

New applications of phosphoric acid supported on alumina ($\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$) as a reusable heterogeneous catalyst for preparation of 2,3-dihydroquinazoline-4(1*H*)-ones, 2*H*-indazolo[2,1-*b*]phthalazinetriones, and benzo[4,5]imidazo[1,2-*a*]pyrimidines

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Abstract An eco-friendly procedure for synthesis of 2,3-dihydroquinazoline-4(1*H*)-one, 2*H*-indazolo[2,1-*b*]phthalazinetrione, and benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives by three-component reaction, with phosphoric acid supported on alumina as catalyst, is described. Noticeable features of the method are that it is solvent-free, work-up is easy, yields are excellent, and the catalyst is reusable.

Keywords 2,3-Dihydroquinazoline-4(1*H*)-ones · 2*H*-indazolo[2,1-*b*]phthalazinetriones · Benzo[4,5]imidazo[1,2-*a*]pyrimidine · $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$

Introduction

Multi-component reactions (MCRs) are important in combinatorial chemistry because of the ability to synthesize target compounds with greater efficiency and atom economy by generating structural complexity in a single step from three or more reactants [1]. In addition, MCRs have the advantage of simplicity and synthetic efficiency over conventional chemical reactions [1]. MCRs have attracted much attention for construction of heterocyclic “drug-like” libraries [1–4].

2,3-Dihydroquinazoline-4(1*H*)-ones are an important class of heterocyclic compounds with a wide range of biological activity and pharmacological properties [5]. They can also be easily oxidized to their quinazolin-4(3*H*)-one analogues, which also have biological activity [5–7].

Phthalazine derivatives have been reported to have anticonvulsant [8], cardio-tonic [9], and vasorelaxant [10] activity. Dihydropyrimidine derivatives have significant therapeutic and medicinal properties [11–13]. Several marine alkaloids

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containing the dihydropyrimidine structure have interesting biological activity, for example antiviral, antibacterial, and anti-inflammatory [14, 15]. Many functionalized derivatives of dihydropyrimidines have been used as calcium channel blockers, antihypertensive agents and α 1A antagonists [16, 17]. Therefore, preparation of this heterocyclic structure has attracted much attention.

Phosphoric acid supported on alumina was prepared for the first time by Araujo et al. [18], by mixing alumina with phosphoric acid. This heterogeneous catalyst was characterized and catalytic evaluation of oleic acid conversion to biofuels and biolubricant was studied [18]. The best catalytic performance was achieved by use of the highest-surface-area alumina impregnated with H_3PO_4 , a solid which combined high total acidity with a large number of mesopores [18]. By use of ^{31}P NMR data [19], two aspects of the structure of the catalyst were confirmed (Scheme 1):

- 1 different phosphorus and aluminium interactions in bridging structures [19]; and
- 2 linear phosphorus and aluminium bonding [19].

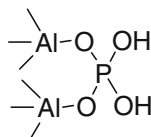
Development of efficient and environmentally benign chemical methods in which heterogeneous recyclable catalysts are used under solvent-free conditions is a major challenge for chemists in organic synthesis [20]. In continuation of our research on solid heterogeneous acidic catalysts [21], we report herein a practical method for synthesis of 2,3-dihydroquinazoline-4(1*H*)-one, 2*H*-indazolo[2,1-*b*]phthalazinetrione, and benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives under thermal solvent-free conditions in the presence of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (50 % w/w) (Schemes 2, 3, 4).

Results and discussion

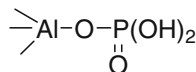
Synthesis of 2,3-dihydroquinazoline-4(1*H*)-ones

To optimize the reaction conditions for preparation of 2,3-dihydroquinazoline-4(1*H*)-ones, we heated isatoic anhydride (1 mmol), aniline (1.1 mmol), and benzaldehyde (1 mmol) at 100 °C in the presence of different amounts of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ as catalyst under solvent-free conditions. It was found that 120 mg catalyst resulted in maximum yield (89 %) in minimum time (33 min). Further increasing the amount of catalyst (150 mg) led to shorter reaction times (1 or 2 min) but with decreasing the yield of the product. Thus, 120 mg catalyst was found to be the optimum quantity and sufficient to promote the reaction. To optimize the reaction temperature we performed this model reaction with $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (120 mg) at

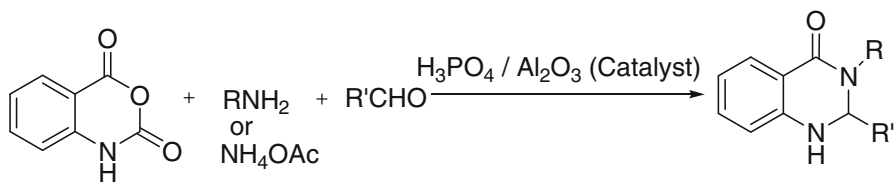
Scheme 1 Structures of phosphoric acid supported on alumina



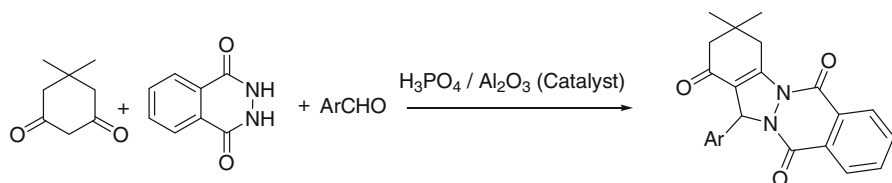
Structure a



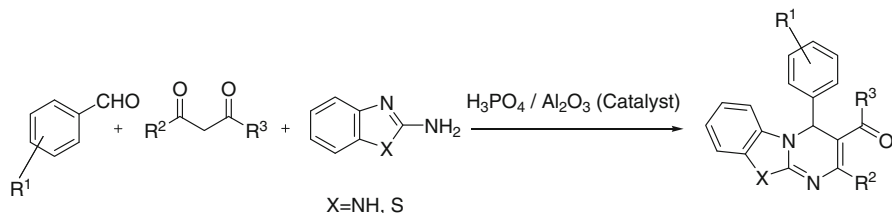
Structure b



Scheme 2 Synthesis of 2,3-dihydroquinazoline-4(1*H*)-ones



Scheme 3 Synthesis of 2*H*-indazolo[2,1-*b*]phthalazinetriones



Scheme 4 Synthesis of benzo[4,5]imidazo[1,2-*a*]pyrimidine

different temperatures under solvent-free conditions. The best results were obtained by use of 120 mg catalyst at 120 °C (Tables 1, 2).

Next, we applied this optimum procedure to a diversity of primary amines or ammonium acetate (as the source of ammonia), aldehydes, and isatoic anhydride. We studied the scope of this reaction for preparation of a variety of 2,3-dihydroquinazolin-4(1*H*)-one derivatives (Table 3). As shown in Table 3, the direct three-component reactions worked well with a variety of aromatic aldehydes

Table 1 Optimization of the amount of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ as catalyst in the reaction of isatoic anhydride (1 mmol), aniline (1.1 mmol), and benzaldehyde (1 mmol) under solvent-free conditions at 100 °C

Entry	Catalyst (mg)	Time (min)	Yield (%) ^a
1	80	60	70
2	100	45	85
3	120	33	89
4	150	31	87

^a Yields refer to the isolated pure products

Table 2 Optimization of the temperature for reaction of isatoic anhydride (1 mmol), aniline (1.1 mmol), and benzaldehyde (1 mmol) in the presence of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (120 mg) as catalyst under solvent-free conditions

Entry	Temperature (°C)	Time (min)	Yield (%) ^a
1	60	52	55
2	80	43	75
3	100	33	89
4	120	30	91
5	150	28	88

^a Yields refer to the isolated pure products

including those bearing electron-withdrawing and electron-donating groups, for example OMe, Cl, Br, and NO_2 , and the desired compounds were obtained in good to high yields (Table 3, Entries 1–31).

We also applied this efficient and environmental friendly approach to the synthesis of heterocyclic 3-(2'-benzothiazolo)-2,3-dihydroquinazolin-4(1*H*)-ones by three-component condensation of 2-aminobenzothiazole, isatoic anhydride, and aromatic or aliphatic aldehydes under thermal solvent-free conditions. The products were obtained in good yields (Scheme 5; Table 3, Entries 9–18).

Three 3-(2'-benzimidazolo)-2,3-dihydroquinazolin-4(1*H*)-one derivatives were synthesized for the first time by three-component condensation reaction of 2-aminobenzimidazole, isatoic anhydride, and aryl aldehydes under the same conditions (Scheme 6; Table 3, Entries 19–21).

If ammonium acetate is used as the source of ammonia (Scheme 2, R = H) in this reaction, 2-aryl-2,3-dihydroquinazolin-4(1*H*)-one derivatives are produced in good to high yields (Table 3, Entries 22–31).

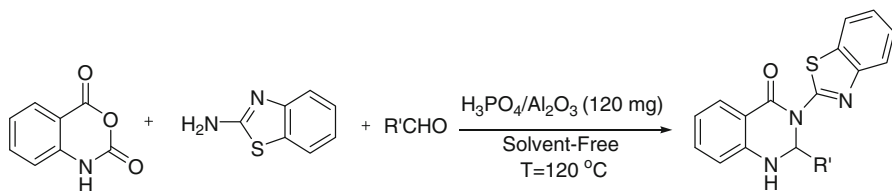
The mechanism suggested for the $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ -catalyzed preparation of 2,3-dihydroquinazoline-4(1*H*)-ones is shown in Scheme 7. According to mechanisms reported in the literature [22, 23, 30], $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ can act as catalyst on isatoic anhydride and produce the reactive intermediate **I**. *N*-Nucleophilic primary amine attack on the carbonyl unit of **I** produces the reactive intermediate **II**, which affords **III** by decarboxylation. Proton transfer by **III** affords the 2-amino-*N*-substituted amide **IV**. Subsequent reaction of the activated aldehyde with **IV** furnishes the imine intermediate **V**. The amide functional group in intermediate **IV** could be formed by tautomerism in the presence of the catalyst. Thus, intermediate **VI** could be prepared by intermolecular nucleophilic attack of the amide nitrogen on the activated imine carbon, and subsequent 1,5-proton transfer yields the final 2,3-dihydroquinazoline-4(1*H*)-ones as products (Scheme 7).

We also investigated recycling of the catalyst under solvent-free conditions, using reaction of isatoic anhydride with aniline and benzaldehyde (Table 3, Entry 1) as a model. After completion of the reaction, the reaction was cooled to room temperature and the crude solid product was dissolved in ethyl acetate. The mixture was filtered for separation of the catalyst. The catalyst was washed with ethyl acetate (2 × 5 mL). The recovered solid catalyst was dried under vacuum and used

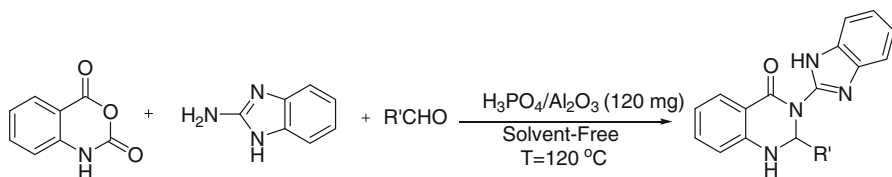
Table 3 Synthesis of 2,3-dihydroquinazoline-4(1*H*)-one derivatives (Scheme 2)

Entry	R (amine)	R' (aldehyde)	Time (min)	Yield (%) ^a	Found m.p. (°C)/(Lit. m.p. (°C)) Ref.
1	Ph	Ph	30	91	214–216/(214–215) [22]
2	Ph	4-NO ₂ C ₆ H ₄	38	89	193–195/(194–196) [23]
3	Ph	4-ClC ₆ H ₄	30	85	213–215/(214–217) [24]
4	Ph	4-MeOC ₆ H ₄	25	90	205–207/(204–205) [23]
5	Ph	4-BrC ₆ H ₄	32	90	219–221/(222–225) [23]
6	4-ClC ₆ H ₄	Ph	38	90	215–218/(216–217) [25]
7	4-MeOC ₆ H ₄	Ph	18	78	208–210/(209–211) [23]
8	4-MeC ₆ H ₄	Ph	30	88	198–205/(196–199) [23]
9	Benzothiazolyl	Ph	14	87	231–234/(233–236) [26]
10	Benzothiazolyl	4-ClC ₆ H ₄	10	82	192–195/(190–193) [26]
11	Benzothiazolyl	4-BrC ₆ H ₄	8	90	228–231/(231–234) [26]
12	Benzothiazolyl	4-MeOC ₆ H ₄	12	93	180–185/(184–186) [26]
13	Benzothiazolyl	2-MeOC ₆ H ₄	16	90	224–231/(225–230) [26]
14	Benzothiazolyl	2-MeC ₆ H ₄	10	88	199–202/(198–200) [26]
15	Benzothiazolyl	CH ₃ (CH ₂) ₅	14	90	146–149/(148–151) [23]
16	Benzothiazolyl	CH ₃ –	12	89	221–223/(215–222) [23]
17	Benzothiazolyl	2,5(MeO) ₂ C ₆ H ₃	8	80	225–226/(Prepared for the first time)
18	Benzothiazolyl	2,3-(Cl) ₂ C ₆ H ₃	7	82	246–248/(Prepared for the first time)
19	Benzoimidazolyl	4-NO ₂ C ₆ H ₄	10	90	>300/(Prepared for the first time)
20	Benzoimidazolyl	2-MeOC ₆ H ₄	9	93	275/(Prepared for the first time)
21	Benzoimidazolyl	2,5-(MeO) ₂ C ₆ H ₃	8	90	235/(Prepared for the first time)
22	H	4-MeOC ₆ H ₄	10	80	193–195/(192–193) [27]
23	H	2,4-(MeO) ₂ C ₆ H ₃	8	83	185–187/(186–187) [22]
24	H	4-NO ₂ C ₆ H ₄	11	87	212–215/(213–214) [22]
25	H	4-MeC ₆ H ₄	9	93	231–234/(233–234) [25]
26	H	4-BrC ₆ H ₄	17	89	202–204/(205–206) [25]
27	H	4-FC ₆ H ₄	15	92	200–202/(199–200) [26, 28]
28	H	3,4-(MeO) ₂ C ₆ H ₃	14	91	210–212/(210–213) [29]
29	H	Ph	9	90	219–222/(221–223) [23]
30	H	4-ClC ₆ H ₄	12	95	206–208/(205/206) [22]
31	H	3-NO ₂ C ₆ H ₄	9	90	214–215/(216–217) [28]

^a Yields refer to the isolated pure products. The desired pure products were characterized by comparison of their physical data (melting points, FT-IR, ¹H NMR and ¹³C NMR) with those of known compounds [22–29]. The reaction was carried out under thermal solvent-free conditions in an oil bath at 100 °C



Scheme 5 Synthesis of heterocyclic 3-(2'-benzothiazolo)-2,3-dihydroquinazolin-4(1*H*)-ones



Scheme 6 Preparation of 3-(2'-benzimidazolo)-2,3-dihydroquinazolin-4(1*H*)-one derivatives

for subsequent catalytic runs. The recovered catalyst was reused five times without any loss of its activity (Fig. 1).

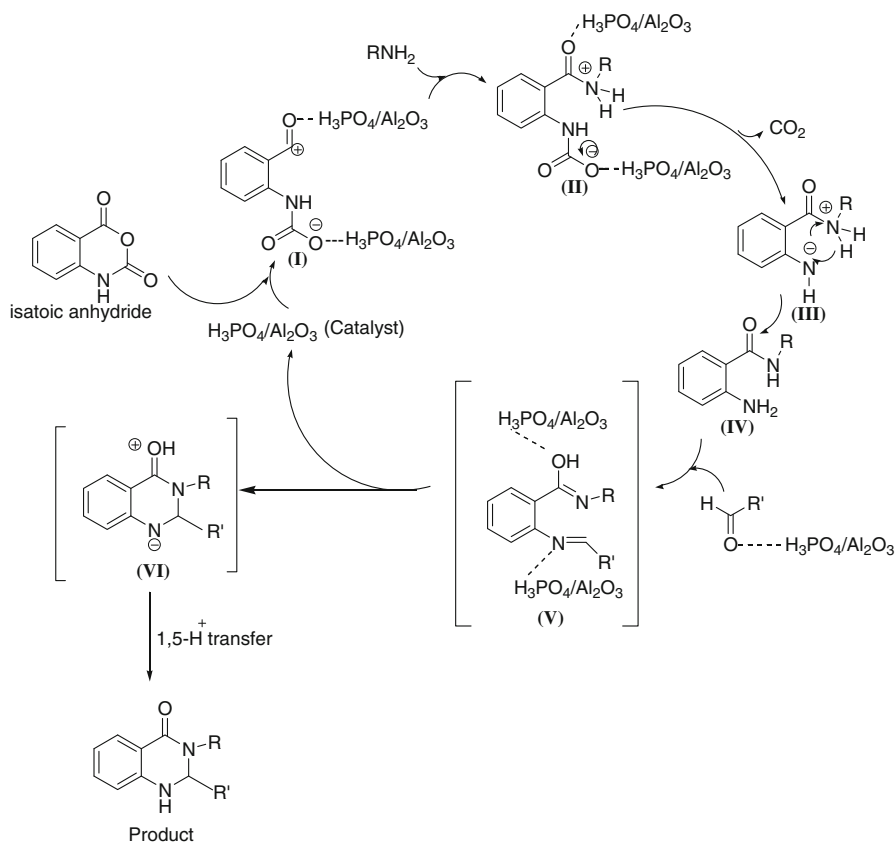
In Table 4 our results from preparation of 2,3-dihydroquinazolin-4(1*H*)-ones are compared with those reported in the literature [22, 24, 25, 30–33]. The table shows that $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ is the most efficient catalyst with regard to reaction times and product yield..

Synthesis of 2*H*-indazolo[2,1-*b*]phthalazinetriones

To optimize the conditions for preparation of 2*H*-indazolo[2,1-*b*]phthalazinetrione derivatives, reaction of benzaldehyde, dimedone, and phthalhydrazide was selected as model system. The reaction was performed at different temperatures (60, 80, 100, 120, and 150 °C) and with different amounts of catalyst (0.08, 0.1, 0.12, and 0.13 g) under solvent-free conditions. The best results were obtained by use of a 1.0:1.0:1.2 molar ratio of dimedone, phthalhydrazide, and aldehyde in the presence of 0.12 g $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ as catalyst at 100 °C under solvent-free conditions (Scheme 3, Tables 5, 6).

Using these optimized reaction conditions, the scope and efficiency of these procedures were investigated for synthesis of a wide variety of substituted 2*H*-indazolo[2,1-*b*]phthalazinetriones. Interestingly, a variety of aryl aldehydes, including *ortho*, *meta*, and *para*-substituted and with electron-donating or electron-withdrawing substituents, participated well in this reaction and gave the 2*H*-indazolo[2,1-*b*]phthalazinetrione derivatives in good to excellent yield (Table 7).

A possible mechanism for formation of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-triones is proposed in Scheme 8. Knoevenagel condensation of dimedone **I** and arylaldehyde **II** forms a heterodiene **III**. Subsequent Michael-type addition of the phthalhydrazide **IV** to the heterodiene **III** followed by cyclization and dehydration affords the corresponding product **VI**.



Scheme 7 Mechanism suggested for $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ catalyzed preparation of 2,3-dihydroquinazoline-4(1*H*)-ones

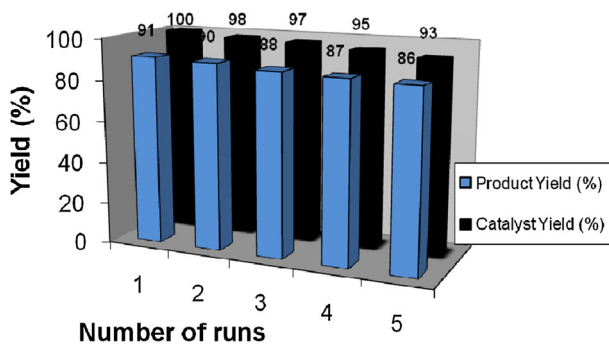


Fig. 1 Results from investigation of the recycling of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ in the synthesis of 2,3-dihydroquinazoline-4(1*H*)-ones

Table 4 Comparison of results obtained by use of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$, $\text{Ga}(\text{OTf})_3$ [22], $\text{KAl}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ (alum) [24], silica sulfuric acid [25], $\text{Al}(\text{H}_2\text{PO}_4)_3$ [30], *p*-TSA [31], Fe_3O_4 nanoparticles [32], copolymer-*P*-TSA [33] as catalysts for synthesis of 2,3-dihydroquinazoline-4(1*H*)-ones

Entry	Catalyst	Conditions	Time (h)	Yield (%) ^a
1	<i>p</i> -TSA (50 mol %)	H_2O	2.5	79
2	$\text{KAl}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ (alum) (200 mg)	EtOH, reflux	4	78
3	$\text{KAl}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O}$ (alum) (200 mg)	H_2O , reflux	1	65
4	$\text{Ga}(\text{OTf})_3$ (1 mol %)	EtOH, reflux	60 min	79
5	Silica sulfuric acid (15 mol.%)	H_2O , 80 °C	4.5	85
6	Silica sulfuric acid (30 mol.%)	EtOH, reflux	6.5	80
7	Silica sulfuric acid (20 mol.%)	Solvent-free, 80 °C	5	80
8	$\text{Al}(\text{H}_2\text{PO}_4)_3$ (16 mol.%)	Solvent-free, 100 °C	35 min	80
9	$\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (120 mg, 50 % w/w)	Solvent-free, 120 °C	30 min	91 (this work)
10	Nano Fe_3O_4 (50 mol.%)	H_2O , reflux	2	80
11	Copolymer- <i>p</i> -TSA (300 mg)	EtOH, reflux	6.5	82

^a Based on the reaction of isatoic anhydride, aniline, and benzaldehyde

Table 5 Optimization of the temperature for reaction of benzaldehyde, dimedone, and phthalhydrazide in the presence of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (0.12 g) as catalyst under solvent-free conditions

Entry	Temperature (°C)	Time(min)	Yield (%) ^a
1	60	3	70
2	80	18	88
3	100	10	93
4	120	9	90
5	150	9	91

^a Yields refer to isolated pure product

Table 6 Optimization of the amount of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ as catalyst for reaction of benzaldehyde, dimedone, and phthalhydrazide under solvent-free conditions at 100 °C

Entry	Catalyst (g)	Time (min)	Yield (%) ^a
1	0.08	25	70
2	0.1	18	88
3	0.12	10	93
4	0.13	9	90

^a Yields refer to isolated pure product

Reusability of catalysts is an important benefit, because of their suitability for commercial application. Thus, recovery and reusability of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ was investigated, with reaction of benzaldehyde, dimedone, and phthalhydrazide as model. In this procedure, after completion of the reaction, the reaction mixture was cooled to room temperature, and the crude solid product was dissolved in ethyl acetate. The mixture was filtered for separation of the catalyst. The catalyst was

Table 7 Preparation of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione derivatives using H₃PO₄-Al₂O₃ as reusable catalyst

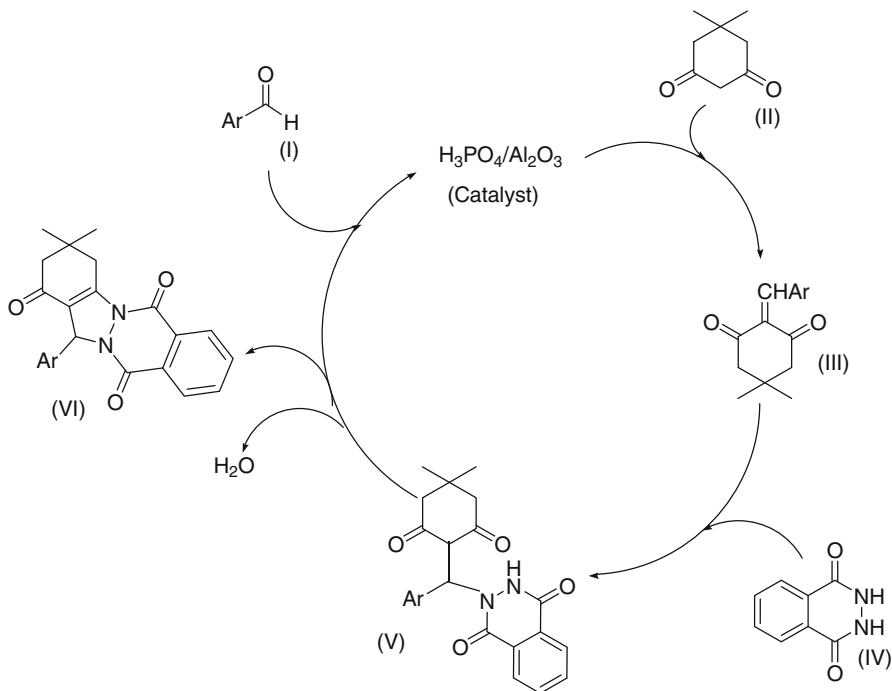
Entry	Aromatic aldehyde	Time (min)	Yield (%) ^a	M.p. (°C) (Lit. m.p. (°C)) [Ref.]
1	Benzaldehyde	10	93	205–207 (207–209) [34] (204–206) [35] (204–206) [36]
2	4-Chlorobenzaldehyde	8	91	260–261 (259–261) [34] (258–260) [35] (262–264) [36]
3	4-Bromobenzaldehyde	10	91	261–263 (258–260) [34] (258–260) [35] (265–267) [36]
4	4-Fluorobenzaldehyde	15	88	220–221 (224–226) [34] (221–223) [35] (217–219) [36]
5	4-Nitrobenzaldehyde	10	85	220–221 (217–219) [34] (216–218) [35] (223–225) [36]
6	2-Chlorobenzaldehyde	14	85	265–267 (264–266) [34] (266–269) [35] (264–266) [36]
7	3-Nitrobenzaldehyde	16	86	270–272 (270–272) [34, 36] (269–271) [35]
8	4-Methylbenzaldehyde	14	80	228–230 (226–228) [34] (226–231) [35] (227–229) [36]
9	3,4,5-Trimethoxybenzaldehyde	8	89	233–235 (232–234) [34] (232–234) [35]
10	2-Methylbenzaldehyde	23	78	240–241 (241–243) [34] (243–245) [35]
11	2,4-Dichlorobenzaldehyde	11	86	217–220 (219–221) [34] (218–220) [35]

Table 7 continued

Entry	Aromatic aldehyde	Time (min)	Yield (%) ^a	M.p. (°C) (Lit. m.p. (°C)) [Ref.]
12	3-Chlorobenzaldehyde	20	76	208–210 (204–206) [34] (207–209) [35]
13	4-Hydroxy-3-methoxybenzaldehyde	15	80	245–247 (250–252) [34] (248–250) [35]
14	4-Methoxybenzaldehyde	10	88	216–217 (218–220) [37]
15	3,4-Dimethoxybenzaldehyde	9	87	206–208 (205–206) [37]

^a Yields refer to isolated pure product. The structures all known products were confirmed by comparison of their melting points and spectral data (FT-IR, ¹H NMR, ¹³C NMR) with those reported in the literature [34–37]

washed with ethyl acetate (2 × 5 ml). The recovered catalyst was dried at 100 °C and used for subsequent catalytic runs. The recovered catalyst was reused five times without any loss of its activity (Fig. 2).



Scheme 8 The suggested mechanism for preparation of 2H-indazolo[2,1-b]phthalazine-1,6,11(13H)-triones

To show the merits of this work we compared results obtained by use of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ with those reported in the literature [35–38] for synthesis of 3,3-dimethyl-13-phenyl-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione by reaction of benzaldehyde, dimedone, and phthalhydrazide. As shown in Table 8, $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ is an effective catalyst with regard to reaction time, amount of the catalyst, and product yield. Thus, this procedure with $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ catalyst is convincingly superior to some catalytic methods reported in the literature (Table 8).

Synthesis of benzo[4,5]imidazo[1,2-*a*]pyrimidines

To prepare benzo[4,5]imidazo[1,2-*a*]pyrimidines more efficiently in minimum time, at low temperature, and with the minimum amount of catalyst, reaction of benzaldehyde (1 mmol), methyl acetoacetate (1 mmol), and 2-aminobenzothiazole (1 mmol) was selected as model system to study the effect of different reaction temperatures (60, 80, 100, 120 and 150 °C) and different amounts of catalyst (0.08, 0.1, 0.12, 0.13, 0.14 g). The best result was obtained by use of a 1.0:1.0:1.0 molar ratio of benzaldehyde, methyl acetoacetate, and 2-aminobenzothiazole in the presence of 120 mg $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ as catalyst at 100 °C under solvent-free conditions (Tables 9, 10).

Using these optimized reaction conditions, the scope and efficiency of the procedure were investigated for synthesis of a wide variety of substituted benzo[4,5]imidazo[1,2-*a*]pyrimidines. Interestingly, a variety of *ortho*, *meta*, and *para*-substituted aryl aldehydes participated well in this reaction and gave the benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives in good to excellent yield (Table 11). Table 11 shows that aromatic aldehydes carrying electron-donating or electron-withdrawing substituents react well under these conditions.

According to the literature [39], the reaction presumably proceeds in two steps. Condensation of aldehyde **1** and the β -dicarbonyl compound **2** by standard Knoevenagel reaction produces 3-benzylidene-2,4-pentanedione **3**. 2-Aminobenzimidazole or 2-aminobenzothiazole **4** then reacts with intermediate **3** by Michael addition and produces intermediate **5**. Cyclization and subsequent dehydration then afford benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives **6** (Scheme 9).

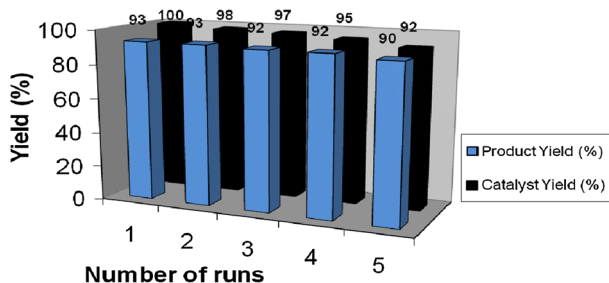


Fig. 2 Results from investigation of the reusability of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ for preparation of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-triones

Table 8 Comparison of results obtained by use of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$, phosphomolybdic acid (PMA)- SiO_2 [38], H_2SO_4 in water-ethanol or ionic liquid [37], *p*-TSA [37], and $\text{Mg}(\text{HSO}_4)_2$ [35] for preparation of 3,3-dimethyl-13-phenyl-3,4-dihydro-2*H*-indazolo[1,2-*b*]phthalazine-1,6,11(13*H*)-trione

Entry	Catalyst	Amount of Catalyst (g)	Time (min)	Yield(%) ^a
1	Phosphomolybdic acid [(PMA)- SiO_2]	1	30	85
2	H_2SO_4 in water-ethanol or ionic liquid	0.015	30	86
3	<i>p</i> -TSA	0.05	10	86
4	$\text{Mg}(\text{HSO}_4)_2$	0.025	10	85
5	$\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$	0.12	10	93 (Present Work)

Table 9 Optimization of temperature in the reaction of benzaldehyde, methyl acetoacetate, and 2-aminobenzothiazole in the presence of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (0.1 g) as catalyst under solvent-free conditions

Entry	Temperature (°C)	Time (min)	Yield (%) ^a
1	60	105	70
2	80	98	85
3	100	90	88
4	120	89	86
5	150	88	85

^a Yields refer to isolated pure product

Table 10 Optimization the amount of $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ as catalyst in the reaction of benzaldehyde, methyl acetoacetate, and 2-aminobenzthiazole under solvent-free conditions at 100 °C

Entry	Catalyst (g)	Time (min)	Yield (%) ^a
1	0.08	95	78
2	0.1	90	88
3	0.12	80	94
4	0.15	78	90

^a Yields refer to isolated pure product

In Table 12 the results obtained in this work are compared with those reported in the literature for use of TMGT [39], and sulfamic acid [40]. The table shows that $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (50 % *w/w*) is the most efficient catalyst for preparation of 4*H*-pyrimido[2,1-*b*]benzazoles with regard to reaction time, temperature, and yield. The catalyst is also widely applicable (Table 12).

We also investigated recycling of the catalyst under solvent-free conditions for reaction of benzaldehyde, ethyl acetoacetate, and 2-aminobenzimidazole as model. After completion of the reaction, the mixture was cooled to room temperature and

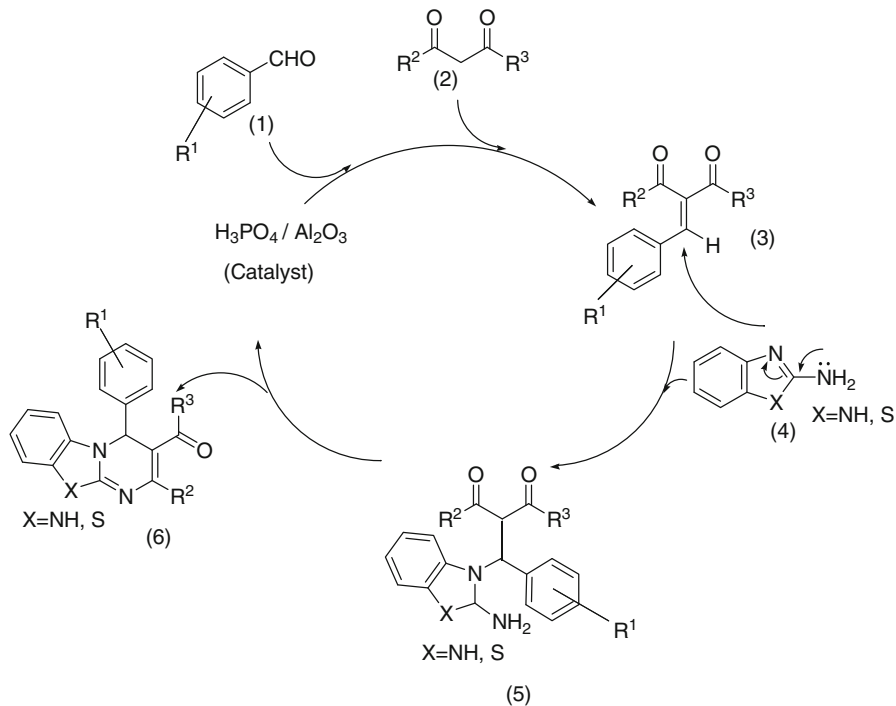
Table 11 One-pot synthesis of benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives by condensation of aldehydes, β -dicarbonyl compounds, and 2-aminobenzimidazole or 2-aminobenzothiazole in the presence of $H_3PO_4-Al_2O_3$ as catalyst at 100 °C

Entry	R ¹	R ²	R ³	X	Time (min)	Yield (%) ^a	Found m.p. (°C) (Lit. m.p. (°C)) [Ref.]
1	C ₆ H ₅	OMe	Me	S	80	94	140–142 (143–145) [39]
2	4-MeOC ₆ H ₄	OMe	Me	S	80	90	153–155 (150–153) [39]
3	4-NO ₂ C ₆ H ₄	OMe	Me	S	80	89	86–88 (78–81) [39]
4	C ₆ H ₅	OEt	Me	S	95	92	173–175 (173–175) [39]
5	4-MeOC ₆ H ₄	OEt	Me	S	80	90	145–147 (140–143) [39]
6	4-BrC ₆ H ₄	OEt	Me	S	90	91	114–116 (110–114) [39]
7	4-O ₂ NC ₆ H ₄	OEt	Me	S	95	88	150–152 (150–152) [39]
8	C ₆ H ₅	OEt	Ph	S	90	87	77–80 (84–86) [39]
9	4-O ₂ NC ₆ H ₄	OEt	Ph	S	95	89	160 dec (158 dec) [39]
10	3-O ₂ NC ₆ H ₄	OMe	Me	S	72	79	>300 (The product was synthesized for the first time)
11	C ₆ H ₅	OEt	Me	N	85	90	275 (>260) [39]
12	3-ClC ₆ H ₄	OEt	Me	N	62	89	>300 (The product was synthesized for the first time)
13	4-MeOC ₆ H ₄	OEt	Me	N	84	82	250–253 (256–258) [39]
14	4-O ₂ NC ₆ H ₄	OEt	Me	N	90	87	228 dec (225 dec) [39]
15	4-MeOC ₆ H ₄	OEt	Ph	N	95	82	200–202 (117–120) [39]
16	4-O ₂ NC ₆ H ₄	OEt	Ph	N	85	88	250 dec (248 dec) [39]
17	4-FC ₆ H ₄	OEt	Me	N	90	80	>300 (>300) [39]
18	4-ClC ₆ H ₄	OEt	Me	N	95	82	>300 (>300) [40]
19	4-BrC ₆ H ₄	OEt	Me	N	75	89	>300 (>300) [40]
20	4-MeOC ₆ H ₄	OEt	Me	N	85	85	280–282 (272–273) [40]
21	4-O ₂ NC ₆ H ₄	OEt	Me	N	90	81	>300 (>300) [40]
22	3-O ₂ NC ₆ H ₄	OEt	Me	N	85	90	297–299 (294–296) [40]
23	C ₆ H ₅	OEt	Me	N	95	95	295–297 (294–296) [40]
24	2,4-Cl ₂ C ₆ H ₃	OEt	Me	N	100	88	>300 (>300) [40]
25	2-ClC ₆ H ₄	OEt	Me	N	80	88	>300 (>300) [40]
26	C ₆ H ₅	Me	Me	N	95	90	>300 (>300) [41]
27	4-FC ₆ H ₄	Me	Me	N	90	90	>300 (>300) [41]
28	4-ClC ₆ H ₄	Me	Me	N	80	89	>300 (>300) [41]
29	4-BrC ₆ H ₄	Me	Me	N	85	94	>300 (>300) [41]
30	4-O ₂ NC ₆ H ₄	Me	Me	N	80	93	>300 (>300) [41]
31	4-MeC ₆ H ₄	Me	Me	N	85	94	277–278 (279–281) [41]
32	3-O ₂ NC ₆ H ₄	Me	Me	N	80	90	>300 (290–292) [41]
33	2,4-Cl ₂ C ₆ H ₃	Me	Me	N	90	89	>300 (>300) [41]
34	2-ClC ₆ H ₄	Me	Me	N	85	87	>300 (>300) [41]
35	4-O ₂ NC ₆ H ₄	OMe	Me	N	80	94	278–279 (281–283.6) [41]
36	3-O ₂ NC ₆ H ₄	OMe	Me	N	44	85	255–257 (267.5–269.5) [40]
37	2,4-Cl ₂ C ₆ H ₃	OMe	Me	N	80	93	280–281 (279.2) [40]
38	4-BrC ₆ H ₄	OMe	Me	N	85	88	263–264 (263–265) [40]

Table 11 continued

Entry	R ¹	R ²	R ³	X	Time (min)	Yield (%) ^a	Found m.p. (°C) (Lit. m.p. (°C)) [Ref.]
39	3,4-(MeO) ₂ C ₆ H ₃	OMe	Me	N	12	76	257–259 (258–261) [40]
40	3-FC ₆ H ₄	OMe	Me	N	80	92	242–244 (247.1–249) [40]

^a Yields refer to the isolated pure products. The desired pure products were characterized by comparison of their physical data (melting points, FT-IR, ¹H and ¹³C NMR) with those of known compounds [39–41]

**Scheme 9** Mechanism suggested for preparation of benzo[4,5]imidazo[1,2-a]pyrimidine derivatives**Table 12** Comparison of results obtained by use of H₃PO₄–Al₂O₃, TMGT, and sulfamic acid in the synthesis of benzo[4,5]imidazo[1,2-a]pyrimidine derivatives

Entry	Catalyst	Amount of catalyst (g)	Conditions	Time	Yield (%)
1	TMGT	0.08	100 °C	5 h	73
2	Sulfamic acid	0.01	85 °C, Solvent-free	8 h	88
3	H ₃ PO ₄ –Al ₂ O ₃ (50 % w/w)	0.12	100 °C, Solvent-free	85 min	95 (this work)

^a Based on the reaction of benzaldehyde, ethyl acetoacetate, and 2-aminobenzimidazole

the crude solid product was dissolved in ethyl acetate. The mixture was filtered for separation of the catalyst. The catalyst was washed with ethyl acetate (4×5 mL) and the recovered catalyst was then dried in an oven at $100\text{ }^{\circ}\text{C}$ for 3 h. The recovered catalyst was then used for subsequent catalytic runs. It was reused five times without any loss of its activity (Fig. 3).

Conclusion

We have developed a green and straightforward procedure for synthesis of 2,3-dihydroquinazoline-4(1*H*)-one, 2*H*-indazolo[2,1-*b*]phthalazinetrione, and benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives using $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ as reusable catalyst under solvent-free conditions. These procedures have several advantages, including cleaner reactions, easier work-up, reduced reaction times, and eco-friendly strategy.

Experimental

General

All reagents were purchased from Merck and Aldrich and used without further purification. $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (50 % w/w) was prepared in accordance with a procedure reported elsewhere [41]. All yields refer to isolated products after purification. Products were characterized by comparison of spectroscopic data (FT-IR, ^1H NMR, ^{13}C NMR spectra) and melting points with those of authentic samples. NMR spectra were recorded on a Bruker Avance DEX 500 MHz instrument. The spectra were measured in CDCl_3 relative to TMS (0.00 ppm). IR spectra were recorded on a Jasco FT-IR 460 plus spectrophotometer. Melting points were determined in open capillaries with a Buchi 510 melting point apparatus. TLC was performed on Polygram SIL G/UV 254 silica gel plates.

General procedure for preparation of 2,3-dihydroquinazoline-4(1*H*)-one derivatives

A stirred mixture of isatoic anhydride (1 mmol), primary amine (1.1 mmol) or ammonium acetate (1.2 mmol), aldehyde (1 mmol) and $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (120 mg, 50 w/w %) was reacted in an oil bath at $120\text{ }^{\circ}\text{C}$ for the appropriate time. After completion of the reaction (monitored by TLC) the mixture was cooled to room temperature and the crude solid product was dissolved in ethyl acetate and filtered for separation of the catalyst. The organic filtrate solution was concentrated. The solid crude product was purified by recrystallization from aqueous EtOH (70 %). All the products were characterized by comparison of their spectroscopic and physical data with those of authentic samples [22–29]. Spectral data of unknown products are given below.

3-(Benzo[d]thiazol-2-yl)-2-(2,5-dimethoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (Table 3, Entry 17)

m.p.: 225–226 °C, IR (KBr) ν/cm^{-1} : 3383, 1671, 1612, 1503, 1439, 1303, 1284, 1237, 753; ^1H NMR (500 MHz, DMSO- d_6): δ (ppm): 8.00 (1H, d, $J = 7.8$ Hz), 7.85 (1H, d, $J = 8.1$ Hz), 7.72 (2H, d, $J = 8.1$ Hz), 7.59 (1H, d, $J = 3.3$ Hz), 7.40 (1H, t, $J = 7.4$ Hz), 7.33 (2H, q, $J = 7.5$ Hz), 6.99 (1H, d, $J = 8.8$ Hz), 6.86 (1H, d, $J = 8.2$ Hz), 6.79–6.76 (2H, m), 6.32 (1H, s), 3.87 (3H, s), 3.49 (3H, s); ^{13}C NMR (125 MHz, DMSO- d_6): δ (ppm): 162.0, 156.9, 152.4, 150.5, 147.5, 146.5, 135.3, 132.5, 128.0, 127.9, 126.1, 124.0, 121.5, 120.9, 118.0, 115.4, 112.7, 112.6, 112.5, 112.4, 65.1, 56.2, 55.0; MS (EI, 70 eV) m/z (%): 43 (23), 57 (24), 69 (32), 77 (19), 105 (18), 132 (32), 149 (21), 210 (25), 238 (17), 268 (80), 283 (100), 417 (79); Anal. Calcd. for: $\text{C}_{23}\text{H}_{19}\text{N}_3\text{O}_3\text{S}$: C, 66.17; H, 4.59; N, 10.07 %. Found: C, 66.16; H, 4.60; N, 10.05 %.

3-(Benzo[d]thiazol-2-yl)-2-(2,3-dichlorophenyl)-2,3-dihydroquinazolin-4(1H)-one (Table 3, Entry 18)

m.p.: 246–248 °C, IR (KBr) ν/cm^{-1} : 3378, 3065, 1639, 1619, 1513, 1432, 1389, 1243, 753, 738; ^1H NMR (500 MHz, DMSO- d_6): δ (ppm): 8.14 (1H, s), 7.99 (1H, d, $J = 6.9$ Hz), 7.92 (1H, s), 7.38 (2H, d, $J = 7.0$ Hz), 7.73–7.68 (2H, m), 7.53 (1H, d, $J = 7.2$ Hz), 7.38 (2H, s), 7.31 (1H, s), 7.18 (1H, d, $J = 7.2$ Hz), 7.04 (1H, d, $J = 6.9$ Hz), 6.88–6.84 (2H, m); ^{13}C NMR (125 MHz, DMSO- d_6): δ (ppm): 161.5, 156.7, 147.3, 145.2, 139.1, 135.6, 132.9, 132.5, 130.6, 129.6, 128.3, 128.2, 126.2, 124.1, 124.0, 121.6, 121.0, 118.7, 115.9, 112.7, 66.8; MS (EI, 70 eV) m/z (%): 43 (16), 57 (21), 77 (36), 105 (25), 130 (19), 186 (24), 211 (20), 254 (17), 276 (89), 291 (100), 390 (17), 425 (20); Anal. Calcd. for: $\text{C}_{21}\text{H}_{13}\text{Cl}_2\text{N}_3\text{OS}$: C, 59.16; H, 3.07; N, 9.86 %. Found: C, 59.20; H, 3.10; N, 9.92 %.

3-(1H-benzo[d]imidazol-2-yl)-2,3-dihydro-2-(4-nitrophenyl) quinazolin-4(1H)-one (Table 3, Entry 19)

m.p.: > 300 °C, IR (KBr) ν/cm^{-1} : 3360, 3209, 3078, 1685, 1613, 1518, 1343, 1243, 1160, 1107, 998; ^1H NMR (500 MHz, DMSO- d_6): δ (ppm): 12.6 (1H, s), 8.34 (1H, d, $J = 5.4$ Hz), 8.17 (2H, d, $J = 8.5$ Hz), 7.79 (1H, d, $J = 7.7$ Hz), 7.59–7.55 (3H, m), 7.45–7.36 (3H, m), 7.16–7.10 (2H, m), 6.94 (1H, d, $J = 7.9$ Hz), 6.81 (1H, t, $J = 7.9$); ^{13}C NMR (125 MHz, DMSO- d_6): δ (ppm): 161.0, 150.4, 148.6, 147.2, 145.7, 138.9(2C), 133.0, 128.3, 127.8(2C), 123.7(2C), 123.3(2C), 117.5, 115.2(2C), 115.0, 113.8, 72.9; MS (EI, 70 eV) m/z (%): 43 (27), 57 (31), 77 (37), 105 (37), 119 (39), 152 (21), 178 (28), 194 (26), 207 (88), 220 (95), 236 (47), 253 (100), 268 (32), 385 (94); Anal. Calcd. for: $\text{C}_{21}\text{H}_{15}\text{N}_5\text{O}_3$: C, 65.45; H, 3.92; N, 18.17 %. Found: C, 65.59; H, 3.76; N, 18.21 %.

3-(1H-benzo[d]imidazol-2-yl) -2-(2-methoxyphenyl) -2,3-dihydroquinazolin-4(1H)-one (Table 3, Entry 20)

m.p.: 275 °C, IR (KBr) ν/cm^{-1} : 3383, 3205, 3208, 2923, 2836, 1669, 1614, 1538, 1494, 1450, 1385, 1278, 1240, 1109, 1020, 747; ^1H NMR (500 MHz, DMSO- d_6): δ

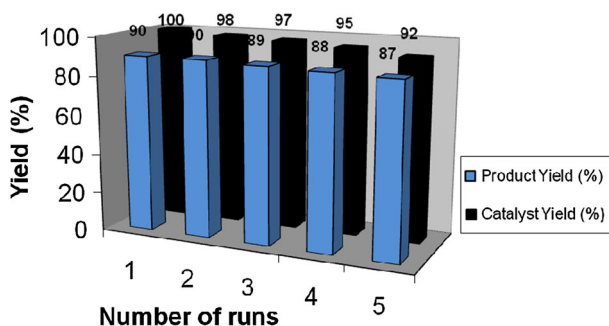


Fig. 3 Results from investigation of recycling of the catalyst in the preparation of benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives

(ppm): 12.54 (1H, s), 7.86 (1H, d, $J = 7.8$ Hz), 7.53 (2H, d, $J = 8.1$ Hz), 7.44 (1H, d, $J = 3.4$ Hz), 7.39 (1H, d, $J = 7.5$ Hz), 7.29 (1H, t, $J = 7.6$ Hz), 7.22 (1H, t, $J = 7.7$ Hz), 7.11–7.05 (3H, m), 6.89 (1H, d, $J = 7.4$ Hz), 6.83 (1H, d, $J = 8.1$ Hz), 6.74 (2H, q, $J = 7.2$ Hz), 3.93 (3H, s); ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) δ (ppm): 162.6, 156.4, 146.5(2C), 139.7, 134.8, 133.0, 129.5, 127.9, 127.2, 125.0, 121.3(2C), 119.6, 117.7, 117.2, 115.3, 113.5, 111.7, 111.4, 64.6, 55.7; MS (EI, 70 eV) m/z (%): 77 (27), 105 (24), 132 (41), 167 (23), 194 (25), 209 (20), 220 (88), 236 (93), 253 (76), 339 (42), 370 (100); Anal. Calcd. for: $\text{C}_{22}\text{H}_{18}\text{N}_4\text{O}_2$: C, 71.34; H, 4.90; N, 15.13 %. Found: C, 71.30; H, 4.61; N, 15.10 %.

3-(1H-benzo[d]imidazol-2-yl)-2-(2,5-dimethoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (Table 3, Entry 21)

m.p.: 235 °C, IR (KBr) ν/cm^{-1} : 3353, 3150, 2928, 1657, 1612, 1533, 1499, 1447, 1388, 1292, 1226, 1048, 1024; ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ (ppm): 12.55 (1H, s), 7.86 (1H, d, $J = 7.6$ Hz), 7.53 (2H, d, $J = 7.5$ Hz), 7.39 (2H, s), 7.30 (1H, t, $J = 7.5$ Hz), 7.12–7.06 (2H, m), 6.97 (1H, d, $J = 8.8$ Hz), 6.84 (1H, d, $J = 8.1$ Hz), 6.77 (2H, q, $J = 6.8$ Hz), 6.43 (1H, s), 3.87 (3H, s), 3.50 (3H, s); ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) δ (ppm): 162.5, 152.3, 150.4, 146.5, 139.7, 134.8, 133.0, 128.4, 127.8, 121.3(2C), 117.8, 117.2(2C), 115.3, 113.5, 112.9, 112.2, 112.1, 111.7, 64.5, 56.1, 55.1; MS (EI, 70 eV) m/z (%): 77 (27), 105 (34), 132 (42), 194 (25), 210 (30), 220 (79), 236 (31), 250 (42), 268 (39), 283 (48), 341 (16), 369 (100), 400 (38); Anal. Calcd. for: $\text{C}_{23}\text{H}_{20}\text{N}_4\text{O}_3$: C, 68.99; H, 5.03; N, 13.99 %. Found: C, 69.01; H, 5.02; N, 13.89 %.

General procedure for preparation of 2*H*-indazolo[2,1-*b*]phthalazinetrione derivatives

A mixture of phthalhydrazide (10 mmol), dimedone (10 mmol), aldehyde (12 mmol), and $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ (0.1 g, 50 % w/w) was heated at 100 °C in an oil bath for the appropriate time (Table 3). After completion (monitored by TLC) the reaction mass was cooled to 25 °C then the solid residue was dissolved in ethyl

acetate. The catalyst was washed with (2×5 ml) ethyl acetate. The recovered catalyst was dried at 100 °C. The filtrate solution was evaporated and the solid crude product was purified by recrystallization from aqueous EtOH (25 %) to obtain the pure products. The compounds were characterized by comparison of their physical and spectral data with those reported in the literature [34–37]. Selected spectral data for one product are given below.

3,3-Dimethyl-13-(4-chlorophenyl)-3,4-dihydro-2H-indazolo[1,2-b]phthalazine-1,6,11(13H)-trione (Table 7, Entry 2)

m.p.: 259–261 °C ^1H NMR (500 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 (125 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.

General procedure for preparation of benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives

A stirred mixture of aldehyde (1 mmol), β -dicarbonyl compound (1 mmol), 2-aminobenzimidazole or 2-aminobenzothiazole (1 mmol), and $\text{H}_3\text{PO}_4\text{-Al}_2\text{O}_3$ as catalyst (0.12 g, 50 % w/w) was reacted in an oil bath at 120 °C for the appropriate time. On completion of the reaction (indicated by TLC) the mixture was cooled to room temperature. The crude solid product was dissolved in ethyl acetate, and filtered for separation of the catalyst. The organic filtrate solution was concentrated. The solid product was purified by recrystallization from aqueous EtOH (96 %). The authenticity of the products was established by comparing their melting points and FT-IR, ^{13}C NMR, and ^1H NMR spectra with those of known compounds [39–41]. The spectral data for the unknown compounds (Table 11, Entries 10 and 12) are given below.

*Methyl-2-methyl-4-(4-methoxyphenyl)-4H-primido[2,1-*b*][1,3]benzothiazole-3-carboxylate (Table 11, Entry 10)*

IR (KBr) (ν): 3415, 3064, 2921, 1702, 1596, 1510, 1432, 1384, 1242, 1081, 738 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 2.49 (s, 3H), 3.76 (s, 3H), 6.57 (s, 1H), 7.08 (d, J = 8.1 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.31–7.28 (m, 1H), 7.53–7.47(m, 2H), 7.77 (d, J = 7.7 Hz, 1H), 8.11 (ddd, J = 10.0 Hz, J = 2.0 Hz, J = 0.9 Hz) 8.31 (t, J = 1.93 Hz, 1H) ppm; ^{13}C NMR (125 MHz, CDCl_3): δ = 23.7, 51.3, 57.2, 102.0, 111.4, 121.9, 122.5, 123.4, 123.9, 124.5, 126.9, 130.0, 132.9, 137.4, 143.2, 148.3, 155.8, 163.6, 166.6 ppm; MS (EI, 70 eV) m/z (%): 381(27), 322(7.4), 259(100), 199(16), 175(6), 134(5); Anal. Calcd for $\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}_4\text{S}$: C, 59.83; H, 3.96; N, 11.02 %; Found: C, 59.66; H, 3.79; N, 10.98 %.

*Ethyl-2-methyl-4-(3-chlorophenyl)-4,10-dihydropyrimido
[1,2-a][1,3]benzimidazole-3-carboxylate: (Table 11, Entry 12)*

IR (KBr) (ν): 3235, 3102, 3025, 2980, 2927, 2853, 1655, 1572, 1515, 1284, 1111, 1013, 835, 730 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ = 1.31 (t, J = 7.10 Hz, 3H), 2.79 (s, 3H), 4.20 (m, 2H), 6.46 (s, 1H), 7.15 (m, 2H), 7.22 (t, J = 7.0 Hz, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.56 (d, J = 7.95 Hz, 1H), 10.4 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ = 14.2, 19.5, 56.3, 60.0, 98.9, 109.6, 116.4, 120.8, 121.1, 122.7, 123.5, 128.7 (2C), 131.3, 133.8, 139.9, 141.0, 146.2, 146.5, 165.7 ppm; MS (EI, 70 eV) m/z (%): 367(50), 338(29), 294(21), 256(100), 228(38), 182(14), 90(7); Anal. Calcd for $\text{C}_{20}\text{H}_{18}\text{ClN}_3\text{O}_2$: C, 65.31; H, 4.93; N, 11.42 %; Found: C, 65.28; H, 4.72; N, 11.41 %.

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