Ligand Coupling Route to Isoflavanones and Isoflavones

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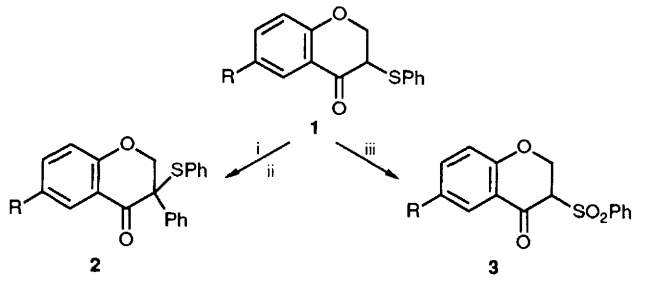
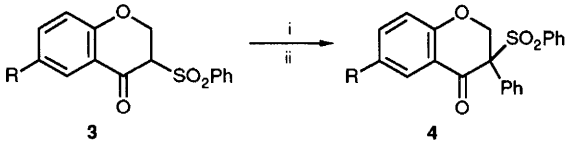
Phenylation of 3-phenylsulfonylchroman-4-ones using Ph_3BiCO_3 leading to the synthesis of isoflavanones and isoflavones is reported.

The isoflavanones, and other isoflavanoids are important classes of biologically active natural products.[1] The biological activities of these compounds include esterogenic, insecticidal, pesticidal and antifungal properties.[2] Even though a number of synthetic methods have been described for both isoflavanones[3] and isoflavones,[4] except for the palladium catalysed Heck-arylation[5] of chrom-3-en-4-ol acetates, the routes are mainly based on direct ring synthesis.

The recently developed bismuth(v) reagents[6] serve as good arylating reagents for ketones, enols and enolates. The use of



Scheme 1 *Reagents and conditions*: i, KH, THF; ii, Ph_3BiCO_3, reflux, 1 h; iii, H_2O_2–HOAc, 0 °C, 8 h



Scheme 2 *Reagents and conditions*: i, KH, THF; ii, Ph_3BiCO_3, reflux, 3 h

these reagents for the synthesis of isoflavanones has been recently reported by Barton *et al.*[7] However, the method suffers from the disadvantages that the phenylation of chroman-4-one afforded the isoflavanone only in low yield and the reaction could not be stopped at the monophenylation stage, whereas phenylation of the 3-formylchroman-4-one furnished the diphenylated product, following *in situ* deformylation of the monophenylated intermediate. Moreover, owing to the ubiquitous aldol condensation in the presence of a base, 3-formylchroman-4-one leads to the formation of a minor amount of dimerised product. Also, the method is not amenable for a direct synthesis of isoflavones.

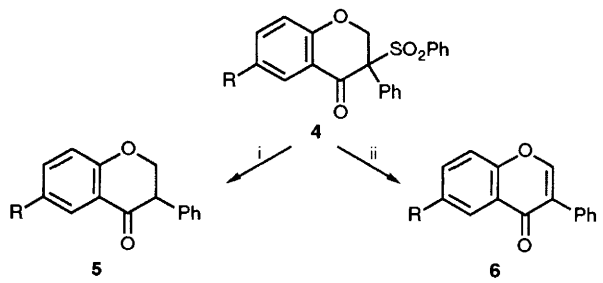
We now report a simple and high yielding, modified, ligand coupling[8] route for the α-phenylation of chroman-4-ones, which permits the synthesis of both isoflavanones and isoflavones from common intermediates, 3-phenyl-3-phenylsulfonylchroman-4-ones, in good yield.

3-Phenylthiochroman-4-ones **1a–d** were prepared by our recently reported procedure.[9] Compound **1a** was subjected to phenylation using Ph_3BiCO_3 in the presence of KH in tetrahydrofuran (THF). However the required product **2a** was obtained in very low yield (20%). Attempted oxidation of **1a** using various reagents, *e.g.* $NaIO_4$, *m*-chloroperbenzoic acid (MCPBA) and magnesium monoperoxyphthalate, failed to yield the desired sulfoxide owing to the occurrence of facile elimination during work-up leading to the chromone. Hence, compounds **1a–d** were converted into the corresponding phenylsulfonyl derivatives **3a–d** quantitatively by treatment with 30% H_2O_2 in acetic acid (Scheme 1).

The phenylation† of **3a–d** was carried out by refluxing the potassium enolate of these 3-phenylsulfonylchroman-4-ones in THF with a slight excess of Ph_3BiCO_3 for 3 h, which furnished the hitherto unknown 3-phenyl-3-phenylsulfonylchroman-4-ones‡ **4a–d** in 80–88% yield (Scheme 2, Table 1).

The reductive removal of the phenylsulfonyl group of compounds **4a–d** was achieved by refluxing in Zn–HOAc[9,10] for 1 h, affording the required isoflavanones **5a–d** in 80–85% yield (Scheme 3).

All the literature methods tried in order to bring about the elimination of phenylsulfinic acid from compound **4a** to obtain the isoflavone were in vain. Surprisingly, treatment of **4a–d** with anhydrous $AlCl_3$ (1.3 equiv.) in dichloromethane at room temperature for 5–10 min yielded the desired isoflavones **6a–d** in almost quantitative yield (Table 2).



Scheme 3 *Reagents and conditions*: i, Zn, HOAc, reflux, 1 h; ii, $AlCl_3$, CH_2Cl_2, room temp., 5–10 min

Table 1 Conversion of compounds **3** into **4** (Scheme 2)

Compd.	R	Yield (%)	M.p., *t*/°C
4a	H	80	205
4b	Me	88	198
4c	Cl	79	226
4d	OMe	85	202

Table 2 Conversion of **4** into **5** and **6** (Scheme 3)

Compd.	R	Yield (%)	M.p., *t*/°C	Compd.	Yield (%)	M.p., *t*/°C
5a	H	80	76	**6a**	95	128
5b	Me	82	50	**6b**	98	110
5c	Cl	80	110	**6c**	92	176
5d	OMe	84	108	**6d**	95	170

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† *Experimental procedure*: the 3-phenylsulfonylchroman-4-one **3** (1 mmol) was added to dry THF (7 ml) containing potassium hydride (*ca.* 1.2 mmol). To this orange enolate solution was added Ph_3BiCO_3 (1.3 mmol). The mixture was refluxed for 3 h and filtered through Celite. The filtrate was concentrated and purified by column chromatography on silica (hexane–ethyl acetate, 9 : 1) to furnish the product **4**.

‡ All the new compounds reported in this communication were thoroughly characterised by spectral and analytical data.