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Solvent Free Microwave Assisted Condensation of Dehydroacetic Acid with Aromatic and Heteroaromatic Aldehydes

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ABSTRACT

A series of 3,4,6-Trisubstituted-2- pyrones were synthesized via microwave assisted Knoevenagel condensation of dehydroacetic acid with aromatic and heteroaromatic aldehydes. The reaction was performed under solvent-free conditions, in a microwave oven and it was found that the condensation was enhanced when compared with conventional method. Further, it was found that the isolated yields were improved (70 to 92%) with very shorter reaction times (4-10 minutes). All the synthesized compounds were characterised by IR and ¹H spectroscopies.

KEYWORDS: Dehydroacetic acid, Aromatic and Heteroaromatic Aldehydes, Microwave Assisted Knoevenagel Condensation.

INTRODUCTION

Microwave assisted organic reactions have emerged as a new 'lead' in organic synthesis. The microwave assisted organic reactions are gaining importance due to the advantages like reaction rate enhancement, improved yields, easier work-up, etc and environmentally friendly processes they offer, as compared to conventional methods (Sharma SV *et al.*, 2002 and Rechar G *et al.*, 1986) Further, microwave heating allows chemist to perform reactions efficiently in the absence of solvents, with dry media conditions. The advantages of using dry media conditions ranges from faster reactions with different selectivity to more economical conditions due to the absence of solvents (Loupy A *et al.*, 2002).

Dehydroacetic acid is a versatile compound and is used in the synthesis of variety of organic compounds which are used as food additives, antihypertensives, antimicrobial, insecticidal, cosmetic and promoters for hematocytes production (Theodore SP *et al.*, 1973, Durakovic S *et al.*, 1994, Gazzaniga A *et al.*, 1994 and Chi Y *et al.*, 1995). Knoevenagel condensation of aldehydes with active Methylene compounds is one of the most important preparation methods of these organic compounds. These reactions are generally catalysed using Lewis acids, bases and surfactants. All these procedures require solvents as reaction media and for extraction and purification and thus create much waste (Knoevenagel E *et al.*, 1904, Willey RH *et al.*, 1955, Rachedi Y *et al.*, 1991, Balalie S *et al.*, 2001 and Baziz NA *et al.*, 2004). Recently, use of microwave dry media technology has been reported as a useful condition for Knoevenagel condensation (Saravanamurugan S *et al.*, 2006 and Baziz NA *et al.*, 2008). Review of literature revealed that no researcher has used heteroaromatic aldehydes with dehydroacetic acid in Knoevenagel condensation and studied the same under microwaves. Therefore, we felt that the Knoevenagel condensation could

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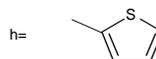
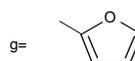
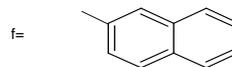
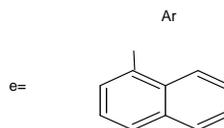
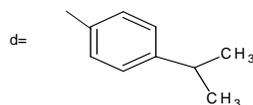
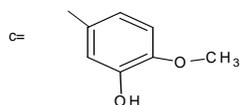
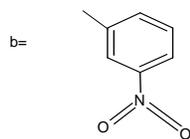
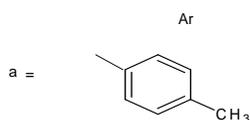
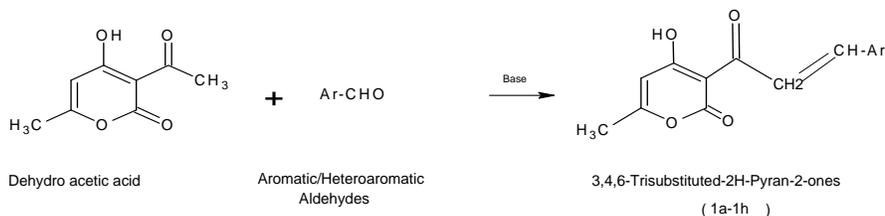
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be a good candidate as a model reaction, in order to compare not only the reaction rate, yield and environment friendly procedures, but also energy consumption for microwave and conventional technologies. The energy consumption should also be considered since it consumes non-renewable resources and produces waste and could also influence in the near future environmental acceptability and economic viability. Energy efficiency of microwave process is rarely discussed in published articles (Gronnow MJ *et al.*, 2005).

MATERIALS AND METHODS

All the chemicals used were obtained from S.D. Fine Chemicals Ltd, Mumbai, Qualigens Fine Chemicals, Mumbai; Himedia Laboratories Pvt.Ltd, Mumbai and CDH (P) Ltd, Delhi. Non-Conventional heating was done in a domestic microwave oven (Sun flame). Melting points were determined in open capillaries using melting point apparatus (Sunbim), expressed in °C and are uncorrected. IR spectra of the compounds was recorded on Analytical FTIR instrument (KBr pellet), ¹H spectra on Bruker AMX 400 MHz using TMS as internal standard and

CHEMICAL REACTION



the values are expressed in δ PPM. The identity of the eight synthesized compounds was confirmed by IR, ¹H NMR spectral data. The microwave data, time, temperature and yield were compared to conventional method.

Conventional Procedure

A mixture of 0.084 gm of dehydroacetic acid and aromatic aldehyde (5 mmol) was added to 20 ml of chloroform containing 0.05 ml of pyridine and 0.05 ml of piperidine. This reaction mixture was reflux condensed on an electrical heating mantle for 6 to 9 hrs. The reaction mixture was evaporated and the crude solid obtained was recrystallised from ethyl alcohol.

Microwave Procedure

A mixture of 0.084 gm of dehydroacetic acid and aromatic aldehyde (5 mmol) was added to 1 gm of neutral alumina contained in a small reaction vessel. To this 0.05 ml of pyridine and 0.05 ml of piperidine were added as catalyst. Then the reaction mixture was irradiated under microwaves at 200W power for 4 to 10 minutes. The product was extracted by chloroform and evaporated. The crude product obtained was recrystallised from ethanol.

RESULTS

The microwave heating effectively reduced the reaction time from 6 to 9 hrs to 4-10 minutes. By using microwave radiation for heating, all the 8 compounds were prepared in yields that were appreciably higher than the conventional method (Table.1). Highest yield improvement was observed for all the 8 compounds when compared with conventional method. The reduced cost of synthesis is clearly advantageous for the proposed solvent free

microwave assisted Knoevenagel condensation in terms of time and energy.

Solvent free microwave assisted reaction of Knoevenagel condensation is a combination in form of synergy between microwave and dry media. The apparatus is very simple and reaction, isolation and purification are performed in reduced stages and using less solvent and energy.

Table.1 Physical data of title compounds and comparative study of conventional v/s microwave method

S.No.	Compound Code	Melting Range ° C	Conventional Method		Melting Range ° C	Microwave method	
			Time (hrs)	% Yield		Time (min)	% Yield
1.	1a	142-149	7	60	145-148	8	75
2.	1b	212-220	7	66	218-221	7	82
3.	1c	196-204	9	74	198-201	10	92
4.	1d	166-172	8	72	168-170	5	88
5.	1e	180-192	6	64	187-191	4	86
6.	1f	175-182	7	66	179-181	9	87
7.	1g	207-212	6	71	210-214	8	90
8.	1h	198-208	7	74	202-209	7	90

1a: 4- Hydroxy-6-methyl-3-[3-(4-methyl phenyl)prop-2-enoyl]-2H-pyran-2-one.

IR: (\square, cm^{-1}) 3600-3200, 1755-1705, 1650-1620, 1550-1500, 1380-1260.

¹H NMR: (CDCl_3): δ 2.31(5,3H,7-CH₃), 2.36 (5,3H,7-CH₃), 5.97 (5,1H,H-5), 7.43 (m,4H,Ar).

1b: 4- Hydroxy-6-methyl-3-[3-(3-nitro phenyl)prop-2-enoyl]-2H-pyran-2-one.

IR: (\square, cm^{-1}) 3400-3150, 1720-1540, 1680-1610, 1500-1405

¹H NMR: (CDCl_3): δ 2.24(3,3H,7-CH₃), 6.22 (m,1H,H-4), 7.61(m,4H,Ar).

1c: 4- Hydroxy-6-methyl-3-[3-(4-methoxy phenyl)prop-2-enoyl]-2H-pyran-2-one.

IR: (\square, cm^{-1}) 3600-3100, 1730-1690, 1650-1580, 1550-1450

¹H NMR: (CDCl_3): δ 2.34(5,3H,7-CH₃), 3.97 (5,3H,7-OCH₃), 6.10 (5,1H,H-5), 7.88 (m,3H,Ar).

1d: 4- Hydroxy-6-methyl-3-[3-(4-isopropyl phenyl)prop-2-enoyl]-2H-pyran-2-one.

IR: (\square, cm^{-1}) 3600-3150, 1770-1720, 1660-1610, 1550-1490, 1370-1250

¹H NMR: (CDCl_3): δ 2.21(5,3H,7-CH₃), 5.97 (5,1H,H-5), 7.44 (5,7H,Isopropyl), 7.81 (m,4H,Ar).

1e: 4- Hydroxy-6-methyl-3-[3-(1-naphthyl)prop-2-enoyl]-2H-pyran-2-one.

IR: (\square, cm^{-1}) 3500-3100, 1750-1700, 1660-1600, 1570-1415.

¹H NMR: (CDCl_3): δ 2.29(5,3H,7-CH₃), 6.00 (5,1H,H-5), 7.44 (m,4H,Ar).

1f: 4- Hydroxy-6-methyl-3-[3-(2-naphthyl)prop-2-enoyl]-2H-pyran-2-one.

IR: (\square, cm^{-1}) 3580-3075, 1765-1710, 1665-1610, 1560-1410.

¹H NMR: (CDCl_3): δ 2.31(5,3H,7-CH₃), 6.12 (5,1H,H-5), 7.54 (m,7H,Ar).

1g: 4- Hydroxy-6-methyl-3-[3-(2-furyl)prop-2-enoyl]-2H-pyran-2-one.

IR: (\square, cm^{-1}) 3550-3200, 1750-1510, 1640-1570, 1540-1430.

¹H NMR: (CDCl_3): δ 2.31(5,3H,7-CH₃), 6.10 (5,1H,H-3), 7.41 (m,3H,Ar).

1h: 4- Hydroxy-6-methyl-3-[3-(2-thienyl)prop-2-enoyl]-2H-pyran-2-one.

IR: (\square, cm^{-1}) 3550-3100, 1700-1490, 1655-1560, 1550-1440.

¹H NMR: (CDCl_3): δ 2.11(5,3H,7-CH₃), 6.21 (5,1H,H-3), 7.56 (m,3H,Ar).

DISCUSSION

The microwave energy reduces the heat-up and cool-down time for reactions. It uses 50% less power than electric furnaces of equivalent capacity. The probable mechanisms involved in microwave heating are Dipolarization, Ohmic heating and Interfacial polarization. A possible explanation for the favourable effect of solvent free microwave is that it enhances dipole-dipole interaction. During the reaction, the transition state involves delocalised anion. The microwave activation effect become important due to enhancement in ionic dissociation and the reactants are transformed into more polar compounds in the transition state.

The Knoevenagel condensation of an active Methylene compound and aldehydes is a convenient route to the synthesis of substituted alkenes. This condensation is normally catalysed by a base like pyridine/ piperidine or

Ammonium acetate to remove the active hydrogen atom, followed by attack of the resulting anion on the carbonyl carbon of the aldehyde. Elimination of a molecule of water results in the formation of a system of extended conjugation.

CONCLUSION

From the above results, we conclude that microwaves produces specific bond activation and also offers advantages over conventional method such as dry media condition, shorter reaction time, better yield, environmentally friendly and low cost.

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