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Solid-State Condensation of 4-Oxo-4*H*-benzopyran-3-Carbaldehydes with Meldrum's Acid

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Abstract:

Solid-state synthesis of 2, 2-dimethyl-5- [(4-oxo-4*H*-chromen-3-yl) methylene]-1, 3-dioxane-4, 6-dione **3(a-h)** by grinding at room temperature. The process is more economical and environmentally benign.

Keywords: Grinding, solid-state, 3-formyl chromone, Meldrum's acid, Knoevenagel reaction.

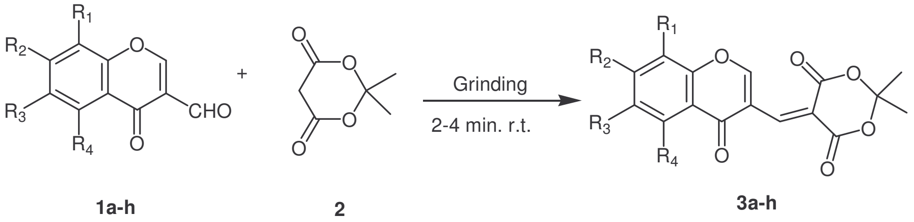
Introduction:

Environmentally friendly chemical process is the vital part of the current chemical research and development. [1] Hence the challenge for sustainable environments calls for the use of clean procedures, which can avoid the use of harmful solvents. We are interested in seeking new processes involving solvent-free reactions; it is an important synthetic procedure from the viewpoint of green and sustainable Chemistry.

In recent years, the progress in the field of solid-state organic reactions is gaining significance both from the mechanistic and synthetic point of view [2]. Number of articles are available reporting solid-state reactions by grinding such as, Grignard reaction,[3] Reformatsky reaction,[4] Aldol condensation,[5] Dickhmann condensation, [6] Knoevenagel condensation, [7] phenol coupling reaction, [8] reduction reaction, [9] Wittig reaction, [10] Grignard and McMurry reaction [11] and others. [12] Most of these reactions are carried out at room temperature, absolutely solvent-free and use only a mortar and pestle. In addition to economical and ecofriendlyness, these procedures are efficient as well. Therefore, we focus on developing the novel procedure involving a solid-state reaction performed by grinding.

Compound having chromone moiety are synthetically versatile molecules with a reactive carbonyl group. They have considerable significance for their biological activities [13] and for their reactivity towards nucleophiles, which allow the synthesis of a wide variety of heterocycles. There are number of methods of Knoevenagel condensation between Meldrum's acid and aromatic aldehydes, which gives arylidene derivatives [14]. They are useful intermediates for the synthesis of heterocyclic compounds with potential pharmacological activities [15]. The condensation reaction of active methylene group with aldehydes function of 3-formyl chromone is studied by different workers [16]. These condensations require acid or base catalyst, prolonged heating period and the product are obtained in low yields. Keeping in view of these observations and in continuation of our work on 3-formyl chromone, [17] in this communication, we wish to introduce a simple route for the condensation of various 4-oxo-4*H*-benzopyran-3-carbaldehyde **1a-h** with active methylene compound, Meldrum's acid **2** at room temperature. The substrate 4-oxo-4*H*-benzopyran-3-carbaldehyde has three active sites; the unsaturated carbonyl group i.e. the pyrone ring, a carbon-carbon double bond and a formyl group. Of these, the formyl group has the highest reactivity towards active methylene compounds.

Scheme 1



Result and discussion:

In Continuation of our ongoing program to develop such solvent-free solid-state reactions, [17b] we wish to report the preparation of arylidenemeldrum's acid from

3-formyl chromone and Meldrum's acid under solvent-free condition. As a model reaction we first decided to investigate the preparation of 2, 2-dimethyl-5-(4-oxo-*4H*-chromen-3ylmethylene)-[1, 3] dioxane-4, 6-dione from **1a** and Meldrum's acid **2** under solvent-free conditions. The progress of the reaction was monitored by TLC and it was observed that the reaction was complete in 4 minute. A variety of 2, 2-dimethyl-5-(4-oxo-*4H*-chromen-3ylmethylene)-[1, 3] dioxane-4, 6-dione were then prepared by simple mixing of **1b-h** and Meldrum's acid **2** in a mortar and grinding the mixture with a pestle at room temperature for the time specified in table-1. The reaction yields are excellent and the reaction times are exceedingly short (2-4 min.). The products were isolated by washing the reaction mixture with water followed by filtrations. This process is fairly general, facial, and efficient and is devoid of any side products. The experimental process is very simple and environmentally benign.

The required 4-oxo-4*H*-benzopyran-3-carbaldehydes was prepared by Vilsmeir-Haack reaction [18] and Meldrum's acid was prepared by known literature method [19].

In conclusion, we have described mild and highly efficient procedure for the synthesis of 2, 2-dimethyl-5-(4-oxo-4*H*-chromen-3ylmethylene)-[1, 3] dioxane-4, 6-dione **3a-h** in solid-state by grinding at room temperature. This process is more economical and environmentally benign

Experimental Section

All products are characterized by IR, ^{1}HNMR spectra. Melting points were obtained on a melting point apparatus with capillary tubes and are uncorrected. IR spectra were recorded on Perkin-Elmer FTIR Spectrophotometer in KBr disc. ^{1}H NMR spectra were recorded on Varian 300 MHz spectrophotometer in $CDCl_3$ as a solvent and TMS as an internal standard. Melting point and other data were recorded in (Table 1)

General Procedure for the Preparation of 3a-h

A mixture of 4-oxo-*4H*-benzopyran-3-carbaldehydes **1a-h** (1 mmol) and Meldrum's acid **2** (0.179g, 1.2 mmol) placed in a mortar was ground with a pestle for 2-4 minutes at room temperature. When TLC showed complete disappearance of starting material, the mixture was quenched with water; the resultant product was filtered, washed with water and recrystallized from ethyl acetate to afford pure corresponding 2, 2-dimethyl-

5-(4-oxo-*4H*-chromen-3ylmethylene)-[1, 3] dioxane-4, 6-dione **3a-h** in excellent yield. The structures of the products were confirmed by IR, ^{1}H NMR spectra.

2,2-dimethyl-5-((4-oxo-4*H*-chromone-3-yl)methylene)-1,3-dioxane-4,6-dione (3a). Yield**:** 88%; mp 182 ^{o}C. IR (KBr):ν_{max} = 3062, 2996, 1732, 1670 1396, 1251 cm^{-1}. ^{1}H NMR (300 Mz, CDCL$_3$): d = 1.8 (6H, s, 2-CH$_3$), 7.2-8.1 (4H, m, aromatic), 8.7 (1H, s, olefinic), 9.6 (1H, s, C$_2$-H of chromone moiety).

5-((6-chloro-4-oxo-4*H*-chromone-3-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (3b). Yield**:** 92%; mp 198 ^{o}C. IR (KBr): ν_{max} = 3061, 2992, 1730, 1669, 1372, 1296, 797 cm^{-1}. ^{1}H NMR (300 Mz, CDCl$_3$): δ = 1.9 (6H, s, 2-CH$_3$), 7.2-8.2 (3H, m, aromatic), 8.6 (1H, s, olefinic), 9.6 (1H, s, C$_2$-H of chromone moiety).

2,2-dimethyl-5-((7-methyl-4-oxo-4*H*-chromone-3-yl)methylene)-1,3-dioxane-4,6-dione (3c). Yield: 87%; mp 186 ^{o}C. IR (KBr): ν_{max} = 3055, 2990, 1710, 1650, 1390, 1280 cm^{-1}. ^{1}H NMR (300 Mz, CDCl$_3$): δ = 2.5 (3H, s, –CH3), 1.9 (6H, s, 2-CH$_3$), 7.2-8.2 (3H, m, aromatic), 8.7 (1H, s, olefinic), 9.6 (1H, s, C$_2$-H of chromone moiety).

5-((6,8-dichloro-4-oxo-4*H*-chromone-3-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (3d). Yield**:** 90%; mp 180 ^{o}C. IR (KBr): ν_{max} = 3065, 2989, 1729, 1674, 1392, 1293, 791 cm^{-1}. ^{1}H NMR (300 Mz, CDCl$_3$): δ = 1.9 (6H, s, 2-CH3), 7.2-8.2 (3H, m, aromatic), 8.6 (1H, s, olefinic), 9.5 (1H, s, C$_2$-H of chromone moiety).

5-((6-chloro-8-methyl-4-oxo-4*H*-chromone-3-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (3e).Yield: 96%; mp 200 ^{o}C. IR (KBr): ν_{max} = 3060, 2996, 1718, 1649, 1396, 1283, 796 cm^{-1}. ^{1}H NMR (300 Mz, CDCl$_3$): δ = 2.5 (3H, s, –CH$_3$), 1.9 (6H, s, 2-CH$_3$), 7.2-7.5 (2H, s, aromatic), 8.6 (1H, s, olefinic), 9.5 (1H, s, C$_2$-H of chromone moiety).

5-((6,7-dichloro-4-oxo-4*H*-chromone-3-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (3f). Yield: 92%, mp 242 ^{o}C. IR (KBr): ν_{max} = 3084, 3018, 1714, 1662, 1392, 1280, 798 cm^{-1}. ^{1}H NMR (300 Mz, CDCl$_3$): δ = 1.8 (6H, s, 2-CH$_3$), 7.2-8.3 (2H, s, aromatic), 8.6 (1H, s, olefinic), 9.5 (1H, s, C$_2$-H of chromone moiety).

5-((6-bromo-4-oxo-4*H*-chromone-3-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (3g). Yield**:** 93%; mp 200 ^{o}C. IR (KBr): ν_{max} = 3063, 2993, 1735, 1664, 1395, 1280, 805 cm^{-1}. ^{1}H NMR (300 Mz, CDCl$_3$): d = 1.8 (6H, s, 2-CH$_3$), 7.2-8.2 (3H, m, aromatic), 8.6 (1H, s, olefinic), 9.6 (1H, s, C$_2$-H of chromone moiety).

Table I. Synthesis of 2, 2-dimethyl-5-(4-oxo-*4H*-chromen-3ylmethylene)-[1, 3] dioxane-4, 6-dione **3a-h** by grinding method

Entry[a]	R_1	R_2	R_3	R_4	Time (min)	Yield (%)[b]	M.P. (°C)
a	H	H	H	H	4	88	182
b	H	H	Cl	H	2.3	92	198
c	H	CH_3	H	H	4	87	186
d	Cl	H	Cl	H	2.3	90	180
e	CH_3	H	Cl	H	2	96	200
f	H	Cl	Cl	H	2.3	92	242
g	H	H	Br	H	3	93	205
h	H	H	F	H	2	95	200

[a] All the products were characterized by IR,^{1}H NMR, spectra.
[b] Yield of isolated product.

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