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# Synthesis of Coumarin Derivatives using Glutamic Acid under Solvent-free Conditions

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**ABSTRACT**

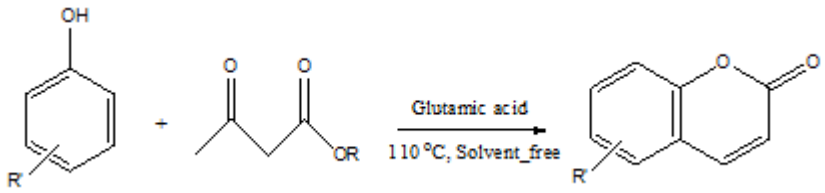
An efficient,simple and one-pot protocol for synthesis of coumarin derivatives on the basis condensation reaction of phenols with ethyl acetoacetate employing glutamic acid as a novel catalyst is described.

**Key words:** One-pot,Glutamic acid, Coumarins, Solvent-Free Conditions.

## INTRODUCTION

Multicomponent reactions are efficient methods in thesynthesis of heterocycles. In Multicomponent reactions synthesis to produce massive amounts of waste,according to the isolation of the complex, toxic and hazardous solvent at each step andwill discovered, economically and environmentallyfriendly. Multicomponent reactions advantages, synthesized of heavy compound molecules by the reaction of small molecule[1].

Coumarins derivatives are heterocyclic units in the field of natural and synthetic organic chemistry due to their wide range of biological and therapeutic properties such asanti-inflammatory, anti-tumor, antioxidant,anti-viral and anti-bacterial activities.Recently, coumarin appropriate analogue functionalized gland known as antibiotics agents, and receptor antagonists have emerged. In addition, several flavonoid containing the coumarin core unit have been isolated from natural sources also show interesting biological properties. However, Thesereactions often require harsh conditions and was happened long reaction time and low efficiency. Kinds of phenols used to replace for synthesiscoumarins[2-9]. Although numerous methods are capable of affecting these synthesis has been previously reported. Glutamic acidhas been used previously as a catalyst for synthesis of organic compound[10],Previously, we have synthesized a number of heterocyclic compounds[11-23]. Herein we report glutamic acida new catalyst for the synthesis of Coumarins at one pot reaction, environmentally friendly easy separation with high yields(Scheme 1).




**Scheme 1:**

All chemicals were obtained from Merck or Flukawithout further purification. Silica gel SILG/UV 254 plates were used for TLC. IR spectra were measured on a Shimadzu IR-470 Spectrophotometer. $^1$H NMR spectra were determined on Bruker400 DRX AVANCE instrument at 400 MHz, respectively.

**Typical procedure adopted for the synthesis of 7-hydroxy-4-methyl-2H-chromen-2-one (S1)**

A mixture of resorsinol (1 mmol), ethyl acetoacetate (1 mmol), and glutamic acid (20 mol%) was stirred at 110°C for a 15 min. The progress of the reaction was monitored by using TLC. After completion of the reaction, the solid catalyst (glutamic acid) was washed with water, and finally purified by recrystallization in ethanol/water.
Data of compounds (S1-S5)

**7-hydroxy-4-methyl-2H-chromen-2-one (S1)**

White powder, Yield: (93%), mp: 187-189$^0$C IR ($\nu_{max}$/cm$^{-1}$)(KBr): 3440(OH), 1683(C=O), 1604(C=C)cm$^{-1}$

$^1$H NMR (400MHz; DMSO-$d_6$) $\delta$ = 2.34 (3H, s, $CH_3$), 6.10 (1H, s, CH), 6.68(1H, d, *J*=2.0 Hz, $H_c$), 6.79(1H, d, *J*=2.0 Hz, $H_b$), 7.76(1H, d, *J*=8.8 Hz, $H_a$),8.85(1H, brs, OH).

**dihydroxy-4-methyl-2H-chromen-2-one (S2)7,8**

White powder, Yield: (90%), mp: 241-243 $^0$C IR ($\nu_{max}$/cm$^{-1}$)(KBr): 3444(OH), 1677(C=O), 1600(C=C)cm$^{-1}$

$^1$H NMR(DMSO) $\nu$ = 2.34(3H, s, $CH_3$), 6.11(1H, s, CH), 6.83-7.09(1H, m, $H_{arom}$), 6.82(1H, d, *J*=8.0 Hz, $H_a$), 7.09(1H, d, *J*=8.0 Hz, $H_b$), 9.30(1H, brs, OH), 10.0(1H, brs, OH).

**5,7-dihydroxy-4-methyl-2H-chromen-2-one (S3)**

White powder, yield (87%), mp: 281-282$^0$C IR ($\nu_{max}$/cm$^{-1}$)(KBr): 3498, 3440(2OH), 1674(C=O), 1602(C=C)

$^1$H NMR(DMSO) $\nu$= 2.47(3H ,s, $CH_3$), 5.82(1H, s, CH), 6.16(1H, d, *J*=2.4 Hz, $H_a$), 6.26(1H, d, *J*=2.4 Hz, $H_b$), 10.37(2H, brs, 2OH).

**7-hydroxy-4,8-dimethyl-2H-chromen-2-one (S4)**

White powder, yield (89%), mp: 261-263 $^0$C IR ($\nu_{max}$/cm$^{-1}$)(KBr): 3494(OH), 1670(C=O), 1606 (C=C)

$^1$HNMR(DMSO): *ä* =2.27, 2.54(6H, s, $2CH_3$), 6.03(1H, s, CH), 6.56(1H, d, *J*=0.8 Hz, $H_a$), 6.60(1H, d, *J*=0.8 Hz, $H_b$).

**4-methyl-2H-chromen-2-one (S5)**

White powder, Yield: (83%), mp: 80-82$^0$C IR ($\nu_{max}$/cm$^{-1}$)(KBr): 1683(C=O), 1604(C=C)cm$^{-1}$

$^1$H NMR (400MHz; DMSO-$d_6$) $\delta$ = 2.34 (3H, s, $CH_3$), 6.10 (1H, s, CH), 6.68(1H, d, *J*=2.0 Hz, $H_c$), 6.79(1H, d, *J*=2.0 Hz, $H_b$), 7.76(1H, d, *J*=8.8 Hz, $H_a$).

## RESULTS AND DISCUSSION

Herein, we report glutamic acid ascatalyst which could provide high yield, an efficient, environmentally friendly, easy separationand simple route for thesynthesis of coumarins.

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