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SYNTHESIS AND CHARACTERIZATION OF 4,6-DIARYL-4,5-DIHYDRO-2H-INDAZOL-3-OLS AND 4,6-DIARYL-2-PHENYL-4,5-DIHYDRO-2H-INDAZOL-3-OLS – A NEW SERIES OF FUSED INDAZOLE DERIVATIVES

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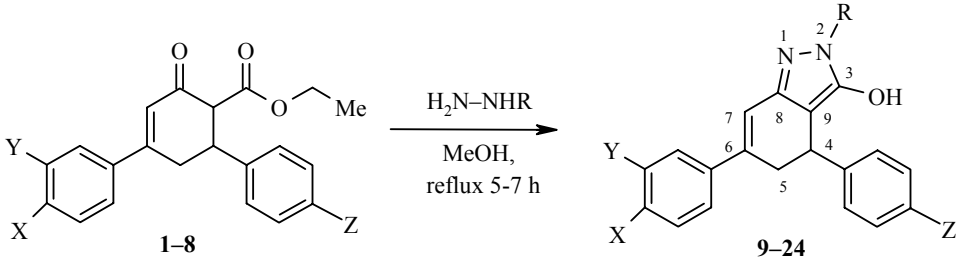
A novel class of 4,6-diaryl-4,5-dihydro-2H-indazol-3-ols and 4,6-diaryl-2-phenyl-4,5-dihydro-2H-indazol-3-ols is synthesized and characterized by melting point, elemental analysis, MS, FT-IR, ^{1}H and ^{13}C NMR, D_2O exchanged ^{1}H NMR, and two-dimensional HSQC spectra.

Keywords: 3,5-diaryl-6-ethoxycarbonylcyclohex-2-en-1-ones, 4,6-diaryl-4,5-dihydro- 2H-indazol-3-ols, 4,6-diaryl-2-phenyl-4,5-dihydro-2H-indazol-3-ols, hydrazine hydrate, phenylhydrazine hydrochloride.

Various structurally diverse indazole derivatives have aroused great interest due to their wide variety of biological properties such as antimicrobial activity [1], inhibition of protein kinase B/Akt [2], antiprotozaal [3], antichagasic [3], leichmanocidal [3], and trypanocidal activities [3], inhibition of S-adenosyl homo-cysteine/methylthioadenosine (SAH/MTA) nucleosidase [4], potent activation of nitric oxide receptors [5], and inhibition of platelet aggregation [5].



9-16 R = H, **17-24** R = Ph; **9-13**, **16-21**, **24** X = H, **14**, **22** X = Br, **15**, **23** X = Me; **9-15**, **17-23** Y = H, **16**,**24** Y = NO_2; **9,14,15,17,22,23** Z = H, **10,18** Z = Me, **11,19** Z = Cl, **12,20** Z = NO_2, **13,16,21,24** Z = OMe

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TABLE 1. Physical and Analytical Characteristics of Compounds **9-24**

Compound	Empirical formula	*m/z* [$M^{+\cdot}$]	Found, % / Calculated, %			mp,°C	Yield, %
			C	H	N		
9	$C_{19}H_{18}N_2O$	291	78.55 / 78.59	6.21 / 6.25	9.61 / 9.65	226	73
10	$C_{20}H_{20}N_2O$	305	78.88 / 78.92	6.59 / 6.62	9.17 / 9.20	230	70
11	$C_{19}H_{17}ClN_2O$	326	70.21 / 70.26	5.26 / 5.28	8.58 / 8.62	234	68
12	$C_{19}H_{17}N_3O_3$	336	68.01 / 68.05	5.07 / 5.11	12.50 / 12.53	212	72
13	$C_{20}H_{20}N_2O_2$	321	74.63 / 74.98	6.27 / 6.29	8.71 / 8.74	204	70
14	$C_{19}H_{17}BrN_2O$	370	61.76 / 61.80	4.61 / 4.64	7.56 / 7.59	232	69
15	$C_{20}H_{20}N_2O$	305	78.89 / 78.92	6.59 / 6.62	9.17 / 9.20	225	60
16	$C_{20}H_{19}N_3O_4$	366	65.70 / 65.74	5.20 / 5.24	11.46 / 11.50	210	68
17	$C_{25}H_{20}N_2O$	364	82.35 / 82.39	5.49 / 5.53	7.64 / 7.69	237	80
18	$C_{26}H_{22}N_2O$	378	82.47 / 82.51	5.82 / 5.86	7.36 / 7.40	242	75
19	$C_{25}H_{19}ClN_2O$	398	75.22 / 75.28	4.78 / 4.80	6.98 / 7.02	251	76
20	$C_{25}H_{19}N_3O_3$	409	73.31 / 73.34	4.65 / 4.68	10.23 / 10.26	224	78
21	$C_{26}H_{22}N_2O_2$	394	79.11 / 79.16	5.58 / 5.62	7.06 / 7.10	219	70
22	$C_{25}H_{19}BrN_2O$	443	67.69 / 67.73	4.28 / 4.32	6.29 / 6.32	238	65
23	$C_{26}H_{22}N_2O$	378	82.46 / 82.51	5.81 / 5.86	7.36 / 7.40	239	60
24	$C_{26}H_{21}N_3O_4$	439	71.01 / 71.06	4.79 / 4.82	9.51 / 9.56	205	75

In recent years there has been a great deal of interest in exploiting more than one proximal functional groups for designing novel structures capable of performing a variety of functions. The present study describes the use of 3,5-diaryl-6-ethoxycarbonylcyclohex-2-en-1-one [6], an intermediate with three versatile functional groups, i.e., ketone, olefin, and ester, for the synthesis of fused indazole derivatives.

In continuation of our earlier work on the synthesis of various biologically active heterocyclic compounds including biolabile piperidone, 1,2,3-selenadiazoles, 1,2,3-thiadiazoles, and 1,2,4,5-tetrazinanes [7-11], we wish to report the development of fused indazoles based on 3,5-diaryl-6-ethoxycarbonylcyclohex-2-en-1-one derivative, thus paving the way for a novel class of 4,6-diaryl-4,5-dihydro-2H-indazol-3-ols **9-16** and 4,6-diaryl-2-phenyl-4,5-dihydro-2H-indazol-3-ols **17**–**24**.

The synthetic strategy for the formation of these fused indazole derivatives involves three steps, which is described as follows. Condensation of the appropriate acetophenone and the appropriate benzaldehyde in the presence of sodium hydroxide yields the respective 1,3-diarylprop-2-en-1-ones. Their reaction with ethyl acetoacetate in the presence of sodium ethoxide gives 3,5-diaryl-6-ethoxycarbonylcyclohex-2-en-1-ones **1-8**.

The formed ketones on treatment with hydrazine hydrate and phenylhydrazine hydrochloride/anhydrous sodium acetate in refluxing methanol yield 4,6-diaryl-4,5-dihydro-2H-indazol-3-ols **9-16** or 4,6-diaryl-2-phenyl-4,5-dihydro-2H-indazol-3-ols **17-24**, respectively (Table 1).

The structures of the compounds are elucidated by melting points, elemental analysis, MS, FT-IR, ^1H and ^{13}C NMR, D_2O exchanged ^1H NMR, and two-dimensional HSQC spectroscopic data.

EXPERIMENTAL

We used TLC to assess the reactions and the purity of the products. All the reported melting points were determined in open capillaries and were uncorrected. IR spectra were recorded in KBr (pellet forms) on a Nicolet-Avatar–330 FT-IR spectrophotometer, and noteworthy absorption values (cm^{-1}) alone are listed. ^1H, D_2O exchanged ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, on a Bruker AMX 400 NMR spectrometer using DMSO-d_6 as a solvent. HSQC spectra were recorded at 500 MHz and on a Bruker DRX 500 NMR spectrometer using DMSO-d_6 as a solvent. The ESI + ve MS spectra were recorded on a Bruker Daltonics LC-MS spectrometer. Satisfactory microanalysis was obtained on a Carlo Erba 1106 CHN analyzer.

By adopting the literature precedent, 1,3-diarylprop-2-en-1-ones [12–14] and 3,5-diaryl-6-ethoxycarbonyl-cyclohex-2-en-1-ones **1-8** [6] were prepared.

Typical Procedure for the Synthesis of 4,6-diphenyl-4,5-dihydro-2H-indazol-3-ols 9–16. A solution of 6-ethoxycarbonyl-3,5-diphenylcyclohex-2-en-1-one **1** (0.1 mol) in methanol (40 ml) is treated with hydrazine hydrate (0.15 mol) and refluxed for 5 h. The reaction mixture is cooled and then poured over crushed ice. The crude product **9** is recrystallized twice using methanol as a solvent. IR, ν, cm^{-1}: 3425, 3060, 2922, 2863, 1607, 1515, 1446, 1369, 758, 695. ^1H NMR, δ, ppm (*J*, Hz): 2.90, 3.1–3.2 (2H, m, H-5); 4.19 (1H, dd, *J* = 11.8, *J* = 9.1, H-4); 6.75 (1H, d, *J* = 7.6, H-7); 9.7 (1H, s, H-2); 11.53 (1H, s, OH); 7.10–7.48 (10H, m, H arom.). ^{13}C NMR, δ, ppm: 34.2 (C-4); 36.2 (C-5); 98.3 (C-9); 113.4 (C-7); 136.2 (C-8); 125.0–128.5 (C arom.); 140.2, 145.3 (*ipso*-C's); 157.2 (C-3). In the D_2O exchanged ^1H NMR spectrum, the broad peak at 11.53 ppm due to –OH proton at C-3 and the broad peak at 9.74 ppm due to –NH proton at C-2 disappeared.

In the HSQC spectrum, one bond correlation (34.2/4.19) between C-4 and H-4a occurs. The ^{13}C resonance at 36.2 ppm has correlations with methylene protons H-5a (36.2/2.90; 36.2/3.20) and hence C-5 resonates at 36.2 ppm. The ^{13}C resonance at 113.4 ppm has correlations with a doublet at 6.75 ppm. The doublet at 6.75 ppm is conveniently assigned to H-7. The cross peak (113.4/6.75 ppm) confirms that the ^{13}C resonance at 113.4 ppm is due to C-7. The ^{13}C resonances at 98.3, 136.2, and 157.2 ppm have no correlations with protons and hence it is due to quaternary carbons. Among the quaternary carbon resonances, the ^{13}C resonance at 140.2 and 143.2 ppm is assigned to *ipso* carbons. The ^{13}C resonances at 136.2 and 157.2 ppm are due to the C-8 and C-3 carbons. The signal at 98.3 ppm is due to C-9 carbon and the C-6 carbon is merged with aromatic carbons.

Compounds 10–16 were synthesized similarly.

6-Phenyl-4-(*p*-tolyl)-4,5-dihydro-2H-indazol-3-ol (**10**). IR, ν, cm^{-1}: 3419, 3060, 3062, 2919, 2858, 1593, 1516, 757, 695. ^1H NMR, δ, ppm (*J*, Hz): 2.21 (3H, s, CH_3 at phenyl ring); 2.87, 3.1-3.2 (2H, m, H-5); 4.14 (1H, dd, *J* = 12.3, *J* = 9.5, H-4); 6.75 (1H, d, *J* = 7.8, H-7); 8.30 (1H, s, H-2); 10.98 (1H, s, OH); 7.02–7.47 (9H, m, H arom.). ^{13}C NMR, δ, ppm: 20.5 CH_3 at phenyl ring; 33.8 (C-4); 36.3 (C-5); 98.5 (C-9); 113.3 (C-7); 136.3 (C-8); 125.0-128.5 (C arom.); 134.8, 140.2, 141.1, 142.2 (*ipso*-C's); 156.4 (C-3).

4-(4-Chlorophenyl)-6-phenyl-4,5-dihydro-2H-indazol-3-ol (**11**). IR, ν, cm^{-1}: 3404, 3054, 2928, 1600, 1535, 1491, 757, 694. ^1H NMR, δ ppm (*J*, Hz): 2.87; 3.1–3.2 (2H, m, H-5); 4.20 (1H, dd, *J* = 12.9, *J* = 8.6, H-4); 6.76 (1H, d, *J* = 8.1, H-7); 8.35 (1H, s, H-2); 11.5 (1H, s, OH); 7.16–7.47 (9H, m, H arom.). ^{13}C NMR, δ, ppm: 33.7 (C-4); 36.1 (C-5); 97.8 (C-9); 113.4 (C-7); 136.2 (C-8); 125.1–128.5 (C arom.); 130.5, 140.1, 141.2, 144.2 (*ipso*-C's); 156.3 (C-3).

4-(4-Nitrophenyl)-6-phenyl-4,5-dihydro-2H-indazol-3-ol (**12**)**.** IR, ν, cm^{-1}: 3422, 3076, 2924, 2847, 1599, 1515, 1437, 1345, 753, 695. ^1H NMR, δ, ppm (*J*, Hz): 2.86, 3.20-3.25 (2H, m, H-5); 4.34 (1H, dd, *J* =12.4, *J* = 8.2, H-4); 6.76 (1H, d, *J* = 7.9, H-7); 9.70 (1H, s, H-2); 11.70 (1H, s, OH); 7.25–8.11 (9H, m, H arom.). ^{13}C NMR, δ, ppm: 34.6 (C-4); 36.0 (C-5); 97.3 (C-9); 113.5 (C-7); 136.2 (C-8); 123.4–128.8 (C arom.); 140.1, 146.2 (*ipso*-C's); 157.2 (C-3).

4-(4-Methoxyphenyl)-6-phenyl-4,5-dihydro-2H-indazol-3-ol (**13**). IR, ν, cm^{-1}: 3417, 3065, 3052, 2930, 2836, 1608, 1511, 1443, 1373, 760, 696. ^1H NMR, δ, ppm (*J*, Hz): 2.85, 3.10–3.20 (2H, m, H-5); 3.64 (3H, s, OCH_3

at phenyl ring); 4.11 (1H, dd, *J* = 11.1, *J* = 9.0, H-4); 6.73 (1H, d, *J* = 8.4, H-7,); 8.40 (1H, s, H-2); 10.70 (1H, s, OH); 7.037.45 (9H, m, H arom.). ^{13}C NMR, δ, ppm: 33.4 (C-4); 36.4 (C-5); 54.9 (OCH_3 at phenyl ring); 98.7 (C-9); 113.4 (C-7); 136.2 (C-8); 125.0–128.5 (C arom.); 137.2, 140.3, 141.0, 157.5 (*ipso*-C's); 156.3 (C-3).

6-(4-Bromophenyl)-4-phenyl-4,5-dihydro-2H-indazol-3-ol (**14**). IR, ν, cm^{-1}: 3402, 3093, 3000, 2927, 2830, 1608, 1526, 1439, 1349, 807, 736. ^{1}H NMR, δ, ppm (*J*, Hz): 2.85, 3.10–3.20 (2H, m, H-5); 4.16 (1H, dd, *J* = 11.6, *J* = 9.4, H-4); 6.76 (1H, d, *J* = 8.6, H-7); 9.70 (1H, s, H-2); 11.72 (1H, s, OH); 7.10–7.82 (9H, m, H arom.). ^{13}C NMR, δ, ppm: 34.4 (C-4); 36.1 (C-5); 97.8 (C-9); 113.3 (C-7); 135.2 (C-8); 126.0–129.7 (C arom.); 131.4, 131.9, 135.2, 139.2 (*ipso*-C's); 157.5 (C-3).

6-(*p*-Tolyl)-4-phenyl-4,5-dihydro-2H-indazol-3-ol (**15**). IR, ν, cm^{-1}: 3422, 3062, 3051, 2928, 2834, 1603, 1510, 1441, 1370, 764, 691. ^{1}H NMR, δ, ppm (*J*, Hz): 2.81, 3.13–3.18 (2H, m, H-5); 2.24 (3H, s, CH_3 at phenyl ring); 4.08 (1H, dd, *J* = 10.8, *J* = 8.9, H-4); 6.70 (1H, d, *J* = 8.6, H-7); 8.38 (1H, s, H-2); 11.21 (1H, s, OH); 7.08–7.38 (9H, m, H arom.). ^{13}C NMR, δ, ppm: 33.0 (C-4); 36.7 (C-5); 21.8 (CH_3 at phenyl ring); 99.2 (C-9); 112.6 (C-7); 134.2 (C-8); 124.7–127.9 (C arom.); 137.0, 140.5, 141.5, 157.2 (*ipso*-C's); 157.2 (C-3).

4,5-Dihydro-4-(4-methoxyphenyl)-6-(3-nitrophenyl)-2H-indazol-3-ol (**16**). IR, ν, cm^{-1}: 3428, 3022, 2925, 2852, 1609, 1525, 1489, 1448, 818, 701. ^{1}H NMR, δ, ppm (*J*, Hz): 2.85, 3.10–3.25 (2H, m, H-5); 4.16 (1H, dd, *J* = 12.3, *J* = 9.0, H-4); 6.77 (1H, d, *J* = 8.1, H-7); 9.82 (1H, s, H-2); 10.90 (1H, s, OH); 6.95–8.24 (8H, m, H arom.). ^{13}C NMR, δ, ppm: 33.4 (C-4); 36.3 (C-5); 99.0 (C-9); 113.5 (C-7); 137.0 (C-8); 116.0-131.4 (C arom.); 137.0, 141.9, 148.2, 157.6 (*ipso*-C's); 156.1 (C-3).

Typical Procedure for the Synthesis of 2,4,6-diaryl-2-phenyl-4,5-dihydro-2H-indazol-3-ols 17-24. A solution of 6-ethoxycarbonyl-3,5-diphenylcyclohex-2-en-1-one **1** (0.1 mol) in methanol (40 ml) is treated with phenylhydrazine hydrochloride (0.15 mol) and anhydrous sodium acetate (0.15 mol) and refluxed for 7 h and then poured over crushed ice. The crude product **17** is recrystallized twice using methanol as a solvent. IR, ν, cm^{-1}: 3425, 3062, 2921, 2862, 1605, 1514, 1445, 1367, 757, 705, 695. ^{1}H NMR, δ, ppm (*J*, Hz): 2.98-3.13, 3.46-3.50 (2H, m, H-5); 4.34 (1H, dd, *J* = 12.0, *J* = 9.2, H-4); 6.86 (1H, d, *J* = 7.9, H-7); 11.73 (1H, s, OH); 7.20-7.58 (15H, m, H arom.). ^{13}C NMR, δ, ppm: 34.4 (C-4); 37.2 (C-5); 99.2 (C-9); 114.5 (C-7); 136.6 (C-8); 125.6-128.6 (C arom.); 140.4, 142.2, 145.4 (*ipso*-C's); 159.2 (C-3). In the D_2O exchanged ^{1}H NMR spectrum, the broad peak at 11.73 ppm due to OH proton at C-3 disappeared.

In the HSQC spectrum, one bond correlation (34.4/4.34) between C-4 and H-4a occurs. The ^{13}C resonance at 37.2 ppm has correlations with methylene protons H-5a (37.2/2.98-3.13; 36.2/3.46–3.50) and hence C-5 resonates at 37.2 ppm. The ^{13}C resonance at 114.5 ppm correlates with a doublet at 6.86 ppm. The doublet at 6.86 ppm is conveniently assigned to H-7. The cross peak (114.5/6.86 ppm) confirms that the ^{13}C resonance at 114.5 ppm is due to C-7. The ^{13}C resonances at 99.2, 136.6, 159.2 ppm have no correlations with protons and hence it is due to quaternary carbons. Among the quaternary carbon resonances, the ^{13}C resonance at 140.4, 142.2, and 145.4 ppm are assigned to *ipso* carbons. The ^{13}C resonances at 136.6 and 159.2 ppm are due to the C-8 and C-3 carbons. The signal at 99.2 ppm is due to C-9 carbon and the C-6 carbon is merged with aromatic carbons.

Compounds 18–24 were synthesized similarly.

2,6-Diphenyl-4-(*p*-tolyl)-4,5-dihydro-2H-indazol-3-ol (**18**). IR, ν, cm^{-1}: 3419, 3062, 3065, 2917, 2857, 1592, 1514, 755, 708, 694. ^{1}H NMR, δ, ppm (*J*, Hz): 2.34 (3H, s, CH_3 at phenyl ring); 2.95–3.10, 3.33–3.69 (2H, m, H-5); 4.01 (1H, dd, *J* = 12.4, *J* = 9.6, H-4); 6.87 (1H, d, *J* = 8.5, H-7); 11.35 (1H, s, OH); 7.02–7.57 (14H, m, H arom.). ^{13}C NMR, δ, ppm: 21.9 (CH_3 at phenyl ring); 33.9 (C-4); 37.3 (C-5); 99.1 (C-9); 114.5 (C-7); 136.3 (C-8); 125.3–128.6 (C arom.); 140.2, 141.3, 142.3 (*ipso*-C's); 159.4 (C-3).

4-(4-Chlorophenyl)-2,6-diphenyl-4,5-dihydro-2H-indazol-3-ol (**19**). IR, ν, cm^{-1}: 3404, 3053, 2926, 1602, 1534, 1492, 756, 711, 695. ^{1}H NMR, δ, ppm (*J*, Hz): 2.95–3.10, 3.26–3.40 (2H, m, H-5); 4.35 (1H, dd, *J* =13.1, *J* = 8.7, H-4); 6.87 (1H, d, *J* = 8.0, H-7); 11.6 (1H, s, OH); 7.26–7.67 (14H, m, H arom.). ^{13}C NMR, δ, ppm: 34.5 (C-4); 37.4 (C-5); 99.3 (C-9); 114.7 (C-7); 136.2 (C-8); 125.1–128.8 (C arom.); 140.1, 141.2, 142.4, 144.2 (*ipso*-C's); 159.3 (C-3).

4-(4-Nitrophenyl)-2,6-diphenyl-4,5-dihydro-2H-indazol-3-ol (**20**). IR, ν, cm^{-1}: 3421, 3075, 2922, 2846, 1597, 1515, 1433, 1346, 752, 708, 693. ^{1}H NMR, δ, ppm (*J*, Hz): 2.96–3.29, 3.40–3.55 (2H, m, H-5); 4.44 (1H, dd, *J* = 12.6, *J* = 8.4, H-4); 6.90 (1H, d, *J* = 8.2, H-7); 11.70 (1H, s, OH);7.35–7.56 (14H, m, H arom.). ^{13}C NMR, δ, ppm: 34.8 (C-4); 37.2 (C-5); 99.2 (C-9); 114.3 (C-7); 136.2 (C-8); 123.4–128.8 (C arom.); 140.1, 142.4, 146.2 (*ipso*-C's); 159.2 (C-3).

4-(4-Methoxyphenyl)-2,6-diphenyl-4,5-dihydro-2H-indazol-3-ol (**21**). IR, ν, cm^{-1}: 3416, 3064, 3051, 2932, 2835, 1606, 1511, 1441, 1372, 759, 712, 693. ^{1}H NMR, δ, ppm (*J*, Hz): 2.94–3.20, 3.22–3.46 (2H, m, H-5); 3.85 (3H, s, OCH_3 at phenyl ring); 4.27 (1H, dd, *J* = 11.4, *J* = 9.1, H-4); 6.85 (1H, d, *J* = 8.6, H-7); 11.40 (1H, s, OH); 7.12-7.55 (14H, m, H arom.). ^{13}C NMR, δ, ppm: 34.8 (C-4); 37.5 (C-5); 55.3 (OCH_3 at phenyl ring); 99.4 (C-9); 114.3 (C-7); 136.2 (C-8); 125.0-128.5 (C arom.); 137.2, 140.3, 141.0, 142.4 (*ipso*-C's); 158.3 (C-3).

6-(4-Bromophenyl)-2,4-diphenyl-4,5-dihydro-2H-indazol-3-ol (**22**). IR, ν, cm^{-1}: 3401, 3092, 2998, 2926, 2831, 1606, 1525, 1437, 1348, 805, 713, 735. ^{1}H NMR, δ, ppm (*J*, Hz): 2.92-2.95, 2.96-3.17 (2H, m, H-5); 4.02 (1H, dd, *J* = 11.8, *J* = 9.5, H-4); 6.87 (1H, d, *J* = 8.8, H-7); 11.71 (1H, s, OH); 7.20-7.90 (14H, m, H arom.). ^{13}C NMR, δ, ppm: 33.8 (C-4); 37.4 (C-5); 99.3 (C-9); 114.3 (C-7); 137.0 (C-8); 116.1-137.0 (C arom.); 142.1, 142.3, 149.0, 157.2 (*ipso*-C's); 159.0 (C-3).

2,4-Diphenyl-6-(*p*-tolyl)-4,5-dihydro-2H-indazol-3-ol (**23**). IR, ν, cm^{-1}: 3421, 3060, 3053, 2927, 2833, 1601, 1512, 1440, 1372, 763, 715, 690. ^{1}H NMR, δ, ppm: 2.92–3.18, 3.20–3.44 (2H, m, H-5); 2.28 (3H, s, CH_3 at phenyl ring); 4.01 (1H, dd, *J* = 11.1, *J* = 8.8, H-4); 6.84 (1H, d, *J* = 8.4, H-7); 11.70 (1H, s, OH); 7.06–7.41 (14H, m, H arom.). ^{13}C NMR, δ, ppm: 33.9 (C-4); 38.7 (C-5); 22.1 (CH_3 at phenyl ring); 99.4 (C-9); 112.7 (C-7); 134.1 (C-8); 123.7-127.7 (C arom.); 137.1, 140.6, 141.4, 157.3 (*ipso*-C's); 159.2 (C-3).

4,5-Dihydro-4-(4-methoxyphenyl)-6-(3-nitrophenyl)-2-phenyl-2H-indazol-3-ol (**24**). IR, ν, cm^{-1}: 3427, 3020, 2924, 2851, 1607, 1523, 1487, 1446, 819, 714, 703. ^{1}H NMR, δ, ppm (*J*, Hz): 2.94–3.28, 3.30-3.44 (2H, m, H-5); 3.82 (3H, s, OCH_3 at phenyl ring), 3.95 (1H, dd, *J* = 12.7, *J* = 9.2, H-4); 6.85 (1H, d, *J* = 8.2, H-7); 11.82 (1H, s, OH); 7.00-8.44 (13H, m, H arom.). ^{13}C NMR, δ, ppm: 34.4 (C-4); 37.8 (C-5); 99.5 (C-9); 114.2 (C-7); 135.2 (C-8); 126.0-129.7 (C arom.); 129.0, 131.4, 131.9, 139.2, 142.2 (*ipso*-C's); 159.0 (C-3).

REFERENCES

1. L. Cecchi, F. Melani, G. Filacchioni, and M. Tredici, *Farmaco*, **39**, 945 (1984).
2. Jong Hee Ko, Seung Woo Yeon, Jung Su Ryu, Tae-Yong Kim, Eun-Ha Song, Hea-Jung You, Rae-Eun Park, and Chung-Kyu Ryu, *Bioorg. Med. Chem. Lett.*, **16**, 6001 (2006).
3. A. Gerpe, G. Aguirre, L. Boiani, H. Cerecetto, M. Gonzalez, C. Olea-Azar, C. Rigol, J. D. Maya, A. Morello, O. E. Piro, V. J. Aran, A. Azqueta, A. L. de Cerain, A. Monge, M. A. Rojas, and G. Yaluff, *Bioorg. Med. Chem.*, **14**, 3467 (2006).
4. X. Li, S. Chu, V. A. Feher, M. Khalili, Z. Nie, S. Margosiak, V. Nikulin, J. Levin, K. G Sprankle, M. E. Tedder, R. Almassy, K. Appelt, and K. M. Yager, *J. Med. Chem.*, **46**, 5663 (2003).
5. D. L. Selwood, D. G. Brummell, J. Budworth, G. E. Burtin, R. O. Campbell, S. Chana, I. G. Charles, P. A. Fernandez, R. C. Glen, M. C. Goggin, A. J. Hobbs, M. R. Kling, Q. Liu, D. J. Madge, S. Meillerais, K. L. Powell, K. Reynolds, G. D. Spacey, J. N. Stables, M. A. Tatlock, K. A. Wheelers, G. Wishart, and C. Woo, *J. Med. Chem.*, **44**, 78 (2001).
6. M. Balasubramanian and A. D'Souza, *Tetrahedron*, **24**, 5399 (1968).
7. M. Gopalakrishnan, P. Sureshkumar, J. Thanusu, V. Kanagarajan, R. Govindaraju, and G. Jayasri, *J. Enz. Inhib. Med. Chem.*, **22**, 709 (2007).
8. M. Gopalakrishnan, P. Sureshkumar, J. Thanusu, C. Prabhu, and V. Kanagarajan, *J. Chem. Res.*, 2, 80 (2007).

9. M. Gopalakrishnan, P. Sureshkumar, V. Kanagarajan, and J. Thanusu, *J. Sulfur Chem*., **28**, 383 (2007).
10. T. Balasankar, M. Gopalakrishnan, and S. Nagarajan, *J. Enz. Inhib. Med. Chem*., **22**, 171 (2007).
11. T. Balasankar, M. Gopalakrishnan, and S. Nagarajan, *Eur. J. Med. Chem*., **40**, 728 (2005).
12. W. Guthrie, *Can. J. Chem*., **69**, 339 (1991).
13. W. Guthrie, *J. Am. Chem. Soc*., **109**, 6609 (1991).
14. A. T. Nielson and W. Houlihan, *J. Org. React*., **16**, 1 (1968).