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Note

Microwave-assisted synthesis of substituted-4-oxo-4*H*-1-benzopyran-3-carboxaldehydes using Vilsmeier reagent over silica gel

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Substituted-4-oxo-4*H*-1-benzopyran-3-carboxaldehydes **2a-h** have been synthesised in good yields under microwave irradiation using Vilsmeier reagent over silica gel in solvent free conditions. The reaction takes place within 2-3.5 min.

Keywords: 4-Oxo-4*H*-1-benzopyran-3-carboxaldehydes, Vilsmeier reagent, microwave irradiation, silica gel, solvent free conditions

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Microwave irradiation has become a very useful tool in organic synthesis and a great number of classical organic reactions have been successfully carried out utilizing microwave dielectric heating technique[1]. Reactions under dry media conditions using inorganic solid supports are gaining more attention because of their enhanced selectivity and milder conditions than those associated with conventional homogeneous reaction procedures[2,3]

Of the different functionalised chromones, 4-oxo-4*H*-1-benzopyran-3-carboxaldehyde (3-formylchromone) is a versatile synthon and the molecules derived from it are equally versatile, as starting materials, for preparing novel heterocyclic systems possessing diverse biological activities[4-8].

Though many methods are known[9-12] for the synthesis of 4-oxo-4*H*-1-benzopyran-3-carboxaldehydes, the Vilsmeier-Haack reaction[5,13] appears to be the most suitable. In Vilsmeier-Haack reaction, DMF-$POCl_3$ plays a dual role of reagent as well as solvent. $POCl_3$ is a highly toxic solvent and its large scale use is a health and environmental hazard. Keeping this in view and the interest in devising clean, efficient and environmentally benign techniques[14] for synthesising organic molecules of synthetic and biological importance, herein is reported the synthesis of substituted-4-oxo-4H-1-benzopyran-3-carboxaldehydes **2a-h** under microwave irradiation using Vilsmeier reagent (V.R.) over silica gel in solvent free conditions (**Scheme I**), which is in continuation to an earlier publication[15] in this series using DMF-$POCl_3$ over silica gel for the synthesis of β-chlorovinyl aldehydes, 2-aryl-3-formylindoles, 2-chloro-3-formyl-quinolines and aromatic aldehydes.

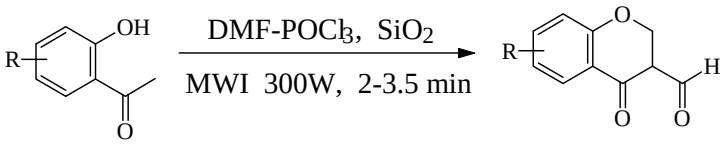
The amount of Vilsmeier reagent and power output were adjusted to get the maximum yield of the products **2a-h**. For optimization of the reaction conditions, it has been found that 0.04 mole of Vilsmeier reagent per 0.01 mole of the substrate furnished the maximum yield. Silica gel (14-16 g) was activated by irradiation at 700 W in a microwave oven for 5 min before use in the reaction. This, alongwith microwave heating at 300 W appeared to be the best compromise between efficiency and safety, as higher power output led to generation of toxic fumes in the oven.

The reaction times and yields of **2a-h** obtained by microwave irradiation and classical[5] methods have been compared in **Table I**.

Though the significant reaction rate enhancement has been observed, the yields of **2g** and **2h** cannot be improved even under microwave irradiation because of the formylation on the benzene ring and formation of tarry material[5].

In order to check the possible intervention of specific (non-thermal) microwave effect, the synthesis of **2a-f** was carried out using a preheated oil bath, as a source of heat, with the same final temperatures and reaction times as measured for the microwave irradiation experiments. The lower yields obtained with conventional heating indicate that the effect of microwaves is not purely thermal **Table II**.

In conclusion, the Vilsmeier-Haack reaction in solvent free conditions, using silica gel as a solid support under microwave irradiation provides an excellent method for the synthesis of substituted-4-oxo-4*H*-1-benzopyran-3-carboxaldehydes. The method, which is rapid and efficient, avoids the employment of the reagent as solvent and is, thus, environmentally benign. Non-thermal effect of microwave iradiation has also been observed.



1a-h **2a-h**

Scheme I

Table I — Comparison of reaction times and yields of **2a-h** under microwave irradiation and classical conditions

Compd	R	m.p. (°C)	Lit. m.p. (°C)	Reaction Time		Yield (%)	
				MWI (min)	Classical (hr)	MWI	Classical
2a	H	150-51	152-53[a]	2.5	13	69	63
2b	6-Cl	166-67	166-68[a]	3	10	77	72
2c	6-Br	190-91	190-93[b]	3.5	10	65	57
2d	6-Me	172-73	174-75[a]	3	14	72	65
2e	6-OMe	163-64	164-66[a]	2.5	8	76	62
2f	6-OEt	134-35	—	2.5	8	78	64
2g	7-OMe	188-89	188-90[a]	2	6	20	06
2h	7-OEt	147-48	—	2.5	7	16	05

[a]From Ref. 5
[b]Aldrich

Table II — Comparison of results of synthesis of **2a-f** under microwave irradiation (MWI) (Power = 300 W) and thermal heating (Δ) at the same final temperatures

Compd	Method	Final temp[a] (°C)	Reaction time (min)	Yield (%)
	Δ	110-12	2.5	30
2a	MWI	110-12	2.5	69
2b	MWI	112-14	3	77
	Δ	112-14	3	43
2c	MWI	112-13	3.5	65
	Δ	112-13	3.5	27
2d	MWI	110-12	3	72
	Δ	110-12	3	33
2e	MWI	112-13	2.5	76
	Δ	112-13	2.5	41
2f	MWI	108-10	2.5	78
	Δ	108-10	2.5	37

[a]Final temperature was measured by immersing a glass thermometer in the reaction mixture immediately after exposure to microwave irradiation and is the approximate temperature range.

Experimental Section

Melting points were determined in open capillaries on Buchi melting point apparatus and are uncorrected. The starting *o*-hydroxyacetophenone derivatives **1b-h** were prepared by reported methods[5,16,17]. Reactions were carried out in a BPL BMO 800 T domestic microwave oven operating at 2450 MHz with maximum output power of 800 W. The identity of products **2a-h** was established on the basis of elemental analyses, spectral data and by comparison of their melting points with authentic samples prepared by known methods.

General procedure for the preparation of 6-ethoxy-4-oxo-4*H*-1-benzopyran-3-carboxaldehyde, 2f

To a well cooled solution of 5-ethoxy-2-hydroxyacetophenone **1f** (1.8 g, 0.01 mole) in DMF (3.1 mL, 0.04 mole), $POCl_3$ (3.68 mL, 0.04 mole) was added dropwise with constant stirring and cooling. The reaction mixture was then allowed to attain RT. Silica gel (15 g) was added to it and properly mixed with the help of a glass rod till free flowing powder was obtained. The dry powder, taken in a borosil beaker (100 mL), was then irradiated in a microwave oven at 300 W for 2.5 min (monitored on TLC after every 30 s). After cooling, crushed ice was added and the mass stirred. It was then extracted with chloroform and the organic layer was washed with water and dried over anhydrous sodium sulphate. The

solid obtained, after removal of the solvent, was purified by recrystallization from acetone to afford **2f** as fluffy white crystals in 78% (1.7 g) yield, m.p. 134-35°C; IR (KBr): 1690, 1645, 1615, 1580 cm^{-1}; MS: *m/z* (%), 220 (M^+ + 2, 10.0), 218 (M^+, 9.4), 191 (100), 162 (85.7), 137 (53.9), 108 (18.5), 79 (22.1), 55 (23.8); ^{1}H NMR ($CDCl_3$): δ 1.45 (t, 3H,-OCH_2 - CH_3), 4.1 (q, 2H, -OCH_2 - CH_3), 7.1 - 7.35 (m, 2H, C_7 - *H* and C_8 - *H*), 7.65 (d, 1H, C_5- *H*, *J* = 3 Hz), 8.5 (s, 1H, C_2 - *H*), 10.4 (s, 1H, - C*H*O).

References

1 (a) Mingos D M P & Baghurst D R, *Chem Soc Rev*, 20, **1991**, 1.
(b) Abramovitch R A, *Org Prep Proced Int*, 23, **1991**, 685.
(c) Caddick S, *Tetrahedron*, 51, **1995**, 10403.
(d) Galema S A, *Chem Soc Rev*, 26, **1997**, 233.
(e) Loupy A, Petit A, Hamelin J, Texier-Boullet F, Jacquault P & Mathe D, *Synthesis*, **1998**, 1213.
(f) Varma R S, *Green Chemistry*, 1, **1999**, 43.
(g) Deshayes S, Liagre M, Loupy A, Luche J-L & Petit A, *Tetrahedron*, 55, **1999**, 10851.
(h) Elander N, Jones J R, Lu S –Y & Stone – Elander S, *Chem Soc Rev*, 29, **2000**, 239.
(i) Lidstorm P, Tierney J, Wathey B & Westman J, *Tetrahedron*, 57, **2001**, 9225.

2 (a) Mckillop A & Young D W, *Synthesis*, **1979**, 401
(b) *ibid*, 481.
(c) Balogh M & Laszlo P, *Organic Chemistry Using Clays* (Springer-Verlag, Berlin), **1993**.

3 (a) Varma R S & Dahiya R, *Tetrahedron Lett*, 38, **1997**, 2043.
(b) Boruah A, Baruah M, Prajapati D & Sandhu J S, *Synth Commun*, 28, **1998**, 653.

4 Ellis G P & Shaw D, *J Med Chem*, 15, **1972**, 865.

5 Nohara A, Umetani T & Sanno Y, *Tetrahedron*, 30, **1974**, 3553.

6 Ellis G P, *Heterocyclic Compounds*, edited by A Weissberger (Interscience, New York), 35, **1977**, 921.

7 Nohara A, Kuriki H, Saijo T, Sugihara H, Kanno M & Sanno Y, *J Med Chem*, 20, **1977**, 141.

8 (a) Ghosh C K, *J Heterocycl Chem*, 20, **1983**, 1437.
(b) Sabitha G, *Aldrichimica Acta*, 29, **1996**, 5.

9 Eiden F & Haverland H, *Arch Pharm*, 300, **1967**, 806.

10 Ellis G P, *J Chem Research (S)*, **1978**, 47.

11 Becket G J P & Ellis G P, *Tetrahedron Lett*, **1976**, 719.

12 Klutchko S, Cohen M P, Shavel J Jr & Strandtmann M von, *J Heterocycl Chem*, 11, **1974**, 183.

13 Nohara A, Umetani T & Sanno Y, *Tetrahedron Lett*, **1973**, **1995**.

14 (a) Paul S, Gupta R & Loupy A, *J Chem Research (S)*, **1998**, 330.
(b) Gupta R, Paul S & Gupta A K, *Indian J Chem Technol*, 5, **1998**, 340.
(c) Gupta M, Paul S, Gupta R & Loupy A, *Org Prep Proceed Int*, 32, **2000**, 280.
(d) Paul S, Gupta M, Gupta R & Loupy A, *Tetrahedron Lett*, 42, **2001**, 3872.
(e) Paul S, Gupta M, Gupta R & Loupy A, *Synthesis*, **2002**, 75.

15 Paul S, Gupta M & Gupta R, *Synlett*, **2000**, 1115.

16 Vogel A I, *A Text Book of Practical Organic Chemistry including Qualitative Organic Analysis*, 3rd edn (E L B S and Longman Group Limited, London), **1973**, 669, 676.

17 (a) *Organic Synthesis*, collective vol 3, **1955**, 280
(b) *ibid*, 452.
(c) Nencki M, *J Prakt Chem*, 25(2), **1882**, 273.
(d) Nencki M & Siber N, *J Prakt Chem*, 23 (2), **1881**, 546.