Rhodium Mediated C–H Bond Functionalization Leading to Carboxylate Derivatives

Cristina Tejel,* M. Pilar del Río, José A. López, and Miguel A. Ciriano

Carboxylic acids and their esters or lactones are among the most common functionalities,[1] and a large number of fine chemicals are accessible from this functionality.[1] Typical organic synthetic procedures[2] towards carboxylic acids include oxidation of alcohols and aldehydes and hydrolysis of nitriles, while carboxylation of organic substrates containing C–X bonds is perhaps the best established approach to carboxylic acids mediated by transition metal complexes.[3] From an atom economy perspective, direct functionalization of C–H bonds to C–CO₂R bonds is a highly desirable alternative, since it avoids classical functional group manipulations. Although scarce, such palladium catalysed reactions were recently reported.[4] From a formal point of view, a COO moiety could be inserted into a C–H bond by the combination of oxygenation and carboxylation involving simply O₂ and CO as attractive and cheap substrates. In this line, 2-metallooxetanes[5] emerge as valuable candidates to test this possibility, since they could be obtained by oxygenation of olefins with dioxygen.[6] Although the reactivity of 2-metallooxetanes is currently in its infancy,[7] two of them have been reported to be suitable for C–X (X = N, O) bond formation, as shown for the reactions of 2-rhoda- and 2-platina-oxetanes with acetonitrile[8] and carbon monoxide,[9] respectively. In this communication we describe new reactions leading to carboxylic acids and lactones, involving the stoichiometric functionalization of an allylic C–H bond of cod with carbon monoxide and dioxygen which proceeds via a discrete 2-dioxoaxetane intermediate.

We previously reported the selective reaction of [Rh₂(C₂H₅)₂(PPh₃)₂] (C₂H₅ = 1.5-cyclooctadiene, PPh₃ = 1,3-diphenyltriazenido) with molecular oxygen to give the dinuclear 2-rhoda[II]oxetane complex [{Rh(PPh₃)₂(OCC₃H₅)}₂] (1, Scheme 1).[6a] Diffusion of carbon monoxide through a dichloromethane solution of 1 at room temperature gave the carbonyl complex [{Rh(CO)₂(μ-PPh₃)₂}₂] (3) quantitatively, along with 4-cyclooctenone (2, 65 %). Although complex 1 contains three different types of metal–X σ-bonds (X = O, N, C), each in principle suitable for carbon monoxide insertion, the reaction predominantly leads to elimination of the oxygenated fragment as 4-cyclooctenone (2). The way in which 2 is eliminated upon exposure of 1 to CO should be similar to the reactions previously reported for the reactions of complex 1 with phosphines.[10] The second organic compound in the reaction (in 35 % yield) was further identified as the cycloocta-2,6-diene carboxylic acid (4) (see Experimental Section). As most relevant resonances, the proton from the –COOH moiety, unobserved at room temperature, was located as a sharp singlet (at δ = 13.67 ppm) at −70 °C in [D₈]-toluene while the carboxylic carbon appeared at the usual chemical shift (δ = 180.7 ppm) in the ¹³C{¹H} NMR spectrum.

On raising the temperature of the reaction, the amount of carboxylic acid 4 increases and becomes the major product at 60 °C in C₆D₆, provided that carbon monoxide is allowed to diffuse slowly through a solution of 1 (Scheme 1).

Dr. C. Tejel, Dr. M. P. del Río, Dr. J. A. López, Prof. M. A. Ciriano
Departamento de Química Inorgánica
Instituto de Ciencia de Materiales de Aragón (ICMA)
CSIC-Universidad de Zaragoza,
Pedro Cerbuna 12, 50009-Zaragoza (Spain)
Fax: (+ 34) 976 761187
E-mail: ctejel@unizar.es

Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author.

Scheme 1. Elimination reactions from the 2-rhoda[III]oxetane complex 1 on reaction with carbon monoxide under different conditions. i) slow diffusion and ii) vigorous stirring. The two nitrogen atoms on 1 and 6 represent the anionic Ph₃P=N ligand. The numbering scheme is used for NMR characterization.

Noticeably, the slow diffusion and dilution of carbon monoxide is crucial for the regioselective synthesis of 4. If the solution of 1 is heated at 60 °C and then mixed with CO at 0 °C under vigorous shaking a different product is formed, i.e. the new 8-oxabicyclo[5.2.1]deca-2,5-dien-9-one (5, Scheme 1). Again [{Rh(CO)₂(μ-PPh₃)₂}] (3) is the single rhodium product. Prolonged heating (100 °C, 3 bar of CO) gave a mixture, probably the thermodynamic one, containing 5 and the isomeric oxabicycles with the olefinic bonds in positions 2,4 (5b) and 3,5 (5c). Compound 5 was identified on the basis of its spectroscopic data (see Experimental Section and Supporting Information). From the six CH signals observed in the apt.¹³C{¹H} NMR
spectrum four of them correspond to the olefinic carbons, while those at δ = 40.3 and 76.9 ppm correspond to C1 and C7 bound to the C=O and O, respectively. As expected, the carboxylic carbon (C9) was observed at a typical chemical shift (δ = 176.3 ppm).

Monitoring the reactions by $^1$H NMR allowed the observation of the common active species leading to cycloocta-2,6-diene carboxylic acid (4) and 8-oxabicyclo[5.2.1]deca-2,5-dien-9-one (5). This species was found to be the eighteen-electron rhodium(III) complex $\left[\text{Rh(PhN}_2\text{Ph)}\left(\text{HO-Cl}_2\text{H}_2\right)\left(\text{CO}\right)\right] \ (6)$ (Scheme 1), which was isolated in a separate experiment working quickly at 0 °C to prevent the elimination reaction. The phenyl groups of 6 are non-equivalent, and the allyl moiety was clearly identified by the sharp resonances at δ = 5.45, 4.71 and 4.53 ppm in the $^1$H NMR spectrum. The alkyl carbon bound to rhodium produces a sharp doublet at δ = 54.8 ppm (J(\text{C,Rh}) = 18.5 Hz) in the $^{13}$C($^1$H)-apt spectrum while the carbon bearing the hydroxyl group gives a sharp singlet at δ = 87.3 ppm. The terminal carbonyl group bound to rhodium was identified by a strong ν(C=O) stretch band at 2083 cm$^{-1}$ with IR spectroscopy.

Complex 6 is the result of the isomerization of the rhodaoxetane(III) complex 1 into the 16 v.e. hydroxy-allyl-allyl species $\left[\text{Rh(PhN}_2\text{Ph)}\left(\text{HO-Cl}_2\text{H}_2\right)\right]$ followed by the coordination of carbon monoxide. We previously reported the hydroxy-allyl-allyl species $\left[\text{Rh(PhN}_2\text{Ph)}\left(\text{HO-Cl}_2\text{H}_2\right)\right]$ without CO ligands (coordination polymer) formed in the reaction of $\left[\text{RhCl}_2(\text{PhN}_2\text{Ph})\right]$ with oxygen through isomerisation of the 2-rhodaoxetane intermediate.$^{[14]}$ Related isomerisation reactions have been previously reported for similar 2-metalloxetane complexes,$^{[15,16]}$ but follow-up reactivity for these species have not been described. In principle, complex 6 could exist in three possible isomeric forms as shown in Figure 1, but the reaction selectively produces only isomer 6a with the carbonyl group in close proximity to the hydroxyl group (as evidenced by NOESY spectroscopy, see Supporting Information).

![Figure 1. Possible stereoisomers of $\left[\text{Rh(PhN}_2\text{Ph)}\left(\text{HO-Cl}_2\text{H}_2\right)\left(\text{CO}\right)\right]$. Isomers 6b and 6c were not observed. The two nitrogen atoms on the rhodium represent the triazenide ligand.](image)

Figure 2 shows the DFT optimized geometry of 6a. The hydroxy-allyl-allyl moiety behaves as a fac-tridentate ligand; a chelating triazenide ligand and one carbonyl group complete an almost octahedral environment for the rhodium. The strong trans-influence of the alkyl carbon (C1) is clearly evidenced by the considerable elongation of the Rh-N1 bond in $\text{trans}$ (2.244 Å) when compared to the other Rh-N3 bond (2.188 Å) $\text{trans}$ to the C4 atom in the allyl group. Within the allyl group, the Rh–C4 bond is found to be shorter (2.200 Å) than the Rh–C6 bond (2.337 Å). The optimized geometries of isomers 6b ($+4.0$ kcal mol$^{-1}$) and 6c ($+4.3$ kcal mol$^{-1}$) are clearly higher in energy (see Supporting Information).

![Figure 2. DFT calculated structure of 6a. Selected distances (Å): Rh–C1 2.094, Rh–C4 2.200, Rh–C5 2.181, Rh–C6 2.337, Rh–N1 2.244, Rh–N3 2.188, Rh–C9 1.906. Only the ipso carbons of the phenyl groups are shown for clarity.](image)

Starting from isolated samples of 6a, the carboxylic acid 4 and the oxabicycle 5 were synthesized and the new organic compounds were isolated (see Experimental Section). Moreover, we have verified that carbon monoxide is not needed for the formation of the carboxylic acid 4 from 6a except for being liberated from the rhodium coordination sphere, while the formation of the lactone 5 requires carbon monoxide as reactant. Furthermore, when the reactions of 6a with $^{13}$CO were carried out under the two different experimental conditions all $^{13}$CO was found to be fully incorporated only into the complex $\left[\left[\text{Rh(13CO)}\right]_2\left[\mu-\text{PhN}_2\text{Ph}\right]\right]$ (3–$^{13}$CO) in both cases, indicating that the carbonyl group in 4 and 5 comes from that previously coordinated to rhodium in complex 6a. In a reverse order, the reactions of the labeled complex 6a–$^{13}$CO with carbon monoxide gave either 4–$^{13}$CO or 5–$^{13}$CO as the sole labeled compounds. The selectivity observed in the labeling experiments indicates that 4 and 5 come from an intramolecular reaction undergone by 6a, and suggests both reactions to proceed through a common intermediate, which would result from the coupling of the carbonyl group (13CO) with the C4 atom (A, Scheme 2). This step is available through a change in the coordination mode of the η$^1$-allyl group into a σ-allyl one, perhaps assisted by the hydroxyl moiety, to produce the carbonyl insertion into the Rh–C4 bond. Precedents for facile reactions of this type assisted by hemilabile ligands are known in palladium chemistry.$^{[11]}$

The way to 4 from A requires a cleavage of the C–OH bond in the organic moiety. A viable possibility is a β-hydroxy elimination reaction from the coordinatively unsaturated acyl intermediate A to give the rhodiumhydroxo(η$^2$,η$^2$-cycloocta-2,5-dien-1-carboxylate) complex (B, Scheme 2). Precedents for β-hydroxy elimination in the coordination sphere of platinum$^{[54, 7a]}$ are known. Reductive elimination of the hydroxy and carbonyl groups (producing the COOH group) renders the diene ligand, which is eventually replaced by carbon monoxide in the rhodium complex, according to the experimental data. This mechanism, proceeding via β-hydroxy elimination from the coordinatively unsaturated intermediate A should be blocked by CO coordination driving the reaction to C (Scheme 2), and thus it readily explains why this reaction channel is suppressed in the presence of CO.
Starting from C (Scheme 2), and with independence of the exact order of steps, formation of 5 would require a nucleophilic attack of the hydroxyl to the acyl group to form a protonated γ-lactone ring. β-hydrogen elimination from the C8–H bond along with the acidic proton would give dihydrogen and 5, probably coordinated to rhodium. Finally, replacement of 5 by carbon monoxide renders the organic compound and the rhodium complex [{Rh(CO)}_{2}(PhN=Ph)]. A similar sequence of reactions involving Cl1 would give a four-membered β-lactone ring, which is disfavoured by ring-strain.

In summary, rhodium complexes bearing a hydroxy-alkyl-allyl moiety are suitable intermediates for the regioselective synthesis of either carboxylic acids or γ-lactones. In these reactions, carbon monoxide is incorporated into the organic fragment along with the formation of new C–C and C=O bonds. Taking together with the oxygenation of L,5-cyclooctadiene to [{Rh(PhN=Ph)(HO–(C=H)H)}] by O2, the carbon monoxide reactions described here disclose a new sequence of stoichiometric reactions for the regioselective functionalization of an allylic C–H bond, which is a main challenge in current chemistry [2]. Further studies to understand the reaction mechanisms and to uncover synthetic applications of this new reaction are underway.

**Experimental Section**

\[
\{(\text{CO})_2\text{Rh(PhN=Ph)}\}\] (3). A suspension of \([\text{Rh}(\text{PhN=Ph})(\text{CH}_3)]\) (1000 mg, 0.12 mmol) in toluene (5 mL) was warmed for 2 h at 80 °C under a CO atmosphere. The resulting red solution was evaporated to dryness, left under vacuum for one day, and the red residue washed with 2 mL of cold hexane. 1H NMR (500 MHz, CD_3OD, 25 °C): δ = 7.66 (d, 3J(HH) = 8.6, 11 Hz, H'H'), 7.04 (m, 3J(HH) = 7.8 Hz, 8H'H'), 6.88 (m, 3J(HH) = 7.4, 11 Hz, 4H'H'); 13C NMR (500 MHz, CD_3OD, 25 °C): δ = 185.9 (d, 3J(CH) = 66.5 Hz), 152.1 (C), 128.9 (C), 129.8 (C), 129.9 (C).

\[
\{(\text{Rh}(\text{PhN=Ph})(\text{HO–(C=H)H}))\}\text{OC}(\text{H}_2)]\] (6). A suspension of \([\text{Rh}(\text{PhN=Ph})(\text{OC}(\text{H}_2)]\) (1) (1000 mg, 0.118 mmol) in toluene (10 mL) was warmed at 100 °C for 1 h 30 min to ensure the full transformation of I into \([\text{Rh}(\text{PhN=Ph})(\text{HO–(C=H)H}))\]. The suspension was cooled at 0 °C and the argon atmosphere was replaced by carbon monoxide. After stirring for 15 min, the resulting brown solution was concentrated to 3 mL and hexane (10 mL) was added under a CO atmosphere to precipitate a brown solid. The mother liquor was decanted and the solid was washed with cold hexane (3 x 2 mL) and dried under vacuum. Yield: 70.3 mg (76 %); 1H NMR (500 MHz, CD_3OD, 25 °C): δ = 7.52 (d, 3J(HH) = 6.8 Hz, 2H'H'), 7.27 (t, 3J(HH) = 7.9 Hz, 2H'H'), 7.17 (t, 3J(HH) = 7.9 Hz, 2H'H'); 7.12 (d, 3J(HH) = 7.9 Hz, 2H'H'); 7.01 (t, 3J(HH) = 7.6 Hz, 1H'H').

References [12-15]
corrections (at 298 K, 1 atm) to the energy have been estimated on the basis of the
frequency calculations.

Acknowledgements

The generous financial support from MICINN/FEDER (Project CTQ2008-03860)
and GA (Gobierno de Aragón, PM 36/2007) is gratefully acknowledged. M.P.R.
thanks GA for a fellowship. Authors thank Dr. Bas de Bruin for useful discussions
and M. Victoria Mendoza for experimental assistance.

Keywords: carboxylic acids • lactones • metallaoxetanes •
rhodium • carbon monoxide

3164; Angew. Chem. Int. Ed. 2008, 47, 3101–3120; b) L. K. Goodfien, K.
Goodfien, N. Rodrigue, M. Blanchot, C. Linder, B. Zimmermann, Pure Appl.


Munday, J. R. Martineili, S. L. Buchwald, J. Am. Chem. Soc. 2008, 130,
2754–2755; c) J. Muzart, Tetrahedron, 2005, 61, 9423–9463; d) A. Haynes,
P. M. Maitis, G. E. Morris, G. J. Sunley, H. Adams, P. W. Badger, C. M.
Bowes, D. B. Cook, P. I. P. Elliott, T. Ghaffar, H. Green, T. R. Griffin, M.
Soc. 2004, 126, 2847–2861; e) E. Daura-Oller, J. M. Poblet, C. Bo, Dalton
Homogeneous Catalysis with Organometallic Compounds, Vol. 1 (Eds:

L. Jin, P. Li, and A. Lei, J. Am. Chem. Soc. 2008, 130, 9429–9433; c) W.-Y.
130, 3304–3306.

[5] For representative examples of LTM-metallaoxetanes, see for example: a) N.
M. Welange, E. Szurimi, P. R. Sharp, J. Am. Chem. Soc. 2009, 131,
8736–8737; b) J. Wu, P. R. Sharp, Organometallics, 2008, 27, 1234–1241
and references therein; c) J. R. Khusnutdinova, L. L. Newman, P. Y. Zavalji,
Cinellis, G. Minigetti, F. Cocco, S. Strocchio, A. Zucca, M. Manassero,
6892–6895; f) B. de Bruin, P. H. M. Buddezaar, A. W. Gal, Angew. Chem.
Szurimi, H. Sham, P. R. Sharp, J. Am. Chem. Soc. 2003, 125, 10522–10523;
and references therein.

Acknowledgements

The generous financial support from MICINN/FEDER (Project CTQ2008-03860)
and GA (Gobierno de Aragón, PM 36/2007) is gratefully acknowledged. M.P.R.
thanks GA for a fellowship. Authors thank Dr. Bas de Bruin for useful discussions
and M. Victoria Mendoza for experimental assistance.

Keywords: carboxylic acids • lactones • metallaoxetanes •
rhodium • carbon monoxide

3164; Angew. Chem. Int. Ed. 2008, 47, 3101–3120; b) L. K. Goodfien, K.
Goodfien, N. Rodrigue, M. Blanchot, C. Linder, B. Zimmermann, Pure Appl.


Munday, J. R. Martineili, S. L. Buchwald, J. Am. Chem. Soc. 2008, 130,
2754–2755; c) J. Muzart, Tetrahedron, 2005, 61, 9423–9463; d) A. Haynes,
P. M. Maitis, G. E. Morris, G. J. Sunley, H. Adams, P. W. Badger, C. M.
Bowes, D. B. Cook, P. I. P. Elliott, T. Ghaffar, H. Green, T. R. Griffin, M.
Soc. 2004, 126, 2847–2861; e) E. Daura-Oller, J. M. Poblet, C. Bo, Dalton
Homogeneous Catalysis with Organometallic Compounds, Vol. 1 (Eds:

L. Jin, P. Li, and A. Lei, J. Am. Chem. Soc. 2008, 130, 9429–9433; c) W.-Y.
130, 3304–3306.

[5] For representative examples of LTM-metallaoxetanes, see for example: a) N.
M. Welange, E. Szurimi, P. R. Sharp, J. Am. Chem. Soc. 2009, 131,
8736–8737; b) J. Wu, P. R. Sharp, Organometallics, 2008, 27, 1234–1241
and references therein; c) J. R. Khusnutdinova, L. L. Newman, P. Y. Zavalji,
Cinellis, G. Minigetti, F. Cocco, S. Strocchio, A. Zucca, M. Manassero,
6892–6895; f) B. de Bruin, P. H. M. Buddezaar, A. W. Gal, Angew. Chem.
Szurimi, H. Sham, P. R. Sharp, J. Am. Chem. Soc. 2003, 125, 10522–10523;
and references therein.
Selective functionalization of 1,5-cyclooctadiene either to the carboxylic acid or to the γ-lactone is achieved by a novel sequence of reactions involving quantitative oxygenation with oxygen, and C–C coupling with carbon monoxide. The rhodium hydroxy-alkyl-allyl complex shown in the inset is the active intermediate promoting the elimination of the organic compounds.