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An efficient one pot synthesis of 3-cyanocoumarins using phase transfer catalysis

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ABSTRACT

An efficient one pot synthesis of 3-cyano and 3-cyano-4-methyl coumarins is being reported starting from 2-hydroxybenzaldehydes and 2-hdroxyacetophenones with ethylcyanoacetate. The reaction was carried out at room temperature using phase transfer catalysis in good yield, short time and easy work up. The structure of the compounds have been confirmed on the basis of their analytical IR, ^{1}H-NMR spectral data.

Key words: 2-hydroxybenzaldehydes, 2-hdroxyacetophenones, ethylcyanoacetate, 3-cyanocoumarins, phase transfer catalysis.

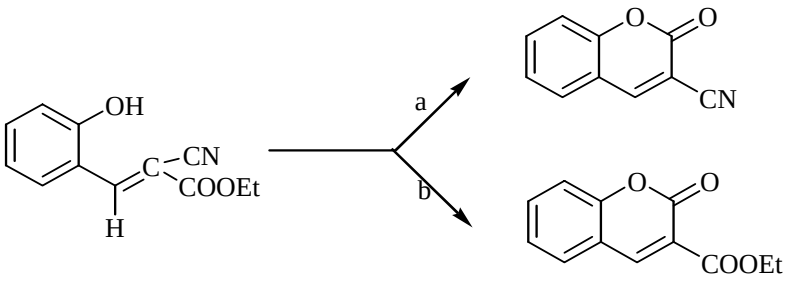
INTRODUCTION

3-Cyanocoumarins have attained enormous importance in recent years as they are required for synthesis of methane dyes[1]. 3-carboxycoumarins[2,3] which are used for synthesis of cephalosporins[4], modified penicillin[5], oxygen bridged tetrahydropyridones[6], isourases[7], etc. The amide obtained from 3-cyanocoumarines exhibit specific inhibitor of α-chymotripsin[8], human leukocytic elastase[9] and polymeric compounds of biological importance[10].

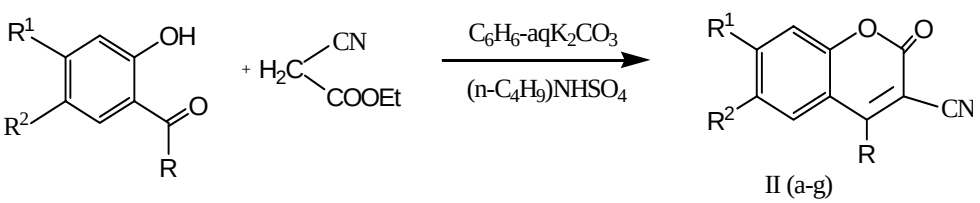
3-Cyanocoumarines have either been obtained by the reaction of 2-hydroxybenzaldehydes with malanonitrile[11] or ethylcyanoacetate[12]. The former reaction takes place in two steps i.e. formation of 2-iminocoumarines in the initial stage which on hydrolysis gives required 3-cyanocoumarins, while the later reaction has to be carried out in anhydrous medium using either mixture of pyridine-pipridine as base or sodium ethoxide in absolute ethanol.

Based on the reports available in the literature and our studies made on the phase transfer catalysed conditions, it can be stated that the base catalysed reactions when are carried out under phase transfer catalysed conditions shows considerable improvement in term of reaction time & yield. Also, the use of anhydrous bases like sodium ethoxide, pyridine, pipridine etc. can be avoided.

Thus it was proposed to undertake study of reaction of 2-hydroxybenazaldehyde and 2-hydroxyacetophenone with ethylcyanoacetate under phase transfer catalysed conditions. The reaction of 2-hydroxybenzaldehyde with ethylcyanoacetate was initially expected to involve condensation between the two to give benzaldehyde derivative which could undergo cyclisation either following path (a) in which carbethoxy group is involved in cyclization and 3-cyanocoumarin is the product or following path (b) in which cyano group is involved in cyclisation and 3-carbethoxy or 3-carboxycoumarin is likely product (Scheme 1).



Scheme 1



Scheme 2

RESULT AND DISCUSSION

A solution of salicyladehyde and ethylcyanoacetate in benzene was stirred magnetically with aqueous potassium carbonate solution at room temperature in the presence of tetra-n-butylammoniumhydrogensulphate. The reaction mixture was monitored on TLC and the starting aldehyde was found to have reacted completely after 30 minutes. The reaction on working up gave a colourless compound (m.p-179-81 ^{0}C) in 82% yield. In IR compound showed absorption at 2231 cm^{-1} (C≡N) and 1718 cm^{-1} (C=O), in ^{1}H-NMR showed peak at δ 7.32-7.62 for two protons (H-5 and H-6) and at 7.6-8.0 for two protons (H-7 & H-8) along with a singlet at 8.78 for one proton (H-4) based on these data compound was identified as 3-cyanocoumarin.

Further this method was successfully employed for the synthesis of 3-cyano-4-methylcoumarin by reacting 2-hydroxyacetophenones with ethylcyanoacetate under similar conditions. Various substituted 3-cyano and 3-cyano-4-methylcoumarins were synthesized by this method (Scheme 2).

EXPERIMENTAL

Synthesis of 3-Cyanocoumarin

A solution of salicyaldehyde (0.4 g) and ethylcyanoacetate (0.38 g) in benzene (20 mL), saturated aqueous potassium carbonate solution (20 mL) and tetra-n-butylammonium hydrogensulphate (0.28) were stirred magnetically at room temperature for 30 minutes. The completion of the reaction was checked by TLC. The benzene layer was separated, washed with water and benzene removed by distillation under vacuum. The residue thus obtained was crystallized from methanol to give 3-cyanocoumarin (0.33 g) as colorless solid.

Table 1: Synthesis of 3-cyanocoumarins

Compd. (s)	R	R_1	R_2	m.pt. (^{0}C)	Lit m.p. (^{0}C)	yield%	IR $\nu_{C\equiv N}$ $\nu_{C=O}$ cm^{-1}	^{1}H-NMR ($CDCl_3$) δ ppm
IIa	H	H	H	179-81	182[11]	82	2231 1718	7.32-7.62 and 7.68-8.0 (each m of 2H,H-5, H-6, H-7 & H-8) and 8.78 (s, 1H,H-4)
IIb	H	OCH_3	H	228	225-30[13]	80	2213 1715	3.40 (s, 3H,OCH_3) 7.16 (d, J=2.Hz,1H,H-8),7.80 (m,2H,H-5,H-6) and 8.90 (s,1H,H-4)
IIc	H	H	CH_3	204-05	205-06[14]	75	2215 1710	2.50 (s, 3H, CH_3), 7.20-7.70(m 3H,H-5, H-7&H-8) and 8.24 (s, 1H,H-4)
IId	CH_3	H	H	188-90	190-92[15]	76	2230 1724	2.75 (s, 3H, CH_3), 7.21-7.50 and 7.51 (each m of 2H,H-5, H-6, H-7& H-8)
IIe	CH_3	H	CH_3	202*		80	2232 1732	2.45 &2.75 (each s, of 3H, 2x CH_3), 7.30(d,J=2.Hz, 1H,H-8), 7.43-7.70 (m,2H,H-5&H-7)
IIf	CH_3	OCH_3	H	220-21	223[13]	75	2226 1718	2.70 (s, 3H,CH_3), 3.92 (s, 3H,OCH_3), 6.80-7.06 (m, 2H,H-6, H-8) and7.65 (d,J=9Hz,1H,H-5)
IIg	CH_3	H	Br	179-80*		80	2235 1737	2.74(s, 3H, CH_3), 7.32 (d,J=2.Hz,1H,H-8) and 7.22-8.18 (m,2H,H-5&H-7)

* IIe (3-cyno-4,6-dimethylcoumarin)
found: C, 73.48; H, 4.74; N, 7.36. requires: C, 72.36; H, 4.52; N, 7.03.
*IIg (6-bromo-3-cyano-4-methylcoumarin)
found: C, 50.78; H, 2.83; N, 5.64 . requires: C. 50.19; H, 2.28; N, 5.32.

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