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A New Palladium-catalyzed Synthesis of 3,4-Disubstituted Coumarins from 3-Alkenoates of *ortho*-Iodophenol, Phenylacetylene and Carbon Monoxide*

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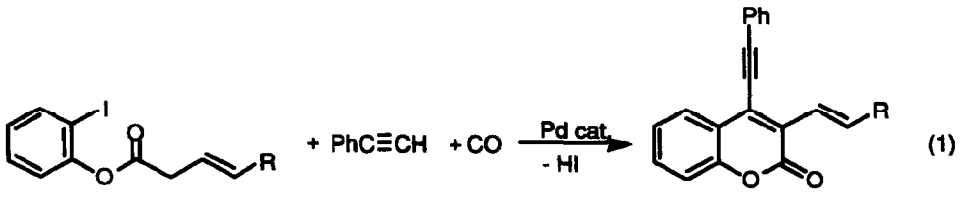
Abstract: Palladium(0) has been found to catalyse the reaction of an aromatic carbon-iodide bond with carbon monoxide, the triple bond of alkynes and the allylic carbon of an *ortho* alkenoic chain to form a 3,4-disubstituted coumarin ring in satisfactory yield under mild conditions.

In the course of our studies aimed at developing synthetic strategies for cyclization reactions we found that palladium(0) complexes could catalyze the formation of coumarins from alkenoates of *ortho*-iodophenol[1]. This reaction was promoted by different types of molecules able to coordinate to palladium. Phenylacetylene in conjunction with carbon monoxide turned out to be among the best promoters. Its action, however, was limited to the 3-butenoic ester insofar as the presence of a carbon substituent on the terminal double bond carbon shifted the reaction towards a new coumarin. The latter was originated from the incorporation of phenylacetylene and carbon monoxide according to the following equation 1 (R=alkyl, aryl):

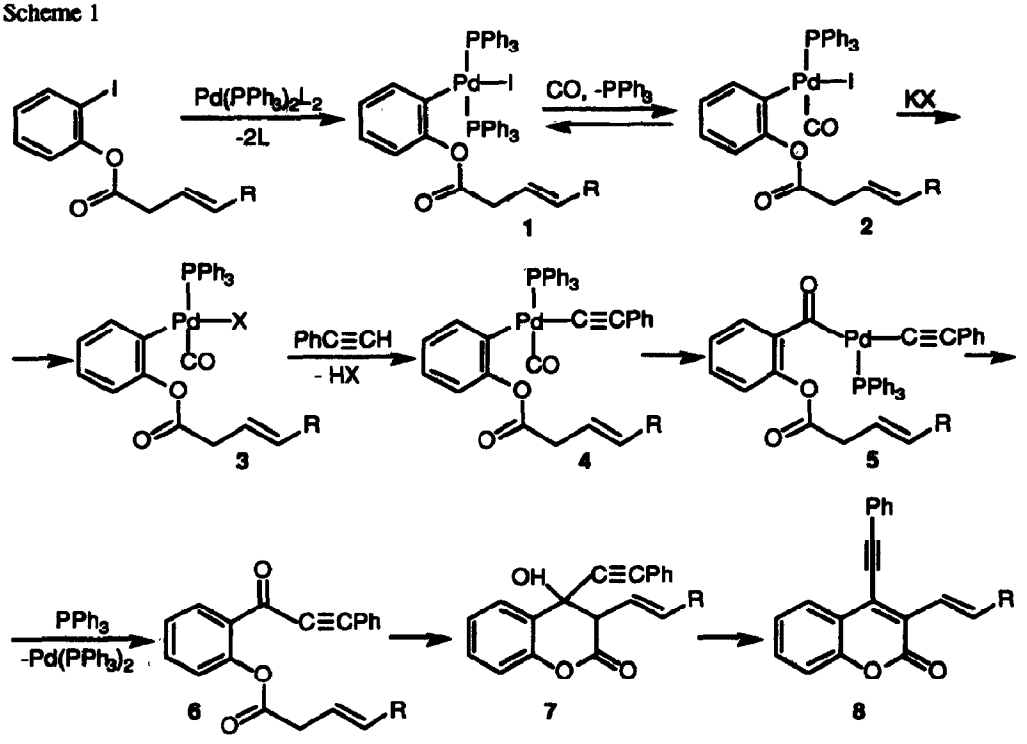


(1)

The behaviour of phenylacetylene, which with similar reaction mixtures can act as a promoter of the formation of 4-methylcoumarin if R=H as well as a substrate for the synthesis of 4-phenylethynyl-3-(1-alkenyl)coumarins if R=alkyl, aryl, is remarkable. An attempt to rationalize the course of these reactions is presented in Schemes 1 and 2 (X=carboxylate, L=ligand).

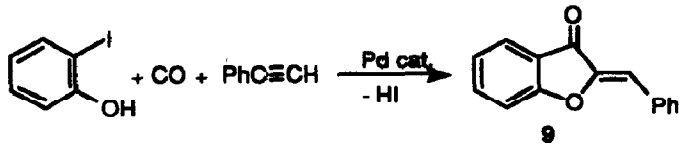
* Dedicated to Professor Helmut Werner in recognition of his fundamental contributions to Organometallic Chemistry.

Scheme 1



Complex **1** originated from the oxidative addition of the aryl halide on the metal undergoes phosphine substitution by carbon monoxide and, in the presence of an alkali carboxylate (butyrate), *trans* substitution of the halide by the alkynyl group[1,2] (compounds **2-4**).

Migration of the phenyl group on carbon monoxide to form **5**, followed by acyl-alkynyl coupling[3] to **6**, then occurs. The other steps are readily explained as a nucleophilic attack of the active methylene group on the carbonyl group leading to **7**, followed by dehydration to **8**. A secondary product, *Z*-aurone (**9**)[4], is also formed from **6** by attack of the phenolic oxygen to the triple bond. This compound had also been obtained by us[4] from the reaction of *ortho*-iodophenol with phenylacetylene and carbon monoxide (eq. 2).



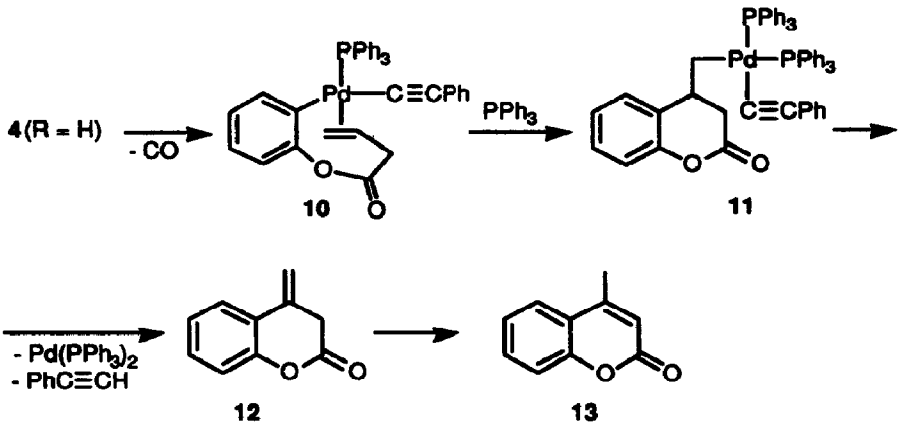
(2)

In the present case the O-acyl bond must be cleaved in order to form a palladium alkoxide able to attack the triple bond. The way by which this cleavage occurs (presumably through participation of the carboxylate anion) has not been ascertained so far.

The proposed intermediate **4** also enables us to explain why phenylacetylene can act as a non innocent ligand and no longer as a substrate in the absence of a substituent on the butenoic double bond. The carbonyl ligand can be displaced by the butenoic double bond (compound **10**) and this time it is the latter that inserts into the arylpalladium bond, thus giving rise to the palladium-bonded precursor of the coumarin ring **11**. The presence of the *cis* alkynyl group, which is placed in the appropriate position for accepting a hydride, favours reductive elimination to reform the original alkyne and the methylenedihydrocoumarin **12**, which immediately isomerizes to the 4-alkylcoumarin **13**.

In addition to the general properties of coumarin derivatives[5] one of the novel coumarin compounds described here (R=Ph) shows fluorescence and this property may be exploited for several applications (see for example ref. 6).

Scheme 2



4-(Phenylethynyl)-3-(1-propenyl)-coumarin ***8*** *(R=Me).* The *o*-iodophenyl ester of 3-pentenoic acid (from 3-pentenoyl chloride and *o*-iodophenol),134 mg (0.443 mmol), phenylacetylene, 83 mg (0.799 mmol), $Pd(PPh_3)_4$, 26 mg (0.022 mmol) and potassium butyrate, 94 mg (0.743 mmol) are stirred in anisole, 4.0 ml, for 24 h at 80°C in a CO atmosphere. Product **8** (R=Me) is separated by CG (58% yield) along with aurone **9** (22%). MS (70 eV), M^+ 286, m/e 285, 257, 239, 226. IR (film, cm^{-1}) 2200, 1720, 1640, 750. ^1H NMR (400 MHz, $CDCl_3$, TMS, the prime refers to protons of the phenylethynyl group): δ 7.99, 1 H, d further split , J 7.9 Hz, H5; 7.69-7.64, 2 H, m, H2', H6'; 7.53-7.42, 4 H, m, H3', H4', H5', H7; 7.36, 1 H, dq, J 15.6, 6.8 Hz (=CHMe); 7.34-7.29, 2 H, m, H6, H8; 6.90, 1 H, dq, J 15.6, 1.8 Hz, (C*H*=CHMe); 2.01, 3 H, dd, J 6.8, 1.7 Hz, Me.

4-Phenylethynyl-3-styryl-coumarin ***8*** *(R=Ph)* was prepared analogously. Yield 63% (aurone **9** 15%). Mp. 178°C (from n-hexane). MS M^+ 348, m/e 331, 319, 302, 289, 271.^1H NMR (prime and double prime

refer to protons of the phenyethynyl and styryl group, respectively): δ 8.27, 1 H, d, J 16.2 Hz, PhCH=; 8.02, 1 H, dd, J 7.9, 1.5 Hz, H5; 7.71-7.68, 2 H, m, H6', H2'; 7.68, 1 H, d, J 16.2 Hz, C*H*=CHPh; 7.63-7.58, 2H, m, (H6", H2"); 7.52, 1 H, td, J 7.7, 1.5 Hz, H7; 7.49-7.43, 3 H, m, H5', H4', H3'; 7.41-7.35, 2 H, m; (H3", H5"); 7.35-7.32, 2 H, m, H6, H8; 7.31, 1 H, tt, J 7.2, 2.1 Hz, (H4").

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