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NOTE

Synthesis of bislactones catalysed by a Pd–dppb system†

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Palladium acetate [$Pd(OAc)_2$] and 1,4-bis(diphenylphosphino)butane (dppb) catalyse regioselective cyclocarbonylation of bisallyl derivatives of bisphenols affording seven-membered ring bislactones in good yields. Double cyclocarbonylation reactions carried out using different conditions afforded bislactones with two different ring sizes (7–6 and 7–5-membered).

Keywords: carbonylation; lactones; bislactones

INTRODUCTION

In recent years intensive efforts have been made to develop new carbonylation-based methodologies for the synthesis of lactones. A number of routes are reported in the literature, and palladium-catalysed carbonylation is an efficient method for the construction of such molecules. Recent examples include the cyclocarbonylation of allylic alcohols and halo-alcohols,[1] alkynes[2] and acetylenic alcohols.[3] The preparation of such compounds can also be achieved by direct insertion of carbon monoxide into four-membered cyclic ethers[4] and the use of phase-transfer catalysis for the lactonization of numerous alcohols.[5] There are other synthetic routes to lactones, including the synthesis of coumarins by palladium-catalysed coupling of 2-iodophenol with carbon monoxide and norbornadiene[6] and the preparation of other six-membered lactones by aromatic thallation and subsequent palladium-catalysed carbonylation.[7]

With few exceptions these palladium-catalysed carbonylation reactions exhibit preference for five- or six-membered rings. Recently two of us have reported that regioselective cyclocarbonylation of 2-allylphenol derivatives, using a $Pd(OAc)_2$ and dppb system as the catalyst,[8] affording five-, six- and seven-membered ring lactones, and good selectivity can be obtained for the five- and seven-membered ring lactones depending on the temperature, solvent and CO/H_2 ratio. In the literature limited data are available for selective carbonylative routes to bislactone rings, i.e. compounds containing two ring lactones.

Our interest in the application of carbonylation reactions in organic synthesis prompted us to examine the possibility of obtaining double carbonylation of bisallyl derivatives of bisphenols using Pd–dppb [dppb = 1,4-bis(diphenylphosphino) butane] as the catalyst system under relatively mild conditions, for the preparation of bisactones containing two different or identical rings. In this paper we report on the preparation of bislactones containing two differently or identically sized rings.

EXPERIMENTAL

Materials and measurements

$Pd(OAc)_2$, dppb, catechol, hydroquinone, 1,5-dihydroxynaphthalene and all allyl halides were purchased from Aldrich.

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Melting points were taken on an electrothermal apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 at room temperature and chemical shifts are reported relative to Me_4Si. IR and MS spectra were obtained, respectively, on Perkin-Elmer 683, and Hewlett-Packard GC/mass MSD 5971 instruments.

General procedure for the cyclocarbonylation reactions

Palladium acetate (0.01 mmol), and dppb (0.04 mmol) were dissolved in 5 ml of dry toluene (or CH_2Cl_2) and the allyl substrate (1 mmol) was added. The autoclave was purged three times with CO and pressurized with CO and H_2. The reaction mixture was heated with stirring for 24 h at 100 °C (oil-bath temperature). The reaction mixture was cooled to room temperature, the solution was concentrated and the residue was extracted with ether. The bislactones were purified by chromatography using a gradient of petroleum ether and diethyl ether as eluents or by the HPLC technique. The yields are summarized in the Tables 1 and 2 and all products were characterized by melting points and spectral data (below)

Compound 1a
M.p. 181–182 °C. IR ($CHCl_3$): 2936, 1742, 1629, 1461, 1203, 1148 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 7.00 (s, 2H), 2.84 (t, J = 7.1 Hz, 4H), 2.50 (t, J = 7.1 Hz, 4H), 2.50 (t, J = 6.6 Hz, 4H), 2.26–2.16 ppm (m, 4H). ^{13}C NMR ($CDCl_3$): δ = 170.3, 141.2, 126.0, 120.0, 31.0, 28.2, 26.4 ppm. MS: *m/z* (%) = 246 (25), 191 (98), 163 (25), 91 (24), 77 (19).

Compound 2a
M.p. 238–240 °C. IR ($CHCl_3$): 3043, 2920, 2850, 1745, 1415, 1203, 1125 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 6.95 (s, 2H), 2.81 (t, J = 7.2 Hz, 4H), 2.51 (t, J = 7.2 Hz, 4H), 2.02 ppm (quintet, J = 7.2 Hz, 4H). ^{13}C NMR ($CDCl_3$): δ = 171.0, 148.9, 130.0, 120.4, 31.0, 27.9, 26.0 ppm. MS: *m/z* (%) = 246 (70), 201 (6), 191 (100), 173 (9), 163 (18), 137 (5), 115 (4), 91 (9), 77 (6), 67 (6), 55 (70), 43 (7).

Compound 3a
M.p. 174–176 °C. IR ($CHCl_3$): 3020, 2929, 2872, 1761, 1652, 1461, 1218, 1197, 1122 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 7.03 (s, 2H), 2.88 (t, J = 7.1 Hz, 4H), 2.48 (t, J = 7.1 Hz, 4H), 2.14 ppm (quintet, J = 7.1 Hz, 4H). ^{13}C NMR ($CDCl_3$): δ = 171.0, 149.6, 129.0, 118.7, 113.8, 30.9, 26.0, 23.9 ppm. MS: *m/z* (%) = 246 (100), 227(7), 218 (7), 201 (32), 192 (30), 191 (61), 173 (16), 163 (36), 147 (13), 146 (11), 135(12) 115 (10), 91 (15), 77 (15), 55 (44), 43 (2).

Compound 4a
Oil. IR ($CHCl_3$): 3020, 2940, 2870, 1765, 1615, 1450, 1210, 1100 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 6.86 (s, 1H), 2.78 (t, J = 7.2 Hz, 4H), 2.48 (t, J = 7.0 Hz, 4H), 2.21 (s, 3H), 2.25–2.14 ppm (m, 4H). ^{13}C NMR ($CDCl_3$): δ = 171.2, 149.4, 130.8, 128.8, 126.9, 31.1, 28.1, 26.5, 9.9 ppm. MS: *m/z* (%) = 260 (58), 205 (100), 177 (42), 91 (17), 55 (33).

Compound 5a
M.p. 265–270 °C. IR ($CHCl_3$): 3020, 3000, 2960, 2880, 1760, 1605, 1500, 1450, 1440, 1385, 1345, 1300, 1125 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 7.92 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 8.5 Hz, 2H), 2.94 (t, J = 7.2 Hz, 4H), 2.46 (t, J = 6.9 Hz, 4H), 2.33–2.22 ppm (m, 4H). ^{13}C NMR ($CDCl_3$): δ = 171.5, 146.5, 128.0, 125.9, 119.2, 31.4, 28.4, 27.4 ppm. MS: *m/z* (%) = 296 (66), 241 (100), 213 (17), 186 (12), 128 (8), 55 (10).

Compound 6a
M.p. 119–120 °C. IR ($CHCl_3$): 3354, 2954, 1736, 1491, 1450, 1228, 1199, 1136 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 6.93 (dd, J = 1Hz, J = 7.9 Hz, 1H), 6.78–6.70 (m, 2H), 6.17 (s, br, 1H), 2.74 (t, J = 7 Hz, 2H), 2.48 (t, J = 7 Hz, 2H), 2.16 ppm (quintet, J = 7 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ = 173.3 153.7, 145.0, 131.2, 120.1, 116.2, 114.4, 31.0, 28.2, 26.3 ppm. MS: *m/z* (%) = 178 (67), 150 (30), 133 (34), 123 (100), 77 (10).

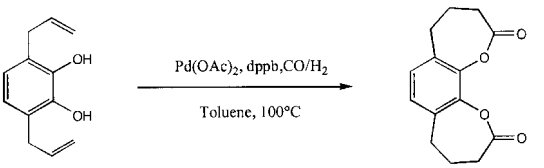
Compound 7
M.p. 109–110 °C. IR ($CHCl_3$): 3362, 3077, 2954, 2871, 1731, 1640, 1511, 1450, 1424, 1346, 1229, 1183, 1133, 965, 921, 900, 883 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 6.86 (s, 1H), 6.66 (s, 1H), 6.09–5.89 (m, 1H), 5.23–5.12 (m, 3H), 6.05 (s, br, 1H), 3.36 (d, J = 6.4 Hz, 2H), 2.74 (t, J = 7.2 Hz, 2H), 2.48 (t, J = 7.1 Hz, 2H), 2.16 ppm (quintet, J = 7 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ = 172.3, 151.6, 145.3, 135.6, 129.3, 124.8, 120.9, 117.1, 116.6, 34.7, 31.0, 27.9, 26.4 ppm. MS: *m/z* (%) = 218 (50), 190 (15), 173 (14), 163 (100), 149 (5), 115 (6), 91 (12), 77 (7), 55 (12).

Compound 8
M.p. 102 °C. IR ($CHCl_3$): 3362, 3077, 2954, 2871, 1731, 1640, 1511, 1450, 1424, 1346, 1229, 1183, 1133, 965, 921, 900, 883 cm^{-1}. ^{1}H NMR ($CDCl_3$):

δ = 6.85 (d, J = 8.7 Hz, 1H), 6.74 (d, J = 8.7 Hz, 1H), 6.02–5.85 (m, 1H), 5.23 (s, br, 1H), 5.06–4.87 (m, 2H), 3.44 (d, J = 5.7 Hz, 2H), 2.68 (t, J = 7.2 Hz, 2H), 2.43 (t, J = 7.1 Hz, 2H), 2.12 ppm (quintet, J = 7 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ = 173.3, 151.9, 145.5, 136.0, 130.0, 124.4, 117.8, 115.3, 114.0, 30.9, 30.2, 25.8, 23.8 ppm. MS: *m/z* (%) = 218 (100), 203 (17), 190 (16), 177 (14), 173 (30), 163 (43), 161 (25), 147 (23), 135 (17), 131 (11), 123 (10), 115 (19), 107 (23), 91 (12), 77 (7), 55 (12).

Compound 3b

M.p. 119–122 °C. IR ($CHCl_3$): 2931, 2854, 1762, 1466, 1209, 1154, 1124 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 7.01 (d, J = 9 Hz, 1H), 6.74 (d, J = 9 Hz, 1H),

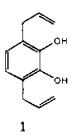
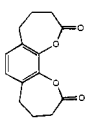
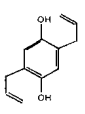
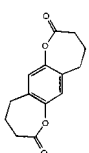
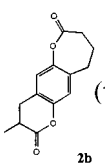
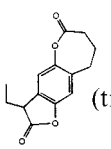
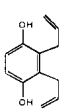
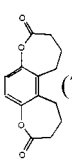
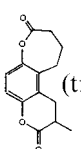
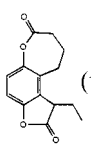
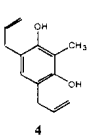
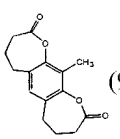
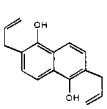
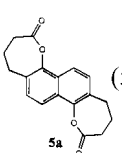


1 **1a**

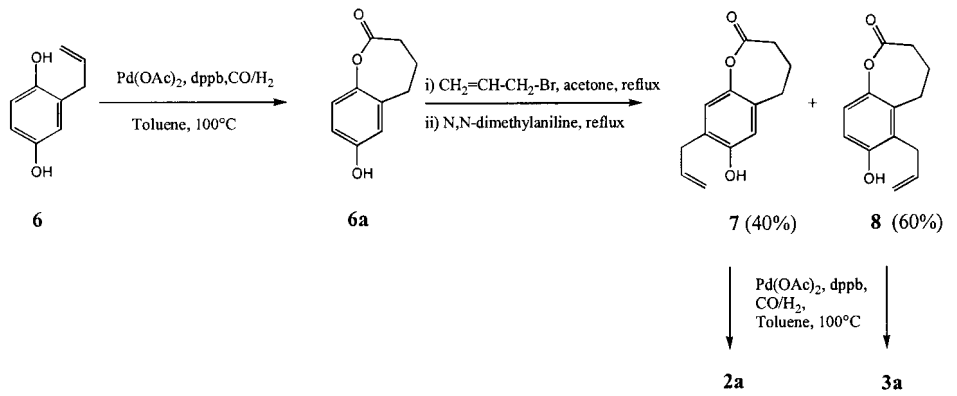
Scheme 1

3.50–2.65 (m, 5H), 2.49 (t, J = 7.1 Hz, 2H), 2.35–2.15 (m, 2H), 1.40 ppm (d, J = 6.2 Hz, 3H). ^{13}C NMR: δ = 171.1, 170.7, 149.5, 148.3, 128.2, 121.6, 119.1, 116.0, 33.5, 30.9, 29.7, 25.5, 23.7, 15.4 ($CDCl_3$) ppm. MS: *m/z* (%) = 246 (100), 218 (18),

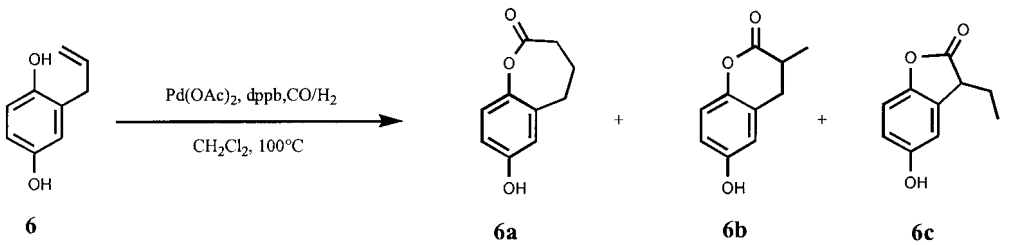
Table 1 Cyclocarbonylation reactions catalysed by $Pd(OAc)_2$–dppb[a]

Entry	Substrate	Products, yield (%)		
1	 **1**	 (79) **1a**		
2	 **2**	 (70) **2a**	 (traces)[b] **2b**	 (traces)[b] **2c**
3	 **3**	 (70) **3a**	 (traces)[b] **3b**	 (traces)[b] **3c**
4	 **4**	 (90) **4a**		
5	 **5**	 (50) **5a**		

[a] General procedure for the cyclocarbonylation reactions were described in the Experimental section.
[b] Substrates **2b, 2c, 3b** and **3c** were detected by GC–MS analysis and their structures confirmed by comparison with authentic samples (see entries 4,6,7 and 9 in Table 2).



Scheme 2



Scheme 3

201 (55), 191 (60), 190 (15), 173 (13), 163 (31), 162 (19), 161 (15), 147 (14), 135 (6), 115 (10), 91 (15), 77 (13), 55 (62), 43 (3).

Compound 6b

M.p. = 130–131 °C. ^{1}H NMR ($CDCl_3$): δ = 6.92 (d, J = 8.5 Hz, 1H), 6.74–6.64 (m, 2H), 4.97 (s, br, 1H), 2.94–2.70 (m, 3H), 1.36 ppm (d, J = 6.0 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ = 171.9, 152.0, 145.7, 124.0, 117.5, 114.7, 114.4, 34.1, 31.7, 15.4 ppm. MS: *m/z* (%) = 178 (100), 150 (70), 135 (41), 133 (13), 122 (22), 107 (26), 94 (17), 77 (12).

Compound 6c

M.p. 94–94 °C. IR ($CHCl_3$): 3394, 3043, 2971, 2935, 1772, 1492, 1470, 1224, 1155 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 6.96 (d, J = 8.2 Hz, 1H), 6.78–6.71 (m, 2H), 5.02 (s, br, 1H), 3.68 (t, J = 5.8 Hz, 1H), 2.04 (dq, J = 5.8 Hz, J = 7.4 Hz, 2H), 0.96 ppm (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ = 177.8, 152.4, 147.7, 128.2, 115.1, 111.5, 111.2, 42.2, 24.2, 10.1 ppm. MS: *m/z* (%) = 178 (70), 150 (100), 135 (50), 133 (15), 122 (16), 107 (29), 77 (14), 65 (11).

RESULTS AND DISCUSSION

We found that, for example, 3,6-bisallylcatechol (**1**) reacts with CO and H_2 in the presence of 10% $Pd(OAc)_2$ and 1,4-bis(diphenylphosphino)butane (dppb) in toluene at 100 °C to give selectively the bis (seven-membered ring) lactone **1a** in 79% isolated yield (Scheme 1).

By reaction of bisallyl derivatives **2–5**, under reaction conditions described previously, double cyclocarbonylation reactions led to bislactones **2a–5a** in 50–90% yields (Table 1).

The synthesis of bislactones in two different steps was also possible. For example, the monoallyl hydroquinone **6** was first cyclocarbonylated in toluene to give 92% of **6a**. The latter, after further allylation and Claisen rearrangement, was converted to the two isomers **7** and **8** and then converted in the corresponding bislactones **2a** and **3a** (Scheme 2).

Using different reaction conditions the bis-cyclocarbonylation reaction can be useful for preparing bislactones with different ring sizes (7–6, 7–5, 6–6). For example, **6** can be carbonylated in CH_2Cl_2 to give a mixture of five-, six- and seven-

Table 2 Cyclocarbonylation reactions of substrates **6**, **7** and **8** with $Pd(OAc)_2$–dppb at 100 °C for 24 h[a]

Entry	Substrate	P_{CO} (psi)	P_{H_2} (psi)	Solvent	Conversion (%)	Products, yield (%)		
1	**6**	500	100	CH_2Cl_2	88	**6a** (65)	**6b** (20)	**6c** (15)
2	**6**	300	300	Toluene	90	**6a** (95)	**6b** (traces)	**6c** (traces)
3	**6**	100	500	CH_2Cl_2	90	**6a** (62)	**6b** (23)	**6c** (15)
4	**7**	500	100	CH_2Cl_2	88	**2a** (65)	**2b** (20)	**2c** (15)
5	**7**	300	300	Toluene	90	**2a** (95)	**2b** (traces)	**2c** (traces)
6	**7**	100	500	CH_2Cl_2	90	**2a** (62)	**2b** (20)	**2c** (18)
7	**8**	500	100	CH_2Cl_2	95	**3a** (63)	**3b** (32)	**3c** (5)
8	**8**	300	300	Toluene	90	**3a** (95)	**3b** (traces)	**3c** (traces)
9	**8**	100	500	CH_2Cl_2	90	**3a** (62)	**3b** (23)	**3c** (15)

[a] General procedure for the cyclocarbonylation reactions as described in the Experimental section.

membered ring monolactones **6a, 6b** and **6c** (Scheme 3).

Compounds **6a, 6b** and **6c**, after allylation, Claisen rearrangement and cyclocarbonylation, can be converted to bislactones containing 7–5, 7–6, 7–7 or 6–7, 6–6, 6–5 or 5–7, 5–6, 5–5 rings. In Table 2 the cyclocarbonylation reactions of **7** and **8** under different reaction conditions for the synthesis of lactones with two different rings are reported

Consistently with the first results on the cyclocarbonylation of allylphenol, toluene is the best solvent for obtaining the seven-membered ring lactone selectively, with conversions ranging from 62 to 99%; CH_2Cl_2, as solvent favours instead the formation of five- and six-membered ring lactones. The method could represent a new synthetic strategy for the synthesis of various bislactone isomers. Several other ligands (PPh_3, dppp, dppe) were inferior to dppb in terms of selectivity and yields.

CONCLUSIONS

The direct double cyclocarbonylation of bisallyl derivatives of bisphenols (or 1,5-dihydroxynaphthalene) can give seven-membered ring bislactones, and bislactones of different ring sizes resulted under modified conditions.

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