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One pot synthesis of 2- amino-5-oxo-4-aryl-5, 6, 7, 8-tetrahydro- 4H-chromenes-3-carboxilic acid ethyl esters

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Abstract

Ethyl esters of 2-cyano-3-arylacrylic acid 1a-b (a = 3- Br- C_6H_4, b= 4- OH- C_6H_4) reacted with 5, 5-dimethyl-1, 3-cyclohexane (2b, R = CH_3) and 1c-d (c= 3- OH- C_6H_4, d= 3- NO_2- C_6H_4) reacted with 1, 3-cyclohexanedione (2a, R = H) and 5, 5-dimethyl-1, 3-cyclohexanedione (2b, R=CH_3) in the presence of alcoholic sodium ethoxide to give the corresponding ethyl esters of 2- amino- 7, 7- dimethyl-5-oxo-4-aryl-5, 6, 7, 8-tetrahydro- 4H- chromenes-3-carboxylic acid 3a-c, 3f and 2- amino-5-oxo-4-aryl-5, 6, 7, 8-tetrahydro- 4H- chromenes-3-carboxilic acid ethyl esters 3d-e. The structures of the compounds 3a-f were confirmed by their ultraviolet (UV), infrared (IR), 1H NMR, 13C NMR, mass spectra and elemental analyses.

Keywords: 4H- chromenes; 1,3-cyclohexanedione; 5,5-dimethyl-1,3-cyclohexanedione; α,β–unsaturated cyanoesters; Knoevenagel adducts; Sodium ethoxide; Michael-cyclization

Introduction

Syntheses of essential bio-active compounds have recently been attracting tremendous attention in the field of organic synthesis. Specially chromene and its derivatives have attracted increasing attention from synthetic chemists due to their miscellaneous biological activities, including antitumor (Raj *et al*., 2010), antibacterial (Mungra *et al*., 2011), antiviral (Conti *et al*., 2014), antioxidative (Mori *et al*., 2006), antidepressant (He *et al*., 2014), antihypertensive (Charles *et al*., 1998), antidiabetic (Rapposelli *et al*., 2011), fungicidal (Meepagala *et al*., 2010), and insecticidal properties (Smetanina *et al*., 2012). Among the various chromene derivatives, 2-amino-4H chromenes have been reported to exhibit highly useful pro-apoptotic properties for the treatment of a wide range of cancer ailments (Kumar *et al*., 2010; Zhang *et al*., 2012). For variety oriented synthesis, the structure of these bioactive molecules could provide chances for drug design in three important regions (the aromatic ring of the benzopyran, substitution at C2-amine, and the substituted group at C4 position). Therefore, substantial efforts have been made over the past decades for the synthesis of 2 amino- 4H-chromenes (Dong *et al*., 2011, Gao *et al*., 2008; Neelakandan *et al*., 2011; Ding *et al*., 2010; Gao *et al*., 2013), which is accomplished using various catalysts including diethylamine (Kulakarni *et al*., 2012), ethylenediamine diacetate (Kolla *et al*., 2012), I_2 (Rajaskhar *et al*., 2012), PEG (Das *et al*., 2011), β-cyclodextrin (Murthy *et al*., 2010), $InCl_3$ (Jayashree *et al*., 2009, Shanthi *et al*., 2008, Yin *et al*., 2013), guanidine (Kalla *et al*., 2013), ammonium acetate (Fujimoto *et al*., 1977), Al_2O_3 (Roudier and Foucaud 1984), Zr $(KPO_4)_2$ (Massimo *et al*., 2005), molecular sieves (Yu *et al*., 2000), aminosilane- modified Fe_3O_4 nanoparticles (Safari *et al*., 2014) and silica-bonded 2-hydroxyethylammonium acetate (HEAA) (Sobhani *et al*., 2013). However, some of these protocols require complex and expensive catalytic systems, prolonged reaction times and complicated operations. Therefore, the introduction of milder, faster and more eco-friendly methods, accompanied with higher yields is needed. A designed Michael addition reaction of active methylene with Knoevenagel adducts generated from benzaldehyde and nucleophiles was tested (Scheme 1, this work). Thus, in continuation of our interest in synthetic tactics for the preparation of heterocyclic compounds, a new sodium ethoxide catalyst methodology for the synthesis of diverse 4-substituted-2-amino- 3-carboxylic acid ethyl ester -4H-chromenes bearing various substituent groups at the C4 position was developed. This methodology differs from the previous classical methods in its simplicity and ready availability of the catalyst. For the synthesis of biologically active compounds and natural products (Dong *et al*., 2011) as key synthons in planning the synthesis of therapeutic agents and exhibiting diverse pharmaceutical activities substituents are the most intensively studied structural motifs, and crucial building blocks.

α, β-Unsaturated cyanoesters 1a–d were prepared via Knoevenagel condensation of the corresponding aldehydes with ethyl cyanoacetate in the presence of a base catalyst as reported in the literature (Jaman *et al*., 2013). Compounds 1a–d were reacted with dimedone/1, 3-cyclohexanedione 2a–b in the presence of sodium ethoxide in ethanol to give tetrahydro-4H-chromenes 3a–f (Scheme 1). In addition, the

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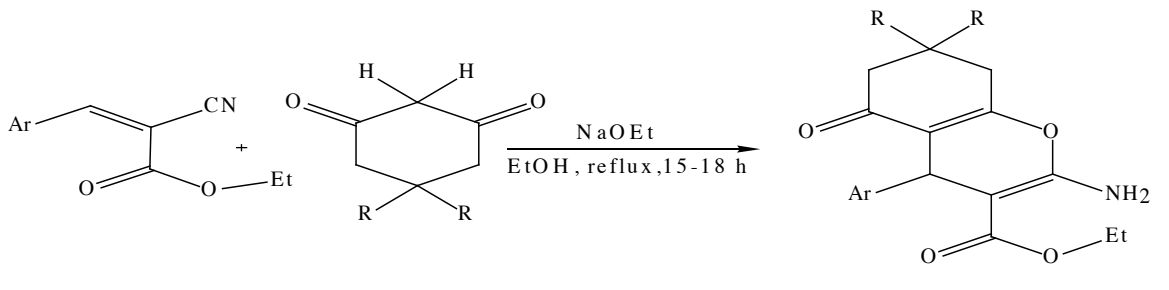


1a ~ 1d

1a Ar = 3- Br- C_6H_4
1b Ar = 4- OH- C_6H_4
1c Ar = 3- OH- C_6H_4
1d Ar = 3- NO_2- C_6H_4

2a ~ 2b

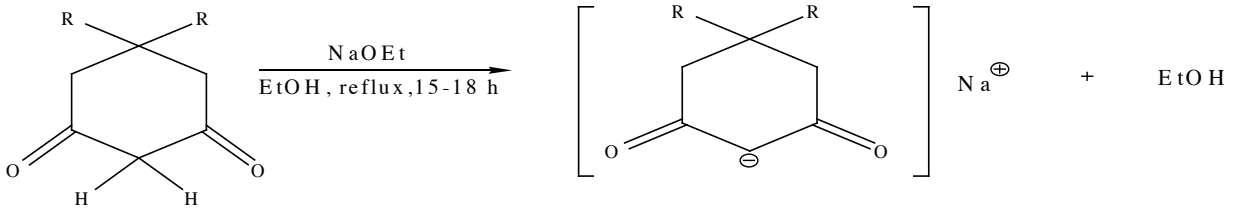
2a R = H
2b R = CH_3

3a ~ 3f

3a R = CH_3, Ar = 3- Br- C_6H_4
3b R = CH_3, Ar = 4- OH- C_6H_4
3c R = CH_3, Ar = 3- OH- C_6H_4
3d R = H, Ar = 3- OH- C_6H_4
3e R = H, Ar = 3- NO_2- C_6H_4
3f R = CH_3, Ar = 3- NO_2- C_6H_4

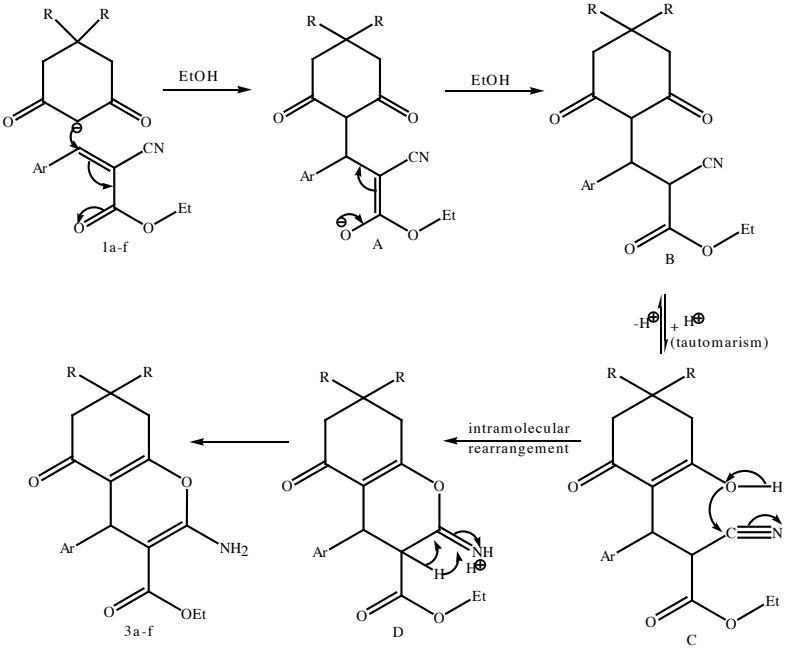
Scheme 1. The structure of tetrahydro-4*H*-chromenes (*3a-f*).

The formation of 4*H*- chromenes (*3a-f*) may be explained by the initial formation of a 1:1 adduct which subsequently underwent cyclization (Scheme 2).



2a-b

2a R=H
2b R=CH_3



Scheme 2. Formation of tetrahydro-4*H*-chromenes 3a-f.

synthesized compounds' structures (3a–f) were characterized and confirmed with the help of their ultraviolet (UV), Infrared (IR), 1H NMR, 13C NMR, Mass spectra and elemental analyses.

Materials and methods

Melting points were determined on an Electrothermal micro melting-point apparatus and uncorrected. The Ultraviolet-Visible spectra of the samples were recorded on a SHIMADZU-UV-160A ultraviolet spectrometer with a scanning range of 800-200 nm using methanol as solvent. IR spectra were recorded with FT-IR 8400S Shimadzu spectrometer in the range 4000-400 cm^{-1}. The 1H NMR and ^{13}C NMR spectra of the samples were recorded on a JEOL ECA-600 operating at 400.17 MHz spectrometer using $CDCl_3$ as solvent with Tetramethylsilane (TMS) as an internal standard.

General procedure

A mixture of α, β -unsaturated cyanoester1a-d (5 mmol), 1, 3-cyclohexanedione 2a ordimedone 2b (5 mmol), 5% sodium ethoxide in dry ethanol (1.5 mmol), and dry ethanol (25 mL) was refluxed for 15-18 hrs. The progress of the reaction was followed by thin-layer chromatography (TLC) on SiO_2 plate using appropriate eluting solvents. After completion of the reaction the mixture was cooled to room temperature and the volume was reduced to one-fourth by evaporation. It was then neutralized with 0.1 M HCl solution, extracted with ether (330 mL) and dried over anhydrous Na_2SO_4. The extracted organic layer was evaporated in a rotary vacuum evaporator, a solid mass obtained which was recrystallized from absolute alcohol.

2-Amino-4-(3/-bromo-phenyl)-7, 7-dimethyl-5-oxo-5, 6, 7, 8-tetrahydro-4H-chromene-3-carboxylic acid ethyl ester, 3a: Yield 94%; white crystalline solid; mp 188°C-190°C; Rf value in TLC 0.52 (Chloroform 1: Pet Ether 4); IR (KBr) ($\upsilon_{max}cm^{-1}$): 3340, 3310 (N-H), 1677, 1630 (C=O), 1575, 1475 (C=C stretching of phenyl), 1357 (C-N stretching), 1235, 1200, 1161 (C-O stretching), 1070 (C-Br, aromatic); ^1H NMR δ (in ppm): 7.07 (m, ArH, 4H), 4.701 (s, C_4 –H, 1H), 3.94 (q, J= 2.5, -$COOC\underline{H}_2CH_3$ at C-3 , 2H),2.461 (m, methylene protons at C-6, 2H), 2.208 (d, J=16.4, C-8, 2H), 1.575 (s, NH_2 protons at C-2, 2H), 1.12 (t, J=5.0 Hz, –$COOCH_2C\underline{H}_3$ at C-3, 3H), 1.093 (s, CH_3 at C-7, 3H), 0.998 (s, another CH_3 at C-7, 3H); ^{13}C NMR δ (in ppm): 196.25 (C=O), 162.55 (C-2), 146.38 (C-9), 131.17, 129.58, 127.57, 122.19 (aromatic C-1, C-4, C-5, C-3), 115.11 (C-10), 50.72 (C-3), 40.88 (C-6), 32.24 (C-8), 29.24 ($\underline{C}H_3$ at C-7), 27.34 (another CH_3 at C-7). Mass: Calculated 420.30, Experimental m/z: 419.07 (100%), 421.07 (97.4%), 420.08 (22.7%), 422.07 (22.0%), 421.08 (3.3%), 423.08 (3.2%). Anal. Found: C, 57.10; H, 5.22; N, 3.23; Calc. for $C_{20}H_{22}BrNO_4$: C, 57.15; H, 5.28; N, 3.33%.

2-Amino-4-(4/-hydroxyphenyl)-7, 7-dimethyl-5-oxo-5, 6, 7, 8-tetrahydro-4H-chromene-3-carboxylic acid ethyl ester, 3b: Yield 89%; white crystalline solid; mp 193°C-195°C; Rf value in TLC 0.68 (Ethyl acetate 1: Chloroform 4); IR (KBr) ($\upsilon_{max}cm^{-1}$): 3423 (O-H stretching), 3315, 2960 (N-H stretching), 1650 (C=O), 1440 (C=C stretching of phenyl), 1371 (C-N stretching), 1039, 1168 (C-O stretching); ^1H NMR δ (in ppm): 9.13 (s, ArOH, 1H), 7.43 (s, NH_2 protons at C-2, 2H), 6.91 (d, J=8.4 Hz, ArH, 2H), 6.58 (d, J=8 Hz, ArH, 2H), 4.40 (s, C_4 –H, 1H), 3.95 (q, J=6.8, -$COOCH_2C\underline{H}_3$ at C-3 , 2H), 2.47 (dd, C-8, 2H), 2.14 (dd, C-6, 2H), 1.09 (t, J=7.2 Hz, –$COOCH_2C\underline{H}_3$ at C-3, 3H), 1.02 (s, CH_3 at C-7, 3H), 0.89 (s, another CH_3 at C-7, 3H): ^{13}C NMR δ (in ppm): 196.04 (C=O), 168.25 (C-2), 161.91 ($COOCH_2CH_3$), 159.14 (C-9), 156.82, 147.86, 128.55, 118.27, 114.62, 112.75 (6C-aromatic), 116.04 (C-10), 78.51 (C-3), 58.8 ($COO\underline{C}H_2CH_3$), 50.13 (C-6), 40.12 (C-8), 32.33 (C-4), 31.94 (C-7), 28.75 (CH_3 at C-7), 26.54 (another $\underline{C}H_3$ at C-7), 14.33 (-$COO\underline{C}H_2CH_3$). Mass: Calculated 357.40, Experimental m/z: 357.16 (100%), 358.16 (22.8.%), 359.16 (3.4%). Anal. Found: C, 67.10; H, 6.41; N, 3.88; Calc. for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92%.

2-Amino-4-(3/-hydroxyphenyl)-7, 7-dimethyl-5-oxo-5, 6, 7, 8-tetrahydro-4H-chromene-3-carboxylic acid ethyl ester, 3c: Yield 82%; Off white crystalline solid; mp 179°C-181°C; Rf value in TLC 0.62 (Ethyl acetate 1: Chloroform 4); IR (KBr) ($\upsilon_{max}cm^{-1}$): 3410 (O-H stretching), 3250, 2956 (N-H stretching), 1650 (C=O), 1452 (C=C stretching of phenyl), 1365 (C-N stretching), 1037, 1100 , 1150 (C-O stretching); ^1H NMR δ (in ppm): 9.13 (s, ArOH, 1H), 7.51 (s, NH_2 protons at C-2, 2H), 6.456-6.984 (m, ArH, 4H), 4.42 (s, C_4 –H, 1H), 3.96 (q, J= 2.4, -$COOC\underline{H}_2CH_3$ at C-3 , 2H), 2.48 (dd, C-8, 2H), 2.16 (dd, C-6, 2H), 1.11 (t, J=7.2 Hz, –-$COOCH_2C\underline{H}_3$ at C-3, 3H), 1.03 (s, CH_3 at C-7, 3H), 0.90 (s, another CH_3 at C-7, 3H): ^{13}C NMR δ (in ppm): 195.78 (C=O), 168.02 (C-2), 162.05 $\underline{C}OOCH_2CH_3$), 159.18 (C-9), 156.80 , 147.69, 128.48, 114.75, 112.75 , 111.28 (6C-aromatic), 115.70 (C-10), 77.88 (C-3), 58.75 ($COO\underline{C}H_2CH_3$), 50.00 (C-6), 40.13 (C-8), 32.97 (C-4), 31.87 (C-7), 28.65 ($\underline{C}H_3$ at C-7), 26.50 (another CH_3 at C-7), 14.24 (-$COO\underline{C}H_2CH_3$). Mass: Calculated 357.40, Experimental m/z: 357.16 (100%), 358.16 (22.8.%), 359.16 (3.4%). Anal. Found: C, 67.10; H, 6.38; N, 3.90; Calc. for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92%.

2-Amino-4-(3/-hydroxyphenyl)-5-oxo-5,6,7, 8-tetrahydro-4H-chromene-3-carboxylic acid ethyl ester, 3d: Yield 93%; Off white crystalline solid; mp 182°C-184°C; Rf value in TLC 0.57 (Ethyl acetate 1: Chloroform 4); IR (KBr)

(υ_{max}cm^{-1}): 3415 (O-H stretching), 3307, 2941 (N-H stretching), 1687 (C=O), 1456 (C=C stretching of phenyl), 1369 (C-N stretching), 1068, 1150, 1200 (C-O stretching); ^{1}H NMR δ (in ppm): 9.13 (s, ArOH, 1H), 7.50 (s, NH_2 protons at C-2, 2H), 6.46-6.98 (m, ArH, 4H), 4.46 (s, C_4 –H, 1H), 3.96 (q, J= 2.4, -COOC$\underline{H}_2$CH$_3$ at C-3 , 2H), 2.59 (t, C-8, 2H), 2.26 (m, C-6, 2H), 1.95 (m, C-7, 2H), 1.10 (t, J=4.9 Hz, –COOCH$_2$C$\underline{H}_3$ at C-3, 3H); ^{13}C NMR δ (in ppm): 196.99 (C=O), 168.00 (C-2), 163.90 (C$\underline{O}$OCH$_2$CH$_3$), 159.22 (C-9), 156.82, 147.86, 128.55, 118.27, 114.62, 112.75 (6C-aromatic), 116.94 (C-10), 77.84 (C-3), 58.72 (COO$\underline{C}$H$_2$CH$_3$), 36.32 (C-6), 32.80 (C-8), 26.30 (C-4), 19.86 (C-7), 14.24 (-COOCH$_2$C$\underline{H}_3$). Mass: Calculated 329.35, Experimentalm/z: 329.13 (100%), 330.13 (20.5.%), 331.13 (3.0%). Anal. Found: C, 65.60; H, 5.79; N, 4.19; Calc. for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.81; N, 4.25%.

2-Amino-4-(3/-nitro-phenyl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carboxylic acid ethyl ester, 3e: Yield 90%; white crystalline solid; mp 182°C-184°C; Rf value in TLC 0.53 (neat chloroform); IR (KBr) (υ_{max}cm^{-1}): 3395, 3280 (N-H stretching), 1695 (C=O), 1528 (C=C stretching of phenyl), 1344 (C-N stretching), 1285, 1183 , 1094 (C-O stretching); ^{1}H NMR δ (in ppm): 8.0726 (s, ArH, 1H)), 7.959 (d, J=8.1 Hz, ArH, 1H), 7.637 (d, J=7.6 Hz0, ArH, 1H), 7.349 (t, J=7.9 Hz, ArH, 1H), 6.303 (s, NH2 protons at C-2, 2H), 4.786 (s, C_4 –H, 1H), 4.006 (q, J= 7.2, -COOC$\underline{H}_2$CH$_3$ at C-3 , 2H), 2.661-2.571 (m, C-6, 2H), 2.323 (t, J=5.8 Hz, C-8, 2H), 1.95 (m, C-7, 2H), 1.105 (t, J=7.2 Hz, –COOCH$_2$C$\underline{H}_3$ at C-3, 3H); ^{13}C NMR δ (in ppm): 196.421 (C=O), 168.555 (C-2), 163.706 (C$\underline{O}$OCH$_2$CH$_3$), 158. 323 (C-9), 148.272, 148.092, 134.908, 128.442, 123.131, 121.260 (6C-aromatic), 116.776 (C-10), 79.388 (C-3), 59.795 (COO$\underline{C}$H$_2$CH$_3$), 36.690 (C-6), 34.112 (C-8), 26.906 (C-4), 20.128 (C-7), 14.135 (-COOCH$_2$C$\underline{H}_3$). Mass: Calculated 358.35, Experimental m/z: 358.12 (100%), 359.12 (20.5%), 360.12 (3.3%). Anal. Found: C, 60.20; H, 5.00; N, 7.79; Calc. for $C_{18}H_{18}N_2O_6$: C, 60.33; H, 5.06; N, 7.82%.

2-Amino-7, 7-dimethyl-4-(3/-nitro-phenyl)-5-oxo-5, 6, 7, 8-tetrahydro-4*H*-chromene-3-carboxylic acid ethyl ester, 3f: Yield 85%; white crystalline solid; mp 174°C-176°C; Rf value in TLC 0.52 (neat chloroform); IR (KBr) (υ_{max}cm^{-1}): 3441, 3303 (N-H stretching), 1691 (C=O), 1521.86 (C=C stretching of phenyl), 1345 (C-N stretching), 1250, 1203, 1164 (C-O stretching); ^{1}H NMR δ (in ppm): 8.069 (t, J=1.8 Hz, ArH, 1H)), 7.945(m, ArH, 1H), 7.612 (m, ArH, 1H), 7.337 (t, J=7.9 Hz, ArH, 1H), 6.423 (s, NH_2 protons at C-2, 2H), 4.749 (s, C4 –H, 1H), 4.014 (q, J= 7.2, -COOC$\underline{H}_2$CH$_3$ at C-3 , 2H), 2.433 (s, C-6, 2H), 2.211 (d, J=16.3 Hz, C-8, 1Hax), 2.143 (d, J=16.3 Hz, 1Heq), 1.102 (t, J=7.1 Hz, –COOCH$_2$C$\underline{H}_3$ at C-3, 3H), 1.065 (s, C-7, 3H), 0.935 (s, another CH$_3$ at C-7, 3H); ^{13}C NMR δ (in ppm): 196.311 (C=O), 168.894 (C-2), 162.141 (C$\underline{O}$OCH$_2$CH$_3$), 158.590 (C-9), 148.181, 148.012, 134.779, 128.578, 123.148, 121.225 (6C-aromatic), 115.569 (C-10), 79.309 (C-3), 59.776 (COO$\underline{C}$H$_2$CH$_3$), 50.938 (C-6), 40.524 (C-8), 34.124 (C-4), 32.207(C-7), 28.983 ($\underline{C}$H$_3$ at C-7), 27.268 (another $\underline{C}$H$_3$ at C-7), 14.138 (-COOCH$_2$C$\underline{H}_3$). Mass: Calculated 386.40, Experimental m/z: 386.15 (100%), 387.15 (22.8%), 388.15 (3.7%). Anal. Found: C, 61.99; H, 5.70; N, 7.19; Calc. for $C_{20}H_{22}N_2O_6$: C, 62.17; H, 5.74; N, 7.25%.

Results and discussion

Compounds 3a-f were synthesized from 1a-d and the corresponding 2a-b in presence of sodium ethoxide in ethanol under refluxing conditions in an analogous manner reported previously. The assignment to the structures of the compounds 3a-f was made on the basis of their UV, IR, 1H NMR, ^{13}C NMR, mass spectra and elemental analyses.

The observed λ_{max} values of compounds 3a-f agree well to the expected values in their UV spectra. The absorption bands in the range 304-290 nm may be assigned to the $\pi\rightarrow\pi^*$ of C=O in these compounds. The weak $n\rightarrow\pi^*$ absorption bands in the cases of these compounds due to C=O were probably masked within the $\pi\rightarrow\pi^*$ absorption range.

The IR data of the compounds 3a-f showed sharp as well as broad bands in the range (υ_{max}) 3440-3250 cm^{-1} indicating the presence of N-H group. The absorption bands at 1700-1650 cm^{-1} indicate the presence of non-conjugated C=O stretching including the cyclohexanedione moieties. The bands at 1580-1440 cm^{-1} were assigned to C=C of aromatic rings and 1370-1345 cm^{-1} for C-N stretching. Additional bands were observed at 1235-1030 cm^{-1} due to these structural units (Bojarski *et al*., 1985).

The N-H protons at ring in the compounds 3a-f were relatively deshielded (δ 7.52-6.43) and appeared as singlet in their 1H NMR spectra due to anisotropy and presence of electronegative oxygen atom attached to this group. In Some compounds (3d, 3e) the proton at position 6 and 7 appeared as a multiplet due to the coupling with the proton at position 6, 7 and 8. The chemical shifts were observed at (δ 2.66-1.95) and the chemical shifts at position 8 observed at (δ 2.59-2.23 appeared as triplet) and other compounds (3a, 3b, 3c, 3f) the proton at position 6 and 8 appeared as a doublet of doublet (δ 2.48-2.14). The C_4-H in these compounds gave signals at (δ 4.78-4.40) as broad singlet. The chemical shifts for the aromatic protons in 3a-f were found in good agreement with the literature values (Silverstein *et al*., 1991, Kemp 1991).

The structures of the compounds 3a-f were further confirmed by their ^{13}C NMR spectra. The chemical shifts of carbonyl

carbon at 5-C were found to be deshielded in the range of δ 196.99-195.78. The chemical shifts of 2-C were also deshielded (δ 168.51-162.91). The chemical shift values for ($\underline{C}OOCH_2CH_3$) in these compounds were observed at (δ 163.70-161.91). The chemical shifts of 9-C were similarly deshielded (δ 159.22-158.59). The 10-C of the compounds showed chemical shift values at δ 116.77-115.11. The chemical shift values for 3-C in these compounds were observed at δ 79.38-77.84. The chemical shift values for 7-C in the compounds (3a, 3b, 3c & 3f) were observed at δ 32.20-31.87 and in the compounds (3d & 3e) were observed at δ 20.12-19.86 due to less deshielded. The chemical shift values for 8-C and 6-C in the compounds (3a, 3b, 3c & 3f) were observed at δ 40.10-40.15 and δ 50.00-50.95 respectively and for (3d & 3e) at 32.80-34.15 and δ 36.32-36.69 respectively due to less deshielded. The chemical shift values for 4-C in these compounds were observed at δ 34.52-32.33.

The ^{13}C NMR chemical shifts for the carbons of aromatic rings were assigned on the basis of a correlation chart available in the literature (Levy and Nelson, 1972).

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References

Bojarski JT, Mokrosz JL, Barton HJ and Paluchowaka MH (1985), Advances in Heterocyclic Chemistry (Review Article) **38:** 229-297.

Charles J, Michael SV, Gabriel SW and Amir HH (1998), Zr-Catalyzed Kinetic Resolution of Allylic Ethers and Mo-Catalyzed Chromene Formation in Synthesis: Enantioselective Total Synthesis of the Antihypertensive Agent (S,R,R,R)-Nebivolol. *J. Am. Chem. Soc*. **120:** 8340–8347.

Conti C, Proietti ML and Desideri N (2014), Synthesis and anti-rhinovirus activity of novel 3-[2-(pyridinyl)vinyl] substituted-2H-chromenes and 4H-chromen-4-ones, *Bioorg. Med. Chem*. **22:** 1201–1207.

Das B, Balasubramnyam P, Reddy GC and Salvanna N (2011), Simple, efficient, and catalyst-free synthesis of (2-amino-4H-1-benzopyran-4-yl) phosphonates in polyethylene glycol, *Helv. Chim. Acta* **94:** 1347–1350.

Ding D and Zhao CG (2010), Organocatalyzed synthesis of 2-amino-8-oxo-5,6,7,8-tretrahydro-4Hchromene-3-carbonitriles, *Treahedron Lett*. **51:** 1322–1325.

Dong AH, Liu XH, Feng JH, Wang M, Lin LL and Feng XM (2011), Efficient Asymmetric Synthesis of 4H-Chromene Derivatives through a Tandem Michael Addition-Cyclization Reaction Catalyzed by a Salen-Cobalt (II) complex, *Eur. J. Org. Chem*. **2011:** 137–142.

Fujimoto A and Sakurai A (1977), A New Selective Preparation of 4H-Chromenes by Reaction of alkyl Cyanoacetate with 3,5-Dibromosalicylaldehyde in the Presence of Ammonium Acetate, **Synthesis 12:** 872–872.

Gao YG and Du DM (2013), Facile synthesis of chiral 2-amino-4-(indol-3-yl)-4H-chromene derivatives using thiourea as the catalyst, *Tetrahedron* **24:** 1312–1317.

Gao SJ, Tsai CH, Tseng C and Yao CF (2008), Fluoride ion catalyzed multicomponent reactions for efficient synthesis of 4H-chromene and N-arylquinoline derivatives in aqueous media, *Tetrahedron* **64:** 9143–9149.

He Y, Chen YY, Shi JB, Tang WJ, Pan ZX, Dong ZQ, Song BA, Li J and Liu XH (2014), New coumarin derivatives: Design, synthesis and use as inhibitors of hMAO, *Bioorg. Med. Chem*. **22:** 3732–3738.

Jaman Z, Jahan K, Akhter K, Romman UKR, Ahmed SM., Siddiki SMAH and Ahmed MG (2013), An efficient synthesis of chromene derivatives through a Tandem Michael addition – cyclisation reaction, *Journal of Bangladesh Chemical Society* **26**(1): 75-82.

Jayashree P, Shanthi G and Perumal PT (2009), Indium Trichloride Catalyzed One-Pot Synthesis of New (2-Amino-3-cyano-4H-chromen-4-yl) Phosphonic Acid Diethyl Ester. Synlett, 6: 917–920.

Kalla RMN, Byeon SJ, Heo MS and Kim I (2013), Synthesis of 2-amino-3-cyano-4H-chromen-4-ylphosphontes and 2-amino-4H-chromenes catalyzed by tetramethylguanidine, *Tetrahedron* **69:** 10544–10551.

Kemp W (1991), Organic Spectroscopy, 3rd Ed., Macmillan.

Kolla SR and Lee YR (2012), Efficient one-pot synthesis of β-phosphono malonates and 2-amino-4Hchromen-4-ylphosphonate derivatives by ethylenediamine diacetate-catalyzed three-component reactions, *Tetrahedron* **68:** 226–237.

Kulakarni MA, Pandurangi VR, Desai UV and Wadgaonkar PP (2012), A practical and highly efficient protocol for multicomponent synthesis of β-phosphono malononitriles and

2-amino-4Hchromen- 4-ylphosphonates using diethylamine as a novel organocatalyst, *C. R. Chim*. **15:** 745–752.

Kumar A, Sharma S, Maurya RA and Sarkar J (2010), Diversity oriented synthesis of benzoxanthene and benzochromene libraries via one-pot, three-component reactions and their anti-proliferative activity, *J. Comb. Chem*. **12:** 20–24.

Levy GC and Nelson GL (1972), Carbon-13 Nuclear Magnetic Resonance for Organic Chemists, John Wiley & Sons, Inc.

Massimo C, Francesco E, Stefano C, Francesca M, Morena N and Ornelio R (2005), Potassium exchanged layered zirconium phosphate as catalyst in the preparation of 4H-chromenes, *Tetrahedron Lett*. **46:** 3497–3499.

Mori J, Iwashima M, Takeuchi M and Saito H (2006), A synthetic study on antiviral and antioxidativechromene derivative, *Chem. Pharm. Bull*. **54:** 391–396.

Meepagala KM, Schrader KK, Burandt CL, Wedge DE and Duke SO (2010), New class of algicidalcompounds and fungicidal activities derived from a chromene amide of Amyristexana, *J. Agric. Food Chem*. **58:** 9476–9482.

Mungra DC, Patel MP, Rajani DP and Patel RG (2011), Synthesis and identification of β-aryloxyquinolines and their pyrano [3,3-c] chromene derivatives as a new class of antimicrobial and antituberculosis agents, *Eur. J. Med. Chem*. **46:** 4192–4200.

Murthy SN, Madhav B, Reddy VP and Nageswar YVD (2010), One-pot synthesis of 2-amino-4Hchromen-4-yl phosphonate derivatives using β-cyclodextrin as reusable catalyst in water, *Tetrahedron Lett*. **51:** 3649–3653.

Neelakandan VL, Selvarangam E, Kiruthika T and Paramasivan T (2011), A Rapid and Efficient Access to 4-Substituted 2-Amino-4H-chromenes Catalyzed by In Cl3, *Synlett* 1389–1394.

Raj T, Bhatia RK, Kapur A, Sharma M, Saxena AK and Ishar MP (2010), Cytotoxic activity of 3-(5-phenyl-3H-[1,2,4] dithiazol-3-yl)chromen-4-ones and 4-oxo-4H-chromene-3- carbothioic acid N-phenylamides, *Eur. J. Med. Chem*. **45:** 790–794.

Rajasekhar M, Rao KUM, Sundar CS, Reddy NB, Nayak SK and Reddy CS (2012), GreenSynthesis and Bioactivity of 2-Amino-4H-chromen-4-yl-phosphonates, *Chem. Pharm. Bull*. **60:** 854–858.

Rapposelli S, da Settiomo F, Digiacomo M, la Motta C, Lapucci A, Sartini S and Vanni M (2011), Synthesis and biological evaluation of 2'-oxo-2,3-dihydro-3'H-spiro [chromene-4,5'-[1,3]oxazolidin]- 3'yl]acetis acid derivatives as aldose reductase inhibitors, *Arch. Pharm. (weinheim)* **344:** 372–385.

Roudier JF and Foucaud A (1984), A Convenient Synthesis of 4H-Chromenes, *Synthesis* **1984:** 159–160.

Safari J and Zarnegar Z (2014), Ultrasonic activated efficient synthesis of chromenes using amino-silane modified Fe3O4 nanoparticles: A versatile integration of high catalytic activity and facile recovery, J. *Mol. Struct*. **1072:** 53–60.

Shanthi G and Perumal PT (2008), Indium-Mediated One-Pot Synthesis of New 4-Allyl-2-amino-4Hchromenes in Water, *Synlett* 2791–2794.

Silverstein RM, Bassler GC and Morill TC (1991), Spectroscopic Identification of Organic Compounds, 5th Ed., John Wiley & Sons, Inc.

Sobhani S and Honarmand M (2013), Silica-Bonded 2-Hydroxyethylammonium Acetate as an Efficient and Recyclable Catalyst for the Synthesis of 2-Amino-4H-chromen-4-yl Phosphonates and β-Phosphonomalonates, *Catal. Lett*. **143:** 476–485.

Smetanina OF, Yurchenko AN, Afiyatullov SS, Kalinovsky AL, Pushilin MA, Khudyakova YV, Slinkina NN, Ermakova SP and Yurchenko EA (2012), Oxirapentyns B–Dproduced by a marine sediment-derived fungus *Isariafelina* (DC.) Fr., *Phytochem. Lett*. **5:** 165–169.

Yin GD, Lai TT, Yan ZS, Chen H, Zheng J and Tao Q (2013), Catalyst-free C-S/C-O bond formation: Synthesis of novel 4-thio-substituted 2-aryl-4H-chromenes from easily available 2-hydroxychalcones, *Tetrahedron* **69:** 2430–2435.

Yu NF, Aramini JM, Germann MW and Huang ZW (2000), Reactions of salicylaldehydes with alkyl cyanoacetates on the surface of solid catalysts: Syntheses of 4H-chromene derivatives, *Tetrahedron Lett*. **41:** 6993–6996.

Zhang G, Zhang Y, Yan J, Chen R, Wang S, Ma Y and Wang R (2012), One-pot enantioselective synthesis of functionalized pyranocoumarins and 2-amino-4H-chromens: Discovery of a type of potent antibacterial agent, *J. Org. Chem*. **77:** 878–888.