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Regiochemistry of Wacker-Type Oxidation of Vinyl Group in the Presence of Neighboring Oxygen Functions. Part 2.

Hélène Pellissier,* Pierre-Yves Michellys and Maurice Santelli*

Laboratoire de Synthèse Organique, ESA n° 6009, Centre de St-Jérôme, Av. Esc. Normandie-Niemen,
13397 Marseille Cedex 20, France.

The regioselectivity of the palladium(II) oxidation of (±)-17α-vinyl-1,3,5(10)-gonatriene derivatives bearing a lactonic bridge on the α or β-face (β-face: obtention of the expected acetyl derivatives; α-face: presence of aldehydes, anti-Markovnikov addition) may be rationalized by an intramolecular coordination of the metal with the two lactonic oxygen atoms. Calculations carried out using ZINDO I method confirm the existence of such a chelation and the possibility of a cis-hydroxy or a cis-acetoxypalladation in the course of the Wacker process. An experimental confirmation was given by the regioselective mono-oxidation of the vinyl group syn to the methoxycarbonyl group of (3*R**,6*S**,9*S**)-3-methoxycarbonyl-3-(2-propyl)-6,9-divinyl-1-oxaspiro[4.4]nonan-2-one. © 1997 Published by Elsevier Science Ltd.

The palladium(II) oxidation of terminal olefins to give methyl ketones (Wacker process) is well established both as an industrial and a synthetic organic reaction.[1] Thus, terminal olefins can be regarded as masked methyl ketones.

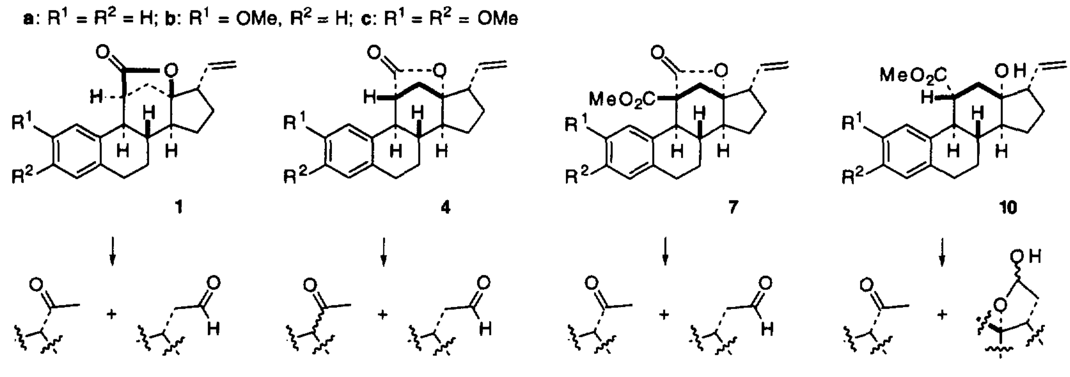
In a precedent paper, we reported that the palladium(II) oxidation of (±)-17α-vinyl-1,3,5(10)-gonatriene derivatives bearing a lactonic bridge on the β–face afford the expected acetyl derivatives. In contrast, when the lactonic bridge is present in the α-face (syn relationship) as for **4** or **7**, aldehydes resulting of an anti–Markovnikov hydroxypalladation are obtained in appreciate yields.[2] Palladium catalyzed oxidation gave unsatisfactory results when cuprous chloride and oxygen were used as co-reagents.[3] Fortunately, palladium acetate-benzoquinone oxidation, performed in the presence of perchloric acid,[4] provided a convenient route to oxidized compounds [$Pd(OAc)_2$, 10%; benzoquinone; $HClO_4$ (0.3 M); acetonitrile].

Treatment of (±)-17α-vinyl-1,3,5(10)-gonatriene derivatives **1**, bearing a lactonic bridge on the β-face, afforded the expected (±)-17α-acetyl-1,3,5(10)-gonatriene derivatives **2** in good yields. However, minor amounts of the unexpected terminal aldehydes **3** were obtained besides ketones **2**.

In marked contrast, oxidation of the isomeric (±)-17α-vinyl-1,3,5(10)-gonatriene derivatives **4**, bearing a lactonic bridge on the α-face, afforded a mixture of methyl ketone derivatives (expected α-acetyl compounds **5** and corresponding epimerized β-acetyl compounds) and aldehydes **6**.

Moreover, aldehydes **9** are major products from (±)-11β-carbomethoxy-17α-vinyl-1,3,5(10)-gonatriene derivatives **7** exhibiting a lactonic bridge on the α-face. Similarly, lactols **12** were obtained, respectively, from the (±)-11α-carbomethoxy-13α-hydroxy-17α-vinyl-1,3,5(10)-gonatriene derivatives **10** along with the acetyl compounds **11**.

E–mail: m.santelli@lso.u-3mrs.fr. Fax: (33) 04 91 98 38 65.



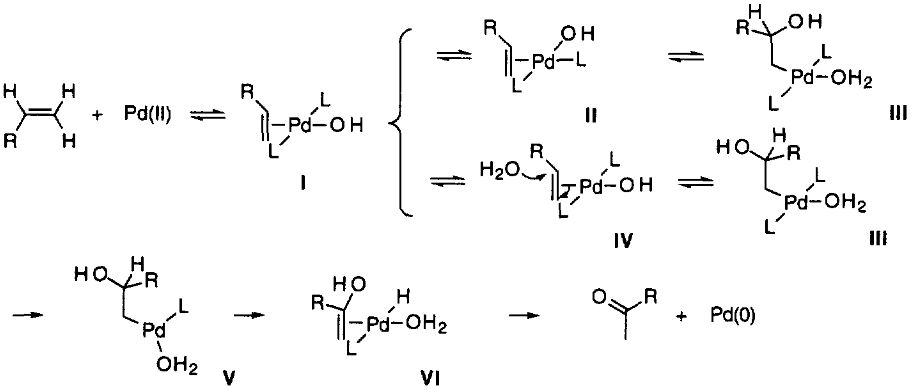
2a: 85%	**3a**: 7%	**5a**: 45%	**6a**: 35%	**8a**: 0%	**9a**: 37%	**11a**: 46%	**12a**: 37%
2b: 79%	**3b**: 14%	**5b**: 42%	**6b**: 28%	**8b**: 38%	**9b**: 45%	**11b**: 58%	**12b**: 22%
2c: 77%	**3c**: 9%	**5c**: 45%	**6c**: 30%	**8c**: 24%	**9c**: 28.5%	**11c**: 54%	**12c**: 22%

In order to facilitate the discussion of these results, we summarize below the accumulated data concerning the oxidation of olefines by palladium salts (see Scheme 1). Cupric chloride is the most usual reoxidizing reagent, in consequence the general mechanism has been postulated basing on kinetic work and involving an excess of chloride anion. Actually, only few studies concerning the oxidation with $Pd(OAc)_2$-benzoquinone system are known.[5]

a) Palladium salts reversibly react with olefins to give square Pd(II)-olefin π-complexes **I**. The trans arrangement of the hydroxo and the olefin ligands is advantageous because of the high trans effect of the ethene group.[6,7]

b) A trans-cis isomerization of complex **I** into **II** (or a ligand-hydroxy substitution) allows a cis-type four center addition of $OH^{(-)}$ leading to an unstable β-hydroxyalkylpalladium complex **III**. A cis-hydroxypalladation is supposed on the basis of kinetic studies without any direct evidence, but is at variance with some stereochemical studies with ethylene-d_2. These latter are rather in agreement with a reversible trans-hydroxypalladation **IV**.[8,9,10] Actually these results were observed in the conditions which do not give the normal Wacker products.[11]

Scheme 1.



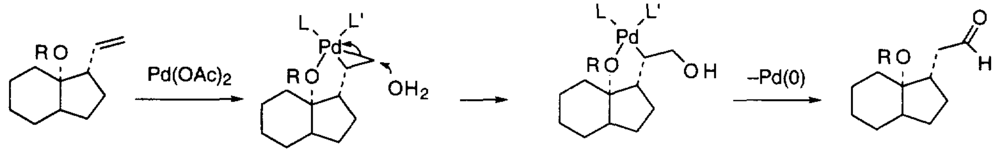
c) Decomposition of the β-hydroxyalkylpalladium complex **III** involves at first the formation of the σ-complex **V** by the loss of a ligand.[9b,9d] Then an hydride shift provides complex **VI** which finally leads to the expected carbonyl compound and the Pd(0) species. Some controversy concerning the exact mode of decomposition of the complex **V** exist. In the case of the oxidation of tetradeuteroethylene in ordinary water, decomposition occurs in such way as to give tetradeuteroacetaldehyde.[12]

d) The homogeneous oxidation of ethylene and terminal olefins is accelerated by addition of small amounts of acid but is inhibited by high concentrations of acid and by the presence of chloride anion. Acceleration by acidic conditions may be due to protonation of the ligands coordinated to the Pd(II) which increases its electrophilicity and reactivity toward olefins.[4,5]

The rate determining step could be the hydroxypalladation step (formation of **III**),[9d,10,13] or more probably, the formation of **V**.[10b,10d] The hydride shift (**V** to **VI**) involves a considerable Pd(II)-H character.[14]

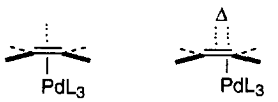
Only few reports involve aldehyde or acetal formations in the course of palladium-catalyzed oxidation of vinyl groups.[15] In most cases, the anti-Markovnikov addition reaction is due to the presence of an heteroatom.[16] The anomalous reaction was explained by postulating that palladium coordinates to the heteroatom and thereby influences the regioselectivity of the hydration step.[17] In a previous work, a coordination between a bimetallic complex (palladium, copper) and the heteroatom was even proposed in order to explain the stereoselectivity of the reaction.[18] However, all these examples only involve open chain compounds and no clear correlation between the relative position of the heteroatom with the double bond and the regiochemical outcome of the reaction has been established. In our case, the lack of copper reagent excludes the formation of such a bimetallic complex. Nevertheless, our results clearly show that the coordination of oxygen atom of the function beared by the α-face with palladium must be an important factor in the regioselectivity of the oxidation process.[19]

The regioselectivity may be rationalized by a nonsymmetrical bonding of palladium to the olefin producing complex **VIII**, caused by intramolecular coordination to the oxygen atom of the substituent . This slippage of the metal away from the methylene of the vinyl group would encourage nucleophilic attack of a water molecule at the methylene carbon, leading to intermediate **IX**. Decomposition of this η^1-Pd complex via β-hydride elimination of Pd–H would yield the observed product **X**.[20,21]



VII **VIII** **IX** **X**

Thus, we expected the regioselectivity of the reaction to be due to the preference for the position of the hydroxy group attack on the olefin coordinated to a Pd(II) center. In the aim to confirm this hypothesis we investigated the electronic structures of olefines coordinated to Pd(II). The first quantum chemical study of this step was made by Eisenstein and Hoffmann in the framework of extended Hückel theory.[22,23] On theoretical grounds, a symmetrically η^2 coordinated ethylene is deactivated toward attack by an external nucleophile.



But a distortion toward a η^1 geometry reactivates the double bond. The passage to activation occurs when the slipping is substantially nearer to a fully formed σ complex. The geometry of the transition state depends also on the nature of the nucleophile. It seems that the oxypalladation is more reactant-like.[24]

With the aim of finding a theoretical interpretation for the origin of the observed regioselectivity, we carried out molecular calculations. The geometry and the electronic structure of various palladium derivatives have been calculated by the ZINDO I method. This latter is the most suitable semi-empirical one for determining structures and energies of molecules with first or second transition row metals.[25,26]

We first calculated the geometry of the following 2-oxoalkylpalladium complex resulting from the oxidation of the complex obtained by the reaction of 3-butenylamine with $PdCl_2$. The structure was confirmed by X-ray analysis which established that a significant interaction exists between the palladium atom and the carbonyl carbon atom C(1).[27] The ZINDO I-optimized geometry is in agreement with the X-ray crystallographic measurements concerning the Pd bond lengths.

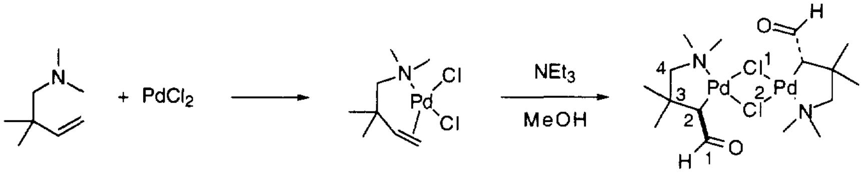


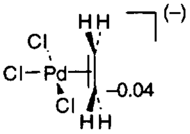
Table 1. Selected Bond Lengths Determined by X-Ray Analysis and ZINDO I Method.

Bond lengths (Å)	X-Ray Analysis	ZINDO I calculations[a]	Bond lengths (Å)	X-Ray Analysis	ZINDO I calculations
Pd–Cl(1)	2.476	2.49	C(1)–C(2)	1.460	1.46
Pd–Cl(2)	2.335	2.34	C(2)–C(3)	1.523	1.52
C(2)–Pd	2.036	2.03	C(3)–C(4)	1.511	1.51
N–Pd	2.076	2.06	C(4)–N	1.512	1.45

[a] H_f = 15289.0 kcal/mol.

Calculations of some η^2-Pd-ethene complexes have confirmed the lowering of the ethene LUMO (π^* orbital of the complexes) at the ZINDO I-level (LUMO of the ethene, 9.52 eV with the present basis)(see Figure 1). This effect is stronger in the case of an hydroxy ligand than that of a Cl ligand. The conformation **14** in which the ethene is perpendicular to the other ligand was found to be less stable than the in-plane conformation **16**. For this latter, calculations indicate that one hydroxy group is near to the carbon atom (C–O distance, 1.43 Å). This means that a cis migration of the hydroxy group occurred. Similar features were observed for the protoned complex **17** (C–O distance, 1.43 Å). Complex **18** (**14** + H_2O) in which ethene is perpendicular to the Pd-OH bonds exhibits an axis of symmetry. For the more stable isomer **19** (**16** + H_2O), two covalent C–O bonds were settled (C–O distance, 1.41 Å) and the complex with a plane of symmetry corresponds to the interaction of glycol with $(H_2O)_2Pd^{(2+)}$. In the case of complex **20** (**18** + H_2O), the presence of a supplementary H_2O ligand lowered the π^* orbital. The complex **21** has a plane of symmetry and results from a trans-hydroxypalladation of the complex $(H_2O)_2Pd^{(2+)}$(ethene). This complex is less stable than its isomer **17** (ΔH_f = 22.3 kcal/mol) resulting from a cis-hydroxy palladation. According to these calculations, an hydroxy attack within the coordination sphere of the complex is more favorable than an attack from the outer side. In contrast, the non-symmetrical complex **22**, corresponding to a trans-hydroxypalladation of **17** is more stable than isomers **18** (ΔH_f = –44.4 kcal/mol) or **19** (ΔH_f = –6.9 kcal/mol). Thus, the relative stability of the products resulting from an hydroxy attack depends of the ligands beared by the palladium.

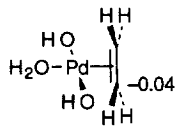
Figure 1. Structures of ethene-palladium complexes. The numbers indicate the net charges of the carbon atoms.



π* orbital: 8.64 eV
(24° OM)

H_f = –1483.6 kcal/mol

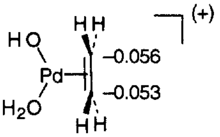
13



π* orbital: 9.05 eV
(28° OM)

H_f = –1894.9 kcal/mol

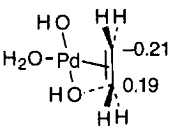
14



π* orbital: 2.79 eV
(24° OM)

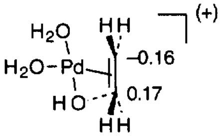
H_f = –1527.07 kcal/mol

15



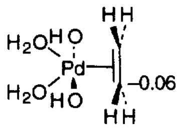
H_f = –1972.6 kcal/mol

16



H_f = –1973.8 kcal/mol

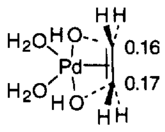
17



π* orbital: 6.34 eV
(29° OM)

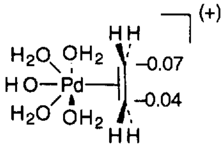
H_f = – 2205.5 kcal/mol

18



H_f = –2343.0 kcal/mol

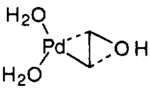
19



π* orbital: 4.24 eV
(36° OM)

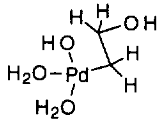
H_f = – 2529.7 kcal/mol

20



H_f = –1951.4 kcal/mol

21

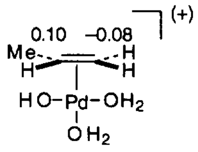


H_f = –2249.9 kcal/mol

22

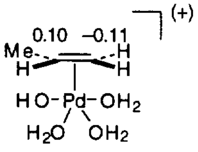
Similarly, calculations were performed for propene-Pd complexes (see Figure 2 and Table 2). The calculated net charges for complexes **23** and **24** were in agreement with a Markovnikov hydroxypalladation. Moreover, in the π* orbital, the substituted carbons bear the largest coefficients. In the case of complex **25**, resulting from the addition of hydrated palladium diacetate to propene, two C–O bonds were formed (C–O distance, 1.41 Å) and the complex corresponds to the interaction of the 1,2-diacetoxypropane with $(H_2O)Pd^{(2+)}$. In the case of **23**, the replacement of one H_2O by Me_2O (**26**) induced a cis-hydroxypalladation on the C(2). Strikingly, no C-O bond was performed after addition of one more H_2O ligand as in **27**.

Figure 2. Structures of some palladium complexes. The numbers indicate the net charges of the carbon atoms.



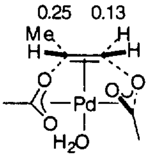
H_f = –2486.5 kcal/mol

23



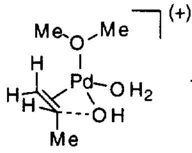
H_f = –2808.1 kcal/mol

24



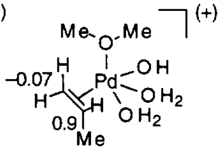
H_f = –4865.2 kcal/mol

25



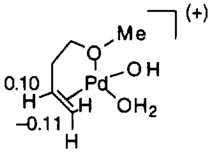
H_f = –3712.3 kcal/mol

26



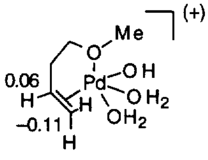
H_f = –3905.0 kcal/mol

27



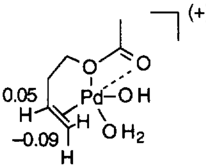
H_f = –3529.8 kcal/mol

28



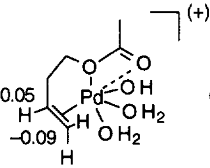
H_f = –3828.6 kcal/mol

29



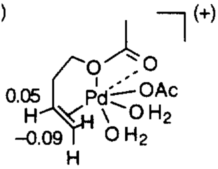
H_f = –4145.1 kcal/mol

30



H_f = –4447.4 kcal/mol

31



H_f = –5638.7 kcal/mol

32

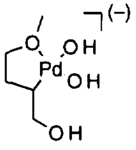
To account for the hypothetical chelation explaining the aldehyde formation, we carried out calculations on 4-methoxy-1-butene and 4-acetoxy-1-butene. Pd-complex with 4-methoxy-1-butene shows a methoxy-Pd bond (C–O distance, 1.82 Å). The addition of one ligand H_2O increased the energy of the π^* orbital (**24** vs **23** : 0.59 eV, **29** vs **28** : 0.66 eV, **31** vs **30** : 0.08 eV). Interestingly, if the calculated net charges were in agreement with a Markovnikov addition, *we note that the larger coefficient of the π^* orbital should be on the primary carbon atom.* So, a *frontier controlled hydroxy addition gave rise to an aldehyde.* Complexation of 4-acetoxy-1-butene led to π-complexes **30** and **31** which possess higher π^* orbital energies. Acetoxy group was linked to the palladium by the two oxygen atoms. For **30** and **31**, *the largest coefficient of the π^* orbital was on the primary carbon atom.* Nevertheless, in the case of **32**, which has an hydroxy group instead of an acetoxy group, the reverse occurred.

Table 2. Electronic structure of (π-olefin)Pd(II) complexes.

Complexes	**23**	**24**	**27**	**28**	**29**	**30**	**31**	**32**	**49**	**51**	**52**
π^*-orbital, no	31	35	41	36	40	42	46	54	84	79	84
energy, eV[a]	3.28	3.87	4.06	3.69	4.35	4.52	4.99	4.71	5.26	5.05	5.44
C(1), Px	0.24	0.42	0.01	0.13	–0.05	–0.28	–0.31	0.33	–0.33	0.36	–0.33
C(1), Py	–0.25	–0.35	0.22	–0.32	0.30	0.36	0.31	–0.21	–0.07	–0.04	–0.01
C(1), Pz	0.13	0.09	–0.41	0.45	–0.42	–0.15	–0.15	0.05	–0.29	0.01	–0.01
C(2), Px	–0.32	–0.45	0.07	–0.22	0.09	0.20	0.21	–0.33	0.31	–0.30	0.26
C(2), Py	0.25	0.27	–0.25	0.28	–0.25	–0.35	–0.31	0.27	0.06	0.05	–0.02
C(2), Pz	–0.08	–0.06	0.34	–0.37	0.39	0.14	0.15	–0.06	0.20	0.04	–0.06

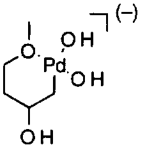
[a] LUMO of the propene at the ZINDO I-level: 9.245 eV.

We calculated the relative stability of the Pd-complexes resulting from the hydroxylation of the π-complexes obtained from 4-methoxy-1-butene. In all cases, *the anti-Markovnikov products were the most stable* (**33** vs **34**, ΔH_f = –12.1 kcal/mol; **35** vs **36**, ΔH_f = –21.6 kcal/mol; **37** vs **39**, ΔH_f = –46.6 kcal/mol).



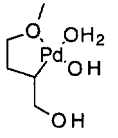
H_f = –3677.8 kcal/mol

33



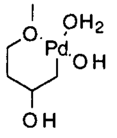
H_f = –3665.7 kcal/mol

34



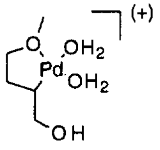
H_f = –3863.3 kcal/mol

35



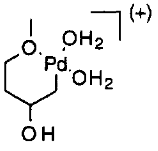
H_f = –3841.7 kcal/mol

36



H_f = –3900.7 kcal/mol

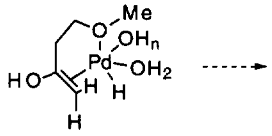
37



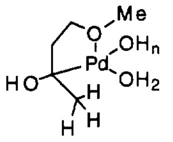
H_f = –3854.1 kcal/mol

38

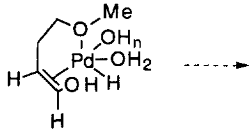
To carry on calculations of the various intermediates of the Wacker process concerning the model 4-methoxy-1-butene, we studied the η^2–PdH complex of the enols **39** and **42** (corresponding to complex **VI**). The minimization of the energy led to a modification of the starting structure (from molecular mechanism geometry optimization) in favor of an exchange of the hydrogen atom between Pd and C. The structures **40-41** and **43-44** after optimization were in agreement with a η^2–Pd complex which can eliminate PdH leading to ketone or aldehyde. The structures of these complexes correspond to the interaction of Pd with the protoned form of the carbonyl group. For this step, the complexes **40-41**, which are the precursors of the ketone, were more stable than complexes **43-44** (**40** vs **43**, ΔH_f = 8.6 kcal/mol; **41** vs **44**, ΔH_f = 3.8 kcal/mol). In the aim to examine the importance of the intramolecular coordination, we carried out calculations about the corresponding open complexes **45** and **46**. Complex **46**, precursor of the aldehyde, proved to be the most stable (**46** vs **45**, ΔH_f = −10 kcal/mol).



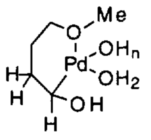
39



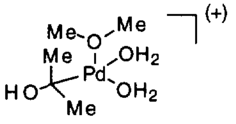
40, n = 1, H_f = −3853.7 kcal/mol
41, n = 2, H_f = −3892.7 kcal/mol



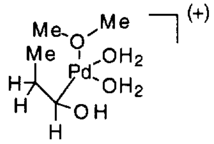
42



43, n = 1, H_f = −3845.1 kcal/mol
44, n = 2, H_f = −3888.9 kcal/mol

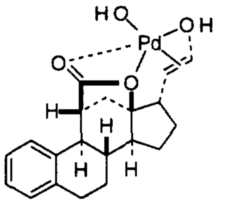


45, H_f = −4003.2 kcal/mol

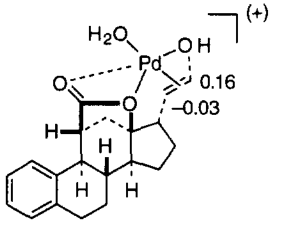


46, H_f = −4013.2 kcal/mol

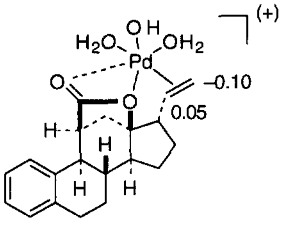
Calculations about steroids have confirmed the results. Complexes can be formed with steroids bearing an α- or β-bridge. As expected, the α-bridged palladium complexes are more stable. As for the above models, a cis-hydroxypalladation sometimes occurred at the terminal carbon atom of the vinyl group for **47** and **48** and on the more substituted carbon atom for **50**. In the other cases, *the largest coefficient of the π* orbital was on the primary carbon atom of the vinyl group* (see Table 2).



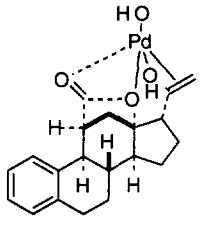
47, H_f = −10571.3 kcal/mol



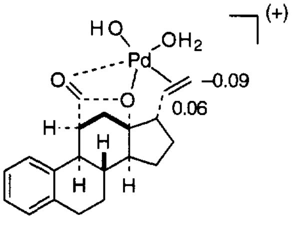
48, H_f = −10642.8 kcal/mol



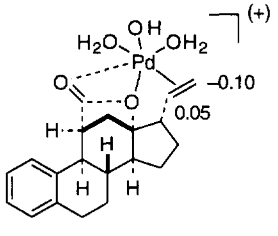
49, H_f = −10857.6 kcal/mol



50, H_f = −10586.2 kcal/mol

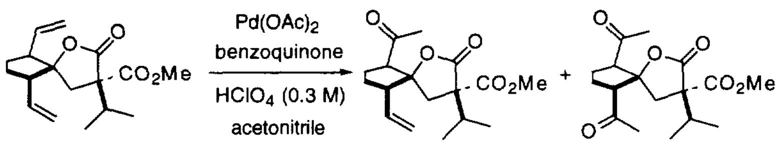


51, H_f = −10557.6 kcal/mol

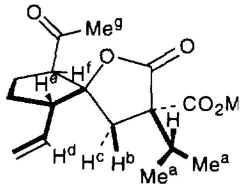


52, H_f = −10854.2 kcal/mol

To test the specific role of the oxygenated function, we performed the oxidation of the divinyl spirolactone **53** in which one vinyl group presents a syn relationship with the methoxycarbonyl group while the second one is away from any heteroatoms. Major product **54** arised from the oxidation of the vinyl group activated by the presence of the ester function. So, *the chelation of the palladium increased the overall rate of the oxidation reaction.* The relative stereochemistry of **54** was determined by a series of 1D, COSY and NOESY experiments (400 MHz). In particular, phase mode NOESY experiments confirmed the vicinal relationship between the *i*-Pr group and its adjacent vinyl group. We observed that H(d)(δ = 5.60 ppm) only gives cross peaks with H(b)(δ = 2.24 ppm) and H(f)(δ = 3.07 ppm), then H(b) and H(a)(δ = 0.88 and 0.80 ppm) produce a cross peak. The relative position of H(e)(δ = 2.80 ppm) and H(g)(δ = 2.06 ppm) was confirmed by the presence of a cross peak. The proximal position of H(c)(δ = 2.54 ppm) and H(f)(δ = 3.07 ppm) was proved by the existence of a cross peak. In contrast, no cross peak has been observed between H(d) and H(c).



53 **54** **55**



CONCLUSIONS

The main results of our calculations at the ZINDO I-level indicate the following features:

- Optimized geometry of some complexes give rise to a more stable structure corresponding to a cis-hydroxypalladation.
- In the case of terminal olefins bearing an oxygenated function located at C(4), the chelation induces an increasing of the coefficient of the complexed π*-orbital at the end of the double bond (C(1)). In contrast, the net atomic charge is mainly present at C(2). This would indicate that the regioselectivity is a frontier orbital-controled reaction.
- In the course of the energy minimization of the η^2-PdH complex of the enols a transfer of hydrogen occurres from palladium to α-carbone.

In conclusion, theoretical and experimental results both confirm the chelation of the palladium by a suitable oxygenated function. This effect can explain the obtention of an aldehyde resulting from an anti-Markovnikov hydration of the distorted Pd(II)-olefin complexes. Moreover, this chelation increases the rate of the expected Wacker-process as we have observed in the course of the oxidation of the spiro-lactone **53**.

EXPERIMENTAL SECTION

General. All reactions were run under argon in oven-dried glassware. TLC was performed on silica gel 60 F_{254}. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz respectively. Carbon-proton couplings were determined by DEPT sequence experiments. MO calculations were performed using HyperChem release 5 package without any modification on a 200 MHz PC.[28] Structures were minimized with the following parameters: restricted Hartree-Fock (RHF) level, minimization algorithm, until the root mean square energy gradient was less than 0.001 kcal/mol Å, accelerated convergence.

Wacker Oxidation of the spiro-lactone 53.

To a solution of 0.1 mmol of palladium acetate (22.4 mg, 0.1 equiv) and 0.5 mmol of benzoquinone (0.54

g, 0.5 equiv) in 10 mL of acetonitrile, 3.1 mL of water and 0.65 mL of perchloric acid (70 %) were successively added. The mixture was stirred 0.5 h at 20 °C under argon. Then a solution of the spirolactone **53** (1 mmol) in 12 mL of acetonitrile was added and stirred at 20 °C for XX h. The mixture was pourred in diethyl ether and washed with a solution of soda (30 %). The aqueous layer was extracted with ether. The combined organic layers were dried over magnesium sulfate, filtrated and concentrated under vacuum. The crude product was purified by chromatography on silica gel.

(3*R,5*S**,6*R**,9*S**)-6-Acetyl-3-methoxycarbonyl-3-(2-propyl)-9-vinyl-1-oxaspiro[4.4]-nonan-2-one (54).** IR 1774, 1720, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.60 (ddd, *J* = 17.2, 10.4, 7.2 Hz, 1H), 5.16 (br d, *J* = 10.4 Hz, 1H), 5.10 (br d, *J* = 17.2 Hz, 1H), 3.80 (s, 3H), 3.07 (dd, *J* = 8.5, 7.1 Hz, 1H), 2.80 (br. q, *J* = 7.2 Hz, 1H), 2.57 (sept., *J* = 6.8 Hz, 1H), 2.54 (1/2 AB, *J* = 14.2 Hz, 1H), 2.24 (1/2 AB, *J* = 14.2 Hz, 1H), 2.1-1.92 (m, 2H), 2.06 (s, 3H), 1.6-1.52 (m, 1H), 1.18-1.08 (m, 1H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 207.8 (s), 173.5 (s), 171.0 (s), 90.8 (s), 136.0 (d), 118.7 (t), 61.0 (s), 58.2 (d), 53.5 (d), 51.0 (q), 34.3 (d), 31.3 (t), 30.5 (q), 26.1 (t), 24.3 (t), 18.4 (q), 18.2 (q). Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 65.91; H, 8.04.

(3*R,6*R**,9*R**)-6,9-Diacetyl-3-methoxycarbonyl-3-(2-propyl)-1-oxaspiro[4.4]-nonan-2-one (55).** IR 1774, 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.82 (s, 3H), 3.34 (t, *J* = 8.3 Hz, 1H), 3.30 (dd, *J* = 9.0, 6.4 Hz, 1H), 2.84 (1/2 AB, *J* = 14.6 Hz, 1H), 2.57 (sept., *J* = 6.8 Hz, 1H), 2.17 (1/2AB, *J* = 14.6 Hz, 1H), 2.17 (s, 3H), 2.07 (s, 3H), 1.83 (quint.d, *J* = 9.6, 6.4 Hz, 1H), 0.88 (d, *J* = 6.8 Hz, 1H), 0.80 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 208.8 (s), 207.5 (s), 173.3 (s), 170.8 (s), 89.8 (s), 60.8 (s), 59.1 (d), 58.5 (d), 53.5 (q), 34.4 (d), 31.8 (t), 31.7 (q), 31.0 (q), 24.8 (t), 24.7 (t), 18.2 (q), 18.1 (q). Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 63.15; H, 7.86.

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