Novel Synthesis of Phenol Derivatives by Palladium-catalysed Cyclocarbonylation of Penta-2,4-dienyl Acetates

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Palladium-catalysed cyclocarbonylation of penta-2,4-dienyl acetates in the presence of NEt_3 and Ac_2O selectively gives phenyl acetates in good yields.

Catalytic cyclocarbonylation has been attracting much attention in recent years because of its potentiality as a synthetic tool.[1–3]. We have recently developed palladium-catalysed cyclocarbonylation of 3-arylallyl acetates and bromides such as cinnamyl acetate to give fused aromatic compounds *via* acylation of the aryl group forming a new six-membered ring.[4–6] During the course of our extensive study on the palladium-catalysed cyclocarbonylation, we have now found a new type of cyclocarbonylation of penta-2,4-dienyl acetates **1** to give selectively phenyl acetates **2** as six-membered cyclization products (Scheme 1).

In the presence of NEt_3, Ac_2O and a catalytic amount of $PdCl_2(PPh_3)_2$, 5-phenylpenta-2,4-dienyl acetate **1a** was smoothly cyclocarbonylated to give 2-acetoxybiphenyl **2a**.† No other identifiable product was detected by GC analysis. Reaction temperatures of 120–140 °C were adequate for the reaction, and Ac_2O and NEt_3 were both essential to obtain the carbonylation product in a high yield.‡ Palladium and platinum phosphine complexes such as $PdCl_2(PPh_3)_2$ and $PtCl_2(PPh_3)_2$ proved to be effective catalysts, whereas some ruthenium complexes such as $RuCl_2(PPh_3)_3$ showed low catalytic activities. Other group 8 metal compounds including $NiBr_2(PPh_3)_2$ and $RhCl(PPh_3)_3$ were inactive. It should be noted that the acetate **1a** was converted to **2a** in much higher yield than the corresponding chloride (33%) or ethyl carbonate (29%), although allylic acetates have been claimed to be poor substrates for carbonylation reactions.[7–9]

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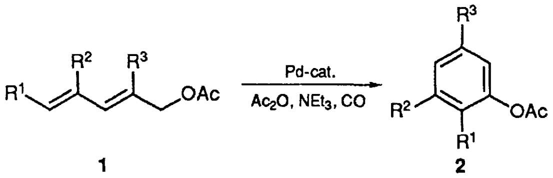
† All the substrates and products of the cyclocarbonylation were fully characterized by ^1H NMR, ^{13}C NMR and IR spectroscopy, and high-resolution electron-impact mass spectrometry.

‡ A reaction in the absence of Ac_2O gave biphenyl-2-ol in 16% and **2** in 11% yield (conv. 100%) as identifiable products, while a reaction in the absence of NEt_3 gave **2** in 9% (based on the starting substrate **1**, conv. 52%).

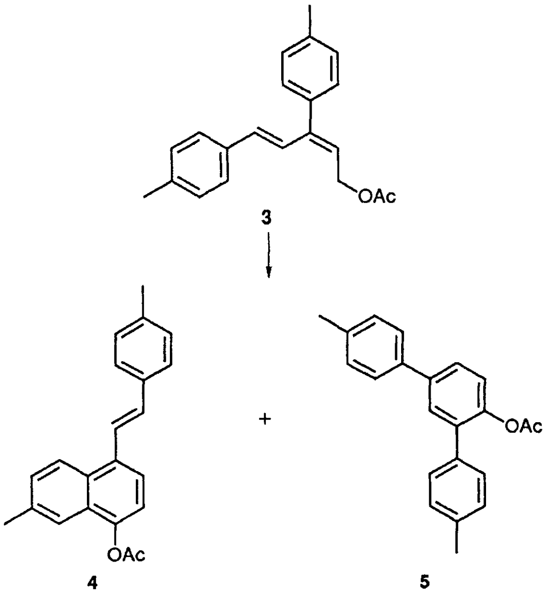
Table 1 Cyclocarbonylation of substituted penta-2,4-dienyl acetates[a]

Run	Substrate	R^1	R^2	R^3	Yield[b] (%)
1	**1a**	Ph	H	H	69 (74)
2	**1b**	p-MeO–C_6H_4	H	H	73
3	**1c**	o-Cl–C_6H_4	H	H	84
4	**1d**	Ph	Me	H	57
5	**1e**	Ph	H	Me	46
6	**1f**	1-Naphthyl	H	H	79
7	**1g**	2-Furyl	H	H	57
8	**1h**	Me	H	H	51[c]
9	**1j**	H	Me	Me	40
10	**1j**	$Bu^nCH{=}CH$	H	H	52[d]

[a] *Reaction conditions*: Substrate 3 mmol, $PdCl_2(PPh_3)_2$ 0.09 mmol, Ac_2O 6 mmol, NEt_3 6.6 mmol, benzene 5 ml, CO 50 atm, 140 °C, 3 h. [b] Isolated yield; GC yield in parentheses. [c] Benzene (2 ml) was used as the solvent. [d] *trans*:*cis* ratio = 79:21.

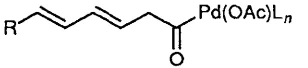


Scheme 1



Scheme 2

As shown in Table 1, various substituted phenyl esters were obtained in moderate to high yields by this unique cyclocarbonylation.† Especially, 5-arylpenta-2,4-dienyl acetates are good substrates for this reaction and substitutents at the 2- or 4-position of the substrates seem to lower the yields of the products. In the reaction of *trans,trans,trans*-undeca-2,4,6-trienyl acetate **1j**, the six-membered ring formation again exclusively occurred to give *o*-(hex-1-enyl)phenyl acetate **2j**, but the product was a mixture of the *cis* and *trans* isomers (run 10). It is noteworthy that the present carbonylation is applicable to the synthesis of 3,5- and 2,3-disubstituted phenyl acetates (runs 4 and 9), which are difficult to prepare by conventional electrophilic substitution reactions of phenol. This exemplifies the effectiveness of our cyclocarbonylation as a synthetic method for substituted phenols. However, when (2*E*,4*E*)-3,5-di(*p*-tolyl)penta-2,4-dienyl acetate **3** was carbonylated under similar reaction conditions, cyclization towards the tolyl group at the 3-position[4] competed with the phenyl acetate formation to give naphthyl acetate **4** (17%) concurrent with the expected 2,4-di(*p*-tolyl)phenyl acetate† **5** (38%) in spite of *E* configuration of the substrate (Scheme 2).



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Previously, Negishi reported that palladium-catalysed cyclocarbonylation of *cis*-penta-2,4-dienyl chlorides in the presence of MeOH and NEt_3 yields cyclopentenone derivatives, and that the *cis* configuration of the substrates is required for the cyclization.[10] Although the catalytic systems are closely related to each other, the cyclocarbonylation described here is in sharp contrast to Negishi's reaction in that only the six-membered products, but not the five-membered ones, are selectively obtained and that substrates of the *trans* configuration undergo smoothly the cyclization. The latter point is especially advantageous from a synthetic point of view. As expected, carbonylation of **1a** under Negishi's conditions resulted in the formation of methyl (3*E*,5*E*)-6-phenylhexa-3,5-dienoate (60%) and methyl (2*E*,4*E*)-6-phenylhexa-2,4-dienoate (13%).

The present reaction is considered to proceed *via* a hexadienoylpalladium complex **6**, which is generated by oxidative addition of a pentadienyl acetate to a Pd^0 species followed by CO insertion. In the absence of a nucleophile such as MeOH, the hexadienoylpalladium complex would undergo *cis–trans* isomerization of the internal double bond and intramolecular insertion of the terminal C=C double bond into the Pd–C bond. Subsequent β-elimination gives a cyclohexadienone, which tautomerizes to afford the corresponding phenol and is finally acetylated by Ac_2O. We must await further investigation to elucidate the reason why the hexadienoyl palladium species selectively cyclizes to form a six-membered ring but not a five-membered one under the present reaction conditions.

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