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Note

Microwave induced, solvent-free Knoevenagel condensation of 4-oxo-(*4H)*-1-benzopyran-3-carbaldehyde with Meldrum's acid using alumina support

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A rapid, solvent-free and environmentally friendly Knoevenagel condensation reaction of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde **1** with Meldrum's acid **2** has been carried out under microwave irradiation. The structures of condensed products **3a-g** have been characterized on the basis of IR and ^{1}H NMR spectral data.

Keywords: Knoevenagel condensation, solvent-free, 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde, Meldrum's acid, microwave irradiation

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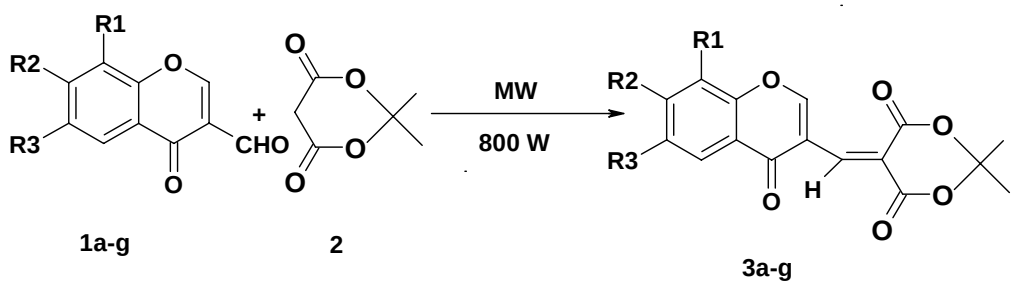
In recent years, there has been a growing interest in the application of microwave irradiation in chemical reaction enhancement, because of its cleaner reactions, decreased reaction time and easier work-up[1-4]. There is increasing interest in the use of microwaves for organic synthesis under solvent-free conditions[5,6] which leads to clean, efficient, environment and eco-friendly technology.

The Knoevenagel condensation is one of the most important, useful and widely employed method for carbon-carbon bond formation in organic reactions[7,8]. It is well-known that the Meldrum's acid undergoes Knoevenagel condensation with aromatic and heteroaromatic aldehydes affording corresponding arylidene derivatives, which are versatile substrates for different kinds of organic reactions[9]. They are useful intermediates for the synthesis of heterocyclic compounds with potential pharmacological activity[10].

In reported methods, the Knoevenagel condensation of aldehydes and Meldrum's acid in ethanol using pipridinum acetate were carried out by conventional heating for two hr reflux[11]. It is also reported by using base such as piperidene in benzene for 3 hr reflux[12]. Excess of pyridine is used for condensation of aldehyde with Meldrum's acid for a long time (8 hr) reflux[13]. It is also carried out by using solvents such as DMF or DMSO (toxic, teratogenic and suspected carcinogens) affording mixtures of unsaturated and Michael addition products[14].

Results and Discussion

In continuation of our work on 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde[15-18] we have developed a newer method for the condensation of various 3-formyl chromones with Meldrum's acid under microwave irradiation using alumina as a solid support for the first time (**Scheme I**). The reactions were carried out by using alumina as well as without alumina. Best results were observed by using alumina support in which time period was reduced and yield was increased as compared to without alumina (**Table I**). The main features of this methodology are easy work up, no requirement of solvent, solid supported and shorter reaction time as compared to reported methods[11-13]. The time period of reaction is reduced from hr to minutes. In addition, products were obtained in excellent yields. All compounds **3a-g** were characterized by IR, ^{1}H NMR and mass spectral data (**Table II**).



Scheme I

Table I — Physical data of compds **3a-g**

Compd	R_1	R_2	R_3	Time (min) without Al_2O_3	Yield[a] (%) without Al_2O_3	Time (min) with Al_2O_3	Yield[a] (%) with Al_2O_3	m.p. (°C)
3a	CH_3	H	Cl	04	90	02	95	200
3b	H	H	Cl	03	90	02	95	198
3c	H	CH_3	H	02	85	01	90	186
3d	Cl	H	Cl	02	90	01	95	180
3e	H	H	H	02	90	01	95	182
3f	H	Cl	Cl	02	87	01	90	242
3g	H	H	Br	02	90	01	95	205

[a] Isolated yield

Table II — Spectral data of compounds **3a-g**

Compd	^{1}H NMR (δ, ppm)	MS (M^+)
3a	2.5 (s, 3H, R_1-CH_3), 1.9 (s, 6H, 2-CH_3), 7.2-7.5 (s, 2H, arom.), 8.6 (s, 1H, olefinic), 9.5 (s, 1H,C_2-H of chromone moiety).	349
3b	1.9 (s, 6H, 2-CH_3), 7.2-8.2 (m, 3H, arom.), 8.6 (s, 1H, olefinic), 9.6 (s, 1H, C_2-H of chromone moiety).	335
3c	2.5 (s, 3H, R_2-CH_3), 1.9 (s, 6H, 2-CH_3), 7.2-8.2 (m, 3H, arom.), 8.7 (s, 1H, olefinic), 9.6 (s, 1H, C_2-H of chromone moiety).	315
3d	1.9 (s, 6H, 2-CH_3), 7.2-8.2 (s, 2H, arom.), 8.6 (s, 1H, olefinic), 9.5 (s, 1H, C_2-H of chromone moiety).	369
3e	1.8 (s, 6H, 2-CH_3), 7.2-8.1 (m, 4H, arom.), 8.7 (s, 1H, olefinic), 9.6 (s, 1H, C_2-H of chromone moiety).	301
3f	1.8 (s, 6H, 2-CH_3), 7.2-8.3 (s, 2H, arom.), 8.6 (s, 1H, olefinic), 9.5 (s, 1H, C_2-H of chromone moiety).	369
3g	1.8 (s, 6H, 2-CH_3), 7.2-8.2 (m, 3H, arom.), 8.6 (s, 1H, olefinic), 9.6 (s, 1H, C_2-H of chromone moiety).	380

Experimental Section

Melting points were measured in open capillaries in a paraffin-bath and are uncorrected. All reactions were carried out in unmodified domestic microwave oven model 800T manufactured by BPL Appliances and Utilities Ltd., Bangalore, India, having maximum power output 800 W and 2450 MHz frequency. The reactions were monitored by TLC [silica, light petroleum-ethyl acetate (8:2)]. IR spectra were recorded as Nujol mulls on FTIR instrument. ^{1}H NMR spectra were recorded at 300 MHz with $CDCl_3$ as solvent and TMS as an internal standard. Mass spectra were recorded on a Micromass Model Quartero II spectrometer.

General Procedure

Without alumina: 4-Oxo-(4*H*)-1-benzopyran-3-carbaldehyde **1a-1g** (10 mmole) and Meldrum's acid 2 (10 mmole) was mixed thoroughly in a 25 mL conical flask and exposed to microwave irradiation at an output of 800 W for 2-4 min (**Table I**). The progress of reaction was checked by TLC. After completion of reaction as indicated by TLC the reaction mixture was cooled and extracted with ethyl acetate. The solvent was removed under vacuum and residual solid was recrystallized from proper solvent. White shiny crystals obtained in 85-90% (**Table I**).

With acidic alumina: 4-Oxo-(4*H*)-1-benzopyran-3-carbaldehyde **1a-1g** (10 mmole) and Meldrum's

acid **2** (10 mmole) was mixed thoroughly with 2 g acidic alumina (from S. D. fine chem., with 99% purity and 0.2% moisture). The reaction mixture was taken in 25 mL conical flask and exposed to microwave irradiation at an output of 800 W for 1-2 min. (**Table I).** The reaction was monitored by TLC. After completion of reaction as indicated by TLC the reaction mixture was extracted with ethyl acetate. The solvent was removed under vacuum and residual solid was recrystallized from proper solvent. White shiny crystals obtained in 90-95% (**Table I**).

Conclusion

In conclusion, we have developed a rapid, solvent-free, environmentally benign and eco-friendly methodology for the Knoevenagel condensation of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde and Meldrum's acid using acidic alumina solid support under microwave irradiation in an excellent yield (90-95%).

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