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# A further step to sustainable palladium catalyzed oxidation: Allylic oxidation of alkenes in green solvents

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ARTICLE INFO	A B S T R A C T				
<i>Keywords:</i> Alkenes, allylic oxidation Green solvents Molecular oxygen Palladium	The palladium catalyzed oxidation of alkenes with molecular oxygen is a synthetically important reaction which employs palladium catalysts in solution; therefore, a solvent plays a critical role for the process. In this study, we have tested several green solvents as a reaction medium for the allylic oxidation of a series of alkenes. Dimethylcarbonate, methyl isobutyl ketone, and propylene carbonate, solvents with impressive sustainability ranks and very scarcely exploited in palladium catalyzed oxidations, were proved to be excellent alternatives for the solvents conventionally employed in these processes, such as acetic acid. Palladium acetate alone or in the combination with <i>p</i> -benzoquinone efficiently operates as the catalyst for the oxidation of alkenes by dioxygen under 5–10 atm. For most substrates, the systems in green solvents showed better selectivity for allylic oxidation products as compared to pure acetic acid; moreover, the reactions in propylene carbonate solutions occurred even faster than in acetic acid.				

## 1. Introduction

The Wacker process for the synthesis of acetaldehyde by the palladium catalyzed oxidation of ethylene with dioxygen is one of the first and the most important applications of transition metal catalysis in industry [1,2]. The chemistry was further extended to higher alkenes opening a convenient pathway to many valuable compounds [3-18]. The use of environmentally benign dioxygen as the terminal oxidant is an important advantage, especially within modern green chemistry requirements. The main issue in palladium catalyzed oxidations consists in ensuring a rapid re-oxidation of reduced palladium, otherwise the irreversible formation of inactive palladium metal would interrupt the catalytic cycle. For this purpose, most applications use auxiliary redox active co-catalysts. The original Wacker catalyst contains CuCl<sub>2</sub> as the co-catalyst and operates at high concentrations of chloride ions [1]. In further developments, CuCl2 was substituted with less corrosive halide-free alternatives, e.g., heteropoly acids, p-benzoquinone (BQ), copper and iron salts [19-22]. In the last 15 years, palladium oxidation chemistry is experiencing a renaissance [4] due to the finding the way to avoid redox co-catalysts using special solvents or ligands. It was discovered that the re-oxidation of palladium by dioxygen could occur in dimethylsulfoxide (DMSO) [23,24] and dimethylacetamide (DMA) media [25-27] ("palladium solo" systems) or with the use of oxidatively

robust ligands (mostly nitrogen-based ligands) [3–7,13,28,29] able to stabilize reduced palladium in solutions ().

Although the most desirable option for liquid phase reactions would be neat conditions; solvents are often strongly required to dissolve the reactants and to control some problematic issues with selectivity, mass transfer, safety, and handling [30,31]. As the mass contribution of the solvent in a whole chemical process is significant; finding more sustainable solvent alternatives would represent an effective strategy to reduce a negative environmental impact [30,31]. As palladium catalyzed oxidations usually involve several simultaneously occurring redox reactions, the choice of solvent is particularly crucial for the catalytic activity and efficient catalyst turnover [11]. The industrial oxidation of ethylene is performed in aqueous solutions; however, organic solvents or mixed-solvent systems should be applied for higher alkenes due to solubility problems. To the best of our knowledge, highly hazardous organic solvents with low sustainability ranks, such as N, N-dimethylformamide, tetrahydrofuran, dichloroethane, DMA, dimethoxyethane, and dioxane, still dominate the scenario of the palladium catalyzed oxidation of alkenes in both laboratory and industry [11]. Acetic acid and DMSO, which are commonly employed in the palladium catalyzed allylic oxidations and in the "palladium solo" systems, are also considered as problematic solvents in modern solvent selection guides [32,33].

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In this study, our efforts have been focused on the development of "greener" solvent alternatives for the palladium catalyzed allylic oxidation of alkenes by dioxygen. Several compounds with high sustainability ranks and very scarcely exploited in palladium catalyzed oxidations, such as dimethylcarbonate (DMC), diethylcarbonate (DEC), methyl isobutyl ketone (MIBK), and propylene carbonate (PC) were tested for this purpose as reaction media for these reactions. Some mixed-solvent systems showed better results in terms of selectivity than pure HOAc and, for some alkenes, even allowed to dispense redox cocatalysts, with the palladium regeneration being performed directly by dioxygen. Pd(OAc)<sub>2</sub> alone or in the combination with BQ efficiently operates as the catalyst for the allylic oxidation of alkenes containing terminal, internal or endocyclic C-C double bonds. The substrate scope includes a series of biomass-based natural compounds, i.e., cis-jasmone, limonene,  $\beta$ -caryophyllene,  $\beta$ -ionone and  $\beta$ -citronellene, as well as 1octene and cyclohexene as model molecules.

## 2. Experimental

All reagents and solvents were acquired from commercial suppliers. *Cis*-jasmone [*cis*-3-methyl-2-(2-pentenyl)–2-cyclopenten-1-one], 1-octene, cyclohexene, (R)-(+)-limonene,  $\beta$ -caryophyllene [(-)-*trans* caryophyllene],  $\beta$ -ionone, *p*-benzoquinone (BQ) and Pd(OAc)<sub>2</sub> were received from Sigma-Aldrich. (-)- $\beta$ -Citronellene [dihydromyrcene, (R)-(-)-3,7-dimethyl-1,6-octadiene] was acquired from Fluka. BQ was purified by column chromatography (silica) using dichloromethane as the eluent. Dimethyl carbonate (DMC) (anhydrous,  $\geq$  99%), diethyl carbonate (DEC) (99%), methyl isobutyl ketone (MIBK) ( $\geq$  98.5%) and propylene carbonate (PC) (anhydrous, 99.7%), were purchased from Sigma-Aldrich. Glacial acetic acid used as a solvent was from VETEC.

Catalytic tests were run in a homemade autoclave with magnetic stirring and a valve dip tube for sampling without the depressurization. Typically, the solution (total volume of 10 mL) of the alkene (0.20 M), palladium acetate (5-10 mM), BQ (if any, 50 mM), and internal standard (bornyl acetate, 0.10 M) was transferred into the reactor. At the end of the run, the autoclave was cooled to room temperature and oxygen was slowly vented out. CAUTION: reactions under superatmospheric pressure of oxygen can cause an unforeseen explosion. These reactions must only be conducted using the appropriate equipment and with rigorous safety precautions. The reaction progress was monitored by gas phase chromatography (GC) analysis of the aliquots periodically sampled from the reactor (GC- Shimadzu GC2010 instrument, FID, Rtx-Wax 30 m or Rtx-5MS 30 m columns). Conversion and selectivity calculations were based on the reacted substrate. Bornyl acetate was used as the internal standard. Average reaction rates were calculated between 0 and ca. 40% conversions.

Reaction products were analyzed/identified by gas chromatography/mass spectrometry (GC-MS, Shimadzu QP2010-PLUS equipment operating at 70 eV) or by NMR spectroscopy (Bruker 400 MHz, CDCl<sub>3</sub>, TMS) after the isolation by a column chromatography (silica gel 60; eluents: hexane and ethyl acetate).

Compound **1b** (two isomers): MS (70 eV, EI): m/z (%): *cis* isomer (shorter GC retention time): 180 (16), 177 (15), 162 (53) [M+-HOAC], 151 (20), 149 (68), 147 (23), 133 (100), 123 (91), 119 (25), 105 (66), 93 (18), 91 (60), 79 (27), 77 (32), 65 (19), 60 (28), 55 (15); *trans* isomer (longer GC retention time): 222 (0.02) [M<sup>+</sup>], 180 (18), 162 (50) [M+HOAC], 151 (21), 147 (22), 133 (41), 123 (100), 119 (18), 105 (40), 91 (40), 77 (19), 65 (9), 55 (12). For NMR data see [34].

Compound **1c**: MS (70 eV, EI): *m/z* (%): 164 (100) [M<sup>+</sup>], 149 (68), 135 (61), 131 (46), 122 (75), 121 (35), 110 (54), 109 (25), 107 (45), 105 (27), 93 (81), 91 (76), 81 (21), 79 (95), 77 (55), 67 (18), 65 (20), 55 (34). For NMR data see [34].

Compound **2b**: MS (70 eV, EI): *m/z* (%):128 (4) [M<sup>+</sup>], 113 (4) [M+-CH<sub>3</sub>], 85 (10), 71 (21), 59 (19), 58 (100).

Compound **3b**: MS (70 eV, EI): *m/z* (%): 140 (11) [M<sup>+</sup>], 98 (81), 97 (31), 83 (30), 81 (27), 80 (49), 79 (100), 70 (27). For NMR data see [35].

Compound **4b** (two isomers): MS (70 eV, EI): *m/z* (%): *trans* isomer (shorter GC retention time): 152 (76), 134 (35) [M+–HOAC], 119 (88) [M+–HOAC–CH<sub>3</sub>], 109 (100), 105 (29), 93 (30), 92 (30), 91 (58) 84 (73), 79 (21), 77 (18); *cis* isomer (longer GC retention time): 152 (59), 134 (53) [M+–HOAC], 119 (100) [M+–HOAC–CH<sub>3</sub>], 109 (88), 105 (32), 93 (29), 92(30), 91(76), 84 (94), 79 (24), 77 (18). For NMR data see [36].

Compound **4c** (two isomers): MS (70 eV, EI): m/z (%): *trans* isomer (shorter GC retention time): 152 (35), 134 (71) [M+–HOAc], 119 (100) [M+–HOAc–CH<sub>3</sub>], 109 (59), 106 (35), 105 (41), 93 (52), 92 (54), 91 (94), 84 (18), 79 (35), 77 (18), 68 (24), 67 (23); *cis* isomer (longer GC retention time): 152 (6), 134 (47) [M+–HOAc], 119 (88) [M+–HOAc–CH<sub>3</sub>], 106 (100), 105 (41), 93 (38), 92 (44), 91 (71), 84 (23), 79 (47), 77 (22), 68 (35), 67 (37) [37]. For NMR data see [38].

Compound **4d**: MS (70 eV, EI): *m/z* (%): 152 (38), 134 (56) [M+–HOAc], 119 (88) [M+–HOAc–CH<sub>3</sub>], 106 (43), 105 (43), 93 (50), 92 (62), 91 (100), 84 (31), 79 (38), 68 (56), 67 (44). For NMR data see [38].

Compound **5b** (two isomers): MS (70 eV, EI): m/z (%): first isomer (shorter GC retention time): 202 (10) [M+-HOAC], 187 (22) [M+-HOAC-CH<sub>3</sub>], 173 (17), 159 (34), 146 (18), 145 (28), 133 (27), 132 (18), 131 (54), 120 (16), 119 (42), 118 (67), 117 (58), 107 (23), 106 (19), 105 (61), 93 (37), 92 (22), 91 (100), 81 (17), 79 (51), 77 (36), 69 (40), 67 (29), 65 (16), 60 (20), 55 (26); second isomer (longer GC retention time): 202 (9) [M+-HOAC], 187 (20) [M+-HOAC-CH<sub>3</sub>], 173 (18), 159 (32), 146 (17), 145 (28), 133 (25), 132 (15), 131 (53), 120 (15), 119 (40), 118 (60), 117 (52), 107 (24), 106 (19), 105 (66), 93 (37), 92 (21), 91 (100), 81 (20), 79 (51), 77 (34), 69 (35), 67 (28), 65 (16), 60 (20), 55 (27). For NMR data see [39].

Compound **5c**: MS (70 eV, EI): *m/z* (%): 202 (13) [M+-HOAc], 187 (26) [M+-HOAc-CH<sub>3</sub>], 173 (24), 159 (36), 146 (21), 145 (34), 133 (30), 132 (20), 131 (63), 120 (16), 119 (39), 118 (31), 117 (48), 107 (23), 106 (20), 105 (63), 93 (39), 92 (22), 91 (100), 81 (15), 79 (51), 77 (34), 69 (39), 67 (27), 65 (16), 60 (15), 55 (24). For NMR data see [39].

Compound **5d**: MS (70 eV, EI): *m/z* (%): 205 (3) [M+-CH<sub>3</sub>], 131 (29), 123 (24), 121 (40), 119 (28), 109 (44), 107 (55), 106 (33), 105 (53), 96 (30), 95 (60), 93 (89), 91 (88), 82 (23), 81 (48), 79 (100), 77 (42), 69 (64), 67 (51), 55 (40).

Compound **6b**: MS (70 eV, EI): *m/z* (%): 250 (0.5) [M<sup>+</sup>], 235 (8) [M+-CH<sub>3</sub>], 190 (27) [M+-HOAC], 175 (100), 157 (20), 147 (37), 134 (22), 133 (22), 131 (28), 119 (20), 105 (27), 91 (28). For NMR data see [40].

Compound **6c**: MS (70 eV, EI): *m/z* (%): 188 (4) [M<sup>+</sup>], 173 (100) [M+-CH<sub>3</sub>], 145 (13), 144 (11), 130 (16), 129 (27), 128 (16), 115 (12). For NMR data see [40].

Compound **6d**: MS (70 eV, EI): *m/z* (%): 193 (1) [M+-CH<sub>3</sub>], 177 (75), 165 (45), 135 (1314), 124 (910), 123 (100), 109 (7), 107 (78), 95 (810), 91 (47), 79 (46), 69 (34).

Compound **7b**: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 25 °C, TMS):  $\delta$  = 5.57–5.64 (m, 1 H), 5.38, (t, J = 4.5, 1 H), 4.89 (d, J = 14.3 Hz, 1 H), 4.86 (d, J = 9.7 Hz, 1 H), 4.38 (s, 2 H), 2.00–2.10 (m, 1 H), 1.99 (s, 3 H), 1.90–2.00 (m, 2 H), 1.57 (s, 3 H), 1.25–1.30 (m, 2 H), 0.93 ppm (d, J = 4.4 Hz, 2 H); <sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>, 25 °C, TMS):  $\delta$  = 171.2, 144.6, 130.2, 130.1, 113.0, 70.6, 37.7, 36.3, 25.7, 21.2, 20.4, 14.16 ppm. NMR data are in accordance with those published in [41].

## 3. Results and discussion

*Cis*-jasmone (**1a**), a natural compound found in the jasmine essential oil, is commonly utilized as fragrance component in many commercial products. We have reported recently the first palladium catalyzed oxidation of this alkene by dioxygen [34]. In the present work, which is directed to finding green reaction media for allylic oxidations, we have chosen *cis*-jasmone as a model substrate.

The oxidation of *cis*-jasmone in the solutions of HOAc containing catalytic quantities of Pd(OAc)<sub>2</sub> and BQ gave mainly allylic acetate **1b** 

	5	10	5 5 5				
0 1a		[Pd] HOAc O <sub>2</sub>		OAc	+ O 1c		
Run	Co-solvent	Т	Time	Conversion	Selectivity for allylic oxidation (%)		Rate <sup>b</sup>
	(vol%)	(°C)	(h)	(%)	1b	total	$(mM h^{-1})$
1 <sup>c</sup>	None	80	0.5	75	82	93	300
			2	96	80	95	
$2^{c}$	DMC (50)	80	0.5	63	85	93	252
			2	98	82	96	
3	DMC (50)	80	0.5	59	78	85	236
			4	99	76	86	
4	DMC (50)	60	1	52	85	95	104
			4	96	85	96	
5	None	60	1	62	55	65	124
			4	96	59	67	
6 <sup>d</sup>	DMC (50)	60	1	25	83	96	100
			8	90	85	96	
7 <sup>e</sup>	DMC (50)	60	1	25	85	95	50
			8	95	86	96	
$8^{\rm f}$	DMC (50)	60	1	20	83	93	40
			8	90	86	97	
9	DMC (70)	60	1	26	85	95	52
			8	88	83	95	
10	DEC (50)	60	1	44	89	96	88
			4	98	83	95	
11	MIBK (50)	60	1	18	90	98	36
			8	90	85	96	
12	MIBK (70)	70	1	34	90	98	70
			6	90	86	98	

<sup>a</sup> Conditions: [*cis*-jasmone] = 0.20 M, [Pd(OAc)<sub>2</sub>] = 10 mM, gas phase – O<sub>2</sub>, 10 atm, solvent – HOAc. Conversion and selectivity calculations were based on the reacted substrate. The rest of the mass balance was mainly due to compound **1c**. DMC – dimethylcarbonate; DEC – diethylcarbonate; MIBK – methyl isobutyl ketone. <sup>b</sup> Average rate calculated between 0 and ca. 40% conversion. <sup>c</sup> [*p*-benzoquinone] = 50 mM. <sup>d</sup> [*cis*-jasmone] = 0.40 M. <sup>e</sup>[Pd(OAc)<sub>2</sub>] = 5 mM. <sup>f</sup> O<sub>2</sub> - 5 atm.

(80% selectivity, ca. 95% *trans*) along with a mixture of other isomeric allylic acetates having the double bond in different positions of the side pentenyl fragment (Table 1, run 1). Along with the allylic oxidation products (total selectivity of 95%), the isomer of *cis*-jasmone, compound **1c**, containing two conjugated C-C double bonds was also formed with ca. 5% selectivity (Table 1). All oxidation products were derived from the reaction of the disubstituted exocyclic C=C bond, whereas the endocyclic tetrasubstituted C=C bond remained intact. A possible reason for low reactivity of the endocyclic C=C bond could be its deactivation by the allylic C=O group. The same reaction performed in a 50 vol% mixture of HOAc and dimethylcarbonate (DMC) was slightly slower; however, it showed nearly the same product selectivity (Table 1, run 2 vs. run 1). DMC is a green biodegradable solvent with low toxicity and much better sustainability score in the solvent selection guides than acetic acid [33].

To our surprise, the oxidation of *cis*-jasmone was catalytic with respect to palladium in the mixed DMC/HOAc solvent even without BQ (Table 1, run 3). At 80 °C, the total selectivity for allylic oxidation was lower than with BQ (86% vs. 96%) due to the contribution of high molecular weight products which could not be detected by GC. However, the selectivity could be improved at lower temperature, 60 °C (Table 1, run 4). Although the reaction occurred slower, it could be nearly completed in 4 h with 85% selectivity for the main product 1b and 96% total selectivity for the allylic acetates. Thus, under the applied conditions, Pd(OAc)<sub>2</sub> operated as a sole catalyst without the assistance of additional redox co-catalysts (i.e., "palladium solo" system). Species of the reduced palladium seem to be stabilized in the solution sufficiently for the direct re-oxidation by dioxygen before their

agglomeration into inactive metal. For comparison, the same reaction in the absence of BQ was run in pure HOAc (Table 1, run 5 vs. run 4). Although no palladium metal was detected, selectivity for allylic oxidation dropped to 67%, with the rest of the mass balance being due to high molecular weight products which could not be detected by GC. This result confirmed the essential role of DMC as the co-solvent in supporting the catalytic cycle at the *cis*-jasmone oxidation.

The reactions with a doubled amount of *cis*-jasmone or with a half amount of palladium acetate gave nearly the same yield of allylic acetates, which means that a turnover number was also doubled, thus illustrating the catalyst stability (Table 1, runs 6 and 7 vs. run 4). The rate positively depended on the palladium concentration (nearly first order) and on the dioxygen pressure (also nearly first order) implying that the regeneration of palladium is probably the slowest reaction of the catalytic process (Table 1, run 4 vs. run 7 and run 8, respectively). The process was successfully performed under 5 atm of dioxygen (Table 1, run 8); however, under 1 atm the catalyst regeneration was not efficient and palladium metal appeared on the reactor walls (nor shown in Table 1). The proportion of DMC in the solvent mixture could be increased to 70 vol% without a negative impact on the reaction selectivity, albeit the reaction was decelerated (Table 1, run 9 vs. run 4).

Diethyl carbonate (DEC) and methyl isobutyl ketone (MIBK) were also tested as the reaction media for the *cis*-jasmone oxidation in the "palladium solo" system (Table 1, runs 10, 11 and 12). Both DEC and MIBK have excellent rankings in solvent sustainability guides occupying the positions comparable with those of ethanol and water [32,33]. The replacement of DMC by DEC did not affect the reaction performance (Table 1, run 10 vs. run 4). In the MIBK/HOAc mixture, the reaction

Oxidation of alkenes with dioxygen catalyzed by Pd(OAc)2<sup>a</sup>.



<sup>a</sup> Conditions: [substrate] = 0.20 M, [Pd(OAc)<sub>2</sub>] = 10 mM, gas phase –  $O_2$ , 10 atm, solvent – HOAc. Conversion and selectivity calculations were based on the reacted substrate. DMC – dimethylcarbonate; DEC – diethylcarbonate; MIBK – methyl isobutyl ketone.

<sup>b</sup> Average rate calculated between 0 and ca. 40% conversion.

occurred slower as compared to DMC and DEC but with the same selectivity (Table 1, runs 11 vs. runs 4 and 10). A slight temperature increase (from 60 to 70 °C) allowed to accelerate the reaction and to decrease the HOAc content in the MIBK reaction mixture (Table 1, run 12). Main product **1b** was obtained with 86% selectivity at 90% conversion for 6 h, with the total selectivity for the allylic oxidation being 98%. As a positive result, it can be noted that the runs in mixed solvents showed better selectivity for main acetate **1b** as compared with the reaction in pure acetic acid (Table 1, runs 1 and 5). It seems that the C-C double bond isomerization in *cis*-jasmone and other undesirable transformations are less favored in the solutions with lower acidity. As reported in our previous work [34], the mixtures of allylic acetates obtained from *cis*-jasmone have a pleasant smell and could be utilized in flavor formulations directly.

Encouraged by the results obtained with *cis*-jasmone, we have applied the "palladium solo" system in mixed solvents for other alkenes (Table 2). First, we tested 1-octene (**2a**) and cyclohexene (**3a**) as model molecules. The oxidation of the terminal C=C bond in 1-octene occurred smoothly in both DMC/HOAc and MIBK/HOAc mixtures (Table 2, runs 1, 2 and 3). No formation of palladium metal occurred in these runs indicating the effective catalyst regeneration. Three isomeric allylic acetates with different locations of the alkene and acetate functionalities were detected as main products with up to 75% total selectivity, along with smaller amounts (20–30%) of 2-octanone **2b**. The selectivity for oxidation in mixed solvents was much higher than in pure acetic acid (Table 2, run 4). The formation of several isomeric allylic

acetates indicated a significant isomerization of the C=C bond in 1octene under the applied conditions. The oxidation of cyclohexene under similar conditions resulted exclusively in allylic acetate **3b** (Table 2, runs 5, 6 and 7). The re-oxidation of palladium was also efficient as no Pd mirror was detected on the reactor walls. However, the conversion of cyclohexene became stagnated at ca. 60% in the DMC and at ca. 30% in MIBK solutions.

The oxidation of trisubstituted endocyclic C=C bonds in limonene (4a) and  $\beta$ -caryophyllene (5a) gave corresponding allylic acetates. However, the selectivity for allylic oxidation was only ca. 40% in both reactions (Table 2, runs 8 and 9). In the run with  $\beta$ -caryophyllene, the product of the endocyclic C=C bond epoxidation (epoxide 5d) was also identified as one of the main products (25% selectivity). The molecule of the next substrate,  $\beta$ -ionone (6a), contains two C-C double bonds: the endocyclic tetrasubstituted and exocyclic disubstituted ones.  $\beta$ -Ionone has showed a relatively high reactivity in the mixed DMC/HOAc solvent being almost completely converted for 6 h at 60 °C (Table 2, run 10). The reaction gave epoxide 6d with 50% selectivity, originated by the oxidation of the endocyclic C=C bond, along with a complex mixture of unidentified products. The only identified product formed from  $\beta$ -citronellene (7a) was allylic acetate 7b derived from the oxidation of the trisubstituted internal C=C bond (Table 2, run 11).

In all reactions shown in Table 2, the palladium re-oxidation was performed directly by dioxygen, i.e., Pd(OAc)<sub>2</sub> operated as the sole catalyst. Although all the alkenes demonstrated a reasonable reactivity in the "palladium solo" system, most of the reactions were either low





<sup>a</sup> Conditions: [cyclohexene] = 0.20 M, [Pd(OAc)<sub>2</sub>] = 10 mM, [*p*-benzoquinone (BQ)] = 50 mM, gas phase – O<sub>2</sub>, 10 atm, 60 °C. Conversion and selectivity calculations were based on the reacted substrate. DMC – dimethyl carbonate; DEC – diethyl carbonate; MIBK – methyl isobutyl ketone; PC – propylene carbonate.

<sup>b</sup> Average rate calculated between 0 and ca. 40% conversion.

<sup>c</sup> 70 °C.

## Table 4 Oxidation of alkenes with dioxygen catalyzed by Pd(OAc)<sub>2</sub>/BQ in dimethyl carbonate (DMC) solutions<sup>3</sup>.



<sup>a</sup> Conditions: [substrate] = 0.20 M, [Pd(OAc)<sub>2</sub>] = 10 mM, [p-benzoquinone (BQ)] = 50 mM, gas phase –  $O_2$ , 10 atm, solvent – DMC. Conversion and selectivity calculations were based on the reacted substrate.

<sup>b</sup> Average rate calculated between 0 and ca. 40% conversion.

selective towards the allylic oxidation or became stagnated at incomplete conversions (cyclohexene). To overcome these limitations, we decided to add BQ in catalytic amounts to the system. Besides the function to re-oxidize palladium during the catalytic cycle, BQ acts as a ligand for palladium and is known to be often capable to improve the catalyst performance. As for the regeneration of BQ, we have previously found that the oxidation of hydroquinone (BQH<sub>2</sub>, the reduced form of BQ) can be performed directly by molecular oxygen under 5–10 atm [42]. Contrarily, under the atmospheric pressure, the reaction of BQH<sub>2</sub> with molecular oxygen is slow and requires the presence of additional

Oxidation of alkenes with dioxygen catalyzed by Pd(OAc)<sub>2</sub>/BQ in methyl isobutyl ketone (MIBK) solutions<sup>a</sup>.



<sup>a</sup> Conditions: [substrate] = 0.20 M, [Pd(OAc)<sub>2</sub>] = 10 mM, [p-benzoquinone (BQ)] = 50 mM, gas phase – O<sub>2</sub>, 10 atm, solvent – MIBK. Conversion and selectivity calculations were based on the reacted substrate.

<sup>b</sup> Average rate calculated between 0 and ca. 40% conversion.

metal co-catalysts, such as copper or manganese salts [8,19,22].

The aim of our further study was to find optimal conditions for the efficient and selective allylic oxidation of alkenes in green reaction media using minimal amounts of acetic acid as the reactant. Cvclohexene, the molecule with no options for the double bond isomerization, was chosen as a model substrate (Table 3). Really, the addition of BQ had a beneficial effect on the reaction, which was completed for 2 h to give allylic acetate **3b** in nearly quantitative yield (run 1 in Table 3 vs. run 6 in Table 2). The oxidation of cyclohexene in DMC/HOAc mixtures occurred slower than in pure acetic acid (Table 3, runs 3-5 vs. run 2). However, the reaction was reasonably fast to be nearly completed in 8 h at 60 °C even with only 10 vol% of HOAc (corresponding to ca. 9 molar equivalents with respect to the substrate, Table 3, run 5). The selectivity for allylic acetate 3b, was improved in DMC solutions as compared to pure acetic acid allowing for nearly quantitative yields. MIBK can be also used as a reaction medium for the oxidation of cyclohexene (Table 3, runs 6 and 7). The reaction rate in MIBK solutions was lower then in DMC at the same concentration of acetic acid (Table 3, run 6 vs. run 4).

Propylene carbonate (PC) is also recognized as an eco-friendly alternative for traditional organic solvents due to its low toxicity, biodegradability, low corrosivity and other attractive characteristics which render PC an excellent position in modern solvent sustainability guides, even better than MIBK and DMC [33,43]. In the present study, we have demonstrated, for the first time to the best of our knowledge, a high potential of PC as a green solvent for the palladium catalyzed oxidation of alkenes. The allylic oxidation of cyclohexene proceeded in the PC solutions at nearly the same rate as in pure HOAc and with even better selectivity (Table 3, runs 8 and 9 vs. run 2). The reaction could be completed in 4 h at 60 °C in the presence of 20 vol% of HOAc (Table 3, run 9). A further reduction in the HOAc concentration was not possible

to perform due to the problems with the solubility of alkene as PC ( $\varepsilon = 64$ ) is much more polar than HOAc ( $\varepsilon = 6$ ), MIBK ( $\varepsilon = 13$ ), and DMC ( $\varepsilon = 3$ ). It should be mentioned that in all other solvents tested (DMC, DEC and MIBK) no problems with miscibility of the components were detected under the conditions employed. The reaction in the PC solution occurred faster than in DMC and MIBK at the same concentrations of HOAc (Table 3, cf. runs 4, 6 and 9). No formation of acetate esters from acetic acid and DMC, DEC or PC was detected under the reaction conditions employed.

The scope of the substrates for the Pd/BQ catalyzed allylic oxidation in green solvents was extended to several other alkenes with different types of C-C double bonds. Representative data obtained by the optimization of reaction variables are collected in Table 4 for DMC, Table 5 for MIBK and Table 6 for PC. For the comparison, the data on the oxidation of these substrates in HOAc solutions under similar conditions are shown in Table 7. The reaction of cis-jasmone (1a) gave allylic acetate 1b as the main product in higher selectivity (ca. 90%) than in pure HOAc (runs 1 and 2 in Table 4, vs. run 2 in Table 7). 1-Octene (2a) and cyclohexene (3a) also gave almost exclusively the corresponding allylic acetates in DMC solutions containing only 10-20 vol% of HOAc (Table 4, runs 3 and 4). For all the substrates, lowering the HOAc concentration in DMC decelerated the reaction. For limonene (4a) and  $\beta$ -caryophyllene (5a), the best balance was achieved at 20 vol% of HOAc (Table 4, runs 5 and 6). For both substrates, only endocyclic double bonds reacted with palladium to give a mixture of allylic acetates in a total selectivity of ca. 90%. The terminal disubstituted double bonds in both molecules 5a and 6a remained intact. A similar situation occurred with  $\beta$ -ionone (**6a**) (Table 4, run 7). The main product **6b** originated by the oxidation of the endocyclic tetrasubstituted double bond, whereas the disubstituted internal C=C bond in a side chain remained intact

Oxidation of alkenes with dioxygen catalyzed by Pd(OAc)<sub>2</sub>/BQ in propylene carbonate (PC) solutions<sup>a</sup>.



<sup>a</sup> Conditions: [substrate] = 0.20 M, [Pd(OAc)<sub>2</sub>] = 10 mM, [*p*-benzoquinone (BQ)] = 50 mM, gas phase –  $O_2$ , 10 atm, solvent – PC. Conversion and selectivity calculations were based on the reacted substrate. <sup>b</sup> Average rate calculated between 0 and ca. 40% conversion.

(probably, due to the deactivation by the allylic C=O group). Due to the relatively low reactivity of  $\beta$ -ionone, reasonable reaction rates were obtained only with 40 vol% of HOAc, otherwise the reaction required for longer reaction times. The reaction with  $\beta$ -citronellene (**7a**) showed excellent selectivity for allylic acetate **7b** originated by the oxidation of the trisubstituted C-C double bond. The terminal monosubstituted olefinic bond was not involved in the oxidation. The only hydrogen in the position allylic to the terminal C=C bond in **7a** is attached to the tertiary carbon atom and therefore it is not easily abstractable, which could be the reason of the low reactivity of this bond towards oxidation under the applied conditions.

MIBK was also found to be an excellent green reaction medium for the palladium catalyzed oxidation of alkenes (Table 5). Similar to that observed in DMC, the reactions occurred slower at lower acetic acid concentrations. Nevertheless, under optimized conditions, all the substrates studied were oxidized in the presence of 10–30 vol% of HOAc at reasonable rates to give corresponding allylic acetates with 85–100% selectivity. Although in most cases, the reactions in MIBK solutions were slower than in pure acetic acid, the selectivity for the allylic oxidation was the same for substrates **4a** and **7a** and higher for the other alkenes (cf. Table 5 and Table 7).

To check the possibility to obtain ketones from olefins, we performed the reactions with *cis*-jasmone (**1a**) under the conditions of run 2 in Table 4 and run 2 in Table 5 using 10 vol% of water instead of acetic acid in DMC and MIBK, respectively. Due to miscibility problems, it was not possible to use more than 10 vol% of water in these solvents. Unfortunately, the attempts were not successful. Practically no olefin conversion was observed in these reactions; moreover, the catalytic system was not stable under such conditions, with palladium mirror being detected on the walls of the reactor after the runs.

Promising results were also obtained for most of the substrates in PC solutions (Table 6). However, high polarity of this solvent could cause the problems with solubility or selectivity. In particular, the oxidation of cis-jasmone (1a) was heavily complicated by a rapid substrate isomerization to give conjugated diene 1c. After 1 h, the reaction showed 82% conversion and only 28% selectivity for allylic oxidation product 1b, with the rest of cis-jasmone being converted into 1c (Table 6, run 1). At longer reaction time, the selectivity for 1b was gradually increased due to the oxidation of 1c by palladium and/or the shift of the isomerization equilibrium towards the more reactive isomer, cis-jasmone 1a, and its further oxidation. All other substrates, except  $\beta$ -caryophyllene (5a), showed excellent performance in PC solutions and gave corresponding allylic oxidation products with 80-98% selectivity at almost complete conversions (Table 6). The content of HOAc in the PC solutions should be at least 20-30 vol%, otherwise the problems with the alkene and/or product solubility appear. For  $\beta$ -caryophyllene (5a), the bulkiest substrate among the alkenes studied, the solubility problems were observed even with 30 vol% of HOAc (Table 6, run 6). The reaction of  $\beta$ -carvophyllene showed high selectivity for allylic oxidation products 5b and 5c up to ca. 40% conversion, after that the reaction mixture turned murky. It is worth mentioning that under the same conditions, the reactions with all alkenes were faster in PC solutions than in DMC and MIBK. Moreover, the reactions in PC were faster than even in pure acetic acid (cf. Table 6 and Table 7). It should be mentioned that for all substrates, the allylic oxidation selectivity was higher or at least the same in PC as well as in DMC and MIBK solutions as compared to the reactions performed in pure acetic acid under similar conditions (Table 7 vs. Tables 4-6).

Oxidation of alkenes with dioxygen catalyzed by Pd(OAc)<sub>2</sub>/BQ in HOAc solutions<sup>a</sup>.



<sup>a</sup> Conditions: [substrate] = 0.20 M, [Pd(OAc)<sub>2</sub>] = 10 mM, [p-benzoquinone (BQ)] = 50 mM, gas phase –  $O_2$ , 10 atm, solvent – acetic acid. Conversion and selectivity calculations were based on the reacted substrate.

<sup>b</sup> Average rate calculated between 0 and ca. 40% conversion.

## 4. Conclusions

As the solvent plays a central role in sustainability, employing solvents with good sustainability ranks is the issue of a great importance for reducing a negative environmental impact of the industrial process. In this work we proposed several green reaction media for the palladium catalyzed allylic oxidation of alkenes by dioxygen. Dimethylcarbonate (DMC), methyl isobutyl ketone (MIBK), and propylene carbonate (PC), the compounds with excellent positions in modern solvent selection guides and very scarcely exploited in palladium catalyzed oxidations, were proved to be excellent alternatives for conventionally used solvents, such as HOAc. The systems with green solvents mostly showed better selectivity than the reactions in pure HOAc and, for some alkenes, even allowed to dispense the use of additional co-catalysts, e.g., p-benzoquinone. Palladium acetate alone or in the combination with p-benzoquinone efficiently operates as the catalyst for the allylic oxidation of alkenes with different types of C=C bonds. The regeneration of *p*-benzoquinone was performed directly by dioxygen at 5-10 atm. We tested a broad range of substrates: a-alkenes and alkenes containing internal disubstituted, trisubstituted and tetrasubstituted C=C bonds, including several biomass-based challenging alkenes. In comparison with pure acetic acid, the reactions in DMC and MIBK solutions were slower for most of the substrates tested, whereas the reactions in PC solutions were faster. Thus, we conclude that DMC, MIBK and PC are highly recommended solvents for the palladium catalyzed allylic oxidation of alkenes, in terms of both the catalyst performance and sustainability.

## CRediT authorship contribution statement

Maíra dos Santos Costa: Conceptualization, Methodology,

Investigation, Writing – original draft. Amanda de Camargo Faria: Methodology, Investigation, Validation. Rayssa L.V. Mota: Methodology, Investigation. Elena V. Gusevskaya: Conceptualization, Supervision, Project administration, Writing – review & editing.

### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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