SHORT PAPER

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Microwave-assisted synthesis of derivatives of chromanones†

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A variety of chromanones are prepared from resorcinol and phloroglucinol in four steps: two of these reactions are conducted under microwave irradiation, the synthesis of cinnamic acids and the cyclisation of *N*-cinnamoylazoles.

Keywords: chromanones, microwave irradiation

The chemistry of polyhydricphenols has been the subject of many investigations in the last past years. These structures are present in many natural compounds of biological interest. We here report a fast preparation of chromanones from resorcinol or phloroglucinol and *p*-substituted benzaldehydes. Two steps of these syntheses which are microwave-assisted allow a fast access (one day) to chromanones from the phenols and benzaldehydes. The use of microwave irradiation is rapidly increasing because of short reaction times and its operational simplicity.[1,2] We have used the strategy of Speranza[3] to obtain these derivatives *i.e.* the Michael reaction of *N*-cinnamoylazoles with phenols.

We have first prepared *(E)*-cinnamic acids by Doebner–Knoevenagel condensation of malonic acid with carbonyl compounds under microwave irradiation as described by Sampath Kumar.[4] The acids were transformed into their chlorides with thionyl chloride in the usual way. The acid chlorides were condensed with imidazole at room temperature to give *N*-cinnamoylazoles.[1] These latter were mixed with DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) and phenol and irradiated without solvent in a domestic microwave oven to afford a mixture of aryl cinnamates and chromanones. The product composition depends on the irradiation time: a longer reaction leads mainly to the chromanones. The results are reported in Table 1. The compounds show spectral data in agreement with literature.

This work provides advantages over the traditional method: simple reaction protocol, shortened reaction times, slightly better yields.

Experimental

Microwave irradiation were carried out using a Whirlpool AVM 350 oven. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 300 spectrometer in DMSO-d6. Silica gel (Merck, 63-200 μm) was used for column chromatography (eluent EtOAc : CH_2Cl_2, 4:1). All compounds were previously described except the NMR spectra of **3c**, **3′b** and **4′c** : **3a**[5], **3b**[6], **3c**[7], **3′a**[6], **3′b**[8], **4a**[9], **4b**[3], **4c**[6], **4′a**[10], **4′b**[10] and **4′c**.[11]

General procedure for microwave-assisted preparation of **3** *and* **4**: A mixture of DBU (0.76g, 5 mmol), *N*-cinnamoylazole (5 mmol) and phloroglucinol or resorcinol (5.5 mmol) was taken in a 250 ml Erlenmeyer flask and subjected to microwave irradiation at 650 watts for an appropriate time. After cooling, the reaction mixture is acidified with hydrochloric acid M and swirled with dichloromethane (20 ml) for 10 minutes. After decantation and one more extraction with dichloromethane, the organic layers were dried over magnesium sulfate. After removal of solvent, the residue was chromatographed; the yields are calculated after this purification.

3c: ^{1}H NMR 6.11 (s, 2H), 6.21 (d, 1H, *J*=2Hz), 7.00 (d, 1H, *J*=15.8Hz), 7.96 (d, 1H, *J*=15.8Hz), 8.05 (d, 2H, *J*=8.4Hz), 8.31 (d, 2H, *J*=8.4Hz), 9.60 (s, 2H); ^{13}C NMR 98.9, 103.1, 120.8, 124.1, 127. 5, 140.2, 148.2, 150.1, 156.0, 158.9, 165.3 .

3′b: ^{1}H NMR 3.80 (s, 3H), 6.23 (s, 1H), 6.89 (d, 1H, *J*=15.7Hz), 6.73–7.12 (m, 4H), 7.92 (d, 1H), 9.74 (s, 1H) ; ^{13}C NMR 55.6, 108.7, 112.4, 112.5, 114.3, 115.3, 126.7, 129.7, 130.3, 149.5, 154.7, 157.8, 162.7, 167.6.

4′c: ^{1}H NMR 2.96 (dd, *J*=15.5 and 7Hz, 1H), 3.15 (dd, *J*=15.5 and 7Hz, 1H), 4.45 (t, *J*=7Hz, 1H), 6.57 (d, *J*=2.4Hz, 1H), 6.59 (d, *J*=8.4 and 2.4Hz, 1H), 6.83 (d, *J*=8.4Hz, 1H), 7.38 (d, *J*=8.6Hz, 2H), 8.16 (d, *J*=8.6Hz, 2H), 9.77 (s, 1H); ^{13}C NMR 37.0, 38.1, 103.2, 111.6, 124.1, 128.5, 128.2, 133.5, 146.6, 150.3, 151.9, 157.5, 167.5.

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Table 1 Microwave-assisted reactions of N-cinnamoylazoles with phenols

Reagents		Irradiation time /min	Products		Ratio 4:3
Azole	Phenol		Ester	Chromanone	
1a	**2a**	1.5	48% **3a**	7% **4a**	0.15
1a	**2a**	3	10% **3a**	43% **4a**	4.3
1b	**2a**	4	21% **3b**	45% **4b**	2.1
1c	**2a**	3	5% **3c**	59% **4c**	11.8
1a	**2b**	3	10% **3′a**	55% **4′a**	5.5
1b	**2b**	4	12% **3′b**	42% **4′b**	3.5
1c	**2b**	3	0% **3′c**	77% **4′c**	

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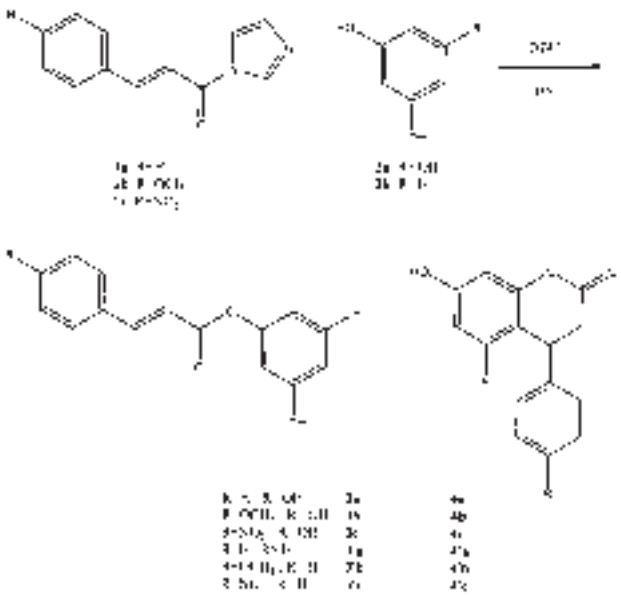
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



Scheme 1

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