Pergamon

Tetrahedron Letters, Vol. 35, No. 32, pp. 5919-5922, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01181-8

Intramolecular Cyclization of *ortho*-Iodophenyl 3-Butenoate to 4-Methylcoumarin: Catalysis by Palladium Complexes

Marta Catellani, Gian Paolo Chiusoli, Maria Chiara Fagnola and Giovanna Solari

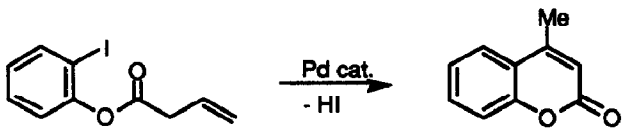
Dipartimento di Chimica Organica e Industriale dell'Università

Viale delle Scienze, I-43100 Parma, Italy

Key Words: coumarin, palladium catalysis, cyclization.

Abstract- A new palladium-catalyzed synthesis of 4-alkylcoumarins is reported, based on intramolecular arylation of the 3-alkenoic chain of an *ortho*-iodophenyl ester.

In the course of our studies, aimed at achieving ring formation from *ortho*-substituted aromatics[1], we have obtained a new synthesis of 4-methylcoumarin, based on the following palladium-catalyzed cyclization (eq. 1):



(1)

The catalyst may be introduced as a palladium(0) complex prepared from palladium *bis*(dibenzylidene)acetone and two molecules of triphenylphosphine. The reaction takes place under mild conditions (80°C) in anisole as solvent, in the presence of an alkali salt of an organic acid (potassium butyrate) as neutralising and gives yields of 4-methylcoumarin above 85% if side reactions are appropriately controlled. The synthesis has general character, although yields rapidly decrease in the presence of increasingly bulky substituents on the terminal double bond carbon.

Intramolecular cyclization to 4-methyl-1-2*H*-benzopyran was obtained by Heck[2a] starting from *ortho*-iodophenyl 3-butenyl ether. Other intramolecular Heck-type reactions[2] with *ortho*-iodoaryl allyl ethers were reported to give five-membered (benzofuran) rings[3]. Analogous reactions with N-allylanilines gave five-membered (indole) rings[4]. The achievement of the six membered ring closure from the *ortho*-iodophenyl ester of 3-butenoic acid has been prevented so far by the absence of control of ester cleavage and isomerization of the double bond from position 3 to 2. In fact the ester is susceptible to attack by acid or basic reagents and can be cleaved in protic solvents, while the allylic group readily undergoes isomerization to 2-butenoate, which is inert towards further reaction and competes with the substrate for coordination sites on

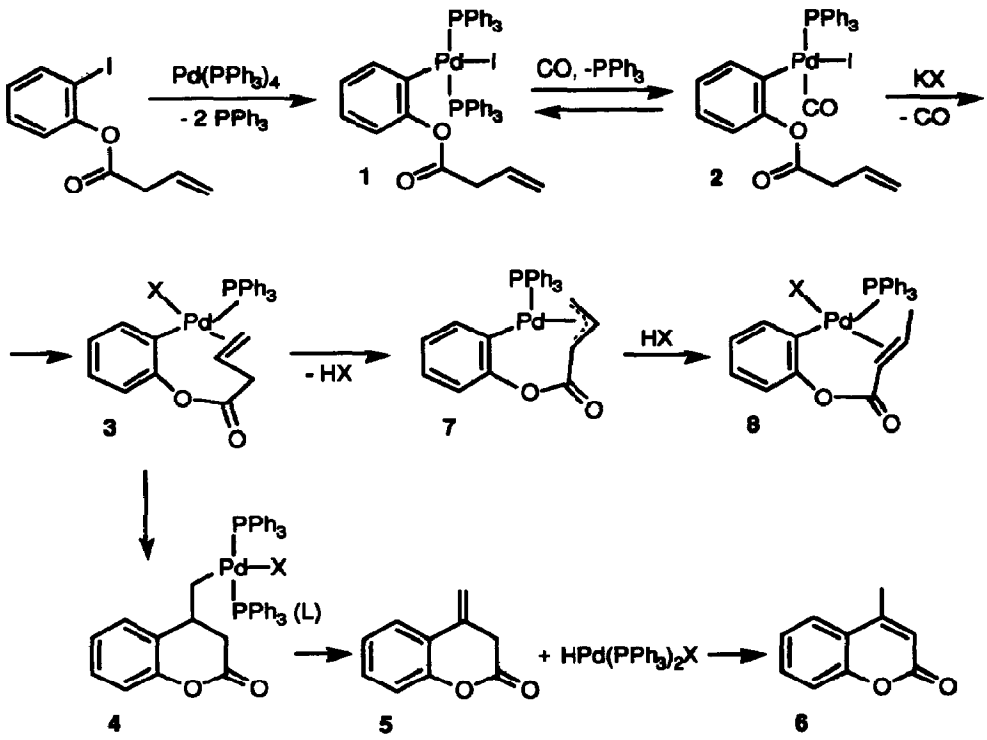
palladium. It has to be observed in this context that if the 3-butenoic chain is replaced by the acrylic one, cyclization does not occur, although it has been obtained with a nickel catalyst[5].

Contrary to olefin arylation, which is not regioselective, the present process is completely regioselective, only the internal carbon of the double bond being involved in cyclization. The allylic carbon does not appear to take part in the process (through formation of an η^3-allylic complex as for example in the synthesis of benzofurans from *ortho*-iodophenol and 1,3-dienes[6]), cyclization occurring as well if the two allylic protons are replaced by methyl groups with formation of 3,3-dimethyl-4-methylene-3,4-dihydrocoumarin. The electron-withdrawing group (carbonyl) adjacent to the allyl group also is not needed, as shown by the above-mentioned reaction[2a] of the corresponding butenyl ether which gives 4-methyl-1-2*H*-benzopyran. The reaction must thus consist of a regioselective attack on the internal carbon of the terminal double bond, followed by reductive elimination of hydrogen iodide.

As shown in the Scheme (L=promoter ligand, X=carboxylate), with triphenylphosphine as ligand the reaction leads to oxidative addition[7] of the substrate to palladium(0), as shown by the isolation of the *trans* complex **1**. The latter gives 4-methylcoumarin on heating, but curiously it does not act as catalyst unless carbon monoxide and a promoter such as phenylacetylene, methyl acrylate or benzonitrile (the latter being the best one) is present in large excess over palladium. No carbon monoxide insertion is observed under our conditions, although intramolecular acylpalladation of unactivated olefins has been reported[2f,8]. Carbon monoxide is likely to help dissociation of one phosphine molecule by coordination to form **2**. Displacement of the carbonyl group by the butenoic double bond gives **3**.

After dissociating triphenylphosphine should reassociate to stabilise the double bond insertion product[9], thus forming **4**, then **5** by β–H elimination[10] (likely through another intermediate) and **6** by palladium hydride-catalysed isomerisation. Apparently triphenylphosphine does not reassociate at a sufficiently high rate, so the added promoter L should play the role of associating to palladium faster than triphenylphosphine, thus curtailing the effect of other competing reactions such as double bond isomerization to **8**, probably through η^3-allylpalladium **7**, and isomerisation (not shown in the Scheme) of the double bond of the starting iodophenyl 3-butenoate to the 2-isomer[11], which all would deactivate the catalytic complex. Iodophenyl 2-butenoate and phenyl 2-butenoate were isolated from the reaction mixture, the latter after hydrogenolysis with hydrogen. It is to be pointed out that no pertinent information was found in the literature on how to promote metal-catalyzed cyclization in the presence of competing isomerisation. When competing reactions are absent, as in the case of *ortho*-iodophenyl 3-butenyl ether, there is no need of a promoter. Also in the case of a rigid chelating phosphine forming a large ring such as *bis*(diphenylphosphino)ferrocene, which can readily dissociate[12] and re-associate, the promoter is not required. Yield drops to 30%, however, owing to extensive isomerisation to iodoaryl 2-butenoate.

Further studies are in progress to clarify the role of promoters and ligands.



Preparation and reaction of complex trans-PdI(o-$C_6H_4OCOCH_2CH{=}CH_2$)(PPh_3)$_2$ (1). *o*-C_6H_4(OCOCH$_2$CH=CH$_2$)I, 167 mg (0.579 mmol), dissolved in toluene, 6.5 ml, is added to Pd(PPh_3)$_4$, 652 mg (0.566 mmol) and toluene, 10.0 ml, at room temperature under nitrogen. The solution becomes progressively clear as the new toluene-soluble complex is formed. After one hour the solvent is removed under vacuum, the solid residue is washed several times with cold diethyl ether and dried at the mechanical pump.

^{1}NMR (400 MHz, $CDCl_3$, TMS): δ 7.58-7.51, 12 H, m; 7.36-7.28, 6 H, m; 7.27-7.19, 12 H, m; 6.52, 1 H, dq, J 7.7, 1.8 Hz (C*H*CPd); 6.39, 1 H, dd, J 7.9, 7.2 Hz (CH *para*, Pd-bonded aryl); 6.21, 1 H, dd further split, J 8.1, 1.2 Hz (C*H*COC=O); 6.02, 1 H, t further split, J 7.0 Hz (C*H*CHCPd); 5.88, 1 H, ddt, J 17.0, 10.4, 6.8 Hz (C*H*=CH$_2$); 5.25, dq, 1 H, J 16.7, 1.5 Hz (CH=C*H*$_2$); 5.24, 1 H, dq, J 10.5, 1.5 Hz (CH=C*H*$_2$); 3.30, 2 H, dt, J 6.9, 1.4 Hz (*CH*$_2$CH=); ^{31}P{H} NMR (81 MHz, $CDCl_3$, external 85% H_3PO_4): δ 23.2. When heated at 80°C in anisole in the presence of an excess of potassium butyrate (3.4 mol) the complex decomposes to 4-methylcoumarin.

General procedure for cyclization reactions. The procedure is illustrated by the following example concerning the preparation of 4-methylcoumarin. In a 25 ml flask with magnetic stirring Pd(*bis*-dibenzylideneacetone)$_2$, 13.2 mg (0.023 mmol), PPh_3, 12.0 mg (0.046 mmol), and potassium butyrate, 95 mg (0.753 mmol), are caused to react with *o*-iodophenyl 3-butenoate, 140 mg (0.486 mmol), in anisole, 4 ml, containing benzonitrile, 61 mg (0.587 mmol), under atmospheric pressure of carbon monoxide at 80°C for 24

h. The products are analyzed by GLC and separated by TLC using n-hexane/ethyl acetate 9/1 as the eluent. 4-Methylcoumarin[13] was obtained with 85% yield and selectivity higher than >90%. No reaction takes place in the absence of CO and benzonitrile. Complex **1** can also be used as catalyst in place of $Pd(dba)_2 + 2PPh_3$.

4-Ethylcoumarin[14] (yield 32%) was obtained from *ortho*-iodophenyl 3-pentenoate. 3,3-Dimethyl-4-methylene-3,4-dihydrocoumarin (yield 50%) was obtained from *ortho*-iodophenyl 2,2-dimethyl-3-butenoate. ^{1}H NMR: δ 7.54, 1 H, dd, J 7.7, 1.5 Hz (C*H*CC=CH_2; 7.36, 1 H, td, J 7.9, 1.6 Hz (C*H*CHCO); 7.18, 1 H, td, J 7.6, 1.2 Hz (C*H*CHCC); 7.08, 1 H, dd, J 8.1, 1.3 Hz (CHCO); 5.57, 1 H, s, (=CH); 5.33, 1 H, s, (=CH); 1.49, 6H, s (2Me). 4-Methyl-1-2*H*-benzopyran[15] (yield 48%) was prepared from *ortho*-iodophenyl 3-butenyl ether together with less than 10% of 3,4-dihydro-4-methylene-1-2*H*-benzopyran. The procedure by Heck[2a] gave 47% and 28% of the two compounds, respectively.

Acknowledgement

The present work has been carried out in the framework of Progetto Finalizzato Chimica Fine 2 of Consiglio Nazionale delle Ricerche.

Mass and NMR spectra have been recorded at Centro Interfacoltà di Misure of the University of Parma.

References

1.- An, Z; Catellani, M; Chiusoli, G.P. *J. Organomet. Chem.* **1989**, *371*, C51; id., ibid. **1990**, *397*, 371; id. *Gazz. Chim. Ital.* **1990**, *120*, 383.
2.- a) Shi, L; Narula, C.K.; Mak, K.T.; Kao, L; Xu, Y; Heck, R.F. *J. Org. Chem.* **1983**, *48*, 3894; (b) Dieck, H.A.; Heck, R.F. *J. Am.Chem. Soc.* **1974**, *96*, 1133; c) Terpko, M.O.; Heck, R.F. *J. Am. Chem. Soc. 1979, 101*, 5281; d) Heck, R.F. *Organic Reactions* **1982**, *27*, 345; e) Grigg, R.; Stevenson, P.; Worakun, T. *Tetrahedron* **1988**, *44*, 2033; f) Tour, J.M.; Negishi, E. *J. Am. Chem. Soc.* **1985**, *107*, 8289; g) Abelman, M.M.; Overman, L.E. *J. Am. Chem. Soc.* **1988**, *110*, 2328; h) Zhang, Y.; O'Connor, B.; Negishi, E.; *J. Org. Chem.* **1988**, *53*, 5588.
3.- Larock, R.C.; Stinn, D.E. *Tetrahedron Lett.* **1988**, *29*, 4687.
4.- Ban, Y.; Wakamatsu, T.; Mori, M. *Heterocycles* **1977**, *7*, 174; Odle, R.; Blevins, B.; Ratcliff, M.; Hegedus, L.S. *J. Org. Chem.* **1980**, *45*, 2709.
5.- Fahey, D.R.; Mahan, J.E. *J. Mol. Chem.* **1978**, *7*, 447.
6.- Larock, R.C.; Berrios-Pena, N.; Narayanan, K. *J. Org. Chem.* **1990**, *55*, 3447.
7.- Amatore, C.; Jutand, A; Suarez, A. *J. Am. Chem. Soc.* **1993**, *115*, 9531 and references therein; Collman, J.P.; Roper, W.R. *Adv. Organomet. Chem.* **1968**, *7*, 53; Halpern, J. *Acc. Chem. Res.* **1970**, *3*, 386.
8.- Negishi, E.I. *Pure Appl. Chem.* **1992**, *64*, 323.
9.- Calderazzo, F. *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 299; Thorn, D.L.; Hoffmann, R. *J. Am. Chem. Soc.* **1978**, *100*, 2079.
10.- Davidson, P.J.; Lappert, M.F.; Pearce, R. *Chem. Rev.* **1976**, *76*, 219.
11.- Formation of the 2-isomer is likely to be catalyzed by the species $HPd(PPh_3)_2X$[16] liberated at the end of the process.
12.- Portnoy, M.; Milstein, D. *Organometallics* **1993**, *12*, 1665; Amatore, C.; Jutand, A.; Khalil, F.; M'Barki, M.A.; Muttier, L. *Organometallics* **1993**, *12*, 3168.
13.- Mali, R.S.; Yadav, V.J. *Synthesis* **1977**, 464.
14.- Garcia-Granda, S.; Diaz, M.R.; Moreiras-Blanco, D.; Marcos-Pascual, C. *Acta Crystallogr., Sec. C, Cryst. Struct. Commun.* **1992**, *C48*, 1513.
15.- Colonge, J.; Guyot, A. *Bull. Soc. Chim. France* **1958**, 325.
16.- Heaton, B.T.; Hébert, S.P.A.; Iggo, J.A.; Metz, F; Whyman, R. *J. Chem. Soc. Dalton Trans.* **1993**, 3081, and references therein.

(*Received in UK* 22 *March* 1994; *revised* 6 *June* 1994; *accepted* 17 *June* 1994)