Reusable silica supported poly phosphoric acid catalyzed three-component synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-trione derivatives

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Abstract

An efficient synthesis of 2*H*-indazolo[2,1-b]phthalazine-1,6,11(13*H*)-trione derivatives from the three-component condensation reaction of phthalhydrazide, dimedone, and aromatic aldehydes under solvent-free conditions in good to excellent yields and short reaction times using reusable silica supported poly phosphoric acid (PPA–SiO_2) as heterogeneous acid catalyst has been investigated.

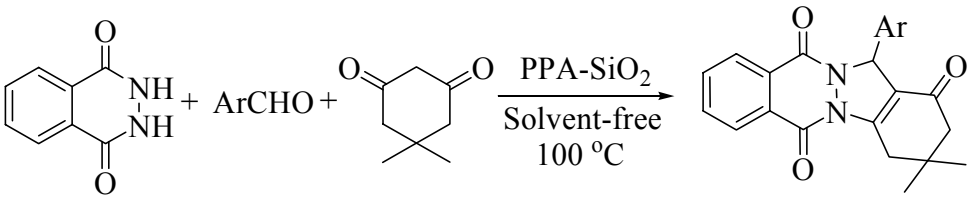
Keywords: PPA–SiO_2, indazolo[2,1-*b*]phthalazine-trione, multi-component reaction, phthalhydrazide, dimedone

Introduction

In recent years, heterogeneous catalysts have gained importance due to economic and environmental consideration.[1-3] Among the various heterogeneous catalysts, particularly, silica supported reagents have advantages of low cost, ease of preparation, and catalyst recycling. These catalysts are generally less expensive, eco-friendly, high reactive, easy to handle and recoverable. In addition, the organic reactions on solid supported reagents have been developed in organic synthesis because of their ease of handling, enhanced reaction rates, greater selectivity, simple workup, and recoverability of catalysts.[1-3]

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 occur very widely in nature and are essential to life. Among a large variety of heterocyclic compounds, heterocycles containing the phthalazine moiety are of interest because they show some pharmacological and biological activities.[4] Phthalazine derivatives were reported to possess anticonvulsant,[5] cardiotonic,[6] and vasorelaxant[7] activities.

Recently the synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-triones has been reported by Bazgir *et al* using *p*-TSA as expensive and non recyclable catalyst.[8] In continuation of our interest in heterogeneous catalysts as well as solvent-free organic reactions,[3] a simple, new, and efficient protocol for the preparation of 2*H*-indazolo[2,1-*b*]phthalazine-trione derivatives using a catalytic amount of recyclable PPA–SiO_2 under solvent-free conditions is described (Scheme 1).



Scheme 1

PPA–SiO_2 is safe, easy to handle, environmentally benign with fewer disposals problems. PPA–SiO_2 was prepared from the reaction of silica gel with poly phosphoric acid.[9a] PPA-SiO_2 has been used in some organic reactions, such as: conversion of carbonyl compounds into oxathioacetals and dithioacetals,[9a] synthesis of amidoalkyl naphthols,[9b] one-pot Knoevenagel condensation, Michael addition and cyclo-dehydration of dimedone and aldehydes.[9c]

Results and Discussions

To choose optimum conditions, first, the effect of temperature on the rate of the reaction was studied for the preparation of 2,2-dimethyl-13-phenyl-2,3-dihydro-1*H*-indazolo[2,1-b]phthalazine-4,6,11(13*H*)-trione from the three-component condensation reaction of phthalhydrazide, dimedone, and benzaldehyde under solvent-free conditions (Table 1). At 80 °C, the reaction proceeded smoothly and almost complete conversion of product was observed. Further increase in temperature to, 100 and 120 °C increased the rate of reaction. Therefore, we kept the reaction temperature as 100 °C (giving short reaction time and high yield).

Next, the study set out to determine optimal amount of PPA–SiO_2, the reaction was carried out by varying amount of the catalyst (Table 1). Maximum yield was obtained with 0.1 g (0.05 mmol H^+)[9] of the catalyst. Further increase in amount of PPA–SiO_2 in the mentioned reaction did not has any significant effect on the product yield.

Table 1. Optimization amount of PPA-SiO_2 (0.1 g, 0.05 mmol H^+)[9] and reaction temperature for preparation 2,2-dimethyl-13-phenyl-2,3-dihydro-1*H*-indazolo[2,1-*b*]phthalazine-4,6,11(13*H*)-trione under solvent-free conditions[b]

Entry	Catalyst (g, mmol)	Temperature (°C)	Time (min)	Yield (%)[a]
1	0.12 g, 0.06 mmol	100	8	91
2	0.10 g, 0.05 mmol	100	8	92
3	0.08 g, 0.04 mmol	100	11	88
4	0.06 g, 0.03 mmol	100	12	80
5	0.04 g, 0.02 mmol	100	13	77
6	0.02 g, 0.01 mmol	100	23	75
7	0.10 g, 0.05 mmol	120	5	90
8	0.10 g, 0.05 mmol	80	10	83

[a] Yields refer to the isolated pure product

[b] The molar ratio of phthalhydrazide, dimedone, and benzaldehyde was chosen 1/1/1.2.

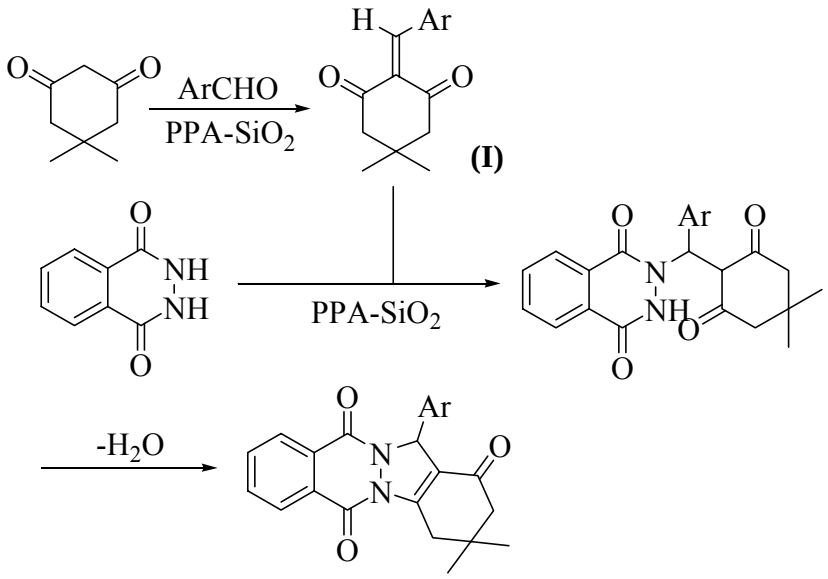
The generality of this reaction was examined using several types of aldehydes. In all cases, the reactions gave the corresponding products in good to excellent yield (Table 2). This methodology offers significant improvements with regard to the scope of this transformation, simplicity in operation and green aspects by avoiding expensive or corrosive catalysts. We also have prepared 5 new analogues of this class of compounds in high yields (Table 2, Entries 9-13).

Table 2. Preparation of 2*H*-indazolo[2,1-*b*]phthalazine-trione derivatives using PPA–SiO_2 as catalyst under solvent-free conditions

Entry	Aldehyde	Time (min)	Yield (%)[a]	M.p. / Lit. m.p.(^oC)[Ref]
1	Benzaldehyde	8	92	207-209 / 204-206[8]
2	4-Chlorobenzaldehyde	6	93	259-261 / 262-264[8]
3	4-Bromobenzaldehyde	8	86	258-260 / 265-267[8]
4	4-Fluorobenzaldehyde	12	82	224-226 / 217-219[8]
5	4-Nitrobenzaldehyde	8	89	217-219 / 223-225[8]
6	2-Chlorobenzaldehyde	12	81	264-266 / 264-266[8]
7	3-Nitrobenzaldehyde	13	86	270-272 / 270-272[8]
8	4-Methylbenzaldehyde	12	79	226-228 / 227-229[8]
9	3,4,5-Trimethoxybenzaldehyde	4	90	232-234
10	2-Methylbenzaldehyde	24	87	241-243
11	2,4-Dichlorobenzaldehyde	9	86	219-221
12	3-Chlorobenzaldehyde	16	78	204-206
13	4-Hydroxy-3-methoxybenzaldehyde	10	92	250-252

[a] Yields refer to the isolated pure products. The desired pure products were characterized by comparison of their physical data (melting points, IR, ^1H and ^{13}C NMR) with those of known compounds.[8] The reaction was carried out under thermal solvent-free conditions in an oil bath at 100 ^oC; The molar ratio of aldehyde / phthalhydrazide / dimedone / PPA–SiO_2 is ((12 / 10 / 10 / 0.5 (1 g))

The suggested mechanism of the PPA–SiO_2 catalyzed transformations is shown in Scheme 2. As reported in the literature the Knoevenagel type coupling of arylaldehyde with active methylene compounds such as dimedone give 2-benzylidene-5,5-dimethylcyclohexane-1,3-dione (**I**).[10] Then, the subsequent 1,4-conjugate addition of phthalhydrazide to the intermediate (**I**) followed by cyclization affords the corresponding products.



Scheme 2

The reusability of the catalyst was tested in the synthesis of 2,2-dimethyl-13-phenyl-2,3-dihydro-1*H*-indazolo[2,1-*b*]phthalazine-4,6,11(13*H*)-trione, as shown in Figure 1. The catalyst was recovered after each run, washed three times with acetone, dried in an oven at 100 ^{o}C for 30 min prior to use and tested for its activity in the subsequent run. The catalyst was tested for 5 runs. It was seen that the catalyst displayed very good reusability (Figure 1).

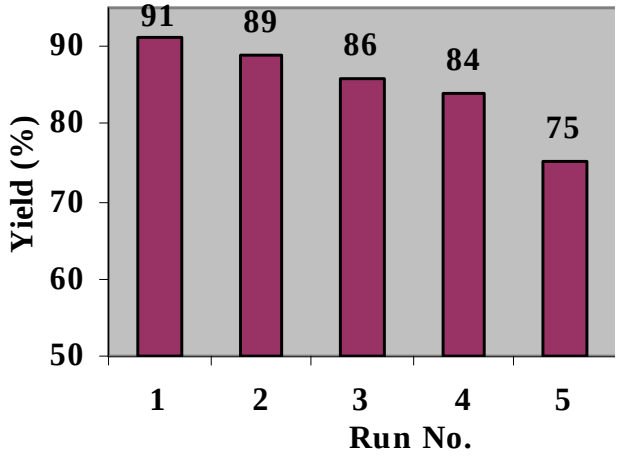


Figure 1. Reusability of the catalyst.

Conclusions

In summary, an efficient protocol for the one-pot preparation of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione derivatives from the three-component condensation reaction of phthalhydrazide, dimedone, and aromatic aldehydes using a commercially available, environmental friendly and

reusable PPA–SiO_2 as catalyst was described. The reactions were carried out under thermal solvent-free conditions with short reaction time and produced the corresponding products in good to excellent yields. Also the catalyst could be successfully recovered and recycled at least for five runs without significant loss in activity. The one-pot nature and the use of heterogeneous solid acid as an eco-friendly catalyst make it an interesting alternative to multi-step approaches. Also, five new analogues of this class of compounds were prepared in high yields.

Experimental Section

General Procedures. All reagents were purchased from Merck and Aldrich and used without further purification. All yields refer to isolated products after purification. PPA-SiO_2 was prepared according to the reported procedure.[9] Products were characterized by comparison of spectroscopic data (IR, ^{1}H NMR, ^{13}C NMR spectra) and melting points with authentic samples. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. The NMR spectra were recorded on a Bruker Avance DPX 300 MHz instrument. The spectra were measured in $CDCl_3$ relative to TMS (0.00 ppm). IR spectra were recorded on a JASCO FT-IR 460plus spectrophotometer. All of the compounds were solid and solid state IR spectra were recorded using the KBr disk technique. Mass spectra were recorded on an Agilent technologies 5973 network mass selective detector (MSD) operating at an ionization potential of 70 eV. Melting points were determined in open capillaries with a BUCHI 510 melting point apparatus. TLC was performed on silica gel polygram SIL G/UV 254 plates.

Typical procedure for the preparation of 3,3-dimethyl-13-phenyl-3,4-dihydro-2*H*-indazolo[1,2-b]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 1)

To a mixture of benzaldehyde (12 mmol), phthalhydrazide (10 mmol) and dimedone (10 mmol), PPA–SiO_2 (1 g, 0.5 mmol of H^+) was added and the mixture was stirred and heated in an oil bath at 100 ^{o}C for appropriate time (Table 2). Completion of the reaction was indicated by TLC (stationary phase: silica gel polygram SIL G/UV 254 plates, and mobile phase: n-hexane / ethyl acetate 80:20). After completion, the reaction mass was cooled to 25 ^{o}C, then the solid residue was dissolved in acetone (40 ml). The catalyst was filtered and reused, the filtrate solution was evaporated. The solid product was purified by recrystallization procedure in aqueous EtOH (25%). [M.p.: 207-209 ^{o}C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.20 (s, 3H), 1.21 (s, 3H), 2.34 (s, 2H), 3.27 (dd, *J* = 1.7, 18.5 Hz, 1H), 3.44 (d, *J* = 18.6 Hz, 1H), 6.47 (s, 1H), 7.31-8.36 (m, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.4, 28.6, 34.6, 38.1, 50.8, 64.8, 118.7, 127.2, 127.6, 127.9, 128.6, 128.9, 129.3, 133.7, 134.6, 136.3, 150.8, 154.4, 156.2, 192.3 ppm; IR (KBr, cm^{-1}): 3027, 2959, 1662, 1618, 1469, 1421, 1360, 1306, 1273, 1145, 1074, 1026, 754, 698.

The desired pure 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:

3,3-Dimethyl-13-(4-chlorophenyl)-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 2). [M.p.: 259-261 ^{o}C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.23 (s, 3H), 1.24

(s, 3H), 2.35 (s, 2H), 3.26 (dd, *J* = 1.8, 19.0 Hz, 1H), 3.45 (d, *J* = 19.0 Hz, 1H), 6.45 (s, 1H), 7.31-8.38 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.6, 28.8, 34.6, 38.1, 50.8, 64.4, 118.2, 127.7, 128.2, 128.6, 128.8, 128.9, 129.1, 133.8, 134.4, 134.7, 134.9, 151.2, 154.4, 156.1, 192.1 ppm; IR (KBr, cm^{-1}): 3037, 2958, 1687, 1654, 1623, 1467, 1390, 1362, 1311, 1268, 1147, 1013, 840, 794, 697.

3,3-Dimethyl-13-(4-bromophenyl)-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 3). [M.p.: 258-260 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 3H), 1.22 (s, 3H), 2.35 (s, 2H), 3.25 (dd, *J* = 1.8, 19.1 Hz, 1H), 3.42 (d, *J* = 19.1 Hz, 1H), 6.43 (s, 1H), 7.30-8.37 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.5, 28.7, 34.6, 38.1, 50.8, 64.5, 118.1, 122.8, 127.8, 128.2, 128.8, 128.9, 129.1, 131.9, 133.7, 134.8, 135.5, 151.2, 154.4, 156.1, 192.2 ppm; IR (KBr, cm^{-1}): 2959, 1654, 1623, 1467, 1409, 1389, 1361, 1311, 1267, 1147, 1105, 1010, 839, 789, 702.

3,3-Dimethyl-13-(4-fluorophenyl)-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 4). [M.p.: 224-226 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.20 (s, 3H), 1.21 (s, 3H), 2.34 (s, 2H), 3.24 (dd, *J* = 1.9, 19.0 Hz, 1H), 3.42 (d, *J* = 19.0 Hz, 1H), 6.44 (s, 1H), 7.00-8.34 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.5, 28.8, 34.6, 38.1, 50.9, 64.2, 115.6, 115.9, 118.3, 127.8, 128.0, 128.9, 129.2, 132.2, 133.7, 134.7, 151.2, 154.4, 156.1, 192.3; ppm; IR (KBr, cm^{-1}): 3072, 2960, 2879, 1665, 1628, 1601, 1509, 1468, 1358, 1313, 1268, 1219, 1159, 1026, 850, 798, 701.

3,3-Dimethyl-13-(4-nitrophenyl)-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 5). [M.p.: 217-219 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.22 (s, 3H), 1.24 (s, 3H), 2.33 (s, 2H), 3.25 (dd, *J* = 2.0, 19.1 Hz, 1H), 3.43 (d, *J* = 19.1 Hz, 1H), 6.50 (s, 1H), 7.57-8.42 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.4, 28.7, 34.7, 38.0, 50.8, 64.2, 117.3, 124.1, 127.8, 128.1, 128.3, 128.6, 128.9, 133.9, 134.9, 143.4, 147.9, 151.7, 154.6, 155.9, 192.1; ppm; IR (KBr, cm^{-1}): 3076, 2958, 1694, 1660, 1617, 1522, 1364, 1276, 1144, 1101, 1017, 857, 791, 720.

3,3-Dimethyl-13-(2-chlorophenyl)-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 6). [M.p.: 264-266 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 3H), 1.23 (s, 3H), 2.34 (s, 2H), 3.24 (dd, *J* = 1.9, 19.0 Hz, 1H), 3.42 (d, *J* = 19.0 Hz, 1H), 6.68 (s, 1H), 7.24-8.41 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.3, 28.7, 34.5, 37.9, 50.8, 63.9, 116.6, 127.1, 127.5, 127.9, 128.6, 129.0, 129.8, 130.4, 132.5, 133.0, 133.5, 134.4, 151.8, 154.1, 156.1, 192.0; ppm; IR (KBr, cm^{-1}): 3058, 2957, 2894, 1662, 1631, 1600, 1467, 1358, 1269, 1150, 1104, 1051, 759, 700.

3,3-Dimethyl-13-(3-nitrophenyl)-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 7). [M.p.: 270-272 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.18 (s, 3H), 1.19 (s, 3H), 2.28 (s, 2H), 3.22 (dd, *J* = 2.0, 19.1 Hz, 1H), 3.35 (d, *J* = 19.1 Hz, 1H), 6.48 (s, 1H), 7.59-8.35 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.4, 28.9, 34.7, 38.3, 51.6, 64.3, 116.9, 127.4, 127.4, 128.5, 128.8, 129.3, 129.9, 131.5, 132.6, 133.0, 133.5, 134.4, 135.5, 151.7, 154.3, 156.4, 192.1; ppm; IR (KBr, cm^{-1}): 3075, 2956, 1671, 1658, 1613, 1358, 1270, 1149, 1104, 1051, 721.

3,3-Dimethyl-13-(4-methylphenyl)-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 8). [M.p.: 226-228 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.22 (s, 3H), 1.23 (s, 3H), 2.31 (s, 3H), 2.36 (s, 2H), 3.24 (dd, *J* = 1.6, 18.7 Hz, 1H), 3.42 (d, *J* = 18.7 Hz, 1H), 6.44 (s,

1H), 7.13-8.36 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4, 28.6, 28.9, 34.8, 38.2, 50.9, 64.9, 118.8, 127.2, 127.8, 127.9, 129.0, 129.3, 129.6, 133.5, 133.6, 134.6, 138.6, 150.9, 154.3, 156.2, 192.3; ppm; IR (KBr, cm^{-1}): 2956, 1660, 1629, 1467, 1359, 1312, 1270, 1142, 1078, 1024, 826, 792, 699.

3,3-Dimethyl-13-(3,4,5-trimethoxyphenyl)-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 9). [M.p.: 232-234 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.23 (s, 3H), 1.24 (s, 3H), 2.36 (s, 2H), 3.21 (d, *J* = 19.1 Hz, 1H), 3.46 (d, *J* = 19.4 Hz, 1H), 3.80 (s, 3H), 3.83 (s, 6H), 6.40 (s, 1H), 6.63 (s, 2H), 7.83-8.37 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.1, 29.0, 34.6, 38.1, 51.0, 56.2, 60.7, 65.0, 104.6, 118.3, 127.7, 128.0, 128.9, 129.0, 131.8, 133.6, 134.6, 138.3, 150.9, 153.4, 154.5, 156.1, 192.2 ppm; IR (KBr, cm^{-1}): 2960, 1656, 1628, 1597, 1507, 1466, 1425, 1361, 1313, 1266, 1125, 1000, 701; MS: m/z (%) = 462 (M^+, 38), 296 (22), 295 (100), 239 (7), 104 (10), 76 (8). [Found: C, 67.49; H, 5.65; N, 6.02. $C_{26}H_{26}N_2O_6$ requires C, 67.52; H, 5.67; N, 6.06 %].

3,3-Dimethyl-13-o-tolyl-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 10). [M.p.: 241-243 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.20 (s, 3H), 1.22 (s, 3H), 2.31 (s, 2H), 2.75 (s, 3H), 3.25 (dd, *J* = 1.9, 19.1 Hz, 1H), 3.44 (d, *J* = 19.0 Hz, 1H), 6.63 (s, 1H), 7.01-7.83 (m, 6H), 8.23 (dd, *J* = 3.2, 5.8 Hz, 1H), 8.36 (dd, *J* = 3.2, 5.9 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.3, 28.3, 28.8, 34.7, 38.0, 50.9, 61.3, 119.8, 125.1, 126.4, 127.6, 128.0, 128.4, 129.0, 129.1, 130.8, 133.5, 134.5, 135.1, 137.1, 150.6, 154.0, 156.0, 192.1 ppm; IR (KBr, cm^{-1}): 3045, 2958, 1661, 1602, 1469, 1359, 1313, 1275, 1146, 1101, 1080, 799, 763, 702; 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); [Found: C, 74.57; H, 5.76; N, 7.21 $C_{24}H_{22}N_2O_3$ requires C, 74.59; H, 5.74; N, 7.25 %].

13-(2,4-Dichlorophenyl)-3,3-dimethyl-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 11). [M.p.: 219-221 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 3H), 1.22 (s, 3H), 2.34 (s, 2H), 3.24 (d, *J* = 19.2 Hz, 1H), 3.40 (d, *J* = 19.1 Hz, 1H), 6.64 (s, 1H), 7.26-7.88 (m, 5H), 8.27 (dd, *J* = 3.2, 5.4 Hz, 1H), 8.37 (dd, *J* = 3.3, 5.6 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 28.4, 28.8, 34.6, 38.0, 50.8, 63.6, 127.6, 127.7, 128.1, 128.6, 129.0, 130.4, 131.8, 133.3, 133.7, 134.6, 135.1, 152.1, 154.3, 156.1, 192.1 ppm; IR (KBr, cm^{-1}): 2964, 1660, 1628, 1468, 1391, 1351, 1312, 1267, 1146, 1101, 832, 701; MS: m/z (%) = 440 (14), 405 (19), 383 (11), 296 (31), 295 (100), 104 (22), 76 (20), 55 (6); [Found: C, 62.56; H, 4.10; N, 6.26 $C_{23}H_{18}Cl_2N_2O_3$ requires C, 62.60; H, 4.11; N, 6.35 %].

13-(3-Chlorophenyl)-3,3-dimethyl-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 12). [M.p.: 204-206 °C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.21 (s, 6H), 2.34 (s, 2H), 3.21 (d, *J* = 19.1 Hz, 1H), 3. 41 (d, *J* = 19.1 Hz, 1H), 6.40 (s, 1H), 7.24-7.86 (m, 6H), 8.24-8.37 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.5, 28.6, 34.7, 38.0, 50.9, 64.3, 117.9, 125.8, 127.0, 127.7, 128.1, 128.9, 129.0, 130.0, 133.7, 134.6, 138.5, 151.2, 154.4, 156.0, 192.1 ppm; IR (KBr, cm^{-1}): 3069, 2957, 2872, 1657, 1626, 1578, 1464, 1360, 1310, 1268, 1145, 788, 701, 677; MS: m/z (%) = 406 (M^+, 30), 296 (48), 295 (100), 239 (11), 149 (7), 130 (7), 104 (21), 76 (19), 55 (8), 43 (7). [Found: C, 67.88; H, 4.70; N, 6.86 $C_{23}H_{19}ClN_2O_3$ requires C, 67.90; H, 4.71; N, 6.89 %].

13-(4-Hydroxy-3-methoxyphenyl)-3,3-dimethyl-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione (Table 2, Entry 13). [M.p.: 250-252 ^{o}C] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.23 (s, 6H), 2.36 (s, 2H), 3.23 (d, *J* = 19.0 Hz, 1H), 3. 44 (d, *J* = 18.9 Hz, 1H), 3.91 (s, 3H), 5.33(br, 1H), 6.40 (s, 1H), 6.77-7.07 (m, 3H), 7.86 (s, 2H), 8.27-8.35 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.4, 28.8, 34.6, 38.1, 51.0, 56.0, 64.8, 111.0, 114.6, 118.6, 119.2, 127.7, 128.0, 128.2, 129.0, 129.2, 133.5, 134.5, 146.0, 146.4, 150.7, 156.1, 192.3 ppm; IR (KBr, cm^{-1}): 3408, 2958, 1660, 1600, 1493, 1359, 1270, 1234, 1135, 1030, 790, 627; 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); [Found: C, 68.88; H, 5.31; N, 6.64 $C_{24}H_{22}N_2O_5$ requires C, 68.89; H, 5.30; N, 6.69 %].

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References

1. Clark, J. H.; Rhodes, C. N. *Clean Synthesis Using Porous Inorganic Solid Catalysts and Supported Reagents*, Royal Society of Chemistry: Cambridge, 2000
2. Gerard, V. S.; Notheisz, F. *Heterogeneous Catalysis in Organic Chemistry*, Elsevier: San Diego, Calif, 2000.
3. (a) Shaterian, H. R.; Shahrekipoor, F.; Ghashang, M. *J. Mol. Catal. A: Chem.* **2007**, *272*, 142. (b) Shaterian, H. R.; Hosseinian, A.; Yarahmadi, H.; Ghashang, M. *Lett. Org. Chem.* **2008**, *5*, 290. (c) Shaterian, H. R.; Hosseinian, A.; Ghashang, M. *Can. J. Chem.* **2008**, *86*, 376. (d) Shaterian, H. R. Yarahmadi, H.; Ghashang, M. *Tetrahedron* **2008**, *64*, 1263. (e) Shaterian, H. R.; Yarahmadi, H. *Tetrahedron Lett.* **2008**, *49*, 1297. (f) Shaterian, H. R.; Yarahmadi, H. *ARKIVOC* **2008**, *(ii)*, 105. (g) Shaterian, H. R.; Yarahmadi, H.; Ghashang, M. *ARKIVOC* **2007**, *(xvi)*, 289. (h) Shaterian, H. R.; Ghashang, M.; Mir, N. *ARKIVOC* **2007**, *(xv)*, 1.
4. (a) Al´-Assar, F.; Zelenin, K. N.; Lesiovskaya, E. E.; Bezhan, I. P.; Chakchir, B. A. *Pharm. Chem. J.* **2002**, *36*, 598. (b) Jain, R. P.; Vederas, J. C. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3655. (c) Carling, R. W.; Moore, K. W.; Street, L. J.; Wild, D.; Isted, C.; Leeson, P. D.; Thomas, S.; O'Conner, D.; McKernan, R. M.; Quirk, K.; Cook, S. M.; Atack, J. R.; Waftord, K. A.; Thompson, S. A.; Dawson, G. R.; Ferris, P.; Castro, J. L. *J. Med. Chem.* **2004**, *47*, 1807.
5. Grasso, S.; DeSarro, G.; Micale, N.; Zappala, M.; Puia, G.; Baraldi, M.; Demicheli, C. *J. Med. Chem.* **2000**, *43*, 2851.
6. Nomoto, Y.; Obase, H.; Takai, H.; Teranishi, M.; Nakamura, J.; Kubo, K. *Chem. Pharm. Bull. (Tokyo)* **1990**, *38*, 2179.
7. Watanabe, N.; Kabasawa, Y.; Takase, Y.; Matsukura, M.; Miyazaki, K.; Ishihara, H.; Kodama, K.; Adachi, H. *J. Med. Chem.* **1998**, *41*, 3367.
8. Sayyafi, M.; Seyyedhamzeh, M.; Khavasi, H. R.; Bazgir, A. *Tetrahedron* **2008**, *64*, 2375.

9. For the preparation and some applications of PPA-SiO_2 please see: (a) Aoyama, T.; Takido, T.; Kodomari, M. *Synlett* **2004**, 2307. (b) Shaterian, H. R.; Hosseinian, A.; Ghashang, M. *Synth. Commun.* **2008**, *38*, 3375. (c) Kantevari, S.; Bantu, R.; Nagarapu, L. *J. Mole. Catal. A: Chem.* **2007**, *269*, 53.
10. (a) Kumar, A.; Maurya, R. A. *Tetrahedron* **2007**, *63*, 1946. (b) Kaupp, G.; Naimi-Jamal, M. R.; Schmeyers, J. *Tetrahedron* **2003**, *59*, 3753. (c) Quiroga, J.; Mejía, D.; Insuasty, B.; Abonía, R.; Nogueras, M.; Sánchez, A.; Cobo, J.; Low, J. N. *Tetrahedron* **2001**, *57*, 6947.

