A Palladium-Catalyzed Synthesis of 4-Aryl-2-oxo-2,5-dihydrofurans[4-Aryl-2(5*H*)-furanones]

Pier Giuseppe CIATTINI, Giorgio ORTAR*

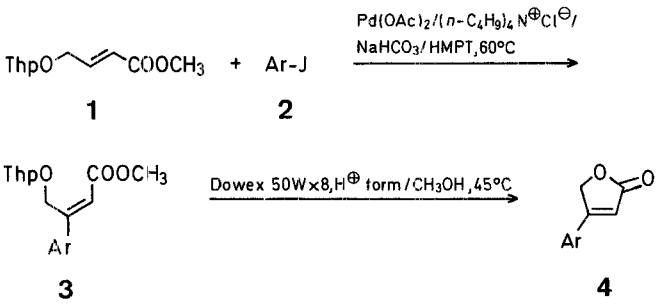
Centro di Studio per la Chimica del Farmaco del C.N.R., Istituto di Chimica Farmaceutica dell' Università, I-00185 Roma, Italy

Palladium-catalyzed arylation of methyl (*E*)-4-(2-tetrahydropyranyloxy)-2-butenoate with aryl iodides and intramolecular cyclocondensation of the resultant 3-aryl derivatives affords 4-aryl-2-oxo-2,5-dihydrofurans in moderate to good yields.

The widespread occurrence of the 2(5*H*)-furanone structural unit in a variety of natural and bioactive products as well as its versatility as a synthetic intermediate has lent considerable importance to the synthesis of this class of heterocycles[1].

The palladium-catalyzed vinylation of organic halides (Heck-type reaction) is a well known method for forming C—C bonds[2]. We have recently reported on a palladium-catalyzed coupling reaction of steroidal 17-enol triflates with methyl (*E*)-4-(2-tetrahydropyranyloxy)-2-butenoate (**1**) as the key step of a new approach to cardenolides[3].

We have now found that compound **1** reacts with various aryl halides (**2**) under solid-liquid phase-transfer conditions[4] in the presence of palladium acetate to give the coupling products **3** which are smoothly cyclized to the title compounds **4**.



Compounds **3** were not isolated and were used in the second step as the crude products.

The (*Z*)-configuration of intermediates **3** was assumed on mechanistic grounds[2,4]; it is consistent with the clean acid-catalyzed cyclization of **3** to **4**. Intermediates similar to **3** have previously been obtained in a five-steps synthesis of 4-arylfuranones from aryl methyl ketones[5].

The process described here provides a useful alternative synthesis of 4-aryl-2(5*H*)-furanones (**4**) from easily available starting materials; it is simple to perform, proceeds under mild conditions, and affords products **4** in moderate to good yields.

2-Oxo-4-phenyl-2,5-dihydrofuran[4a, 4-Phenyl-2(5*H*)-furanone]; Typical Procedure:

A mixture of methyl (*E*)-4-(2-tetrahydropyranyloxy)-2-butenoate[3] (**1**; 300 mg, 1.5 mmol), iodobenzene (204 mg, 1 mmol), palladium

Table. 4-Aryl-2-oxo-2,5-dihydrofurans **(4)** prepared

4	Ar	Yield [%][a]	m.p. [°C] (solvent)	Molecular Formula[b] or Lit. m.p. [°C]	M.S. (M^+)[c] *m/e* (rel.int.)	I.R. (KBr)[d] ν[cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int})[e] δ[ppm]
a	C_6H_5—	71	92–93.5° (acetone/hexane)	91–92.5°[6]	160 (65)	1795, 1747, 1620	5.20 (d, 2H, J = 2 Hz, 5,5-H_2); 6.37 (t, 1H, J = 2 Hz, 3-H); 7.4–7.8 (m, 5H_{arom})
b	3-H_3C—C_6H_4—	70	87–88° (acetone/hexane)	$C_{11}H_{10}O_2$ (174.2)	174 (71)	1793, 1738, 1621	2.40 (s, 3H, CH_3); 5.22 (d, 2H, J = 2 Hz, 5,5-H_2); 6.38 (t, 1H, J = 2 Hz, 3-H); 7.2–7.5 (m, 4H_{arom})
c	4-H_3C—C_6H_4—	59	114–116° (acetone/hexane)	$C_{11}H_{10}O_2$ (174.2)	174 (81)	1790, 1729, 1620	2.40 (s, 3H, CH_3); 5.20 (d, 2H, J = 2 Hz, 5,5-H_2); 6.33 (t, 1H, J = 2 Hz, 3-H); 7.30, 7.47 (ABq, 4H, J_{AB} = 9 Hz, arom)
d	4-H_3CO—C_6H_4—	65	119–120.5° (benzene)	119.5–120°[7]	190 (100)	1792, 1735, 1621	3.87 (s, 3H, OCH_3); 5.17 (d, 2H, J = 2 Hz, 5,5-H_2); 6.23 (t, 1H, J = 2 Hz, 3-H); 7.00, 7.50 (ABq, 4H, J_{AB} = 9 Hz, arom)
e	3-H_3COOC—C_6H_4—	60	150–151° (methanol)	$C_{12}H_{10}O_4$ (218.2)	218 (85)	1790, 1744, 1725, 1624	4.00 (s, 3H, $COOCH_3$); 5.33 (d, 2H, J = 2 Hz, 5,5-H_2); 6.37 (t, 1H, J = 2 Hz, 3-H); 7.6–8.4 (m, 4H_{arom})
f	3-$HOCH_2$—C_6H_4—	59	101–102° (acetone/CCl_4)	$C_{11}H_{10}O_3$ (190.2)	190 (100)	3428, 1816, 1727, 1614	2.3 (m, 1H, OH); 4.78 (br. s, 2H, CH_2—OH); 5.23 (d, 2H, J = 2 Hz, 5,5-H_2); 6.40 (t, 1H, J = 2 Hz, 3-H); 7.4–7.7 (m, 4H_{arom})
g	4-Br—C_6H_4—	48	161–163° ($CHCl_3$)	164°[8]	238 (100)	1794, 1738, 1619	5.20 (d, 2H, J = 2 Hz, 5,5-H_2); 6.40 (t, 1H, J = 2 Hz, 3-H); 7.40, 7.65 (ABq, 4H, J_{AB} = 9 Hz, arom)

[a] Yield of isolated product based on aryl halide **2**.
[b] The microanalyses were in good agreement with the calculated values: C ±0.26, H ±0.08.
[c] Recorded on a Hewlett-Packard 5930 A spectrometer.
[d] Recorded on a Perkin-Elmer 983 spectrophotometer.
[e] Recorded on a Varian EM-390 spectrometer.

acetate (11 mg, 0.05 mmol), tetrabutylammonium chloride (296 mg, 1 mmol), sodium hydrogen carbonate (210 mg, 2.5 mmol), and hexamethylphosphoric triamide (3 ml) is stirred at 60°C for 24 h. The mixture is then diluted with water (20 ml) and extracted with ether (2 × 20 ml). The organic phase is washed with water (2 × 20 ml), dried with sodium sulphate, and evaporated. A mixture of the residue (357 mg) and Dowex 50W × 8 resin (200–400 mesh, $H^{\oplus}$ form, 357 mg) in methanol (5 ml) is stirred at 45°C for 2 h. The resin is then filtered off and washed with methanol. The filtrate is evaporated and the residue (228 mg) is chromatographed on a silica gel column (7 g) with benzene/ethyl acetate (97/3) as eluent; yield of **4a**: 113 mg (71% based on iodobenzene); m.p. 92–93.5°C (Ref.[6], m.p. 91–92.5°C).

Received: May 15, 1985

* Address for correspondence.

[1] Brownbridge, P., Egert, E., Hunt, P.G., Kennard, O., Warren, S. *J. Chem. Soc. Perkin Trans. 1* **1981**, 2751; and references cited therein.
Rao, Y.S. *Chem. Rev.* **1976**, 625.
[2] Heck, R.F. *Org. React.* **1982**, *27*, 345.
[3] Harnisch, W., Morera, E., Ortar, G. *J. Org. Chem.* **1985**, *50*, 1990.
[4] Jeffery, T. *J. Chem. Soc. Chem. Commun.* **1984**, 1287.
[5] Schmitt, J., Suquet, M., Comoy, P., Boitard, J., Callet, G., Clim, T., Le Meur, J. *Bull. Soc. Chim. Fr.* **1966**, 953.
[6] Krauser, S.F., Watterson, A.C. *J. Org. Chem.* **1978**, *43*, 3400.
[7] Perold, G.W., Hundt, H.K.L. *J. Chem. Soc.* [C] **1966**, 1924.
[8] Falsone, G., Wingen, H.P. *Arch. Pharm. (Weinheim)* **1984**, *317*, 802.