst, as shown in Table 1, entry 4 (**2a** yield was 80%). On the other hand, the use of 4 mol % of KI or the use of PdCl₂/KCl instead of PdI₂/KI led to inferior results (Table 1, entries 5 and 6, respectively). Lower yields of **2a** were also obtained working in other ILs, such as BmimCl, BmimPF₆, BmimN(CN)₂, or BmimOTf (Table 1, entries 7–10).

The next experiments were aimed at verifying the recyclability of the catalyst-IL system and at generalizing the process to other variously substituted substrates, using BmimBF₄ as the reaction medium at 100 °C for 5 h. Regarding the recycling experiments, the reaction crude deriving from the reaction carried out under the same conditions as those reported in Table 1, entry 3, was extracted several times with diethyl ether, to isolate the product, while the residue (containing the catalyst dissolved in the IL), after drying under vacuum, was used again by adding to it fresh substrate **1a** and morpholine (1:1 ratio). After stirring at 100 °C for 5 h, **2a** was obtained again, with practically the same yield as the parent reaction (85%, Table 2, entry 1, run 2). The recycling procedure was then repeated up to 5 times, without any appreciable loss of catalytic activity (Table 2, entry 1, runs 3–7).

Table 1. Iodocyclodehydration of 4-mercapto-3-methyl-1-phenylpent-1-yn-3-ol (**1a**) to 3-iodo-4,5-dimethyl-2-phenylthiophene (**2a**) under different conditions ^a.

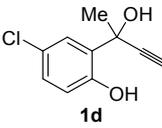
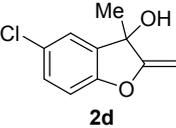
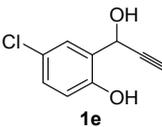
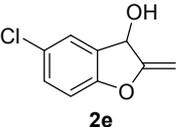
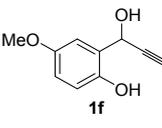
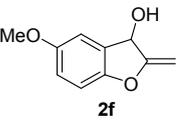
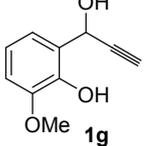
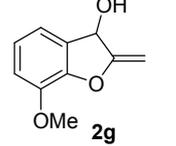
Entry	Ionic Liquid	T (°C)	Conversion of 1a ^b (%)	Yield of 2a ^c (%)
1	BmimBF ₄	70	80	60
2 ^d	BmimBF ₄	70	100	82
3	BmimBF ₄	100	100	86
4 ^e	BmimBF ₄	100	100	80
5 ^f	BmimBF ₄	100	100	63
6 ^g	BmimBF ₄	100	100	65
7	BmimCl	100	100	51
8	BmimPF ₆	100	100	58
9	BmimN(CN) ₂	100	100	63
10	BmimOTf	100	60	23

^a Unless otherwise noted, all cycloisomerization reactions were carried out for 5 h under nitrogen with a substrate concentration of 0.25 mmol of **1a** per mL of ionic liquid. The morpholine:**1a**:KI: PdI₂ molar ratio was 50:50:5:1. The formation of a complex mixture of products accounted for the difference between substrate conversion and the yield of **2a**. ^b Based on isolated unreacted **1a**. ^c Isolated yield based on starting **1a**. ^d The reaction time was 8 h. ^e The reaction was carried out with 1 mol % of PdI₂. ^f The reaction was carried with 4 mol % of KI. ^g The reaction was carried with PdCl₂+5KCl rather than with PdI₂ + 5KI.

Table 2. Recyclable Synthesis of 2-methylene-2,3-dihydrobenzofuran-3-ols (**2**) by PdI₂/KI-catalyzed cycloisomerization of 2-(1-hydroxyprop-2-ynyl)phenols (**1**) in BmimBF₄ ^a.

Entry	1	2	Yield of 2 (%) ^b						
			Run 1 ^c	Run 2 ^c	Run 3 ^c	Run 4 ^c	Run 5 ^c	Run 6 ^c	Run 7 ^c
1			86	85	87	86	85	86	87
2			84	86	82	75	72	73	72
3			70	71	71	68	70	69	70

Table 2. Cont.

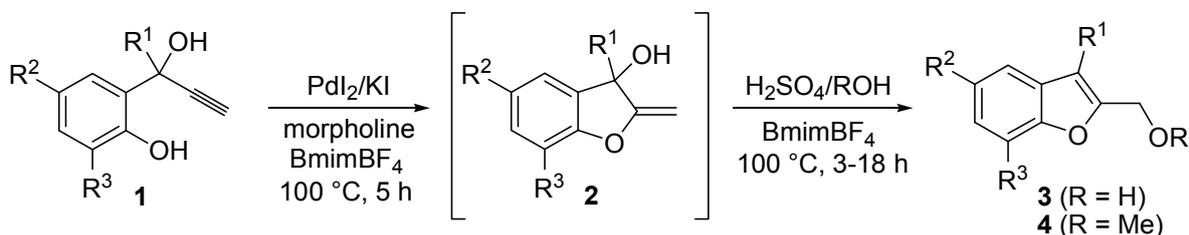
Entry	1	2	Yield of 2 (%) ^b						
			Run 1 ^c	Run 2 ^c	Run 3 ^c	Run 4 ^c	Run 5 ^c	Run 6 ^c	Run 7 ^c
4			78	80	78	80	81	81	80
5			80	81	79	80	78	81	79
6			75	77	76	77	75	76	78
7			76	76	77	75	78	74	77

^a All reactions were carried out at 100 °C in BmimBF₄ under nitrogen for 5 h with a substrate concentration of 0.25 mmol of **1** per mL of ionic liquid. The morpholine:1:KI:PdI₂ molar ratio was 50:50:5:1. Conversion of **1** was quantitative in all cases. ^b Isolated yield based on starting **1**. ^c Run 1 corresponds to the 1st experiment, the next runs to recycles. See text for details.

The method was then extended to other 2-(1-hydroxyprop-2-ynyl)phenols **1b–g**, bearing different (either electron-withdrawing or electron-donating) substituents on the aromatic ring and at the benzylic position. As can be seen from the results shown in Table 2, entries 2–7, good yields of the corresponding methylenedihydrobenzofurans **2b–g** were consistently obtained. We also checked the catalyst-solvent recyclability in all cases, still with satisfactory results, products being obtained in comparable yields with respect to the parent reactions (Table 2, entries 2–7).

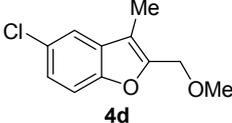
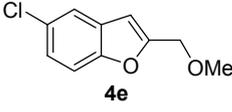
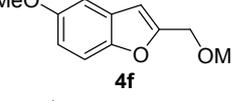
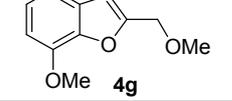
2-Methylene-2,3-dihydrobenzofuran-3-ols **2** are known to be useful precursors for the preparation of functionalized benzofurans [18,42]. In particular, we previously reported that they can easily undergo acid-catalyzed allylic isomerization to give 2-hydroxymethylbenzofurans **3** or acid-catalyzed allylic nucleophilic substitution to give 2-methoxymethylbenzofurans **4** [18]. We have now found that it is possible to directly obtain either benzofurans **3** or **4** in a one-pot fashion by Pd-catalyzed cycloisomerization of **1** in BmimBF₄, followed by acid catalyzed allylic isomerization or nucleophilic substitution, without the need for isolating compounds **2**. Thus, the reaction mixture resulting from the cycloisomerization process was allowed to cool down to room temperature, and then H₂SO₄ in water or in MeOH was added. After 3–18 h at 100 °C, the corresponding benzofuran derivatives **3** and **4** were obtained in high yields (Table 3). Clearly, no IL recyclability was possible for this one-pot transformation.

Table 3. Synthesis of 2-hydroxymethylbenzofurans **3** and 2-methoxymethylbenzofurans **4** by one-pot PdI₂/KI-catalyzed cycloisomerization of 2-(1-hydroxyprop-2-ynyl)phenols – allylic isomerization or allylic nucleophilic substitution ^a.



Entry	1	R	t (h)	3 or 4	Yield of 3 or 4 ^b (%)
1		H	3		65
2		H	3		55
3		H	3		54
4		H	3		71
5		H	3		56
6		H	3		52
7		H	3		54
8	1a	Me	18		80
9	1b	Me	18		65
10	1c	Me	18		52

Table 3. Cont.

Entry	1	R	t (h)	3 or 4	Yield of 3 or 4 ^b (%)
11	1d	Me	15		70
12	1e	Me	18		52
13	1f	Me	18		55
14	1g	Me	18		60

^a All cycloisomerization reactions were carried out at 100 °C in BmimBF₄ under nitrogen for 5 h with a substrate concentration of 0.25 mmol of **1** per mL of ionic liquid. The morpholine:1:KI:PdI₂ molar ratio was 50:50:5:1. The allylic isomerization or allylic nucleophilic substitution was carried out in a one-pot fashion by adding H₂SO₄ in water or in MeOH (R = H or Me, respectively; 0.75 M) to the reaction crude deriving from the cycloisomerization reaction, and allowing the resulting mixture to stir a 100 °C for the required time. Conversion of **1** was quantitative in all cases. ^b Isolated yield based on starting **1**.

3. Experimental

3.1. General

Melting points were taken on a Reichert Thermovar apparatus and are uncorrected. ¹H-NMR and ¹³C-NMR spectra were recorded at 25 °C in CDCl₃ solutions with a Bruker DPX Avance 300 spectrometer operating at 300 MHz and 75 MHz, respectively, with Me₄Si as internal standard. Chemical shifts (δ) and coupling constants (*J*) are given in ppm and in Hz, respectively. IR spectra were taken with a JASCO FT-IR 4200 spectrometer. Mass spectra were obtained using a Shimadzu QP-2010 GC-MS apparatus at 70 eV ionization voltage. Microanalyses were carried out with a Carlo Erba Elemental Analyzer Mod. 1106. All reactions were analyzed by TLC on silica gel 60 F₂₅₄ (Merck) or on neutral alumina (Merck) and by GLC using a Shimadzu GC-2010 gas chromatograph and capillary columns with polymethylsilicone + 5% polyphenylsilicone as the stationary phase (HP-5). Column chromatography was performed on silica gel 60 (Merck, 70–230 mesh) or neutral alumina 90 (Merck, 70–230 mesh). Evaporation refers to the removal of solvent under reduced pressure.

3.2. Preparation of Substrates

Starting 2-(1-hydroxyprop-2-ynyl)phenols **1** were prepared and characterized as already described [43].

3.3. Preparation of Ionic Liquids

Ionic liquid BmimOTf [44] was prepared according to a literature procedure. All other ionic liquids were prepared as previously described [17].

3.4. General Procedure for the PdI₂/KI-Catalyzed Cycloisomerization of 2-(1-Hydroxyprop-2-ynyl)phenols **1** to Give 2-Methylene-2,3-Dihydrobenzofuran-3-ols **2**

To a Schlenk flask containing PdI₂ (1.8 mg, 5.0×10^{-3} mmol), KI (4.2 mg, 2.5×10^{-2} mmol) and BmimBF₄ (1 mL) was added, under nitrogen, a solution of **1** (0.25 mmol) in Et₂O (1.5 mL). The diethyl ether was eliminated under vacuum, and then morpholine (22.0 mg, 0.25 mmol) was added under nitrogen. The resulting mixture was allowed to stir under nitrogen at 100 °C for 5 h. After cooling, the mixture was extracted with Et₂O (6 × 2 mL), to separate the product, while the residue, still containing the catalysts dissolved in the IL, was used as such for the recycling experiments (see below). The collected ethereal phases were concentrated, and products **2** were purified by column chromatography on silica gel using hexane-AcOEt from 95:5 to 9:1 as the eluent. The yields obtained in each experiments are reported in Table 2.

Recycling Procedure. To the residue obtained as described above, still containing the catalyst dissolved in the ionic liquid, was added under nitrogen a solution of **1** (0.25 mmol) in Et₂O (1.5 mL). Diethyl ether was removed under vacuum, morpholine (22.0 mg, 0.25 mmol) was added, and then the same procedure described above was followed.

3.5. General Procedure for the One-Pot Synthesis of 2-Hydroxymethylbenzofurans **3** and 2-Methoxymethylbenzofurans **4** Starting From 2-(1-Hydroxyprop-2-ynyl)phenols **1**

To a Schlenk flask containing PdI₂ (1.8 mg, 5.0×10^{-3} mmol), KI (4.2 mg, 2.5×10^{-2} mmol) and BmimBF₄ (1 mL) was added, under nitrogen, a solution of **1** (0.25 mmol) in Et₂O (1.5 mL). The diethyl ether was eliminated under vacuum, and then morpholine (22.0 mg, 0.25 mmol) was added under nitrogen. The resulting mixture was allowed to stir under nitrogen at 100 °C for 5 h. After cooling, a solution of H₂SO₄ in ROH (R = H or Me, 0.75 M) (670 μL, 0.5 mmol) was added under nitrogen (together with 100 μL of MeOH when R = Me), and the mixture was allowed to stir at 100 °C for 3 h (R = H) or overnight (18 h, R = Me). After cooling, the mixture was extracted with Et₂O (6 × 2 mL). The collected ethereal phases were concentrated, and products **3** (R = H) and **4** (R = Me) were purified by column chromatography on silica gel using hexane-AcOEt from 95:5 to 9:1 as the eluent. The yields obtained in each experiment are reported in Table 3.

3.6. Characterization of Products

All products **2**, **3**, and **4** were characterized by comparison with the characterization data already reported by us [18].

4. Conclusions

In conclusion, we have found that the PdI₂/KI-catalyzed cycloisomerization of 2-(1-hydroxyprop-2-ynyl)phenols (**1**) to give 2-methylene-2,3-dihydrobenzofuran-3-ols (**2**) can be conveniently carried out in BmimBF₄ as the reaction medium. When compared with MeOH [18], the use of BmimBF₄ as the solvent required a higher temperature (100 °C vs. 40 °C) and a longer reaction time (5 h vs. 2 h); moreover, the yields obtained in BmimBF₄ were similar or slightly inferior with respect to those obtained under the

“classical” conditions (using MeOH as the solvent) [18]. However, the use of the ionic liquid has allowed to recycle the solvent-catalytic system several times, without appreciable loss of catalytic activity. Moreover, in BmimBF₄, 2-methylene-2,3-dihydrobenzofuran-3-ols (**2**) could be expediently converted into functionalized benzofurans (2-hydroxymethylbenzofurans **3** or 2-methoxymethylbenzofurans **4**) in a one-pot fashion by subsequent acid-catalyzed allylic isomerization or allylic nucleophilic substitution.

Acknowledgments

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Conflicts of Interest

The authors declare no conflict of interest.

References

1. Adcock, H.V.; Davies, P.W. π -Acid mediated insertion of alkynes into carbon-heteroatom σ -bonds. *Synthesis* **2012**, *44*, 3401–3420.
2. Yamamoto, Y. Transition-metal-catalyzed cycloisomerizations of α,ω -dienes. *Chem. Rev.* **2012**, *112*, 4736–4769.
3. Watson, I.D.G.; Toste, F.D. Catalytic enantioselective carbon-carbon bond formation using cycloisomerization reactions. *Chem. Sci.* **2012**, *3*, 2899–2919.
4. Marinetti, A.; Jullien, H.; Voituriez, A. Enantioselective, transition metal catalyzed cycloisomerizations. *Chem. Soc. Rev.* **2012**, *41*, 4884–4908.
5. Herndon, J.W. The Chemistry of the carbon–transition metal double and triple bond: Annual survey covering the year 2009. *Coord. Chem. Rev.* **2011**, *255*, 3–100.
6. Krause, N.; Winter, C. Gold-catalyzed nucleophilic cyclization of functionalized allenes: A powerful access to carbo- and heterocycles. *Chem. Rev.* **2011**, *111*, 1994–2009.
7. Belmont, P.; Parker, E. Silver and gold catalysis for cycloisomerization reactions. *Eur. J. Org. Chem.* **2009**, *2009*, 6075–6089.
8. Soriano, E.; Marco-Contelles, J. Mechanistic insights on the cycloisomerization of polyunsaturated precursors catalyzed by platinum and gold complexes. *Acc. Chem. Res.* **2009**, *42*, 1026–1036.
9. Majumdar, K.C.; Debnath, P.; Roy, B. Metal-catalyzed heterocyclization: Formation of five- and six-membered oxygen heterocycles through carbon-oxygen bond forming reactions. *Heterocycles* **2009**, *78*, 2661–2728.
10. Zeni, G.; Larock, R.C. Synthesis of heterocycles via palladium π -olefin and π -alkyne chemistry. *Chem. Rev.* **2004**, *104*, 2285–2309.
11. Gabriele, B.; Salerno, G.; Costa, M. PdI₂-catalyzed synthesis of heterocycles. *Synlett* **2004**, *14*, 2468–2483.
12. Gabriele, B.; Veltri, L.; Plastina, P.; Mancuso, R.; Vetere, M.V.; Maltese, V. Copper-catalyzed synthesis of substituted furans and pyrroles by heterocyclodehydration and tandem heterocyclodehydration-hydration of 3-yne-1,2-diols and 1-amino-3-yn-2-ol derivatives. *J. Org. Chem.* **2013**, *78*, 4919–4928.

13. Spina, R.; Colacino, E.; Gabriele, B.; Salerno, G.; Martinez, J.; Lamaty, F. Synthesis of pyrrolin-4-ones by Pt-catalyzed cycloisomerization in PEG under microwaves. *J. Org. Chem.* **2013**, *78*, 2698–2702.
14. Gabriele, B.; Mancuso, R.; Veltri, L.; Maltese, V.; Salerno, G. Synthesis of substituted thiophenes by palladium-catalyzed heterocyclodehydration of 1-mercapto-3-yn-2-ols in conventional and nonconventional solvents. *J. Org. Chem.* **2012**, *77*, 9905–9909.
15. Gabriele, B.; Mancuso, R.; Lupinacci, E.; Veltri, L.; Salerno, G.; Carfagna, C. Synthesis of benzothiophene derivatives by Pd-catalyzed or radical-promoted heterocyclodehydration of 1-(2-mercapto-phenyl)-2-yn-1-ols. *J. Org. Chem.* **2011**, *76*, 8277–8286.
16. Gabriele, B.; Plastina, P.; Vetere, M.V.; Veltri, L.; Mancuso, R.; Salerno, G. A simple and convenient synthesis of substituted furans and pyrroles by CuCl₂-Catalyzed heterocyclodehydration of 3-yne-1,2-diols and *N*-Boc- or *N*-Tosyl-1-amino-3-yn-2-ols. *Tetrahedron Lett.* **2010**, *51*, 3565–3567.
17. Gabriele, B.; Mancuso, R.; Lupinacci, E.; Spina, R.; Salerno, G.; Veltri, L.; Dibenedetto, A. Recyclable catalytic synthesis of substituted quinolines: Copper-catalyzed heterocyclization of 1-(2-aminoaryl)-2-yn-1-ols in ionic liquids. *Tetrahedron* **2009**, *65*, 8507–8512.
18. Gabriele, B.; Mancuso, R.; Salerno, G. A novel synthesis of 2-functionalized benzofurans by palladium-catalyzed cycloisomerization of 2-(1-hydroxyprop-2-ynyl)phenols followed by acid-catalyzed allylic isomerization or allylic nucleophilic substitution. *J. Org. Chem.* **2008**, *73*, 7336–7341.
19. Plastina, P.; Gabriele, B.; Salerno, G. Palladium-catalyzed oxidative aminocarbonylation of alkynols. *Synthesis* **2007**, 3083–3087.
20. Gabriele, B.; Mancuso, R.; Salerno, G.; Ruffolo, G.; Plastina, P. Novel and convenient synthesis of substituted quinolines by copper- or palladium-catalyzed cyclodehydration of 1-(2-aminoaryl)-2-yn-1-ols. *J. Org. Chem.* **2007**, *72*, 6873–6877.
21. Greaves, T.L.; Drummond, C.J. Solvent nanostructure, the solvophobic effect and amphiphile self-assembly in ionic liquids. *Chem. Soc. Rev.* **2013**, *42*, 1096–1120.
22. Rehman, A.; Zeng, X. Ionic liquids as green solvents and electrolytes for robust chemical sensor development. *Acc. Chem. Res.* **2012**, *45*, 1667–1677.
23. Patel, D.D.; Lee, J.-M. Applications of ionic liquids. *Chem. Rec.* **2012**, *12*, 329–355.
24. Wong, W.-L.; Wong, K.-Y. Recent development in functionalized ionic liquids as reaction media and promoters. *Can. J. Chem.* **2012**, *90*, 1–16.
25. Payagala, T.; Armstrong, D.W. Chiral ionic liquids: A compendium of syntheses and applications (2005–2012). *Chirality* **2012**, *24*, 17–53.
26. de Maria, P.D.; Yang, Z.; Kohlmann, C.; Greiner, L.; Lozano, P.; García-Verdugo, E.; Zhao, H.; Gamemara, D.; Saenz Méndez, P.; Dennewald, D.; *et al.* *Ionic Liquids in Biotransformations and Organocatalysis: Solvents and Beyond*; Domínguez de Maria, P., Ed.; Wiley-VCH: Weinheim, Germany, 2012.
27. Dupont, J. From molten salts to ionic liquids: A “nano” journey. *Acc. Chem. Res.* **2011**, *44*, 1223–1231.
28. Hallett, J.P.; Welton, T. Room-temperature ionic liquids: Solvents for synthesis and catalysis. *Chem. Rev.* **2011**, *111*, 3508–3576.

29. Hubbard, C.D.; Illner, P.; van Eldik, R. Understanding chemical reaction mechanisms in ionic liquids: Successes and challenges. *Chem. Soc. Rev.* **2011**, *40*, 272–290.
30. Zhang, Q.; Zhang, S.; Deng, Y. Recent advances in ionic liquid catalysis. *Green Chem.* **2011**, *13*, 2619–2637.
31. Wilkes, J.S.; Wasserscheid, P.; Welton, T.; Gordon, C.M.; Muldoon, M.J.; Wagner, M.; Hilgers, C.; Davis, J.H.; Holbrey, J.D.; Rogers, R.D.; *et al.* *Ionic Liquids in Synthesis*, 2nd ed.; Wasserscheid, P., Welton, T., Eds.; Wiley-VCH: Weinheim, Germany, 2008.
32. Ohtaka, A. Recyclable polymer-supported nanometal catalysts in water. *Chem. Rec.* **2013**, *13*, 274–285.
33. Gawande, M.B.; Branco, P.S.; Varma, R.S. Nano-magnetite (Fe₃O₄) as a support for recyclable catalysts in the development of sustainable methodologies. *Chem. Soc. Rev.* **2013**, *42*, 3371–3393.
34. Colacino, E.; Martinez J.; Lamaty, F.; Petrikeeva L.S.; Khemchyan, L.L.; Ananikov, V.P.; Beletskaya, I.P. PEG as an alternative reaction medium in metal-mediated transformations. *Coord. Chem. Rev.* **2012**, *256*, 2893–2920.
35. Yuan, D.; Huang, B. Progress in organic synthesis reactions catalyzed by palladium supported on magnetic nanoparticles. *Chin. J. Org. Chem.* **2012**, *32*, 1368–1379.
36. Liu, H.; Jia, Z.; Ji, S. Research progress in supported catalysts for Heck reaction. *Chin. J. Catal.* **2012**, *33*, 757–767.
37. Gu, Y. Multicomponent reactions in unconventional solvents: State of the art. *Green Chem.* **2012**, *14*, 2091–2128.
38. Arpad, M. Efficient, selective, and recyclable palladium catalysts in carbon-carbon coupling reactions. *Chem. Rev.* **2011**, *111*, 2251–2320.
39. Beletskaya, I.P.; Tyurin, V. Recyclable nanostructured catalytic systems in modern environmentally friendly organic synthesis. *Molecules* **2010**, *15*, 4792–4814.
40. Bellina, F.; Chiappe, C. The Heck reaction in ionic liquids: Progress and challenges. *Molecules* **2010**, *15*, 2211–2245.
41. Lim, C.W.; Lee, I.S. Magnetically recyclable nanocatalyst systems for the organic reactions. *Nano Today* **2010**, *5*, 412–434.
42. Gabriele, B.; Mancuso, R.; Salerno, G. Acid-catalysed or radical-promoted allylic substitution of 2-methylene-2,3-dihydrobenzofuran-3-ols with thiol derivatives: A novel and expedient synthesis of 2-(thiomethyl)benzofurans. *Eur. J. Org. Chem.* **2010**, *2010*, 3459–3464.
43. Gabriele, B.; Mancuso, R.; Salerno, G.; Plastina, P. A novel palladium-catalyzed dicarbonylation process leading to coumarins. *J. Org. Chem.* **2008**, *73*, 756–759.
44. Crosthwaite, J.M.; Aki, S.N.V.K.; Maginn, E.J.; Brennecke, J.F. Liquid phase behavior of imidazolium-based ionic liquids with alcohols. *J. Phys. Chem. B* **2004**, *108*, 5113–5119.

Sample Availability: Samples of the compounds **2a–j**, **3a–j**, and **4a–j** are available from the authors.