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# Synthesis and biological evaluation of some new Aryl acid N'-(1H-indazole-3-carbonyl)-hydrazide derivatives

**T. Chandrasekhar, L. Vinay Kumar, A. Babul Reddy, P. Jagan Naik and G. Narayana Swamy***

*Department of Chemistry, Sri Krishnadevaraya University, Anantapur, A.P. India*

**ABSTRACT**

*Amide coupling of 1H-Indazole-3-carboxylic acid hydrazide with substituted aryl acids affords thirteen novel Aryl acid N'-(1H-indazole-3-carbonyl)-hydrazide derivatives. The acid hydrazide was synthesized by the hydrazine reaction with 1-H-Indazole-3-carboxylic acid methyl ester which was obtained by esterification of indazole-3-carboxylic acid.*

**Keywords:** 1H-Indazole-3-carboxylic acid, 1H-Indazole-3-carboxylic acid hydrazide, substituted aryl acids, diacyl hydrazines, HATU, antimicrobial activity.

## INTRODUCTION

Recent drug discovery efforts are highly focused towards design and synthesis of small molecules of protein kinase C-β/AKt inhibitiors.[1, 2] A wide ranges of heterocyclic ring systems has been studied for the development of novel chemical entities as lead molecules in the drug discovery paradigm. Indazole derivatives are one of the privileged structural fragments in medicinal chemistry having broad spectrum of potent pharmacological activities including anti-inflammatory, anti-tumor, or HIV protease inhibition.[3-6] Numerous compounds containing Indazole moiety have been shown to exhibit estrogen receptor,[7] antifungal, antibacterial activity.[8] Among the important heterocycles, many of the natural and synthetic Indazole–based heterocycles with diverse mechanism of action have been reported as lead anticancer, [9] 5-$HT_2$, 5-$HT_3$ and 5-$HT_4$ receptor antagonisms.[10-13]

The search for an efficient synthesis of the indazole ring system has been a long standing goal. However to date, methods reported for the synthesis of indazoles have met with only limited success. Most of the syntheses of the indazole derivatives reported in the literature proceed from benzene precursors in which the pyrazole moiety was generated by ring closure starting from isatins, phenylhydrazines or o-toluidines.[14,15] To the best our knowledge, indazole-3-carboxilic acid has been synthesized conveniently for many years.[16, 17] However, further modifications were very limited.[18, 19]

## EXPERIMENTAL SECTION

Chemicals and solvents used were either purchased from commercial suppliers or purified by standard techniques. All experiments involving air-sensitive reagents were performed under an inert atmosphere in oven-dried glassware. The monitoring of reaction and checking of purity of the product were done using pre-coated Merck silica gel 60 $F_{254}$ plates and compounds were visualized by irradiating with UV light or by exposing to $I_2$ vapours, and or by staining with Ninhydrine stain followed by heating. Melting points were measured on a yanagimoto micro melting

apparatus and are uncorrected. The $^1$H NMR spectra were recorded on a Varian 400 MHz spectrometer in DMSO as a solvent and TMS as an internal standard. IR spectra were recorded on Perkin-Elmer 1420 Spectrophotometer. The mass spectra were determined using a Thermo finnigan LCQ DECA XP MAX (ION TRAP) LCMS MS Mass spectrometer using direct infusion technique. The Elemental analyses were performed for C, H, and N using a Perkin-Elmer analyser.

**General procedure for the preparation of 1H-Indazole-3-carboxylic acid methyl ester (2):** To a solution of 1H-Indazole-3-carboxylic acid (**1)** (4 g, 24.66 mmol, 1equiv.) in methanol (40 mL) at R.T, catalytic amount of $H_2SO_4$ was added. The resulting solution was stirred at reflux temperature for 2h, briefly cooled to room temperature and methanol was evaporated under vacuo. The residue was treated with ice water (50 mL) and the precipitated product was extracted with Ethyl acetate (80 mL), washed with brine solution (50 mL), and dried over $Na_2SO_4$. The solvent was evaporated under vacuo to afford **2** (4.31 g), Yield - 98.99%, mp 162-164 $^0$C; IR ($\nu_{max}$, KBr/cm$^{-1}$): 3327 (br), 3211 (w), 2991 (m), 1731 (vs), 1638 (vs), 1535 (vs), 1467 (m), 1368 (s), 1232 (s), 1128 (s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 3.9 (s, 3H, $CH_3$), 7.32 (t, 1H, *J* = 4.2 Hz, ben-H), 7.4 (t, 1H, *J* = 4.4 Hz, ben-H), 7.65 (d, 1H, *J* = 6.4 Hz, ben-H), 8.18 (d, 1H, *J* = 6.2 Hz, ben-H), 13.98 (s, 1H, NH); LCMS MS (APCI, m/z): 177.02 (M + H)$^+$; Anal.calcd for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 60.78; H, 4.12; N, 15.28.

**General procedure for the preparation of 1H-Indazole-3-carboxylic acid hydrazide (3):** To a solution of 1H-Indazole-3-carboxylic acid methyl ester (**2)** (4.2 g, 23.86 mmol, 1 equiv.) in ethanol (42 mL) at R.T, hydrazine hydrate was added (1.79 g, 35.79 mmol, 1.5 equiv) and resulting solution was stirred at reflex temperature for 4h. It was briefly cooled to room temperature and ethanol was evaporated at 60$^0$C under high vacuo. The solid material was washed with diethyl ether (40 mL × 2) to give **3** (4.12 g), Yield - 98%, mp 198-201 $^0$C; IR ($\nu_{max}$, KBr/cm$^{-1}$): 3366 (br), 3327 (w), 3211 (s), 1731 (vs), 1673 (vs), 1608 (s), 1535 (vs), 1468 (m), 1349 (m), 1242 (s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 4.5 (s, 2H, $NH_2$), 7.23 (t, 1H, *J* = 4.2 Hz, ben-H), 7.4 (t, 1H, *J* = 4.4 Hz, ben-H), 7.68 (d, 1H, *J* = 6.4 Hz, ben-H), 8.08 (d, 1H, *J* = 6.2 Hz, ben-H), 9.6 (s, 1H, NH), 13.68 (s, 1H, N-NH ); LCMS MS (APCI, m/z): 177.04 (M + H)$^+$; Anal.calcd for $C_8H_8N_4O$: C, 54.54; H, 4.58; N, 31.80. Found: C, 53.86; H, 4.02; N, 31.12.

**General procedure for the preparation of Aryl acid N'- (1H-indazole-3-carbonyl) - hydrazide derivatives (4a-m):** To a solution of 1H-Indazole-3-carboxylic acid hydrazide (**3)** (0.100 g, 0.57 mmol, 1equiv) in DMF (5 mL), HATU (0.216 g, 0.57 mmol, 1 equiv), Aryl acids (0.57 mmol, 1equiv), DIPEA (0.146 g, 1.13 mmol, 2 equiv) were added and the mixture was stirred at room temperature for 2-6h. The ice water (10 mL) was poured into reaction mixture to precipitate solid which was filtered, washed with water (20 mL × 2), and diethyl ether (20 mL × 2). The solid material was recrystalized from Ethanol/DMF to give **4a-m.** The melting points and yields are reported in Table - 1.

**N'-(4-chlorobenzoyl)-1H-indazole-3-carbohydrazide (4a):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3366 (br), 3227 (s), 1925 (w), 1614 (vs), 1568 (vs), 1483 (vs), 1238 (s), 1122 (m), 1014 (m), 937 (m), 741(s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 7.28 (t, 1H, *J* = 4.2 Hz, ben-H), 7.44 (t, 1H, *J* = 4.4 Hz, ben-H), 7.65 (m, 3H, ben-H), 7.99 (d, 2H, *J* = 6.4 Hz, ben-H), 8.12 (d, 1H, *J* = 6.2 Hz, ben-H), 10.45 (s, 1H, CONH), 10.52 (s,1H, CONH), 13.9 (s, 1H, N-NH); LCMS MS (APCI, m/z): 314.82, 315.82, (M + H)$^+$; Anal.calcd for $C_{15}H_{11}Cl\ N_5O_2$: C, 57.24; H, 3.52; N, 17.80. Found: C, 56.64; H, 2.98; N, 17.12.

**N'-(4-(trifluoromethyl)benzoyl)-1H-indazole-3-carbohydrazide (4b):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3292 (br), 1685 (vs), 1650 (s), 1622 (vs), 1542 (vs), 1482 (vs), 1239 (s), 1120 (m), 1021 (m), 924 (m), 756 (s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 7.28 (t, 1H, *J* = 4.2 Hz), 7.44 (t, 1H, *J* = 4.4 Hz), 7.7 (d, 1H, *J* = 4.2 Hz), 7.96 (d, 2H, *J* = 4.6 Hz), 8.18 (t, 3H), 10.5 (s, 1H), 10.75 (s, 1H), 13.9 (s, 1H); LCMS MS (APCI, m/z): 348.90 (M + H)$^+$; Anal.calcd for $C_{16}H_{11}F_3N_4O_2$: C, 55.18; H, 3.18; N, 16.09. Found: C, 54.64 H, 2.68, N, 15.49.

**N'-picolinoyl-1H-indazole-3-carbohydrazide (4c):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3440 (br), 2111 (s), 1600 (m), 1114 (br), 843 (s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 7.2-7.3 (m, 3H), 7.45 (t, 1H, *J* = 4.4 Hz), 7.65 (d, 1H, *J* = 6.2 Hz), 8.18 (d, 1H, *J* = 6 Hz), 8.8 (d, 2H, *J* = 4 Hz), 10.5 (brs, 1H), 10.8 (brs, 1H), 13.8 (s, 1H); LCMS MS (APCI, m/z): 282.06, (M + H)$^+$; Anal.calcd for $C_{14}H_{11}N_5O_2$: C, 59.78; H, 3.94; N, 24.90. Found: C, 59.06; H, 3.09; N, 24.10.

**N'-(6-chloronicotinoyl)-1H-indazole-3-carbohydrazide (4d):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3251 (br), 3148 (m), 2943 (w), 1674 (vs), 1647 (s), 1588 (vs), 1562 (s), 1456 (s), 1380 (s), 1286 (m), 1246 (s), 952 (m), 843 (m); $^1$HNMR (DMSO-$d_6$) δ (ppm): 7.28 (t, 1H, *J* = 4.2 Hz), 7.44 (t, 1H, *J* = 4.4 Hz), 7.65-7.77 (m, 2H), 8.13 (d, 1H, *J* = 6.2 Hz), 8.35 (dd,

1H, *J* = 2 Hz and *J* = 4 Hz, pyridine-H), 8.95 (s, 1H), 10.5 (s, 1H), 10.8 (s, 1H), 13.9 (s, 1H); LCMS MS (APCI, m/z): 316.32, 317.22 (M + H)$^+$; Anal.calcd for $C_{14}H_{10}ClN_5O_2$: C, 53.26; H, 3.19; N, 22.18. Found: C, 52.64; H, 2.64; N, 21.54.

**N'-(pyrazine-2-carbonyl)-1H-indazole-3-carbohydrazide (4e):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3254 (br), 1692 (vs), 1663 (s), 1578 (vs), 1438 (vs), 1351 (s), 1246 (m), 1084 (m), 1020 (m), 935 (m), 875 (m), 744 (s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 7.28 (t, 1H, *J* = 4.2 Hz), 7.44 (t, 1H, *J* = 4.4 Hz), 7.68 (d, 1H, *J* = 6.4 Hz), 8.15 (d, 1H, *J* = 6.2 Hz), 8.82 (d, 1H, *J* = 2.8 Hz), 8.92 (d, 1H, *J* = 3.2 Hz), 9.25 (s, 1H, Py-H), 10.5 (s, 1H), 10.88 (s, 1H), 13.9 (s, 1H); LCMS MS (APCI, m/z): 283.28 (M + H)$^+$; Anal.calcd for $C_{13}H_{10}N6O_2$: C, 55.32; H, 3.57; N, 29.77. Found: C, 54.94; H, 2.92; N, 29.05.

**N'-(1H-pyrrole-2-carbonyl)-1H-indazole-3-carbohydrazide (4f):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3360 (br), 3233 (w), 3068 (s), 1954 (w), 1691(vs), 1660 (s), 1572 (vs), 1543 (s), 1443 (vs), 1369 (s), 1111 (m), 1003 (m), 916 (m), 858 (m), 749 (s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 7.28 (t, 1H, *J* = 4.2 Hz), 7.44 (t, 1H, *J* = 4.4 Hz), 7.6-7.7 (m, 4H,), 8.15 (d, 1H, *J* = 6.2 Hz), 8.3 (s, 1H, pyrrole-NH), 10.5 (s, 1H), 10.63 (s, 1H), 13.9 (s, 1H); LCMS MS (APCI, m/z): 270.16 (M + H)$^+$; Anal.calcd for $C_{13}H_{11}N_5O_2$: C, 57.99; H, 4.12; N, 26.01. Found: C, 57.06; H, 3.68; N, 25.48.

**N'-(3-methylthiophene-2-carbonyl)-1H-indazole-3-carbohydrazide (4g):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3268 (vs), 1688 (vs), 1672 (m), 1583 (vs), 1481 (s), 1381 (s), 1227 (m), 1118 (m), 858 (m), 726 (s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 2.3 (s, 3H, Me), 7.05 (d, 1H, *J* = 5.4 Hz), 7.28 (t, 1H, *J* = 4.2 Hz), 7.45 (t, 1H, *J* = 4.4 Hz), 7.68 (d, 2H, *J* = 4.4 Hz), 7.68 (d, 2H, *J* = 5.6 Hz), 8.18 (d, 1H, *J* = 6.2 Hz), 10.18 (brs, 1H), 10.6 (brs, 1H), 13.9 (s, 1H); LCMS MS (APCI, m/z): 301.15, (M + H)$^+$; Anal.calcd for $C_{14}H_{12}N_4O_2$ S: C, 55.99; H, 4.03; N, 18.65. Found: C, 55.28; H, 3.62; N, 17.92.

**N'-(1H-indazole-3-carbonyl)-1,2,3-thiadiazole-4-carbohydrazide (4h):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3379 (br), 3272 (m), 3076 (w), 1705 (vs), 1651 (s), 1586 (vs), 1536 (m), 1473 (vs), 1401 (s), 1374 (s), 1249 (m), 1173 (m), 1003 (m), 916 (m); $^1$HNMR (DMSO-$d_6$) δ (ppm): 7.28 (t, 1H, *J* = 4.2 Hz), 7.45 (t, 1H, *J* = 4.4 Hz), 7.68 (d, 1H, *J* = 6.4 Hz), 8.18 (d, 1H, *J* = 6.2 Hz), 9.93 (s, 1H, thiadiazole-H), 10.65 (brs, 1H), 11.10 (brs, 1H), 13.9 (brs, 1H); LCMS MS (APCI, m/z): 289.18, (M + H)$^+$; Anal.calcd for $C_{11}H_8N_6O_2S$: C, 45.83; H, 2.80; N, 29.15. Found: C, 45.24; H, 2.20; N, 28.12.

**N'-(1H-indazole-3-carbonyl)-5-methylisoxazole-3-carbohydrazide (4i):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3428 (br), 3304 (s), 2950 (w), 1694 (s), 1664 (vs), 1568 (vs), 1458 (vs), 1178 (m), 1010 (m), 916 (m), 848 (m),740 (s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 2.82 (s, 3H, Me), 6.66 (s, 1H, isoxazole-H), 7.28 (t, 1H, *J* = 4.2 Hz), 7.46 (t, 1H, *J* = 4.4 Hz), 7.68 (d, 1H, *J* = 6.4 Hz), 8.18 (d, 1H, *J* = 6.2 Hz), 10.5 (s, 1H), 10.7 (s, 1H), 13.9 (s, 1H); LCMS MS (APCI, m/z): 286.13, 287.13, (M + H)$^+$; Anal.calcd for $C_{13}H_{11}N_5O_3$: C, 54.74; H, 3.89; N, 24.55. Found: C, 54.04; H, 3.16; N, 23.68.

**N'-(3-methyl-1H-pyrazole-5-carbonyl)-1H-indazole-3-carbohydrazide (4j):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3436 (br), 3019 (w), 1634 (br), 1401 (vs), 1215 (m), 1046 (m), 847 (m), 757 (vs); $^1$HNMR (DMSO-$d_6$) δ (ppm): 2.3 (s, 3H, Me), 6.5 (s, 1H, pyrazole-H), 7.28 (t, 1H, *J* = 4.2 Hz), 7.45 (t, 1H, *J* = 4.4 Hz), 7.68 (d, 1H, *J* = 6.4 Hz), 8.18 (d, 1H, *J* = 6.2 Hz), 9.9 (s, 1H), 10.25 (s, 1H), 13.13 (s, 1H), 13.9 (s, 1H); LCMS MS (APCI, m/z): 285.08, (M + H)$^+$; Anal.calcd for $C_{13}H_{12}N_6O_2$: C, 54.93; H, 4.25; N, 29.56. Found: C, 54.63; H, 3.89; N, 29.01.

**N'-(5-phenylfuran-2-carbonyl)-1H-indazole-3-carbohydrazide (4k):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3272 (br), 1682 (vs), 1654 (s), 1580 (vs), 1479 (s), 1449 (m), 1349 (vs), 1193 (m), 1020 (m), 917 (m), 862 (m); $^1$HNMR (DMSO-$d_6$) δ (ppm): 7.28 (t, 1H, *J* = 4.2 Hz), 7.4-7.55 (m, 7H), 7.68 (d, 1H, *J* = 6.4 Hz), 8.0 (d, 1H, *J* = 5.6 Hz), 8.18 (d, 1H, *J* = 6.2 Hz), 10.42 (s, 1H), 10.61 (s, 1H), 13.89 (s, 1H); LCMS MS (APCI, m/z): 346.91, (M + H)$^+$; Anal.calcd for $C_{19}H_{14}N_4O_3$: C, 65.89; H, 4.07; N,16.18. Found: C, 65.45; H, 3.62; N, 15.76.

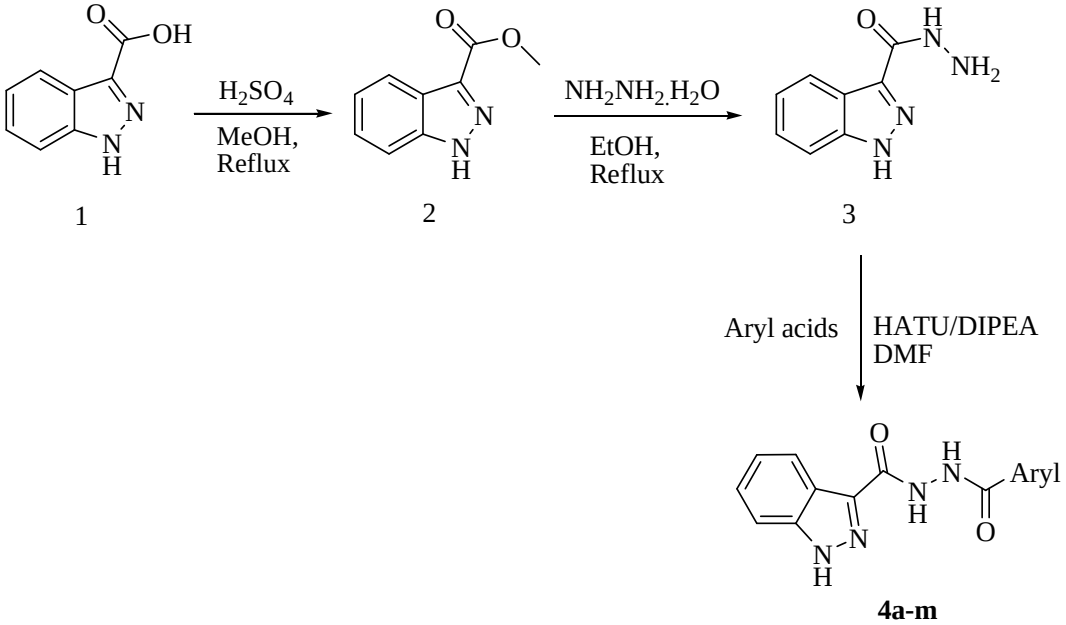
**N'-(1-phenyl-5-(trifluoromethyl)-1H-pyrazole-4-carbonyl)-1H-indazole-3-carbohydrazide (4l):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3468 (br), 3237 (m), 1655 (vs), 1629 (s), 1536 (vs), 1470 (vs), 1439 (m), 1347 (vs), 1202 (m), 1165 (m), 921 (m), 776 (m), 750 (s); $^1$HNMR (DMSO-$d_6$) δ (ppm): 6.9-7.1 (m, 5H), 7.28 (t, 1H, *J* = 4.2 Hz), 7.45 (t, 1H, *J* = 4.6 Hz), 7.65 (d, 1H, *J* = 6.4 Hz), 8.18 (d, 1H, *J* = 6.2 Hz), 10.05 (s, 1H), 10.25 (brs, 1H), 11.75 (s, 1H, pyrazole-H), 13.8 (brs, 1H); LCMS MS (APCI, m/z): 415.22, 416.22, (M + H)$^+$; Anal.calcd for $C_{19}H_{13}F_3N_6O_2$: C, 55.08; H, 3.16; N, 20.28. Found: C, 54.68; H, 2.86; N, 19.64.

**3-(2-chloro-6-fluorophenyl)-N'-(1H-indazole-3-carbonyl)-5-methylisoxazole-4-carbohydrazide (4m):** IR ($\nu_{max}$, KBr/cm$^{-1}$): 3336 (br), 3253 (w), 1688 (vs), 1652 (s), 1610 (s), 1571 (s), 1479 (vs), 1410 (s), 1370 (vs), 1352 (m), 1251 (m), 1192 (m), 1020 (m), 925 (m), 898 (m), 790 (m); $^1$HNMR (DMSO-$d_6$) δ (ppm): 2.81 (s, 3H, Me), 7.28 (t, 1H, *J* = 4.2 Hz), 7.4-7.5 (m, 3H), 7.62-7.76 (m, 2H), 8.18 (d, 1H, *J* = 6.2 Hz), 10.25 (s, 1H), 10.45 (s, 1H), 13.8 (s, 1H); LCMS MS (APCI, m/z): 414.11, 415.11 (M + H)$^+$; Anal.calcd for $C_{19}H_{13}$ Cl F $N_5O_3$: C, 55.15; H, 3.17; N, 16.92. Found: C, 54.68; H, 2.79; N, 16.38.

## RESULTS AND DISCUSSION

Thus, we are very interested in transforming indazole-3-carboxilic acid to some novel Aryl acid N'-(1H-indazole-3-carbonyl)-hydrazidederivatives **(4a-m**), which should be useful precursors for achieving new biologically active indazole-3-substituted compounds.

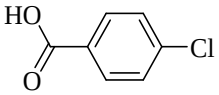
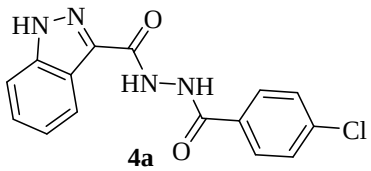
**Scheme 1. Synthetic route of the title compounds 4a-m**

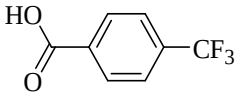
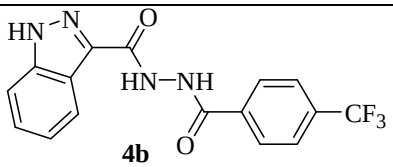
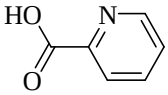
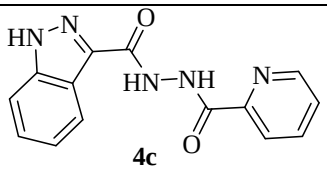
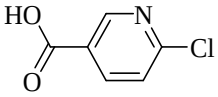
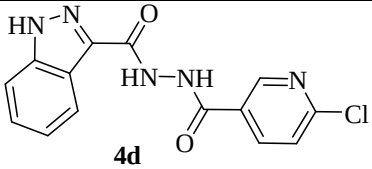
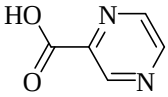
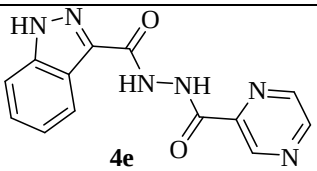
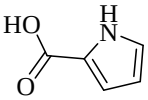
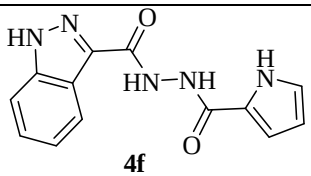
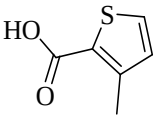
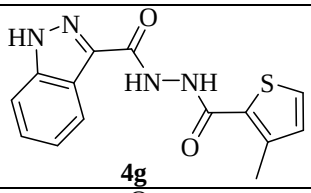
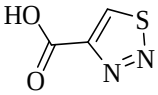
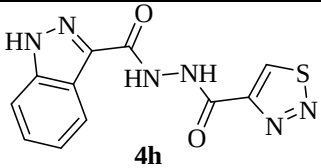
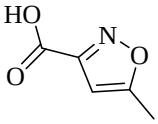
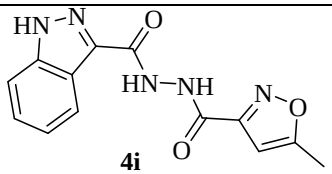
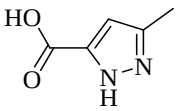
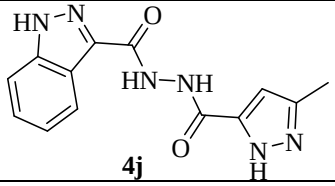


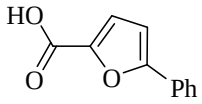
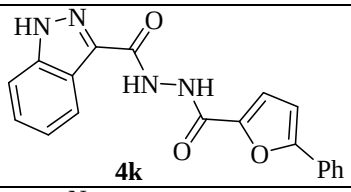
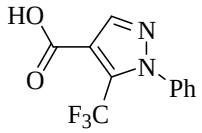
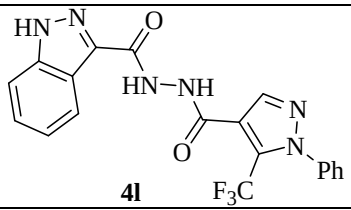
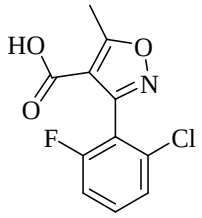
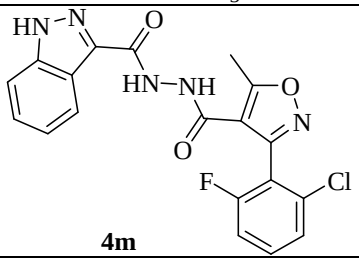

1 2 3 **4a-m**

Here in, we wish to report the synthesis of aryl acid N'-(1H-indazole-3-carbonyl)-hydrazide derivatives by the reaction of 1H-Indazole-3-carboxylic acid hydrazide **(3)** with some substituted aryl acids (**Table 1, Entry 1-13**) as shown in scheme 1. Initially, treatment of 1H-Indazole-3-carboxylic acid (1) with catalytic amount of $H_2SO_4$ in refluxing methanol produced 1H-Indazole-3-carboxylic acid methyl ester **(2).** Treatment of **(2)** with Hydrazine hydrate in refluxing EtOH gave a 1H-Indazole-3-carboxylic acid hydrazide **(3).** Finally this was coupled with some substituted aryl acids in the presence of O-(7-Azabenzotriazole-1-Yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU) as amide coupling agent and Ethyl-diisopropyl-amine (DIPEA) as base in N,N-Dimethyl-formamide (DMF) to give Aryl acid N'-(1H-indazole-3-carbonyl)-hydrazide derivatives (**4a-m, Table 1**).

**Table 1. Synthesis of Aryl acid N'-(1H-indazole-3-carbonyl)-hydrazide derivatives (4a-m):**

| Entry | Aryl acids | Title compounds (**4a-m**) | Mp ($^0$C) | Yields (%)[a] |
|---|---|---|---|---|
| 1 |  |  **4a** | 274-277 | 90 |

| | | | | |
|---|---|---|---|---|
| 2 |  |  **4b** | 303-306 | 91 |
| 3 |  |  **4c** | 225-228 | 64 |
| 4 |  |  **4d** | 272-275 | 92 |
| 5 |  |  **4e** | 276-279 | 94 |
| 6 |  |  **4f** | 248-251 | 87 |
| 7 |  |  **4g** | 269-272 | 95 |
| 8 |  |  **4h** | 228-231 | 91 |
| 9 |  |  **4i** | 210-213 | 96 |
| 10 |  |  **4j** | 272-275 | 94 |

| | | | | |
|---|---|---|---|---|
| 11 |  |  **4k** | 275-278 | 96 |
| 12 |  |  **4l** | 268-271 | 92 |
| 13 |  |  **4m** | 298-301 | 90 |

[a] *Isolated yields*

In addition, we also attempted the reaction with other reagents such as N-Hydroxybenzotrizole (HOBT) and (3-Dimethylamino-propyl)-ethyl-carbodiimide (EDC.HCl), but the yield could not be improved further. Some representative results are summarized in **Table 1.**

**Biological activity**

**Antibacterial activity:** The compounds **4a-m** were screened for their antibacterial activity against human pathogenic bacteria such as Escherichia coli (MTCC46), Pseudomonas aeruginosa (MTCC442), Staphylococcus aureus (MTCC87) and Streptococcus pyogene. The minimum inhibition concentration (MIC) was determined using the tube dilution method.[20] DMF was used as a blank and Ciprofloxacin as standard and the results are reported in **Table 2**.

Compounds **4b-i**, and **4k-m** showed moderate activity against Escherichia coli, Pseudomonas aeruginosa, staphylococcus aureus and streptococcus pyogene. Compound **4a** showed moderate activity against Pseudomonas aeruginosa, staphylococcus aureus and streptococcus pyogene but didn't exhibit activity against Escherichia coli. Compound **4j** showed moderate activity against Escherichia coli, staphylococcus aureus and streptococcus pyogene but didn't exhibit activity against Pseudomonas aeruginosa.

**Table 2. In Vitro antibacterial activity for compounds 4a-m**

| Compounds | Zone of Inhibition (mm) | | | |
|---|---|---|---|---|
| | *Escherichia coli* | *Pseudomonas aeruginosa* | *Staphylococcus aureus* | *Streptococcus pyogene* |
| **4a** | - | 12 | 12 | 14 |
| **4b** | 11 | 12 | 14 | 14 |
| **4c** | 11 | 14 | 11 | 09 |
| **4d** | 12 | 14 | 16 | 14 |
| **4e** | 13 | 13 | 12 | 11 |
| **4f** | 12 | 13 | 15 | 12 |
| **4g** | 14 | 13 | 10 | 10 |
| **4h** | 12 | 11 | 15 | 12 |
| **4i** | 10 | 12 | 12 | 11 |
| **4j** | 13 | - | 12 | 12 |
| **4k** | 14 | 13 | 15 | 15 |
| **4l** | 13 | 14 | 12 | 15 |

| | | | | |
|---|---|---|---|---|
| **4m** | 11 | 14 | 14 | 13 |
| **Ciprofloxacin** | 17 | 21 | 21 | 23 |

**Antifungal activity:** The compounds **4a-m** were screened also for antifungal activities (**Table 3**) against Aspergillus niger and Helminthosporium oryzae using fungicide Griseofulvin in DMF as the standard.

**Table 3. In Vitro antifungal activity for compounds 4a-m**

| Compounds | Zone of Inhibition (mm) | |
|---|---|---|
| | *Aspergillus niger* | *Helminthosporium oryzae* |
| **4a** | 07 | 06 |
| **4b** | 10 | 09 |
| **4c** | 09 | 09 |
| **4d** | 10 | 08 |
| **4e** | 11 | 09 |
| **4f** | 12 | 11 |
| **4g** | 09 | 11 |
| **4h** | 13 | 11 |
| **4i** | 11 | 13 |
| **4j** | 12 | 09 |
| **4k** | 08 | 09 |
| **4l** | 10 | 09 |
| **4m** | 10 | 10 |
| **Griseofulvin** | 15 | 14 |

Antifungal activity of compounds **4a-m** was compared with that of the antifungal drug Griseofulvin. **Table-3** showed that compounds **4b**, **4d-f**, **4h-j**, **4l** and **4m** showed high activity against fungi Aspergillus niger. Where as compounds **4a**, **4c**, **4g** and **4k** exhibited moderate activity against fungi Aspergillus niger when compared with Griseofulvin. Compounds **4f-l** and **4m** showed high activity against Helminthosporium oryzae. Where as compounds **4a-e** and **4j-l** exhibited moderate activity against fungi Helminthosporium oryzae.

## CONCLUSION

We have successfully prepared 13 novel aryl acid N'-(1H-indazole-3-carbonyl)-hydrazide derivatives (4a-m) by amide coupling of some substituted aryl acids with 1H- indazole-3- carboxylic acid hydrazide and also assayed for their invitro antibacterial activity and antifungal activity, because the literature gives results enormously interesting on these subjects.

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