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Synthesis, characterization and antimicrobial activity of novel pyrrole derivatives

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ABSTRACT

*4-(1,3-dioxoisoindolin-2-yl)benzohydrazide (**1**) undergoes facile condensation with aromatic aldehydes to afford the corresponding N'-arylidene-4-(1,3-dioxoisoindolin-2-yl)benzohydrazide (**2a-e**) in good yields. Cyclo condensation of compounds (**2a-e**) with maleic anhydride yields 1-(4-(1,3-dioxoisoindolin-2-yl)benzamido)-5-oxo-2-aryl-2,5-dihydro-1H-pyrrole-3-carboxylic acid (**3a-e**). The structures of these compounds were established on the basis of analytical and spectral data. All the newly synthesized compounds were evaluated for their antibacterial and antifungal activities.*

Keywords: 4-(1,3-dioxoisoindolin-2-yl)benzohydrazide, pyrrole, antibacterial and antifungal activities.

INTRODUCTION

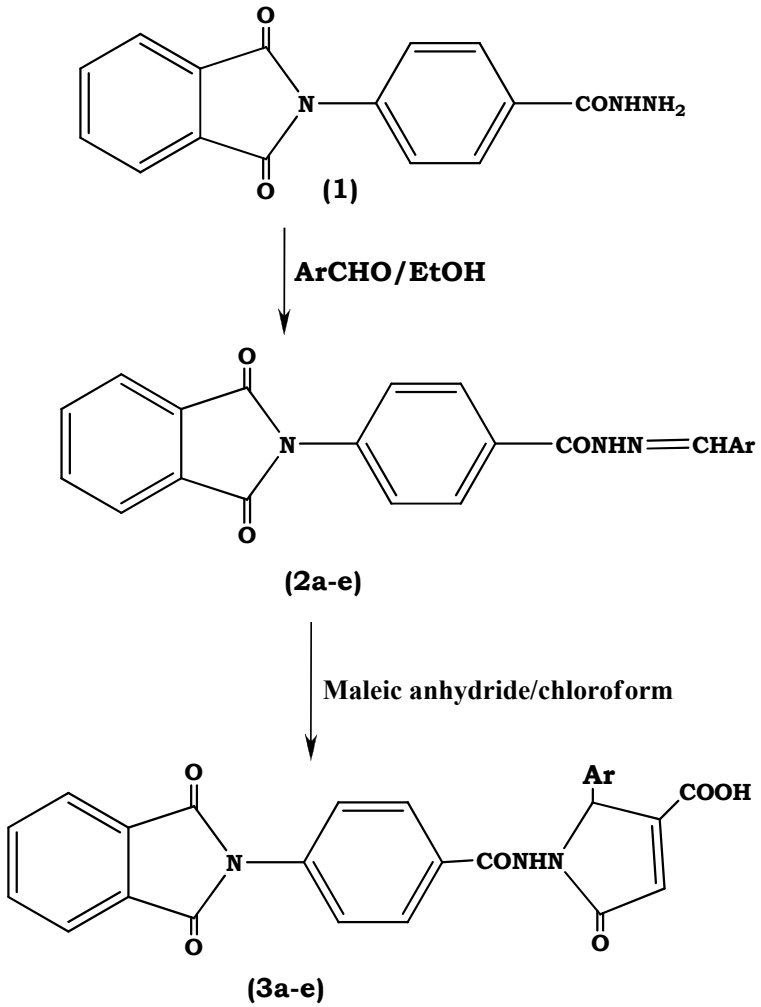
Heterocyclised products based on hydrazides display diverse biological activities including antibacterial, antifungicidal, analgesic, anti-inflammatory properties [1-10]. These heterocyclic systems find wide use in medicine, agriculture and industry. One of the hydrazides, 2-(1,3-dioxoisoindolin-2-yl)aceto hydrazide and their condensed products play a vital role in medicinal chemistry[11-13]. 2-pyrrole and its arylidene compounds give good pharmacological properties [14-20]. Hence, it was thought of interest to merge both of pyrrole and phthlamide moieties which may enhance the drug activity of compounds to some extent, or they might possess some of the above mentioned biological activities. From this point of view, the objective of the present work is to prepare new derivatives of phthlamide containing pyrrole moiety. Hence the current communication covers the study of 1-(4-(1,3-dioxoisoindolin-2-yl)benzamido)-5-oxo-2-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylic acid. The synthetic approach is shown in scheme-1.

MATERIALS AND METHODS

Melting points were determined in open capillary tubes and were uncorrected. The IR spectra were recorded in KBr pellets on a Nicolet 400D spectrometer and ^{1}H NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz and 100 MHz, respectively. LC-MS of selected samples taken on LC-MSD-Trap-SL_01046.

Preparation of N'-arylidene-4-(1,3-dioxoisoindolin-2-yl) benzohydrazide (2a-e): The mixture of 4-(1,3-dioxoisoindolin-2-yl)benzohydrazide (1) (0.1mmole) and subsituted aromatic aldehydes(0.1mmole) (a-e) in EtOH (15ml) was refluxed for 60-150 minutes. The solid separated was collected by filtration, dried and recrystallized from EtOH. The yields, melting points and other characterization data of these compounds are given in Table -1.

Scheme-I



Where Ar = (a) C_6H_5, (b) 4-OH-C_6H_4, (c) 2-OH-C_6H_4,

(d) 4-OCH_3-C_6H_4, (e) 4-OH-3-OCH_3-C_6H_3

Table:-1 Analytical Data and Elemental Analysis of Compounds (2a-e)

Compd.	Molecular formula (Mol. wt.)	LC-MS Data	Yield	M.P.* ^{0}C	Elemental Analysis					
					%C		% H		%N	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
2a	$C_{22}H_{15}N_3O_3$ (369)	376	84	232-235	71.54	71.5	4.06	4.0	11.38	11.3
2b	$C_{22}H_{15}N_3O_4$ (385)	393	79	234-236	68.57	68.5	3.89	3.8	10.90	10.9
2c	$C_{22}H_{15}N_3O_4$ (385)	392	80	233-236	68.57	68.5	3.89	3.8	10.90	10.8
2d	$C_{23}H_{17}N_3O_4$ (399)	407	82	236-240	69.17	69.1	4.26	4.2	10.52	10.5
2e	$C_{23}H_{17}N_3O_5$ (415)	426	83	238-244	66.50	66.5	4.09	4.0	10.12	10.1

***** *Uncorrected*

Preparation of 1-(4-(1,3-dioxoisoindolin-2-yl)benzamido)-5-oxo-2-aryl-2,5-dihydro-1H-pyrrole-3-carboxylic acid (3a-e): A mixture of N'-arylidene-4-(1,3-dioxoisoindolin-2-yl) benzohydrazide (2a-e) (0.1mmole) and Maleic anhydride (0.1mmole) in chloroform (50ml) was refluxed for 4.5-6 hrs. The reaction mixture was allowed to stand for 45hrs, the solid was filtered. The product thus formed was recrystallized from EtOH to give 1-(4-(1,3-

dioxoisoindolin-2-yl)benzamido)-5-oxo-2-aryl-2,5-dihydro-1H-pyrrole-3-carboxylic acid (3a-e), which were obtained in 70-80% yield. The yields, melting points and other characterization data of these compounds are given in Table -2.

RESULTS AND DISCUSSION

It was observed that 4-(1,3-dioxoisoindolin-2-yl)benzohydrazide (1) undergoes facile condensation with various aromatic aldehydes to afford the corresponding N'-arylidene-4-(1,3-dioxoisoindolin-2-yl) benzohydrazide (2a-e). The structures of (2a-e) were confirmed by elemental analysis and IR spectra showing an absorption band at 1620-1640 (C=N), 3030-3080 cm^{-1} (C-H, of Ar.), 1725-1750 cm^{-1} (-CO). ^1H NMR : 6.98 – 7.96 (8H, m) (Ar - H), 11.80-11.81 (1H, s) (-CONH), 8.43-8.80 (1H, s) (-N=CH), 2d, 2e; 3.90 (3H, s) (-OCH_3),2b,2c 3.5(2H,s)(OH).The C, H, N analysis data of all compounds are presented in Table -1.

The structures assigned to 1-(4-(1,3-dioxoisoindolin-2-yl)benzamido)-5-oxo-2-aryl-2,5-dihydro-1H-pyrrole-3-carboxylic acid (3a-e) were supported by the elemental analysis and IR spectra showing an absorption bands at 1720cm^{-1}(C=O of pyrrole ring), 3040-3058 cm^{-1}(C-H, of Ar.),3450-3550 cm^{-1}(-OH),1660-1670 cm^{-1} (-CO of -COOH). ^1H NMR: 7.16-7.94 (13H, m,Ar-H), 5.63(1H,s, C_2H of the ring), 7.18(1H,s,C_4H),12.96(1H,s)(-COOH), 3b,3c; 3.5(2H,s)(OH),3d,3e; 3.90 (3H, s) (-OCH_3). The C, H, N, S analysis data of all compounds are presented in Table-2.

Table:-2 Analytical Data and Elemental Analysis of Compounds (3a-e)

Compd.	Molecular formula (Mol. wt.)	LC-MS Data	Yield	M.P.* ^0C	Elemental Analysis					
					%C		% H		%N	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
3a	$C_{26}H_{17}N_3O_6$ (467)	489	78	211-212	66.81	66.7	3.67	3.6	8.99	8.9
3b	$C_{26}H_{17}N_3O_7$ (483)	506	75	214-216	64.60	64.5	3.54	3.5	8.69	8.6
3c	$C_{26}H_{17}N_3O_7$ (483)	507	77	213-215	64.60	64.5	3.54	3.5	8.69	8.6
3d	$C_{27}H_{19}N_3O_7$ (497)	519	71	216-218	65.19	65.1	3.85	3.8	8.45	8.4
3e	$C_{27}H_{19}N_3O_8$ (513)	528	70	209-211	63.16	63.1	3.73	3.7	8.18	8.1

***** *Uncorrected*

The examination of elemental analytical data reveals that the elemental contents are consistence with the predicted structure shown in Scheme-1. The IR data also direct for assignment of the predicted structure. The final structure of all compounds is confirmed by LC-MS. LC-MS data of Samples 3b and 3e gives the molecular ion peak (m/z) at 506 and 528 respectively. These values are corresponds to their molecular weight.

BIOLOGICAL SCREENING

Antibacterial activities

The antibacterial activities of all the compounds were studied against gram-positive bacteria (*Staphylococcus aureus and Bacillus subtilis*) and gram-negative bacteria (*E.coli, and klebsiella promioe*) at a concentration of 50µg/ml by agar cup plate method. A methanol system was used as control in this method. Similar conditions using tetracycline as a control was used standard for comparison. The area of inhibition of zone measured in mm. Compounds 3d and 3e were found more toxic for microbes. Other compounds found to be less or moderate active than tetracycline Tables -3.

Table:-3 Antibacterial Activity of Compounds [3a-e]

Compounds	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	*Bacillus subtilis*	*E.coli*	*Klebsiella promioe*
3a	54	49	67	61
3b	53	55	65	73
3c	51	56	64	55
3d	58	67	75	62
3e	59	65	78	75
Tetracycline	60	68	80	77

Antifungal Activities

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro. Plant pathogenic organisms used were *Nigrospora Sp, Aspergillus niger, Botrydepladia thiobromine, and Rhizopus nigricum, Fusarium oxyporium*. The antifungal activities of all the compounds (3a-e) were measured on each of these plant

pathogenic strains on a potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200g, dextrose 20g, agar 20g and water 1ml. Five days old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at 120^{o}C for 15 min. at 15atm. pressure. These media were poured into sterile Petri plates and the organisms were inoculated after cooling the Petri plates. The percentage inhibition for fungi was calculated after five days using the formula given below:

Percentage of inhibition = 100(X-Y) / X

Where,
X = Area of colony in control plate
Y = Area of colony in test plate

The fungicidal activity displayed by various compounds (3a-e) is shown in Tables-4.

Table:-4 Antifungal Activity of Compounds (3a-e)

Zone of Inhibition at 1000 ppm (%)					
Compounds	***Botrydepladia Thiobromine***	***Rhizopus Nigricum***	***Aspergillus Niger***	***Nigrospora Sp.***	***Fusarium oxyporium***
3a	60	61	59	58	64
3b	58	58	57	62	62
3c	72	67	61	69	68
3d	64	59	58	61	63
3e	69	70	67	59	66

REFERENCES

[1] R. Kalsi;M. Shrimali; T. N. Bhalla; J. P. Barthwal. *Indian J. Pharm. Sci.* **2006**, 41, 353.
[2] Y. Janin. *Bioorg. Med. Chem.**2007,*** 15, 2479.
[3] E. Gursoy; N. Guzeldemirci-Ulusoy. *Eur. J. Med. Chem.* **2007**, 42, 320.
[4] M. R. Rao; K. Hart; N. Devanna and K. B. Chandrasekhar. *Asian J. Chem.***2008**, 20, 1402.
[5] K. B. Kaymakcıoglu; E. E. Oruc; S. Unsalan; F. Kandemirli;N. Shvets; S. Rollas; D. Anatholy.*Eur. J. Med. Chem.***2006**,.41, 1253.
[6] M. R. Shiradkar; K. K. Murahari;H. R. Gangadasu; T. Suresh; C. C. Kalyan; D. Panchal, R. Kaur; P. Burange;J.Ghogare;V.Mokale;M.Raut. *Bioorg.Med. Chem.*,**2007**, 15, 3997.
[7] S. Gemma;G. Kukreja; C. Fattorusso; M. Persico;M. Romano; M. Altarelli;L. Savini; G. Campiani; E. Fattorusso; N. Basilico. *Bioorg. Med. Chem. Lett.* **2006**,16, 5384.
[8] D. Sriram; P. Yogeeswari; K. Madhu. *Bioorg. Med. Chem. Lett.* **2006**, 15, 4502.
[9] A. Nayyar; R. Jain.*Curr. Med. Chem.* **2006**, 12, 1873.
[10] R. M. Fikry; N. A. Ismael;A. A. El-Bahnasawy; A. A. Sayed El-Ahl. *Phosphorus Sulfur and Silicon.* **2006**, 179, 1227.
[11] Al- Mawsawi LQ;R. Dayam;L. Taheri;M. Witvrouw; Z. Debyser; N. Neamati. *Bioorg. Med. Chem. Lett.* **2007**, 17(23) 6472.
[12] C. Plasencia; R. Daym; Q. Wang; J. Pinski; T. R. Jr. Burke; D. I. Quinn and N. Neamati. *Mol. Cancer Ther.* **2005**, 4(7) 1105.
[13] H. Zhao; N. Neamati; S. Sunder; H. Hong; S. wang; G. W. Milne; Y. Pommier;T. R. Jr. Burke. *J. Med. Chem.* **1997**,40(6) 937.
[14] LQ Al- Mawsawi; R.Dayam; L.Taheri; M.Witvrouw; Z.Debyser;N.Neamati. *Bioorg. Med. Chem. Lett.* **2007**, 17(23), 6472.
[15] C.Plasencia; R.Daym; Q.Wang; J.Pinski; T. R. Jr. Burke; D. I.Quinn and N. Neamati. *Mol. Cancer Ther.* **2005**, 4(7) 1105.
[16] K.M.Thaker . *Ind. J. Chem.*,**2003**,42B,1544.
[17] V.S.Ingle;A.R.Sawale; R.D. Ingle and R.A. Mane. *Ind. J. Chem.*, **2000**,40, 124.
[18] R.C. Sharma and D.Kumar. *J. Ind. Chem. Soc.*,**2000**,77, 492.
[19] A.Bijev. *Lett.Drug Des. Discov.*, **2006**,3, 506.
[20] H.Zhao; N.Neamati; S.Sunder; H.Hong; S.Wang; G.W.Milne; Y.Pommier; T. R. Jr. Burke. *J. Med. Chem.* **1997**, 40(6) 937.