Ligand Coupling Route to Isoflavanones and Isoflavones

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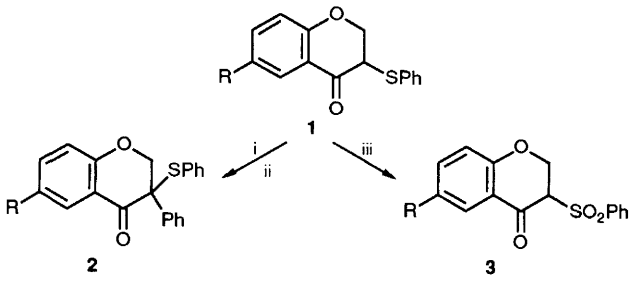
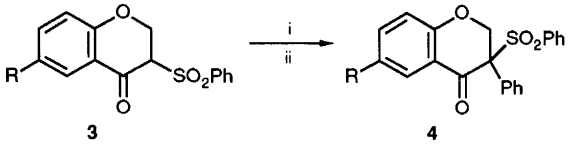
Phenylation of 3-phenylsulfonylchroman-4-ones using Ph_3BiCO_3 leading to the synthesis of isoflavanones and isoflavones is reported.

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).

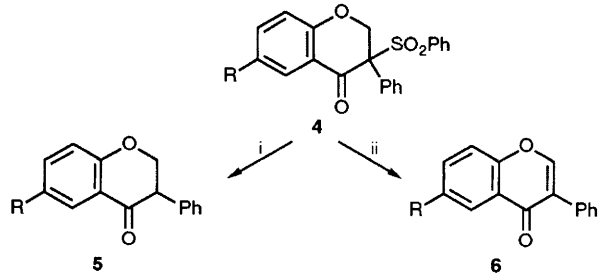
The phenylation† of **3a–d** was carried out by refluxing the potassium enolate of these 3-phenylsulfonylchroman-4-ones in THF with a slight excess of Ph_3BiCO_3 for 3 h, which furnished the hitherto unknown 3-phenyl-3-phenylsulfonylchroman-4-ones‡ **4a–d** in 80–88% yield (Scheme 2, Table 1).

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

† *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.



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

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).

K.C.S. is grateful to IIT, Madras, for a fellowship. We thank Professor G. Schröder and Dr H. Röttele, Univ. of Karlsruhe, Germany, Dr K. Nagarajan, Searle (India) Ltd. Bombay, and RSIC, IIT, Madras for spectral data., and Professor A. Vasella, Univ. of Zurich and Dr S. Vancheesan, IIT, Madras for a gift of triphenylbismuth.

Received, 4th November 1991; Com. 1/05596H

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