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Palladium-catalysed cyclocarbonylation reactions in dimethyl carbonate, an eco-friendly solvent and ring-opening reagent

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Dimethyl carbonate (DMC) is used as an alternative and eco-friendly solvent for selective cyclocarbonylation reactions of allyl phenol derivatives for the synthesis of lactones; in some cases, depending on the reaction condition, DMC behaves as a ring-opening reagent producing methoxycarbonyl compounds. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: 2-allyl phenols; allyl naphthols; cyclocarbonylation; lactones; palladium; dimethyl carbonate

INTRODUCTION

Transition-metal-catalysed cyclocarbonylation reactions represent an interesting synthetic strategy for the preparation of cyclic compounds, e.g. lactones and lactams.[1–8] Various routes to lactones have been described in the past decade, and palladium-based catalysts are among the most efficient for such carbonylation reactions.[9,10]

A few years ago we reported that the combination of palladium acetate ($Pd(OAc)_2$) and 1,4-bis-(diphenylphosphino) butane (dppb) formed an efficient homogeneous catalytic system for the selective cyclocarbonylation of allyl phenols and other bis-allyl phenols.[11,12]

The reaction afforded new important five-, six- and seven-membered ring lactones (Scheme 1) and it has been noted that the solvent can play an important role in terms of yield and regioselectivity: in toluene, for example, the seven-membered ring lactone was the major product; in dichloromethane, the six- and five-membered lactones were favoured.

Recently, in view of the possible need for future development of environmentally sustainable processes, we validated the efficiency of $Pd(OAc)_2$–dppb on the cyclocarbonylation of natural substrates such as for example estrone and cardanol derivatives.[13,14] We also reported the heterogeneous cyclocarbonylation reactions of allylphenols, using Pd–C as a catalytic system.[15] Continuing our research on cyclocarbonylation reactions, with a view to their possible future development as environmentally sustainable processes, we have investigated these reactions in alternative solvents having a low environmental impact, such as dialkyl carbonates.

The eco-sustainability of dimethyl carbonate (DMC) began from its low-cost industrial production through the new methanol–carbon monoxide cuprous-chloride-catalysed process and developed because of its reduced toxicity smaller energy requirement, lowest boiling point and lower flammable point compared with other solvents (e.g. toluene, CH_2Cl_2, $CHCl_3$).[16–40] These parameters are of fundamental importance with regard to a possible sustainable scale-up of the cyclocarbonylation reactions.

In particular, the advantages of DMC could go beyond of being an attractive eco-friendly solvent due to its reduced toxicity; it is a well-known reagent used in different classes of reactions. As reported by Tundo and Selva,[41] DMC, depending on the experimental conditions, can exhibit a versatile and tunable chemical reactivity, either as a methoxycarbonylating or as a methylating agent.

Therefore we report in this paper our results on the selective cyclocarbonylation reactions of allyl phenols performed in dialkyl carbonate using $Pd(OAc)_2$ and dppb as the catalytic system. In particular, we show that the efficiency of the catalytic system in such an eco-solvent is maintained and that, in some cases, DMC behaves as a reactant producing opening of the lactone ring.

RESULTS AND DISCUSSION

As reported previously, treatment of 2-allyl phenol (**1a**) with $Pd(OAc)_2$ and dppb in toluene under 1/5 carbon

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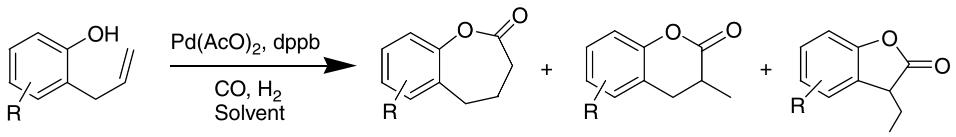


Scheme 1.

Table 1. Cyclocarbonylation reactions of the substrates **1a**–**c** catalysed by Pd(OAc)$_2$–dppb[a]

Run	Substrate	Time (h)	T (°C)	P_{CO} (psi)	P_{H_2} (psi)	Ligand	Conversion[b] (%)	Product (%)[c]			
								2a–c	**3a–c**	**4a–c**	**5a–c**
1	**1a**	24	100	10	0	dppb	45	25	8	67	0
2	**1a**	24	100	100	0	dppb	93	4	7	89	0
3	**1a**	24	100	100	500	dppb	40	7	20	35	38
4	**1a**	48	100	100	500	dppb	90	0	0	35	65
5	**1a**	48	120	100	500	dppb	97	3	8	17	72
6	**1a**	48	100	100	0	PPh$_3$	0.5	0	0	0	*0*
7	**1b**	24	100	100	0	dppb	100	11	4	85	0
8	**1b**	48	100	100	0	dppp	75	4	5	49	42
9	**1b**	96	120	100	0	dppp	100	25	11	38	26
10	**1b**	48	100	100	0	dppe	30	10	10	70	10
11	**1b**	96	120	100	0	dppe	90	20	4.9	0.1	75
12	**1c**	24	100	100	0	dppb	30	0.2	0.3	99	0.5
13	**1c**	96	100	100	0	dppb	90	0.1	0.4	99	0.5

[a] Reaction conditions: substrate (1.0 mmol), catalyst Pd(OAc)$_2$ (0.01 mmol); dppb (0.04 mmol); solvent (5 ml).
[b] Determined by gas chromatography (GC)–MS analysis.
[c] Isolated distributions.

monoxide and hydrogen resulted in 90% conversion with good selectivity toward the seven-membered ring lactone **4a**, with trace amounts of the six- and five-membered ring lactones **3a** and **2a**.

In a similar manner, performing the reaction in DMC in place of toluene, the yields toward the seven-membered ring lactone were maintained at a high level, as was the selectivity (Table 1, run 2).

Trace amounts of the six- and five-membered ring lactones **3a** and **2a** were also present, and in some cases, depending on the reaction conditions, 4-(2-hydroxy-phenyl)-butyric acid methyl ester (**5a)** was formed (Scheme 2).

2-Allyl-4-hydroxybenzaldehyde (**1b)** and 1-allyl-naphthalen-2-ol (**1c)** were also studied for such transformations (Schemes 2 and 3) and the results are summarized in Table 1.

Other alkyl carbonates, such as diethyl carbonate and diphenyl carbonate, were also considered, but the yields and selectivities were lower than in the case of DMC.

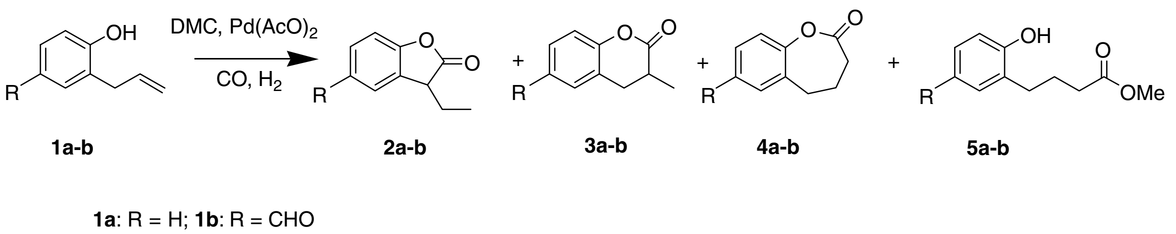
Carbon monoxide, of course, is of fundamental importance for cyclocarbonylation; but other parameters, such as temperature, time, ligands, presence of molecular hydrogen (H_2), can play a key role in terms of yield and selectivity of the reaction.

For example, the formation of the seven-membered ring lactone was preferred at 100 °C (Table 1, run 2); however, at higher temperature (higher than 120 °C), longer reaction time and in the presence of H_2 (Table 1, runs 4 and 5), the formation of the methoxycarbonyl compound was favoured.

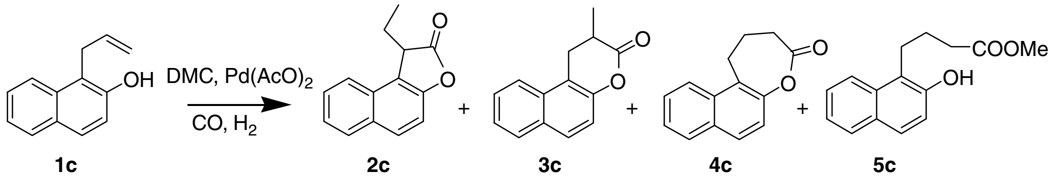
No reaction was observed at 80 °C or at lower temperatures, and no reaction occurs when monodentate phosphine ligands, such as triphenyl phosphine (Table 1, run 6), or a mixture of them with dppb were used. Other bidentate phosphine ligands, such as 1,2-diphenyl phosphine ethane (dppe) and 1,3-diphenyl phosphine propane (dppp), produced low yield but the selectivity was maintained (Table 1, runs 10 and 11). In particular, in the case of dppe at 100 °C, the conversion was 30% with good selectivity toward the seven-membered ring **4b** (Table 1, run 10). On performing the same reaction at 120 °C, the conversion was 90% and the selectivity was in favour of the 4-(2-hydroxy-5-methyl-phenyl)-butyric acid methyl ester (**5b**; Table 1, run 10).

The reaction, however, can be tuned either in favour of the lactone or in favour of methoxycarbonyl compound simply by changing the reaction time and temperature.

Table 2 reports the regioselectivity of the reaction for different solvents and different catalytic systems (homogeneous, heterogeneous) and it is possible to observe that, in the case of the heterogeneous system (Table 2, run 8), the conversion is maintained at a high level but the selectivity towards **5a** is lower compared with the homogeneous system.



Scheme 2.

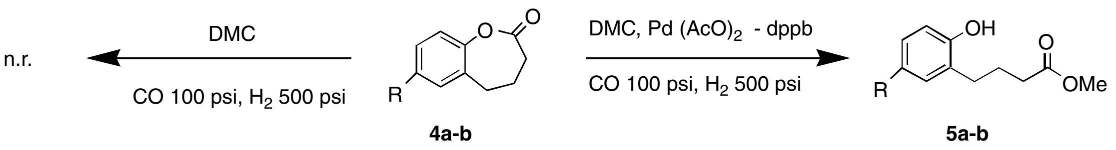


Scheme 3.

Table 2. Cyclocarbonylation reactions of the substrate **1a** using different solvent and catalytic systems

Run	Time (h)	T (°C)	Catalyst[a]	Solvent	P_{CO} (psi)	P_{H_2} (psi)	Conversion[b] (%)	Product (%)[c]			
								2a	**3a**	**4a**	**5a**
1	24	100	$Pd(OAc)_2$–dppb	Toluene	100	100	95	2	3	95	
2	24	100	$Pd(OAc)_2$–dppb	DMC	100	100	93	4	7	89	
3	24	120	$Pd(OAc)_2$–dppb	CH_2Cl_2	100	500	98	76	18	6	
4	36	100	$Pd(OAc)_2$–dppb	DMC	100	500	40	7	20	35	38
5	48	100	$Pd(OAc)_2$–dppb	DMC	100	500	90	0	0	35	65
6	24	120	Pd/C–dppb	Toluene	300	500	70	25	30	45	
7	24	120	Pd/C–dppb	CH_2Cl_2	100	500	95	85	15	0	
8	40	120	Pd/C–dppb	DMC	100	0	99	9	7	29	55

[a] Reaction conditions: substrate (1.0 mmol), dppb (0.04 mmol), solvent (5 ml). Catalyst $Pd(OAc)_2$ (0.01 mmol) or catalyst Pd/C (0.01 mmol palladium).
[b] Determined by GC–MS analysis.
[c] Isolated yields.



Scheme 4.

The formation of the methoxycarbonyl compounds **5a**–**b** can be tentatively explained by considering that the lactones **4a**–**b**, once formed, can be opened by DMC, which behaves as a methoxycarbonylating agent.

Further investigations devoted to justifying the mechanism of ring opening have confirmed that lactone formation is preliminary to their ring-opening reaction.

Experiments carried out *ad hoc* to support this mechanism have shown that, on reacting lactones **4a**–**b** in DMC in the presence of catalytic amounts of palladium–dppb catalyst, the ring-opening reaction occurs in 24 h; on the contrary, no reaction was observed in the absence of palladium catalyst or using other solvents (toluene, CH_2Cl_2, $CHCl_3$) under the same reaction conditions (Scheme 4).

The involvement of nucleophilic species was demonstrated to be important in the mechanism of methoxycarbonylation by DMC;[41,42] for our cases this role can be attributed to Pd–H or Pd–OCH_3 as key intermediates in the ring-opening reactions.

We cannot exclude the involvement of methanol, generated *in situ* by a palladium-catalysed reduction from DMC, in the ring opening of the lactone compounds.

CONCLUSIONS

In summary, we have demonstrated that in the palladium-catalysed cyclocarbonylation reaction of allyl phenols performed in DMC, yields and regioselectivity for the seven-membered ring lactone are maintained at a high level, similar to that performed in toluene under analogous reaction conditions (temperature, reaction times and CO/H_2 molar ratio). In contrast to the other solvents, DMC at high temperature and longer reaction time behaved as a reactant, promoting the formation of methoxycarbonyl compounds.

EXPERIMENTAL

Materials and measurements

Most chemicals were used as obtained from commercial sources. $Pd(OAc)_2$, dppb are commercially available (Aldrich). 2-Allyl phenol (**1**), 2-allyl benzaldehyde, 2-allyl-4-hydroxybenzaldehyde (**2**) and 1-allyl-naphthalen-2-ol (**3**) were prepared according to literature procedures.[43,44]

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 at room temperature and chemical shifts are reported relative to tetramethylsilane. IR spectra were performed on a Jasco FT-IR-430 instrument. Mass spectrometry (MS) analyses were performed using a GC mass spectrometer 5971 (Hewlett Packard) equipped with an electron impact ionization (EI) source interface at 70 eV.

General procedure for the cyclocarbonylation reactions

In a typical experiment, to a 45 ml Parr autoclave fitted with a glass liner and stirring bar, were added $Pd(OAc)_2$ (0.01 mmol Pd), dppb (0.04 mmol), 5 ml of DMC and the allyl phenol derivative (1 mmol). The autoclave was purged three times with carbon monoxide and successively pressurized with carbon monoxide and hydrogen. The reaction mixture was heated at 100 or 120 °C (oil-bath temperature) and stirred for 24–96 h (see Tables 1 and 2).

The reaction mixture was cooled to room temperature, filtered, the solvent evaporated under vacuum and the residue purified by column chromatography (using silica gel (Merck 60) as stationary phase and petroleum ether–diethyl ether as the eluant). This procedure was used to isolate the new esters **5a**, **5b** and **Si** as pure compounds. Lactones **2a**, **2b**, **2c**, **3a**, **3b**, **3c**, **4a**, **4b**, **4c** are known compounds and the spectral data are in accord with the literature data (see Refs 11 and 15). The representative data for compounds **5a**, **5b** and **5c** are as follows

*4-(2-Hydroxy-phenyl)-butyric acid methyl ester (**5a**)*

Oil, FT-IR (cm^{-1}): 3417, 2952, 2923, 2852, 1712, 1455, 1362, 1232, 1100, 789.

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.15–6.75 (m, 4H), 6.46 (s, 1H, OH), 3.69 (s, 3H, OCH_3), 2.65(t, $J = 7$ Hz, 2H), 2.39 (t, $J = 7$ Hz, 2H), 2.05 (quintuplet, $J = 7$ Hz, 2H).

^{13}C NMR (200 MHz, $CDCl_3$) δ (ppm): 176.3, 154.3, 130.1, 127.5, 127.1, 120.3, 115.7, 51.8, 32.9, 29.3, 24.9.

MS (EI) m/z (%): 194 (19); 163 (20), 162 (31), 134 (9), 120 (33), 119 (9), 117 (33), 108 (13), 107 (100), 91 (19), 87 (10), 79 (15), 78 (12), 77 (41), 55 (36), 51 (12) amu. Anal. Calcd for $C_{11}H_{14}O_3$ (194.09). C, 68.02; H, 7.27. Found: C, 68.63; H, 7.30.

*4-(2-Hydroxy-5-methyl-phenyl)-butyric acid methyl ester (**5b**)*

Sticky solid at room temperature. FT-IR (cm^{-1}): 3323, 2953, 2920, 2850, 1734, 1669, 1591, 1507, 1438, 1375, 1280, 1252, 1105, 826.

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 9.82 (s, 1H, CHO), 8.36 (s, br, 1H, OH), 7.64–7.66 (m, 2H), 6.99 (d, $J = 8.7$ Hz, 1H), 3.73 (s, 3H, OCH_3), 2.72 (t, $J = 7.6$ Hz, 2H), 2.43 (t, $J = 6.8$ H_3, 2H), 2.01–1.87 (m, 2H).

^{13}C NMR (200 MHz, $CDCl_3$) δ (ppm): 191.4, 175.4, 160.9, 132.1, 130.8, 129.3, 128.2, 116.2, 52.0, 32.84, 29.2, 24.5.

MS (EI) m/z (%): 222 (M^+, 12), 191 (11), 190 (16), 162 (32), 149 (19), 148 (12), 147 (11), 135 (33), 91 (11), 79 (11), 78 (10), 77 (32), 55 (100), 51(15) amu. Anal. Calcd for $C_{12}H_{14}O_4$ (222.09): C, 64.85; H, 6.35. Found: C, 64.86; H, 6.36.

*4-(2-Hydroxy-naphthalen-1-yl)-butyric acid methyl ester (**5c**)*

This compound, obtained in a trace amount, has been identified only by GC–MS analysis.

MS (EI) m/z (%): 244 (M^+, 33), 212 (20), 184 (49), 183 (6), 170 (13), 169 (16), 167 (12), 158 (23), 157 (100), 129 (47), 128 (50), 127 (21), 115 (14), 102 (5), 55 (5), 51 (5) amu.

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