2024
11(1), 656

Chemical Biology
LETTERS

Synthesis, anticancer activity and molecular docking study of (*E*)-4-(3,4-Dichlorophenyl)-2-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2*H*)-one derivatives

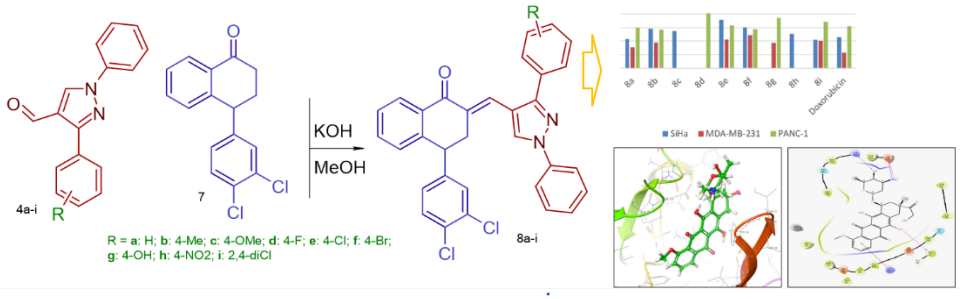
Kudikala Sadanandam, Prasad Pinnoju, S.K. Manasa, Madderla Sarasija*

Department of Chemistry, Satavahana University, Karimnagar, Telangana, India

Submitted on: 17-Nov-2023, Accepted and Published on: 12-Jan-2024

Article

ABSTRACT



A novel series of (E)-4-(3,4-Dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives were synthesized by Claisen-Schmidt condensation of 4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1(2H)-one and 1,3-diphenyl-1H-pyrazole-4-carbaldehyde. All the synthesized targets were evaluated for their cytotoxicity against a panel of three cancer cells (SiHa, MDA-MB-231 and PANC-1). Among the tested compounds, many of them exhibited significant anticancer activity, the compound 8a was found to be the most promising analogue in this series with IC50 values of 1.56 µM on breast cancer cells.

Keywords: Claisen-Schmidt condensation, Sertralone, pyrazole aldehyde, cytotoxic activity, molecular docking study.

INTRODUCTION

Pyrazole and its derivatives are considered a pharmacologically important active scaffold that possesses almost all types of pharmacological activities such as anticancer, anti-inflammatory, anti-fungal, antibacterial, anti-insecticidal, analgesic, antiviral, anticonvulsant, anti-diabetic, antipyretic, anti-arrhythmic, anti-depressant, anti-hyperglycemic, antioxidant, herbicidal etc.[1-9] Indeed, Phenazone was the first pyrazole which was commercially available as antipyretic agent.[10] Now the fascinating medicinal potential of pyrazole could be analyzed by the lists of drugs available in market such as; Celecoxib,[11] Lonazolac,[12] Mepirizole,[13] Rimonabant,[14] acomplia,[15] Cimetidine,[16] Fipronil,[17] Dexacoxib[18] etc. In addition, tetralone scaffold and its derivatives are not only important as pharmacological agents but these also serve as precursors for natural products and compounds of medicinal importance. Many of substituted tetralones have played a substantial role in organic synthesis due to their strong reactivity and suitability as a starting material for a range of synthetic heterocyclic compounds, pharmaceuticals along with biological activities as well as precursors of many natural products and their derivatives. Many α-tetralone derivatives are building blocks that have been used in the synthesis of therapeutically functional compounds like some antibiotics, antidepressants, acetylcholinesterase inhibitors effective for treating Alzheimer's disease and alkaloids possessing antitumor activity. In addition, 2-benzylidene-1-tetralone derivatives are also known for their antitumor,[19] antifungal[20] and antimicrobial properties.[21] The 2-benzylidene -1-tetralone has not previously been evaluated as a possible scaffold for developing AR antagonists. Sertraline hydrochloride is a tetralone derivative, marked drug it is an inhibitor of synaptosome serotonin uptake, an important pharmaceutical agent for the treatment of depression as well as dependency and other anxiety-related disorders.[22-24] On the other hand, many more nitrogen heterocyclic compounds were reported as anticancer agents.[25]

Based on earlier reports, herein is reported a hybrid novel series of (E)-4-(3,4-Dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives synthesized by Claisen-Schmidt condensation of 4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1(2H)-one and 1,3-diphenyl-1H-pyrazole-4-carbaldehyde and further evaluated

*Corresponding Author: Dr. Madderla Sarasija, Department of Chemistry, Satavahana University, Karimnagar, Telangana, India
Email: lionsarasija@gmail.com

URN:NBN:sciencein.cbl.2024.v11.656
DOI: 10.62110/sciencein.cbl.2024.v11.656

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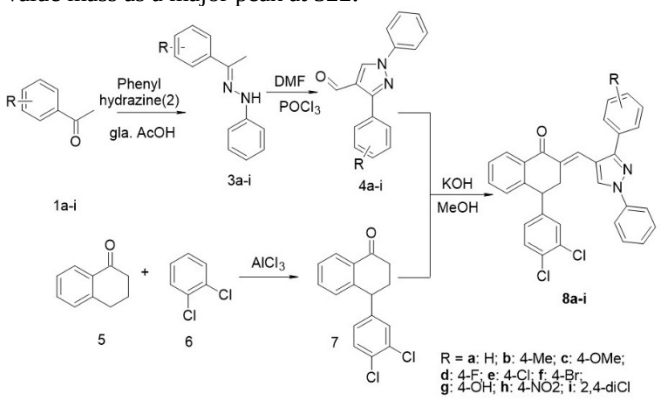
their potential as anti-cancer heterocycles via in-vitro cellular assay and molecular docking on CDK-8 kinase.

Result and Discussion

Chemistry

The target (*E*)-4-(3,4-dichlorophenyl)-2-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives were synthesized by the condensation of 4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1(2H)-one (**7**) and 1,3-diphenyl-1H-pyrazole-4-carbaldehyde (**4a-i**)[26] in the presence of potassium hydroxide in methanol medium at room temperature in good yield listed in table-1. The synthesized derivatives were well characterized by using various analytical methods such as ^{1}HNMR, ^{13}CNMR and mass spectrometry. In the ^{1}HNMR spectrum the compound (E)-4-(3,4-dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one **(8a)** showed three characteristic doublets of doublets at δ 3.39 (dd, J= 4.0, 15.6 Hz,1H, CH) 3.43 (dd, J= 4.0, 15.6 Hz,1H, CH) & 4.59 (t, J= 5.6Hz, 1H, CH), were corresponds to tetralone ring CH2 & CH protons respectively. The compounds showed pyrazole ring protons at δ 8.79 ppm. In the ^{13}CNMR spectrum two aliphatic carbon peaks appeared at δ 34.1 & 42.2 ppm and another characteristic carbonyl carbon appeared at δ 186.0 ppm. In mass spectrum the compounds showed m/z + H value mass as a major peak at 522.



Scheme-1: Preparation of (E)-4-(3,4-dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives (8a-i)

Table 1. Chemical synthesis data of synthesized compounds

Compds	R	Melting Point (^{0}C)	Reaction Time (h)	Yield (%)
8a	hydrogen	122-124	6	76
8b	4-methyl	118-120	4	78
8c	4-methoxy	131-133	5	79
8d	4-chloro	148-150	5	78
8e	4-fluoro	142-144	4	75
8f	4-bromo	139-141	5	78
8g	4-hydroxy	157-159	6	64
8h	4-nitro	145-147	6	69
8i	2,4-dichloro	136-138	6	72

Anticancer Activity

(E)-4-(3,4-dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives (8a-i) were evaluated to determine their cytotoxic activity against three different human tumor cell lines as cervix (SiHa), breast (MDA-MB-231) and pancreatic carcinoma (PANC-1) (SiHa, MDA-MB-231 and PANC-1 using the Sulforhodamine B assay method. Doxorubicin is used as standard. The GI50 values are listed in Table 2. From the screening results, Interestingly, the compounds 8a, 8h and 8i showed potent activity against as Cervix (SiHa) cell lines with compared to doxorubicin, the compounds 8a, 8b and 8g showed good anticancer activity on breast (MDA-MB-231) cell lines and the compounds 8a, 8b and 8f exhibited maximum anticancer activity on pancreatic carcinoma (PANC-1).

Table-2 : Anticancer activity of (E)-4-(3,4-dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives (**8a-i**) GI_{50} values in micro molar (µm).

Compounds	SiHa	MDA-MB-231	PAN-1
8a	2.15	1.56	2.98
8b	2.89	1.89	2.85
8c	2.74	--	--
8d	--	--	4.05
8e	3.55	2.12	3.15
8f	3.01	2.43	2.86
8g	--	1.88	3.69
8h	2.52	--	--
8i	2.11	2.00	3.42
Doxorubicin	2.31	1.15	3.10

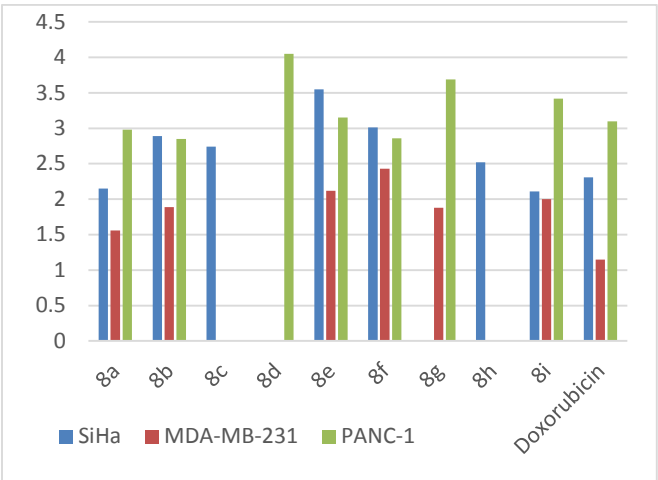


Figure 1: Anticancer activity of synthesized compounds on SiHa, MDA-MB-231 and PANC-1 cells.

Molecular Docking Study

In silico molecular docking studies lead to innovation in synthesizing novel drugs as this study requires less time and can be performed with many ligands and easy to compare between the ligand scores. The ligands were sketched in chem draw and saved it in mol2 format. All the sketched molecules were converted to energy minimized 3D structures by using lig prep module for in-silico protein-ligand docking using Schrödinger 11.4. Each molecule was docked separately. Initially the molecule was loaded; torsions were set and saved it in PDB format. All the heteroatoms were removed from the 5FGK. PDB (CDK8-CYCC in complex with 8-[3-(3-Amino-1H-indazol-6-yl)-5-chloro-pyridine-4-yl]-2,8-diaza-spiro[4.5]decan-1-one).
The Mediator complex-associated cyclin-dependent kinase CDK8 has been implicated in human disease, particularly in colorectal cancer where it has been reported as a putative oncogene to make complex receptor free of any ligand before docking. Receptor grid generated using glide module. The best conformation was chosen with the lowest docked energy after the docking search was completed. The interactions of 5FGK protein and ligand conformations, including hydrogen bonds and the bond lengths were analyzed. Molecular docking study was performed by using maestro (Schrödinger 11.4) which was a suite of automated docking tools and was used to predict the affinity, activity, binding orientation of ligand with the target protein and to analyze best conformations, the protein with all the 10 were loaded individually evaluated. We observed that the compound 8a and 8d derivatives showed best fit and best potent dock score then compared with doxorubicin.

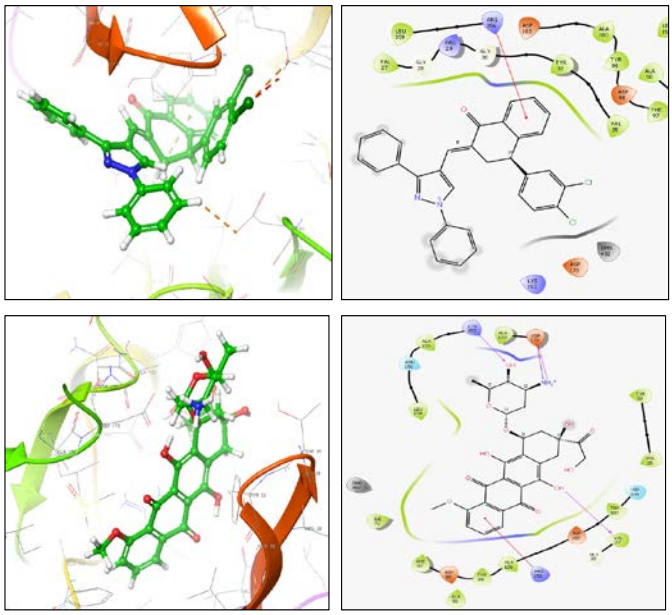


Figure 2. Intraction of synthesized compoud – 8a and doxorubicin with amino acids of cyclin-dependent kinase CDK8

Table-3 : Molecular Docking study of (E)-4-(3,4-dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives (**8a-i**)

Compounds	Dock Score (5FGK) Kcal/mol
8a	-6.925
8b	-6.136
8c	-4.628
8d	-6.483
8e	-6.049
8f	-6.122
8g	-6.289
8h	-6.179
8i	-5.704
Doxorubicin	-7.065

Experimental

The ^{1}HNMR (400 MHz) and ^{13}CNMR (100 MHz) spectra were recorded on Bruker Avance II 400 spectrometer using $CDCl_3$ as solvent and TMS as the internal standard, the chemical shifts are expressed in δ ppm. Mass spectra were recorded on SHIMADZU LCMS 2020 mass spectrometers. The progress of reactions was monitored by TLC (Silica gel, aluminum sheets 60 F254, Merck).

General procedure for preparation of (E)-4-(3,4-dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives:

A solution of 4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1(2H)-one (7, 11mmol), 1,3-diphenyl-1H-pyrazole-4-carbaldehyde (4a-i), 10mmol) and potassium hydroxide (20mmol) in methanol was taken into RBF and stirred at room temperature for 4-6hr. completion of the reaction monitored by TLC. After completion of the reaction, the reaction mixture poured in ice-cold water and neutralised with 1N HCl to solid precipitated out. Filter the solid, wash with water, dried and the product purified by column chromatography using silica gel and ethyl acetate:hexane (5-30%) to pure (E)-4-(3,4-dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives (8a-i).

Spectral data

(E)-4-(3,4-dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one (8a): Off-white solid; Yield: 76%; M.P.: 122-124°C; Rf: 0.4 (30% EtOAc: n-Hexane); ^{1}HNMR (DMSO-d_6, 400MHz): δ 3.39 (dd, J= 4.0, 15.6 Hz,1H, CH), 3.43 (dd, J= 4.0, 15.6 Hz,1H, CH), 4.59 (t, J= 5.6Hz, 1H, CH), 7.10-7.12 (dd, J= 2.0, 4.4Hz, 1H, ArH), 7.19-7.21 (d, J= 7.6Hz, 1H, ArH), 7.38-7.64 (m, 13H, ArH), 7.95-7.97 (d, J= 7.6Hz, 2H, ArH), 8.04-8.06 (d, J= 6.8Hz, 1H, ArH), 8.79 (s, 1H, PyH); ^{13}CNMR (DMSO-d_6, 100MHz): δ 34.1, 42.2, 115.8, 119.0, 127.0, 127.6, 127.8, 128.3, 128.6, 128.7, 128.8, 129.3, 129.5, 129.9, 130.6, 131.0, 131.7, 131.7, 131.9, 132.7, 133.9, 139.0, 144.3, 144.7, 153.3, 186.0; Mass: m/z 522 [M+H]+;

Elemental Analysis: Calculated: C, 73.71; H, 4.25; Cl, 13.60; N, 5.37; $C_{32}H_{22}Cl_2N_2O$ Found: C, 73.68; H, 4.21; Cl, 13.62; N, 5.35.

(E)-4-(3,4-dichlorophenyl)-2-((1-phenyl-3-(p-tolyl)-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one (8b): Off-white solid; Yield: 78%; M.P.: 118-120°C; Rf: 0.41 (30% EtOAc: n-Hexane); ^{1}HNMR (DMSO-d_6, 400MHz): δ 2.33 (s, 3H, -CH3), 3.39 (dd, J= 4.0, 15.6 Hz,1H, CH), 3.47 (dd, J= 4.0, 15.6 Hz,1H, CH), 4.60 (bt, 1H, CH), 7.10-7.12 (d, J= 8.8Hz, 1H, ArH), 7.19-7.21 (d, J= 7.6Hz, 1H, ArH), 7.31-7.64 (m, 12H, ArH), 7.94-7.96 (d, J= 8.0Hz, 2H, ArH), 8.04-8.06 (d, J= 7.6Hz, 1H, ArH), 8.76 (s, 1H, PyH); ^{13}CNMR (DMSO-d_6, 100MHz): δ 20.9, 34.1, 42.2, 115.7, 119.0, 127.0, 127.6, 127.8, 128.2, 128.3, 128.5, 128.8, 129.1, 129.3, 129.5, 129.9, 130.6, 131.0, 131.5, 132.8, 133.9, 138.2, 139.0, 144.8, 153.4, 186.0; Mass: m/z 536 [M+H]+; Elemental Analysis: Calculated: C, 74.02; H, 4.52; Cl, 13.24; N, 5.23; $C_{33}H_{24}Cl_2N_2O$ Found: C, 73.98; H, 4.50; Cl, 13.20; N, 5.28;

(E)-4-(3,4-dichlorophenyl)-2-((3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one (8c): Off-white solid; Yield: 79%; M.P.: 131-133°C; Rf: 0.40 (30% EtOAc: n-Hexane); ^{1}HNMR (DMSO-d_6, 400MHz): δ 3.36 (dd, J= 4.0, 15.6 Hz,1H, CH), 3.47 (dd, J= 5.2, 15.6 Hz,1H, CH), 3.80 (s, 3H, -OCH3), 4.56 (t, J= 5.2, 1H, CH), 7.04-7.10 (m, 3H, ArH), 7.17-7.19 (d, J= 7.6Hz, 1H, ArH), 7.32-7.61 (m, 10H, ArH), 7.87-7.97 (d, J= 8.0Hz, 2H, ArH), 8.02-8.04 (d, J= 7.6Hz, 1H, ArH), 8.72 (s, 1H, PyH); ^{13}CNMR (DMSO-d6, 100MHz): δ 34.1, 42.2, 55.2, 114.1, 115.5, 118.8, 124.2, 126.8, 127.5, 127.7, 127.9, 128.3, 128.4, 128.9, 129.3, 129.5, 129.6, 129.9, 130.0, 130.6, 131.0, 131.4, 132.8, 139.0, 144.2, 144.7, 153.1, 159.5, 185.9; Mass: m/z 552 [M+H]+; Elemental Analysis: Calculated: C, 71.87; H, 4.39; Cl, 12.86; N, 5.08; $C_{33}H_{24}Cl_2N_2O_2$ Found: C, 71.84; H, 4.42; Cl, 12.84; N, 5.07;

(E)-(E)-4-(3,4-dichlorophenyl)-2-((3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one (8d): Off-white yellow solid; Yield: 78%; M.P.: 148-150°C; Rf: 0.40 (30% EtOAc: n-Hexane); ^{1}HNMR (DMSO-d_6, 400MHz): δ 3.37 (dd, J= 4.4, 15.6 Hz,1H, CH), 3.47 (dd, J= 5.2, 15.6 Hz,1H, CH), 4.56 (bt, 1H, CH), 7.09-7.11 (d, J= 8.8Hz, 1H, ArH), 7.19-7.21 (d, J= 7.6Hz, 1H, ArH), 7.34-7.64 (m, 12H, ArH), 7.94-7.96 (d, J= 8.0Hz, 2H, ArH), 8.04-8.06 (d, J= 7.6Hz, 1H, ArH), 8.78 (s, 1H, PyH); ^{13}CNMR (DMSO-d_6, 100MHz): δ 34.1, 42.2, 115.6, 115.7, 115.8, 119.0, 127.0, 127.3, 127.6, 127.8, 128.3, 128.4, 128.7, 128.8, 129.3, 129.5, 130.0, 130.2, 130.3, 130.6, 131.0, 132.0, 132.7, 133.9, 138.9, 144.3, 144.7, 152.2, 186.0; Mass: m/z 540 [M+H]+; Elemental Analysis: Calculated: C, 71.25; H, 3.92; Cl, 13.14; F, 3.52; N, 5.19; $C_{32}H_{21}Cl_2FN_2O$ Found: C, 71.22; H, 3.88; Cl, 13.11; F, 3.50; N, 5.14;

(E)-2-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1(2H)-one (8e): Off-white yellow solid; Yield: 75%; M.P.: 142-144°C; Rf: 0.40 (30% EtOAc: n-Hexane); ^{1}HNMR (DMSO-d_6, 400MHz): δ 3.38-3.53 (m, 2H, CH) 4.58 (t, J= 5.6Hz, 1H, CH), 7.07-7.10 (dd, J= 2.0, 8.0Hz, 1H, ArH), 7.18-7.20 (d, J= 7.6Hz, 1H, ArH), 7.39-7.64 (m, 12H, ArH), 7.94-7.96 (d, J= 8.0Hz, 2H, ArH), 8.04-8.07 (dd, J= 1.2, 8.0Hz, 1H, ArH), 8.78 (s, 1H, PyH); ^{13}CNMR (DMSO-d_6, 100MHz): δ 34.1, 42.2, 115.8, 119.0, 127.1, 127.2, 127.6, 127.8, 128.3, 128.8, 129.3, 129.5, 129.8, 130.0, 130.6, 130.8, 131.0, 132.2, 132.7, 133.4, 133.9, 138.9, 144.3, 144.7, 151.8, 185.9; Mass: m/z 556 [M+H]+; Elemental Analysis: Calculated: C, 69.14; H, 3.81; Cl, 19.13; N, 5.04; $C_{32}H_{21}Cl_3N_2O$ Found: C, 69.11; H, 3.77; Cl, 19.10; N, 5.05;

(E)-2-((3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1(2H)-one (8f): Off-white yellow solid; Yield: 78%; M.P.: 139-141°C; Rf: 0.40 (30% EtOAc: n-Hexane); ^{1}HNMR (DMSO-d_6, 400MHz): δ 3.37 (m, 2H, CH), 4.56 (bt, 1H, CH), 7.08-7.10 (d, J= 8.4Hz, 1H, ArH), 7.18-7.20 (d, J= 7.6Hz, 1H, ArH), 7.39-7.62 (m, 10H, ArH), 7.71-7.73 (d, J= 8.0Hz, 2H, ArH), 7.94-7.96 (d, J= 8.0Hz, 2H, ArH), 8.05-8.07 (d, J= 7.6Hz, 1H, ArH), 8.78 (s, 1H, PyH); ^{13}CNMR (DMSO-d_6, 100MHz): δ 34.1, 42.2, 115.8, 119.0, 122.1, 127.0, 127.2, 127.6, 127.8, 128.3, 128.8, 129.3, 129.5, 129.7, 130.0, 130.0, 130.6, 131.1, 131.1, 131.7, 132.2, 132.7, 133.9, 138.9, 144.3, 144.7, 151.9, 185.9; Mass: m/z 601 [M+H]+; Elemental Analysis: Calculated: C, 64.02; H, 3.53; Br, 13.31; Cl, 11.81; N, 4.67; $C_{32}H_{21}Cl_2BrN_2O$ Found: C, 64.02; H, 3.53; Br, 13.31; Cl, 11.81; N, 4.67;

(E)-4-(3,4-dichlorophenyl)-2-((3-(4-hydroxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one (8g): Off-white yellow solid; Yield: 64%; M.P.: 157-159°C; Rf: 0.47(30% EtOAc: n-Hexane); ^{1}HNMR (DMSO-d6, 400MHz): δ 3.37 (m, 2H, CH) 4.58 (t, J= 5.2Hz, 1H, CH), 6.87-6.90 (d, J= 8.4Hz, 1H, ArH), 7.11-7.15 (m, 1H, ArH), 7.19-7.21 (d, J=7.2Hz, 1H, ArH), 7.31-7.64 (m, 10H, ArH), 7.77-7.99 (m, 3H, ArH), 8.04-8.06 (d, J= 8.0Hz, 1H, ArH), 8.73 (s, 1H, PyH); ^{13}CNMR (DMSO-d6, 100MHz): δ 33.7, 41.8, 118.2, 119.5, 125.0, 127.3, 127.8, 128.0, 128.9, 129.4, 129.4, 129.8, 130.2, 130.5, 131.0, 132.3, 133.5, 134.0, 134.7, 137.5, 144.7, 185.6; Mass: m/z 538 [M+H]+; Elemental Analysis: Calculated: C, 71.52; H, 4.13; Cl, 13.19; N, 5.21; $C_{32}H_{22}Cl_2N_2O_2$ Found: C, 71.51; H, 4.10; Cl, 13.20; N, 5.22;

(E)-4-(3,4-dichlorophenyl)-2-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one (8h): Off-white yellow solid; Yield: 69%; M.P.: 145-147°C; Rf: 0.41 (30% EtOAc: n-Hexane); ^{1}HNMR (DMSO-d_6, 400MHz): δ 3.37 (m, 2H, CH) 4.60 (bt, 1H, CH), 7.05-7.07 (d, J= 8.4Hz, 1H, ArH), 7.19-7.21 (d, J=7.2Hz, 2H, ArH), 7.39-7.65 (m, 10H, ArH), 7.79-8.03 (m, 2H, ArH), 8.06-8.08 (d, J= 8.0Hz, 2H, ArH), 8.83 (s, 1H, PyH); ^{13}CNMR (DMSO-d_6, 100MHz): δ 34.0, 41.5, 118.2, 119.3, 126.6, 127.6, 127.8, 128.0, 128.2, 128.9, 129.2, 129.4, 129.7, 129.8, 130.5, 131.5, 132.7, 133.5, 133.9, 135.7, 138.8, 142.5, 145.2, 150.3, 185.9; Mass: m/z 591 [M+H]+; Elemental Analysis: Calculated: C, 67.85; H, 3.74; Cl, 12.52; N, 7.42; $C_{32}H_{21}Cl_2N_3O_3$ Found: C, 67.81; H, 3.70; Cl, 12.47; N, 7.37;

(E)-4-(3,4-dichlorophenyl)-2-((3-(2,4-dichlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one (8i): Off-white yellow solid; Yield: 72%; M.P.: 136-138°C; Rf: 0.40 (30% EtOAc: n-Hexane); ^{1}HNMR (DMSO-d_6,

400MHz): δ 3.37 (m, 2H, CH) 4.56 (t, J= 5.2Hz, 1H, CH), 7.05-7.08 (dd, J= 2.0, 8.0Hz, 1H, ArH), 7.21-7.24 (m, 2H, ArH), 7.38-7.63 (m, 10H, ArH), 7.82-7.83 (d, J= 2.0Hz, 1H, ArH), 7.95-8.00 (m, 3H, ArH), 8.93 (s, 1H, PyH); ^{13}CNMR (DMSO-d_6, 100MHz): δ 33.9, 41.8, 117.3, 119.1, 126.3, 127.6, 127.8, 128.0, 128.2, 128.9, 129.2, 129.4, 129.6, 129.8, 130.5, 131.0, 132.7, 133.5, 133.9, 134.7, 138.8, 144.9, 185.8; Mass: m/z 591 [M+H]+; Elemental Analysis: Calculated: C, 65.11; H, 3.42; Cl, 24.02; N, 4.75; $C_{32}H_{20}C_{l4}N_2O$ Found: C, 65.07; H, 3.45; Cl, 24.00; N, 4.72;

CONCLUSION

In the present study synthesized a novel series of (E)-4-(3,4-Dichlorophenyl)-2-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-3,4-dihydronaphthalen-1(2H)-one derivatives were synthesised by Claisen-Schmidt condensation of 4-(3,4-dichlorophenyl)-3,4-dihydronaphthalen-1(2H)-one and 1,3-diphenyl-1H-pyrazole-4-carbaldehyde in the presence of KOH in good yield. All the synthesised targets were evaluated for their cytotoxicity against a panel of three cancer cell lines (SiHa, MDA-MB-231 and PANC-1). Among the tested compounds many of them exhibited significant anticancer activity, the compound 8a was found to be the most promising analogue in this series tested three cancer cell lines.

ACKNOWLEDGEMENT

The authors are thankful to the Department of Chemistry, Satavahana University for providing laboratory facility.

CONFLICT OF INTEREST

Authors declare that there is no conflict of interest for this work.

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