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A convenient catalytic synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-triones on reusable silica supported Preyssler heteropolyacid

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Efficient synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione derivatives was achieved by one-pot three-component condensation reaction of phthalhydrazide, dimedone, and aromatic aldehydes under solvent-free conditions. Good to excellent yields were obtained at short reaction times on the reusable silica supported Preyssler heteropolyacid catalyst.

Keywords: Indazolo[2,1-*b*]phthalazine-trione, Phthalhydrazide, Dimedone, Preyssler, Heteropolyacid

INTRODUCTION

In the past few decades, the synthesis of new heterocyclic compounds has been a subject of great interest due to their wide applicability. Heterocyclic compounds widely occur in the nature and are essential to life. Among the large variety of heterocyclic compounds, heterocycles containing the phthalazine moiety are of interest because of their pharmacological and biological activities [1]. Phthalazine derivatives were reported to possess vasorelaxant [2], cardiotonic [3] and anticonvulsant [4] properties. A number of methods have been reported in the literature for the synthesis of phthalazine derivatives [5,6]. In recent decades, heteropolyacids (HPAs) have been used as catalysts for fine organic synthetic processes, thus being important for industries related with fine chemicals [7], including flavors, pharmaceuticals and food industries [8]. Heteropolyacids are more active catalysts than conventional inorganic and organic acids for various reactions in solutions [9]. They are used as industrial catalysts for several liquid phase reactions [10–13]. Among heteropolyacids, polytungstic acids are the most widely used catalysts owing to their high acid strengths, thermal stabilities, and low reducibilities. Catalysts based on heteropolyacids as Brønsted acids have many advantages over liquid acid catalysts. They are non-corrosive and environmentally benign, presenting fewer disposal problems. Solid heteropolyacids have attracted much attention in organic synthesis owing to easy work-up procedures, easy filtration, and minimization of cost and waste generation due to recycling and reuse of the catalysts [14-16]. Supported heteropolyacid on silica gel has been used as an effective catalyst for Diels Alder [17] and Fries rearrangement [18], as well as for Friedel-Crafts reactions [19]. In recent years, heterogeneous catalysts have gained importance due to economic and environmental considerations [1,3,20]. Among the various heterogeneous catalysts, particularly, heteropolyacids supported on silica gel have the advantages of low cost, ease of preparation, and catalyst recycling. These catalysts are generally less expensive, eco-friendly, highly reactive, easy to handle and recoverable.

EXPERIMENTAL

Materials

All chemicals were obtained from Merck and were used as received.

Instruments

^{1}H NMR spectra were recorded on a FT NMR Bruker 400 MHz spectrometer at 298 K. Melting points were recorded on an Electrothermal type 9100 apparatus and were uncorrected. Chemical shifts were reported in ppm (δ-scale) relative to the internal standard TMS (0.00 ppm); the solvent was

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used as a reference. IR spectra were recorded on a Buck 500 scientific spectrometer (KBr pellets). The products were identified by comparison of their m.p., IR and NMR spectra with those of authentic samples.

Preparation of silica supported Preyssler heteropolyacid catalyst, $H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (50%)

$H_{14}[NaP_5W_{30}O_{110}]$, ($H_{14}$–$P_5$) was prepared by passing a solution of the potassium salt in water through a column (50 cm × 1 cm) of Dowex 50W×8 in the H^+ form and evaporating the eluate to dryness under vacuum. Supported heteropolyacid catalyst was obtained according to our previous report [21–24] by impregnating the support (SiO_2 powder) with an aqueous solution of $H_{14}[NaP_5W_{30}O_{110}]$, ($H_{14}$–$P_5$). After stirring the mixture, the solvent was evaporated, the product was dried at 120 ºC and was calcined at 250 ºC in a furnace prior to use.

General Procedure for the synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione derivatives

A mixture of dimeone (1 mmol), aldehydes (1.5 mmol), phthalhydrazide (1 mmol) and silica supported Preyssler heteropolyacid catalyst (0.07 g) was heated under reflux conditions for the appropriate time (Table **2**). The reaction was monitored by TLC. After completion, the reaction mass was cooled to room temperature and was washed with water, then the solid residue was isolated and dissolved in CH_2Cl_2. The catalyst was filtered; the solvent was evaporated from the reaction mixture. The solid product was purified by re-crystallization from aqueous C_2H_5OH (25%). The products were characterized by comparison of their physical data with those of known compounds.

The spectral data of some representative 2*H*-indazolo[1,2–*b*]phthalazine-1,6,11(13*H*)-triones are given below.

3,4-Dihydro-3,3-dimethyl-13-phenyl-2*H*-indazolo[2,1-b]phthalazine-1,6,11(13*H*)-trione **(4a)** [25]:

Yellow powder. M.p. 203–205 °C; IR (KBr) ν_{max}/cm^{-1}: 2953, 1564, 1572; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.31 (m, 2H), 7.85 (d, 2H, J = 3.2, 7.6 Hz), 7.43 (d, 2H, J = 7.2 Hz), 7.32 (m, 3H), 6.46 (s, 1H), 3.44 (d, 1H, J = 18.8 Hz), 3.26 (d, 1H, J = 2.4, 18.8 Hz), 2.36 (s, 2H), 1.23 (s, 6H); ^{13}CNMR ($CDCl_3$, 100 MHz) δ: 192.0, 156.0, 154.4, 150.8, 136.3, 134.5, 133.5, 129.0, 128.6, 128.0, 127.5, 127.1, 118.6, 65.1, 50.7, 38.0, 34.5. 28.7, 28.4; MS, *m*/*z* (%): 372 (M+, 15), 295 (100), 104 (84), 76 (67). Anal. calcd for $C_{23}H_{20}N_2O_3$: C 74.18, H 5.41, N 7.52; found: C 74.26, H 5.36, N 7.49.

3,4-Dihydro-3,3-dimethyl-13-(4-chlorophenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **(4b)** [25]:

Yellow powder. M.p. 261–263 ºC; IR (KBr) ν_{max}/cm^{-1}: 2950, 1651, 1628; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.31 (m, 2H), 7.86 (m, 2H), 7.35 (d, 2H, J = 8.4 Hz), 7.31 (d, 2H, J = 8.4 Hz), 6.43 (s, 1H), 3.40 (d, 1H, J = 18.8 Hz), 3.25 (dd, 1H, J = 2.0, 18.8 Hz), 2.36 (s, 2H), 1.24 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 192.0, 156.0, 154.3, 151.0, 134.9, 134.6, 134.5, 133.5, 129.0, 128.9, 128.5, 128.0, 127.6, 118.0, 64.2, 50.9, 38.0, 34.6, 28.7, 28.4; Anal. calcd for $C_{23}H_{19}ClN_2O_3$: C 67.90, H 4.71, N 6.89; found: C 67.96, H 4.80, N 6.77.

3,4-Dihydro-3,3-dimethyl-13-(4-bromophenyl)-2*H*indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **(4c)** [25]:

White powder. M.p. 265–267 ^{o}C; IR (KBr) ν_{max}/cm^{-1}: 2956, 1655, 1623; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.20 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 2.35 (s, 2H, CH_2CO), 3.39 (d, J= 19.1 Hz, 2H), 6.40 (s, 1H, CHN), 8.32 (m, 8H, Ph); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 28.5, 28.7, 34.6, 38.1, 50.7, 64.5, 118.0, 122.7, 127.6, 128.1, 128.8, 128.9, 129.1, 131.9, 133.6, 134.7, 135.4, 151.1, 154.3, 156.0, 192.2; MS, m/z (%): 451 (Mþ, 7), 295 (100), 104 (28), 76 (34). Anal. calcd for $C_{23}H_{19}BrN_2O_3$: C, 61.21; H, 4.24; N, 6.21%. Found: C, 61.12; H, 4.16; N, 6.31%.

3,4-Dihydro-3,3-dimethyl-13-(4-methylphenyl)-2*H*indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **(4d)** [25]:

Yellow powder. M.p.: 226–228 ºC; IR (KBr) ν_{max}/cm^{-1}: 2955, 1660, 1628, 1466, 1357, 1313, 1270, 1144, 1076, 1025, 826, 793, 699. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.29 (m, 2H), 7.84 (m, 2H), 7.30 (d, 2H, J = 8.0 Hz), 7.15 (d, 2H, J = 7.6 Hz), 6.44 (s, 1H), 3.42 (d, 1H, J = 18.8 Hz), 3.25 (dd, 1H, J = 2.0, 18.8 Hz), 2.32 (s, 2H), 2.31 (s, 3H), 1.21 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 192.1, 156.0, 154.1, 150.6, 138.5, 134.7, 133.3, 133.5, 129.4, 129.2, 127.9, 127.7, 118.7, 64.7, 51.0, 38.0, 34.6, 28.7, 28.4, 21.0; Anal. calcd for $C_{24}H_{22}N_2O_3$: C 74.59, H 5.74, N 7.25; found: C 74.60, H 5.68, N 7.38.

3,4-Dihydro-3,3-dimethyl-13-(4-nitrophenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **(4e)** [25]:

Yellow powder. M.p.: 217–219 ºC; IR (KBr) ν_{max}/cm^{-1}: 3075, 2957, 1693, 1660, 1616, 1520, 1365, 1275, 1143, 1100, 1018, 857, 793, 720. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 88.34 (m, 2H), 8.20 (d, 2H, J = 8.8 Hz), 7.90 (d, 2H, J = 1.6, 5.6 Hz), 7.65 (d, 2H, J = 8.8 Hz), 6.50 (s, 1H), 3.41 (d, 1H, J = 19.2 Hz), 3.26 (d, 1H, J = 2.0, 19.2 Hz), 2.33 (s, 2H), 1.23 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 192.0, 155.8, 154.5, 151.5, 147.8, 143.5, 134.7, 133.8, 128.7, 128.5, 128.1, 128.0, 127.7, 124.0, 117.2, 64.0, 50.8, 38.0, 34.8, 28.9, 28.4; Anal. calcd for $C_{23}H_{19}N_3O_5$: C 66.18, H 4.59, N 10.07; found: C 66.23, H 4.50, N 10.02.

3,4-Dihydro-3,3-dimethyl-13-(3-nitrophenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **(4f)** [26]:

Yellow powder. M.p.: 270–272 ºC; IR (KBr) ν_{max}/cm^{-1}: 3075, 2954, 1670, 1657, 1612, 1358, 1270, 1147, 1105, 1050, 720. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.33 (m, 2H), 8.17 (d, 2H, J = 7.2 Hz), 7.90 (m, 3H), 7.58 (t, 1H, J = 7.2 Hz), 6.53 (s, 1H), 3.45 (d, 1H, J = 19.6 Hz), 3.28 (d, 1H, J = 2.0, 19.6 Hz), 2.37 (s, 2H), 1.23 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 192.0, 156.0, 154., 151.8, 148.5, 138.6, 134.2, 133.9, 129.6, 129.0, 128.5, 128.2, 127.7, 123.7, 121.4, 117.3, 64.0, 50.8, 38.0, 34.6, 28.7, 28.3; Anal. calcd for $C_{23}H_{19}N_3O_5$: C 66.18, H 4.59, N 10.07; found: C 66.19, H 4.66, N 10.03.

3,4-Dihydro-3,3-dimethyl-13-(4-fluorophenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **(4g)** [25]:

Yellow powder. M.p. 218–220 ºC; IR (KBr) ν_{max}/cm^{-1}: 2950, 1668, 1660; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.30 (m, 2H), 7.85 (m, 2H), 7.40 (m, 2H), 7.03 (t, 2H, J = 8.8 Hz), 6.45 (s, 1H), 3.40 (d, 1H, J = 18.8 Hz), 3.25 (d, 1H, J= 2.4, 18.8 Hz), 2.36 (s, 2H), 1.23 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 192.0, 163.9, 161.5, 156.0, 154.4, 151.0, 134.6, 133.6, 132.0, 129.0, 128.8, 128.0, 127.7, 118.1, 115.7, 115.6, 64.2, 50.9, 38.1, 34.5, 28.7, 28.4; Anal. calcd for $C_{23}H_{19}FN_2O_3$: C 70.76, H 4.91, N 7.18; found: C 70.83, H 4.84, N 7.26.

3,4-Dihydro-3,3-dimethyl-13-(2-chlorophenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **(4h)** [26]:

Yellow powder. M.p.: 264–266 ºC, IR (KBr) ν_{max}/cm^{-1}: 3056, 2958, 2893, 1660, 1630, 1600, 1466, 1358, 1269, 1150, 1105, 1053, 757, 700. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.29 (m, 2H), 7.86 (m, 2H), 7.47 (d, 1H, J = 6.8Hz), 7.30 (m, 3H), 6.69 (s, 1H), 3.40 (d, 1H, J = 18.8 Hz), 3.25 (d, 1H, J = 2.0, 18.8 Hz), 2.32 (s, 2H), 1.24 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 192.0, 156.3, 154.1, 151.9, 134.6, 133.5, 133.0, 132.5, 130.6, 129.7, 129.0, 128.7, 128.0, 127.7, 127.3, 64.1, 50.8, 38.1, 34.6, 28.9, 28.4; Anal. calcd for $C_{23}H_{19}ClN_2O_3$: C 67.90, H 4.71, N 6.89; found: C 70.01, H 4.67, N 6.94.

13-(3-chlorophenyl)-3,3-dimethyl-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (**4i**) [26]:

Yellow powder. M.p.: 204–206 ºC; IR (KBr) ν_{max}/cm^{-1}: 3067, 2959, 2870, 1656, 1626, 1578, 1465, 1360, 1312, 1269, 1145, 789, 700, 677; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (s, 6H), 2.35 (s, 2H), 3.20 (d, 1H , J 19.1 Hz), 3. 42 (d, 1H, J 19.1 Hz), 6.40 (s, 1H), 7.30 (m, 4H), 7.85 (d, 2H, J 3.3, 5.7 Hz), 8.29 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.5, 28.6, 34.6, 38.0, 50.8, 64.1, 117.8, 125.8, 127.0, 127.5, 128.1, 128.9, 129.0, 130.0, 133.6, 134.5, 138.5, 151.2, 154.4, 156.0, 192.1 ppm; MS: m/z (%) = 406 (M^+, 30), 296 (48), 295 (100), 239 (11), 149 (7), 130 (7), 104 (21), 76 (19), 55 (8), 43 (7). MS: m/z (%) = 406 (M+, 30), 296 (48), 295 (100), 239 (11), 149 (7), 130 (7), 104 (21), 76 (19), 55 (8), 43 (7). Anal. calcd for $C_{24}H_{22}N_2O_3$: C, 67.90; H, 4.71; N, 6.89; found: C, 67.98; H, 4.78; N, 6.94.

3,4-Dihydro-3,3-dimethyl-13-(3,4-dichlorophenyl)-2*H*indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **(4j)** [26]:

Yellow powder. M.p.: 219–221 ºC ; IR (KBr) ν_{max}/cm^{-1}: 2965, 1660, 1627, 1469, 1390, 1352, 1314, 1265, 1145, 1100, 830, 701; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.31 (m, 2H), 7.88 (m, 2H), 7.44 (m, 2H), 7.31 (d, 1H, J = 2.0, 7.6 Hz), 6.38 (s, 1H), 3.40 (d, 1H, J = 19.2 Hz), 3.26 (d, 1H, J = 1.6, 19.2 Hz), 2.35 (s, 2H), 1.24 (s, 6H); ^{13}CNMR ($CDCl_3$, 100 MHz) δ: 192.0, 155.8, 154.6, 151.5, 136.7, 134.6, 133.8, 133.1, 132.8, 130.6, 128.9, 128.7, 128.1, 127.6, 126.8, 117.4, 63.8, 50.5, 38.0, 34.6, 28.6, 28.5; MS: m/z (%) = 440 (14), 405 (19), 383 (11), 296 (31), 295 (100), 104 (22), 76 (20), 55 (6); Anal. calcd for $C_{23}H_{18}Cl_2N_2O_3$: C 62.60, H 4.11, N 6.35; found: C 62.65, H 4.23, N 6.30.

3,4-Dihydro-3,3-dimethyl-13-(3,4,5-trimethoxyl)-2*H*indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione **(4k):**

Yellow powder. M.p.: 232–234 ºC; IR (KBr) ν_{max}/cm^{-1}: 2960, 1655, 1627, 1595, 1506, 1465, 1425, 1363, 1311, 1265, 1125, 1000, 700; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.32 (m, 2H), 7.81 (m, 2H), 6.63 (s, 2H), 6.40 (s, 1H), 3.82 (m, 9H), 3.45 (d, 1H, J = 18.8 Hz), 3.22 (d, 1H, J = 2.0, 18.8 Hz), 2.37 (s, 2H), 1.25 (s, 6H); ^{13}CNMR ($CDCl_3$, 100 MHz) δ: 192.1, 156.2, 154.5, 153.3, 150.5, 138.1, 134.5, 133.6, 131.7, 129.0, 128.8, 128.0, 127.8, 118.2, 104.5, 65.0, 60.8, 56.1, 50.9, 38.2, 34.7,

29.7, 28.8, 28.1; MS: m/z (%) = 462 (M^+, 38), 296 (22), 295 (100), 239 (7), 104 (10), 76 (8). Anal. calcd for $C_{26}H_{26}N_2O_6$: C 67.52, H 5.67, N 6.06; found: C 67.61, H 5.74, N 6.02.

3,3-dimethyl-13-o-tolyl-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione **(4l):**

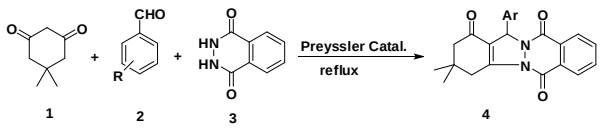
Yellow powder. M.p.: 241–243 ºC; IR (KBr) ν_{max}/cm^{-1}: 3045, 2959, 1663, 1600, 1467, 1359, 1314, 1275, 1145, 1103, 1082, 797, 764, 701; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20 (s, 3H), 1.21 (s, 3H), 2.30 (s, 2H), 2.77 (s, 3H), 3.26 (d, 1H, *J* 1.9, 19.1 Hz), 3.45 (d, 1H, *J* 19.0 Hz), 6.62 (s, 1H), 7.11 (m, 4H), 7.82 (m, 2H), 8.20 (d, 1H, *J* 3.2, 5.8 Hz), 8.36 (d, 1H, *J* 3.2, 5.9 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.4, 28.3, 28.7, 34.7, 38.0, 50.8, 61.4, 119.8, 125.2, 126.4, 127.5, 128.0, 128.4, 129.1, 129.3, 130.8, 133.5, 134.6, 135.2, 137.0, 150.6, 154.0, 156.0, 192.2 ppm; MS: m/z (%) = 386 (M+, 4), 295 (27), 279 (32), 167 (73), 149 (100), 113 (21), 104 (13), 83 (13), 71 (35), 70 (29), 57 (48), 43 (27), 41 (24); Anal. calcd for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25; found: C, 74.65; H, 5.80; N, 7.31.

13-(4-hydroxy-3-methoxyphenyl)-3,3-dimethyl-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione **(4m):**

Yellow powder. M.p.: 250–252 ºC; IR (KBr) ν_{max}/cm^{-1}: 3406, 2957, 1660, 1600, 1495, 1360, 1270, 1235, 1135, 1030, 791, 627; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (s, 6H), 2.35 (s, 2H), 3.24 (d, 1H, *J* 19.0 Hz), 3. 45 (d, 1H, *J* 18.9 Hz), 3.90 (s, 3H), 5.31 (br, 1H), 6.40 (s, 1H), 6.79 (m, 2H), 7.08 (s, 1H), 7.29 (s, 1H), 7.86 (s, 2H), 8.30 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.3, 156.2, 150.7, 146.5, 146.0, 134.5, 133.4, 129.3, 129.0, 128.1, 128.0, 127.6, 119.2, 118.5, 114.7, 111.0, 64.7, 56.0, 51.0, 38.2, 34.5, 28.7, 28.5 ppm; MS: m/z (%) = 418 (M+, 11), 415 (12), 295 (76), 231 (14), 162 (100), 132 (23), 104 (81), 77 (22), 76 (29), 51 (13), 50 (13); Anal. calcd for $C_{24}H_{22}N_2O_3$: C, 68.89; H, 5.30; N, 6.69; found: C, 68.95; H, 5.38; N, 6.76

RESULTS AND DISCUSSION

In continuation of our work on the catalytic properties of heteropolyacids [22–24], herein, we report a suitable method for the use of silica supported Preyssler heteropolyacid (50%) as a catalyst for the synthesis of 2,2-dimethyl-13-phenyl-2,3-dihydro-1*H*indazolo[2,1-*b*]phthalazine-4,6,11(13*H*)-trione (Scheme **1**).

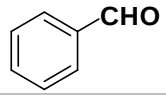
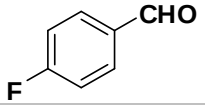
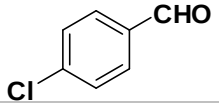
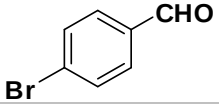
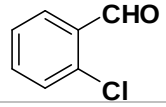
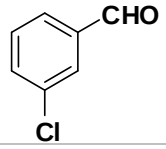
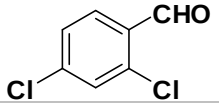
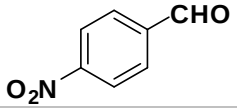
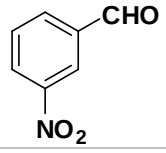
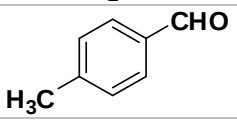
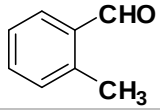
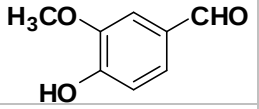
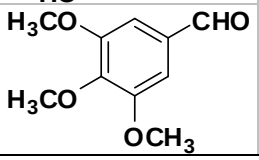


Scheme **1**

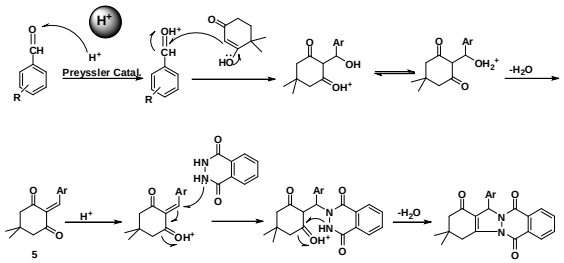
Dimedone **1**, phthalhydrazide **3**, and aromatic aldehydes **2a-m** in the presence of silica supported Preyssler heteropolyacid (50%) undergo a fast reaction under reflux at solvent-free conditions for several minutes to produce 2*H*-indazolo[2,1–*b*]phthalazine-1,6,11(13*H*)-triones **4a-m** (Table **1**). At these optimized reaction conditions, the scope and the efficiency of the procedures were explored for the synthesis of a wide variety of substituted 2*H*-indazolo[2,1-*b*]phthalazine-triones. The results are summarized in Table **1**. As shown in Table **1**, the direct three-component reactions worked well with a variety of aryl aldehydes including those bearing electron-withdrawing and electron-donating groups such as Me, OMe, Cl, F, Br and NO_2, and the desired compounds were obtained in high to excellent yields. This methodology offers significant improvements with regard to the scope of transformation, simplicity of operation, and green aspects avoiding expensive or corrosive catalysts. The structures of the products were established from their spectral properties (^{1}H NMR, ^{13}C NMR), elemental analysis and by comparison with available literature data. The formation of products **4a-4i** can be rationalized by initial formation of heterodiene **5 (**Scheme **2)** using the standard Knoevenagel condensation of dimedone with aromatic aldehyde in the presence of a catalytic amount of silica supported Preyssler heteropolyacid (50%). Subsequent Michael-type addition of phthalhydrazide to the heterodienes followed by cyclization and dehydration afford the corresponding products **4a-4i** (Scheme **2**, Table **1**).

A possible mechanism for the formation of entries **4a**–**g**, **4h**–**k** in Table **1** is proposed in Scheme **2**. It is reasonable to assume that entries **4a**–**g**, **4h**–**k** in Table **1** result from the initial formation of the heterodiene **5** by standard Knoevenagel condensation of dimedone **1** and aldehyde **2**. Then, the subsequent Michael-type addition of the phthalhydrazide **3** to the heterodyne **5** followed by cyclization affords the corresponding products (Table **1**, entries **4a-g**, **4h-k**) and Scheme **2**.

Table 1. Synthesis of 2*H*-indazolo[2,1-*b*] phthalazine-1,6,11(13*H*)-trione derivatives in the presence of silica supported Preyssler heteropolyacid (50%) under reflux conditions

Entry	Compound	Aldehyde	Time (min)	[a]Yield (%)
1	4a		8	94
2	4b		6	85
3	4c		7	87.5
4	4d		6	92
5	4e		7.5	88
6	4f		10	91.5
7	4g		7	93.5
8	4h		11	89
9	4i		15	80.5
10	4j		6.5	89
11	4k		7	89.5
12	4l		14	82.5
13	4m		9	84.5

[a] Isolated yield.



Scheme **2**

To recognize the capability of the present method in comparison with reported methods for the preparation of 2*H*-indazolo[2,1–*b*]phthalazine-1,6,11(13*H*)-trione derivatives from dimedone, aromatic aldehydes and phthalhydrazide, the model reaction of dimedone, benzaldehyde and phthalhydrazide was described. The reusability of the catalyst was tested in the synthesis of 3,3-dimethyl-13-phenyl-3,4-dihydro-1*H*-indazolo[1,2–*b*]phthalazine-1,6,11(2*H*,13*H*)-trione. HPA on silica is relatively inert toward HPAs, at least above a certain loading level, although some chemical interactions take place between HPA and SiO_2, the interaction involving the hydroxyl groups of silan and the acidic protons of heteropolyacids. The results show a decrease in the acidity of the silica supported Preyssler heteropolyacid in the following way: 10 %< 20 %< 30 %< 40% <50%. (Table 2).

Table 2. Synthesis of 3,3-dimethyl-13-phenyl-3,4-dihydro-1*H*-indazolo[1,2-*b*]phthalazine-1,6,11(2*H*,13*H*)-trione (**4a**) in the presence of silica supported Preyssler heteropolyacid under reflux conditions

[a]Yield (%)	Catalyst	Entry
28	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (10%)	1
43	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (20%)	2
60	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (30%)	3
72	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (40%)	4
94	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (50%)	5

[a] Isolated yield.

The catalyst was recovered after each run, washed with CH_2Cl_2, dried in an oven at 90 °C for 50 min prior to use and tested for its activity in the subsequent run. The catalyst was tested for 5 runs and it displayed very good reusability. The whole amount of the product could be isolated from the reaction mixture simply by CH_2Cl_2 extraction, and the catalyst system could be recovered and recharged with fresh substrates. Screening the system for five subsequent runs, the product was obtained in 93 %, 91%, 90%, 88% and 88% yields, respectively (Table **3**).

Table 3. Recycling of a silica supported Preyssler heteropolyacid catalyst $H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (50%) in the synthesis of 3,3-dimethyl-13-phenyl-3,4-dihydro-1*H*-indazolo[1,2-*b*]phthalazine-1,6,11(2*H*,13*H*)-trione (**4a**) under reflux conditions

Run	[a]Yield (%)
1	93
2	91
3	90
4	88
5	88

[a]Isolated yields and yields obtained in the first, second, third, fourth and fifth reuse of the catalyst.

CONCLUSIONS

A very simple and convenient procedure was described for the synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione catalyzed by a three-component condensation reaction of dimedone, aromatic aldehydes and phthalhydrazide using the non-corrosive, and environmentally benign (green) silica supported Preyssler type heteropolyacid $H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (50%) under solvent-free conditions. In addition, it is possible to apply the tenets of green chemistry to the generation of biologically interesting products in solvent-free media, which is less expensive and less toxic than using organic solvents. Also, the catalyst is recyclable and could be reused without significant loss of activity. Even after three reaction runs, the catalytic activity of silica supported Preyssler heteropolyacid, $H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (50%), was almost the same as that of the freshly used catalyst.

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УДОБЕН КАТАЛИТИЧЕН СИНТЕЗ НА 2Н- ИНДАЗОЛО[2,1-В]ФТАЛАЗИН-ТРИ-ОНИ ВЪРХУ ВЪЗОБНОВЯЕМА ХЕТЕРОПОЛИКИСЕЛИНА ТИП PREYSSLER ВЪРХУ СИЛИЦИЕВ ДИОКСИД

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(Резюме)

Ефективен метод за синтез на 2Н- индазоло[2,1-b]фталазин-три-он производни е осъществен чрез едностъпкова три компонентна кондензация на фталов хидразид, димедон и ароматни алдехиди при условия без разтворител. Получени са добри до отлични добиви за кратко реакционно време върху възобновяема хетерополикиселина тип Preyssler като катализатор при използване на носител силициев диоксид.