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ECO-FRIENDLY SYNTHESIS OF 3-CYANO AND 3-CYANO-4 METHYL-COUMARINS UNDER SOLVENT FREE CONDITIONS

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ABSTRACT

A facile microwave assisted synthesis of 3-cyano & 3-cyano-4-methylcoumarins using flyash as solid support under solvent free conditions is described.

Keywords : 2-Hydroxybenzaldehydes , 2-hydroxyacetophenones, malanonitrile, triton-B, 3-cyanocoumarins, microwave irradiation, solvent free reactions.

INTRODUCTION

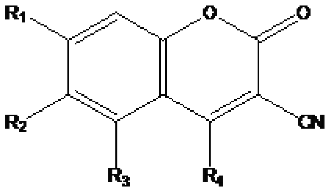
Coumarins constitute an important class of naturally occurring compounds because of their vast range of applications such as anticoagulants[i], anti HIV agents[ii, iii] anthelmintics, hypnotics and insecticides[iv-vi] . These are also used as sensitizers for photographic emulsions.[vii] 3-Cyano and 3-cyano-4-methylcoumarins (a subclass of naturally occurring coumarins) are the synthetic analogues which have been found to exhibit varying degree of pharmacological properties and have been used for the synthesis of various other class of compounds including coumarin carboxylic acids, esters, aldehydes etc. These are intermediates for the synthesis of various pharmacological compounds.

3-Cyanocoumarins have largely been prepared by reacting 2-hydroxybenzaldehydes with malanonitile or ethylcyanoacetate in the presence of pyridine or piperidine which are highly toxic in nature and are to be avoided according to modern recommendations to save our enjoinment. Another modification to this method includes above condensation under phase transfer catalysed conditions using aqueous potassium carbonate-benzene as the biphase medium. But this again involves the use of highly carcinogenic organic solvent during the reaction.

Herein we report an eco-friendly method for the synthesis of 3-cyano and 3-cyano-4-methylcoumarins involving condensation of 2-hydroxybenzaldehydes and 2-hydroxyacetophenones with malanonitile in presence of triton-B adsorbed on flyash as solid support using microwave irradiations. This method avoids the use of organic solvents as media for the reactions which makes the protocol eco-friendly.

Further, condensation of 2-hydroxybenzaldehydes with malanonitile generally initially form the 2-iminobenzopyran derivatives which have to be hydrolysed to give the coumarins. But the present method has the advantage that the 3-cyanocoumarins are obtained in a single step directly and the intermediate imino compounds are not isolated. The method has further been extended for the synthesis of 3-cyano-4-methylcoumarins by condensing 2-hydroxyacetophenones with malanonitrile under similar conditions. Validity of above procedure was shown by preparing differently substituted 3-cyano and 3-cyano-4-methyl coumarins and identity of the compounds were confirmed from their IR and ^{1}H NMR spectra.

Table 1



Compounds	R_1	R_2	R_3	R_4	Time (sec)	Yield(%)	MR(°C)	lit MP (°C)
I	H	H	H	H	20	85	179-80	182[X]
II	H	CH_3	H	H	25	85	204-05	205-06[XI]
III	OCH_3	H	H	H	30	86	228-29	225-30[XII]
IV	OCH_3	H	OCH_3	H	25	79	228-29	-
V	H	H	H	CH_3	30	80	190-91	191-92[XIII]
VI	H	CH_3	H	CH_3	30	82	204-05	-
VII	OCH_3	H	H	CH_3	25	88	220-21	223[XII]
VIII	H	OCH_3	H	CH_3	30	90	189-90	-
IX	H	Br	H	CH_3	35	90	180-82	-

MATERIALS AND METHODS

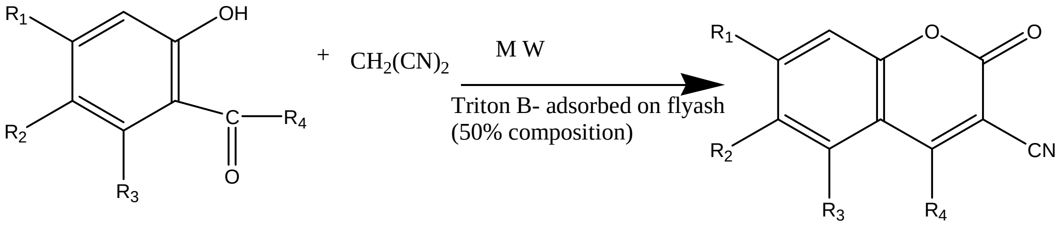
Experimental

Melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on Perkin-Elmer Spectrum BX-series FTIR and ^{1}H NMR spectra on Bruker Avance II 400 MHz NMR spectrometer using tetramethylsilane as internal standard. The reaction was carried out in domestic microwave oven (Samsung, Model No. CE II8 KF, output energy 900W, frequency 2450 MHz) using 30% power for all experiments.

General experimental procedure :

A mixture of o-hydroxybenzaldehyde/o-hydroxyacetophenone (5mmol), malanonitrile (5mmol) and the base i.e. triton-B adsorbed on flyash (50% composition) was prepared by adding few drops of acetone, air dried and was subjected to microwave irradiations. Completion of the reaction was checked on TLC and the reaction mixture was dissolved in chloroform. Organic layer was filtered to remove flyash and solvent was distilled off from filterate. The residue was washed with water, dried and recrystalized from methanol to get the desired product.

Scheme 1 Synthesis of 3-cyanocoumarins



Spectral data of compounds (I-IX)

I IR (Nujol) : 2200 (C≡N), 1700 cm^{-1} (C = O) ; ^{1}H NMR (CD_3COCD_3) : δ 7.32 to 7.62 and 7.68 to 8.0 (each m of 2H, H-5 & H-6, H-7 & H-8) and 8.77 (s, 1H, H-4).

II IR (Nujol) : 2215 (C≡N), 1710 cm^{-1} (C = O) ; ^{1}H NMR ($CDCl_3$) : δ 2.50 (s, 3H, CH_3), 7.20 to 7.70 (m, 3H, H-5, H-7 & H-8) and 8.84 (s,1H, H-4).

III IR (Nujol) : 2200 ($C\equiv N$), 1710 cm^{-1} ($C = O$) ; ^1H NMR ($DMSO - D_6$) : δ 3.40 (s, 3H, OCH_3), 7.16 (d, J = 2.0Hz, 1 H, H-8), 7.80 (m, 2H, H-5 & H-6) and 8.90 (s, 1H, H-4).

IV IR (Nujol) : 2210 ($C\equiv N$), 1710 cm^{-1} ($C = O$) ; ^1H NMR ($DMSO\text{-}D_6$) : δ 3.90 & 3.95 (each s of 3H, 2 × OCH_3), 6.55 & 6.64 (each d of 1H, J = 2.0Hz, H-6 & H-8) and 8.65 (s, 1H, H-4) ; Anal Calcd for $C_{12}H_9O_4N$: C, 62.34 ; H, 3.90 ; N, 6.06. Found : C, 62.00; H, 3.78; N, 6.00%.

V IR (Nujol) : 2200 ($C\equiv N$), 1720 cm^{-1} ($C = O$) ; ^1H NMR ($CDCl_3$) : δ 2.75 (s 3H, CH_3) , 7.21 to 7.50 (m, 2H, H-5 & H-6) and 7.51 to 7.82 (m, 2H, H-7 & H-8).

VI IR (Nujol) : 2212 ($C\equiv N$), 1700 cm^{-1} ($C = O$) ; ^1H NMR ($CDCl_3$) : δ 2.45 and 2.75 (each s of 3H, 2 × CH_3), 7.30 (d, J = 9.0 Hz, 1H, H-8) and 7.43 to 7.70 (m, 2H, H-5 & H-7) : Anal Calcd for $C_{12}H_9O_2N$: C, 72.00 ; H, 4.50 ; N, 7.00. Found : C, 71.82; H, 4.37; N, 6.89%.

VII IR (Nujol) : 2200 ($C\equiv N$), 1710 cm^{-1} ($C = O$) ; ^1H NMR ($CDCl_3$) : δ 2.70 (s, 3H, CH_3), 3.92 (s, 3H, OCH_3), 6.80 to 7.06 (m, 2H, H-6 & H-8) and 7.65 (d, J = 9.0Hz, 1H, H-5).

VIII IR (Nujol) : 2204 ($C\equiv N$), 1710 cm^{-1} ($C = O$) ; ^1H NMR ($CDCl_3$) : δ 2.75 (s, 3H, CH_3), 3.93 (s, 3H, OCH_3), and 7.08 to 7.44 (m, 3H, H-5, H-7 & H-8) : Anal Calcd for $C_{12}H_9O_3N$: C, 66.98 ; H, 4.19 ; N, 6.51. Found : C, 66.72; H, 4.02; N, 6.32%.

IX IR (Nujol) : 2200 ($C\equiv N$), 1719 cm^{-1} ($C = O$) ; ^1H NMR ($CDCl_3$) : δ 2.74 (s, 3H, CH_3), 7.32 (d, J = 9.0 Hz, 1H, H-8) and 7.72 to 8.18 (m, 2H, H-5 & H-7) ; Anal Calcd for $C_{11}H_6O_2NBr$: C, 50.00 ; H, 2.27 ; N, 5.30. Found : C, 50.20; H, 2.00; N, 5.10%.

CONCLUSION

Present method is rapid, efficient, one step process for the synthesis of 3-cyanocoumarins avoiding use of toxic solvents at all stages of the reaction and is thus eco-friendly.

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