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Research Paper

Synthesis and anti-HIV activity of novel N-((1, 3-substituted diphenyl-1*H*-pyrazole-4-yl)methylene)-2-methylindoline-1-amine derivatives using MTT method

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Abstract: A new series of novel N-((1, 3-substituted diphenyl-1*H*-pyrazole-4-yl)methylene)-2-methylindoline-1-amine derivatives has been synthesized by microwave assisted green chemical approach. All the synthesized compounds were evaluated for their anti-HIV activity using MTT method. Most of the compounds shown moderate to potent activity against two strains of Human Immunodeficiency virus (HIV-I and HIV-II). Among all compounds, three compounds **5c**, **5d**, **5e**, **5j**, **5m** and **5o** shown potent activity (5c, IC₅₀ = 9.07 µg/ml), (5d, IC₅₀ = 12.55 µg/ml), (5e, IC₅₀ = 8.05 µg/ml), (5j, IC₅₀ = 8.01 µg/ml), (5m, IC₅₀ = 10.09 µg/ml), (5o, IC₅₀ = 8.21 µg/ml), while **5f** and **5i** shown moderately active against MT-4 cells.

Introduction

The human immunodeficiency virus(HIV) has now been established as the causative agent of the acquired immunodeficiency syndrome (AIDS) for over 20 years.^[1-2] The current therapy against the human immunodeficiency virus type 1 (HIV-1), which is the etiological agent of acquired immunodeficiency syndrome (AIDS), is based on six of categories drugs: nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs/NtRTIs); nonnucleoside reverse transcriptase inhibitors (NNRTIs); protease inhibitors (PIs); cell entry inhibitors [fusion inhibitors (FIs) and co-receptor inhibitors (CRIs)]; and integrase inhibitors(INIs).^[3]

In the present era, acquired HIV (Human Immunodeficiency Virus) is the most fatal disorder for which no completely successful chemotherapy has been developed so far. A variety of anti-HIV agents rely on inhibition of key enzymes involved with the virus life cycle. Over 20 anti-retroviral medications have now been approved for the treatment of HIV-infected individuals.^[4] HAART (Highly active anti-retroviral therapy) has demonstrated that targeting multiple enzymes provides one means of circumventing this problem, with combination therapies directed against both the HIV reverse transcriptase and the protease enzymes showing good results in reducing viral loads in HIV-1 infected patients.^[5] The highly potent and selective inhibitor of HIV-1 reverse transcriptase is

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NNRTIs which are structurally and chemically dissimilar group of anti-retrovirals.^[6] Moreover, pyrazole framework containing compounds are well known for its antimicrobial,^[7] anti-inflammatory^[7] analgesic^[7] anti HIV, anticancer and hypoglycaemic activities.^[8] Numerous pyrazoles are utilized as insecticides and pesticides due to their herbicidal and fungicidal activity.^[9] Recently, pyrazoles containing aryl substituted emerged as p38 Kinase inhibitors, antiparasitic activities.^[10]

Materials and Methods

All Melting points of the synthesized compounds were recorded by open capillary method and are uncorrected. Formation of the compounds was routinely checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV. All the reaction was carried out in Q-pro-M microwave synthesizer. The IR spectra were recorded on a Shimadzu FT-IR-8400 instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using Direct Injection Probe technique. ¹H NMR was determined in CDCl₃/DMSO solution on a Bruker Ac 400 MHz spectrometer. Elemental analysis of the all the synthesized compounds were carried out on Elemental Vario EL III Carlo Erba 1108 model and the results are in agreements with the structures assigned.

Synthesis of N-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-2-methylindolin-1-amines (5a-o)

All the pyrazole aldehydes **4a-o** derivatives were prepared by reported method.^[11] Equimolar amounts of neat reactants i.e. 2-Methyl indolin-1-amine and substituted pyrazolaldehydes were taken in an Erlenmeyer flask, dissolved in Methanol which was taken 10 time w/v of the reactants and served as the solvent. Very few drops of Acetic acid were added

in the reaction mixture to catalyze the reaction in the forward direction. The reaction mixture was then subjected to MWI for a specific time (see Physical data Table) at low power (180 W). The progress of the reaction was monitored by TLC examination at an interval of every 10 seconds. On completion of reaction, the reaction mixture was cooled at R.T. which afforded us the solid crystals of the desired product. The product thus obtained was filtered, washed with cold methanol, dried, and recrystallized from Rectified Spirit.

Assay Method

A 20 ml of MTT (7.5 mg/ml) solution (warmed to 37 °C) was added to each well outer row of the micro titer plates using the titertek multi drop dispenser. Then Incubated the trays at 37 °C in a CO₂ incubator for 1 h. Remove a constant volume of medium (e.g., 150 µl) from each cup using a multichannel pipette or a micro plate washer (Biotek EL404, a double, aspiration and dispensing, 96-channel washer, should be used as the brusque movement of the plate or of the manifold head of an 8 or 12 channel washer will lead to suspension of the cell clusters and subsequent aspiration of part of the cells, if not all) without disturbing the MT-4 or C8166 cell clusters containing the formazan crystals. Lyse the cells (and infectious virus) and solubilise the formazan crystals by adding 100 µl of the acidified Triton X-100 isopropanol solution to each cup using the micro plate washer (or a multichannel pipette).

Complete dissolution of the formazan crystals by placing the plates on a vibrating platform shaker for 10 min. Read the absorbance in an eight-channel computer-controlled Multiskan Ascent reader and stacker at two wavelengths (540 and 690 nm). Subtract the absorbance measured at 690 nm from the absorbance at 540 nm to eliminatethe effects of scattering by cell debris. Use the first

column wells for background subtraction because they contain all reagents except for cells, virus and compounds. CC_{50} is the concentration of compound that reduced the absorbance (OD₅₄₀) of the mock-infected control sample by 50%. The concentration achieving 50% protection according to the above formula is defined as IC_{50} .

$$IC_{50} = ((ODT)HIV - (ODC)HIV) / ((ODC)mock - (ODC)HIV) \times 100$$

Where (ODT)HIV is the OD measured with a given concentration of the test compound in the HIV-infected cells; (ODC) HIV is the OD measured for the control untreated, HIV-infected cells (column 11), which stands for 100% infection-related CPE; and (ODC) mock is the OD measured for the control untreated, mock-infected cells (column 11), which stands for 0% infection-related CPE.

Five compounds were studied for anti HIV activities according to the EC_{50} values measured on the wild-type HIV-1 cell line: strong anti-HIV effect $0 < IC_{50} < 10 \mu g/ml$ (Compounds 5c, 5d, 5e, 5f and 5i).

Result and Discussion

In our previous efforts, we have developed novel anti-HIV agents^[12-14] and further to developed new anti-HIV agents,^[15-17] we have synthesized diverse N-((1, 3-substituted diphenyl-1*H*-pyrazole-4-yl)methylene)-2-methylindoline-1-amine by the reaction of N-amino 2-methyl indoline and respected aldehydes. (Scheme-1). All the synthesized compounds **5a-o** was screened for their in vitro anti-HIV activity against human HIV cell line. These compounds required to achieve 50% protection of MT-4 cells from the HIV-1 induced cytopathogenicity, as determined by the MTT method. To synthesize N-amino 2-methyl indoline (scheme-1) a mixture of 2-methyl indoline and HCl was stirred at 0-5°C for half an hour and slowly add $NaNO_2$ to it till permanent blue colour

appears in starch iodide paper. Then filter it and take it into water-alcohol mixture and add Zn dust to it. Then slowly add CH_3COOH and reflux it for 6 hrs. After extract with toluene and distilled out toluene to get solid N-amino 2-methyl indoline and subjected it with substituted pyrazole aldehyde, Methanol and Acetic acid in MW for appropriate time (30-60 sec) to get desired molecules (Table-1).

Conclusion

We have developed a novel, rapid and efficient methodology for the synthesis of novel N-((1, 3-substituted diphenyl-1*H*-pyrazole-4-yl)methylene)-2-methylindoline-1-amine derivatives and exhibits their in vitro anti-HIV activity using MTT method. Among them compounds 5c, 5d, 5e, 5j, 5m and 5o have been found potent active while two compounds namely 5f and 5i found moderately active. The main significance of this procedure is good yield, easy workup procedure for biologically active compounds.

Spectral Data

N-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (**5a**)

IR (cm^{-1}): 3492, 3048, 2973, 2926, 2850, 1590, 1533, 1491, 1472, 1405, 1250, 887, 750 ^1H NMR ($DMSO-d_6$) δ ppm: 1.39(d, 3H), 2.45(d, 2H), 3.14(m, 1H), 6.46-6.50(d, 1H), 6.61-6.63(t, 1H), 7.08-7.15(t, 2H), 7.22-7.26(t, 3H), 7.53-7.57(t, 3H), 7.71-7.75(t, 2H), 7.91-7.95(t, 2H), 8.20(s, 1H), 8.45(s, 1H); MS: m/z : 378.18; Anal. Calcd. for $C_{25}H_{22}N_4$: C, 79.34; H, 5.86; N, 14.80; Found: C, 79.30; H, 5.81; N, 14.75.

N-((3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (**5b**)

IR (cm^{-1}): 3495, 3051, 2970, 2931, 2856, 889, 1599, 1529, 1498, 1475, 1408, 1251, 750, 686 ^1H NMR ($DMSO-d_6$) δ ppm:

1.35(d, 3H), 4.46-4.51(m, 1H), 2.77-2.81(d, 1H), 3.46-3.52(q, 1H), 7.09-7.15(q, 2H), 6.82-6.86(t, 1H), 7.33-7.37(t, 1H), 7.60(s, 1H), 7.47-7.53(m, 4H), 7.33-7.37(t, 1H), 7.71-7.75(d, 2H), 7.81-7.85(d, 2H), 8.40(s, 1H); MS: m/z : 412.15; Anal. Calcd. for $C_{25}H_{21}ClN_4$: C, 72.72; H, 5.13; Cl, 8.59; N, 13.57; Found: C, 72.65; H, 5.09; Cl, 8.55; N, 13.52.

N-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methyl-indolin-1-amine (5c)

IR (cm^{-1}): 3497, 3057, 2970, 2930, 2855, 1590, 1530, 1515, 1493, 1473, 1405, 1257, 885, 750 ^1H NMR (DMSO- d_6) δ ppm: 1.49(d, 3H), 2.78-2.82(d, 2H), 4.47-4.55(m, 1H), 6.51(d, 1H), 6.75-6.79(t, 1H), 6.82-6.86(t, 2H), 7.31-7.37(t, 1H), 7.60-7.68(m, 4H), 7.81-7.83(d, 2H, $J=8.0$ Hz), 8.20(s, 1H), 8.14-8.16(d, 2H, $J=8.0$ Hz), 8.81(s, 1H); MS: m/z : 423.17; Anal. Calcd. for $C_{25}H_{21}N_5O_2$: C, 70.91; H, 5.00; N, 16.54; O, 7.56 Found: C, 70.86; H, 4.96; N, 16.50; O, 7.51.

N-((3-(4-hydroxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methyl-indolin-1-amine (5d)

IR (cm^{-1}): 3492, 2975, 2931, 2851, 1587, 1533, 1489, 1475, 889, 1408, 3049, 1250, 750, 3625, 678 ^1H NMR (DMSO- d_6) δ ppm: 1.59(d, 3H), 2.88-2.92(d, 2H), 4.47-4.58(m, 1H), 5.12(s, 1H), 6.61(d, 1H), 6.69-6.72(t, 1H), 6.82-6.86(d, 2H), 7.41-7.47(t, 2H), 7.80-7.83(d, 2H), 7.90-7.98(m, 4H), 8.10(s, 1H), 8.24(s, 1H), 8.71(s, 1H); MS: m/z : 394.18; Anal. Calcd. for $C_{25}H_{22}N_4O$: C, 76.12; H, 5.62; N, 14.20; O, 4.06; Found: C, 76.07; H, 5.58; N, 14.14; O, 4.00.

N-((3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (5e)

IR (cm^{-1}): 3497, 3147, 3055, 2970, 2939, 2852, 1589, 1530, 1493, 1474, 1402, 1256, 1278, 883, 750 ^1H NMR (DMSO- d_6) δ ppm: 1.53(d, 3H), 2.68-2.72(d, 2H), 4.37-4.45(m, 1H), 3.21(s, 3H), 6.55(d, 2H),

6.75-6.81(t, 1H), 6.92-6.96(d, 2H, $J=8.0$ Hz), 7.21-7.27(t, 1H), 7.61-7.68(m, 5H), 7.82-7.84(d, 2H, $J=8.0$ Hz), 8.29(s, 1H), 8.81(s, 1H); MS: m/z : 408.20; Anal. Calcd. for $C_{26}H_{24}N_4O$: C, 76.45; H, 5.92; N, 13.72; O, 3.92; Found: C, 76.41; H, 5.88; N, 13.69; O, 3.87.

2-Methyl-N-((3-(2-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)indolin-1-amine (5f)

IR (cm^{-1}): 3498, 3052, 2974, 2932, 2857, 1590, 1534, 1496, 1475, 1510, 1407, 1250, 886, 750 ^1H NMR (DMSO- d_6) δ ppm: 1.59(d, 3H), 2.58-2.62(d, 2H), 4.39-4.46(m, 1H), 6.43(d, 1H), 6.76-6.81(t, 1H), 6.91-6.98(t, 2H), 7.22-7.27(t, 1H), 7.56-7.61(t, 2H), 7.70-7.75(t, 1H), 7.86-7.89(t, 1H), 8.10-8.20(m, 4H), 8.74(s, 1H), 8.91(s, 1H); MS: m/z : 423.17; Anal. Calcd. for $C_{25}H_{21}N_5O_2$: C, 70.91; H, 5.00; N, 16.54; O, 7.56; Found: C, 70.85; H, 4.97; N, 16.50; O, 7.53.

N-((3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (5g)

IR (cm^{-1}): 3490, 1495, 2858, 2935, 1470, 2976, 890, 1600, 1529, 1405, 3055, 1250, 750, 587 ^1H NMR (DMSO- d_6) δ ppm: 1.56(d, 3H), 2.68-2.73(d, 2H), 4.37-4.45(m, 1H), 6.41(d, 1H), 6.65-6.69(t, 1H), 6.72-6.76(t, 2H), 7.32-7.36(t, 1H), 7.59-7.68(m, 4H), 7.71-7.73(d, 2H, $J=8.0$ Hz), 8.04-8.06(d, 2H, $J=8.0$ Hz), 8.32(s, 1H), 8.71(s, 1H); MS: m/z : 456.09; Anal. Calcd. for $C_{25}H_{21}BrN_4$: C, 65.65; H, 4.63; Br, 17.47; N, 12.25; Found: C, 65.61; H, 4.60; Br, 17.44; N, 12.19.

2-Methyl-N-((1-phenyl-3-(thiophen-2-yl)-1H-pyrazol-4-yl)-methylene)-indolin-1-amine (5h)

IR (cm^{-1}): 3485, 3423, 3389, 3304, 3275, 1683, 1647, 1597, 1564, 1531, 1485, 1402, 1367, 1383, 1298, 1267, 1219, 704, 750, 715, 663 ^1H NMR (DMSO- d_6) δ ppm: 1.27-1.29(d, 3H), 4.38-4.43(m, 1H), 2.64-2.69(d, 1H), 3.34-3.40(q, 1H), 7.00-7.11(m, 4H), 6.70-6.74 (t, 1H), 7.64 (s,

1H), 8.23 (s, 1H), 7.68-7.70 (d, 2H), 7.27-7.28 (d, 1H), 7.18-7.22 (t, 1H), 7.34-7.40 (m, 3H); MS: *m/z*: 384.14; Anal. Calcd. for C₂₃H₂₀N₄S: C, 71.85; H, 5.24; N, 14.57; S, 8.34; Found: C, 71.80; H, 5.19; N, 14.52; S, 8.30.

N-((3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (5i)

IR (cm⁻¹): 3495, 3047, 2973, 2930, 2854, 1599, 1534, 1490, 1475, 1409, 1257, 1074, 887, 750 ¹H NMR (DMSO-*d*₆) δ ppm: 1.58(d, 3H), 2.71-2.84(d, 2H), 4.07-4.15(m, 1H), 6.53(d, 1H), 6.76-6.79(t, 1H), 6.81-6.86(t, 2H), 7.31-7.33(d, 2H), 7.49(t, 1H), 7.62-7.69(m, 4H), 8.15(d, 2H, *J*=8.0Hz), 8.40(s, 1H), 8.71(s, 1H); MS: *m/z*: 396.18; Anal. Calcd. for C₂₅H₂₁FN₄: C, 75.74; H, 5.34; F, 4.79; N, 14.13; Found: C, 75.70; H, 5.29; F, 4.73; N, 14.09.

N-((3-(3-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (5j)

IR (cm⁻¹): 3497, 3040, 2963, 2939, 2844, 1590, 1529, 1480, 1465, 1256, 1078, 897, 759 ¹H NMR (DMSO-*d*₆) δ ppm: 1.61(d, 3H), 2.72-2.74(d, 2H), 4.08-4.14(m, 1H), 6.57(d, 1H), 6.71-6.76(t, 1H), 7.01-6.06(t, 2H), 7.30-7.33(d, 1H), 7.48(t, 1H), 7.61-7.71(m, 4H), 8.19(d, 2H), 8.10(s, 1H), 8.45(s, 1H), 8.74(s, 1H); MS: *m/z*: 423.17; Anal. Calcd. for C₂₅H₂₁N₅O₂: C, 70.91; H, 5.00; N, 16.54; O, 7.56; Found: C, 70.95; H, 4.98; N, 16.52; O, 7.43.

N-((3-(2-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (5k)

IR (cm⁻¹): 3485, 3037, 2943, 2920, 2864, 1589, 1544, 1480, 1419, 1267, 1084, 897, 760 ¹H NMR (DMSO-*d*₆) δ ppm: 1.55(d, 3H), 2.61-2.64(d, 2H), 4.17-4.21(m, 1H), 6.63(d, 1H), 6.75-6.80(t, 1H), 6.91-6.96(t, 3H), 7.30-7.35(t, 2H), 7.48(t, 1H), 7.62-7.68(m, 4H), 8.16(d, 1H), 8.41(s, 1H), 8.61(s, 1H); MS: *m/z*: 412.15; Anal. Calcd. for C₂₅H₂₁ClN₄: C, 72.72; H, 5.13; Cl,

8.59; N, 13.57; Found: C, 72.69; H, 5.19; Cl, 8.65; N, 13.62.

N-((3-(3-Bromophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (5l)

IR (cm⁻¹): 3485, 3037, 2983, 2894, 1589, 1491, 1419, 1267, 887, 751 ¹H NMR (DMSO-*d*₆) δ ppm: 1.55(d, 3H), 2.81-2.84(d, 2H), 4.17-4.25(m, 1H), 6.63(d, 1H), 6.75-6.80(t, 1H), 6.80-6.87(t, 2H), 7.30-7.34(d, 1H), 7.46(s, 1H), 7.51(t, 1H), 7.61-7.68(m, 4H), 8.17(d, 2H), 8.50(s, 1H), 8.72(s, 1H); MS: *m/z*: 456.09; Anal. Calcd. for C₂₅H₂₁BrN₄: C, 65.65; H, 4.63; Br, 17.47; N, 12.25; Found: C, 65.51; H, 4.50; Br, 17.34; N, 12.09.

N-((3-(3-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (5m)

IR (cm⁻¹): 3485, 3057, 2983, 2935, 2844, 1544, 1492, 1475, 1267, 897, 752 ¹H NMR (DMSO-*d*₆) δ ppm: 1.45(d, 3H), 2.78-2.82(d, 2H), 4.18-4.25(m, 1H), 6.60(d, 1H), 6.76-6.81(t, 1H), 6.87-6.91(t, 2H), 7.32-7.36(d, 1H), 7.48(s, 1H), 7.53(t, 1H), 7.68-7.75(m, 4H), 8.19(d, 2H), 8.55(s, 1H), 8.82(s, 1H); MS: *m/z*: 396.18; Anal. Calcd. for C₂₅H₂₁FN₄: C, 75.74; H, 5.34; F, 4.79; N, 14.13; Found: C, 75.60; H, 5.27; F, 4.79; N, 14.08.

N-((3-(2-Methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (5n)

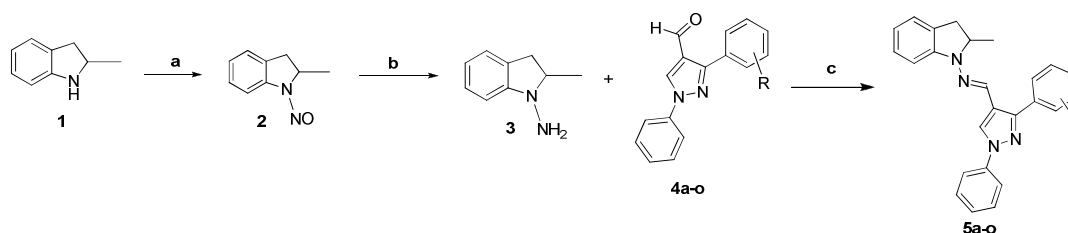
IR (cm⁻¹): 3485, 3037, 2983, 1587, 1480, 1476, 1267, 1084, 897, 760 ¹H NMR (DMSO-*d*₆) δ ppm: 1.48(d, 3H), 2.51-2.54(d, 2H), 3.10(s, 3H), 4.17-4.25(m, 1H), 6.52(d, 1H), 6.71-6.78(t, 1H), 6.88-6.95(m, 4H), 7.32-7.36(t, 1H), 7.59(t, 1H), 7.63-7.69(m, 4H), 8.15-8.17(d, 1H), 8.49(s, 1H), 8.61(s, 1H); MS: *m/z*: 408.20; Anal. Calcd. for C₂₆H₂₄N₄O: C, 76.45; H, 5.92; N, 13.72; O, 3.92; Found: C, 76.31; H, 5.78; N, 13.65; O, 3.88.

N-((3-(2-Hydroxyphenyl)-1-phenyl-1*H*-pyrazol-4-yl)methylene)-2-methylindolin-1-amine (5o)

IR (cm⁻¹): 3625, 3493, 3039, 2978, 2921, 2881, 1597, 1533, 1480, 1479, 879, 1418, 1251, 749, 679 ¹H NMR (DMSO-*d*₆) δ ppm: 1.58(d, 3H), 2.61-2.64(d, 2H), 4.07-4.15(m, 1H), 5.25(s, 1H), 6.53(d, 1H), 6.61-6.68(t, 1H), 6.89-6.96(m, 4H), 7.34-7.39(t, 1H), 7.61(t, 1H), 7.73-7.79(m, 4H), 8.05-8.11(d, 1H), 8.45(s, 1H), 8.71(s, 1H); MS: *m/z*: 394.18; Anal. Calcd. for C₂₅H₂₂N₄O: C, 76.12; H, 5.62; N, 14.20; O, 4.06; Found: C, 76.17; H, 5.68; N, 14.24; O, 4.10.

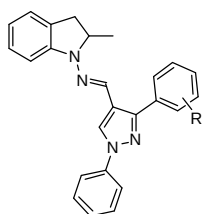
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Scheme-1 synthesis of N-((1,3-substituted diphenyl-1*H*-pyrazole-4-yl)methylene)-2-methylindoline-1-amine. Reagent and condition: (a) NaNO₂, HCl, 0-5°C (b) Zn, CH₃COOH, 6hrs, reflux (c) Methanol, MW, 180 W, 30-60 sec

Table 1. Physical and activity data of substituted **5a-o**.



Entry	Substitution R	Melting Range (°C)	Time(sec)	Yield %	IC ₅₀ μ g/ml	CC ₅₀ μ g/ml
5a	H	140-142	40	95	>65.67	65.67
5b	4-Cl	148-150	20	96	>69.43	69.43
5c	4-NO ₂	188-190	30	98	>9.07	9.07
5d	4-OH	166-168	20	97	>12.55	12.55
5e	4-OCH ₃	172-174	30	93	>8.05	8.05
5f	2-NO ₂	182-184	40	92	>24.98	24.98
5g	4-Br	142-144	30	95	>112.00	112.00
5h	Thiophenyl	156-158	30	96	>125	125
5i	4-F	158-160	30	90	>17.19	17.19
5j	3-NO ₂	132-134	30	92	>8.01	8.01
5k	2-Cl	142-144	40	88	>28.23	28.23

5l	3-Br	162-164	40	94	>89.4	89.4
5m	3-F	128-130	30	92	>10.09	10.09
5n	2-OCH ₃	148-150	40	86	>17.21	17.21
5o	2-OH	140-142	30	94	>8.21	8.21

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