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Synthesis and characterization of new (2E,2'E)-3,3'-(((3--hydroxypropane-1,2-diyl)bis(oxy))bis(2,1-phenylene))bis(1-phenylprop-2-en-1-one) and its transformation into 2,3-bis (2-(1,3-diphenyl-4,5-dihydro-1H-pyrazol-5-yl)phenoxy)propan-1-ol

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Abstract

In this paper, new (2E,2'E)-3,3'-(((3-hydroxypropane-1,2-diyl)bis (oxy))bis (2,1-phenylene))bis(1-phenylprop-2-en-1-one)(**2a**) was prepared in good yield by condensation reaction of acetophenone with bisaldehyde(**1a**) in ethanolic NaOH solutions at room temperature. The (2E,2'E)-3,3'-(((3-hydroxypropane-1,2-diyl)bis-(oxy))bis(2,1-phenylene))bis(1-phenylprop-2-en-1-one) (**2a**) was immediately reacted with phenyl hydrazine under refluxing conditions in the presence of potassium hydroxide to obtain the corresponding 2,3-bis(2-(1,3-diphenyl-4,5-dihydro-1H-pyrazol-5-yl)phenoxy)propan-1-ol(**3a**). The newly synthesized compounds confirmed by melting point and TLC and their structure were established by various analytical techniques such as IR, ^{1}H-NMR, ^{13}C-NMR and elemental analysis.

Keywords: Synthesis; bischalcone; bispyrazoline; bisaldehyde.

Introduction

The synthesis of heterocyclic compounds is a major challenge in modern heterocyclic chemistry due to their potential biological activities [1]. Pyrazolines are one of the heterocyclic compounds containing two nitrogen atoms in the five membered rings [2]. They are used extensively as useful synthon in organic chemistry and drug designing [3,4]. Chalcones are valuable starting materials for the synthesis of various heterocyclic compounds like pyrazolines, pyrazoles and isoxaxolines, etc. [5]. Chalcones exhibit many pharmacological activities, including antimicrobial, anti-inflammatory, antioxidant, anticancer, antifungal, antimitotic, antimalarial, cytotoxic and antitumor activities [1,6,7]. Pyrazolineshave been found topossess a wide range of biological activities such as antimicrobial, antifungal, antiamoebic, anti-inflammatory, analgesic, antidepressant, anticonvulsant, antitumor, insecticidal, antiviral and anti HIV properties [8-11]. Among the methods employed in the synthesis of pyrazolines, the condensation of a variety of substituted chalcones with hydrazine and its derivatives is commonly used [12]. There are several recent reports for the synthesis of bischalcone and bispyrazoline compounds; for example, the bischalcones were prepared *via* condensation of bisbenzaldehydes with

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(un) substituted acetophenones in ethanolic KOH solution [13]. The pyrazoline derivatives were synthesized by the cyclization of various -1-[2-(alkoxy)phenyl]-3-(furan-2-yl)prop-2-en-1-one with N-substituted phenyl hydrazine in the presence of CH_3COOH in ethanol [14]. The bispyrazolines were prepared by the reaction of bischalcones with hydrazine in acetic acid [15].

Based on the interest in the chemistry of arylatedpyrazolines, we report here the synthesis and structures of a new series of bischalcone and bis-pyrazoline compounds, which have been characterized by spectra data. In the present work, (2E,2'E)-3,3'-(((3-hydroxypropane-1,2-diyl)bis(oxy))bis-(2,1-phenylene))bis(1-phenylprop-2-en-1-one) (**2a**) was synthesized by the reacting of acetophenone with 2,2'-((3-hydroxypropane-1,2-diyl)bis(oxy))-bisbenzaldehyde(**1a**) in the presence of an aqueous solution of sodium hydroxide and ethanol at room temperature by Claisen-Schmidt condensation method. The reaction between synthesized (2E,2'E)-3,3'-(((3--hydroxypropane-1,2-diyl)bis(oxy))bis-(2,1-phenylene))bis(1-phenylprop-2-en-1-one)(**2a**)and phenyl hydrazine in presence of potassium hydroxide led to synthesis of novel 2,3-bis(2-(1,3-diphenyl-4,5-dihydro-1H-pyrazol-5-yl)-phenoxy)propan-1-ol(**3a**).

Experimental

General

To monitor the reactions, as well as, to establish the identity and purity of reactants and products, thin layerchromatography was performed on silica gel-G plates, using petroleum ether-ethyl acetate mixture (4:1) as a solving system. Melting points are uncorrected and recorded on an electrothermal 9200 digital melting point apparatus. The IR spectra of the synthesized compounds were recorded -on Shimadzu Varian Model-4300 FT-IR spectrophotometer using potassium bromide. The ^1H and ^{13}C NMR spectra were run on a Bruker DPX 400 spectrometer operating at 400 MHz and 100 MHz, respectively, using $CDCl_3$ as solvent and TMS as internal standard. The elemental analyses were carried out on a Perkin-Elmer series II 2400 equipment.

Synthesis of 2,2'-((3-hydroxypropane-1,2-diyl) bis(oxy))-bisbenzaldehyde(1a)

To the stirred solution of salicyldehyde (24.4 g, 0.2mol) in hot ethanol was added sodium hydroxide (8 g, 0.2mol) in absolute ethanol (100 mL). The mixture was warmed and 2, 3-dibromo propanol (10.28 mL, 0.1mol) was added. Sufficient ethanol (300 mL) to produce a homogeneous solution was then added. The progress of the reaction was monitored by thin layerchromatography (TLC). The solution was refluxed under nitrogen for 100 h and then cooled and let stand at 0º. The cream colored crystals produced were washed with waterand – recrystallized from ethanol. The resulting crystals were collected by filtration and dried in vacuum desiccators over P_4O_{10}.

Cream crystals; m.p: 109-110 °C, -yield: 84%. IR (KBr): 3466 (OH), 2875 (CHO), 1682 (C=O) cm^{-1}.^{1}H-NMR (400 MHz, $CDCl_3$): δ= 10.2 (s, 2H, H--7), 7.02-7.8 (m, 6H, H-3, 4, 5), 6.96 (s, 2H, H-2) 4.520 (m, 2H, H-8), 4.317 (d, 1H, H-9), 3.9 (s, 2H, H-10), 2 (s, 1H, OH) ppm.^{13}C-NMR (100 MHz, $CDCl_3$): *δ*= 190.25 (CH, C-7), 160 (C, C-1), 134 (CH, C-3), 130.3 (CH, C-5), 122.11 (C, C-6), 119.08 (CH, C-4), 114.7 (CH, C-2), 80 (CH, C-9), 73 (CH, C-8), 64.3 (CH, C-10) ppm-.Anal.calcd For $C_{17}H_{16}O_5$ (300.31): C,

67.85; H, 5.37; O, 26.54. Found: C, 67.55; H, 5.06; O, 26.20 %.

Synthesis of (2E,2'E)-3,3'-(((3-hydroxypropane-1,2-diyl)bis(oxy))-bis(2,1-phenylene))bis(1-phenylprop-2-en-1-one) (2a)

A mixture of acetophenone (0.4 g, 3.35 mmoles), 2,2'-((3-hydroxypropane-1,2-diyl) bis(oxy))bisbenzaldehyde(**1a**)(0.5 g, 1.66mmoles) and 10 mL of 20% NaOH in EtOH (20 mL) was stirred for 12 h at room temperature. The progress of thereaction was monitored by TLC. Brown colored solid obtained was isolated by filtration, washed by water and recrystallized from ethanol.

Brown solid;m.p: 125-135 °C,yield: 80%.R_f: 0. 41. IR (KBr): 1654 (C=O), 1600 (C=C), 3406 (OH), 1242 (C-O)cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$-):δ=7.61 (d, J_{trans}=15.6 Hz,2H,H-3), 7.57 (dd, $J_{P,O}$= 1.7, 7.6 Hz,4H, H-5' and H-9'), 7.3 (s, 2H, H-7'),7. 28 (t, 4H, H-6' and H-8'),7.26 (d, $J_{P,O}$= 1.7, 7.6 Hz,2H, H-5), 7.24 (d, J_{trans}=15.6 Hz, 2H,H-2),7.18 (t, 2H, H-7), 6.65 (m, 4H, H-6 and H-8), 4.03 (d, 2H, H-10), 3.9 (m, 1H, H-11), 3.71 (d, 2H, H-12), 3.62 (s, 1H, OH)ppm.^{13}C-NMR (100 MHz,$CDCl_3$): δ= 189.7 (C, C-1), 154.4 (C, C-9), 141.01 (CH, C-3),137.9 (CH, C-7'), 134.8 (C, C-4'), 134.5 (CH, C-5' and C-9'),129.2 (CH, C-6' and C--8'),128.5 (CH, C-5),125.8 (C, C-4),121.3 (CH, C-7),121.3 (CH, C-2 and C-6), 114.3 (CH, C-8), 84.8 (CH, C-11), 67.6 (CH, C-10), 62.6 (CH, C-12)ppm. Anal.Calcd. For$C_{33}H_{28}O_5$(504.19): C, 78.35; H, 5.48; O, 15.73. Found: C, 78.32;H, 5.42; O, 15.71 %.

Synthesis of2,3-bis(2-(1,3-diphenyl-4,5-dihydro-1H-pyrazol-5-yl)-phenoxy)propan-1-ol(3a)

To the stirred solution of (2E,2'E)-3,3'-(((3-hydroxypropane-1,2-diyl)bis-(oxy))bis(2,1-phenylene))bis(1-phenylprop-2-en-1-one)(2a) (0.5 g, 0.99mmoles) in absolute ethanol (30 mL) was added phenyl hydrazine -(0.58mL, 5.9mmoles) and KOH (0.38 g, 6.9 mmoles) and the reaction mixture was refluxed for 24 h. The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was cooled to room temperature and then the reaction mixture was acidified with dilute HCl to neutral. The precipitate obtained was filtered, dried and recrystallized from EtOH to give pure product.

Olivaceous solid; m.p: 145-155°C,yield: 65 %.R_f: 0.66. IR (KBr): -1597 (C=N), 1238 (C-O), 3209 (OH)cm^{-1}.^{1}H-NMR (400 MHz, $CDCl_3$): δ=8.1 (dd, $J_{P,O}$= 1.6, 7.8 Hz,4H, H-5' and H-9'),7.6 (m, 6H,H-6', H-7' and 8'),7.5 (dd, 4H,H-14 and H-16),7.4 (d, $J_{P,O}$= 1.6, 7.8 Hz,2H, H-7),7.2 (d, 2H, H-8), 7 (m, 8H, H-9, H-13, H-15 and H-17), 6.9 (d, 2H, H-10), 4.6 (dd, J_{XM}= 12.1, J_{XA}= 6.7 Hz,2H, H_X), 4.3 (s, 2H, H-18), 4.3 (s, 1H, H-19), 4.3 (s, 2H, H-20), 4.3 (dd, J_{MX}= 12.1, J_{MA}= 17.3 Hz,2H, H_M),4.2 (dd, J_{AX}= 6.6, J_{AM}= 17.7 Hz,2H, H_A), 4.2 (s, 1H, OH)ppm.^{13}C-NMR (100 MHz, $CDCl_3$): δ= 153 (C, C-5), 151.9 (C, C-11),151.3 (C, C-12), 128.8 (C, C-6), 128.5 (CH, -C-5' and C-9'),128 (CH, C-6' and C-8'), 127 (C, C-4'), 126 (CH,C-14 and C-16), 125 (CH, C-7' and C-9), 124 (CH, C-15),123 (CH, C-7), 120 (CH, C-13 and C-17),113 (CH, C-8), 112 (CH, C-10),66.30 (CH, H-19),64 (CH, H-18), 63.9 (CH, H-20), 60.8 (CH, C-3), 41.9 (CH, C-4) ppm. Anal.-Calcd.For$C_{45}H_{40}N_4O_3$ (684.82): C, 79.65; H, 6.81; N, 7.27; O, 6.20. Found: C, 79.63; H, 6.79;N, 7.25; O, 6.18 %.

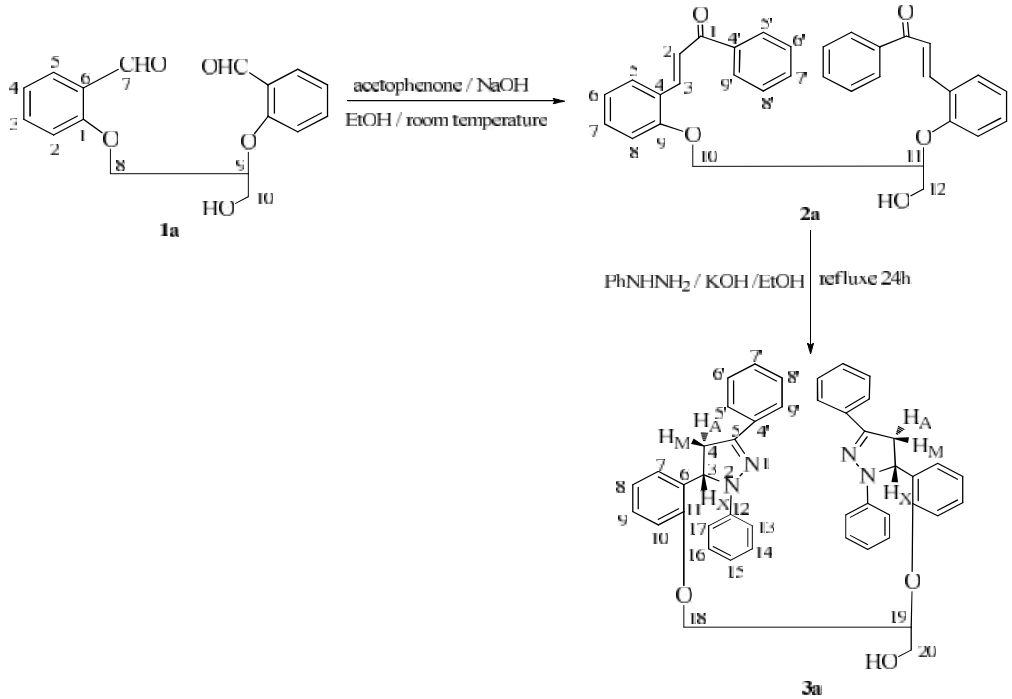
Results and discussion

The reaction routes for the synthesis of the compounds are shown in Scheme 1. The(2E,2'E)-3,3'-(((3-hydroxypropane-1,2-diyl)bis (oxy))bis(2,1-phenylene))-

bis(1-phenylprop-2-en-1-one)(**2a**)was prepared in excellent yield by the Claisen-Schmidt reaction of acetophenone with 2,2'-((3-hydroxypropane-1,2-diyl)bis(oxy))-bisbenzaldehyde(**1a**) in the presence of aqueous ethanolic sodium hydroxide-.The2,3-bis(2-(1,3-diphenyl-4,5-dihydro-1H-pyrazol-5-yl)phenoxy)-propan-1-ol(**3a**) was synthesized by cyclization of (2E,2'E)-3,3'-(((3--hydroxypropane-1,2-diyl)bis (oxy))bis-(2,1-phenylene))bis(1-phenylprop-2-en-1-one)(**2a**) with phenyl hydrazine in dry ethanol in the presence of potassium hydroxide. The assigned structures of the newly synthesized compounds were confirmed on the basis of their elemental and spectral analysis (IR, ^{1}H-NMR, ^{13}C-NMR).

The IR spectra of (2E,2'E)-3,3'-(((3-hydroxypropane-1,2-diyl)bis-(oxy))bis(2,1-phenylene))bis(1-phenylprop-2-en-1-one)(**2a**)showed an absorption band due to the unsaturated carbonyl group at 1654 cm^{1}.Theabsorptionbandsappearedin the region at 1600 cm^{-1} were attributed to the C=C stretching. Additional band was observed due to the OH group in3406. Their ¹H-NMR spectra showed two broad doublets resonating atd7.61 and 7.24 could be assigned to H-3 and H-2, respectively. The coupling value of 15.9 Hz between these vinyl hydrogens confirmed the presence of bischalcone in the trans form. In the ^{13}C-NMR spectra of (2E,2'E)-3,3'-(((3--hydroxypropane-1,2-diyl)bis(oxy))bis-(2,1-phenylene))bis (1-phenylprop-2-en-1-one)(**2a**), the chemical shift values of carbon atoms C-2 (121.3), C-3 (141.01), C-12 (62.6) and C=O (189.7). IR spectra of2,3-bis(2-(1,3-diphenyl-4,-5-dihydro-1H-pyrazol-5-yl)phenoxy)-propan-1- ol(**3a**) show C=N stretch at 1597 cm^{-1}. In the ^{1}H-NMR spectra of2,-3-bis(2-(1,3-diphenyl-4,5-dihydro-1H-pyrazol-5-yl)phenoxy)propan-1-ol(**3a**), the three hydrogen atoms attached to the C-4 and C-5 carbon atoms of the heterocyclic ring were observed as a doublet of doublet at d 4.2-4.3 ($H_{A,}$ $J_{AM\ (gem)}$= 17.2-17.8 Hz), 4.3 (H_{M},$J_{AX\ (trans)}$= 6.7-7.1 Hz) and 4.6-4.61 (H_{X},$J_{MX\ (cis)}$= 12-12.2).In the ^{13}C-NMR spectra, the signals resonating at 60.8, 41.9 and 153 could be generated by the C-3, C-4 and C-5, respectively which are belonging to the pyrazoline ring.

The elemental analysis data of these compounds showed good agreements with calculated values of % C, H and N.



Scheme 1. Synthesis of (2E,2'E)-3,3'-(((3-hydroxypropane-1,2-diyl)bis(oxy))bis(2,1-phenylene))bis(1-phenylprop-2-en-1-one)(**2a**) and2,3-bis (2-(1,3-diphenyl-4,5-dihydro-1H-pyrazol-5-yl)phenoxy)propan-1-ol(**3a**)

Conclusion

The pyrazoline derivatives exhibit a wide variety of pharmacological activities. Therefore, the synthesis of these compounds is always of interest. In view of the biological activities of both chalcone and pyrazoline compounds, we report here the synthesis of a new series of bischalcone and bispyrazoline derivatives.

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References

[1] S.Y. Hassan, *J. Braz. Chem. Soc*., **2011**, *22*, 1286-1298.

[2] M. Yusuf, P. Jain, *Arab* J *Chem.*, **2011**, 1-44.

[3] P. Gothwal, G. Malhotra,Y.K. Srivastava, *IJGHC*, **2012**, *1*, 39-45.

[4] J.D. Mahale, S.C. Manoja, N.G. Belsare, P.R. Rajput, *Indian J. Chem.*, **2010**, *49 B*, 505-511.

[5] S.Nimbalkar,*Int J Chem.*,**2012**, *4*, 108-115.

[6] P.M. Rachmale, *IJPSR*, **2012**, *3 (3)*,901-908.

[7] A.N.Mayekar, H. Li, H.S. Yathirajan, B. Narayana, N. SuchethaKumari, *Int J Chem.*,**2010**, *2*, 114-123.

[8] S. Kumar, S. Bawa, S. Drabu, R. Kumar, H. Gupta,*Recent Pat Antiinfect Drug Discov* ,**2009**, *4*, 154-163.

[9] K.A. Parmar, J.R. Vihol, Y.M. Dabhi, Sh. D. Sutariya, *J. Chem. Pharm. Res.*, **2012**, *4(3)*, 1584-1588.

[10] N.M. Abunada, H.M. Hassaneen, N.G. Kandile, O.A. Miqdad, *Molecules*,**2008**, *13*, 1011-1024.

[11] S. Shah N.N, H.M. Ziauddin, M. Zameer, Sh.S. Hingole, M.A.Baseer, *J. Chem. Pharm. Res.*, **2010**, *2(6)*,441-445.

[12] B. Dipankar, C. Hirakmoy, B. Asish, C. Abhijit, *Int. Res J Pharm. App Sci.*, **2011**, *1(1)*, 68-80.

[13] F.F. Barsoum,H.M. Hosni,A.S. Girgis, *Bioorg. Med. Chem.*, **2006**, *14*, 3929-3937.
[14] M. Rani, M. Yusuf, S.A. Khan, P.P. Sahota, G. Pandove, *Arab J Chem.*, **2011**, 1-7.
[15] B. Insuasty, H. Martinez, J. Quiroga, R.Abonía,M.Nogueras, J.Cobo, *J. Heterocyclic Chem.*, **2008**, *45*, 1521-1524.