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Microwave assisted synthesis and characterization of 1-[4-(3-substituted-acryloyl)-phenyl]-pyrrole-2,5-diones

K. Aravind* and A. Ganesh

Department of Chemistry, Osmania University, Hyderabad, India

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ABSTRACT

*A series of 1-[4-(3-Substituted-acryloyl)-phenyl]-pyrrole-2,5-diones**(5a-f)** were synthesized and characterized. All the compound synthesized from 1-(4-Acetyl-phenyl)-pyrrole-2,5-dione**(3)** and substituted benzaldehydes**(4a-f)** by using Claisen-Schmidt Condensation reaction under conventional heating method and microwave irradiation methods. All the compoundswere characterized based on spectroscopic analysis such as IR, ^{1}H-NMR and Mass spectral data.*

Keywords: 1-(4-Acetyl-phenyl)-pyrrole-2,5-dione, Claisen-Schmidt Condensation, microwave irradiation, Chalcones.

INTRODUCTION

Chalcones are widely distributed in nature and are known to have multipronged activity, they exhibit wide spectrum of biological activities, such as antibacterial [1], antifungal [2], anti-inflammatory [3], antipyretic [4], antiinvasive [5], antiproliferatine [6] and antitumor [7] activities. A number of chalcone derivatives, have also been found to inhibit several important enzymes in cellular systems, including xanthine oxidase [8], aldose reductase [9], epoxide hydrolase [10], protein tyrosine kinase [11] and quinone reductase [12]. Chalcones and their analogues are especially important starting materials or intermediates for the synthesis of naturally occurring flavonoids [13], flavones, flavanonse, aurones and various nitrogen-containing heterocyclic compounds. Derivatives of maleic anhydride and maleimide are a class of organic compounds with numerous applications in synthetic chemistry [14]. A search of the literature revealed that some *N*-substituted maleimides have important biological properties, such as antimicrobial activity [15] and antitumor activity [16]. As part of our research aims to synthesized new compounds with improve biological activities. Recently several structurally interesting compounds with substituted maleic anhydride and maleimide moieties have been isolated as bioactive compounds.

MATERIALS AND METHODS

Melting points were determined on THOMAS-HOOVER melting point apparatus & they were uncorrected. All the required chemicals used were obtained from Aldrich chemicals. Each reaction was monitored by thin layer chromatography (TLC) using appropriate solvent system, which was selected by trial & error method on silica gel precoated TLC plates obtained from E. Merk. All the NMR spectra were recorded on a BRUKER 300 NMR Spectrometer in DMSO-D_6 solvent system. Chemical shifts (δ) were reported relative to TMS as an internal standard on the δ scale. Infra-red spectroscopy (IR) spectra were determined on SCHIMADZU FT-IR instrument by

potassium bromide (KBr). All the mass spectra were obtained in a suitable solvent & they were reported in *m/z* value as a molecular ion peak.

Scheme-I: Synthesis of Pyrrole-2,5-dione Substituted chalcones(5a-f):

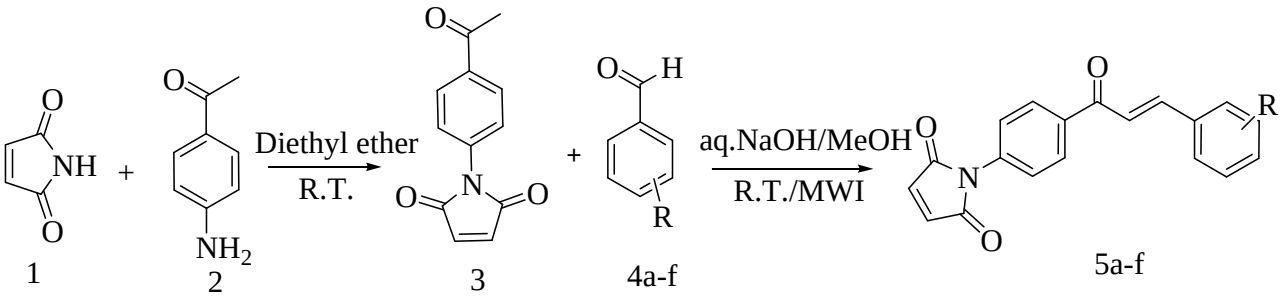

Table-1: Physical data of 1-[4-(3-Substituted-acryloyl)-phenyl]-pyrrole-2,5-diones (5a-f):

S.No	Compds.	M.P. (°C)	Reaction time		Yield	
			Conventional (hr)	MWI (min)	Conventional	MWI
5a	Phenyl	197-199	8	4	62	84
5b	4-Methyl phenyl	178-180	7	4	68	86
5c	4-Methoxy phenyl	165-167	7	3	71	90
5d	4-Chloro phenyl	176-178	8	5	67	84
5e	4-Bromo phenyl	167-169	8	5	66	84
5f	4-Nitro phenyl	200-202	8	4	58	80

RESULTS AND DISCUSION

The starting compound 1-(4-acetyl-phenyl)-pyrrole-2,5-dione**(3)**, is precursor for the preparation of the1-[4-(3-Substituted-acryloyl)-phenyl]-pyrrole-2,5-diones**(5a-f)**, was obtained by a reaction involving maleic anhydride**(1)** and 4-Aminoacetophenone**(2)** in diethyl ether. The final target compounds synthesized by condensation of 1-(4-acetyl-phenyl)-pyrrole-2,5-dione**(3)** and substituted benzaldehydes**(4a-g)** in the presence of alkali. This reaction carried out two different methods, conventional heating method and microwave irradiation method. In recent years, there is an increasing interest in the use of microwave-induced rate acceleration technologyin organic synthesis in view of the mild, clean, convenient, greater selectivity, easier workup, spontaneity of the reaction process in comparison to the conventional solution phase reactions and the associated ease of manipulation. It is of note that this technique offers an environmentally friendly process of organic synthesis.The structures were established through IR, ^{1}H NMR, Mass spectrometry. IR spectrum of the compound **5a** showed a characteristic peak at 1662 cm^{-1} confirming the presence chalcones part of carbonyl group. The ^{1}H NMR of Compound **5a** represented two doublets at δ 7.78 - 7.82 and δ 7.98 - 8.02 for H_α proton and H_β proton. In the mass spectrum of the compound molecular ion peak was obtained at *m/z* 304. Details of the characterization of the compound reported below in experimental data. These confirm the structures of the compounds(**5a-f).**

General procedure:

Synthesis of 1-(4-Acetyl-phenyl)-pyrrole-2,5-dione(3):

A solution of maleic anhydride(9.7g, 0.1mol) and 4-aminoacetophenone(13.5g, 0.1mol) in diethyl ether at room temperature stirring for 2hr. Reaction progress checked by TLC. After completion of the reaction that reaction mixture was filtered and washes it with water to give compound in 90% yield, as a light yellow solid, m.p. 164°C.

Synthesis of 1-[4-(3-substituted phenyl-acryloyl)-phenyl]-pyrrole-2,5-diones(5a-g):

Microwave irradiation method:

A mixture of 1-(4-Acetyl-phenyl)-pyrrole-2,5-dione**(3)** (0.22g, 1mmol), substituted benzaldehydes**(4a-f)** (1mmol), methanol(10ml) and 20% sodium hydroxide(2ml) in were irradiated under microwave at 180 watt for 3-5min. with 30sec intervals. The reactions progresses were checked by TLC. After completion of the reactions the reactions

mixture poured into ice cold water and neutralized with dil. HCl, the resulting solid was filtered, dried and recrystallized from ethanol to obtain 1-[4-(3-substituted phenyl-acryloyl)-phenyl]-pyrrole-2,5-diones**(5a-g)**.

Conventional heating method:
To a solution of 1-(4-Acetyl-phenyl)-pyrrole-2,5-dione**(3)** (0.22g, 1mmol), substituted benzaldehydes**(4a-f)** (1mmol), methanol(20ml) and 20% sodium hydroxide(2ml) were stirred for 7-8hr at room temperature. The reaction progresses were monitored by TLC. After completion of the reaction the reactions mixture poured into ice cold water and neutralized with dil. HCl, the resulting solid was filtered, dried and recrystallized from ethanol to obtain 1-[4-(3-substituted phenyl-acryloyl)-phenyl]-pyrrole-2,5-diones**(5a-g)**.

Analytical data:
1) 1-[4-(3-Phenyl-acryloyl)-phenyl]-pyrrole-2,5-dione(5a):
IR (KBr): 3083, 1704, 1662, 1604 cm^{-1}; ^1H NMR ($DMSOd_6$): δ 7.23 (2H, s, pyrrole-H), 7.47 - 7.49 (3H, m, Ar-H), 7.58 (2H, d, Ar-H), 7.78 - 7.82 (1H, d, *J* = 16 Hz, H_α), 7.90 - 7.93 (2H, m, Ar-H), 7.98 - 8.02 (1H, d, *J* = 16 Hz, H_β), 8.28 - 8.30 (2H, d, Ar-H); Mass: m/z 303. Molecular ion peak at 304 (M+1).

2) 1-[4-(3-*p*-Tolyl-acryloyl)-phenyl]-pyrrole-2,5-dione(5b):
IR (KBr): 3078, 1712, 1665, 1603 cm^{-1}; ^1H NMR (DMSO-d6): δ 3.30 (3H, s, CH_3), 7.24 (2H, s, pyrrole-H), 7.28 - 7.31 (2H, d, Ar-H), 7.55 - 7.57 (2H, d, Ar-H), 7.75 - 7.79 (1H, d, *J* = 16 Hz, H_α), 7.80 - 7.82 (2H, d, Ar-H), 7.80 - 7.84 (1H, d, *J* = 16 Hz, H_β), 8.26 - 8.28 (2H, d, Ar-H); Mass: m/z 317. Molecular ion peak at 318 (M+1).

3) 1-{4-[3-(4-Methoxy-phenyl)-acryloyl]-phenyl}-pyrrole-2,5-dione(5c):
IR (KBr): 3093, 1712, 1660, 1608 cm^{-1}; ^1H NMR (DMSO-d6): δ 3.88 (3H, s, OCH_3), 6.97 (2H, d, Ar-H), 7.28 (2H, s, pyrrole-H), 7.41 (1H, d, J = 16 Hz, H_α), 7.56–7.65 (4H, m, Ar-H), 7.82 (1H, d, J = 16 Hz, H_β), 8.13 – 8.15 (2H, d, Ar-H); Mass: m/z 333. Molecular ion peak at 334 (M+1).

4) 1-{4-[3-(4-Chloro-phenyl)-acryloyl]-phenyl}-pyrrole-2,5-dione(5d):
IR (KBr): 3071, 1716, 1669, 1602 cm^{-1}; ^1H NMR (DMSO-d6): δ 7.24 (2H, s, pyrrole-H), 7.42 - 7.44 (2H, d, Ar-H), 7.51 - 7.55 (1H, d, *J* = 16 Hz, H_α), 7.58 - 7.63 (4H, m, Ar-H), 7.80 - 7.85 (1H, d, *J* = 16Hz, H_β), 8.13 – 8.15 (2H, d, Ar-H); Mass: m/z 337. Molecular ion peak at 338 (M+1).

5) 1-{4-[3-(4-Bromo-phenyl)-acryloyl]-phenyl}-pyrrole-2,5-dione(5e):
IR (KBr): 3078, 1711, 1658, 1597 cm^{-1}; ^1H NMR (DMSO-d6): δ 7.14 (2H, s, pyrrole-H), 7.39 - 7.41 (2H, d, Ar-H), 7.37 - 7.41 (1H, d, *J* = 16 Hz, H_α), 7.45 - 7.49 (4H, m, Ar-H), 7.78 - 7.82 (1H, d, *J* = 16 Hz, H_β), 8.08 - 8.10 (2H, d, Ar-H); Mass: m/z 337. Molecular ion peak at 338 (M+1).

6) 1-{4-[3-(4-Nitro-phenyl)-acryloyl]-phenyl}-pyrrole-2,5-dione(5f):
IR (KBr): 3071, 1716, 1660, 1608 cm^{-1}; ^1H NMR (DMSO-d6): δ 7.25 (2H, s, pyrrole-H), 7.61 - 7.63 (2H, d, Ar-H), 7.86 - 7.88 (1H, d, *J* = 16 Hz, H_α), 8.15 - 8.21 (3H, m, H_β and Ar-H), 8.30 - 8.33 (4H, d, Ar-H); Mass: m/z 348. Molecular ion peak at 349 (M+1).

CONCLUSION

We have used an easy, high yielding, convenient and green methods for the synthesis of 1-[4-(3-Substitutedphenyl-acryloyl)-phenyl]-pyrrole-2,5-diones under microwave irradiation. The process proved to be a simple, environmentally friendly technique with high yields and high rate of acceleration was achieved in performing the reaction in microwave irradiation technique.

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REFERENCES

[1] V.K. Ahluwalia, N. Kaila, S. Bala, *Indian J. Chem.*, **1986**, 25B, 663.
[2] A. Furlan, R.L.E. Zacchino, *Arch. Pharm. Chem. Life Sci*., **2005**, 338, 87.

[3] S.J. Won, C.T. Liu, L.T. Tsao, J.R. Weng, H.H. Ko, J.P. Wang, C.N. Lin, *Eur. J. Med. Chem.*, **2005**, 40, 103.
[4] E.J. DeLeon, M.J. Alcaraz, J.N. Dominguez, J. Charris, M.C. Terencio, *Inflamm. Res.*, **2003**, 52, 24.
[5] S. Mukherjee, V. Kumar, A.K. Prasad, H.G. Raj, M.E. Bracke, C.E. Olsen, S.C. Jain, V.S. Parmar, *Bioorg. Med. Chem*., **2001**, 9, 337.
[6] F.C. Chen, *Bioorg. Med. Chem.,* **2002**, 10, 2795.
[7] G. Saydam, H.H. Aydin, F. Sahin, O. Kucukoglu, E. Erciyas, E. Terzioglu, F. Buyukkececi, S.B. Omay, *Leuk. Res.*, **2003**, 27, 57.
[8] S. Sogawa, Y. Nihro, H. Ueda, T. Miki, H. Matsumoto, T. Satoh, *Biol. Pharm. Bull.*, **1994**, 17, 251.
[9] S. Iwata, N. Nagata, A. Omae, S. Yamaguchi, Y. Okada, S. Shibata, T. Okuyama, *Biol. Pharm. Bull.,* **1999**, 22, 323.
[10] C. Morisseau, G. Du, T.W. Newman, B.D. Hammock, *Arch. Biochem. Biophys.*, **1998**, 356, 214.
[11] O. Nerya, R. Musa, S. Khatib, S. Tamir, *J. Phytochemistry*, **2004**, 65, 1389.
[12] C.L. Miranda, G.L.M. Aponso, J.F. Stevens, M.L. Deinzer, D.R. Buhler, *Cancer Lett.,* **2000**, 149, 21.
[13] 13. T.A. Geissmann, *The chemistry of flavonoid compounds;* Pergamon Press: Oxford, 1962
[14] V.D. Kiselev, A.G. Sakhabutdinov, I.M. Shakirov, A.I. Konovalov, *J. Org. Chem. USSR (Engl. Transl.),* **1991**, 27, 1437.
[15] V.C. Filho, T. Pinheiro, R.J. Nunes, R.A. Yunes, A.B. Cruz, *Farmaco.*, **1994**, 49, 675.
[16] F. Kratz, U. Beyer, P. Schumacher, M. Kruger, H. Zahn, T. Roth, H.H. Fiebig, H. Unger, *Bioorg. Med. Chem. Lett.*, **1997**, 7, 617.