An efficient condensation of 4-oxo-4*H*-benzopyran-3-carbaldehydes with 3-methyl-1-phenyl-1*H*-pyrazol-5 (4*H*)-one

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Abstract
An efficient synthesis of 3-methyl-4- [(4-oxo-4*H*-chromen-3-yl) methylene]-1-pheny-1*H*-pyrazol-5-(4*H*)-ones **3a-m** in solid-state by grinding without solvent at room temperature.

Keyword: Grinding, solid-state, 3-formyl chromone, pyrazolinone, Knoevenagel reaction

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Introduction

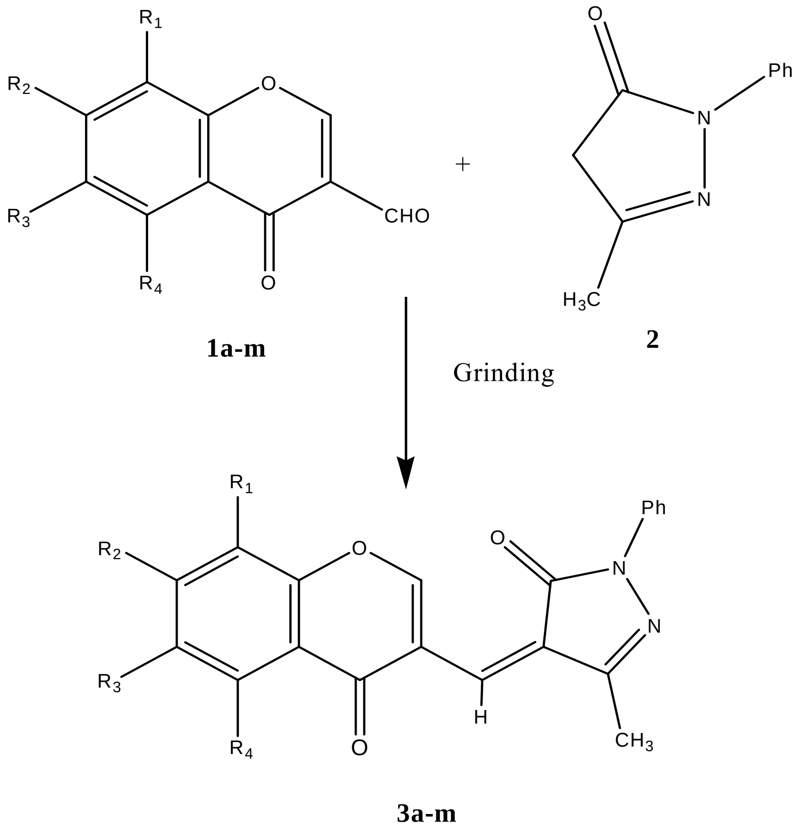
Environmental concern in research and industry are increasing with the increasing pressure to reduce the amount of pollutants produced, including organic solvents whose recoveries mandated by ever more strict laws. Hence the challenge for sustainable environments calls for the use of clean procedures, which can avoid the use of harmful solvents. We are interested in seeking new processes involving solvent-free reactions, for these methods many advantages such as reduced pollution, low cost, and simplicity in processing. These factors are beneficial to industry as well as to enviorment.[1]In recent times, the progress in the field of solid-state organic reactions is gaining significance both from the mechanistic and synthetic point of view.[2-4] Most article have appeared reporting solid-state reactions by grinding such as, Grignard reaction,[5] Reformatsky reaction,[6] Aldol condensation,[7] Dickhmann condensation,[8] phenol coupling reaction,[9] reduction reaction[10] and others.[11] Most of these reactions are carried out at room temperature, absolutely solvent-free and use only a mortar and pestle. In addition too economical and environmentally friendly, 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 [12] and for their reactivity towards nucleophiles, which allow the synthesis of a wide variety of heterocycles. The condensation reaction of active methylene group with aldehydes function of 3-formyl chromone is studied by different workers.[13] these condensations require acid or base catalyst and 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,[14] herein we wish to report a mild and highly efficient method for the synthesis of 3-methyl-4- [(4-oxo-4*H*-chromen-3-yl)-methylene]-1-phenyl-1*H*-pyrazol-5 (4*H*)-ones by grinding in mortar and pestle in excellent yield.

In this communication, we have developed a newer root for the condensation of various 4-oxo-4*H*-benzopyran-3-carbaldehyde **1a-m** with active methylene compound such as 3- methyl-1-phenyl-1*H*-pyrazol-5 (4*H*)-ones **2** ground in mortar and pestle 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.

Results and Discussion

In order to verify the role of grinding, we have examined the model reaction of **1a-m** and **2** stirred and left standing at room temperature for overnight, reaction remained incomplete. To keep this method simple, economical and efficient, we have used a glass mortar and pestle to repeat this experiment under the same conditions. Surprisingly, the reaction completes within 2 minutes and the color of the ground substance changed (yellow to red color). It leads to the almost quantitative formation of the Knoevenagel product **3a-m**.



Isolation of the product is achieved by quenching in water, followed by filtration and drying. This process is fairly general, facial, efficient and is devoid of any side products. The process is environmentally benign and experimental process is very simple.

The required 4-oxo-4*H*-benzopyran-3-carbaldehydes was prepared by Vilsmeir-Haack reaction[15] and 3-methyl-1-phenyl-1*H*-pyrazol-5 (4*H*)-one was prepared by known literature method.[16]

In conclusion, we have described a highly efficient procedure for the synthesis of 3-methyl-4-[(4-oxo-4*H*-chromen-3-yl) methylene]-1-phenyl-1*H*-pyrazol-5(4*H*)-ones in solid state by grinding at room temperature. This process is more economics and environmentally benign.

Experimental Section

General procedures. All products are known compounds and their physical data, IR, ^{1}H NMR spectra were essentially identical with those of authentic samples. Melting pints were obtained on a melting point apparatus with capillary tubes and are uncorrected. IR spectra were recorded on Perkin-Elmer FT Spectrophotometer in KBr disc. ^{1}H NMR spectra were recorded on Varian 300 MHz spectrophotometer in CDCl3 as a solvent and TMS as an internal standard. Melting point and other data were recorded in table 1.

Table 1. Reaction of 4-oxo-4*H*-benzopyran-3-carbaldehyde and 3- methyl-1-phenyl-1*H*-pyrazol-5 (4*H*)-one by grinding method

Product	R_1	R_2	R_3	R_4	Yield (%) b	Melting point (^{0}C)
3a	H	H	H	H	83	228-230
3b	H	H	CH_3	H	80	238-240
3c	CH_3	H	CH_3	H	77	280-282
3d	H	CH_3	H	CH_3	80	213-215
3e	H	CH_3	H	H	82	200-202
3f	H	H	Br	H	85	232-234
3g	Cl	H	Cl	H	84	290-291
3h	H	CH_3	Cl	H	90	253-254
3i	Cl	H	H	Cl	88	290-292
3j	H	Cl	Cl	H	86	266-268
3k	H	CH_3	CH_3	H	80	248-250
3l	Cl	H	H	H	85	218-220
3m	H	H	Cl	H	85	236-238

[a] All the products were characterized by IR,^{1}H NMR, spectra and by comparison of their physical cheristeristics with those of the authentic compounds.
[b] Yield of isolated product.

Synthesis of 3-methyl-4-[(4-oxo-4*H*-chromen-3-yl) methylene]-1-phenyl-1*H*-pyrazol-5(4*H*)-ones

A mixture of 4-oxo-4*H*-benzopyran-3-carbaldehydes **1a-m** (1mmol) and 3- methyl-1-phenyl-1*H*-pyrazol-5 (4*H*)-ones **2** (1mmol) placed in a mortar was ground with a pestle for 2 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 dioxan to afford pure corresponding 3-methyl-4- [(4-oxo-4*H*-chromen-3-yl) methylene]-1-phenyl-1*H*-pyrazol-5 (4*H*)-ones **3a-m** in excellent yield. The structure of the products were confirmed by IR, ^{1}H NMR and comparison with authentic samples prepared according to literature methods.[14]

3-Methyl -4- [(6-methyl-4-oxo-4*H*-chromen-3-yl) methylene]-1-phenyl-1*H*-pyrazol-5 (4*H*)-one (3f). Yield: 80%; Orange red crystals; mp 238-240 ° C (Lit. mp 239 ° C); IR (KBr): 3063 (=C-H, Ar-H), 1790 (C=O, Pyrazolinyl), 1685 (C=N, Pyrazolinyl), 1654 (C=O, chromone), 1460 (γ-pyrone), 2900 (aliphatic C-H str.) cm^{-1}; ^{1}H NMR (300 Mz, CDCL$_3$): δ = 2.4 (s, 3H, R$_3$ -CH$_3$), 2.5 (s, 3H, Pyrazolinyl -CH$_3$), 7.2-8.2 (m, 9H, arom. and olefinic, 10.8 (s, 1H, C$_2$-H of chromone moiety).

3-Methyl -4- [(6-Bromo-4-oxo-4*H*-chromen-3-yl) methylene]-1-phenyl-1*H*-pyrazol-5 (4*H*)-one (3f). Yield: 85%; Orange red; mp 232-234 ° C (Lit[14b]. 234 ° C); IR (KBr): 3063 (=C-H, Ar-H), 1790 (C=O, Pyrazolinyl), 1685 (C=N, Pyrazolinyl), 1654 (C=O, chromone), 1460 (γ-pyrone), 780(C-Br) cm^{-1}; ^{1}H NMR (300 Mz, CDCL$_3$): δ = 2.5(s, 3H, Pyrazolinyl –CH3), 7.2-8.1 (m, 9H arom. and olefinic), 10.8 9s, 1H, C$_2$-H of chromone moiety).

3-Methyl -4- [(6-chloro-7-methyl-4-oxo-4*H*-chromen-3-yl) methylene]-1-phenyl-1*H*-pyrazol-5 (4*H*)-one (3h). Yield; 90%; Red crystals; mp 253-254 ° C (Lit[14b]. 255); IR (KBr): 3063 (=C-H, Ar-H), 1790 (C=O, Pyrazolinyl), 1685 (C=N, Pyrazolinyl), 1654 (C=O, chromone), 1460 (γ-pyrone), 680 (O-substituted methyl and –Cl group). 2885 (aliphatic C-H str.) cm^{-1}; ^{1}H NMR (300 Mz, CDCl$_3$): δ= 2.3 (s, 3H, R2=CH3), 2.4 (s, 3H, Pyrazolinyl–CH3), 7.2-7.9 (m, 8H, arom. and olefinic), 10.9 (s, 1H, C$_2$-H of chromone moiety).

3-Methyl -4- [(6, 7-dichloro-4-oxo-4*H*-chromen-3-yl) methylene]-1-phenyl-1*H*-pyrazol-5 (4*H*)-one (3j). Yield; 86%; Orange red crystals; mp 266-268 ° C (Lit[14b]. 268); IR (KBr): 3063 (=C-H, Ar-H), 1790 (C=O, Pyrazolinyl), 1685 (C=N, Pyrazolinyl), 1654 (C=O, chromone), 1460 (γ-pyrone), 690 (o-substituted –Cl group) cm^{-1}; ^{1}H NMR (300 Mz, CDCl$_3$): δ = 2.4 (s, 3H, Pyrazolinyl –CH3), 7.5-7.9 (m, 8H, arom. and olefinic), 10.7 (s, 1H, C$_2$-H of chromone moiety).

3-Methyl -4- [(6-bromo-4-oxo-4*H*-chromen-3-yl) methylene]-1-phenyl-1*H*-pyrazol-5 (4*H*)-one (3m). Yield; 85%; Red crystals; mp 236-238 ° C (Lit ° C[14b]. 238); IR (KBr): 3063 (=C-H, Ar-H), 1790 (C=O Pyrazolinyl), 1685 (C=N, Pyrazolinyl), 1654 (C=O, chromone), 1460 (γ-pyrone), 750 (C-Cl) cm^{-1}; ^{1}H NMR (300 Mz, CDCl$_3$): δ 2.4 (s, 3H, Pyrazolinyl), 7.1-8.2 (m, 9H, aromatic and olefinic protons), 10.8(s, 1H, C$_2$-H of chromone moiety).

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References

1. Tanaka, K.; Toda, F. *Chem. Rev*. **2000**, *100*, 1025.
2. Toda, F. *Synlett* **1993**, 303.
3. Singh, N. B.; Singh, R. J.; Singh, N. P. *Tetrahedron* **1994**, *50*, 6441.
4. Desiraju, G. R.; *Solid-state ionics* **1997**, *101*, 839.
5. Toda, F.; Takumi, H.; Yamaguchi, H.; *Chem. Exp*. **1989**, *4*, 507.
6. Tanaka, k.; Kishigami, S.; Toda, F. *J. Org. Chem.* **1991**, *56*, 4333.
7. Toda, F.; Tanaka, K.; Hamai, K. *J. Chem. Soc., Perkin Trans. I* **1990**, 3207.
8. Toda, F.; Suzuki, T.; Higa, S. *J. Chem. Soc*., *Perkin Trans. I* **1998**, 3521.
9. Toda, F.; Tanaka, K.; Iwata, S. *J. Org. Chem*. **1989**, *54*, 3007.
10. Toda, F.;Kiyoshige, K.; Yagi, M. *Angew. Chem*., *Int. Ed.* **1989**, *28*, 320.
11. (a) Schmeyers, T.; Toda, F.; Boys, J.;Kaupp, G. *J. Chem. Soc., Perkin Trans*. **1998**, *2*, 989. (b) Xiao, J. P.; Wang, Y. L.; Zhau, Q. X. *Synth. Commun*. **2001**, *31*, 661. (c) Li, J. P.; Wang, Y. L.; Wang H.; Luo, Q. F.; Wang, X. Y. *Synth. Commun*. **2001**, *31*, 781. (d) Scott, J. L.; Raston, C. L. *Green Chem*. **2000**, *2*, 245. (e) Wang, Z. X.; Hua, L. Q. *Green Chem*. **2004**, *60*, 90.
12. Gerwick, W. H.; Lopez, A.; Van Duyne, G. D.; Clardy, J.; Ortiz, W.; Buez, A.; *Tetrahedron Lett*. **1979**, *270*, 1986.
13. (a) Polyakov, V. K.; Shevtsova, R. G.; *Ukr. Khim. Zh.* (Russ. Ed.). **1981**, *47(1)*, 85. (b) Treibs, A.; William, R.; Dieter, L. *Ann. Chem*. **1981**, *3*, 306. (c) Prousek, J. *Collect. Czech. Chem. Commun.* **1993**, *58(12)*, 3014. *Chem. Abstract* **1994**, *120*, 217542j.
14. (a) Shingare, M. S.; Karale, B. K.; Gill, C. H.; Ganage, K. N.; Bachute, M. T. *Ind. J. Heterocyclic Chem*. **1999**, *9(2)*, 153; (b) Karale, B. K.; Chavan, V. P.; Mane, A. S.; Hangarge, R. V.; Gill, C. H.; Shingare, M. S. *Synth. Commun*. **2002**, *32(4)*, 497-502. (c) Hangarge, R. V.; Jarikote, D. V.; Shingare, M. S. *Green Chemistry* **2002**, *4*, 266.
15. Nohara, A.; Umetani, T.; Sanno, Y. *Tetrahedron* **1974**, *30(19)*, 3553.
16. Vogel's *Textbook of Practical Organic Chemistry*, Fifth Edition, ELBS, Longman Scientific and Technical: England. 1989, Reprinted 1994, p 1150.