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NOTE

A Facile and Efficient Synthesis of 3-(1*H*-Benzimidazol-2-yl)chromen-2-ones

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A facile and efficient synthesis of 3-(1*H*-benzimidazol-2-yl)-chromen-2-ones (**3**) by condensation of chromen-2-one-3-carboxylates (**1**) with *o*-phenylenediamine (**2**) is being reported. The reaction has been done under microwave as well as under conventional conditions. The structures of all the products have been confirmed by spectral and analytical data.

Key Words: Chromen-2-one-3-carboxylate, *o*-Phenylenediamine, N,N-Dimethyl formamide, Polyphosphoric acid.

Coumarin derivatives are reported to cure Alzheimer's disease[1]. Its other derivatives are known to be biologically active compounds, especially for their anti-HIV and antibiotic activities[2-4]. For example, novobiocin is a 2*H*-chromen-2-one derived antibiotic used as a competitive inhibitor of the bacterial ATP binding gyrase B subunit, blocking the negative supercoiling of relaxed DNA[2-4]. The coumarin ring is a common constituent of bioactive compounds such as calanolides[5] and lipid lowering agents[6]. Recent studies have revealed that coumarin and its derivatives exhibit several other medicinal applications[7], such as antifungals[8], ACE inhibitors[9], antibacterials[10] and antitubercular agents[11].

Compounds bearing benzimidazole moiety are reported to possess a number of interesting biological activities such as antiulcer[12], antihypertensive[12], antiviral[12], antifungal[12] and anticancer[12]. They are also reported to possess antitubercular[13], antiallergic[14], antioxidant[15], antimicrobial[16] and *in vitro* anti-HIV-1[17]. As these two moieties are associated with a broad range of biological activities, here we wish to report a facile and efficient synthesis of compounds containing the biologically active chromen-2-one as well as the benzimidazole ring systems under conventional and also under microwave conditions.

Melting points are uncorrected and are determined in open capillary tubes in sulphuric acid bath. TLC was performed on silica gel-G and spotting was done using iodine or UV light. IR spectra were recorded using Perkin-Elmer 1000 instrument in KBr phase, ^{1}H NMR on VARIAN 400 MHz instrument and Mass spectra recorded on Agilent-LC-MS instrument giving only $M^{+\cdot}$ +1 and $M^{+\cdot}$ -1 values. Experiments under microwave irradiation were carried out by using Kenstar domestic microwave oven (MOD: OM-34ECR).

General procedure for the synthesis of 3 (conventional method): A mixture of **1** (0.5 g, 0.01 mol), **2** (0.5 g, 0.01 mol) and freshly prepared polyphosphoric acid (PPA) (10 mL) was heated in oil-bath at 130-140 ºC for 5 h. The progress of the reaction was monitored by TLC. After the complete disappearance of the starting material spot on TLC, the reaction mixture was cooled to room temperature and poured in ice-cold water (100 mL). The separated solid was filtered, thoroughly washed with water and dried to obtain a crude product. It was recrystallized from hexane-chloroform to yield pure **3**.

General procedure for the preparation of polyphosphoric acid: A mixture of phosphorus pentoxide (18 g, 0.03 mol) and *o*-phosphoric acid (9 mL, 0.01 mol) was heated on an oil-bath at 140-150 ºC for 1.5 h, when a thick syrupy liquid consisting of polyphosphoric acid is obtained. This liquid was used as such for condensation reactions.

Compound 3b: IR (KBr, ν_{max}, cm^{-1}): 3255-3021 (OH), 1714 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$/DMSO-d_6): δ 7.11-8.88 (m, complex, 8H aryl protons), 11.9 (s, 1H, hydroxyl proton) 12.4 (s, 1H, NH, proton), Mass: m/z 279 ($M^{+\cdot}$+1): Elemental analysis ($C_{16}H_{10}N_2O_3$), C. 69.07, H. 3.26; N. 10.07. Found. C. 70.9, H. 3.28; N. 10.11.

Compound 3c: IR (KBr, ν_{max}, cm^{-1}): 1714 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$/DMSO-d_6): δ 4.35 (S, 3H, methoxy protons) and 7.11-8.88 (m, complex, 8H aryl protons) and 11.88 (s, 1H, NH, proton), Mass: m/z 293 ($M^{+\cdot}$+1). Elemental

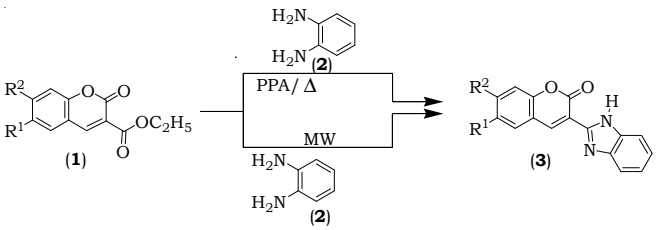
analysis ($C_{17}H_{12}N_2O_3$), C. 69.87, H. 4.14; N. 9.58. Found. C. 70.21, H. 4.18; N. 9.88.

Compound 3d: IR (KBr, ν_{max}, cm^{-1}): 1714 (C=O). ^1H NMR (400 MHz, $CDCl_3$/DMSO-d_6): δ 7.11-8.88 (m, complex, 7H aryl protons) and 12.2 (s, 1H, NH, proton), Mass: m/z 331 ($M^{+\cdot}$+1). Elemental analysis ($C_{16}H_{10}N_2O_2Cl_2$), C. 58.03, H.2.43; N. 8.46. Found. C. 59, H. 2.88; N. 9.12.

Preparation of 3 by microwave irradiation (MWI) technique: A mixture of **1** (0.01 mol) and **2** (0.01 mol) in dry DMF (10 mL) was taken in a 50 mL Erlenmeyer flask and subjected to microwave irradiation in domestic microwave oven at 450 W level for a period of 5 min. The completion of reaction was monitored by TLC. The reaction mixture was cooled to room temperature and poured into ice-cold water (50 mL). The separated solid was filtered, washed with water and dried to obtain crude **3**. It was recrystallized from hexane-chloroform to obtain pure **3**.

Reaction of chromen-2-one-3-carboxylate[18] (**1a**, *i.e.*, **1**, $R^1 = R^2 = H$), with *o*-phenylenediamine (**2**), in hot polyphosphoric acid (PPA), for 5 h, gave a product which has been characterized as 3-(1*H*-benzimidazol-2-yl)-chromen-2-one (**3a**, *i.e.*, 3, $R^1 = R^2 = H$), on the basis of its spectral data. Thus, its IR spectrum in KBr, showed a medium broad band at 3210-2980 cm^{-1} due to NH group and at 1738 cm^{-1} due to lactone C=O group. Its ^1H NMR spectrum in DMSO-d_6/TMS showed signals at δ 7.12-8.88 (complex, m, 9H, aryl protons), 12.38 (s, 1H, NH). Its mass spectrum when recorded in the CI method showed a molecular ion peak at 263 (base peak) corresponding to a molecular mass of 262.

3a (*i.e.*, **3**, $R^1 = R^2 = H$) could also be prepared by an alternative method. Thus, **1a** (*i.e.*, **1**, $R^1 = R^2 = H$) on treating with **2** in N,N-dimethyl formamide (DMF) under microwave condition for 5 min, gave a product identical with **3a** (*i.e.*, **3**, $R^1 = R^2 = H$) in all respects (m.p., m.m.p. and co-TLC analysis) (**Scheme-I**).



Scheme-I

The above reaction of **1a** (*i.e.*, **1**, $R^1 = R^2 = H$), with **2** was found to be a general one, the other compounds namely, 3-(1*H*-benzimidazole-2-yl)-6-hydroxy-chromen-2-one (**3b**, *i.e.*, **3**, R^1 = OH, $R^2 = H$), 3-(1*H*-benzimidazole-2-yl)-6-methoxy-chromen-2-one (**3c**, *i.e.*, **3**, $R^1 = OCH_3$, R = H) and 3-(1*H*-benzimidazol-2-yl)-6,7-dichloro-chromen-2-one (**3d**, *i.e.*, $R^1 = R^2 = Cl$) have been prepared in both the methods. The results are summarized in Table-1. A comparison between the two methods shows that in the microwave technique the reaction time is drastically reduced and the yields are comparable.

TABLE-1
PHYSICAL DATA OF COMPOUNDS **3a-d**

Compd.	R^1	R^2	m.p. (ºC)	Method-A (Conventional)		Method-B (MWI)	
				Yield (%)	Time (h)	Yield (%)	Time (min)
3a	H	H	188	80	4.0	84	3.5
3b	OH	H	210	71	4.5	81	4.0
3c	OCH_3	H	248	68	5.0	80	3.0
3d	Cl	Cl	231	70	5.0	82	3.5

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REFERENCES

1. (a) B. Rajitha, K.M. Rao and P.N. Reddy, *Indian J. Chem.*, **43B**, 417 (2004); (b). J.V. Madhu, V.N. Kumar and B. Rajitha, *Synth. Commun.*, **38**, 1799 (2008).
2. (a) A. Murakami, G. Rao, M. Omura, M. Yano, C. Ito, H. Furukawa, D. Takahashi, K. Koshimizu and H. Ohigashi, *Bioorg. Med. Chem. Lett.*, **10**, 59 (2000); (b) N. Guravaiah and V.J. Rao, *Phosphorus, Sulfur Silicon Rel. Elem.*, **185**, 361 (2010).
3. (a) Y. Xia, Z.-Y. Yang, P. Xia, T. Hackl, E. Hamel, A. Mauger, J.-H. Wu and K.-L. Lee, *J. Med. Chem.*, **44**, 3932 (2001); (b) T. Ara, K.Z. Khan and K. Tasneem, *Synth. Commun.*, **39**, 4416 (2009).
4. Y.-L. Chen, K.-C. Fang, J.-Y. Sheu, S.-L. Hsu and C.-C. Tzeng, *J. Med. Chem.*, **44**, 2374 (2001).
5. T. Yamaguchi, T. Vukuda, F. Vishibashi and M. Iwao, *Tetrahedron Lett.*, **47**, 3755 (2006).
6. G.V.M. Sharma, A. Illangovan, V.L. Narayanan and M.K. Gurjar, *Tetra-hedron Lett.*, **59**, 95 (2003).
7. G.R. Madhavan, V. Balraju, B. Mallesham, R. Chakrabarti and B.B. Lohray, *J. Bioorg. Med. Chem. Lett.*, **13**, 2547 (2003).
8. I.A. Raad, R. Terreux, P. Richomme, E.-L. Matera, C. Dumontet, J. Raybaud and Duilt, *J. Bioorg. Med. Chem.*, **14**, 6979 (2004).
9. G. Redighiero and C. Antonello, *Bull. Chim. Farm.*, **97**, 592 (1958).
10. A.K. Mittal and O.P. Singhal, *J. Indian Chem. Soc.*, **59**, 373 (1982).
11. D.R. Buckle and H. Smith, *J. Med. Chem.*, **18**, 391 (1975).
12. I. Islam, E.B. Skibo and R.T. Dorr, *J. Med. Chem.*, **34**, 2954 (1991).
13. T. Fukuda, T. Saito and S. Tajima, *Arzneim-Forsh./Drug Res.*, **34**, 805 (1984).
14. H. Nakano, T. Inoue and N. Kawasaki, *Chem. Pharm. Bull.*, **47**, 1573 (1999).
15. B. Can-Eke, M.O. Puskullu and M. Iscan, *Chem.-Biol. Internat.*, **65**, 113 (1998).
16. C. Kus, G. Ayhan-Kicigil and M. Iscan, *Arch. Pharm. Res.*, **27**, 156 (2004).
17. F.S.G. Soliman, S.M. Rida and T. Kappe, *Arch. Pharm.*, **317**, 951 (1984).
18. K.D. Gupta, R.M. Chatterjee and K.R. Das, *Indian J. Chem.*, **20B**, 511 (1981).