

## NOVEL RING CLOSURE CARBONYLATION REACTION OF 1,5-CYCLOOCTADIENE IN THE PRESENCE OF Pd(II)-CATALYSTS

Curtis B. ANDERSON<sup>a</sup> and Rade MARKOVIĆ<sup>b</sup>

<sup>a</sup> Department of Chemistry,  
University of California, Santa Barbara, California 93106, U.S.A.

<sup>b</sup> Faculty of Chemistry,  
University of Belgrade, P.O. Box 550, 11001 Belgrade, Yugoslavia

Received January 17, 1992

Accepted March 10, 1992

---

Oxidative carbonylation of 1,5-cyclooctadiene in methylene chloride-methanol mixture, catalyzed by Pd(II)-salts, gave rise to a bicyclic, bifunctional product under mild experimental conditions. The mechanism, involving multiple carbon monoxide and double bond insertions into the Pd(II)-carbon  $\sigma$ -bond, has been proposed, as being consistent with the outcome of this novel ring closure reaction.

---

In the past few years there has been enhanced activity concerning the synthesis of the functionalized cyclic compounds by means of the Pd(II)-catalyzed cyclization of nonconjugated 1,5-dienes<sup>1-3</sup>. Several examples of these reactions are available, recent cases being the oxidative transformations of 1,5-cyclooctadiene (1,5-COD) (ref.<sup>4</sup>) and other 1,5-dienes<sup>5</sup> to the corresponding bicyclic or cyclic compounds, using PdCl<sub>2</sub>-Pb(OAc)<sub>4</sub> and PdCl<sub>2</sub>-MnO<sub>2</sub>-*p*-benzoquinone catalyst-oxidant systems, respectively.

We now wish to report the novel ring closure carbonylation of 1,5-cyclooctadiene initiated, under mild experimental conditions, by palladium(II)-salts. It has been shown that catalytic carbonylation of conjugated dienes *I* yields primarily monoesters, diesters<sup>6</sup> and/or  $\beta$ -alkoxy esters<sup>7</sup> in alcohols, acting as a solvent and reacting species. The details of the general reaction scheme will not be repeated here<sup>8</sup>, but the common catalytic intermediates *II* and *III* are responsible for the formation of monoesters *IVa* and  $\beta$ -alkoxy esters *IVb* (Scheme 1).

Since the intramolecular insertion of the double bond into the carbon-palladium(II)  $\sigma$ -bond of the intermediate *II* (*II*  $\rightarrow$  *V*) or *III* (*III*  $\rightarrow$  *VI*) can be useful synthetically on account of the formation of various cyclic products<sup>9</sup>, we decided to explore and find experimental conditions for the ring closure of 1,5-cyclooctadiene.

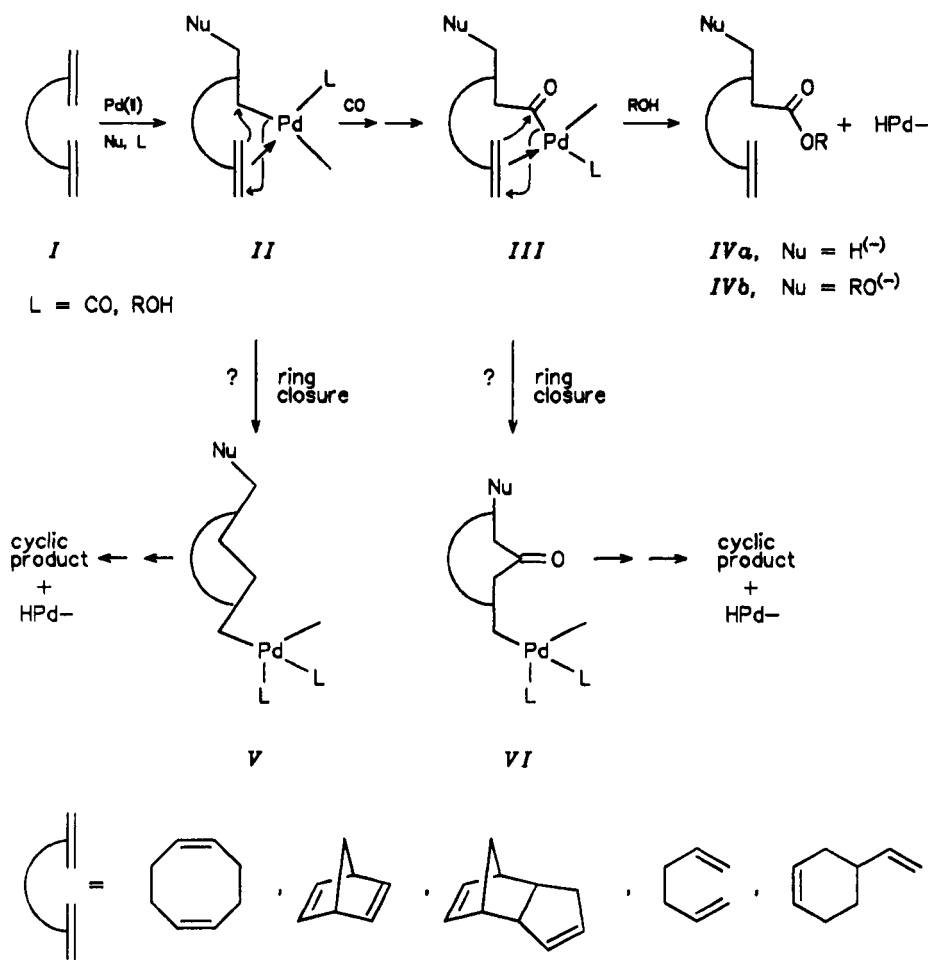
### EXPERIMENTAL

*General.* <sup>1</sup>H NMR spectra in ppm ( $\delta$ -scale) were recorded on a Varian F-60 and Varian XL-100 spectrometer in CdCl<sub>2</sub> as solvent unless otherwise stated. IR spectra ( $\nu$  in cm<sup>-1</sup>) were taken on a Perkin-Elmer

Model 283 spectrometer. Mass spectra were recorded on a AEI MS-902 spectrometer. Gas chromatographic (GC) analyses and separations were carried out on a Loenco model 15 C-E and Hewlett-Packard model 775, both equipped with a thermal conductivity detector. GC columns used for analytical and preparative runs were packed with 10% and 20% Carbowax 4000 on Chromosorb W 60/80 mesh, non-acid washed. For higher temperatures Carbowax 20 M on Chromosorb W 60/80 mesh, non-acid washed was used. Microanalyses were performed by Chemalytics Inc. (Tempe, Arizona).

Catalytic Carbonylation of 1,5-COD in Methylene Chloride–Methanol Solution in the Presence of PdCl<sub>2</sub>–CuCl<sub>2</sub>–NaOAc as a Catalyst–Oxidant System

The experimental procedure used in this work for the catalytic carbonylation has been described previously<sup>8</sup>. A mixture of 0.1 g (0.56 mmol) of palladium chloride, 2.2 g (27 mmol) of sodium acetate, 3.6 g

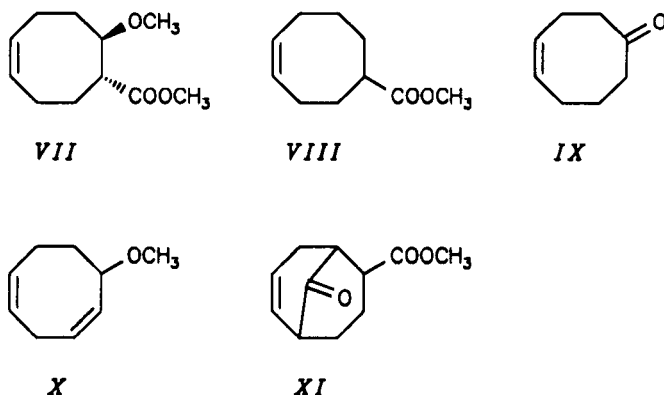


SCHEME 1

(27 mmol) of copper(II) chloride and 4 ml (32 mmol) of 1,5-cyclooctadiene in methylene chloride (50 ml)–methanol (3 ml) solution was placed into the 250 ml Pyrex bottle. After evacuation, carbon monoxide was introduced to well stirred solution under pressure (417 kPa) and the reaction mixture was heated to 100 °C for the period of 24 h. A brown-black suspension was worked-up and GC analysis on a 3 m × 0.6 cm column of 20% Carbowax 4000 on non-acid washed 60/80 mesh Chromosorb operated at 160 °C and 68 kPa, showed the presence of five products (Table I, run 3). Three compounds with retention times of 3, 5 and 12 min were those found in catalytic carbonylation of 1,5-COD at 100 °C in methanol as solvent (Table I, run 1): methyl 4-cyclooctenecarboxylate (*VIII*) (16.5%), 4-cyclooctenone (*IX*) (13%) and 2,5-cyclooctadienyl methyl ether (*X*) (5%). The compounds *VIII* – *X* were identified by co-injection with authentic samples and mass spectrometry. A complete description of characterization for *XVIII*, *IX* and *X* was presented elsewhere<sup>10</sup>. The fourth bifunctional compound (retention time 37 min) characterized as methyl *trans*-8-methoxycyclooctenecarboxylate (*VII*) (24%) by comparison of the spectral and physical data to those of the independently synthesized authentic sample was also found as a main product in catalytic carbonylation of 1,5-COD in methanol (Table I, run 1). The product with the longest retention time (125 min) purified by a careful fractional distillation at 148 – 149 °C (67 Pa), was detected as 2-carbomethoxybicyclo[3.3.1]nonan-9-one (*XI*) (30%): <sup>1</sup>H NMR (CDCl<sub>3</sub>): 3.6 s, 3 H (CO<sub>2</sub>CH<sub>3</sub>); 2.65 m, 1 H (HCCO<sub>2</sub>CH<sub>3</sub>); 2.4 m, 2 H (α-carbonyl hydrogens). IR spectrum (neat): 1 735, 1 700, 1 450, 1 250, 1 030 cm<sup>-1</sup>. Mass spectrum, *m/z* (rel. %): 196 (M<sup>+</sup>, 10), 165 (12.5), 137 (8.8), 109 (5.5), 124 (26.5), 67 (28), 55 (100) 43 (13). For C<sub>11</sub>H<sub>16</sub>O<sub>3</sub> (197.1) calculated: 67.25% C, 8.12% H; found: 67.35% C, 6.17% H.

The 2,4-dinitrophenylhydrazone derivative of *XI* melted at 134 – 135 °C. The total yield of the organic products *VII*, *VIII*, *IX*, *X* and *XI*, determined on the basis of the limiting copper(II) salt was 45% in a ratio of 24 : 17 : 13 : 5 : 30.

In order to account for the rest of the organic material the carbonylation experiment was repeated under the same conditions but the work-up of the reaction mixture was different. Therefore, after the completion of the reaction the whole mixture was transferred to a distillation apparatus for efficient fractionation. The temperature was increased by gentle heating and 0.322 g of distillate collected at 57 – 60 °C in the flask cooled in a dry ice–acetone bath. GC analysis indicated the presence of two components and the minor one isolated by preparative GC (0.092 g; 1.45 mmol) was identified as methyl formate by comparison of retention time and IR spectra with an authentic sample. The one with longer retention time was identified as methanol. The yield of methyl formate based on the limiting reagent was calculated to be 17.5%. The described work-up of the reaction mixture afforded in addition to methyl formate, five known products *VII* – *XI* and the traces of the undesired isomerized compounds<sup>10</sup>. The overall yield including methyl formate was 62%.



Catalytic Carbonylation of 1,5-COD in the Presence of Pd(OAc)<sub>2</sub>-CuCl<sub>2</sub>-NaOAc System

Bicyclic product *XI* was also prepared from 1,5-COD by catalytic carbonylation according to the procedure described above, by using Pd(OAc)<sub>2</sub>-CuCl<sub>2</sub> as catalyst-oxidant system (molar ratio 0.56 : 54) in methanol-methylene chloride mixture (Table I, run 2). After the work-up GC analysis of the reaction mixture showed the following composition: *VII* (30%), *VIII* (3%), *IX* (20%), *X* (11%), *XI* (28%) and other unidentified isomerized products (8%). The total yield of the products *VII* - *XI* was 69% without methyl formate included (11%).

Catalytic Carbonylation of 1,5-COD in the Presence of Pd(OAc)<sub>2</sub>-Cu(OAc)<sub>2</sub>-NaOAc System

The procedure was the same as above with Pd(OAc)<sub>2</sub>-Cu(OAc)<sub>2</sub>-NaOAc molar ratio (0.56 : 22 : 44) and using methanol as a solvent (Table I, run 4). The yield was 26% and GC indicated the following composition: *VII* (30%), *VIII* (3%), *IX* (20%), *X* (23%), *XI* (28%) and unidentified isomerization products (8%) of shorter retention times.

## RESULTS AND DISCUSSION

We already mentioned that the pronounced interest in the synthesis of functionalized cyclic compounds as important precursors in organic and natural product chemistry,

TABLE I  
Oxidative catalytic carbonylation of 1,5-COD

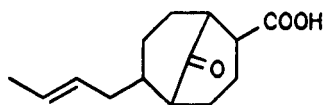
Run <sup>a</sup>	Catalyst mmol	Oxidant mmol	NaOAc mmol	Solvent ml	Products <sup>b</sup> , %					Unknown %	Total yield <sup>c</sup> %	C. N. <sup>d</sup>
					<i>VII</i>	<i>VIII</i>	<i>IX</i>	<i>X</i>	<i>XI</i>			
1	Na <sub>2</sub> PdCl <sub>4</sub> 0.50	CuCl <sub>2</sub> 40	84	CH <sub>3</sub> OH 200	89	2	4	1	0	4	91	36
2	Pd(OAc) <sub>2</sub> 0.56	CuCl <sub>2</sub> 54	54	CH <sub>3</sub> OH 6 CH <sub>2</sub> Cl <sub>2</sub> 100	30	3	20	11	28	8	69	19.6
3	PdCl <sub>2</sub> 0.56	CuCl <sub>2</sub> 27	27	CH <sub>3</sub> OH 3 CH <sub>2</sub> Cl <sub>2</sub> 50	24	17	13	5	30	11	45	9.5
4	Pd(OAc) <sub>2</sub> 0.56	Cu(OAc) <sub>2</sub> 22	44	CH <sub>3</sub> OH 50	30	3	20	11	28	8	26	4

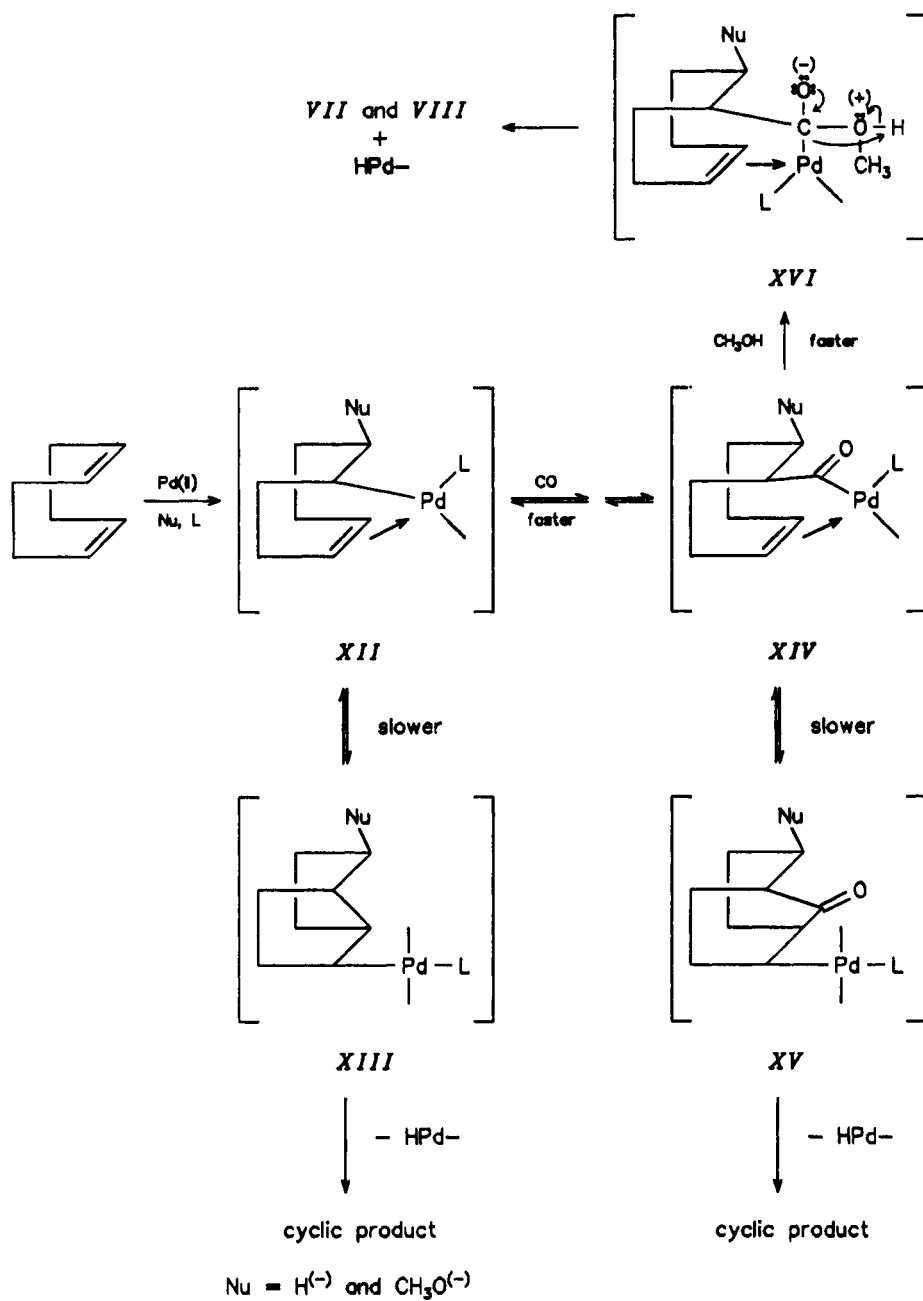
<sup>a</sup> 10% Molar excess of diene; reaction temperature 100 °C; reaction time 24 h; CO pressure 300 kPa (runs 2 and 3); reaction temperature 20 °C; reaction time 44 h; CO pressure 200 kPa (run 1); reaction time 80 h; CO pressure 300 kPa (run 4). <sup>b</sup> Relative percentage of the organic products. <sup>c</sup> Yield determined by an internal GC standard, or based on an oxidant as limiting reagent. <sup>d</sup> Catalytic turnover number (mmol of organic products/mmol of catalyst).

initiated our study of palladium(II)-mediated cyclization of 1,5-cyclooctadiene. This diene was chosen as a starting substrate for its expected ease of cyclization. When catalytic carbonylation of 1,5-COD was carried out in methanol, in the presence of  $\text{Na}_2\text{PdCl}_4$  as a catalyst, under the conditions shown in Table I (run 1), methyl *trans*-8-methoxy-4-cyclooctenecarboxylate (*VII*) and methyl 4-cyclooctenecarboxylate (*VIII*) were formed as carbonylated products (total yield 91%; ratio 89 : 2) along with the undesired oxidation products *IX* and *X*, isolated in a very small yield<sup>10</sup>. Under such experimental conditions we could see no evidence for the formation of the bicyclic products.

One of the intermediates of the catalytic cycle in the carbonylation reaction of 1,5-COD, yielding *VII* and *VIII*, is the species *XII*, formed by *trans*-palladation via preformed metal  $\pi$ -complex (Scheme 2). The reasonable hypothesis explaining the absence of a bicyclic product is that the reaction of carbon monoxide with the intermediate *XII* (*XII*  $\rightarrow$  *XIV*) proceeds much faster, than the preferential, concurrent *cis*-insertion of the double bond into the carbon-metal  $\sigma$ -bond (*XII*  $\rightarrow$  *XIII*).

The formation of another type of bicyclic product is possible<sup>9</sup> by an initial intramolecular attack of the double bond on the carbonyl of an acyl-palladium(II) complex *XIV*. Nevertheless the transformation of 1,5-cyclooctadiene to *VII* and *VIII* represents the principal mechanistic pathway in methanol. Obviously, the nucleophilic attack of this solvent of relatively high nucleophilicity, on the acyl-palladium(II)  $\sigma$ -bond is substantially faster (*XIV*  $\rightarrow$  *XVI*), than the desired cyclization reaction (*XIV*  $\rightarrow$  *XV*). It follows that by decreasing the nucleophilic power of methanol by mixing it with some nonpolar solvent, an intramolecular participation of the sterically unhindered double bond might become competitive (step *XIV*  $\rightarrow$  *XV*). Especially noteworthy is that Chiu-soli et al.<sup>11</sup> reported the carbonylation of 1,5-cyclooctadiene and crotyl chloride with nickel tetracarbonyl in a nonpolar solvent, containing the low concentration of methanol. The bicyclic product *XVII* was then formed via similarly postulated transannular cyclization reaction. Consequently, it seemed very likely to us, that the solvent mixture of methylene chloride and methanol (50 : 3 ratio; v/v) with the  $\text{PdCl}_2$ - $\text{CuCl}_2$ - $\text{NaOAc}$  proportions given in Table I (run 3) may promote the double bond insertion into the palladium-carbon  $\sigma$ -bond of the acyl-palladium(II) complex *XIV*. Under these reaction conditions the nucleophilic reactivity of methanol is strongly inhibited. The suspension was flushed with nitrogen, evacuated, and with the constant shaking carbon monoxide introduced under pressure (300 kPa) at room temperature. The temperature of the oil

*XVII*



SCHEME 2

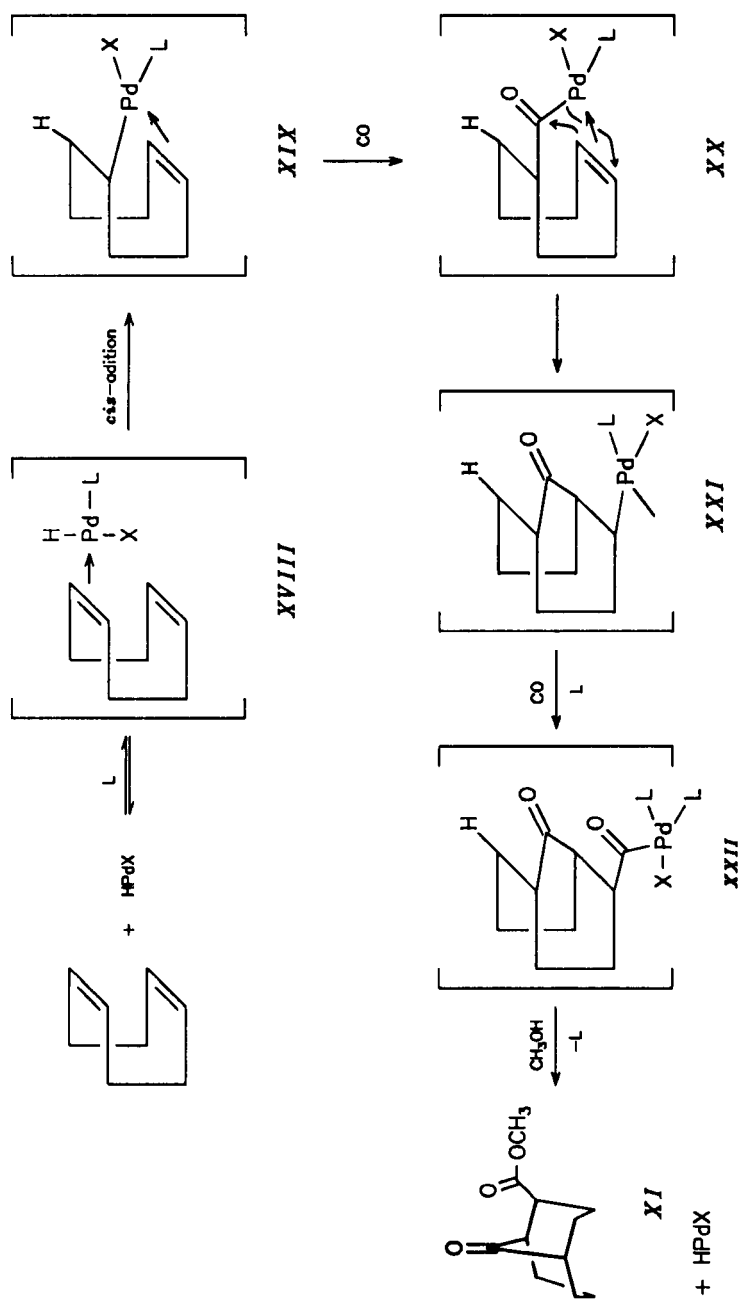
bath was raised to 100 °C and after 24 h a brown-black suspension was obtained. After the usual extractive work-up, GC analysis showed the presence of five products VII – XI, the four of which (VII – X) were those identified previously. The new product was identified as 2-methoxycarbonylbicyclo[3.3.1]nonan-9-one (XI).

As can be seen from the Table I (run 2), changing Pd(OAc)<sub>2</sub> to PdCl<sub>2</sub> as a catalyst, led to the similar product composition of the organic products VII – XI, but Pd(OAc)<sub>2</sub> was more effective catalyst. Catalytic number was 19.6 compared to 9 with PdCl<sub>2</sub> as a catalyst.

The determination of the structure of the bicyclic  $\gamma$ -keto ester XI was based on the following physical and chemical evidence. The neat IR spectrum indicates the presence of two carbonyl groups. The absorption at 1 735 cm<sup>-1</sup> together with the strong absorptions at 1 250, 1 450 and 1 030 cm<sup>-1</sup> are due to the methoxycarbonyl group. This is confirmed by the characteristic singlet in the <sup>1</sup>H NMR spectrum at  $\delta$  3.6 ppm, which integrated correctly for three protons in the methyl group. The IR absorption for the second carbonyl group appears at 1 700 cm<sup>-1</sup>, which is typical for the keto group in a six-membered ring. Furthermore, the multiplet signal centered at  $\delta$  2.4 ppm in the <sup>1</sup>H NMR spectrum must represent 2 hydrogens  $\alpha$  to the carbonyl group. In addition, the bicyclic compound XI gives an orange 2,4-diphenylhydrazone, m.p. 134 – 135 °C. The NMR integration permits an unequivocal assignment for one proton on the tertiary carbon atom bearing the methoxycarbonyl group ( $\delta$  2.65 ppm, multiplet integrated for one proton of HCCO<sub>2</sub>CH<sub>3</sub>). The molecular peak in the mass spectrum at  $m/z$  supports the molecular formula C<sub>11</sub>H<sub>16</sub>O<sub>3</sub>. The mass spectrum, besides indicating the molecular ion at  $m/z$  196, had fragments at  $m/z$  165 (M – OCH<sub>3</sub>) and 137 (M – CO<sub>2</sub>CH<sub>3</sub>) which are indicative of the methoxycarbonyl residue. Elemental analysis is in accordance with the suggested formula (see Experimental). The most likely mechanism leading to the bicyclic compound XI, as depicted in Scheme 3, begins with the *cis*-addition of the hydrido-palladium(II) species (HPdX) to 1,5-COD. In turn HPdX is generated in situ by dehydropalladiation from the intermediate XVI (Scheme 2). The result of this stereospecific reaction is  $\sigma$ - $\pi$ -palladium(II) complex XIX.

A subsequent carbonylation of XIX, followed by the double bond insertion into the palladium(II)-carbon  $\sigma$ -bond of an intermediate XX, forms the bicyclic Pd(II)- $\sigma$ -complex XXI. The last steps of the reaction cycle involve the second CO insertion and methanolysis of the acyl-palladium  $\sigma$ -complex XXII. The elimination of Pd(II)-hydride with the simultaneous liberation of organic product XI completes the catalytic cycle.

Interestingly, while the formation of usual carbonylation products VII and VIII is generally preferred in methanol as a solvent (Table I, run 1), the bicyclic product formation (30% of XI with respect to the other organic compounds) becomes also a favorable competitive process in methanol, though in the chloride-free reaction medium with Pd(OAc)<sub>2</sub> as a catalyst and Cu(OAc)<sub>2</sub> as an oxidant (Table I, run 4). It is difficult to explain this finding, but the weaker coordination of the acetate group to palladium



SCHEME 3



most probably enhances the possibility for the double bond insertion into the metal-carbon  $\sigma$ -bond, as a key step in palladium(II)-catalyzed carbonylation of 1,5-COD. However, the yield was low (26%) and based on the catalytic number only 4 mmol of organic compounds can be obtained in this manner from 1 mmol of 1,5-COD.

Obviously from the synthetic point of view this kind of the multiple insertion of carbon monoxide and the coordinated double bond into Pd(II)-carbon  $\sigma$ -bond affords an attractive approach to the synthesis of double functionalized bicyclic products. On the other hand, palladium(II)-induced cyclization, as is often the case in organometallic chemistry, is not the single reaction path.

#### REFERENCES

1. Stille J. K., Tanaka M. J.: *J. Am. Chem. Soc.* **109**, 3785 (1987).
2. Henry P. M., Davies M., Ferguson G., Phillips S., Restivo R.: *Chem. Commun.* **1974**, 112.
3. Henry P. M.: *Palladium-Catalyzed Oxidation of Hydrocarbons*. D. Reidel Publishing Co., Dordrecht 1980.
4. Brewis S., Hughes P. R.: *Chem. Commun.* **1965**, 489.
5. Antonsson T., Moberg C., Tottie L., Heumann A.: *J. Org. Chem.* **54**, 4914 (1989).
6. Tsuji J., Hosaka S., Kiji J., Sasuki T.: *Bull. Chem. Soc. Jpn.* **39**, 141 (1966).
7. Hines L. F., Stille J. K.: *J. Am. Chem. Soc.* **94**, 485 (1972).
8. Anderson C. B., Marković R.: *Collect. Czech. Chem. Commun.* **56**, 663 (1991).
9. Tour J. M., Negishi E.: *J. Am. Chem. Soc.* **107**, 8289 (1985).
10. Marković R.: *Thesis*. University of California, Santa Barbara 1981.
11. Guerrieri F., Chiusoli G. P.: *J. Organometal. Chem.* **15**, 209 (1968).