The Reims Journey Towards Discovery and Understanding of Pd-Catalyzed Oxidations

Jean Le Bras, Jacques Muzart

To cite this version:

Jean Le Bras, Jacques Muzart. The Reims Journey Towards Discovery and Understanding of Pd-Catalyzed Oxidations. Catalysts, 2020, 10 (1), pp.111. 10.3390/catal10010111 . hal-02524094

HAL Id: hal-02524094
https://hal.univ-reims.fr/hal-02524094v1

Submitted on 25 Jun 2020

catalysts

Review

The Reims Journey Towards Discovery and Understanding of Pd-Catalyzed Oxidations

Jean Le Bras and Jacques Muzart *

Institut de Chimie Moléculaire de Reims, UMR 7312, CNRS-Université de Reims Champagne-Ardenne,
B.P. 1039, 51687 Reims Cedex 2, France; jean.lebras@univ-reims.fr
* Correspondence: jacques.muzart@univ-reims.fr

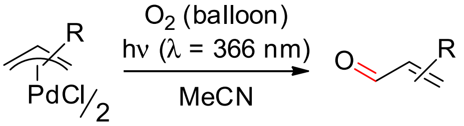
Received: 9 December 2019; Accepted: 7 January 2020; Published: 12 January 2020

Abstract: This review recounts the development by the authors of the Pd-catalyzed procedures devoted to various kinds of oxidation. Starting with reactions assisted with UV light, the research has explored reactions under light-free conditions: allylic oxidation, alcohol oxidation, etherification, Wacker oxidation and dehydrogenations with, always, accompanying efforts towards mechanism determination.

Keywords: palladium; catalysis; oxidations; dehydrogenations; C–H activation

1. Introduction

Our initial studies on Pd-catalyzed oxidations results from our observation in the early 1980s of the formation of unsaturated carbonyl compounds from irradiation with UV light of bis(μ-chloro)bis(η^3-allyl)dipalladium complexes in oxygenated acetonitrile (Scheme 1) [1]. That result urged us to look for such reactions under catalytic conditions. This activity progressively led us to study a variety of Pd-catalyzed oxidations under light-free conditions. The aim of the present account is to highlight the main results that we obtained in the area over the years.

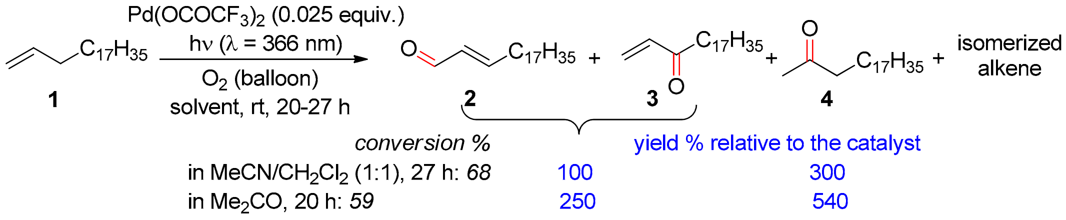


Scheme 1. Photocatalyzed oxidation of bis(μ-chloro)bis(η^3-allyl)dipalladium complexes

2. UV-Light-Assisted Oxidation

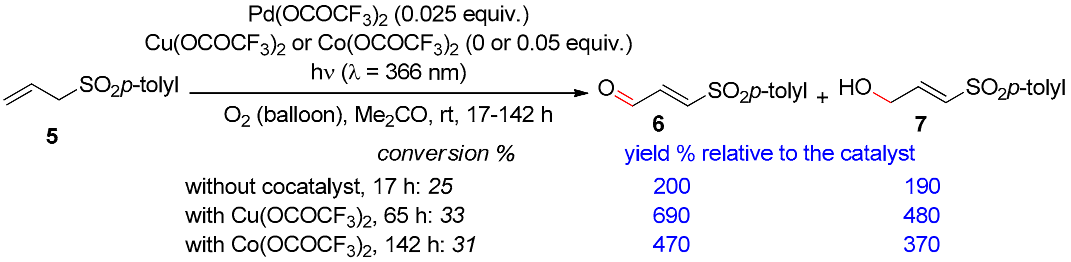
2.1. Ethylenic Compounds

The easy formation at room temperature of η^3-allylpalladium complexes from alkenes and $Pd(OCOCF_3)_2$ reported by Trost and Metzner [2] urged us to use this Pd salt as a catalyst for the photo-assisted oxidation of alkenes [3,4]. For an example, the reaction of 1-eicosene (**1**) in $MeCN/CH_2Cl_2$ afforded a mixture of saturated and unsaturated ketones **2** to **4** (Equation (1)). Some migration of the double bond of **1** was a competing reaction [5,6]. In contrast to the isomerization, ketones **2** to **4** were not produced in the absence of light. Switching to acetone as the solvent increased the ketone yields. Similar results were obtained using $[(\eta^3\text{-}CH_2CHCHC_3H_7)Pd(OCOCF_3)]_2$ as the catalyst whereas the turnover number was inferior to 1 with $Pd(OAc)_2$ [4]. Under alkene-free conditions, monitoring the irradiation of an acetone solution of $Pd(OCOCF_3)_2$ showed the adsorption of oxygen [4]. That led us to suspect the formation of peroxydic species. Nevertheless, ketones **2** to **4** were also produced from the reaction of **1** in the presence of radical and $^1O_2$ traps [4].



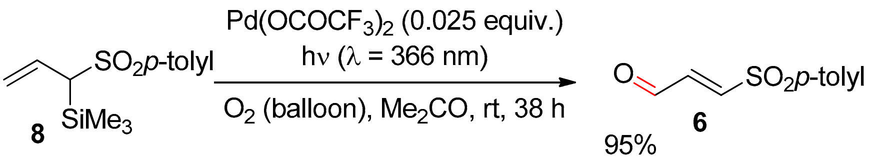
(1)

The process was used for the oxidation of allylsulfones [7]. Under the above conditions, **5** led to a mixture of unsaturated aldehyde **6** and alcohol **7** (Equation (2)). The yields were improved with a cocatalyst such as $Cu(OCOCF_3)_2$ or $Co(OCOCF_3)_2$.



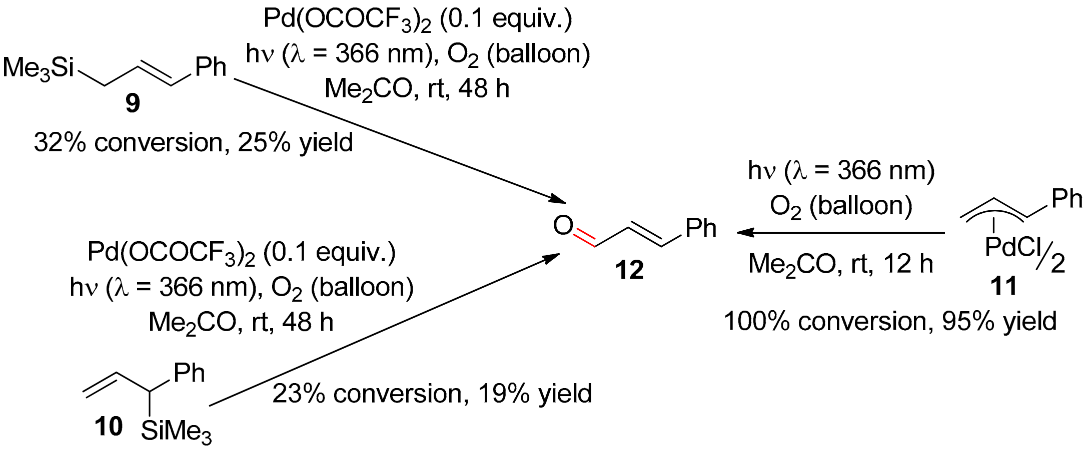
(2)

Under both $Pd(OCOCF_3)_2$ catalysis and UV light, allylsulfones substituted with a trimethylsilyl group underwent cleavage of the allyl-Si bond. Thus, full conversion of **8** occurred in 38 h leading to **6** in 95% yield (Equation (3)) [8]. Lower conversions were mediated by other Pd catalysts.

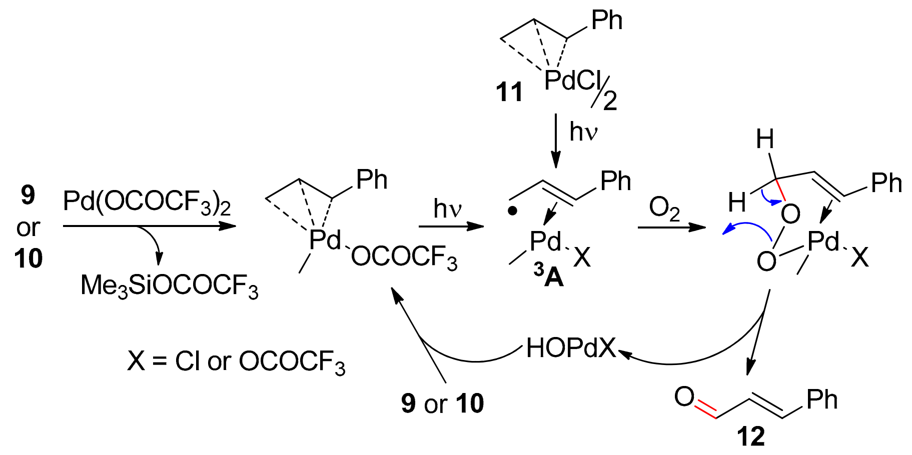


(3)

The mechanism of the reaction of allylsilanes was studied using l-phenyl-3-(trimethylsilyl)-l-propene (**9**) and l-phenyl-1-(trimethylsilyl)-2-propene (**10**) as substrates, and comparison with the reactivity of corresponding allylpalladium chloride **11** [9]. The latter would be dissymmetric due to the different substitution of the allyl unit extremities [10–12]. Cinnamaldehyde (**12**) was selectively obtained from irradiation of either **9** and **10** in the presence of catalytic $Pd(OCOCF_3)_2$, or **11** (Scheme 2). That contrasts from oxidations of the free phenylallyl radical which gave mixtures of oxidation products in 1- and 3-position [9,13,14]. Consequently, the regiospecificity of the reactions of **9**, **10** and **11** excluded the formation of the free phenylallyl radical. The formation of η^3-allylpalladium complexes from allylsilanes and Pd^{II} salts is known [15]. Thus, a common intermediate, which would be a dissymetric η^3-allylpalladium complex, has been proposed (Scheme 3). Light-mediated cleavage of the longer C–Pd bond would lead to intermediate ^{3}**A** [16,17] which reacts with oxygen to afford a peroxopalladium complex. The latter evolves towards aldehyde **12**, liberating HOPdX which would be involved in the subsequent catalytic cycle.



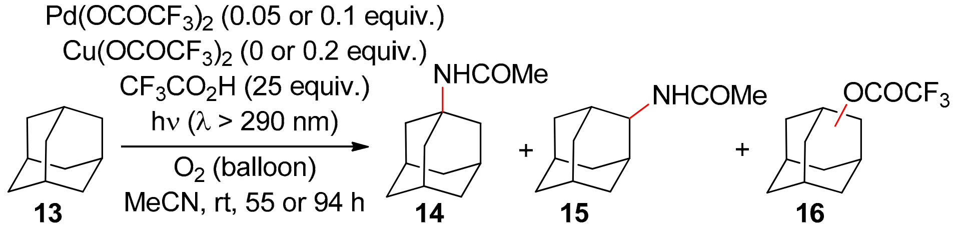
Scheme 2. Three photochemical reactions leading to cinnamaldehyde.



Scheme 3. Plausible reaction pathways leading to cinnamaldehyde from allylsilanes **9** and **10**.

2.2. Alkanes

Irradiation with UV light of a MeCN solution of adamantane (**13**) containing trifluoroacetic acid and catalytic $Pd(OCOCF_3)_2$ afforded adamantanyl acetamides **14** and **15** in quantitative yields versus the amount of palladium (Equation (4)) [18]. The reaction became catalytic with $Cu(OCOCF_3)_2$ as the cocatalyst and provided traces of adamantanyl trifluoroacetates **16**. The mechanism of these reactions remains obscure, the %**14**/%**15** ratio indicating a radical or electrophilic process [19].

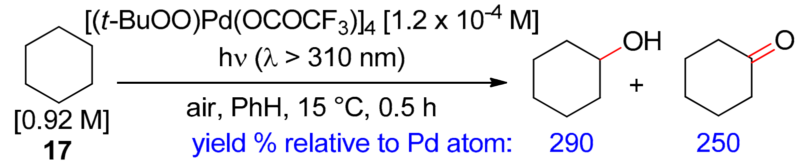


13 **14** **15** **16**

	yield % relative to Pd catalyst		
$Pd(OCOCF_3)_2$ (0.1 equiv.) without $Cu(OCOCF_3)_2$, 55 h:	73	25	0
$Pd(OCOCF_3)_2$ (0.05 equiv.) with $Cu(OCOCF_3)_2$, 94 h:	295	127	traces

(4)

Oxidation of cyclohexane (**17**) and 3-methylhexane (**18**) was performed using light and peroxopalladium complexes [20]. Thus, $[(t\text{-BuOO})Pd(OCOCF_3)]_4$ in air led, from **17**, to cyclohexanol and cyclohexanone with a slight catalytic character (Equation (5)). A similar result arose with $[(t\text{-BuOO})Pd(OCOCH_3)]_4$. The oxidation of **18** mainly occurred at the level of the tertiary C–H bond.

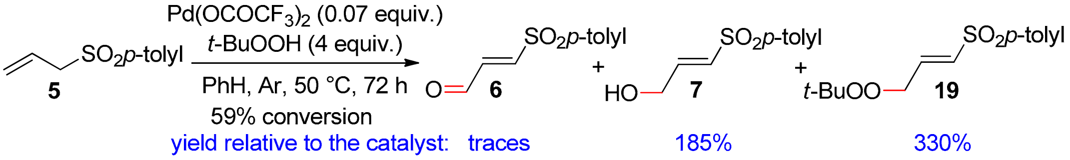


(5)

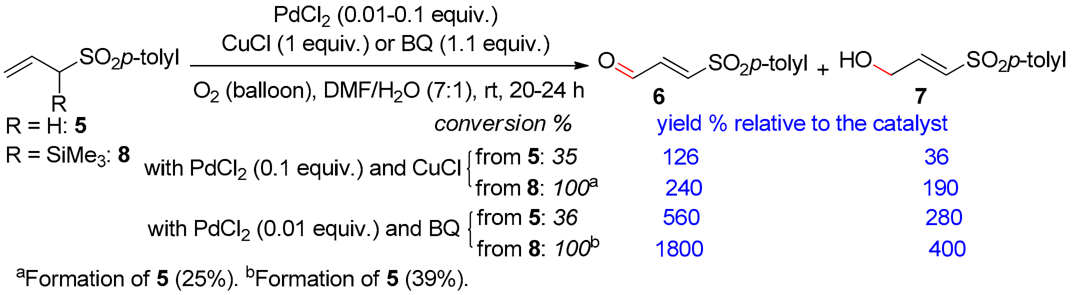
3. Allylic Oxidation

3.1. 1-(p-Toluenesulfonyl)-2-Propene and 1-(Trimethylsilyl)-1-(p-Toluenesulfonyl)-2-Propene

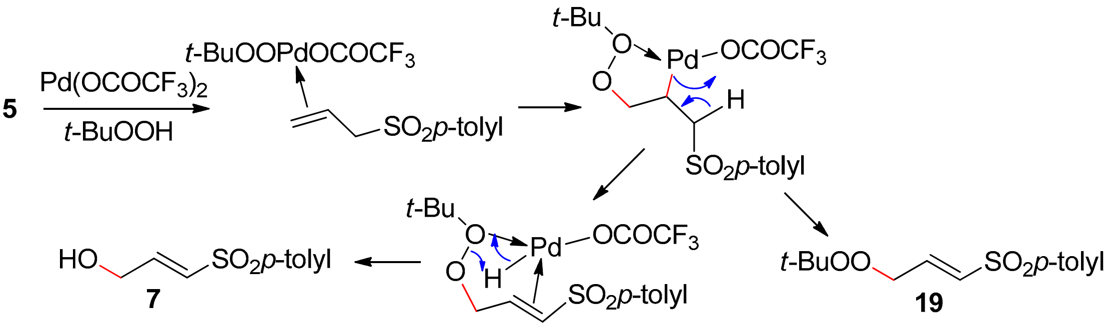
The Pd^{II}-catalyzed oxidation of allylsulfone **5** was carried out with *t*-BuOOH or oxygen in conjunction with either CuCl or benzoquinone (BQ) (Equations (6) and (7)) [21]. Under the former conditions, the main products were alcohol **7** and peroxide **19**, which could be produced from a η^2-olefin palladium complex formed from **5** and $t\text{-BuOOPdOCOCF}_3$ (Scheme 4) [22].



(6)



(7)

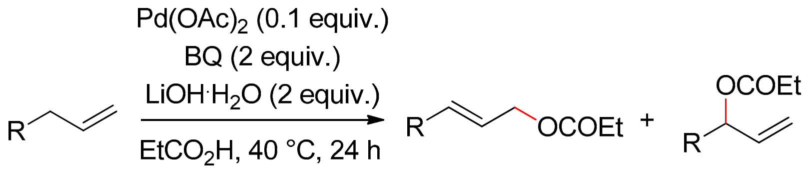


Scheme 4. $Pd(OCOCF_3)_2$-catalyzed oxidation of allylsulfone **5** with *t*-BuOOH.

Submitting allylsilane **8** to the $PdCl_2$/CuCl or BQ system under oxygen mainly led to the desilylated compound **5**. (Equation (7)) [21]. Aldehyde **6** and alcohol **7** were concomitantly produced.

3.2. Terminal Alkenes

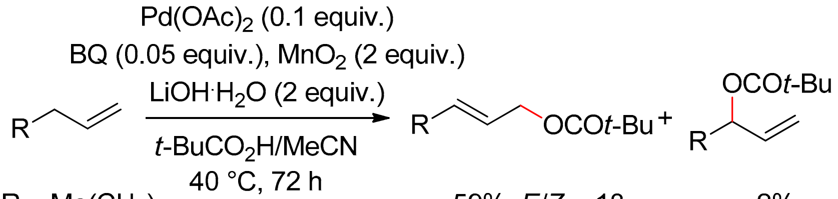
Various conditions have been reported for the synthesis of allylic carboxylates via Pd^{II}-catalyzed allylic oxidation of olefins in carboxylic acids [23,24]. After the observation of the improvement of the $Pd(OAc)_2$-catalyzed allylic acetoxylation of allylbenzene with BQ as the stoichiometric oxidant in the presence of base but with inconsistent yields, we performed the efficient, reproducible and regioselective allylic acyloxylation of terminal alkenes using lithium hydroxide as the additive and propionic acid as the solvent (Equation (8)) [25].



R = *p*-$MeOC_6H_4$:	71.5%, *E*/*Z* = 15	1.5%
R = *o*-$MeOC_6H_4$:	63%, *E*/*Z* = 7	1%
R = *o*-$AcOC_6H_4$:	77%, *E*/*Z* = 16	trace
R = PhCH(OH):	64%, *E*	0%
R = *o*-$BrC_6H_4CH(OH)$:	74%, *E*	0%
R = $Me(CH_2)_6CH(OH)$:	68%, *E*	0%
R = $Me(CH_2)_6$:	71%, *E*/*Z* = 7	9%

(8)

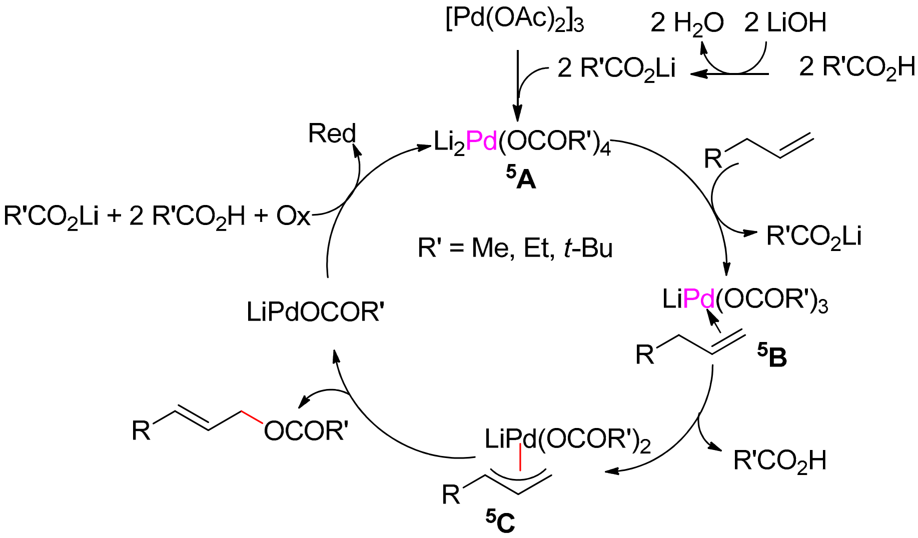
The reaction of 1-decene was less selective (Equation (8)). The regioselectivity increased with the more-hindered pivalic acid but to the detriment of the conversion. Improved results were finally obtained using a BQ/MnO_2 mixture as the oxidant (Equation (9)) [25]. This modified procedure was well adapted to the oxidation of homoallylic alcohols but led to lower yields with allylarenes (compare Equations (8) and (9)).



R = $Me(CH_2)_6$:	59%, *E*/*Z* = 18	2%
R = *o*-$MeOC_6H_4$:	51%, *E*/*Z* = 6	trace
R = PhCH(OH):	78%, *E*	0%
R = *p*-$ClC_6H_4CH(OMe)$:	64%, *E*	0%

(9)

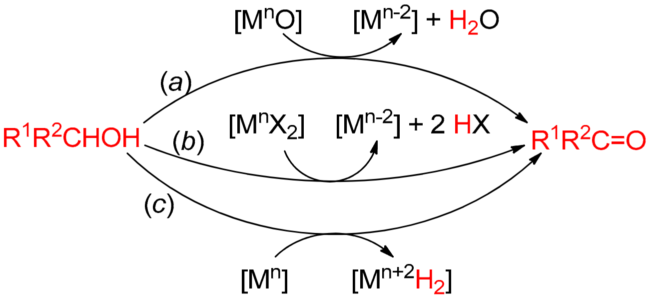
Careful analysis by Electrospray Ionization Mass Spectrometry (ESI–MS) of the allylic acyloxylation under the above conditions led to identification of different clusters, especially those corresponding to intermediates having the Pd atom (in mauve color) in the proposed catalytic cycle depicted in Scheme 5. Palladium acetate, which is a trimer in the solid state [26], reacts with the in-situ formed salt of the carboxylic acid to afford ^{5}**A**. Coordination of the substrate to ^{5}**A** leads to η^2-alkenyl intermediate ^{5}**B**, which evolves towards an η^3-allyl complex ^{5}**C**. Subsequent intramolecular acetoxylation delivers the product and Pd^0. The reoxidation of Pd^0 completes the catalytic cycle.



Scheme 5. Proposed mechanism of the Pd-catalyzed allylic acyloxylation.

4. Alcohol Oxidation

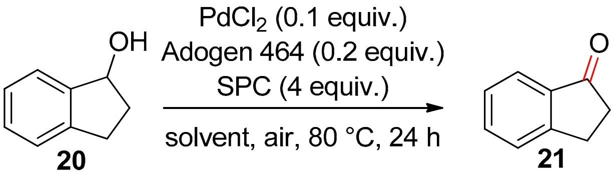
The transformation of alcohols into the corresponding carbonyl compounds with metal oxides and metal salts may occur through three pathways (Scheme 6). Instead of the term "oxidation" used for reactions following paths *a* and *b*, those arising via path *c* are often called "dehydrogenation" or "oxidative dehydrogenation". Most Pd-catalyzed oxidation of alcohols occur via paths *b* and *c* [27]. As shown below, we have developed procedures for such reactions using various species to regenerate the catalyst.



Scheme 6. The three pathways of metal-mediated oxidation of alcohols.

4.1. With Sodium Percarbonate

Despite its name, sodium percarbonate (SPC) is not a persalt. SPC, which is a versatile oxidizing agent for organic synthesis [28,29], is the association of sodium carbonate with hydrogen peroxide with the formula Na_2CO_3,1.5 H_2O_2. In the course of the screening of metal chlorides for the catalytic oxidation of 1-indanol (**20**) by SPC in 1,2-dichloroethane (DCE) in the presence of Adogen 464 [30], we discovered that the reaction with $PdCl_2$ effectively occurred even in the absence of SPC. That led us to the procedure documented in Section 4.2. In contrast, SPC is required with solvents such as acetonitrile, hexane and benzene, leading selectively to 1-indanone (**21**) from **20** (Equation (10)) [31].



20 **21**

conversion %, yield %

MeCN: *81*, 79; hexane: *77*, 74; PhH: *80*, 79 (10)

4.2. With 1,2-Dichloroethane

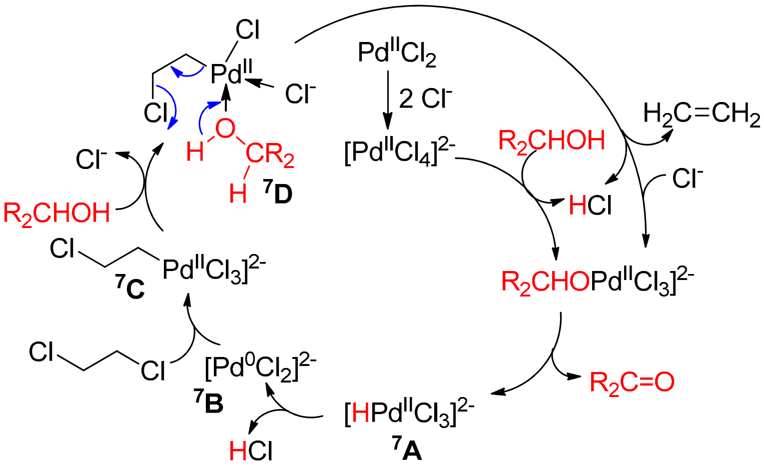
The $PdCl_2$-catalyzed oxidation of alcohols in DCE containing sodium carbonate and catalytic amounts of Adogen 464 (Equation (11)) involves the regeneration of active Pd species by the solvent, leading to the formation of ethylene. The formation of the latter has been highlighted by its reaction with iodine, giving 1,2-diiodooethane [32]. The method is efficient for saturated and benzylic secondary alcohols. Some overoxidation of primary alcohols occurred leading to acids which react with the solvent to afford esters. Isomerization of secondary allylic alcohols to saturated ketones may compete with the oxidation (Equation (11)).

$$R^1R^2CHOH \xrightarrow[\text{ClCH}_2\text{CH}_2\text{Cl, air, reflux, 5-24 h}]{\text{PdCl}_2\text{ (0.05 equiv.)}\;\text{Adogen 464 (0.1 equiv.)}\;\text{Na}_2\text{CO}_3\text{ (2 equiv.)}} R^1R^2C{=}O$$

time h, *conversion %*, selectivity %

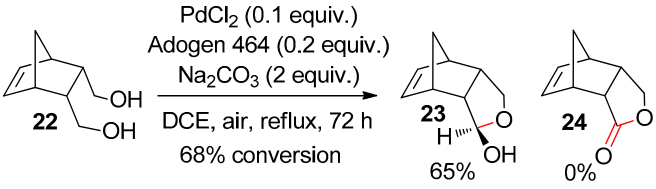
1-indanol: 5.5, *100*, 86; 9-hydroxyfluorene: 11, *100*, 91;
2-naphthalenemethanol: 22, *100*, 68[a]; isophorol: 20, *77*, 69;
cyclooctanol: 24, *87*, 95; 1-octadecanol: 24, *64*, 39[b];
eicos-1-en-3-ol: 24, *69*, 33[c]; benzoin: 24, *89*, 67[d]
[a]Plus (2-naphthyl)$CO_2(CH_2)_2Cl$, 16%.
[b]Plus $Me(CH_2)_{16}CO_2(CH_2)_2Cl$, 54%.
[c]Plus eicosan-3-one, 58%.
[d]Plus PhCHO, 12% and $PhCO_2(CH_2)_2Cl$, 19%. (11)

As the plausible mechanism, we initially suspected the insertion of Pd^0 into a C–Cl bond of DCE to afford $ClCH_2CH_2PdCl$ which would undergo β-Cl elimination leading to ethylene and $PdCl_2$ [32]. According to a theoretical study, $ClCH_2CH_2PdCl$ would rather be the active species reacting with the alcohol [33]. The process is, however, carried out in the presence of Adogen 464 which reacts with $PdCl_2$ to afford the soluble palladium salt $[PdCl_4]^{2-}$ [34]. These remarks led us to propose the catalytic cycle depicted in Scheme 7. Hydridopalladium ^{7}**A** formed after the first alcohol oxidation leads to Pd^0 species ^{7}**B** via elimination of HCl. Insertion of ^{7}**B** into DCE affords ^{7}**C**. Coordination of the alcohol to the latter gives ^{7}**D**. Subsequent elimination of ethylene and HCl leads to an alkoxypalladium intermediate.

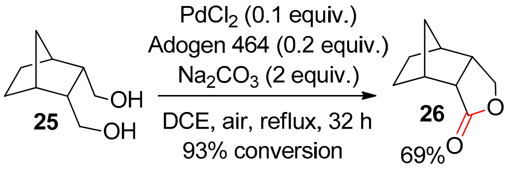


Scheme 7. PdCl$_2$-catalyzed oxidation of alcohols with 1,2-dichloroethane.

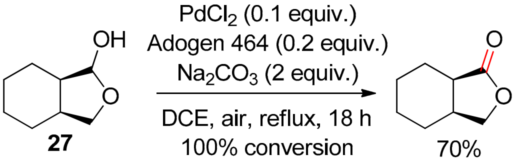
The PdCl$_2$/Adogen 464/DCE procedure effected the lactonisation of various 1,4- and 1,5-diols except that of *cis*-*endo*-2,3-bis(hydroxymethyl)bicyclo [2.2.1]hept-5-ene (**22**) which led to lactol **23** (96% selectivity) (Equation (12)) although the corresponding saturated diol **25** provided lactone **26** (Equation (13)) [35]. Oxidation of lactol **23** into lactone **24** did not occur under the Pd conditions, but arose using pyridinium dichromate in CH$_2$Cl$_2$ (83% yield [36]) [37] or the Swern oxidation method [38]. The PdCl$_2$/Adogen 464/DCE procedure is however able to oxidize α lactol such as **27** (Equation (14)).



(12)

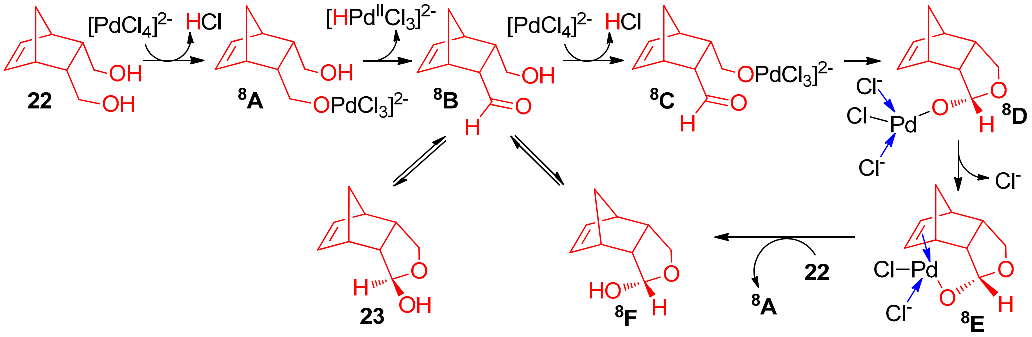


(13)



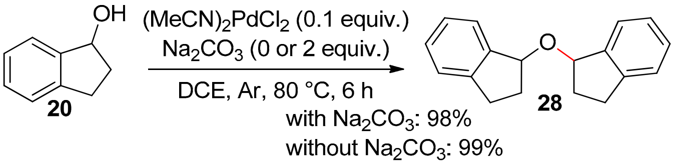
(14)

The above results clearly demonstrated that the lack of formation of **24** from **22** under Pd-conditions was attributable to the C=C bond. Analysis of both the plausible intermediates of the process and literature [39–41] led to the proposal of Scheme 8. The reaction of hydroxyaldehyde ^{8}**B** obtained via ^{8}**A** leads to alkoxypalladium intermediate ^{8}**C**. Subsequent intramolecular reaction occurs through the stereoselective approach of the alkoxypalladium moiety to one face of the aldehyde to afford ^{8}**D**. In contrast to the intermediate obtained from **25**, ^{8}**D** undergoes a ligand exchange leading to palladacycle ^{8}**E**. The syn relationship between O-Pd and C-H bonds, which would allow a β-H elimination leading to the carbonyl unit [42,43], is prevented in ^{8}**E**. That favors alkoxyde exchange with diol **22** to afford ^{8}**F**. The latter is in equilibrium with ^{8}**B** which evolves towards **23**, that is, the more stable isomer [44–46]. The apparent absence of **23** evolution under the PdCl$_2$/Adogen 464/DCE conditions would be a "no reaction" reaction [47,48], which involves ^{8}**B**, ^{8}**C**, ^{8}**D**, ^{8}**E**, alcoholysis and equilibration regenerating the starting substrate.



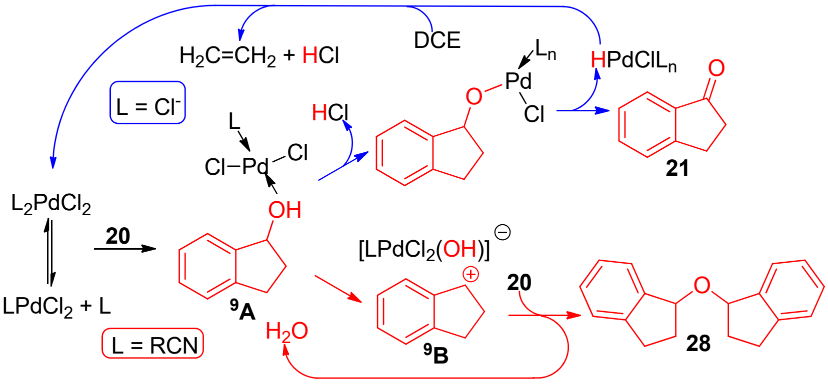
Scheme 8. The "no reaction" reaction of lactol **23**.

As depicted in Equation (11), the $PdCl_2$/Adogen 464/DCE procedure efficiently oxidizes 1-indanol (**20**) into 1-indanone (**21**). The oxidation was also effective using the soluble catalyst (n-$Bu_4N)_2PdCl_4 \cdot 0.5$ H_2O (92% conversion, 90% yield) instead of the $PdCl_2$/Adogen 464 association [31]. Surprisingly, soluble $(MeCN)_2PdCl_2$ produced di(1-indanyl) oxide (**28**) in high yields, even in the absence of the base (Equation (15)) [49].



(15)

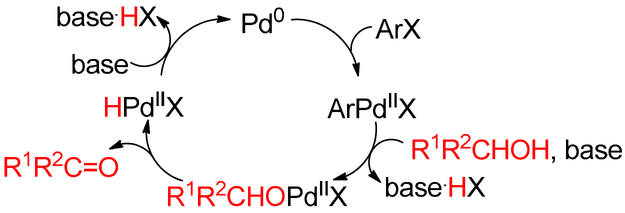
We rationalized the formation of **21** and **28** through two competitive pathways catalyzed with L_2PdCl_2 (L = Cl^- or RCN), that is with $[PdCl_4]^{2-}$ and $(RCN)_2PdCl_2$, respectively (Scheme 9) [49]. In contrast to the anionic catalyst (L = Cl^-), the neutral catalyst (L = RCN) is electrophilic [50–53]. Exchange of ligand between L_2PdCl_2 and **20** affords ^{9}**A**. The evolution of ^{9}**A** depends on the electrophilicity of the L_2PdCl_2. Transition metals having Lewis acid properties mediate the formation of ethers from alcohols [31,54]. Consequently, ^{9}**A** formed from the anionic catalyst evolves towards **21** via the ketonisation pathway [32,33], while ^{9}**A** formed from $(RCN)_2PdCl_2$ undergoes heterolytic cleavage of the C–OH bond leading to ionic species ^{9}**B**. The latter reacts with **20** to give ether **28**, water and the starting catalyst.



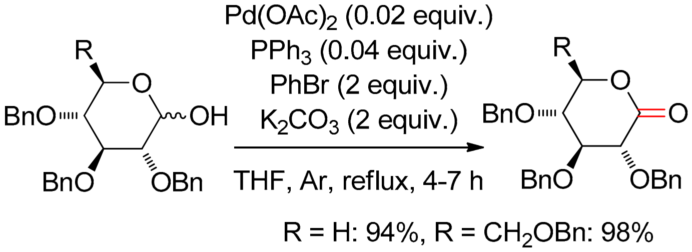
Scheme 9. Dependence of the reaction pathway on the electrophilicity of the catalyst.

4.3. With Aryl Bromide

The Yoshida procedure of oxidation of alcohols used a Pd catalyst with an aryl halide as hydrogen acceptor and a base (Scheme 10) [55,56]. We used this procedure for the oxidation with high yields of benzyl-protected sugar hemiacetals into lactones (Equation (16)) [57].



Scheme 10. Pd^{II}-catalyzed oxidation of alcohols with aryl halides.



(16)

4.4. Dehydrogenation

Over the last thirty years, growing attention has been devoted to the use of ionic liquids and molten salts as solvents for organic synthesis [58–60]. The strong interest for catalyzed reactions is due to the immobilization of the catalyst in the ionic liquid or molten salt that would allow the recycling of the tandem catalyst/solvent. These unusual solvents have been used for various catalytic oxidations [61–63]. Our above studies with $(n\text{-Bu}_4\text{N})_2\text{PdCl}_4\cdot 0.5\,\text{H}_2\text{O}$ (see Section 4.2) and Heck reaction in molten n-Bu$_4$NBr [64] urged us to carry out Pd-catalyzed oxidations in this medium.

Initial experimentation using **20**, catalytic $PdCl_2$ and n-Bu$_4$NBr at 120 °C led to a mixture of **21** and indane. The reductive cleavage of the C–OH bond of **19** indicated in-situ formation of hydrogen [65] and/or [Pd]H_2 species [66]. Addition of cyclohexene as a hydrogen acceptor increased the selectivity towards **21**. Finally, the best result was obtained under a gentle flow of argon which removes hydrogen gas (Equation (17)) [67]. Under these conditions, the recycling of both catalyst and n-Bu$_4$NBr was relatively efficient. Secondary benzylic alcohols provided the corresponding ketones in good yields. The method is less selective for primary benzylic alcohols and is ineffective from allylic and saturated alcohols. Subsequent experiments showed that recycling was more efficient with $Pd(OAc)_2$ than with $PdCl_2$, the yield obtained from 4th reuse of the catalyst/*n*-Bu_4NBr association being 92% (94% conversion) with the former and 64% (67% conversion) with the latter [68].

$$R^1R^2CHOH \xrightarrow[\substack{\text{gentle flow of argon} \\ 120\ °C,\ 6\text{-}72\ h}]{\substack{PdCl_2\ (0.03\ \text{equiv.}) \\ n\text{-}Bu_4NBr\ (1.5g/mmol)}} R^1R^2C{=}O \tag{17}$$

time h, *conversion %*, yield %

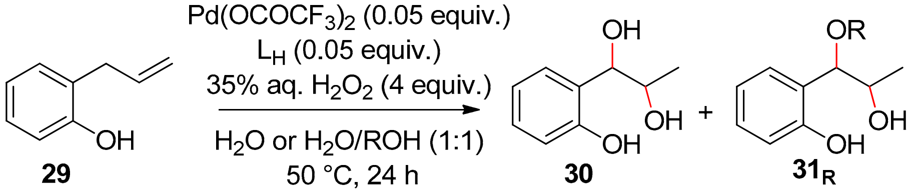
1-indanol: 22, *100*, 90; 9-hydroxyfluorene: 48, *81*, 73;
1-tetralol: 24, *89*, 83; 1-phenylpropan-1-ol: 72, *100*, 91;
benzhydrol: 48, *77*, 97; benzoin: 48, *70*, 68;
2-naphthalenemethanol: 48, *51*, 24[a];
benzylalcohol: 6, *100*, 4[b].

[a] Plus 2-methylnaphthalene.
[b] Plus $PhCO_2n$-Bu (51%) and PhMe.

5. Allylphenols Oxidation

Green chemistry has led the chemical community to intensify research on aqueous procedures [69–75], and we previously used the hydrophilic ligand $[(HOCH_2CH_2NHCOCH_2)_2NCH_2]_2$ ($\mathbf{L_H}$) for copper-catalyzed allylic oxidations in water [76]. The intramolecular Wacker oxidation of allylphenol (**29**) leads to 2-methylbenzofuran [77,78] or 2*H*-chromene [79] depending on the reaction conditions. Thus, we were interested in performing such a reaction in aqueous media with a $Pd^{II}/\mathbf{L_H}$ catalytic system.

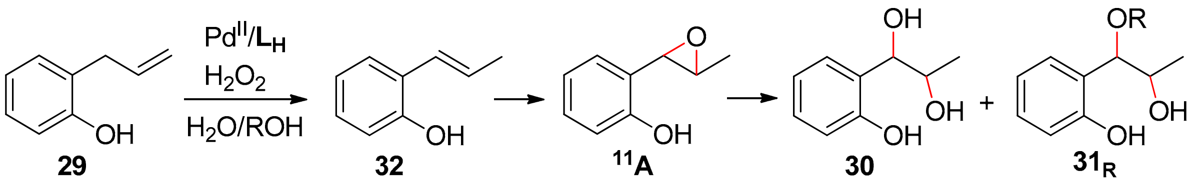
Treatment of **29** with aqueous H_2O_2 and catalytic amounts of both $Pd(OCOCF_3)_2$ and $\mathbf{L_H}$ at 50 °C in water afforded diol **30** instead of the cyclization products (Equation (18)) [80]. Reaction in a mixture of water and methanol led to **30** and hydroxyl methyl ether $\mathbf{31_{Me}}$. Similar compounds were produced in H_2O/EtOH and H_2O/*i*-PrOH, or using 2-allyl-4-methylphenol and 2-allyl-6-methylphenol.



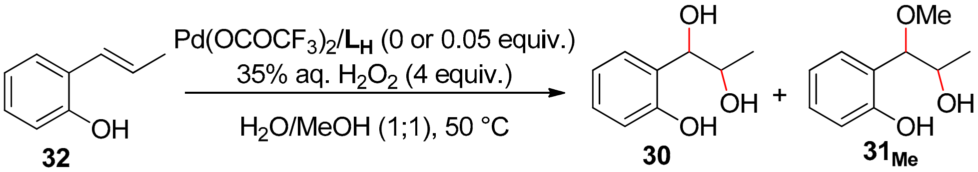
H_2O:	50%	
H_2O/MeOH:	35%	47%
H_2O/EtOH:	43%	38%
H_2O/*i*-PrOH:	38%	38%

(18)

The report of Jacobs' team about the phenol-mediated epoxidation of alkenes by H_2O_2 under metal-free conditions [81] led us to propose in 2005 the mechanism depicted in Scheme 11 [80]. Pd-catalyzed isomerization of **29** affords **32** [82]. Activation by the phenolic OH of the epoxidation of **32** provides $^{\mathbf{11}}$**A**. The high instability of such a compound [83] brings on spontaneous ring opening leading to **30** and $\mathbf{31_R}$. However, the strong acceleration of the palladium-catalyzed reaction of **32** (Equation (19)) indicates some participation of $Pd(OCOCF_3)_2/\mathbf{L_H}$ in the process [80]. In fact, epoxides are very sensitive to Pd catalysis [84]. Complementary mechanistic experiments and ESI-MS studies supported the proposed reaction pathway [85].



Scheme 11. Domino reaction of 2-allylphenol.



	30	**31$_{Me}$**
with Pd^{II}/**L**$_H$, 24 h, 100% conversion, yield:	33%	55%
without Pd^{II}/**L**$_H$, 60 h, 55% conversion, yield:	7%	20%

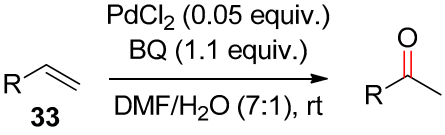
(19)

Recycling of the Pd(OCOCF$_3$)$_2$/**L**$_H$ catalytic system led to gradual loss of activity, the 4th reuse in H_2O/MeOH yielding 35% and 24% of **30** and **31$_{Me}$**, respectively, from **29** [85].

6. Wacker Oxidation

Tsuji's conditions of the Wacker reaction use $PdCl_2$ catalyst in DMF/H_2O and oxidants such as copper salts/O_2 or benzoquinone [86]. According to investigations through isotope effects, kinetic, stereochemical and theoretical studies [87–90], the mechanism involves alkene coordination to $PdCl_2$, followed by hydroxypalladation and β-hydride elimination leading to a palladium–enol η^2-complex. The latter evolves towards the ketone, liberating HCl and Pd^0. The catalyst is regenerated from Pd^0 through reaction with BQ. Mechanistic details remain however matter of debate [87].

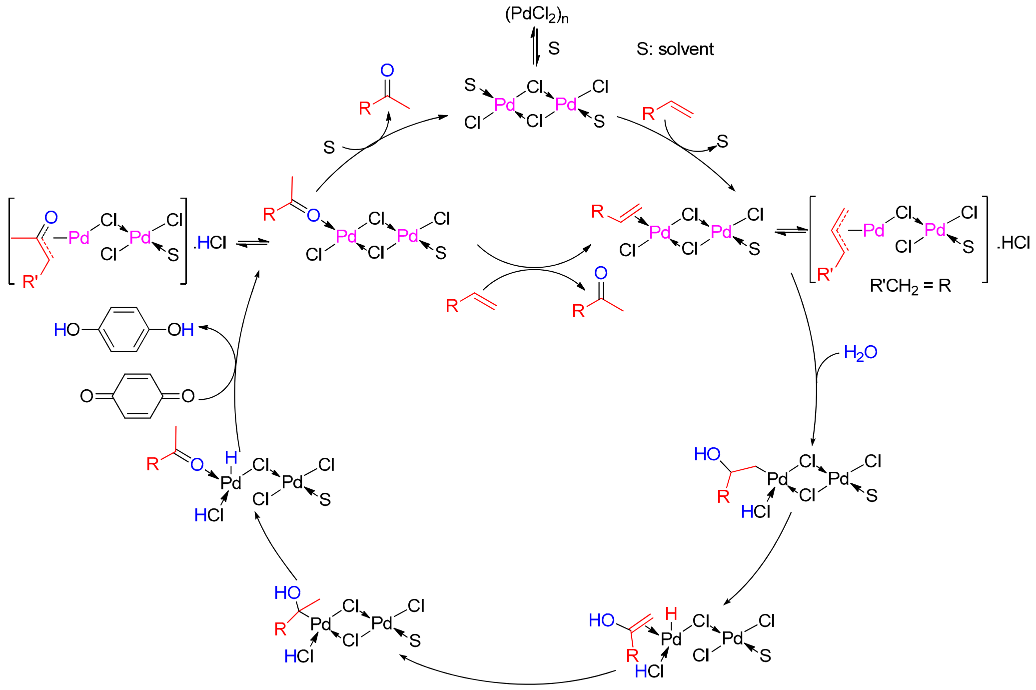
Our interest in the Pd-catalyzed oxidations and in the synthetic properties of DMF [91–93] and BQ [94] urged us to investigate the Wacker reaction of terminal alkenes **33** with ESI-MS, using BQ as the terminal oxidant (Equation (20)) [95].



33a: 1-octene, **33b**: 1-decene, **33c**: 4-allylanisole
33d: 4-allyl-1,2-dimethoxybenzene
33e: 5-hexenoic acid, **33f**: 10-undecenoic acid

(20)

ESI–MS monitoring of the reactions showed that dinuclear palladium complexes were more involved as active catalytic intermediates than mononuclear species. Tests of complexation suggested a reoxidation of Pd occurring before the decoordination of the product. These studies associated to kinetic experiments led us to propose the catalytic cycle depicted in Scheme 12, in which intermediates having the Pd atom in mauve color correspond to clusters detected by ESI–MS.

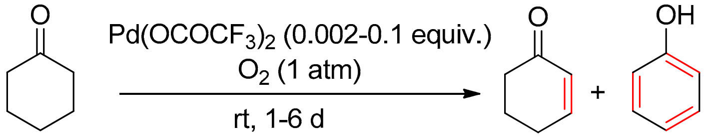


Scheme 12. Proposed catalytic cycle for the Wacker reaction in DMF/H_2O in the presence of benzoquinone.

Compared with the usual mechanism, the most important differences are the involvement of mainly dinuclear Pd species and the reoxidation of a Pd-hydride complex before decomplexation of the ketone.

7. Cyclohexanone Dehydrogenation

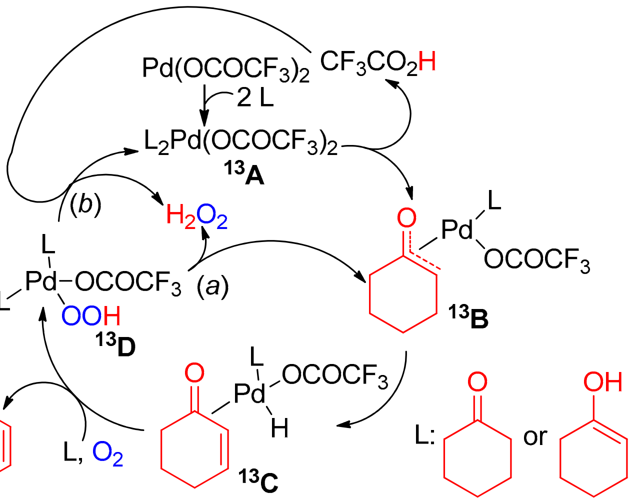
In 1982, we disclosed the room temperature $Pd(OCOCF_3)_2$-catalyzed dehydrogenation of cyclohexanones under oxygen atmosphere (Equation (21)) [96]. Pd procedures were previously reported but using mainly stoichiometric amounts of Pd^{II} [97].



0.002 equiv., 6 d, 5% conversion:	5%	
0.02 equiv., 1 d, 11% conversion:	10%	
0.02 equiv., 5 d, 64% conversion:	50%	13%
0.1 equiv., 1 d, 42% conversion:	29%	12%

(21)

Cyclohexenone was selectively produced at low conversion. Increase of the latter led to over-oxidation giving phenol. The proposed catalytic cycle (Scheme 13) maintains the formal oxidation state of Pd^{II} throughout the reaction. Coordination of cyclohexanone or its enol form to $Pd(OCOCF_3)_2$ provides ^{13}**A**, which led to oxo-η^3-allyl palladium complex ^{13}**B** in liberating CF_3CO_2H. Hydrogen abstraction by palladium provides ^{13}**C** which undergoes insertion of oxygen and ligand exchange giving 2-cyclohexenone and hydroperoxy complex ^{13}**D**. The latter leads to H_2O_2 and either ^{13}**B** (path *a*) or ^{13}**A** by reacting with CF_3CO_2H (path *b*).



Scheme 13. Pd(OCOCF$_3$)$_2$-catalyzed dehydrogenation of cyclohexanone.

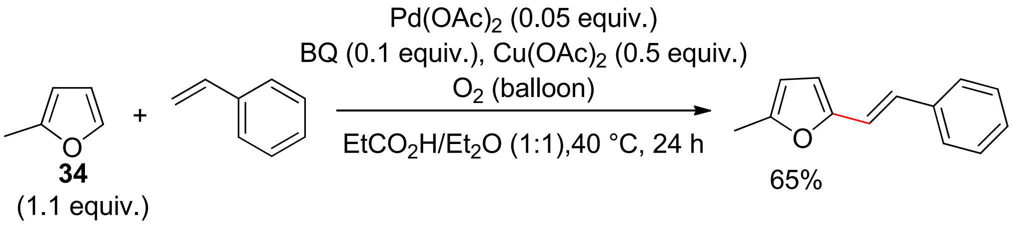
This oxidation process was, in 1982, one of the first reports on the regeneration of active Pd^{II} species using only oxygen [98–100]. The pathway leading to PdOOH from PdH and O$_2$, that is **^{13}D** from **^{13}C** remains however a matter of debate [98–101].

A number of procedures are now available for the Pd-catalyzed dehydrogenation of carbonyl compounds [102]. Moreover, such a dehydrogenation may be a step of a domino reaction involving the Heck reaction, decarboxylative Heck reaction or dehydrogenative Heck reaction [103].

8. Dehydrogenative Heck Reaction

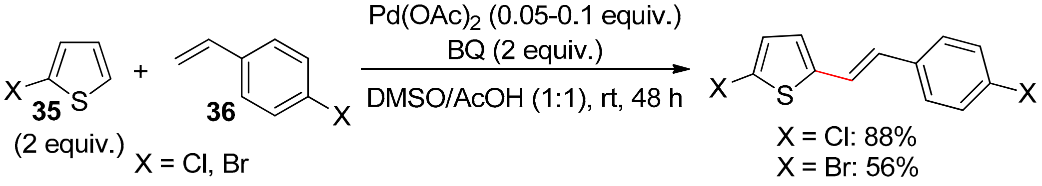
Disclosed in 1970, the Heck reaction is traditionally the synthesis of an arylalkene from the Pd^0-catalyzed cross-coupling of an aryl halide with an alkene [104]. Previously, Fujiwara's team reported the synthesis of stilbene from the reaction of benzene with styrene and PdCl$_2$, leading to two turnovers of palladium [105]. Such a cross-coupling, for which we adopted the name "dehydrogenative Heck reaction" (DHR) [106], may be more respective of the atom economic principle [107], and has been intensively studied over the last twenty years [108].

Our studies focused on the coupling of furan **34** with styrene. Screening various experimental conditions initially led to the best results with catalytic Pd(OAc)$_2$ and the BQ/Cu(OAc)$_2$/O$_2$ oxidizing system (Equation (22)). The method was used for the DHR of various furans and styrenes with high regio- and stereoselectivities (30 examples, 50%–78% yields) [109].



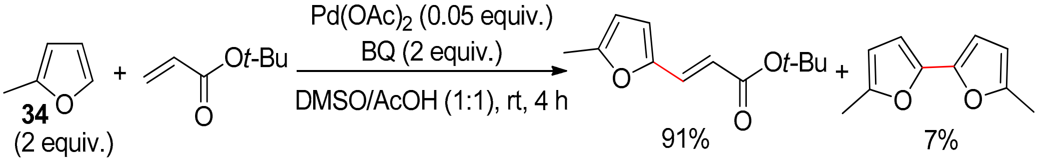
(22)

Kinetic investigations showed an induction period which depends on the nature of the furan, the transformation being faster with electron-rich furans. This led us to investigate the influence of ligands and solvents on the activity of the catalyst. The use of DMSO/AcOH as solvent mixture and BQ as oxidant led to a catalytic system showing no induction period at room temperature, leading to cross-coupling of furans and thiophenes with styrenes, and compatible with halogenated substrates such as **35** and **36** (Equation (23)) [110]. The positive influence of DMSO on the efficiency of Pd(OAc)$_2$-catalyzed oxidations is largely documented in the literature [111,112]. Ligation of DMSO to the trimer [Pd(OAc)$_2$]$_3$ affords the dimeric active species Pd(OAc)$_2$(DMSO)$_2$ [113,114], which may react with the arene leading to ArPdOAc(DMSO)$_2$. Subsequent ligand exchange with BQ could give the less electron-rich species ArPdOAc(BQ)(DMSO), which would be susceptible to easily coordinate to electron-rich styrenes [110].

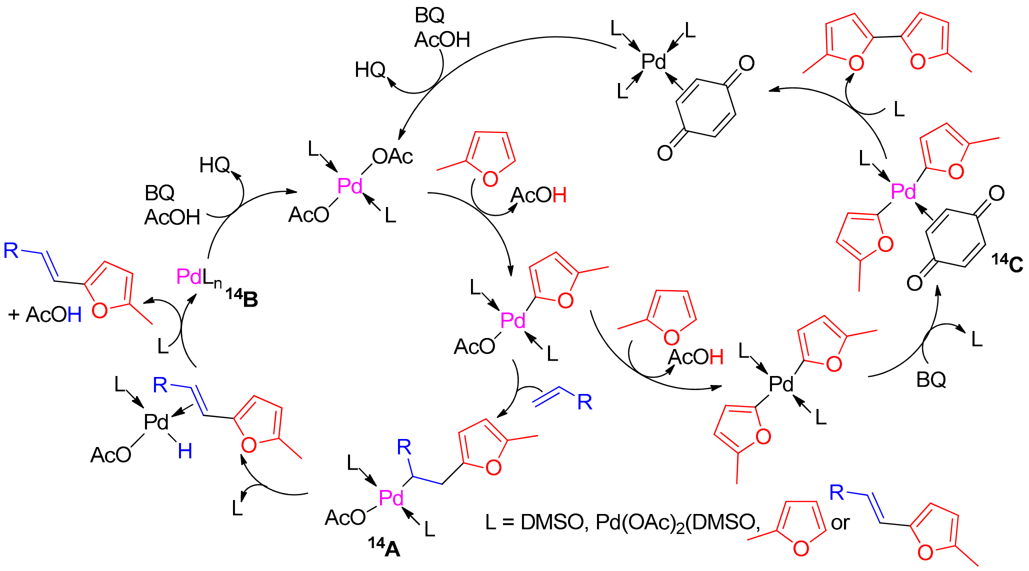


(23)

The mechanism of the reaction of **34** with *tert*-butyl acrylate under these conditions (Equation (24)) has been investigated by ESI–MS leading to identification of clusters corresponding especially to Pd^{II} and Pd^0 intermediates ^{14}**A**, ^{14}**B** and ^{14}**C**, leading us to propose the catalytic cycle shown Scheme 14 [115].



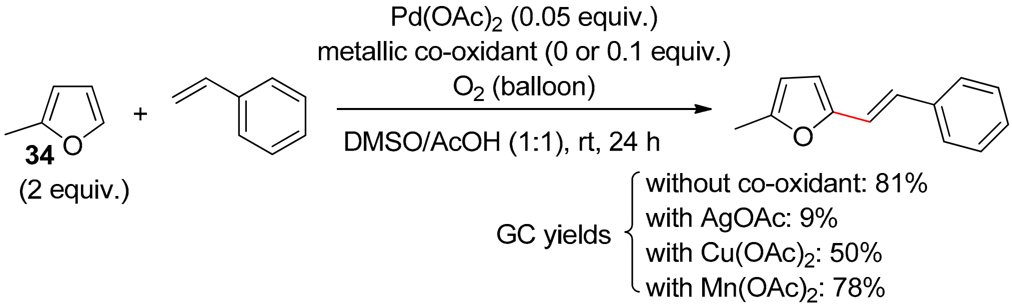
(24)



Scheme 14. Pd^{II}-catalyzed C-H activation.

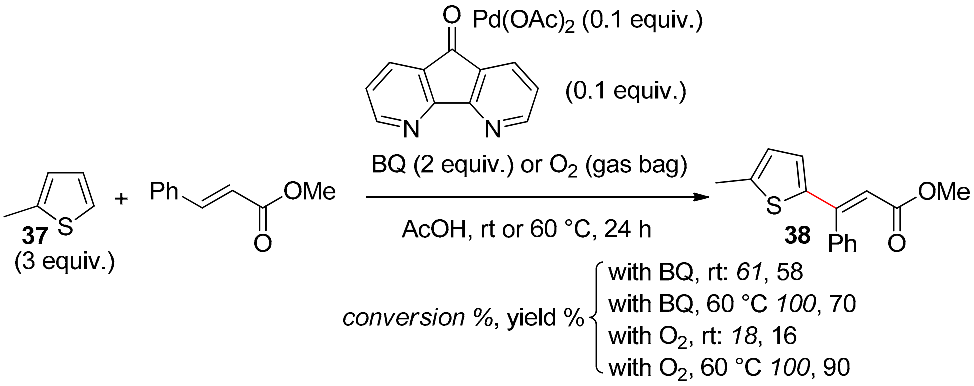
Catalytic amounts of metallic co-oxidants are often required for efficient DHRs under oxygen [108]. We observed, however, that such additives are not always beneficial. Indeed, the room temperature Pd(OAc)$_2$-catalyzed reaction of **34** with styrene in oxygenated DMSO/AcOH afforded the cross-coupling product in higher yield in their absence (Equation (25)). Thus, these mild experimental conditions were used for the efficient DHR of furans, thiophenes and indoles with styrenes (29 examples, 42%–95%

yields) [116]. ESI–MS studies of mixtures of $Pd(OAc)_2$ and AgOAc have shown the formation of mixed species; which could be inactive towards the DHR.



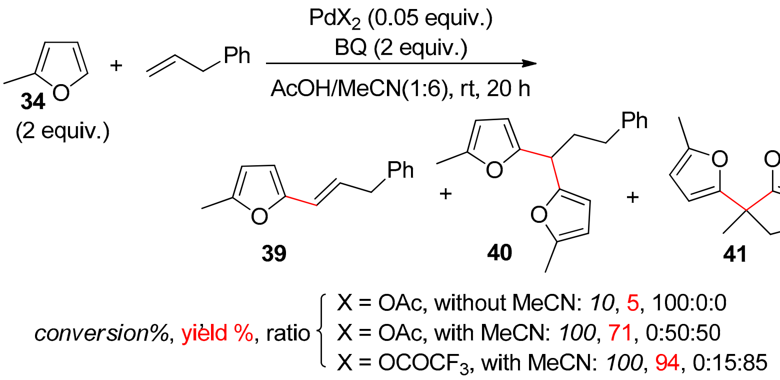
(25)

The reaction of thiophene **37** with a hindered alkene such as methyl cinnamate under conditions of Equation (24) occurred with 5% conversion leading to traces of DHR product **38** [117]. With AcOH as the solvent instead of the AcOH/DMSO mixture, the conversion increased to 20%. Testing various ligands led to an efficient DHR with 4,5-diazafluorenone (Equation (26)). Moreover, increase of the temperature to 60 °C with O_2 instead of BQ led to **38** in 90% isolated yield. Consequently, these conditions have been used for the cross-coupling of furans and thiophenes with various hindered alkenes (19 examples, 51%–96% yield). According to kinetics and competitive experiments as well as ESI–MS studies, 4,5-diazafluorenone influences the C–H bond activation, the alkene insertion, the stereoselectivity and the regeneration of the catalyst [117].



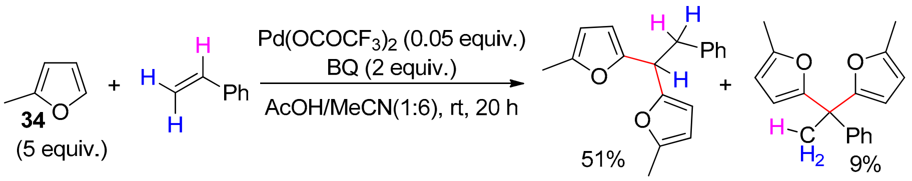
(26)

Under conditions of Equation (24) except the presence of DMSO, a low yield of the DHR product **39** was obtained from the sluggish reaction of **34** with allylbenzene (Equation (27)) [118]. Surprisingly, addition of MeCN as a co-solvent suppressed the formation of **39** and increased the conversion leading to a 1:1 mixture of difurylalkanes **40** and **41**. Moreover, switching to $Pd(OCOCF_3)_2$ as the catalyst increased the **40** + **41** yield to 94% (Equation (27)).

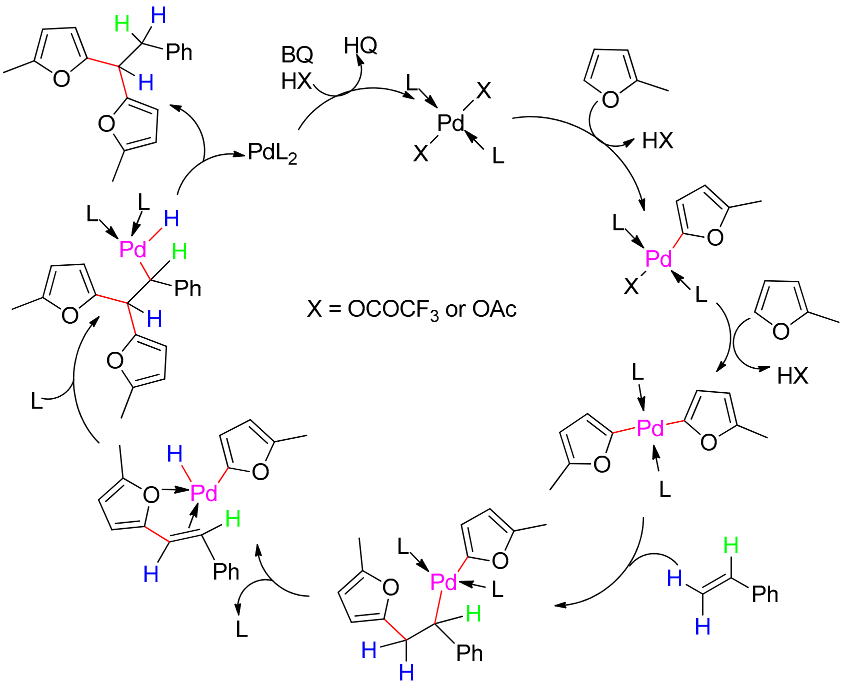


(27)

Suspecting the formation of **41** from prop-1-en-1-ylbenzene via isomerization of allylbenzene [82], the reaction was repeated with styrene [118]. Difurylalkanes were also obtained (Equation (28)). Labelling experiments led to assignment of the hydrogen shifts shown in Equation (28) and, associated ESI–MS studies, to propose the catalytic cycle depicted in Scheme 15 [118].



(28)



Scheme 15. Diaddition of 2-methylfuran to styrene.

9. Conclusions

Starting at the end of the 1970s with oxidations of CH or CH_2 units under UV light, our research evolved towards light-free reactions in various media: organic solvents, water, molten salts, leading to alcohol oxidation, dehydrogenation, etherification or formation of C–C bonds. We have always been strongly focused on the mechanisms; these lead us to various proposals, especially those based on ESI–MS results. Some reactions and mechanisms have been serendipitously discovered [119], but nevertheless, in most cases, they were the fruit of deep investigations and reflection, rather than good fortune.

Funding: This research received no external funding.

Acknowledgments: We are grateful to colleagues and students from the Universities of Grenoble, Lille, Marseille, Moscow, Prague, Reims and York whose names are cited in the references, for their involvement in the above reactions. We thank CNRS for the freedom in the choice of our research activities.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Muzart, J.; Pale, P.; Pète, J.-P. Preparation of conjugated carbonyl compounds by photolysis of η^3-allylpalladium complexes. *J. Chem. Soc. Chem. Commun.* **1981**, *14*, 668–669. [CrossRef]
2. Trost, B.M.; Metzner, P.J. Reaction of olefins with palladium trifluoroacetate. *J. Am. Chem. Soc.* **1980**, *102*, 3572–3577. [CrossRef]
3. Muzart, J.; Pale, P.; Pète, J.-P. Photoactivation of alkenes oxidation by molecular oxygen in the presence of palladium. *Tetrahedron Lett.* **1982**, *23*, 3577–3578. [CrossRef]
4. Muzart, J.; Pale, P.; Pète, J.-P. Catalyse par le palladium et la lumière ultra-violette de l'oxydation d'alcènes par l'oxygène moléculaire. *J. Organomet. Chem.* **1988**, *353*, 267–273. [CrossRef]
5. Sen, A.; Lai, T.-W. Catalytic isomerization of alkenes by palladium(II) compounds. An alternative mechanistic view. *Inorg. Chem.* **1981**, *20*, 4036–4038. [CrossRef]
6. Sen, A.; Lai, T.-W. Mechanism of palladium(II)-catalyzed carbon-carbon double bond isomerization in olefins. *Inorg. Chem.* **1984**, *23*, 3257–3258. [CrossRef]
7. Muzart, J.; Riahi, A.; Pète, J.-P. Oxydation régiosélective de sulfones allyliques catalysée par le palladium et la lumière: Formation d'aldéhydes et alcools α,β-éthyléniques β-sulfonylés. *J. Organomet. Chem.* **1985**, *280*, 269–279. [CrossRef]
8. Riahi, A.; Cossy, J.; Muzart, J.; Pète, J.-P. Palladium catalyzed oxidation of allylsilanes with U.V. light and molecular oxygen. *Tetrahedron Lett.* **1985**, *26*, 839–842. [CrossRef]
9. Muzart, J.; Riahi, A. Oxygenation under UV light of allylsilanes catalyzed by palladium(II) and of (.eta. 3-allyl)palladium complexes: A mechanistic approach. *Organometallics* **1992**, *11*, 3478–3481. [CrossRef]
10. Hütter, P.; Butters, T.; Winter, W.; Handschuh, D.; Woelter, W. Die kristall- und molekülstruktur des dimeren π-allylpalladiumchlorid-Complexes von testosteron. *Liebigs Ann. Chem.* **1982**, 1111–1120. [CrossRef]
11. Hughes, R.P.; Day, C.S. Steric blocking of $\eta^3 \rightarrow \eta^1 \rightarrow \eta^3$ isomerizations of an η^3-allylic ligand. Crystal and molecular structures of 1,3-chloropalladation products of cis-9-methylenebicyclo [6.1.0]nonane and cis-7-methylenebicyclo[4.1.0]heptane. *Organometallics* **1982**, *1*, 1221–1225. [CrossRef]
12. Keinan, E.; Roth, Z. Regioselectivity in organo-transition-metal chemistry. A new indicator substrate for classification of nucleophiles. *J. Org. Chem.* **1983**, *48*, 1769–1772. [CrossRef]
13. Walling, C.; Zavitsas, A.A. The copper-catalyzed reaction of peresters with hydrocarbons. *J. Am. Chem. Soc.* **1963**, *85*, 2084–2090. [CrossRef]
14. Corey, E.J.; Walker, J.C. Organoiron-mediated oxygenation of allylic organotin compounds. A possible chemical model for enzymatic lipoxygenation. *J. Am. Chem. Soc.* **1987**, *109*, 8108–8109. [CrossRef]
15. Kliegman, J.M. The palladium(II) cleavage of allylsilanes. *J. Organomet. Chem.* **1971**, *29*, 73–77. [CrossRef]
16. Crozet, M.P.; Muzart, J.; Pale, P.; Tordo, P. Photolyse des complexes η^3–allylpalladium: Étude par résonnance paramagnétique électronique des nitroxydes allyliques formés en présence de nitrosodurène. *J. Organomet. Chem.* **1983**, *244*, 191–200. [CrossRef]
17. Vermeersch, G.; Marko, J.; Muzart, J. Photoreactivity of η^3-allylpalladium complexes studied by CINDP. *J. Chem. Soc. Perkin Trans.* **1986**, 383–389. [CrossRef]
18. Muzart, J.; Hénin, F. Activation de liaisons carbone-hydrogène d'alcanes par l'association de complexes métalliques électrophiles et de lumière ultra-violette. *C. R. Acad. Sci. Paris Série II* **1988**, *307*, 479–482.

19. Barton, D.H.R.; Boivin, J.; Gastiger, M.; Morzycki, J.; Hay-Motherwell, R.S.; Motherwell, W.B.; Ozbalik, N.; Schwartzentruber, K.M. Functionalization of saturated hydrocarbons. Part 4. The Gif system for selective oxidation using molecular oxygen. *J. Chem. Soc. Perkin Trans.* **1986**, 947–955. [CrossRef]
20. Muzart, J.; Nizova, G.V.; Riahi, A.; Shul'pin, G.B. Oxidation of alkanes by peroxide complexes of palladium. *J. Gen. Chem. USSR* **1992**, *62*, 964.
21. Muzart, J.; Pète, J.-P.; Riahi, A. Palladium-catalyzed allylic oxidation of 1-(*p*-toluenesulfonyl)-2-propene and 1-(trimethylsilyl)-1-(*p*-toluenesulfonyl)-2-propene. *J. Organomet. Chem.* **1987**, *331*, 113–119. [CrossRef]
22. Mimoun, H.; Charpentier, R.; Mitschler, A.; Fischer, J.; Weiss, R. Palladium(II) *tert*-butyl peroxide carboxylates. New reagents for the selective oxidation of terminal olefins to methyl ketones. On the role of peroxymetalation in selective oxidative processes. *J. Am. Chem. Soc.* **1980**, *102*, 1047–1057. [CrossRef]
23. Muzart, J. Oxydation d'alcènes: Induction par les métaux de la formation de liaison C-O en position allylique. *Bull. Soc. Chim. Fr.* **1986**, *1*, 65–77.
24. Beccalli, E.M.; Broggini, G.; Martinelli, M.; Sottocornola, S. C-C, C-O, C-N bond formation on sp^2 carbon by Pd(II)-catalyzed reactions involving oxidant agents. *Chem. Rev.* **2007**, *107*, 5318–5365. [CrossRef] [PubMed]
25. Thiery, E.; Aouf, C.; Belloy, J.; Harakat, D.; Le Bras, J.; Muzart, J. Palladium-catalyzed allylic acyloxylation of terminal alkenes in the presence of a base. *J. Org. Chem.* **2010**, *75*, 1771–1774. [CrossRef] [PubMed]
26. Skapski, A.C.; Smart, M.L. The crystal structure of trimeric palladium(II) acetate. *J. Chem. Soc. Chem. Commun.* **1970**, *11*, 658–659. [CrossRef]
27. Muzart, J. Palladium-catalysed oxidation of primary and secondary alcohols. *Tetrahedron* **2003**, *59*, 5789–5816. [CrossRef]
28. Muzart, J. Sodium perborate and sodium percarbonate in organic synthesis. *Synthesis* **1995**, *1995*, 1325–1347. [CrossRef]
29. McKillop, W.R. Sanderson, Sodium perborate and sodium percarbonate: Cheap, safe and versatile oxidising agents for organic synthesis. *Tetrahedron* **1995**, *51*, 6145–6166. [CrossRef]
30. Adogen 464 is a registered trademark of Ashland Chemical Co. for methyltrialky1(C8-C10) ammonium chloride. CAS Number 72749-59-8.
31. Aït-Mohand, S.; Lunak, S.; Muzart, J. Chlorides and acetylacetonates of transition metals as catalysts for the oxidation of 1-indanol by sodium percarbonate. *Chem. Ber.* **1997**, *130*, 1655–1658. [CrossRef]
32. Aït-Mohand, S.; Hénin, F.; Muzart, J. Palladium(II)-mediated oxidation of alcohols using 1,2-dichloroethane as Pd(0) reoxidant. *Tetrahedron Lett.* **1995**, *36*, 2473–2476. [CrossRef]
33. Rothenberg, G.; Humbel, S.; Muzart, J. Palladium-catalyzed oxidation of alcohols to carbonyl compounds with 1,2-dichloroethane as the primary oxidant: A theoretical study. *J. Chem. Soc. Perkin Trans.* **2001**, *10*, 1998–2004. [CrossRef]
34. Bouquillon, S.; du Moulinet d'Hardemare, A.; Averbuch-Pouchot, M.-T.; Hénin, F.; Muzart, J. Synthesis and characterization of monomeric and dimeric palladium(II)-ammonium complexes; Their use for the catalytic oxidation of alcohols. *Polyhedron* **1999**, *18*, 3511–3516. [CrossRef]
35. Aït-Mohand, S.; Muzart, J. Palladium-catalyzed oxidative cyclization of 1,4-and 1,5-diols in 1,2-dichloroethane. *J. Mol. Catal. A Chem.* **1998**, *129*, 135–139. [CrossRef]
36. Aït-Mohand, S. Catalyse de réactions d'oxydation: utilisation du percarbonate de sodium et régénération d'espèces palladiées actives par le 1,2-dichloroéthane. Doctoral Thesis, Reims University, Reims, France, 1997.
37. Taniguchi, T.; Ogasawara, K. Specific asymmetric mono-epoxidation of *meso* 2,3-*syn*-*bis*-allylic alcohols having a bicyclo[2.2.1]heptane framework. *Tetrahedron Lett.* **1997**, *38*, 433–436. [CrossRef]
38. Taniguchi, T.; Goto, Y.; Ogasawara, K. Preparation of a promising cyclobutanone chiral building block: Utilization its stereochemistry and utilization. *Synlett* **1997**, *1997*, 707–709. [CrossRef]
39. Jaeschke, G.; Seebach, D. Highly enantioselective ring opening of cyclic *meso*-anhydrides to isopropyl hemiesters with Ti-TADDOLates: An alternative to hydrolytic enzymes? *J. Org. Chem.* **1998**, *63*, 1190–1197. [CrossRef]
40. March, J. *Advanced Organic Chemistry*, 4th ed.; John Wiley: New York, NY, USA, 1992; p. 393.
41. Aït-Mohand, S.; Hénin, F.; Muzart, J. Palladium-catalyzed oxidations: Inhibition of a Pd-H elimination by coordination of a remote carbon carbon double bond. *Organometallics* **2001**, *20*, 1683–1686. [CrossRef]

42. Chung, K.; Banik, S.M.; De Crisci, A.G.; Pearson, D.M.; Blake, T.R.; Olsson, J.V.; Ingram, A.J.; Zare, R.N.; Waymouth, R.M. Chemoselective Pd-catalyzed oxidation of polyols: Synthetic scope and mechanistic studies. *J. Am. Chem. Soc.* **2013**, *135*, 7593–7602. [CrossRef]
43. Li, Y.; Lin, Z. Understanding the reaction mechanisms of Pd-catalysed oxidation of alcohols and domino oxidation-arylation reactions using phenyl chloride as an oxidant. *Org. Chem. Front.* **2014**, *1*, 1188–1196. [CrossRef]
44. Corey, E.J.; Palani, A. A method for the selective oxidation of 1,4-diols to lactols. *Tetrahedron Lett.* **1995**, *36*, 3485–3488. [CrossRef]
45. Corey, E.J.; Palani, A. A mechanistic model for the selective oxidation of 1,4-diols to γ-lactols by *o*-iodoxybenzoic acid. *Tetrahedron Lett.* **1995**, *36*, 7945–7948. [CrossRef]
46. Lieb, F.; Niewöhner, U.; Wendisch, D. 6-(3-Carbamoylbicyclo[2.2.1]hept-2-yl)hexansäuren, eine neue klasse von TxA_2-antagonisten. *Liebigs Ann. Chem.* **1987**, *1987*, 607–615. [CrossRef]
47. For the introduction of this expression and its use, see, respectively: Berson, J.A.; Willcott, M.R. Bredt rule Interdictions of cyclopropane rearrangements.The vinylnortricyclenes. *J. Org. Chem.* **1965**, *30*, 3569–3572. [CrossRef]
48. Baldwin, J.E.; Dunmire, D.A. The "No Reaction" reaction of 1-vinylnortricyclene to tricyclo[4.2.1.0^{3,7}]non-3-ene. *J. Org. Chem.* **2000**, *65*, 6791–6794. [CrossRef] [PubMed]
49. Bouquillon, S.; Hénin, F.; Muzart, J. The critical role of the coordination environment of palladium dichloride on the course of its reaction with secondary benzylic alcohols; selective oxidation or etherification catalysts. *Organometallics* **2000**, *19*, 1434–1437. [CrossRef]
50. Sen, A.; Lai, T.-W. Catalysis by solvated transition-metal cations. Novel catalytic transformations of alkenes by tetrakis(acetonitrile)palladium ditetrafluoroborate. Evidence for the formation of incipient carbonium ions as intermediates. *J. Am. Chem. Soc.* **1981**, *103*, 4627–4629. [CrossRef]
51. Sen, A.; Lai, T.-W. Oligomerization and isomerization of olefins by η^3-allyl complexes of palladium. The role of the allyl group. *Organometallics* **1983**, *2*, 1059–1060. [CrossRef]
52. Lipshutz, B.H.; Pollart, D.; Monforte, J.; Kotsuki, H. Pd(II)-catalyzed acetal/ketal hydrolysis/exchange reactions. *Tetrahedron Lett.* **1985**, *26*, 705–708. [CrossRef]
53. Tenaglia, A.; Kammerer, F. Palladium(II)-catalyzed dehydrative cyclization of *cis*-4-alkylcycloalken-2-ols. Synthesis of tricyclic spiroketals in a one-pot sequence. *Synlett* **1996**, *1996*, 576–578. [CrossRef]
54. Salehi, P.; Iranpoor, N.; Behbahani, F.K. Selective and efficient alcoholyses of allylic, secondary-and tertiary benzylic alcohols in the presence of iron (III). *Tetrahedron* **1998**, *54*, 943–948. [CrossRef]
55. Tamaru, Y.; Yamamoto, Y.; Yamada, Y.; Yoshida, Z. Palladium catalyzed oxidations of secondary alcohols. *Tetrahedron Lett.* **1979**, *20*, 1401–1404. [CrossRef]
56. Tamaru, Y.; Yamada, Y.; Inoue, K.; Yamamoto, Y.; Yoshida, Z. Oxidation of primary and secondary alcohols by the catalysis of palladium. *J. Org. Chem.* **1983**, *48*, 1286–1292. [CrossRef]
57. Bessmertnykh, A.; Hénin, F.; Muzart, J. Palladium-catalyzed oxidation of benzylated aldose hemiacetals to lactones. *Carbohydr. Res.* **2004**, *339*, 1377–1380. [CrossRef] [PubMed]
58. Welton, T. Room-temperature ionic liquids. Solvents for synthesis and catalysis. *Chem. Rev.* **1999**, *99*, 2071–2083. [CrossRef] [PubMed]
59. Dupont, J.; de Souza, R.F.; Suarez, P.A.Z. Ionic liquid (molten salt) phase organometallic catalysis. *Chem. Rev.* **2002**, *102*, 3667–3692. [CrossRef] [PubMed]
60. *Ionic Liquids in Synthesis*; Wasserscheid, P.; Welton, T. (Eds.) Wiley: Weinheim, Germany, 2003.
61. Muzart, J. Ionic liquids as solvents for catalyzed oxidations of organic compounds. *Adv. Synth. Catal.* **2006**, *348*, 275–295. [CrossRef]
62. Betza, D.; Altmann, P.; Cokoja, M.; Herrmann, W.A.; Kuhn, F.E. Recent advances in oxidation catalysis using ionic liquids as solvents. *Coord. Chem. Rev.* **2011**, *255*, 1518–1540. [CrossRef]
63. Dai, C.; Zhang, J.; Huang, C.; Lei, Z. Ionic liquids in selective oxidation: Catalysts and solvents. *Chem. Rev.* **2017**, *117*, 6929–6983. [CrossRef]
64. Bouquillon, S.; Ganchegui, B.; Estrine, B.; Hénin, F.; Muzart, J. Heck arylation of allylic alcohols in molten salts. *J. Organomet. Chem.* **2001**, *634*, 153–156. [CrossRef]
65. Keresszegi, C.; Mallat, T.; Baiker, A. Selective transfer dehydrogenation of aromatic alcohols on supported palladium. *New J. Chem.* **2001**, *25*, 1163–1167. [CrossRef]

66. Murahashi, S.; Shimura, T.; Moritani, I. Conversion of alcohols into unsymmetrical secondary or tertiary amines by a palladium catalyst. Synthesis of *N*-substituted pyrroles. *Chem. Commun.* **1974**, *22*, 931–932. [CrossRef]
67. Ganchegui, B.; Bouquillon, S.; Hénin, F.; Muzart, J. Palladium-catalyzed dehydrogenation of benzylic alcohols in molten ammonium salts, a recyclable system. *Tetrahedron Lett.* **2002**, *43*, 6641–6644. [CrossRef]
68. Ganchegui, B. Transformations palladocatalysées et utilisation d'un sel fondu comme solvant. Doctoral Thesis, Reims University, Reims, France, 2004.
69. Li, C.-J. Organic reactions in aqueous media—with a focus on carbon-carbon bond formation. *Chem. Rev.* **1993**, *93*, 2023–2035. [CrossRef]
70. Li, C.-J.; Chen, L. Organic chemistry in water. *Chem. Soc. Rev.* **2006**, *35*, 68–82. [CrossRef] [PubMed]
71. Hailes, H.C. Reaction solvent selection: The potential of water as a solvent for organic transformations. *Org. Process Res. Dev.* **2007**, *11*, 114–120. [CrossRef]
72. Chanda, A.; Fokin, V.V. Organic synthesis "on water". *Chem. Rev.* **2009**, *109*, 725–748. [CrossRef]
73. Lamblin, M.; Nassar-Hardy, L.; Hierso, J.-C.; Fouquet, E.; Felpin, F.-X. Recyclable heterogeneous palladium catalysts in pure water: Sustainable developments in Suzuki, Heck, Sonogashira and Tsuji–Trost reactions. *Adv. Synth. Catal.* **2010**, *352*, 33–79. [CrossRef]
74. Le Bras, J.; Muzart, J. From metal-catalyzed reactions with hydrosoluble ligands to reactions in and on water. *Curr. Org. Synth.* **2011**, *8*, 330–334. [CrossRef]
75. Harry, N.A.; Radhika, S.; Neetha, M.; Anilkumar, G. Recent advances and prospects of organic reactions "on water". *ChemistrySelect* **2019**, *4*, 12337–12355. [CrossRef]
76. Le Bras, J.; Muzart, J. Water-soluble and reusable copper catalyst for the allylic benzoyloxylation of olefins. *Tetrahedron Lett.* **2002**, *43*, 431–433. [CrossRef]
77. Meulemans, T.M.; Kiers, N.H.; Feringa, B.L.; van Leeuwen, P.W.N.M. Catalytic oxidation of homoallylalcohols to α-alkoxytetrahydrofurans by a Pd-nitro complex and molecular oxygen. *Tetrahedron Lett.* **1994**, *35*, 455–458. [CrossRef]
78. Roshchin, A.I.; Kel'chevski, S.M.; Bumagin, N.A. Synthesis of benzofurans via Pd^{2+}-catalyzed oxidative cyclization of 2-allylphenols. *J. Organomet. Chem.* **1998**, *560*, 163–167. [CrossRef]
79. Larock, R.C.; Wei, L.; Hightower, T.R. Synthesis of 2H-1-benzopyrans by Pd-catalyzed cyclization of *o*-allylic phenols. *Synlett* **1998**, 522–524. [CrossRef]
80. Chevrin, C.; Le Bras, J.; Hénin, F.; Muzart, J. One-pot catalytic synthesis of 2-(1,2-dihydroxypropyl)-phenol derivatives from 2-allylphenols in aqueous media. *Synthesis* **2005**, *2005*, 2615–2618. [CrossRef]
81. Wahlen, J.; De Vos, D.E.; Jacobs, P.A. Activation of hydrogen peroxide through hydrogen-bonding interaction with acidic alcohols: epoxidation of alkenes in phenol. *Org. Lett.* **2003**, *5*, 1777–1780. [CrossRef] [PubMed]
82. Hassam, M.; Taher, A.; Arnott, G.E.; Green, I.R.; van Otterlo, W.A.L. Isomerization of allylbenzenes. *Chem. Rev.* **2015**, *115*, 5462–5569. [CrossRef]
83. Lattanzi, A.; Senatore, A.; Massa, A.; Scettri, A. Novel highly regioselective $VO(acac)_2$/TBHP mediated oxidation of *o*-alkenyl phenols to *o*-hydroxybenzyl ketones. *J. Org. Chem.* **2003**, *68*, 3691–3694. [CrossRef]
84. Muzart, J. Pd-mediated reactions of epoxides. *Eur. J. Org. Chem.* **2011**, *2011*, 4717–4741. [CrossRef]
85. Thiery, E.; Chevrin, C.; Le Bras, J.; Harakat, D.; Muzart, J. Mechanism insights into the palladium^{II}-catalyzed hydroalkoxylation of 2-allylphenols. *J. Org. Chem.* **2007**, *72*, 1859–1862. [CrossRef]
86. Tsuji, J. Synthetic applications of the palladium-catalyzed oxidation of olefins to ketones. *Synthesis* **1984**, *1984*, 369–384. [CrossRef]
87. Keith, J.A.; Henry, P.M. The Mechanism of the Wacker reaction: A tale of two hydroxypalladations. *Angew. Chem. Int. Ed.* **2009**, *48*, 9038–9049. [CrossRef] [PubMed]
88. Comas-Vives, A.; Stirling, A.; Lledós, A.; Ujaque, G. The Wacker process: Inner- or outer-sphere nucleophilic addition? New insights from ab initio molecular dynamics. *Chem. Eur. J.* **2010**, *16*, 8738–8747. [CrossRef] [PubMed]
89. Anderson, B.J.; Keith, J.A.; Sigman, M.S. Experimental and computational study of a direct O_2-coupled Wacker oxidation: Water dependence in the absence of Cu salts. *J. Am. Chem. Soc.* **2010**, *132*, 11872–11874. [CrossRef]
90. Nair, N.N. Ligand exchanges and hydroxypalladation reactions of the Wacker process in aqueous solution at high Cl^- concentration. *J. Phys. Chem. B* **2011**, *115*, 2312–2321. [CrossRef]
91. Muzart, J. *N*,*N*-Dimethylformamide: Much more than a solvent. *Tetrahedron* **2009**, *65*, 8313–8323. [CrossRef]

92. Le Bras, J.; Muzart, J. *N*,*N*-Dimethylformamide and *N*,*N*-dimethylacetamide as carbon, hydrogen, nitrogen and/or oxygen sources. In *Solvents as Reagents in Organic Synthesis, Reactions and Applications*; Wu, X.-F., Ed.; Wiley-VCH: Hoboken, NJ, USA, 2017; pp. 199–314.
93. Le Bras, J.; Muzart, J. Recent uses of *N*,*N*-dimethylformamide and *N*,*N*-dimethylacetamide as reagents. *Molecules* **2018**, *23*, 1939. [CrossRef]
94. Vasseur, A.; Muzart, J.; Le Bras, J. Ubiquitous benzoquinones, multitalented compounds for palladium-catalyzed oxidative reactions. *Eur. J. Org. Chem.* **2015**, *2015*, 4053–4059. [CrossRef]
95. Harakat, D.; Muzart, J.; Le Bras, J. ESI-MS mechanistic studies of Wacker oxidation of alkenes: Dinuclear species as catalytic active intermediates. *RSC Adv.* **2012**, *2*, 3094–3099. [CrossRef]
96. Muzart, J.; Pète, J.-P. Dehydrogenation of cyclohexanones catalyzed by palladium (II) trifluoroacetate. *J. Mol. Catal.* **1982**, *15*, 373–376. [CrossRef]
97. Muzart, J. One-pot synthesis of α, β-unsaturated carbonyl compounds through palladium-mediated dehydrogenation of ketones, aldehydes, esters, lactones and amides. *Eur. J. Org. Chem.* **2010**, 3779–3790. [CrossRef]
98. Gligorich, K.M.; Sigman, M.S. Mechanistic questions about the reaction of molecular oxygen with palladium in oxidase catalysis. *Angew. Chem. Int. Ed.* **2006**, *118*, 6612–6615. [CrossRef] [PubMed]
99. Muzart, J. Molecular oxygen to regenerate $\mathrm{Pd^{II}}$ active species. *Chem. Asian J.* **2006**, *1*, 508–515. [CrossRef] [PubMed]
100. Gligorich, K.M.; Sigman, M.S. Recent advancements and challenges of $\mathrm{palladium^{II}}$-catalyzed oxidation reactions with molecular oxygen as the sole oxidant. *Chem. Commun.* **2009**, *26*, 3854–3867. [CrossRef]
101. Konnick, M.M.; Stahl, S.S. Reaction of molecular oxygen with a $\mathrm{Pd^{II}}$-hydride to produce a $\mathrm{Pd^{II}}$-hydroperoxide: Experimental evidence for an HX-reductive-elimination pathway. *J. Am. Chem. Soc.* **2008**, *130*, 5753–5762. [CrossRef]
102. Le Bras, J.; Muzart, J. The Saegusa oxidation and related procedures. *Org. React.* **2019**, *98*, 1–172.
103. Le Bras, J.; Muzart, J. Pd-catalyzed domino dehydrogenation/Heck-type reactions of carbonyl compounds. *Adv. Synth. Catal.* **2018**, *360*, 2411–2428. [CrossRef]
104. *The Mizoroki-Heck Reaction*; Oestreich, M. (Ed.) Wiley: Chichester, UK, 2009.
105. Fujiwara, Y.; Moritani, I.; Matsuda, M.; Teranishi, S. Aromatic substitution of olefin. IV Reaction with palladium metal and silver acetate. *Tetrahedron Lett.* **1968**, *9*, 3863–3865. [CrossRef]
106. Ferreira, E.M.; Zhang, H.; Stoltz, B.M. C–H bond functionalizations with palladium(II): Intramolecular oxidative annulations of arenes. *Tetrahedron* **2008**, *64*, 5987–6001. [CrossRef]
107. Trost, B.M. Atom economy—a challenge for organic synthesis: Homogeneous catalysis leads the way. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259–281. [CrossRef]
108. Le Bras, J.; Muzart, J. Intermolecular dehydrogenative Heck reactions. *Chem. Rev.* **2011**, *111*, 1170–1214. [CrossRef] [PubMed]
109. Aouf, C.; Thiery, E.; Le Bras, J.; Muzart, J. Palladium-catalyzed dehydrogenative coupling of furans with styrenes. *Org. Lett.* **2009**, *11*, 4096–4099. [CrossRef] [PubMed]
110. Vasseur, A.; Muzart, J.; Le Bras, J. Dehydrogenative Heck reaction of furans and thiophenes with styrenes under mild conditions and influence of the oxidizing agent on the reaction rate. *Chem. Eur. J.* **2011**, *17*, 12556–12560. [CrossRef] [PubMed]
111. Larock, R.C.; Hightower, T.R.J. Synthesis of unsaturated lactones via palladium-catalyzed cyclization of alkenoic acids. *J. Org. Chem.* **1993**, *58*, 5298–5300. [CrossRef]
112. Muzart, J. Oxidation adjacent to oxygen of alcohols catalyzed by palladium/dimethyl sulfoxide. In *Comprehensive Organic Synthesis*, 2nd ed.; Molander, G.A., Knochel, P., Eds.; Elsevier: Amsterdam, The Netherlands; Oxford, UK, 2014; Volume 7, pp. 295–301.
113. Stash, A.I.; Perepelkova, T.I.; Kravtsova, S.V.; Noskov, Y.G.; Romm, I.P. Palladium(II) diacetate complex with dimethyl sulfoxide: Structure and properties. *Koord. Khim.* **1998**, *24*, 40–43. *Russ. J. Coord. Chem.* **1998**, *24*, 36–39.
114. Zierkiewicz, W.; Privalov, T. A theoretical study of the essential role of DMSO as a solvent/ligand in the $\mathrm{Pd(OAc)_2}$/DMSO catalyst system for aerobic oxidation. *Organometallics* **2005**, *24*, 6019–6028. [CrossRef]
115. Vasseur, A.; Harakat, D.; Muzart, J.; Le Bras, J. ESI-MS studies of the dehydrogenative Heck reaction of furans with acrylates using benzoquinone as the reoxidant and DMSO as the solvent. *J. Org. Chem.* **2012**, *77*, 5751–5758. [CrossRef]

116. Vasseur, A.; Harakat, D.; Muzart, J.; Le Bras, J. Aerobic dehydrogenative Heck reactions of heterocycles with styrenes: A negative effect of metallic co-oxidants. *Adv. Synth. Catal.* **2013**, *355*, 59–67. [CrossRef]
117. Vasseur, A.; Laugel, C.; Harakat, D.; Muzart, J.; Le Bras, J. Ligand-promoted reactivity of alkenes in dehydrogenative Heck reactions of furans and thiophenes. *Eur. J. Org. Chem.* **2015**, *2015*, 944–948. [CrossRef]
118. Thiery, E.; Harakat, D.; Le Bras, J.; Muzart, J. Pd-catalyzed oxidative coupling of 2-alkylfurans with olefins through C-H activation: Synthesis of difurylalkanes. *Organometallics* **2008**, *27*, 3996–4004. [CrossRef]
119. Rulev, A.Y. Serendipity or the art of making discoveries. *New J. Chem.* **2017**, *41*, 4262–4268. [CrossRef]