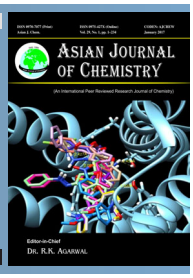
Asian Journal of Chemistry; Vol. 29, No. 1 (2017), 187-190

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2017.20249



Synthesis and Biological Studies of Novel Coumarin Derivatives Comprising Azo Functional Group

K. BABU[1] and K. THARINI[2,*]

[1]PG and Research Department of Chemistry, Rajah Serfoji Government College (Autonomous), Thanjavur-613 005, India
[2]PG and Research Department of Chemistry, Government Arts College, Tiruchirappalli-620 022, India

*Corresponding author: E-mail: kbabu.chemistry@gmail.com

Received: 17 August 2016; *Accepted*: 26 September 2016; *Published online*: 29 October 2016; AJC-18124

Some novel coumarin derivatives have been synthesized by diazotization of 4-aminoacetophenone and subsequent coupling reaction with salicylaldehyde and further treatment of obtained product with various active methelene compounds. The structures of compounds are confirmed by IR, NMR, GC-MS spectra and evaluated their antimicrobial activity by using disc diffusion method.

Keywords: 4-Aminoacetophenone, Diazotization, Claisen-Schmidt reaction, Malanonitrile.

INTRODUCTION

Coumarins derivatives are one of the most important families of heterocyclic compounds and present in various natural products. They have been widely used as starting materials and intermediates in the synthetic organic chemistry. Most of the coumarin derivatives are used in pharmaceutical, perfumery and agrochemical industries for various purposes [1-8]. Furthermore, these compounds also used as fluorescent brighteners, efficient laser dyes, additives in food and cosmetics [9-12]. In view of versatile application of coumarin analogs and in continuation of previous studies towards heterocyclic compounds [13-15], herein we focused on the design of some novel coumarin derivatives in order to examine their biological activities.

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Paragon 1000 FTIR spectrophotometer as potassium bromide discs. ^{1}H NMR spectra were obtained on a Brucker (400 MHz) instrument in $CDCl_3$ solutions using tetramethylsilane as an internal standard. *J* Values are given in Hz. Mass spectra were obtained at the Indian Institute of Chemical technology, Hyderabad, India. All the basic chemicals were purchased from Merck (India), S.D. Fine Chemicals (India).

Preparation of 1-[4-(chlorodiazenyl)phenyl]ethanone (2): A suspension of 4-nitroaniline (5.52 g, 40 mmol) in hydrochloric acid (36 mL) and water (16 mL) was heated to 70 °C until complete dissolution. The clear solution was poured into ice water, which was diazotized below 5 °C with sodium nitrite (2.8 g, 40 mmol) dissolved in water (10 mL) for 20-30 min.

Synthesis of 5-[(4-acetylphenyl)diazenyl]-2-hydroxybenzaldehyde (4): The cold diazonium solution (**2**) obtained from above step was added over the course of 30 min at 0-5 °C to a solution of salicylaldehyde (**3**) (4.26 mL, 40 mmol) in water (75 mL) containing sodium hydroxide (1.6 g) and sodium carbonate (14.8 g). During the addition process solid was formed, the solution was vigorously stirred to complete the reaction. After complete addition, small amount of urea was added to decompose the unreacted nitrous acid. The product was collected by vacuum filtration, washed with NaCl solution and finally dried. The pure product was obtained by recrystallization of crude sample in ethanol. Yield: 87 %, m.p.: 150-152 °C, R_f: 0.60, IR (KBr, cm^{-1}): 3423.12, 3242.55, 2859.26, 1699.49, 1599.01,1262.12, 735.66; ^{1}H NMR ($CDCl_3$, δ ppm): 2.67 (s, 3H, $COCH_3$), 7.13-7.16 (d,1H, Ar-H), 7.94-8.26 (m, 6H, Ar-H), 10.05 (s, 1H, OH), 11.41 (s, 1H, CHO), ^{13}H NMR ($CDCl_3$, δ ppm), 29.70 ($COCH_3$), 113.38, 114.73, 116.66, 118.00, 119.72, 123.10, 123.58, 123.74, 124.57, 124.72, 125.44, 126.39.

General procedure for synthesis of novel coumarin derivatives (5a-e): A mixture of 5-[(4-acetylphenyl)diazenyl]-2-hydroxybenzaldehyde (**1a-1g**) and ethylacetoacetate/ethylcyanoacetate/diethylmalonate/malaononitrile/acetylacetone in 0.01 mol, 1:1 ratio was taken in pestle and mortar. This mixture was grinded up to 30 min in presence of few drops of piperidine at room temperature. During the reaction progress heat was generated, the solid material turn into liquid and finally solid formed. The mixture was cooled and poured into ice cold water

and stirred vigorously. The precipitated compound was filtered, dried and recrystallized from ethanol.

3-Acetyl-6-[(4-acetylphenyl)diazenyl]-2H-chromen-2-one (5a): Yield: 94 %, m.p.: 128-130 °C, R_f: 0.60, IR (KBr, cm^{-1}): 3430.77, 3050.41, 1744.05, 1681.42, 1606.75, 1359.65, 1267.01, 843.57; ^{1}H NMR ($CDCl_3$, δ ppm): 2.68 (s, 3H, $COCH_3$), 2.76 (s, 3H, $COCH_3$), 7.51-7.54 (d, 1H, Ar-H), 7.92-8.02 (m, 6H, Ar-H), 8.12-8.15 (d, 2H, Ar-H) 8.62 (s, 1H, CH=C), ^{13}C NMR ($CDCl_3$, δ ppm), 29.38 ($COCH_3$), 29.64 ($COCH_3$), 113.43 (CH=C), 114.04, 115.74, 120.338, 127.66, 128.92, 129.97, 130.75, 131.68, 131.93, 132.18, 145.73, 153.04 (12Ar-C), 186.64 (COO), 196.48 (CO).

6-[(4-Acetylphenyl)diazenyl]-2-imino-2H-chromene-3-carbonitrile (5b): Yield: 92 %, m.p.: 144-146 °C, R_f: 0.64, IR (KBr, cm^{-1}): 3415.85, 3334.53, 2192.29, 1652.25, 1606.707, 1419.56, 842.73; ^{1}H NMR ($CDCl_3$, δ ppm): 2.70 (s, 3H, $COCH_3$), 7.71 (s, 1H, Ar-H), 7.88-8.40 (m, 6H, Ar-H), 8.41 (s, 1H, CH=C), ^{13}C NMR ($CDCl_3$, δ ppm), 26.6 ($COCH_3$), 117.91 (CH=C) 120.09 (C-CN), 122.17, 122.48, 127.42, 128.76, 129.37, 131.22, 140.69, 144.63, 145.09, 153.81, 163.49, 194.76.

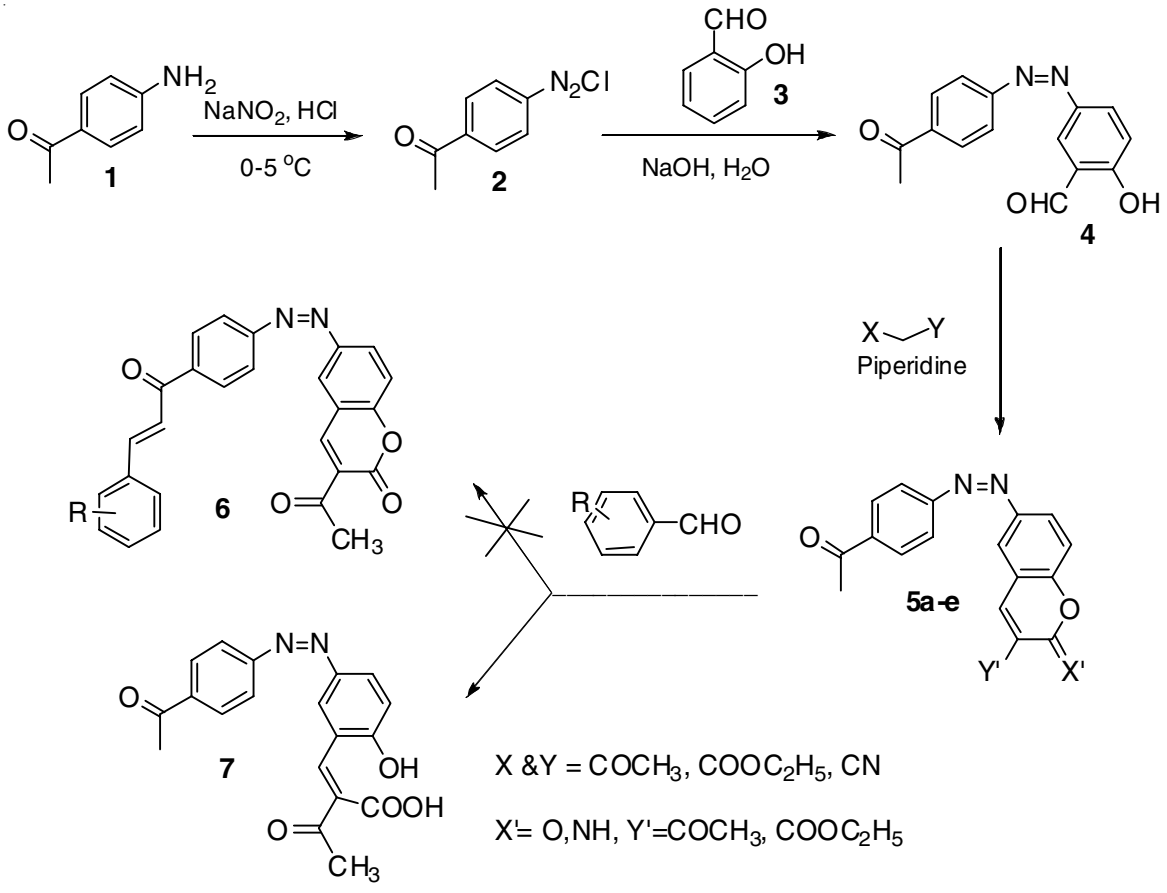
Ethyl 6-[(4-acetylphenyl)diazenyl]-2-imino-2H-chromene-3-carboxylate (5c): Yield: 85 %, m.p.: 140-142 °C, R_f: 0.65, IR (KBr, cm^{-1}): 3434.30, 3295.53, 2982.58, 1737.40, 1687.89, 1639.69, 1531.27, 1215.53, 844.22., ^{1}H NMR ($CDCl_3$, δ ppm): 1.42-1.44 (t, 3H, CH_3), 2.58 (s, 3H, $COCH_3$), 4.33-4.35 (q, 2H, CH_2), 7.45-7.48 (d, 2H, Ar-H), 7.99-8.02 (d, 2H, Ar-H), 8.22-8.47 (m, 3H, Ar-H) 8.83 (s, 1H, CH=C), 11.70 (NH); ^{13}C NMR ($CDCl_3$, δ ppm), 14.04 (CH_3), 26.85 ($COCH_3$), 60.15 (CH_2), 115.35 (CH=C), 117.11, 120.95, 121.94, 122.84, 123.87, 124.21, 125.08, 129.40, 138.42, 149.18, 154.73, 164.64, 165.00, 197.48.

Ethyl 6-[(4-acetylphenyl)diazenyl]-2-oxo-2H-chromene-3-carboxylate (5d): Yield: 90 %, m.p.: 148-150 °C, R_f: 0.60, IR (KBr, cm^{-1}): 3423.08, 3242.42, 2859.24, 1699.35, 1599.01, 1262.00, 735.52; ^{1}H NMR ($CDCl_3$, δ ppm): 1.42-1.44 (t, 3H, CH_3), 2.59 (s, 3H, $COCH_3$), 4.32-4.34 (q, 2H, CH_2), 7.45-7.48 (d, 2H, Ar-H), 7.99-8.02 (d, 2H, Ar-H), 8.22-8.45 (m, 3H, Ar-H) 8.82 (s, 1H, CH=C), ^{13}C NMR ($CDCl_3$, δ ppm), 12.10 (CH_3), 29.72 ($COCH_3$), 54.71 (CH_2), 99.32 (CH=C), 120.63, 125.24, 127.40, 128.02, 128.11, 129.14, 129.63, 131.88, 132.34, 136.77, 150.00, 160.00, 198.28.

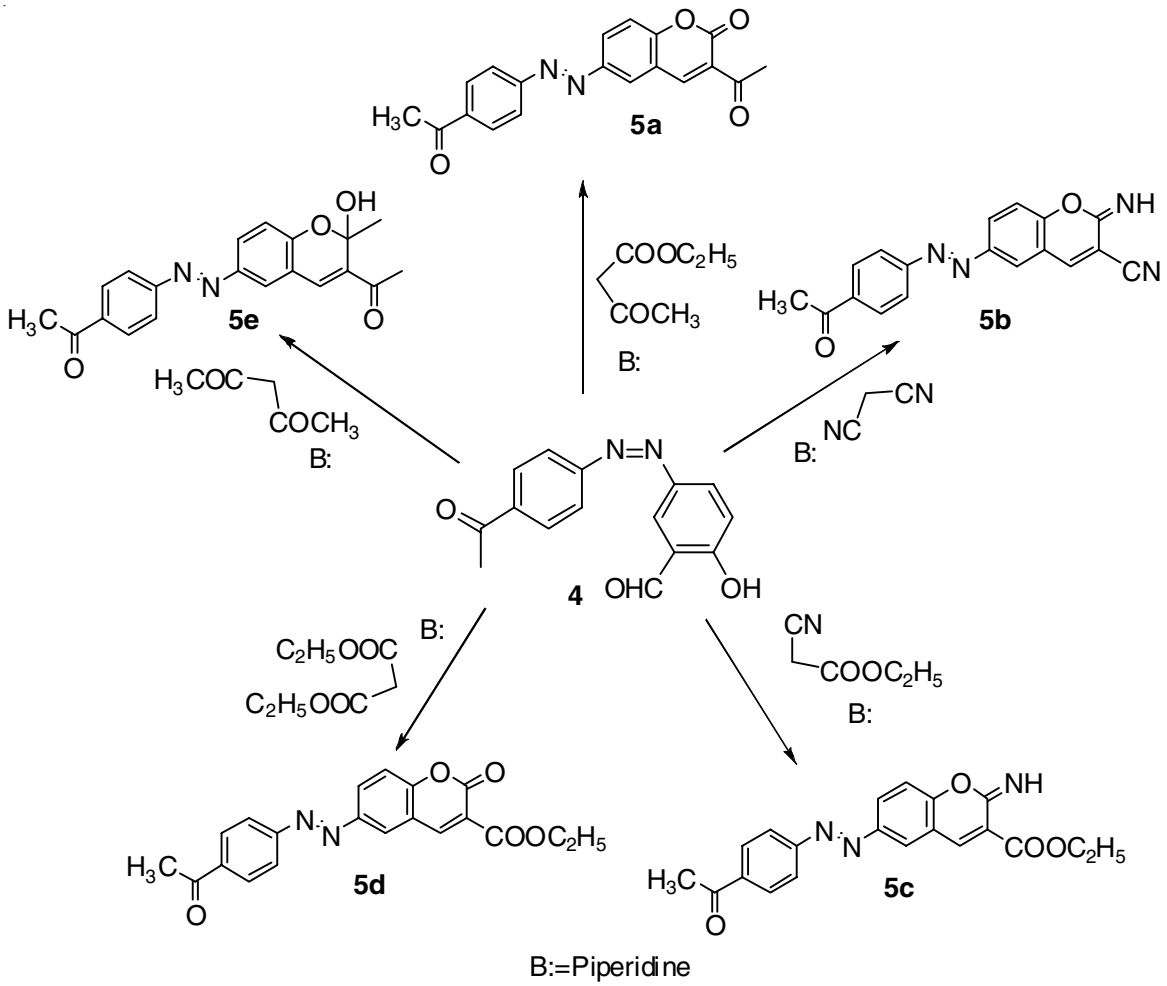
1-[4-{(3-Acetyl-2-hydroxy-2-methyl-2H-chromen-6-yl)-diazenyl}phenyl]ethanone (5e): Yield: 96 %, m.p.: 132-134 °C, R_f: 0.62, IR (KBr, cm^{-1}): 3430.77, 3050.41, 1744.05, 1681.42, 1606.75, 1359.65, 1267.01, 843.57; ^{1}H NMR ($CDCl_3$, δ ppm): 1.89 (CH_3), 2.54 (s, 3H, $COCH_3$), 2.76 (s, 3H, $COCH_3$), 4.78 (OH), 7.11-7.14 (d, 1H, Ar-H), 7.53 (s, 1H, Ar-H), 7.93-8.10, (d, 2H, Ar-H), 8.30 (s, 1H, CH=C); ^{13}C NMR ($CDCl_3$, δ ppm), 24.26 ($2COCH_3$), 26.50 (CH_3), 102.10 (CH=C), 115.74, 120.26, 122.30, 128.06, 128.45, 128.98, 129.41, 130.41, 143.67, 153.80, 163.73, 193.74 (CO).

RESULTS AND DISCUSSION

This work explains about synthesis of some novel coumarin derivatives by using following synthetic steps. The product **4** obtained by diazotization of *p*-aminoacetophenone (**1**) into 1-[4-(chlorodiazenyl)phenyl]ethanone (**2**) which further coupled with salicylaldehyde (**3**). The compound **4** involved condensation



Scheme-I



Scheme-II

TABLE-1
ANTIMICROBIAL ACTIVITY DATA OF NOVEL COUMARIN DERIVATIVES (**5a-e**)

Sample	Zone of inhibition (mm in diameter)				
	Bacillus subtilis	*Staphylococcus aureus*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Aspergillus niger*
PC*	15	20	24	20	06
C	-	-	-	-	_
5a	14	15	12	16	_
5b	13	14	12	14	_
5c	14	16	14	20	_
5d	15	18	15	14	_
5e	14	15	14	13	15

reactions with various active methelene compounds (ethylacetoacetate, ethylcyanoacetate, acetylacetone, malanonitrile and diethyl-malonate) produced corresponding coumarin derivatives (**5a-e**). Actually, we planned to synthesize chalcone (**6**) from product **5a-e** in order to make some heterocyclic compounds but unfortunately product **7** was formed. The synthetic route of compounds **5a-e** are given in **Schemes I** and **II**.

The physical data as well as UV-visible, FT-IR, ^{1}H NMR and ^{13}C NMR spectral data confirmed formation of the desired products. All the synthesized compounds showed good activity against selective bacteria than the fungus (Table-1).

Conclusion

A new series of coumarin derivatives were successfully synthesized and structure of these compounds proposed with help of various spectroscopic techniques such as UV-visible, FT-IR, ^{1}H NMR, ^{13}C NMR and GC-MS techniques. The *in vitro* antimicrobial activities of these compounds examined and most of the compounds showed more active against selective bacterial and fungal pathogens.

REFERENCES

1. O. Kennedy and R. Zhorenes, in eds.: R. O'Kennedy and R.D. Thornes, Coumarins: Biology, Applications and Mode of Action; John Wiley & Sons: Chichester, UK (1997).
2. P. Chiu, L.T. Leung and C.B.B. Ko, *Nat. Prod. Rep.*, **27**, 1066 (2010).
3. (a) V. Boucard, G. Broustal and J.M. Campagne, *Eur. J. Org. Chem.*, 225 (2007); (b) G.J. Florence, N.M. Gardner and I. Paterson, *Nat. Prod. Rep.*, **25**, 342 (2008).
4. D. Jansone, L. Leite, M. Fleisher, J. Popelis, I. Mazheika, E. Lukevics, G. Melikyan and A. Ayetisvan, *Khim. Geterotsikl. Soedin.*, **3**, 298 (1998).

5. L.X. Yang, H.B. Li, X.M. Wu, H. Bai, Q.J. Zhang and Y. Zhao, *Chin. Chem. Lett.*, **16**, 1189 (2005).
6. Y. Dong, K. Nakagawa-Goto, C. Lai, S. Morris-Natschke, K. Bastow and K. Lee, *Bioorg. Med. Chem. Lett.*, **20**, 4085 (2010).
7. B.C. Raju, A.K. Tiwari, J.A. Kumar, A.Z. Ali, S.B. Agawane, G. Saidachary and K. Madhusudana, *Bioorg. Med. Chem.*, **18**, 358 (2010).
8. H.M. Bilgin, M. Atmaca, B.D. Obay, S. Ozekinci, E. Tasdemir and A. Ketani, *Exp. Toxicol. Pathol.*, **63**, 325 (2011).
9. G. Slapsytë, V. Dedonytë, J.R. Lazutka, J. Mierauskienë, V. Morkunas, R. Kazernaviciutë, A. Pukalskas and P.R. Venskutonis, *Molecules*, **18**, 4419 (2013).
10. I. Manolov and N.D. Danchev, *Eur. J. Med. Chem. Chim. Ther.*, **30**, 531 (1995).
11. Z.M. Nofal, M.I. El-Zahar and S.S. Abd El-Karim, *Molecules*, **5**, 99 (2000).
12. L. Raev, E. Voinov, I. Ivanov and D. Popov, *Pharmazie*, **45**, 696 (1990).
13. K. Babu, D. Selvi and P. Pitchai, *Der Pharma Chemica*, **7**, 89 (2015).
14. K. Babu, P. Pitchai and R.M. Gengan, *J. Chem. Pharm. Res.*, **7**, 275 (2015).
15. K. Babu, P. Pitchai, M. Sathiyaseelan and A. Nepolraj, *Der Pharma Chemica*, **7**, 95 (2015).