Synthesis, Characterization and Biological Activityof some novelphenyl-2H, 1'H-[3, 4'] bipyrazolyl derivatives.

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Abstract
An important class of heterocyclic molecule called bi-pyrazolyl and its derivatives has both chemical and biological applications. In this study, substituted acetophenones and substituted hydrazine are used to create bi-pyrazolyl derivatives, which are then synthesised and characterised.Substituted acetophenones, substituted hydrazine, and DMF were used in the first phase of the synthesis of 1-substituted-3-aryl-1H-pyrazole-4-carbaldehydes derivatives in phosphorus trichloride ($POCl_3$) using a scientific microwave oven 20%, 140 watts. In the second phase, various phenyl-2H, 1'H-[3, 4] bipyrazolyl derivatives with good yield were produced by reacting substituted hydrazine, acetone, and 10% NaOH with 1-substituted 3-aryl-1H-pyrazole-4-carbaldehydes derivatives in the scientific microwave oven (20%, 140 watts). FT-IR, H1NMR, and 13CNMR were used to characterise each of the produced compounds. By using PASS, all of the produced compounds were examined for biological activity.

Keywords:-DMF, substituted hydrazine, phosphorus trichloride, QSAR study, microwave irradiation.

I. Introduction

The first bipyrazolyl series was created in 1893[1]. Since then, numerous articles about bipyrazolyl derivatives have been published in the literature [2]. These substances represent a very exceptional class of pharmacologically relevant heterocycles. They may have antitumor[3], anti-inflammatory[4], antimicrobial, cytotoxic[5, 6], antiallergic[7], cardiovascular[8], and diuretic[9] properties, for instance. As insecticides[10], herbicides[11], fungicides[12–14], in the photography and paint industries[15], and in the manufacture of heat-resistant polymers, bipyrazoles were also discovered to be useful. Additionally, bipyrazole derivatives have been employed as free radical scavengers[16] and to prevent or treat a number of conditions brought on by active oxygen.

Bipyrazolyl derivatives are often created using cyclization procedures[17]. However, 1, 3-dipolar cycloaddition[18], which uses diarylnitrilimines or diazocompounds as reagents, is one of the most flexible methods for the synthesis of five-membered heterocycles. These methods have also been utilised to produce bipyrazoles. Since 1978, it has been known that hydrazones can form azomethine imine intermediates that can go through a 1,3-dipolar cycloaddition by inducing a thermal 1,2-hydrogen shift. A protonated substrate has been shown to intramolecularly aid the hydrazone-azomethine imine isomerization under benign conditions[19] if a carbonyl group is present in the proper location.However, in the majority of instances, high-activated dipolarophiles must be added to thermally generated

azomethineimines under reflux in high-boiling solvents with extended reaction durations[20]. The reaction's synthetic usefulness is decreased by these requirements.

Considering the significance of bipyrazolyl derivatives, we aimed to create novel substances like as 2-(2, 4-Dinitro-phenyl)-5-methyl-3'-phenyl-2H,1'H-[3,4']bipyrazolyl[5-a], 5-Methyl-2,3'-diphenyl-2H,1'H-[3,4']bipyrazolyl[5-b], 3'-(4-Methoxy-phenyl)-5-methyl-2-phenyl-2H,1'H-[3,4']bipyrazolyl [5-c], 2-(2,4-Dinitro-phenyl)-3'-(4-methoxy-phenyl)-5-methyl-2H,1'H-[3,4']bipyrazolyl [5-d], 3'-(4-Methoxy-phenyl)-5-methyl-2,1'-diphenyl-2H,1'H-[3,4']bipyrazolyl [5-e], 2-(2,4-Dinitro-phenyl)-3'-(4-methoxy-phenyl)-5-methyl-1'-phenyl-2H,1'H-[3,4']bipyrazolyl [5-f], 5-Methyl-3'-(4-nitro-phenyl)-2-phenyl-2H,1'H-[3,4']bipyrazolyl [5-g], 2-(2,4-Dinitro-phenyl)-5-methyl-3'-(4-nitro-phenyl)-2H,1'H-[3,4']bipyrazolyl[5-h], 5-Methyl-3'-(4-nitro-phenyl)-2,1'-diphenyl-2H,1'H-[3,4']bipyrazolyl [5-i] and 2-(2,4-Dinitro-phenyl)-5-methyl-3'-(4-nitro-phenyl)-1'-phenyl-2H,1'H-[3,4']bipyrazolyl [5-j].

PASS

A user-selected (set of) compound's 565 likely biological functions are predicted by the software programme PASS (s). 5-hydroxytryptamine antagonists, neuromuscular blockers, antibiotics, antidepressants, antiviral medicines, contraceptives, tumour necrosis factor antagonists, and many other substances are included in these actions. PASS predictions have led to the discovery of novel pharmaceutical substances with impacts on anxiety, inflammation, hypertension, cancer, and other conditions. Chemical libraries of millions of chemicals are covered by PASS.

According to various functions, as illustrated in equation, the biological activities of chemical compounds are related to their physical characteristics (1).

Biological activity = f (physicochemical properties)…….. (1)

As a result, "the biological activity spectrum" is described as a quality that is "intrinsic" to a material and solely dependent on its physicochemical properties. Based on SAR analysis of the training set, which contains hundreds of chemicals with various biological functions, PASS is able to predict this spectrum. The qualitative descriptions of biological activities are included in PASS.

Importance of PASS

1. Since it takes time and money to experimentally determine a drug's biological function, using PASS is frequently important.

2. PASS is a useful tool for finding compounds with the desired qualities and no undesired side effects.

3. It is used to select the compounds that are the most likely from the pool of samples that are available for a particular screening.

4. To identify further relevant screens for a specific component.

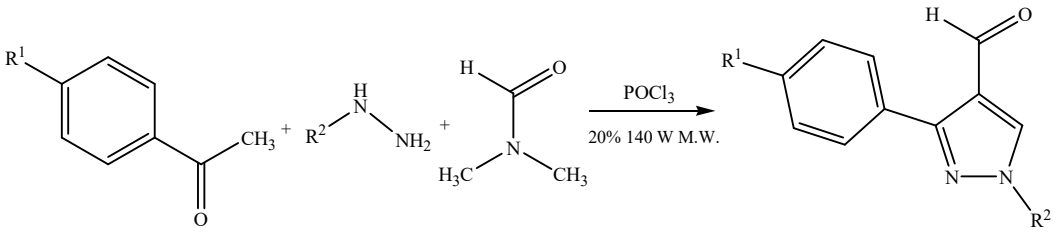
The current study uses PASS as a technique to create the medicine with the highest potential activity because of the significance of PASS.

II. Experimental

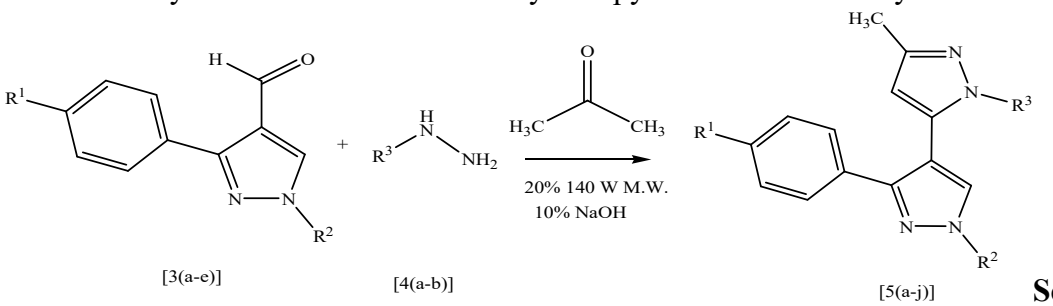
The melting points were discovered in uncorrected open capillary tubes. The 1H NMR spectra were taken in $CDCl_3$ with TMS as an internal standard on a Bruker spectrometer at 400 MHz, and the IR spectra were captured in KBr pellets on a Nicolet 400D spectrometer. Selected samples collected with the LC-MSD-Trap-SL 01046 and LC-MS TLC was used to test the compounds' purity on silica-G plates. Using pass software, anti-microbial activities are checked.

Synthesisof1-substituted-3-aryl-1H-pyrazole-4-carbaldehydes(3a-e): In 100 mL round bottom flask 0.02 mol substituted acetophenone**(1a-c)**, 0.02 mol substituted hydrazine **(2a-b)** and 10 mL DMF were mixed in ethanol (30 mL). $POCl_3$ solution (1 mL) was added and microwaves were used to irradiate the reaction mixture for 4-5 minutes at 20% microwave power (140 W).TLC was used to confirm the reaction's completion (Ethyl acetate: Hexane 1:9). The reaction mixture was put into crushed ice after being allowed to cool at room temperature. To obtain pure products, the solid was filtered, washed with a little amount of ethanol, then refined by recrystallization from ethanol **(3a-e)**(**Scheme-I**).

Synthesisof phenyl-2H, 1'H-[3, 4'] bipyrazolyl (5a-j): A 100 mL round bottom flask 0.001 mol3-Phenyl-1H-pyrazole-4-carbaldehyde **(3a-e)**, 0.001 mol substituted hydrazine **(4a-b)**, 10 mL acetone were mixed in ethanol (30 mL) and 10% NaOH solution were added. Microwaves were used to irradiate the reaction mixture for 5-7 minutes at 20% microwave power (140 W). TLC was used to confirm the reaction's completion (Ethyl acetate: Hexane 1:9). The reaction mixture was put into crushed ice after being allowed to cool at room temperature. To obtain pure products, the solid was filtered, washed with a little amount of ethanol, then refined by recrystallization from ethanol **(5a-j)**(**Scheme-II**).Table 1 summarises the specifics of the microwave-induced bipyrazolyl synthesis.



Scheme-I: Synthesisof1-substituted-3-aryl-1H-pyrazole-4- carbaldehydes



Scheme-II: Synthesisofphenyl-2H, 1'H-[3, 4'] bipyrazolyl

2-(2, 4-Dinitro-phenyl)-5-methyl-3'-phenyl-2H, 1'H-[3, 4']bipyrazolyl (5a): Yield: 83%; Time (min.): 5; m.p.214^{0}C;m.f. $C_{19}H_{14}N_6O_4$;IR (KBr, $\nu_{max,}$ cm^{-1}): 1124.14 (C-N), 1241.86 (N-N), 1492.90 (-NO_2), 1583.56 (C=N), 3095.75 (Ar-CH), 3309.85 (NH);^{1}HNMR (δ ppm):

2.33 (s, 3H, CH_3), 6.45 (s, 1H, =CH), 7.42-7.44 (d, 1H,=CH), 7.61-7.64 (m, 5H, C_6H_5), 7.81-7.84 (d, 1H, =CH), 8.44-8.47 (d, 1H, =CH), 8.75 (s,1H, =CH), 9.52 (s, 1H, NH) ; ^{13}C NMR(δ ppm): 13.50(–CH_3), 108.03(=CH), 115.16(=C<),121.58(=CH), 126.58(2×=CH), 127.58(=CH), 128.20(=CH),129.00(2×=CH), 130.50(=CH), 136.34(=C<), 137.17(=C<), 138.60(=CH), 142.34(=C<),144.30(=C<), 145.20 (=C<), 146.58(=C<), 150.00(=C<); MS:*m/z* (M^+1 390).

5-Methyl-2, 3'-diphenyl-2H, 1'H-[3, 4'] bipyrazolyl (5b): Yield: 76%; Time (min.): 5; m.p. 209^{0}C; m.f. $C_{19}H_{16}N_4$; IR (KBr, $\nu_{max,}$ cm^{-1}):1075.24(C-N), 1217.24(N-N), 1504.20(C=C), 1600.35(C=N), 3021.24(Ar-CH), 3300.56(NH) ; ^{1}HNMR (δ ppm): 2.33(s, 3H, CH_3), 6.45(s, 1H, =CH), 7.37- 7.40(m, 5H, C_6H_5),7.60-7.64(m, 5H, C_6H_5),7.91 (s, 1H, =CH), 9.52 (s, 1H, NH); ^{13}C NMR(δ ppm):13.47(–CH_3), 108.48(=CH), 115.16(=C<), 124.21(2×=CH), 126.23(2×=CH), 127.58(=CH), 128.00(=CH), 128.43(2×=CH), 128.94(2×=CH), 137.17(=C<), 138.60(=CH), 139.71(=C<), 142.22(=C<), 144.40(=C<), 149.78 (=C<);MS :*m/z* (M^+1 300).

3'-(4-Methoxy-phenyl)-5-methyl-2-phenyl-2H, 1'H-[3,4'] bipyrazolyl (5c): Yield:78%; Time(min.): 6; m. p. 217^{0}C; m. f. $C_{20}H_{18}N_4O$; IR (KBr, $\nu_{max,}$ cm^{-1}):1160.36(OCH_3), 1217.24(N-N), 1500.04(C=C), 1577.84(C=N), 3012.04(Ar-CH), 3300.56(NH) ; ^{1}HNMR (δ ppm): δ 2.36(s, 3H, CH_3), 4.00(s, 3H, OCH3), 6.44(s, 1H, =CH), 7.51-7.54 (m, 5H, C_6H_5),7.71-7.74(m, 4H, C_6H_4), 7.89(s, 1H, =CH), 9.59(s, 1H, NH); ^{13}C NMR(δ ppm):13.43(–CH_3), 55.34(OCH_3), 108.46(=CH),114.23(2×CH), 115.10(=C<), 124.65(2×=CH), 127.34(=CH), 128.41(2×=CH), 128.94(2×=CH), 137.15(=C<), 138.83(=C<), 139.74(=C<), 142.35(-CH), 144.41(=C<), 149.48(=C<), 160.04(=C<); MS : *m/z* (M^+1 330).

2-(2,4-Dinitro-phenyl)-3'-(4-methoxy-phenyl)-5-methyl-2H,1'H-[3,4']bipyrazolyl(5d): Yield:81%; Time(min.): 6; m. p. 229^{0}C; m. f. $C_{20}H_{16}N_6O_5$; IR (KBr, $\nu_{max,}$ cm^{-1}):1295(C-O), 1515(-NO_2), 1595(C=N), 1600 (C=C), 3040(Ar-H), 3333(-NH); ^{1}HNMR (δ ppm): δ 2.33(3H,s,CH_3), 3.80(3H,s,OCH_3), 6.44(H,s,=CH), 6.97-7.73(4H,m,C_6H_4), 7.42(H,d,=CH), 7.93(H,d,=CH), 8.48(H,d,=CH), 8.78(H,s,=CH), 9.52(H,d,NH); ^{13}C NMR(δ ppm): 13.44(–CH_3), 55.37(OCH_3), 108.47(=CH), 114.21(2×=CH),115.07(=C<), 121.22(=CH), 128.22(=CH), 128.40(2×=CH), 130.13(=CH), 136.81(=C<), 137.14(=C<), 138.84(=CH), 142.38(=C<), 144.42(=C<), 145.41(=C<), 146.51(=C<), 149.50(=C<), 160.07(=C<); MS : *m/z* (M^+1 496).

3'-(4-Methoxy-phenyl)-5-methyl-2,1'-diphenyl-2H,1'H-[3,4']bipyrazolyl (5e): Yield:79%; Time(min.): 6; m. p. 212^{0}C; m. f $C_{26}H_{22}N_4O$; IR (KBr, $\nu_{max,}$ cm^{-1}):1293(C-O), 1598(C=N), 1605 (C=C), 3042(Ar-H),; ^{1}HNMR (δ ppm): δ 2.36(3H,s,-CH_3), 3.82(3H,s,OCH_3), 6.44(H,s,=CH), 6.97-7.73(4H, m, C_6H_4), 7.11-7.31(5H,m,C_6H_5), 7.33-7.72(5H,m,C_6H_5), 8.27(H,s,=CH);^{13}C NMR(δ ppm): 13.45(–CH_3), 55.35(OCH_3), 108.48(=CH), 114.23(2×=CH) ,115.09(=C<), 118.95(2×=CH), 124.36(=CH), 124.68(2×=CH), 126.85 (=C<), 127.36 (=C<), 128.41(2×=CH), 128.96(2×=CH), 129.50(2×=CH),137.17(=C<), 139.71(=C<), 139.90 (=C<), 142.37(=C<), 144.40 (=C<), 149.49(=C<), 160.05(=C<); MS : *m/z* (M^+1 406).

2-(2,4-Dinitro-phenyl)-3'-(4-methoxy-phenyl)-5-methyl-1'-phenyl-2H,1'H-[3,4']bipyrazolyl (5f): Yield:83%; Time(min.): 6; m. p. 241^{0}C; m. f. $C_{26}H_{20}N_6O_5$; IR (KBr, $\nu_{max,}$ cm^{-1}):1288(C-O), 1515 (-NO_2), 1583(C=N), 1585 (C=C), 3045(Ar-CH); ^{1}HNMR (δ ppm): δ 2.37(3H,s,-CH_3), 3.82(3H,s,OCH_3), 6.44 (H,s,=CH),6.96-7.72(4H,m ,C_6H_4) , 7.31-

7.70(5H,m,C_6H_5), 7.41(H,d,=CH), 8.26(H,s,=CH),8.47(H,d,=CH) ,8.79 (H, s, =CH); ^{13}C NMR(δ ppm): 13.43(–CH_3), 55.36(OCH_3), 108.50(=CH), 114.24(2×=CH), 115.11(=C<) , 118.96(2×=CH), 121.21(=CH), 124.37 (=CH), 126.86(=C<), 128.21(=CH), 128.42(2×=CH), 129.51(2×=CH), 130.11(=CH), 136.81(=C<),137.18(=C<), 139.91(=C<),142.36(=C<),144.41(=C<),145.41(=C<),146.51(=C<),149.51(=C<),160.06(=C <); MS : *m/z* (M^+1 496).

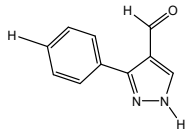
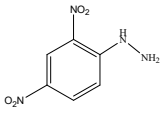
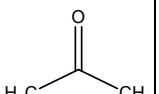
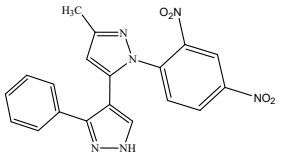
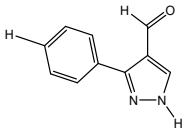
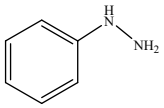
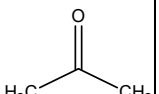
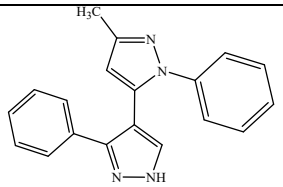
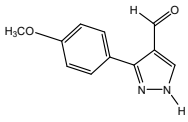
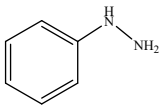
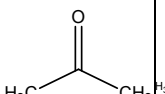
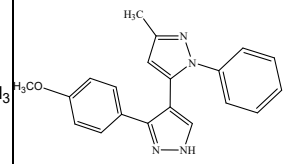
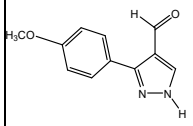
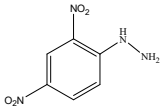
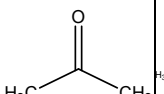
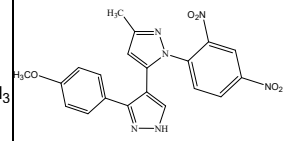
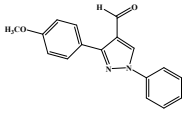
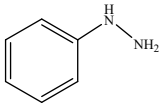
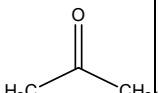
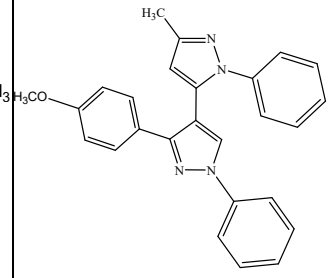
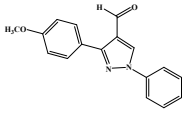
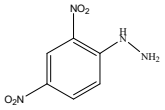
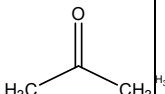
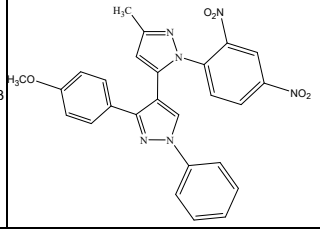
5-Methyl-3'-(4-nitro-phenyl)-2-phenyl-2H,1'H-[3,4']bipyrazolyl (5g):
Yield:81%; Time(min.): 7; m. p. 249^{0}C; m. f. $C_{19}H_{15}N_5O_2$,; IR (KBr, $\nu_{max,}$ cm^{-1}):1062.78(C-N), 1217.08(N-N), 1421.54(-NO_2), 1589.34(C=N),1614.42(C=C), 3095.75(Ar-CH), 3309.85(NH) ;^{1}HNMR (δ ppm): 2.38(s, 3H, CH_3), 6.46(s, 1H, =CH),7.41-7.44(m, 5H, C_6H_5),7.90(s, 1H, =CH), 8.21-8.24(m, 4H, C_6H_4), 9.56(s, 1H,NH); ^{13}C NMR(δ ppm): 13.42(-CH_3), 108.47(=CH), 115.09(=C<),123.88(2×=CH), 124.68(2×=CH), 127.32(=CH), 127.93(2×=CH), 128.94(2×=CH), 137.17(=C<), 138.79(=CH), 139.70(=C<), 142.37(=C<), 144.39(=C<), 147.49(=C<), 149.52 (=C<); MS : *m/z* (M^+1 345).

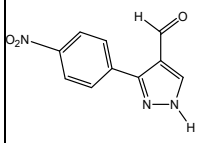
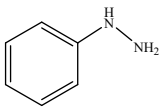
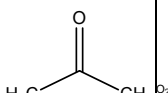
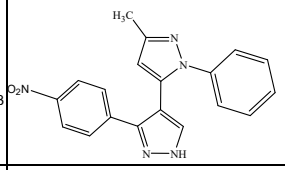
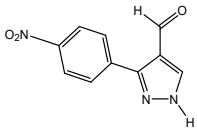
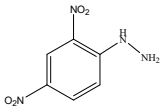
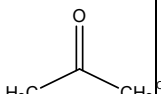
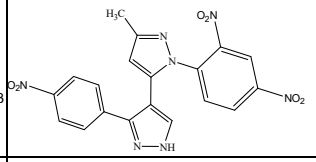
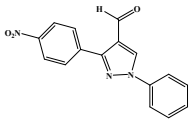
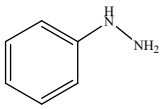
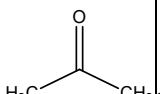
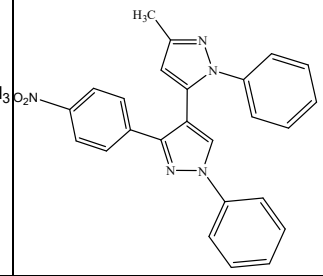
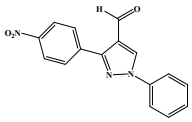
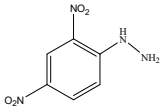
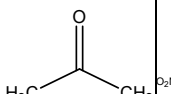
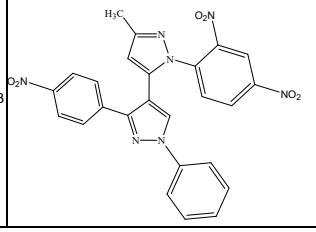
2-(2,4-Dinitro-phenyl)-5-methyl-3'-(4-nitro-phenyl)-2H,1'H-[3,4']bipyrazolyl(5h):
Yield:76%; Time(min.): 6; m. p. 239^{0}C; m. f. $C_{19}H_{13}N_7O_6$; IR (KBr, $\nu_{max,}$ cm^{-1}):1594 (C=C), 1520(-NO_2), 1598(C=N), 3033 (Ar-CH), 3330 (-NH); ^{1}HNMR (δ ppm): δ 2.34(3H,s,-CH_3), 6.44(H,s,=CH),7.41(H, d, =CH), 7.80-8.24(4H, m, C_6H_4), 7.90(H,d,=CH), 8.47(H,d,=CH), 8.77(H,s,=CH) 9.51(H,d,NH),; ^{13}C NMR(δ ppm): 13.44(–CH_3), 108.47(=CH), 115.07(=C<), 121.21(=CH), 123.96(2×=CH), 127.92(2×=CH), 128.21(=CH), 130.11(=CH), 136.81(=C<), 137.19(=C<), 138.83(=CH), 142.36(=C<), 144.42 (=C<), 145.02(=C<), 146.52(=C<), 147.50 (=C<), 149.48(=C<); MS : *m/z* (M^+1 435).

5-Methyl-3'-(4-nitro-phenyl)-2,1'-diphenyl-2H,1'H-[3,4']bipyrazolyl(5i): Yield:77%; Time(min.): 6; m. p. 232^{0}C; m. f. $C_{25}H_{19}N_5O_2$; IR (KBr, $\nu_{max,}$ cm^{-1}):1513(-NO_2), 1595 (C=N), 1600 (C=C), 3040 (Ar-CH); ^{1}HNMR (δ ppm): δ 2.36(3H,s,-CH_3), 6.45(H,s,=CH), 7.11-7.31(5H, m, C_6H_5), 7.33-7.72(5H,m,C_6H_5), 7.80-8.24(4H,m,C_6H_4),8.27(H,s,=CH); ^{13}C NMR(δ ppm): 13.43(–CH_3), 108.49(=CH), 115.09(=C<), 118.95(2×=CH), 121.20(=CH), 123.94(2×=CH), 124.36(=CH), 126.85 (=C<), 127.91(2×=CH), 128.20(=CH), 129.50(2×=CH), 130.10(=CH), 136.80(=C<), 137.17(=C<), 139.90 (=C<), 142.37(=C<), 144.40 (=C<), 145.00(=C<)146.50(=C<), 147.49 (=C<), 149.50(=C<);MS : *m/z* (M^+1 421).

2-(2,4-Dinitro-phenyl)-5-methyl-3'-(4-nitro-phenyl)-1'-phenyl-2H,1'H-[3,4']bipyrazolyl (5j): Yield:79%; Time(min.):6; m. p. 237^{0}C; m. f. $C_{25}H_{17}N_7O_6$; IR (KBr, $\nu_{max,}$ cm^{-1}):1525(-NO_2), 1610 (C=C), 1635 (C=N), 3050 (Ar-CH); ^{1}HNMR (δ ppm): δ 2.34(3H,s,-CH_3), 6.47(H,s,=CH), 7.33-7.72(5H,m,C_6H_5), 7.80-8.24(4H,m,C_6H_4), 7.42(H,d,=CH), 8.26(H,s,=CH), 8.48(H,d,=CH), 8.78(H,s,=CH); ^{13}C NMR(δ ppm): 13.42(–CH_3), 108.44(=CH), 115.06(=C<), 118.95(2×=CH), 121.22(=CH), 123.94(2×=CH),124.34(=CH), 126.85 (=C<), 127.93(2×=CH), 128.25(=CH), 129.50(2×=CH), 130.12(=CH),136.80(=C<), 137.16(=C<), 139.91 (=C<), 142.36(=C<), 144.43 (=C<), 145.03(=C<) 146.51(=C<), 147.49 (=C<),149.52(=C<);MS : *m/z* (M^+1 511).

TABLE-1
PREPARATION OF BIPYRAZOLYL UNDER MICROWAVE IRRADIATION

Comp.	Substrate			Product	Time (min.)	m.p. (^{0}C)	Yield (%)
	1	2	3				
5a					5	215	84
5b					5	209	74
5c					5	215	78
5d					6	229	81
5e					5	212	79
5f					6	241	83

5g					7	249	81
5h					6	239	69
5i					5	232	77
5j					5	237	79

III. Result and discussion

1. The substances [3(a-e)] to [5(a-j)] display the range of potential biological actions.
2. From virtually all the compounds [3(a-e) to [5(a-j)], only two activities, namely HMGCS2 expression enhancer and Liver fibrosis therapy, are expected.
3. The compounds [5-g] and [5-i] are anticipated to exhibit spectacular HMGCS2 expression enhancer activity. Additionally, because of the phenyl ring, [5-g] is anticipated to be more active than the monocyclic molecule [5-i].
4. Each of the compounds [3(a-e)] and [5(a-j)] is anticipated to have therapeutic potential for liver fibrosis. But out of all the compounds, [5-b] is probably the most active.
5. The bipyrazolyl compound [5-b] is likewise anticipated to have spectacular signal transduction pathways inhibitor activity. This is more likely to have substrate activity for the cyclin-dependent kinase 2 inhibitor.
6. It is also anticipated that some of the drugs in this series will have MAP3K5 inhibitor, hepatic disorders therapy, CDK9/cyclin T1 inhibitor, UGT2B12 substrate, Cyclin-dependent kinase inhibitor, and CYP19A1 expression inhibitor properties.

7. Due to the differences from the known pharmacological drugs, several of the compounds have Pa values between 0.5 and 0.7, making it conceivable for them to demonstrate activities. They are also most likely new chemical entities.

The substances [5-g] and [5-i] are proposed for the expression enhancer activity of the gene HMGCS2, which controls the synthesis of ketone bodies in the liver and extrahepatic organs.

QSAR Analysis of Activities with PASS:

A number of biological functions were examined in relation to structure using the computer programme PASS. Using the structures of derivatives [5(a-j)], software was used to forecast the probabilities of being active [Pa] and inactive [Pi] given a set of biological activities. The following three activities were projected to have the highest probabilities for the chemical series [5(a-j)].

i) HMGCS2 expression enhancer(ii) MAP3K5 inhibitor(iii) Liver fibrosis treatment.

(i) HMGCS2 expression enhancer:

The gene HMGCS2, which regulates ketone body synthesis, is found in the liver and several extrahepatic tissues, including the colon. This gene's expression alters when the CaCo-2 colonic epithelial cells differentiate. HMGCS2 is mostly detected in differentiated cells of the human colonic epithelium, according to immunohistochemistry utilising specific antibodies. The test indicates that HMGCS2 is a direct target of c-Myc, which contains HMGCS2 transcriptional activity. Blocking Miz-1's trans activating activity, which often takes place through a Sp1-binding site in the gene's proximal promoter, mediates c-Myc trans repression. 90% of Myc-dependent colon and rectum tumours had decreased expression of the human HMGCS2 gene.HMGCS2 protein expression is down-regulated in carcinomas with moderate and poor differentiation. Additionally, it is down-regulated in 80% of small intestinal tumours without Myc.

(ii) MAP3K5 inhibitor:

288 melanomas with the MAP3K5 popularity screen were still present in the harbour. All MAP3K5-mutated samples included the wild type of BRAF, proving that the two mutations are mutually exclusive. According to a functional analysis of the MAP3K5 R256C mutation, the decreased MKK4 activation caused by increased binding of the inhibitory protein thioredoxin led to higher proliferation and anchorage-independent growth of melanoma cells. This mutation indicates a possible target for the development of novel melanoma treatments.

(iii)Liver fibrosis treatment:

As a result of an imbalance between fibrous hyperplasia and fibrous breakdown, liver fibrosis is the excessive loss of fibrous connective tissue in the liver. The body's response to damage healing is called fibrous hyperplasia. Continuous fibrous hyperplasia of the liver and the development of liver fibrosis can result from repeated chronic liver parenchyma necrosis and inflammation, which can be caused by a variety of factors. Liver fibrosis is a necessary stage for chronic liver disorders to progress into liver cirrhosis from the pathological alterations of various chronic liver diseases. It is stated that while liver cirrhosis cannot be reversed, hepatic fibrosis can.

Table 2
PREDICTIONS OF BIOLOGICAL ACTIVITIES BY PASS

Comp.	HMGCS2 expression enhancer	MAP3K5 inhibitor	Liver fibrosis treatment
	Pa	Pa	Pa
5a	0.606	0.498	0.438
5b	0.606	0.576	0.605
5c	0.539	0.521	0.442
5d	0.553	0.459	0.358
5e	0.511	0.513	0.250
5f	0.577	0.434	0.207
5g	0.702	0.516	0.472
5h	0.609	0.501	0.448
5i	0.694	0.507	0.260
5j	0.636	0.478	0.252

IV. Conclusion

As a result, we have developed a quick and efficient method that might be used in the creation of new drugs for the selective synthesis of new 5-methyl-2, 1, 3'-triphenyl-2H, 1'H-[3, 4'] bipyrazolyl in an aqueous medium.

V. Acknowledgments

The Central Instrumental Facility, SavitribaiPhule, Pune University, Pune, India, and the DST-FIST-financed Central Instrumentation Laboratory, Dada PatilMahavidyalaya, Karjat, Dist- Ahmednagar, India, are gratefully acknowledged by the authors for their assistance with spectrum analysis and financial support.

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