FACILE SYNTHESIS OF ISOFLAVONES BY THE CROSS-COUPLING REACTION OF 3-IODOCHROMONE WITH ARYLBORONIC ACIDS

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We describe a convenient preparation of isoflavones by the cross-coupling reactions of 3-iodochromone (**1**) with arylboronic acids (**2**) catalyzed by tetrakis(triphenylphosphine)palladium(0).

KEYWORDS isoflavone; 3-iodochromone; phenylboronic acid; cross-coupling reaction; tetrakis(triphenylphosphine)palladium

Isoflavonoids are widely distributed in plants, especially in Leguminosae, Moraceae, Iridaceae and Rosaceae. Some of these isoflavonoids have physiological such activities as estrogenic, antispastic, antibacterial, antiprotozoal, and insecticidal.[1)]

Synthesis of isoflavones is needed to confirm the structures of natural products, and for this the long-established methods of ring closure of a C_1 unit onto a deoxybenzoin are still widely used. While the addition of one-carbon unit to a deoxybenzoin can be accomplished efficiently, synthesis of the deoxybenzoin itself may proceed in rather poor yields, and starting materials are not readily available.

Recently the cross-coupling reactions of arylhalides with alkenes, alkynes, and arylboronic acids catalyzed by Pd-complex have been studied extensively.[2)] We have applied the reaction to the novel and efficient synthesis of isoflavones (**3**) by using tetrakis(triphenylphosphine)palladium as a catalyst.

A typical experiment can be described as follows. Isoflavone (**3a**): To a solution of 3-iodochromone (**1**) (0.5 mmol), $Pd(PPh_3)_4$ (0.05 mmol), and 1 ml of 2M-Na_2CO_3 in benzene (20 ml) was added phenylboronic acid (**2a**) (2 mmol) in 2 ml of ethanol under argon with stirring at room temperature. The reaction mixture was refluxed for 15 h followed by the addition of 1 ml of 30% H_2O_2 to oxidize excess phenylboronic acid. After being stirred for 1 h at room temperature the mixture was poured into ice and extracted with CH_2Cl_2 (3 x 15 ml). The organic layer was washed with water and dried over anhydrous Na_2SO_4. Removal of the solvent gave a pale yellow product which was purified by silica gel chromatography with benzene as an eluent to give isoflavone (**3a**), mp 135 °C, in 97.8% yield. Palladium(0) catalyzed the cross-coupling reactions of other arylboronic acids (**2b-2e**), prepared by the reported method[3)] through the corresponding Grignard reagents, with 3-iodochromone (**1**) using the above general procedure, are summarized in Table I. The results show that the cross-coupling reaction of substituted arylboronic acids (**2**) with **1** is a quite general and simple method for the synthesis of isoflavones (**3**). When palladium acetate was used as the catalyst instead of $Pd(PPh_3)_4$, the yield of isoflavone was decreased to ca. 30%.

Thiophen-2-boronic acid (**4**) was also coupled with **1** under the same condition to afford **5**, mp 138-139 °C, in 70.2% yield. This implies that we could introduce aromatic and heterocyclic ring systems into the 3-position of chromone under the mild condition in the presence of "Pd" catalyst.

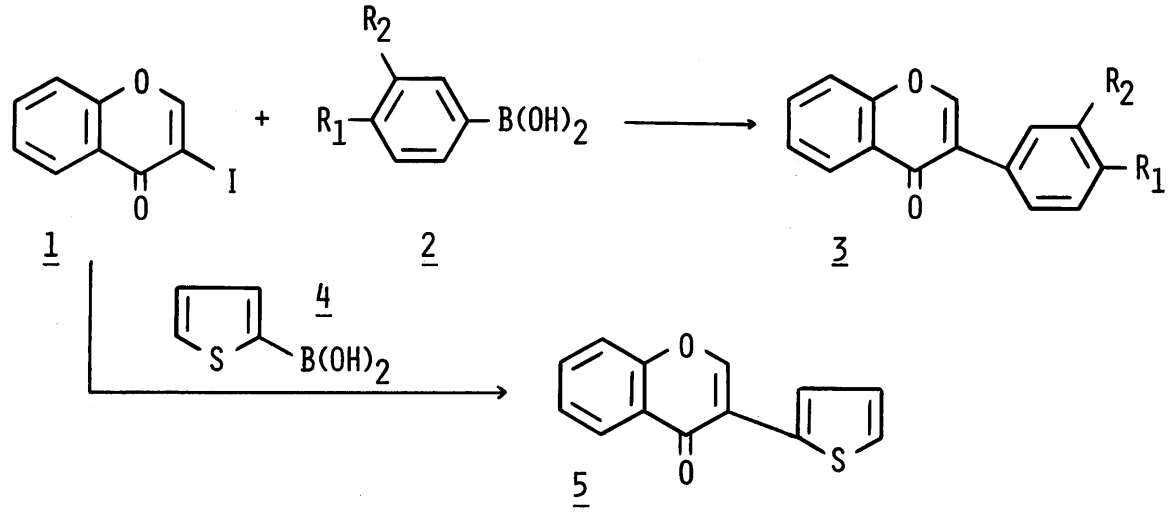

Table I. Reactions of 3-Iodochromone (1) with Arylboronic Acids (2) Catalyzed by $Pd(PPh_3)_4$

	Arylboronic acid (2) R_1	R_2	Yeild of 3 (%)[a]	mp of 3 (°C)
a	H	H	97.8	135
b	CH_3	H	93.2	154–156
c	OCH_3	H	94.1	144
d	OCH_3	OCH_3	95.8	144–145
e	$-O-CH_2-O-$		92.8	158

a) Satisfactory spectroscopic data were obtained for all 3 and yields were after the isolation by the silica gel column chromatography.

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