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Research Article
Comparative Study of Microwave-assisted and Conventional Synthesis of 3-[1-(s-phenylimino) Ethyl]-2H-chromen-2-ones and Selected Hydrazone Derivatives

Olayinka O. Ajani, Olufemi Ajayi, Joseph A. Adekoya, Taiwo F. Owoeye, Bamidele M. Durodola and Olatunde M. Ogunleye

Department of Chemistry, School of Natural and Applied Sciences, College of Science and Technology, Covenant University, PMB 1023, Ota, Ogun State, Nigeria

Abstract
In this study, 3-acetylcoumarin 1, used as the essential precursor was synthesized by the reaction of salicyaldehyde with ethyl acetoacetate in the presence of a catalytic amount of piperidine in solvent-free medium. Schiff bases 2-9 were obtained by the condensation reaction of 3-acetylcoumarin, 1 with various aniline derivatives while reaction of 3-hydrazinoquinoxalin-2-one with four different 6-susbtituted 3-acetylcoumarins afforded the corresponding hydrazones 10-13. Both Schiff bases and hydrazone products were synthesized under microwave irradiation method and conventional synthetic strategy for comparative study. The microwave assisted reaction was remarkably successful and gave both Schiff bases and hydrazones in higher yields at shorter reaction time compared to conventional heating method. The characterization of the synthesized compounds were structurally confirmed by analytical data as well as spectroscopic means which involved ^{1}H-and ^{13}C-nmr, ir, UV-visible and mass spectra.

INTRODUCTION

Over the years, coumarin (2H-chromen-2-one), as well as its analogues, has attracted considerable attention from organic and medicinal chemists due to its photophysical and photochemical behavior (Trenor *et al.*, 2004). Coumarins are naturally occurring benzopyrone derivatives identified in plants and are characterized by extensive chemo-diversity and various pharmacological activities (Rabtti *et al.*, 2012). Recently, coumarin derivatives are well known fluorescence dyes for their high photoluminescence (PL) quantum efficiencies (Lu *et al.*, 2002). The coumarin ring system has a central position in various classes of naturally occurring compounds (Nicolaou *et al.*, 2000). A number of natural and synthetic compounds containing the coumarin nucleus have been reported to exhibit a wide spectrum of biological activity and fluorescence in the visible light range. Due to its unique sweet smell and stability, coumarin has long been recognized as an important raw material in the fragrance industry. It is widely used in hand soaps, detergents, lotions and perfumes at concentrations usually extending from 0.01-0.80%. Coumarins have been reported to possess, among others, anticoagulant (Anderson *et al.*, 2002), antitubercular (Gursoy and Karali, 2003), antileucemic (Kotali *et al.*, 2008), antimicrobial (Satyanarayana *et al.*, 2008), anti-inflammatory (Kontogiorgis *et al.*, 2006), anti-HIV (Mateeva *et al.*, 2002), analgesic (Jayashree *et al.*, 2008), anticancer (Zhang *et al.*, 2013), antitumoral (Al-Soud *et al.*, 2008), anticonvulsant (Luszczki *et al.*, 2009), antiplatelet (Roma *et al.*, 2007), antifungal (Montagner *et al.*, 2008), antiviral (Neyts *et al.*, 2009), antibacterial (Siddiqui *et al.*, 2008) and antimalarial (Lisgarten *et al.*, 2003) activities. The intestinal anti-inflammatory properties of coumarin and coumarin derivatives, such as esculetin, 4-hydroxycoumarin and 4-methyl esculetin, have also been associated with their antioxidant properties (Witaicenis *et al.*, 2010). Dietary exposure to coumarins is quite significant and it has been estimated that the average Western diet contains approximately 1 g day^{-1} of mixed coumarin derivatives (Lacy and O'Kennedy, 2004).

Furthermore, coumarin has a significant use in the electroplating industry, mostly in the automotive area, to provide high polished quality to chrome plated steel but this use is presently declining. It confers shining properties to metallic part of automobile. This may be as a result of the high hydrophobic nature of this compound. The synthesis of a new cation receptor which combined coumarin and anthraquinone with ether units was earlier reported and the binding properties of such cation guests was studied (Ryu *et al.*, 2007). Polymers having photocrosslinkable functionality, such as coumarin, represent an active field of research in polymer science because of their technological applications in the fields of holographic elements (Lutz *et al.*, 2008), nonlinear optical materials (Scott *et al.*, 2001), photolithography (Nechifor, 2009) and liquid crystalline materials (Yavari *et al.*, 2006). In a similar manner, Schiff bases have often been used as chelating ligands in the field of coordination chemistry and their metal complexes have been of great interest to researchers for many years. It is well known that N and S atoms play a key role in the coordination of metals at the active sites of many metallo-biomolecules (Singh *et al.*, 2006). In view of numerous applications of coumarin templates and multi-drug resistance challenge, it is conceivable to synthesize more derivatives of this scaffold for continuous therapeutic application and valuable drug designs. Hence, the aim of this present study is to synthesize some valuable Schiff bases of coumarin and selected hydrazones for future drug design and development.

MATERIALS AND METHODS

General conditions: All chemical compounds were obtained commercially and were made available by the Department of Chemistry, Covenant University. Solvents used were of analytical grade and, when necessary, were purified and treated by standard methods. Organic solutions were dried over anhydrous Na_2SO_4 and concentrated with a RE-2000B buchi rotary evaporator. Melting points were determined in open capillary tubes on a Stuart melting point apparatus and were uncorrected. The IR spectra were run in the Nicolet IR 100 (Fourier-Transform); while UV of all the samples were run in ethanol using UV-Genesys spectrophotometer. The mass spectral data were obtained from waters GCT premier spectrophotometer. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded in DMSO-d_6 using NMR Bruker DP×400 spectrophotometer operating at 400 MHz and 100 MHz respectively. Compounds were routinely checked by TLC on silica gel G plates using $CHCl_3$:CH_3OH (9:1, v/v) or CH_3COCH_3:C_6H_6 (1:9, v/v) solvent system and the developed plates were visualized under UV light. The elemental analysis (C, H, N) of compounds were performed using a Carlo Erba-1108 elemental analyzer. Results were found to be in good agreement with the calculated values. The microwave assisted syntheses were carried out using a CEM Discover monomode oven operating at 2450 MHz monitored by a PC computer and temperature control was fixed at 140°C within the power modulation of 300 and 400 W. Stirring was provided by an *in situ* magnetic stirrer while reactions were performed in sealed tube within a ramp time of 75 sec to 2 min.

Synthesis of 3-acetylcoumarin (1)

Procedure A-conventional method (COM): To a mixture of salicyaldehyde (8.60 mL, 81.89 mmol) and ethyl acetoacetate (11.50 mL, 90.13 mmol) was added ethanol (30 mL) to make homogeneous solution. Catalytic amount of piperidine (0.20 mL, 1.64 mmol) was added to the solution above and refluxed for 10 min to afford a crude yellow crystal. The crude product was purified by recrystallization in methanol and cooled to obtain a solid which was filtered by suction and dried to afford yellow 3-acetylcoumarin, 1 (4.10 g, 89.00%).

Procedure B-Microwave Assisted Method (MAM): To a mixture of salicyaldehyde (8.60 mL, 81.89 mmol) and ethyl acetoacetate (11.50 mL, 90.13 mmol) was added catalytic amount of piperidine (0.20 mL, 1.64 mmol) and swirled thoroughly. The mixture was irradiated in microwave oven at 400 W for 1 min. The solid product was filtered, dried and recrystallized from methanol to afford pure 3-acetyl coumarin 1. M.p. 122-123°C; R_f 0.71 {CHCl$_3$:CH$_3$OH (9:1, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.27 (s, 3H, CH$_3$), 7.42-7.84 (m, 4H, Ar-H), 8.57 (s, 1H, Het-H); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 195.0 (C = O), 158.3 (C = O), 154.5, 147.0 (2×C), 134.4 (2×C), 130.7 (2×C), 118.1, 30.0 (CH$_3$) ppm; λ$_{max}$ in nm (log ε in mol^{-1} cm^{-1}): 335 (4.88), 296 (5.08), 209 (5.21); FT-IR (KBr) ν: 2925 (CH aliphatic), 1746 (C = O ester), 1685 (C = O), 1606 (C = C), 1369 cm^{-1}; MS-ESI (m/z): 189.05 (M + 1, 2%), 188.04 (M$^+$, 39%), 173.01 (M-CH$_3$, 100%), 145.03 (M-COCH$_3$, 7%), 118.04 (MH-COCH$_3$-CO), 89.03 (8%); Anal. Calcd. for C$_{11}$H$_8$O$_2$ (Mr = 188.18): C 70.21, H 4.29. Found C 70.10, H 4.41.

General procedure for the synthesis of schiff bases, 3-[1-(s-phenylimino) ethyl]-2H-chromen-2-one 2-9

General procedure for A-Conventional Method (COM): The 3-Acetylcoumarin (1.0 g, 5.3 mmol) was dissolved in ethanol (30 mL). To this solution was added an appropriate substituted aniline derivatives (5.3 mmol) and swirled thoroughly. The reacting mixture was then refluxed for required period of time and was allowed to cool to afford a solid which was filtered by suction and dried to afford Schiff bases 2-9 in low yields.

General procedure for B-Microwave Assisted Method (MAM): To a mixture of 3-acetylcoumarin 1 (1.0 g, 5.3 mmol) and appropriate aniline (5.3 mmol) derivative was added ethanol (20 mL) and swirled thoroughly. The resulting mixture was then irradiated in microwave oven at 300 W for the required period of time and allowed to cool to ambient temperature for proper crystallization. The solid obtained was filtered by suction and dried to afford the expected Schiff bases 2-9 in improved yields. The following compounds 2-9 below were prepared in the manner given in the general procedure above.

3-[1-(4-Bromophenylimino) ethyl]-2H-chromen-2-one (2): Prepared from 1 (1.0 g, 5.3 mmol) and 4-bromoaniline (0.9 g, 5.3 mmol). M.p. 117-118°C; R_f 0.66 {CHCl$_3$:CH$_3$OH (9:1, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.09 (s, 3H, CH$_3$), 7.21-7.23 (d, J = 8.02 Hz, 2H, Ar-H), 7.43-7.85 (m, 4H, Ar-H), 7.76-7.78 (d, J = 8.11 Hz, 2H, Ar-H), 8.54 (s, 1H, Het-H); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 19.3 (CH$_3$), 113.4, 116.1, 118.3, 121.7, 122.9 (2×C), 125.2, 127.5, 128.6, 132.6, 132.8 (2×C), 150.1, 153.2, 159.1, 175.8 (C = O) ppm; λ$_{max}$ in nm (log ε in mol^{-1} cm^{-1}): 299 (5.08), 209 (5.29); FT-IR (KBr) ν: 2723 (CH aliphatic), 1747 (C = O of esters), 1612 (C = C aromatic), 1560 (C = N of imine), 1376 (C-O of esters), 756 (C-Br), 723 (Ar-H aromatic) cm^{-1}; MS-ESI (m/z): 343.03 (MH, 3%), 342.02 (M$^+$, 68%), 340.02 (M-2, 72%), 261.10 (M-Br, 4%), 171.05 (NH$_2$C$_6$H$_4$Br, 21.5%), 143.04 (100%), 115.05 (53%), 89.03 (7%), 77.03 (Ph$^+$, 3%); Anal. Calcd. for C$_{17}$H$_{12}$NBrO$_2$ (Mr = 342.19): C 59.67, H 3.53, N 4.09. Found C 59.81, H 3.66, N 3.89.

3-[1-(3-Nitrophenylimino) ethyl]-2H-chromen-2-one (3): Prepared from 1 (1.0 g, 5.3 mmol) and 3-nitroaniline (0.7 g, 5.3 mmol). M.p. 107-109°C; R_f 0.53 {CHCl$_3$:CH$_3$OH (9:1, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.04 (s, 3H, CH$_3$), 7.37-7.66 (m, 4H, Ar-H), 7.56 (s, 1H, Het-H), 7.71-7.96 (m, 3H, ArH), 7.81 (s, 1H, ArH); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 19.9 (CH$_3$), 113.1, 116.6, 118.3, 118.7, 122.7, 125.4, 127.8, 128.2, 128.7, 132.2, 132.9, 149.1, 149.7, 153.3, 159.4, 175.6 (C = O) ppm; λ$_{max}$ in nm (log ε in mol^{-1} cm^{-1}): 335 (4.89), 296 (5.09), 209 (5.20); FT-IR (KBr) ν: 2723 (CH aliphatic), 1745 (C = O of esters), 1612 (C = C aromatic), 1559 (C = N of imine), 1376 (C-O of esters), 1208 (NO$_2$), 723 (Ar-H aromatic) cm^{-1}; MS-ESI (m/z): 188.04 (MH-C$_6$H$_5$NO$_2$, 93%), 173.01 (M-CH$_3$-C$_6$H$_5$NO$_2$, 100%), 145.03 (MH-C$_6$H$_5$NO$_2$-COCH$_3$, 20%), 118.04 (MH-C$_6$H$_5$NO$_2$-COCH$_3$-CO), 89.03 (8%); Anal. Calcd. for C$_{17}$H$_{12}$N$_2$O$_4$ (Mr = 308.29): C 66.23, H 3.92, N 9.09. Found C 66.11, H 3.79, N 9.18.

3-[1-(4-chlorophenylimino) ethyl] 2H-chromen-2-one (4): Prepared from 1 (1.0 g, 5.3 mmol) and 4-chloroaniline (0.7 g, 5.3 mmol). M.p. 105-106°C; R_f 0.47 {CHCl$_3$:CH$_3$OH (9:1, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.12 (s, 3H, CH$_3$), 7.02-7.04 (d, J = 8.00 Hz, 2H, Ar-H), 7.44-7.88 (m, 4H, Ar-H), 7.45-7.47 (d, J = 8.10 Hz, 2H, Ar-H), 8.14 (s, 1H, Het-H); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 30.0 (CH$_3$), 102.5, 105.3, 116.0 (2×C),

118.1, 124.2, 124.3 (2×C), 130.7 (2×C), 134.4 (2×C), 147.0 (2×C), 154.5, 158.3 (C = O) ppm; λ_{max} in nm (log ε in mol^{-1} cm^{-1}): 338 (4.77), 296 (4.96), 209 (5.11); FT-IR (KBr) ν: 2723 (CH aliphatic), 1745 (C = O of esters), 1612 (C = C aromatic), 1559 (C = N of imine), 1376 (C-O of esters), 756 (C-Cl), 723 (Ar-H aromatic) cm^{-1}; MS-ESI (m/z): 297.91 (M$^+$, 28%), 261.49 (M-Cl, 31.4%), 246.48 (M-CH$_3$Cl, 44.6%), 172.11 (M-CH$_3$C$_6$H$_4$Cl, 10.2%), 119.13 (27.3%), 112.17 (PhCl, 19.1%), 74.22 (12.1%); Anal. Calcd. for C$_{17}$H$_{12}$NClO$_2$ (Mr = 297.74): C 68.58, H 4.06, N 4.70. Found C 68.73, H 4.21, N 4.56.

3-[1-(4-Bromo-2-methylphenylimino) ethyl]-2H-chromen-2-one (5): Prepared from 1 (1.0 g, 5.3 mmol) and 4-bromo-2-methylaniline (0.99 g, 5.3 mmol). M.p. 95-96°C; R$_f$ 0.44 {CHCl$_3$:CH$_3$OH (9:1, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.11 (s, 3H, CH$_3$), 2.87 (s, 3H, CH$_3$), 7.13 (d, J = 7.57 Hz, 1H, ArH), 7.33 (s, 1H, ArH), 7.42-7.85 (m, 4H, Ar-H), 7.55 (s, 1H, Het-H), 7.59 (d, J = 7.57 Hz, 1H, ArH); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 17.9 (CH$_3$), 20.3 (CH$_3$), 113.2, 116.4, 118.9, 121.3, 124.7, 125.3, 127.7, 128.5, 129.8, 132.7 (2×C), 135.6, 145.1, 153.9, 159.3, 175.8 (C = O) ppm; λ_{max} in nm (log ε in mol^{-1} cm^{-1}): 335 (4.62), 296 (4.83), 209 (4.97); FT-IR (KBr) ν: 2723 (CH aliphatic), 1745 (C = O of esters), 1612 (C = C aromatic), 1558 (C = N of imine), 1376 (C-O of esters), 756 (C-Br), 723 (Ar-H aromatic) cm^{-1}; MS-ESI (m/z): 359.03 (1.8%), 358.02 (19.4%), 357.03 (2.2%), 356.33 (MH$^+$, 13%), 328.31 (M-C$_2$H$_4$, 73.4%), 276.11 (M-Br, 100%), 261.14 (M-CH$_3$Br, 63%), 260.13 (MH-CH$_3$Br, 5%), 172.11 (MH-CH$_3$-[BrC$_6$H$_4$CH$_3$], 11%), 138.17 (21%), 137.33 (12%); Anal. Calcd. for C$_{18}$H$_{14}$NBrO$_2$ (Mr = 356.21): C 60.69, H 3.96, N 3.93. Found C 60.83, H 3.78, N 3.77.

3-[1-(3-Bromo-4-methylphenylimino) ethyl]-2H-chromen-2-one (6): Prepared from 1 (1.0 g, 5.3 mmol) and 3-bromo-4-methylaniline (0.66 mL, 5.3 mmol). M.p. 114-115°C; R$_f$ 0.50 {CHCl$_3$:CH$_3$OH (9:1, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.11 (s, 3H, CH$_3$), 2.87 (s, 3H, CH$_3$), 7.13 (d, J = 7.57 Hz, 1H, ArH), 7.33 (s, 1H, ArH), 7.42-7.85 (m, 4H, Ar-H), 7.55 (s, 1H, Het-H), 7.59 (d, J = 7.57 Hz, 1H, ArH); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 17.9 (CH$_3$), 20.3 (CH$_3$), 113.2, 116.4, 118.9, 121.3, 124.7, 125.3, 127.7, 128.5, 129.8, 132.7 (2×C), 135.7, 145.1, 153.9, 159.3, 175.8 (C = O) ppm; λ_{max} in nm (log ε in mol^{-1} cm^{-1}): 335 (4.78), 296 (4.96), 209 (5.13); FT-IR (KBr) ν: 2723 (CH aliphatic), 1742 (C = O of esters), 1612 (C = C aromatic), 1557 (C = N of imine), 1376 (C-O of esters), 757 (C-Br), 723 (Ar-H aromatic) cm^{-1}; MS-ESI (m/z): 359.03 (3.7%), 358.02 (15.9%), 357.11 (M+1, 20.6%), 356.31 (MH$^+$, 47%), 328.77 (M-C$_2$H$_4$, 64.1%),

276.44 (M-Br, 100%), 261.14 (M-CH$_3$Br, 63%), 260.27 (MH-CH$_3$Br, 5%), 172.41 (MH-CH$_3$-[BrC$_6$H$_4$CH$_3$], 22%), 137.21 (15%), 135.79 (8%), 78.96 (12%); Anal. Calcd. for C$_{18}$H$_{14}$NBrO$_2$ (Mr = 356.21): C 60.69, H 3.96, N 3.93. Found C 60.88, H 4.02, N 3.81.

3-[1-(2-Bromo-4-methylphenylimino) ethyl]-2H-chromen-2-one (7): Prepared from 1 (1.0 g, 5.3 mmol) and 2-bromo-4-methylaniline (0.66 mL, 5.3 mmol). M.p. 109-110°C; R$_f$ 0.56 {CHCl$_3$:CH$_3$OH (9:1, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.08 (s, 3H, CH$_3$), 2.35 (s, 3H, CH$_3$), 7.10 (d, J = 7.98 Hz, 1H, ArH), 7.18 (d, J = 7.98 Hz, 1H, ArH), 7.39 (s, 1H, ArH), 7.41-7.86 (m, 4H, Ar-H), 7.57 (s, 1H, Het-H); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 19.9 (CH$_3$), 21.2 (CH$_3$), 110.2, 113.7, 116.1, 118.9, 124.6, 125.2, 127.9, 128.4, 129.3, 132.7, 135.8, 139.4, 143.8, 153.5, 159.4, 175.5 (C = O) ppm; λ_{max} in nm (log ε in mol^{-1} cm^{-1}): 335 (4.91), 296 (5.12), 209 (5.24); FT-IR (KBr) ν: 2723 (CH aliphatic), 1739 (C = O of esters), 1612 (C = C aromatic), 1556 (C = N of imine), 1376 (C-O of esters), 756 (C-Br), 723 (Ar-H aromatic) cm^{-1}; MS-ESI (m/z): 357.04 (M + 1, 12%), 356.18 (M$^+$, 11%), 340.02 (M-CH$_2$, 2%), 276.11 (M-Br, 100%), 261.09 (M-CH$_3$Br, 51%), 260.09 (MH-CH$_3$Br, 3%), 172.05 (MH-CH$_3$-[BrC$_6$H$_4$CH$_3$], 8%), 138.05 (22%), 137.55 (18%); Anal. Calcd. for C$_{18}$H$_{14}$NBrO$_2$ (Mr = 356.21): C 60.69, H 3.96, N 3.93. Found C 60.54, H 3.87, N 4.04.

3-[1-(Phenylimino) ethyl]-2H-chromen-2-one (8): Prepared from 1 (1.0 g, 5.3 mmol) and aniline (0.45 mL, 5.3 mmol). M.p. 117-119°C; R$_f$ 0.50 {CHCl$_3$:CH$_3$OH (9:1, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.13 (s, 3H, CH$_3$), 6.98-7.42 (m, 5H, ArH), 7.45-7.89 (m, 4H, Ar-H), 8.51 (s, 1H, Het-H); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 19.9 (CH$_3$), 113.1, 116.2, 118.1, 119.5 (2×C), 125.4, 127.1, 127.8, 128.3, 130.0 (2×C), 132.7, 136.2, 153.1, 159.6, 175.3 (C = O) ppm; FT-IR (KBr) ν: 2723 (CH aliphatic), 1745 (C = O of esters), 1612 (C = C aromatic), 1558 (C = N of imine), 1376 (C-O of esters), 723 (Ar-H aromatic) cm^{-1}; Anal. Calcd. for C$_{17}$H$_{13}$NO$_2$ (Mr = 263.29): C 77.55, H 4.98, N 5.32. Found C 77.72, H 5.05, N 5.17.

3-[1-(Methylimino) ethyl]-2H-chromen-2-one (9): Prepared from 1 (1.0 g, 5.3 mmol) and methylamine (0.2 mL, 5.3 mmol). M.p. 114-116°C; R$_f$ 0.53 {CHCl$_3$:CH$_3$OH (9:1, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 1.13 (s, 3H, CH$_3$), 2.17 (s, 3H, CH$_3$), 7.42-7.84 (m, 4H, Ar-H), 8.51 (s, 1H, Het-H); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 17.8 (CH$_3$), 31.7 (CH$_3$), 114.1, 116.8, 118.2, 125.4, 127.3, 128.7, 132.8 (2×C), 153.1, 159.4 (C = O) ppm; λ_{max} in nm (log ε in mol^{-1} cm^{-1}): 335 (5.11), 296 (5.30), 212 (5.31);

FT-IR (KBr) v: 2723 (CH aliphatic), 1744 (C = O of esters), 1612 (C = C aromatic), 1558 (C = N of imine), 1376 (C-O of esters), 723 (Ar-H aromatic) cm^{-1}; Anal. Calcd. for C$_{12}$H$_{11}$NO$_2$ (Mr = 201.22): C 71.63, H 5.51, N 6.96. Found C 71.72, H 5.42, N 6.74.

General procedure for the synthesis of 3-{2-[1-(6-substituted-2-oxo-2H-chromen-3-yl)ethy lidene] hydrazinyl}quinoxalin-2(1H)-one, 10-13

General procedure A-conventional method (COM): In a 250 mL round-bottomed flask, unsubstituted or 6-substituted 3-acetylcoumarin (5.7 mmol) and 3-hydrazinoquinoxalin-2(1H)-one, (1.0 g, 5.7 mmol) in dry DMF (20 mL) were taken. The reaction mixture was refluxed at 90-95°C for 3 h and the solvent was distilled off. The solid product obtained was filtered, dried and recrystallized from methanol to afford 10-13.

General procedure B-Microwave Assisted Method (MAM): To a ground mixture of 3-hydrazino quinoxalin-2(1H)-one, (1.0 g, 5.7 mmol) and unsubstituted or 6-substituted 3-acetylcoumarin (5.7 mmol), was added dry DMF (20 mL) in a 250 mL round-bottomed flask. The reaction mixture was irradiated in a microwave oven at 400W for 1 min and the solvent was distilled off. The solid product obtained was filtered, dried and recrystallized from methanol to afford 3-{2-[1-(6-substituted-2-oxo-2H-chromen-3-yl)ethylidene] hydrazinyl} quinoxalin-2(1H)-one, 10-13. The following compounds 10-13 below were prepared in the manner in the general procedure given above.

3-{2-[1-(2-Oxo-2H-chromen-3-yl)ethylidene] hydrazinyl}quinoxalin-2(1H)-one (10): Prepared from 3-hydrazinoquinoxalin-2(1H)-one (1.0 g, 5.7 mmol) and 3-acetylcoumarin, 1 (1.07 g, 5.7 mmol). M.p. 238-241°C; R$_f$ 0.58 {CH$_3$COCH$_3$:C$_6$H$_6$ (1:9, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.07 (s, 3H, CH$_3$), 7.00 (s, 1H, NH, D$_2$O, exchangeable). The 7.09-8.27 (m, 4H, Ar-H), 7.54 (s, 1H, Het-H, C = CH), 7.42-7.84 (m, 4H, Ar-H), 8.00 (s, 1H, NH, D$_2$O, exchangeable); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 159.4 (C = O), 158.0 (C = O), 157.6, 155.6, 153.0, 142.7, 133.5, 131.7, 129.1, 128.3, 127.9, 125.9, 125.4, 123.5, 123.3, 118.1, 116.1, 115.2, 4.0 ppm; λ$_{max}$ in nm (log ϵ in mol^{-1} cm^{-1}): 212 (4.58), 327 (3.65s), 344 (3.68), 365 (3.32s); FT-IR (KBr) v: 3240 (N-H), 1740 (C = O ester), 1685 (C = O), 1606 (C = C), 1563 (C = N), 1381 (C-O) cm^{-1}; MS-ESI (m/z): 346 (M$^+$, 35%), 331 (53%), 201 (13%), 186 (82%), 161 (100%), 15 (3%); Anal. Calcd. for C$_{19}$H$_{14}$N$_4$O$_3$ (Mr = 346.34): C 65.90, H 4.05, N 16.18. Found: C 65.94, H 4.08, N 16.21.

3-{2-[1-(6-Bromo-2-oxo-2H-chromen-3-yl)ethylidene] hydrazinyl}quinoxalin-2(1H)-one (11): Prepared from 3-hydrazinoquinoxalin-2(1H)-one (1.0 g, 5.7 mmol) and 6-bromo-3-acetyl coumarin (1.52 g, 5.7 mmol). M.p. 265-266°C; R$_f$ 0.71 {CH$_3$COCH$_3$:C$_6$H$_6$ (1:9, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.07 (s, 3H, CH$_3$), 7.00 (s, 1H, NH, D$_2$O, exchangeable). 7.09-8.27 (m, 4H, Ar-H), 7.31-8.19 (m, 3H, Ar-H), 7.54 (s, 1H, Het-H, C = CH), 8.00 (s, 1H, NH, D$_2$O, exchangeable); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 159.4 (C = O), 158.0 (C = O), 157.6, 155.6, 152.0, 142.7, 134.2, 133.5, 131.7, 130.3, 129.1, 125.9, 124.4, 123.5, 123.3, 119.8, 118.2, 115.2, 4.0 ppm; λ$_{max}$ in nm (log ϵ in mol^{-1}cm^{-1}): 210 (4.10), 325 (3.51), 345 (3.41), 414 (3.32); FT-IR (KBr) v: 3135 (N-H), 1740 (C = O), 1665 (C = O), 1575 (C = N), 1288 (m), 1130 (m) cm^{-1}; MS-ESI (m/z): 425 (M$^+$, 38%), 345 (12%), 161 (100%), 155 (63%), 75 (25%); Anal. Calcd. for C$_{19}$H$_{13}$N$_4$O$_3$Br (Mr = 425.24): C 53.65, H 3.06, N 13.18. Found: C 53.66, H 3.08, N 13.21.

3-{2-[1-(6-Chloro-2-oxo-2H-chromen-3-yl)ethylidene] hydrazinyl}quinoxalin-2(1H)-one (12): Prepared from 3-hydrazinoquinoxalin-2(1H)-one (1.0 g, 5.7 mmol) and 6-chloro-3-acetyl coumarin (1.27 g, 5.7 mmol). M.p. 245-246°C; R$_f$ 0.73 {CH$_3$COCH$_3$:C$_6$H$_6$ (1:9, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.07 (s, 3H, CH$_3$), 7.00 (s, 1H, NH, D$_2$O, exchangeable), 7.09-8.27 (m, 4H, Ar-H), 7.54 (s, 1H, Het-H, C = CH), 7.36-8.02 (m, 3H, Ar-H), 8.00 (s, 1H, NH, D$_2$O, exchangeable); ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 159.4 (C = O), 158.0 (C = O), 157.6, 155.6, 151.1, 142.7, 133.5, 131.7, 131.0, 129.5, 129.1, 126.8, 125.9, 123.6, 123.5, 123.3, 118.0, 115.2, 4.0 ppm; λ$_{max}$ in nm (log ϵ in mol^{-1}cm^{-1}): 224 (4.11), 310 (3.71s), 332 (3.41), 360 (3.97s), 396 (4.22); FT-IR (KBr) v: 3387 (N-H), 1740 (C = O ester), 1648 (C = O), 1612 (C = C), 1570 (C = N), 1375 (C-O ester), 1290 (m) cm^{-1}; MS-ESI (m/z): 380.5 (M$^+$, 40%), 345 (15%), 160 (100%), 15 (5%); Anal. Calcd. for C$_{19}$H$_{13}$N$_4$O$_3$Cl (Mr = 380.78): C 59.92, H 3.42, N 14.72. Found: C 59.90, H 3.39, N 14.70.

3-{2-[1-(6-Methyl-2-oxo-2H-chromen-3-yl)ethylidene] hydrazinyl}quinoxalin-2(1H)-one (13): Prepared from 3-hydrazinoquinoxalin-2(1H)-one (1.0 g, 5.7 mmol) and 6-methyl-3-acetyl coumarin (1.15 g, 5.7 mmol). M.p. 183-185°C; R$_f$ 0.59 {CH$_3$COCH$_3$:C$_6$H$_6$ (1:9, v/v)}; ^{1}H NMR (DMSO-d$_6$, 400 MHz) δ: 2.07 (s, 3H, CH$_3$), 2.34 (s, 3H, CH$_3$), 7.00 (s, 1H, NH, D$_2$O, exchangeable), 7.09-8.27 (m, 7H, 2 Ar-H), 7.54 (s, 1H, Het-H, C = CH), 8.00 (s, 1H, NH, D$_2$O, exchangeable). ^{13}C NMR (DMSO-d$_6$, 100 MHz) δ: 159.4 (C = O), 158.0 (C = O), 157.6, 155.6, 150.0, 142.7, 135.1, 133.5, 132.0, 131.7, 129.1, 127.0, 125.9, 123.5, 123.3, 122.1, 116.9, 115.2, 21.7, 5.0 ppm; λ$_{max}$ (log ϵ$_{max}$): 210 (3.11), 320 (3.67), 342 (3.17), 350 (3.84), 360

(3.51), 408 (3.57); FT-IR (KBr) v: 3118 (N-H), 1742 (C = O), 1665 (C = O), 1571 (C = N), 1273 (m) cm^{-1}; MS-ESI (m/z): 360 (M$^+$, 35%), 346 (20%), 161 (100%), 158 (60%), 72 (18%), 15 (7%); Anal. Calcd. for C$_{20}$H$_{16}$N$_4$O$_3$ (Mr = 360.37): C 66.67, H 4.44, N 15.56. Found: C 66.68, H 4.47, N 15.59.

RESULTS AND DISCUSSION

Coumarins have been established as well-known naturally occurring oxygen-heterocyclic compounds isolated from various plants. They are the family of lactones containing benzopyrone skeletal framework that have enjoyed isolation from plant as well as total synthesis in the laboratory. Molecular characterization and structural activity relationship studies have shown Schiff bases to be highly relevant scaffolds in drug design and medicinal research. Hence, the formation of the Schiff bases of 3-acetylcoumarin was embarked upon in this project study. In the continuation of our effort on the exploration of microwave assisted synthesis as an eco-friendly strategy (Ajani *et al.*, 2009), we have herein compared the synthesis of imine and selected hydrazones of 3-acetylcoumarin under conventional and microwave assisted methods. First and foremost, 3-acetylcoumarin, 1, used as the essential precursor in this study, was synthesized by the reaction of salicyaldehyde with ethyl acetoacetate in the presence of catalytic amount of piperidine using ethanol as the solvent by adopting the standard procedure we earlier reported (Ajani and Nwinyi, 2010) (Fig. 1). Subsequently, 3-acetylcoumarin, 1 was treated with substituted anilines to afford the Schiff bases 2-8, while its condensation with methylamine resulted in the formation of imino template 9. Thus, condensation reaction of 3-acetylcoumarin with aniline derivatives and methyl amine resulted in Schiff bases 2-8 and alkylimino compound 9 as shown in Fig. 2. In addition, selected hydrazone scaffold 10 was obtained from the reaction of 3-hydrazino-2-quinoxalinone with 3-acetyl coumarin whereas when, the 3-acetylcoumarin was replaced with three different 6-substituted-3-acetylcoumarin (6-Br, 6-Cl, 6-CH$_3$) derivatives, the hydrazones 11-13 were obtained, respectively (Fig. 3).
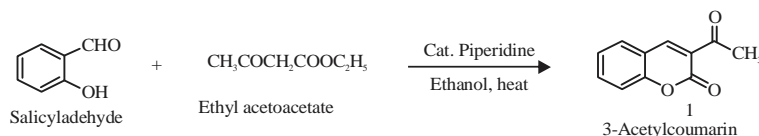

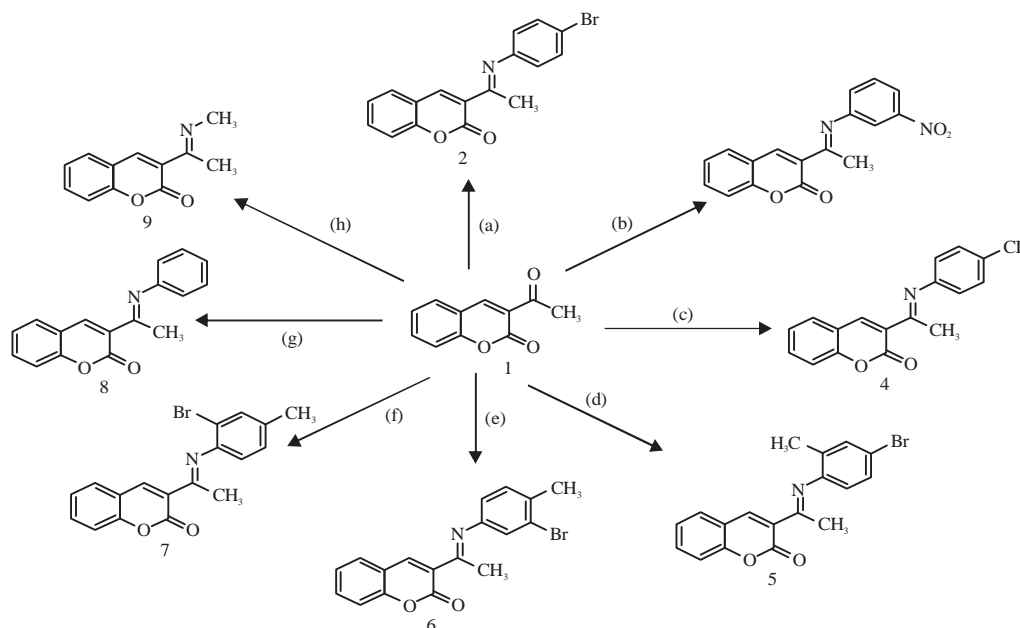Fig. 1: Equation of reaction for the formation of 3-acetylcoumarin

Fig. 2(a-h): Synthesis of the schiff bases of 3-acetylcoumarin, reaction condition and reagent used: Dissolved in EtOH and heated under reflux or in microwave, (a) 4-Bromoaniline, (b) 3-Nitroaniline, (c) 4-Chloroaniline, (d) 4-Bromo-2-methhylaniline, (e) 3-Bromo-4-methylaniline, (f) 2-Bromo-4-methylaniline, (g) Aniline and (h) Methylamine
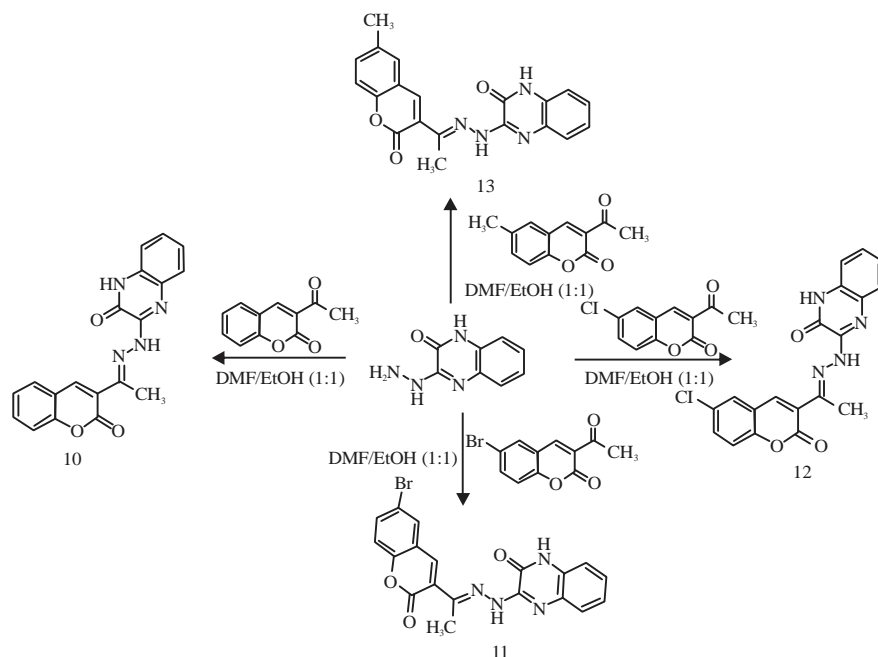
Fig. 3: Synthesis of selected hydrazones 10-13 from 6-substitued 3-acetylcoumarin

Table 1: Comparison of the conventional and microwave assisted synthesis for 1-13

Comp codes	Yield for COM (%)	Time (min)	Yield for MAM (%)	Time (min)	Power (Watt)
1	91.50	15	92.60	1	300
2	15.20	210	68.71	2	300
3	14.14	150	71.21	2	300
4	45.56	190	76.63	2	300
5	64.50	180	81.22	3	300
6	58.92	210	79.01	2	300
7	47.91	180	77.82	2	300
8	41.92	150	82.13	1	300
9	28.08	210	59.08	1	300
10	59.40	180	84.00	1	400
11	61.00	180	86.00	1	400
12	70.20	180	91.00	1	400
13	51.70	180	73.20	1	400

Comp code: Compound code, COM: Conventional method and MAM: Microwave assisted method

Moreover, for comparative study, all the products were synthesized by using two different methods which are conventional method (COM) and microwave assisted methods (MAM). The synthesis of 1 under conventional (91.5%) and microwave irradiation technique (92.6%) showed almost the same % yield (>90%). This might be as a result of the fact that the compound 1 is kinetically controlled product. This excellent yield was in agreement with the value reported by Pangal *et al.* (2013) in that it was >90%. Nonetheless, the higher yield (98%) they reported for this precursor 1 might be due to nature of their work-up technique and solventless environment used (Pangal *et al.*, 2013). However, it is worthy

to note that the synthesis of both imino frameworks 2-9 and hydrazone derivatives 10-13 were highly favoured under microwave method in term of higher product yields and shorter reaction times. The reaction was completed within 1-2 min with yield of 92.60-68.71%. Thermodynamic justification for faster reaction rate under microwave could be explained by the works of Gude *et al.* (2013) who established, by Arrhenius equation, that the reaction rate under microwave was 1000 fold higher than that from conventional heating approach. According to microwave synthetic approach, the 6-chloro substituted 3-acetylcoumarin reacted vigorously with 3-hydrazinoquinoxalin-2(1H)-one to give 12 in high yield (91.00%) followed by 6-bromo substituted 3-acetylcoumarin to give 86.00% of 11. The un-substituted 3-acetylcoumarin, upon treatment with 3-hydrazinoquinoxalin-2(1H)-one gave 84.00% of 10 while 6-methyl substituted 3-acetyl coumarin condensed with 3-hydrazinoquinoxalin-2(1H)-one to afford 13 in 73.20% which is the lowest yield of all the hydrazones 10-13 (Table 1). All the Schiff bases were herein obtained in higher yields under high thermal condition in microwave reactor. This was contrary to the observation of Bhagat *et al.* (2013) who reported that salicylaldehyde-based Schiff bases synthesis under thermal conditions led to lower yields with tedious work-up. The nature of solvent used and the heteroaromatic nucleus present in the coumarin Schiff base might have contributing effect in this regard. On the other hand, the utilization of conventional method by heating under reflux, instead of microwave assisted approach, resulted in the yields

Table 2: Physico-chemical properties of synthesized compounds 1-13

Comp code	Molecular formular	Mole. Wt.	Melting point (°C)	R_{fa}	Elemental analysis calcd (%) (found %)		
					C	H	N
1	$C_{11}H_8O_3$	188.18	122-123	0.71[b]	70.21 (70.10)	4.29 (4.41)	-
2	$C_{17}H_{12}BrNO_2$	342.19	117-118	0.66[b]	59.67 (59.81)	3.53 (3.66)	4.09 (3.89)
3	$C_{17}H_{12}N_2O_4$	308.29	107-109	0.53[b]	66.23 (66.11)	3.92 (3.79)	9.09 (9.18)
4	$C_{17}H_{12}ClNO_2$	297.74	105-106	0.47[b]	68.58 (68.73)	4.06 (4.21)	4.70 (4.56)
5	$C_{18}H_{14}BrNO_2$	356.21	95-96	0.44[b]	60.69 (60.83)	3.96 (3.78)	3.93 (3.77)
6	$C_{18}H_{14}BrNO_2$	356.21	114-115	0.50[b]	60.69 (60.88)	3.96 (4.02)	3.93 (3.81)
7	$C_{18}H_{14}BrNO_2$	356.21	109-110	0.56[b]	60.69 (60.54)	3.96 (3.87)	3.93 (4.04)
8	$C_{17}H_{13}NO_2$	263.29	117-119	0.50[b]	77.55 (77.72)	4.98 (5.05)	5.32 (5.17)
9	$C_{12}H_{11}NO_2$	201.22	114-116	0.53[b]	71.63 (71.72)	5.51 (5.42)	6.96 (6.74)
10	$C_{19}H_{16}N_4O_3$	348.36	238-241	0.58[c]	65.90 (65.94)	4.05 (4.08)	16.18 (16.21)
11	$C_{19}H_{13}BrN_4O_3$	425.24	265-266	0.71[c]	53.65 (53.66)	3.06 (3.08)	13.18 (13.21)
12	$C_{19}H_{13}ClN_4O_3$	380.78	245-246	0.73[c]	59.92 (59.90)	3.42 (3.39)	14.72 (14.70)
13	$C_{20}H_{16}N_4O_3$	360.37	183-185	0.59[c]	66.67 (66.68)	4.44 (4.47)	15.56 (15.59)

[a]: Eluting solvent system, [b]: $CHCl_3:CH_3OH$ (9:1, v/v), [c]: $CH_3COCH_3:C_6H_6$ (1:9, v/v), Comp code: Compound code, Mol. Wt.: Molecular weight and Calcd (%): Percentage calculated

of 70.20 to 14.14% over several minutes (150-210 min), except for the 3-acetylcoumarin which was obtained in 91.50% yield within 15 min (Table 1).

Furthermore, the structural elucidation of the imino product was confirmed by using product 3-[1-(4-chlorophenylimino) ethyl] 2H-chromen-2-one 4, as the main representative. In a nutshell, the ^{1}H-NMR spectrum of 4 in deuteriated DMSO showed a 3H singlet at δ of 2.12 ppm while two proton doublet of aromatic resonated at δ of 7.02-7.04 with coupling constant of 8.00 Hz and at δ of 7.45-7.47 ppm with coupling constant of 8.10 Hz. The multiplet at δ of 7.44-7.88 ppm was due to the presence of four aromatic benzenoid protons while the singlet with chemical shift δ 8.14 ppm was as a result of the hetero ring system of coumarin. This deshielded downfield resonance of the aromatic protons experienced herein corroborated the conformational properties of aromatic multi-layered compounds documented by Kudo and Tanatani (2015). The ^{13}C-NMR spectrum of 4 showed the presence of seventeen carbon atoms which is in agreement with the proposed structure of 4. The lowest carbon resonated at 19 ppm (CH_3) while the highest carbon was that of carbonyl of lactone at δ 175.7 ppm, which correlated well with the earlier reported value from Al-Kawkabani et al. (2013) who investigated the synthesis of novel 2H,8H-pyrano[2,3-f]chromene-2,8-dione based scaffolds under tandem knoevenagel condition. The result of the electronic transition of uv-visible spectrum of 4 in methanol gave rise to wavelength (λ_{max}) ranging from 209-338 nm. The first wavelength (λ_{max} = 209 nm) for compound 4 was as a result of π→π* transition indicating the presence of C = C of aromatic protons whereas the bathochromic shift observed at the highest wavelength in 4 (λ_{max} = 338 nm) was as a result of π→n transition which may be

ascribed to the chromophoric C = N group; characteristic of K bands of C = N functional group (Komurcu et al., 1995). According to the IR spectrum of 4, the absorption bands at 2723 cm^{-1} and 1612 cm^{-1} depicted the presence of CH aliphatic and C = C aromatic, respectively. The C = O of ester absorbed at 1745 cm^{-1} and doubly confirmed by a C-O bending vibration at 1376 cm^{-1}. The carbonyl frequency herein reported (1745 cm^{-1}) was further confirmed by comparing it with the findings of Lewis et al. (1994) who documented the various C = O stretching absorption vibration frequencies in infrared spectra to range between 1685-1748 cm^{-1}. In addition, the frequencies at the fingerprint regions 756 and 723 cm^{-1} were due to the presence of C-Cl and Ar-H aromatic bending respectively. The molecular ion peak m/z 297.91 correlated well with the molecular mass of 4 and the base peak was found at m/z 261.49 which was as a result of M-Cl fragmentation pattern. The mass spectrum of 4 was also characterized by the occurrence of some daughter fragments at m/z 246.48, 172.11, 119.13, 112.17 and 74.22 with the intensities of 44.60, 10.20, 27.30, 19.10 and 12.10%, respectively.

The result of the physical parameters such as molecular formular, molecular weight, melting point R_f as well as the elemental analysis are as shown in Table 2. In detail, the molecular weight of the compound ranged from 188.18 (for 1) to 425.24 g mol^{-1} (for 11), while the melting point of the compounds varied between 95-96°C for imino compound 5 to 265-266°C for hydrazone 11. Coincidentally, the compound 11 with the highest molecular weight has the highest melting point. The progress of the reaction was monitored by Thin Layer Chromatography (TLC) spotting using suitable eluting solvent system as presented in Table 2. The R_f values were duly calculated from the spots and were
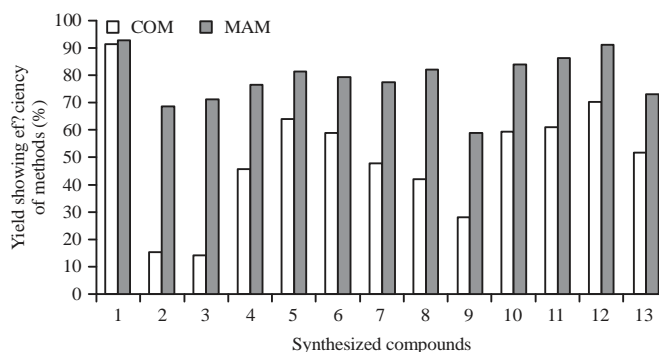
Gursoy, A. and N. Karali, 2003. Synthesis, characterization and primary antituberculosis activity evaluation of 4-(3-coumarinyl)-3-benzyl-4-thiazolin-2-one benzylidenehydrazones. Turk. J. Chem., 27: 545-552.

Jayashree, B.S., S. Arora and Y. Nayak, 2008. Antioxidant analgesic and anti-inflammatory activities of some selected heteroaryl substituted coumarins. Pharmacologyonline, 2: 404-410.

Komurcu, S.G., S. Rollas, M. Ulgen, J.W. Gorrod and A. Cevikbas, 1995. Evaluation of some arylhydrazones of *p*-aminobenzoic acid hydrazide as antimicrobial agents and their *in vitro* hepatic microsomal metabolism. Bollettino Chimico Farmaceutico, 134: 375-379.

Kontogiorgis, C.A., K. Savvoglou and D.J. Hadjipavlou-Litina, 2006. Antiinflammatory and antioxidant evaluation of novel coumarin derivatives. J. Enzyme Inhibition Med. Chem., 21: 21-29.

Kotali, A., I.S. Lafazanis, A. Papageorgiou, E. Chrysogelou, T. Lialiaris and Z. Sinakos, 2008. Synthesis, characterization and antileucemic activity of 7-hydroxy-8-acetylcoumarin benzoylhydrazone. Molbank. 10.3390/M574

Kudo, M. and A. Tanatani, 2015. Conformational properties of aromatic multi-layered and helical oligoureas and oligoguanidines. New J. Chem., 39: 3190-3196.

Lacy, A. and R. O'Kennedy, 2004. Studies on coumarins and coumarin-related compounds to determine their therapeutic role in the treatment of cancer. Curr. Pharamaceut. Des., 10: 3797-3811.

Lewis, R.N., R.N. McElhaney, W. Pohle and H.H. Mantsch, 1994. Components of the carbonyl stretching band in the infrared spectra of hydrated 1,2-diacylglycerolipid bilayers: A reevaluation. Biophys. J., 67: 2367-2375.

Lisgarten, J.N., B.S. Potter, J. Aymami, H. Oketch-Rabah and R.A. Palmer, 2003. Crystal structure and conformation of the antimalarial drug 5,7-methoxy-8-(3-methyl-1-buten-3-ol)-coumarin. J. Chem. Crystallogr., 33: 149-153.

Lu, Z.Y., T.S. Yuan, Y.L. Chen, X.Q. Wei, W.G. Zhu and M.G. Xie, 2002. Synthesis of a novel blue-light-emitting polymer material bearing coumarin pendants. Chin. Chem. Lett., 13: 674-677.

Luszczki, J.J., M. Andres-Mach, W. Cisowski, I. Mazol, K. Glowniak and S.J. Czuczwar, 2009. Osthole suppresses seizures in the mouse maximal electroshock seizure model. Eur. J. Pharmacol., 607: 107-109.

Lutz, C., T.S. Otis, V. DeSars, S. Charpak, D.A. DiGregorio and V. Emiliani, 2008. Holographic photolysis of caged neurotransmitters. Nat. Methods, 5: 821-827.

Mateeva, N.N., R.N. Kode and K.K. Redda, 2002. Synthesis of novel flavonoid derivatives as potential HIV-integrase inhibitors. J. Heterocyclic Chem., 39: 1251-1258.

Montagner, C., S.M. de Souza, C. Groposoa, F.D. Monache, E.F. Smania and A. Smania Jr., 2008. Antifungal activity of coumarins. Zeitschrift Naturforschung C, 63: 21-28.

Nechifor, M., 2009. Synthesis and properties of some aromatic polyamides with coumarin chromophores. React. Funct. Polym., 69: 27-35.

Neyts, J., E. De Clercq, R. Singha, Y.H. Chang and A.R. Das *et al.*, 2009. Structure-activity relationship of new anti-hepatitis C virus agents: Heterobicycle-coumarin conjugates. J. Med. Chem., 52: 1486-1490.

Nicolaou, K.C., J.A. Pfefferkorn, A.J. Roecker, G.Q. Cao, S. Barluenga and H.J. Mitchell, 2000. Natural product-like combinatorial libraries based on privileged structures. 1. General principles and solid-phase synthesis of benzopyrans. J. Am. Chem. Soc., 122: 9939-9953.

Pangal, A., J.A. Shaikh, G. Muiz, V. Mane and K. Ahmed, 2013. Novel 3-acetylcoumarin Schiff's base synthesis from different acid hydrazide. Int. Res. J. Pharm., 4: 108-110.

Rabtti, E.M.A., M.M. Natic, D.M. Milojkovic-Opsenica, J.D. Trifkovic, I.M. Vuckovic, V.E. Vajs and Z.L. Tesic, 2012. RP TLC-based lipophilicity assessment of some natural and synthetic coumarins. J. Braz. Chem. Soc., 23: 522-530.

Roma, G., M. Di Braccio, G. Grossi, D. Piras and G. Leoncini *et al.*, 2007. Synthesis and *in vitro* antiplatelet activity of new 4-(1-piperazinyl)coumarin derivatives. Human platelet phosphodiesterase 3 inhibitory properties of the two most effective compounds described and molecular modeling study on their interactions with phosphodiesterase 3A catalytic site. J. Med. Chem., 50: 2886-2895.

Ryu, B.J., E.J. Cho and K.C. Nam, 2007. Synthesis and metal binding properties of anthraquinone bridged with coumarin. Bull. Korean Chem. Soc., 28: 1585-1587.

Satyanarayana, V.S.V., P. Sreevani, A. Sivakumar and V. Vijayakumar, 2008. Synthesis and antimicrobial activity of new Schiff bases containing coumarin moiety and their spectral characterization. Arkivoc, 17: 221-233.

Scott, B.J., G. Wirnsberger and G.D. Stucky, 2001. Mesoporous and mesostructured materials for optical applications. Chem. Mater., 13: 3140-3150.

Siddiqui, Z.N., M. Asad and S. Praveen, 2008. Synthesis and biological activity of heterocycles from chalcone. Med. Chem. Res., 17: 318-325.

Singh, K., M.S. Barwa and P. Tyagi, 2006. Synthesis, characterization and biological studies of Co(II), Ni(II), Cu(II) and Zn(II) complexes with bidentate Schiff bases derived by heterocyclic ketone. Eur. J. Med. Chem., 41: 147-153.

Trenor, S.R., A.R. Shultz, B.J. Love and T.E. Long, 2004. Coumarins in polymers: From light harvesting to photo-cross-linkable tissue scaffolds. Chem. Rev., 104: 3059-3078.

Vahabi, V. and F. Hatamjafari, 2014. Microwave assisted convenient one-pot synthesis of coumarin derivatives via pechmann condensation catalyzed by FeF$_3$ under solvent-free conditions and antimicrobial activities of the products. Molecules, 19: 13093-13103.

Witaicenis, A., L.N. Seito and L.C. Di-Stasi, 2010. Intestinal anti-inflammatory activity of esculetin and 4-methylesculetin in the trinitrobenzenesulphonic acid model of rat colitis. Chemico-Biological Interactions, 186: 211-218.

Yavari, I., H. Djahaniani and F. Nasiri, 2006. The crystal structure of *tert*-butyl coumarin-3-carboxylate. J. Iran. Chem. Soc., 3: 46-50.

Zhang, T., Z. Yan, Y.F. Li and N. Wang, 2013. Simplified aminocoumarin analogues as anticancer agents: Amino isosteric replacement in the noviose moiety resulted in substantial enhancement of antiproliferative activity. Chin. Chem. Lett., 24: 719-722.