Iranian Journal of Organic Chemistry Vol. 2, No. 2 (2010) 367-370

A novel synthesis of *N*-(4-nitrophenyl)-2-oxo-2*H*-chromene-3-carboxamide, *N*-(4-bromophenyl)-2-oxo-2*H*-chromene-3-carboxamide and methyl-4-morpholino-2-oxo-2*H*-chromene-3-carboxylate from the reaction of coumarins with aliphatic and aromatic aminoes

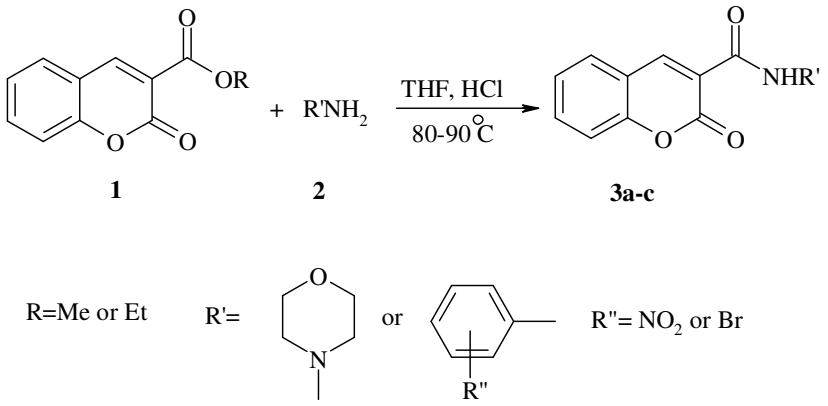
Manzarbanoo Esnaashari Isfahani,* M. Miri
Department of Chemistry, Islamic Azad University, North Tehran Branch, Tehran, Iran.

Abstract: One-pot two component synthesis of *N*-(4-nitrophenyl)-2-oxo-2*H*-chromene-3-carboxamide, *N*-(4-bromophenyl)-2-oxo-2*H*-chromene-3-carboxamide and methyl-4-morpholino-2-oxo-2*H*-chromene-3-carboxylate, from the reaction of coumarin derivatives with morpholin or aromatic amines, such as *P*-nitroaniline, *P*-bromoaniline, is described.

Keywords: Knovenagel condensation; Coumarin; Morpholin; *P*-nitroaniline; *P*- boromoaniline.

Introduction

Coumarin derivatives are very important in synthesis of organic chemistry. Some of these compounds have shown various biological activities. Coumarin has many applications in several field pharmaceutical, agricultural, perfume and pesticide industries [1, 2].
A considerable number of natural or synthetic coumarin derivatives display pharmaceutical properties with a wide range of activity and others, are useful for optical applications [3]. Recent developments on long wavelength fluorescent compounds have been reviewed [4]. Synthesis of fluorescent 3-benzoxazol-2-yl-coumarins, from the reaction of coumarin-3-carboxylic acids and benzoxazoloyl, such as nitro and sulphonic, has been studied [5, 6].
In this work, we report the results of the reaction between alkyl-2-oxo-2*H*-chromene-3-carboxylate with primary amines such as *p*-nitroaniline, *p*-boromo aniline or morpholin, without opening of the lactone ring to give *N*-(4-nitrophenyl)-2-oxo-2*H*-chromene-3-carboxamide, *N*-(4-bromophenyl) -2-oxo-2*H*-chromene-3-carboxamide and methyl-4-morpholino-2-oxo-2*H*-chromene-3-carboxylate in excellent yields (Scheme1).



Scheme 1

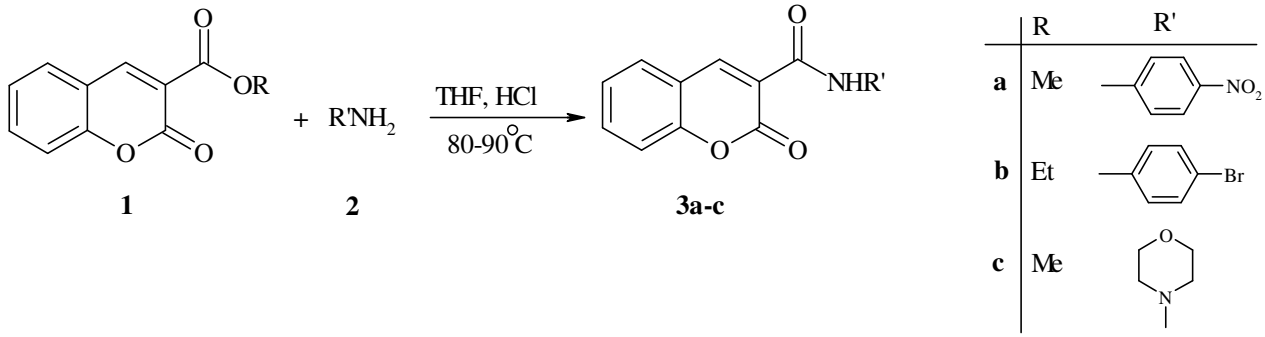
*Corresponding author. Fax: +(98) 21 22214312; Tel.: +(98) 21 22215670; E-mail: *mb_esnaashari@yahoo.com, E-mail: m_asnaashari@iau-tnb.ac.ir*

Results and Discussion

The above two-component reaction leads to stable *N*-(4-nitrophenyl) -2-oxo-2*H*-chromene-3-carboxamide **3a**, *N*-(4-bromophenyl) -2-oxo-2*H*-chromene-3-carboxamide **3b** and methyl-4-morpholino-2-oxo-2*H*-chromene-3-carboxylate **3c**. The structure of compounds **3a-c** was evaluated based on detailed spectroscopic studies. Thus, the IR spectrum of compound **3a**, showed peaks at 3365, 1715, 1630, 1599 and 1387 cm^{-1} indicating the presence of NH, C=O, C=C and N=O functional groups respectively. The ^{1}H NMR spectrum showed aromatic protons in the region of δ= 6.87 (1 H, *t*, *J*= 7.4 and 7.5 Hz), 6.94 (1 H, *d*, *J*= 8.2 Hz), 7.26 (1 H, *t*, *J*= 7.6 and 8.2 Hz), 7.31 (1 H, *d*, *J*= 7.6 Hz), 8.37 (1 H, *s*, =CH), 11.22 (NH). In ^{13}C NMR spectrum all the aromatic carbons appeared in the region of δ=112.9-155.2 and the carbonyl carbon resonated at δ=166.9 and 166.6.

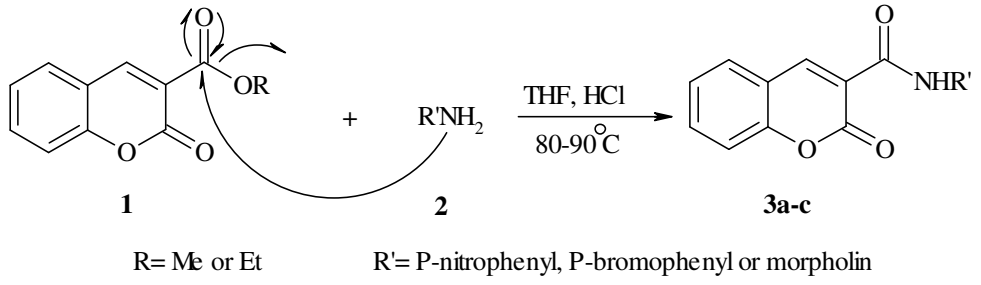
The spectral data of compound **3b**, in IR spectrum, stretching frequencies at 3445 (NH), 166.6 and 1728 C=O and 166.9 C=C cm^{-1}. The ^{1}H NMR spectrum showed the presence of aromatic protons in the region of δ=6.72 (1 H, *d*, *J*=8.1 Hz), 6.78 (1 H, *t*, *J*=7.4 and 7.3 Hz), 6.95 (1 H, *d*, *J*=7.3 Hz), 7.04 (1 H, *t*, *J*=8.1 and 7.4 Hz), 7.19 (1 H, *d*, *J*=10.2 Hz), 7.30 (1 H, *d*, *J*=10.2 Hz), 8.61 (=CH), 11.29 (NH). In ^{13}C NMR spectra all the aromatic carbons appeared in the region of δ=112.9-153.9 and the carbonyl carbon resonated at δ=165.9 and 166.1.

The spectral data of compound **3c**, in IR spectrum, stretching frequencies at 1712 C=O, 1575 C=C cm^{-1}. The ^{1}H NMR spectrum showed the presence of 2.84 and 3.94 aliphatic protons in the region of 2.84 and 3.94 and the aromatic protons in the region of δ= 6.72 (1 H, *d*, *J*=8.1 Hz), 6.78 (1 H, *t*, *J*=7.4 and 7.3 Hz), 6.95 (1 H, *d*, *J*=7.3 Hz), 7.04 (1 H, *t*, *J*=8.1 and 7.4 Hz), 7.19 (1 H, *d*, *J*=10.2 Hz), 7.30 (1 H, *d*, *J*=10.2 Hz), 8.61 (=CH), 11.29 (NH), 2.84 and 3.94 (CH_2 of morpholin). In ^{13}C NMR spectra all the aromatic carbons appeared in the region of δ=114.7-161.2 and the carbonyl carbon resonated at δ=166.3 and 166.9 (Scheme 2).



Scheme 2

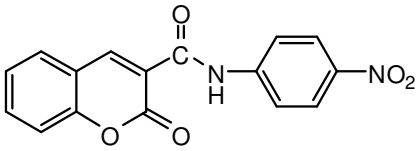
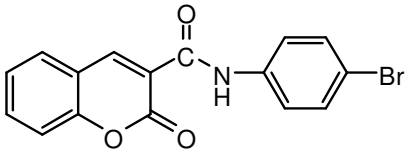
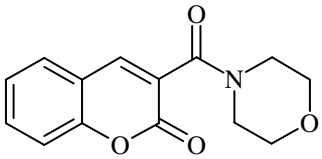
The mechanism of the reaction of coumarin derivatives containing with morpholin or amino aromatic amines, such as *p*-nitroaniline, *p*-bromoaniline, has been shown in scheme 3. This reaction has easily carried out in alkaline environment and chloroform as a solvent (Scheme 3).



Scheme 3

In conclusion, we have found that the one-pot two component reaction between alkyl-2-oxo-2*H*-chromene-3-carboxylate with primary amines such as *p*-nitroaniline, *p*-boromo aniline or morpholin, without opening of the lactone ring to give *N*-(4-nitrophenyl)-2-oxo-2*H*-chromene-3-carboxamide, *N*-(4-bromophenyl) -2-oxo-2*H*-chromene-3-carboxamide and methyl-4-morpholino-2-oxo-2*H*-chromene-3-carboxylate in excellent yields (Scheme 1).

Table 1: Synthesis of coumarin derivatives with morpholin or aromatic amines, such as *p*-nitroaniline, *p*-bromoaniline.

Entry	R'	Product	Time (h)	Yield (%)	mp. °C
1	*p*-Nitroaniline		15	52	237-239
2	*p*-Boromoaniline		15	49	212-214
3	Morpholine		15	58	216-218

Experimental

Melting points measured on an Electronthermal 9100 apparatus. IR spectra were recorded on a shimadzu IR-470 spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER DRX-300 AVANCE spectrometer at 400.13 and 100.77 MHz in $CDCl_3$ usibg *TMS* an internal standard. The reagents used in this work were purchased from Fluka chemical compounds and used without further purification.

Synthesis of N-(4-nitro phenyl-2-oxo)-2H-chromen-2-one ($C_{16}H_{10}N_2O_5$) **3a**:
General procedure:
To a stirred solution of coumarin (1.03g, 5 mmol) and 20cm^3 $CHCl_3$ as a solvent was added *p*-nitroaniline (0.7g, 5 mmol) in the presence of 0.5 cc HCl as acid catalyzed and 10 cc THF. Then the reaction mixture was heated with stirring at 80-90°C. After 15 hours stiring, the product was filtered and washed with 20 cc cold diethyl ether to extract as a red crystal.

N-(4-nitrophenyl)-2-oxo-2H-chromene-3-carboxamide ($C_{16}H_{10}N_2O_5$) **3a**:
Red crystal, (0.14g, 52 %), mp= 237-239°C, IR (KBr) (ν_{max}/cm^{-1}): 3365 (NH), 3063 (CH, aromatic), 1720 (C=O), 1630, 1599 (C=C), 1484 and 1327 (NO_2). ^{1}H NMR (300 MHz, TMS, $CDCl_3$): δ= 11.22 (1 H, *s*, NH), 8.41 (1 H, *s*, =CH), 7.31 (1 H, *d*, *J*=7.6 Hz, CH), 7.23 (1 H, *t*, *J*=7.6 and 8.2 Hz, CH), 6.94 (1 H, *d*, *J* = 8.2 Hz, CH), 6.85 (1 H, *t*, *J*=7.6 and 7.4 Hz, CH), ppm. ^{13}C NMR (75 MHz, TMS, $CDCl_3$): δ= 112.9-132.8 (11 *C*H aromatic), 137.7 (=*C*H), 155.2 (***C***-C-O), 166.3 (***C***-CO-N), 166.6 and 166.9 (2 *C*=O) ppm.

N-(4-boromophenyl)-2-oxo-2H-chromene-3-carboxamide ($C_{16}H_{10}NO_3Br$) **3b**:
Violet sediment, (0.13g, 49 %), mp=212-214°C, IR (KBr) (ν_{max}/cm^{-1}): 3445 (NH), 3010 (CH,aromatic), 1720 (C=O), 1601 and 1509 (C=C), cm^{-1}. ^{1}H NMR (300 MHz, TMS, $CDCl_3$): δ= 11.29 (1 H, *s*, NH), 8.61 (1 H, *s*, =CH), 7.30 (1 H, *d*, *J*=10.2 Hz, CH), 7.19 (1 H, *d*, *J*=10.2 Hz, CH), 7.04 (1 H, *t*, *J* = 8.1 and 7.4 Hz,

CH), 6.95 (1 H, *d*, *J*=7.4 Hz, CH), ppm. ^{13}C NMR (75 MHz, TMS, $CDCl_3$): δ = 112.9-132.8 (11 *C*H aromatic), 137.6 (=CH), 153.9 (C-C-O), 160.6 (***C***-CO-N), 165.9 and 166.1 (2 *C*=O) ppm.

3-(morpholine-4-carbonyl)-2H-chromene-2-one *($C_{14}H_{13}NO_4$)* **3c**:
Pink crystalline, (0.16g, 58 %), mp= 216.4-218.4°C, IR (KBr) (ν_{max}/cm^{-1}): 3063 (CH,aromatic) 2927 (CH, aliphatic), 1712 (C=O), 1575 and 1487 (C=C), 1453 (CH_2) cm^{-1}. ^{1}H NMR (300 MHz, TMS, $CDCl_3$): δ= 8.56 (1 H, *s*, =CH), 7.95 (1 H, *d*, *J*=7.3 Hz, CH), 7.91 (1 H, *t*, *J*=7.5 and 8.2 Hz, CH), 6.94 (1 H, *d*, *J* = 8.2 Hz, CH), 6.85 (1 H, *t*, *J*=7.5 and 7.3 Hz, CH), ppm. ^{13}C NMR (75 MHz, TMS, $CDCl_3$): δ = 45.5 (2 CH_2), 65.8 (2 CH_2), 114.7 (C=C-C=O), 117.1-133.0 (6 C, aromatic), 161.2 (C-CO-N), 166.6 and 166.9 (2 C=O) ppm.

References

[1] Seshadri, T. R.; President, F. N. I. *National Institute of Sciences of India*, Jan 2, Vol. 35, **1968**.
[2] Coumarin-wikipedia the free encyclopedia, http://en.wikipedia.org/wiki/coumarin
[3] Charitos, C.; Kokotos, G. and Tzougraki, C., *J. Heterocycl. Chem.* **2001**, *38*, 153.
[4] Mama, J. *Advances in Colour Science and Technology* **1999**, *2(3),* 162.
[5] Luan, X. H.; Cerqueira, N. M. F. S. A.; Oliveira, A. M. A. G.; Rodrigues, L. M.; Coelho, P.; Oliveira, A. M. F. *Advances in Colour Science and Technology* **2002**, *5*, 18.
[6] Elnagdi, M. H.; Abdallah, S. O.; Ghoneim, K. M.; Ebied, E. M. and Kassab, K. N. *J. Chem. Res. (S)*, **1997**, *44-5* (M), 375.
.