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RESEARCH PAPER

Amorphous Mesoporous Iron Aluminophosphate Catalyst for the Synthesis of 1,5-Benzodiazepines

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Abstract: A simple and versatile method for the synthesis of 1,5-benzodiazepines from *o*-phenylenediamine and ketones in the presence of solvents and under solvent-free conditions that used an amorphous mesoporous iron aluminophosphate as catalyst was developed. High yields with excellent selectivity were obtained with a wide variety of ketones under mild reaction conditions. The catalyst had the advantages of ease of preparation, ease of handling, simple recovery, reusability, non toxicity, and being inexpensive.

Key words: benzodiazepine; amorphous metal aluminophosphate; mesoporous iron aluminophosphate; *o*-phenylenediamine; ketone; solvent free synthesis

Benzodiazepines and their derivatives have broad and important pharmacological properties [1–4]. They are widely used as anticonvulsant, analgesic, hypnotic, sedative, and antidepressive agents. In addition, 1,5-benzodiazepines are key intermediates for the synthesis of various fused ring benzodiazepines derivatives [5–7]. Due to their wide biological, industrial, and synthetic applications [8–10], the synthesis of these compounds has received a great deal of attention. The general and simplest method to construct the ring skeletons of 1,5-benzodiazepine is the acid catalyzed reactions of *o*-phenylenediamines (OPDA) or *o*-aminothiophenol (*o*-ATP) with ketones, α,β-unsaturated carbonyl compound, or β-haloketones [11,12].

Many of the synthesis methods of 1,5-benzodiazepines suffer from one or more limitations, such as long reaction times, occurrence of side reactions [13], severe reaction conditions, low yields, use of corrosive chemicals (e.g., HCl gas, trifluoroacetic acid) and hazardous reagents (e.g., pyridine, piperidine, halogenated hydrocarbon), high-boiling solvent (e.g., dimethylformamide), and tedious work-up procedures. Catalysts such as BF_3-Et_2O [14], $NaBH_4$ [15], ceric ammonium nitrate [16], PPA/SiO_2 [17], MgO/$POCl_3$ [18], $Yb(OTf)_3$ [19], AcOH under microwave conditions [20], NBS [21], polymer-supported $FeCl_3Sc(OTf)_3$ [22], and ionic liquids [23] have been used to improve reaction efficiency. The main disadvantages of these catalysts are that they get lost in the work-up procedure, cannot be recovered or reused, and are highly toxic and expensive [24]. Therefore, a better catalyst for the synthesis of 1,5-benzadiazepines is needed to achieve mild reaction conditions, operational simplicity, economic viability, and selectivity.

The use of heterogeneous catalysts such as Al_2O_3/P_2O_5 [25] and sulfated zirconia [26] is advantageous. The application of aluminophosphates as heterogeneous catalytic materials in organic synthesis is growing significantly. Our group has recently reported the catalytic activity of amorphous metal aluminophosphates as effective and recyclable materials in organic transformations [27–30]. To synthesize diazepines by an effective and environmentally benign route, we have condensed OPDA with various ketones in the presence of metal aluminophosphates as catalyst. This solvent-free protocol using a heterogeneous catalyst provides an excellent route for an eco-friendly and economic synthesis of benzodiazepines. We report for the first time a facile method for the synthesis of 1,5-benzodiazepines by the condensation of OPDA with ketones with an amorphous mesoporous iron aluminophosphate catalyst in the presence of a solvent and under solvent-free conditions.

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1 Experimental

1.1 Catalyst preparation

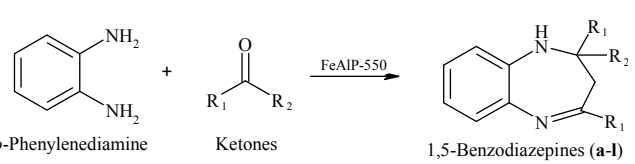
The iron aluminophosphate (FeAlP) catalyst was prepared by co-precipitation [27–30]. Aluminum nitrate ($Al(NO_3)_3 \cdot 9H_2O$), ferric nitrate ($Fe(NO_3)_3 \cdot 9H_2O$), and 85% H_3PO_4 in a definite molar ratio (Al:Fe:P = 0.95:0.025:1) were dissolved in 500 ml of deionized water and stirred vigorously. The solution was heated to 60–70 °C, and then 28% ammonia was added continuously till a precipitate was obtained (pH 9). The precipitate was filtered, washed with deionized water, dried at 120 °C, and calcined at 550 °C for 5 h. The obtained catalyst is denoted FeAlP-550.

1.2 General procedure for the synthesis of 1,5-benzodizepines

A mixture of OPDA (1 mmol) and ketone (2.5 mmol), 5 ml of solvent (when used), and 0.2 g of catalyst were mixed in a 100 ml round bottom flask and heated with stirring in a temperature controlled oil bath at 80 °C (Scheme 1). The progress of reaction was monitored by thin layer chromatography. The reaction mixture was treated with 1:1 (v/v) water and CH_2Cl_2 and centrifuged to separate the solid catalyst. The organic layer was concentrated and the product was separated by silica gel (100–200 mesh) column chromatography using an ethyl acetate-*n*-hexane (2:8) mixture as eluent.

1.3 Characterization of product

The yield and structure of the products were characterized by their melting point and FTIR, ^{1}H NMR, ^{13}C NMR, and mass spectrometry (MS). Melting points were recorded on an Electrothermal melting point apparatus. FTIR spectra were recorded using a Nicolet IR 200 instrument and the KBr pellet technique. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DSX-300 spectrometer at 300/400 MHz and 75/100 MHz, respectively. Chemical shifts are reported downfield from tetramethylsilane (TMS). Multiplicity is indicated using the following abbreviations: s (singlet), d (doublet), dd (double doublet), t (triplet), m (multiplet), and bs (broad singlet). The mass spectra of the filtrate were recorded on an automated GC-MS Shimadzu QP 5000 GC-17A, EI-Mode Model.



o-Phenylenediamine Ketones 1,5-Benzodiazepines (**a-l**)

Scheme 1. Condensation of OPDA with ketones for the synthesis of 1,5-benzodiazepines.

Compound **a**: Yellow solid; mp 137–139 °C; IR (KBr, cm^{-1}) ν 3295, 1633, 1593, 1437; ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 6H, $2CH_3$), 2.23 (s, 2H, CH_2), 2.38 (s, 3H, CH_3), 2.98 (br s, 1H, NH), 6.74–7.27 (m, 4H, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 29.9, 30.5, 45.1, 68.5, 121.8, 122.1, 125.6, 126.8, 137.9, 140.6, 172.5.

Compound **b**: Yellow solid; mp 137–138 °C; IR (KBr, cm^{-1}) ν 3327, 1635, 1568, 1442; ^{1}H NMR ($CDCl_3$) δ 0.95–1.66 (m, 6H, $2CH_3$), 1.71–2.13 (m, 4H, CH_2), 2.37 (s, 3H, CH_3), 2.69 (q, 2H, CH_2), 3.65 (br s, 1H, NH), 6.75–7.57 (m, 3H, C_6H_3); ^{13}C NMR ($CDCl_3$) δ 8.6, 11.2, 26.8, 35.6, 35.7, 42.3, 70.5, 121.8, 125.1, 126.2, 127.1, 137.8, 140.6, 175.6.

^{13}C NMR ($CDCl_3$), δ: 8.6, 11.2, 26.8, 35.6, 35.7, 42.3, 70.5, 121.8, 125.1, 126.2, 127.1, 137.8, 140.6, 175.6.

Compound **c**: Yellow solid; mp 144–145 °C; IR (KBr, cm^{-1}), ν 3322, 1630, 1595; ^{1}H NMR ($CDCl_3$) δ 0.73–1.65 (m, 16H, $2CH_2$ and $4CH_3$), 2.35–2.52 (m, 2H, CH_2), 2.85 (q, 1H, CH), 3.78 (br s, 1H, NH), 6.67–7.42 (m, 4H, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 7.5, 7.8, 11.5, 12.2, 28.1, 28.3, 35.5, 46.1, 68.9, 117.7, 118.1, 125.6, 132.7, 140.0, 142.4, 173.6.

Compound **d**: Yellow solid; mp 138–139 °C; IR (KBr, cm^{-1}) ν 3327, 1620, 1568, 1430, 1372; ^{1}H NMR ($CDCl_3$) δ 1.20–2.50 (m, 15H, $7CH_2$ and CH), 3.90 (br s, 1H, NH), 6.55–7.77 (m, 4H, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 23.1, 24.3, 24.5, 28.8, 33.5, 38.2, 39.2, 54.2, 67.1, 118.8, 119.2, 126.8, 132.1, 139.3, 143.4, 178.2.

Compound **e**: Yellow solid; mp 137–139 °C; IR (KBr, cm^{-1}), ν 3322, 1626, 1568, 1442, 1365; ^{1}H NMR ($CDCl_3$) δ 0.85–2.36 (m, 19H, $9CH_2$ and CH), 3.48 (br s, 1H, NH), 6.85–7.60 (m, 4H, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 21.5, 21.7, 23.4, 23.5, 24.5, 25.1, 33.2, 34.4, 39.3, 40.6, 52.4, 63.1, 121.5, 126.4, 129.6, 138.2, 142.4, 178.5.

Compound **f**: Yellow solid; mp 136–137 °C; IR (KBr, cm^{-1}), ν 3328, 1623, 1550, 1442, 1360; ^{1}H NMR ($CDCl_3$) δ 1.15–2.45 (m, 19H, $9CH_2$ and CH), 3.95 (br s, 1H, NH), 6.52–7.70 (m, 4H, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 22.7, 23.1, 24.3, 24.5, 27.2, 28.1, 33.5, 34.3, 38.2, 39.2, 54.2, 55.4, 67.1, 118.8, 119.2, 126.8, 132.1, 139.3, 143.4, 178.2.

Compound **g**: Yellow solid; mp 151–152 °C; IR (KBr, cm^{-1}), ν 3332, 1637, 1598, 1426; ^{1}H NMR ($CDCl_3$) δ 1.70 (s, 3H, CH_3), 2.95 (d, 1H, CH_2), 3.15 (d, 1H, CH_2), 3.35 (br s, 1H, NH), 6.65–7.10 (m, 2H, C_6H_4), 7.25–7.48 (m, 10H, C_6H_5), 7.55–7.68 (m, 2H, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 29.7, 41.4, 74.3, 121.6, 122.0, 125.4, 126.7, 127.3, 127.4, 128.3, 128.5, 128.8, 129.6, 138.1, 139.2, 140.6, 145.3, 166.3.

Compound **h**: Pale yellow crystalline solid; mp 98–99 °C; IR (KBr, cm^{-1}) ν 3318, 1630, 1598; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.72 (s, 3H), 2.26 (s, 3H), 2.32 (s, 3H), 2.98 (d, 1H), 3.05 (d, 1H), 3.43 (br s, 1H, NH), 6.74–6.76 (m, 1H), 6.98–7.02 (m, 6H), 7.21–7.23 (m, 1H), 7.47–7.50 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 21.2, 29.8, 42.9, 73.1, 121.3, 121.4, 125.2, 126.0, 127.1, 128.5, 128.6, 128.9, 129.2, 136.4, 137.0, 138.2, 139.7, 140.3, 145.0, 166.8.

Compound **i**: Yellowish solid; mp 114–116 °C; IR (KBr,

cm^{-1}), ν 3325, 1135, 1640, 1594, 1190; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.71 (s, 3H), 2.85 (d, 1H), 2.98 (d, 1H), 3.73 (s, 3H), 3.77 (s, 3H), 6.65–6.78 (m, 4H), 6.95–7.02 (m, 2H), 7.18–7.25 (m, 2H), 7.42–7.55 (m, 4H).

Compound **j**: Yellow crystalline solid; mp 219–220 °C; IR (KBr, cm^{-1}) ν 3339, 1636, 1599; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.65 (s, 3H), 2.77 (d, 1H), 2.89 (d, 1H), 4.18 (br s, NH), 6.57–6.64 (m, 4H), 6.81–7.00 (m, 1H), 7.10–7.18 (m, 1H), 7.28–7.55 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.2, 42.0, 72.6, 114.4, 114.6, 120.5, 120.9, 124.9, 125.8, 127.0, 128.2, 130.0, 137.9, 139.5, 155.3, 158.6, 166.8.

Compound **k**: Yellow solid; mp 145–146 °C; IR (KBr, cm^{-1}) ν 3325, 1640, 1589, 1198, 574; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.72 (s, 3H), 2.87 (d, 1H), 3.00 (d, 1H), 2.65 (br s, NH), 6.97–6.98 (m, 1H), 7.00–7.04 (m, 6H), 7.18–7.24 (m, 1H), 7.45–7.48 (m, 4H).

Compound **l**: Red crystalline solid; mp 156–158 °C; IR (KBr, cm^{-1}) ν 3325, 1642, 1597; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.83 (s, 3H), 2.96 (d, 1H), 3.27 (d, 1H), 3.52 (br s, NH), 6.97–6.98 (m, 1H), 7.00–7.02 (m, 6H), 7.21–7.22 (m, 1H), 7.45–7.47 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.0, 42.9, 73.4, 121.3, 122.2, 123.5, 123.4, 126.8, 127.6, 127.7, 129.6, 137.2, 138.8, 144.6, 146.9, 148.4, 154.1, 163.8.

2 Results and discussion

2.1 Effect of solvent in the condensation of OPDA and cyclohexanone

Initially, a reaction between OPDA and cyclohexanone was carried out for the evaluation of FeAlP-550 as the catalyst under different reaction conditions (Table 1). In the first stage, the effect of solvent was studied using the different solvents of CH_2Cl_2, H_2O, C_2H_5OH, $C_2H_2Cl_2$, and $CHCl_3$ as well as under solvent-free conditions. The reaction in the different solvents needed long reaction time and gave low yield. From among the tested solvents, ethanol was chosen as the solvent at 80 °C (Table 1, entry 3).

2.2 Catalyst screening

Although the target catalyst was iron aluminophosphate, the catalytic activity studies were also conducted using hydrated alumina ($Al(OH)_3$), aluminium phosphate (AlP), iron phosphate (FeP), and hydrated iron oxide ($Fe_2O_3{\cdot}xH_2O$) calcined at 120 and 550 °C. This was because the preparation of iron aluminophosphate by the procedure followed in the present work had the possibility of the formation of these materials along with iron aluminophosphate. Hence, we also wanted to characterize the catalytic activity, if any, of these materials.

Table 1 Optimization of solvent conditions for the reaction of OPDA and cyclohexanone using FeAlP-550 as catalyst

Entry	Temperature (°C)	Solvent	Yield* (%)
1	50	dichlolromethane	60
2	100	water	20
3	80	ethanol	94
4	85	dichloroethane	69
5	65	chloroform	57

* Isolated yield.

Table 2 Effect of catalyst under different reaction conditions for the condensation of OPDA and cyclohexanone

Entry	Catalyst	Yield[a] (%)
1	blank	trace[b]
2	$Al(OH)_3$-120	30
3	$Al(OH)_3$-550	25
4	AlP-120	54
5	AlP-550	58
6	FeP-120	68
7	FeP-550	70
8	$Fe(OH)_3$-120	65
9	$Fe(OH)_3$-550	69
10	FeAlP-120	70
11	FeAlP-550	94

Reaction conditions: diamine 1 mmol, ketone 2.5 mmol, catalyst 0.3 g in 5 ml of ethanol, 80 °C, 120 min.

[a]Isolated yield. [b]Isolated yield after 10 h.

The catalytic activity of the various materials expressed as the percentage of isolated yield of product in the condensation of OPDA and cyclohexanone is presented in Table 2. The condensation reaction did not give much yield of the expected product in the absence of a catalyst. The reaction was very slow with only traces of products in the absence of a catalyst. All the materials were found to be active for the condensation reaction between OPDA and cyclohexanone in the presence of ethanol as solvent. There was not much difference in their catalytic activity and the effect of the temperature of calcination, except in the case of iron aluminophosphate. FeAlP calcined to 550 °C exhibited excellent catalytic activity and resulted in the best isolated yield of diazepines.

2.3 Efficiency of catalyst under solvent-free conditions at different temperatures

The reaction was further investigated under solvent-free conditions at different temperatures in the presence of the active FeAlP-550 catalyst. The reaction did not proceed rapidly at room temperature (rt) under solvent-free conditions. However, the yield after 2 h was found to be 50% (Table 3). When the reaction was allowed to continue for 10 h, a product yield of 85% was achieved. When the reaction temperature was increased, a higher yield of diazepines of 96% was obtained at 80 °C. The yield was a function of temperature under solvent-free conditions. An optimum temperature of 80 °C was required for a better yield, which is explained in the mechanism (Scheme

Table 3 Effect of reaction temperature for the condensation of OPDA and cyclohexanone under solvent-free conditions using FeAlP-550 as catalyst

Entry	Temperature (°C)	Yield[a] (%)
1	rt	50
2	54	78
3	80	96
4	rt	85[b]

Reaction conditions: diamine 1 mmol, ketone 2.5 mmol, catalyst 0.2 g, 120 min. [a]Isolated yield. [b]Isolated yield after 10 h.

2). This gave a sufficient number of ketones available on the surface of the catalyst to propagate the reaction.

2.4 Reusability of catalyst in the condensation of OPDA and cyclohexanone

We also investigated the reusability of the FeAlP-550 catalyst, both in the presence of ethanol and under solvent-free conditions. The catalyst was recovered by dissolving the reaction mixture in 1:1 (v/v) water and CH_2Cl_2 and filtered to separate the solid catalyst. The catalyst was separated by simple filtration, washed with acetone, dried at 120 °C, and calcined at 550 °C. The catalyst was reused at least four times in the same reaction without appreciable loss in catalytic activity. The results of the catalyst reusability are shown in Table 4.

2.5 Synthesis of benzodiazepines both in the presence of ethanol as solvent and under solvent-free conditions

To look at the application of FeAlP as a general catalyst for the synthesis of 1,5-benzodiazepines, the condensation reactions under optimized conditions using a variety of aliphatic, alicyclic ketones, and substituted acetophenones were carried out. The results are presented in Table 5. All the ketones condensed smoothly with OPDA in the presence of FeAlP-550 without forming any side products. The only noticeable difference in the reactivity of the various ketones was in the time taken to get a significant yield of the expected diazepine products. It is noteworthy that the condensation of the various ketones with OPDA in the presence of FeAlP-550 was superior in terms of yield and selectivity for products as compared to other catalysts reported in the literature.

Under the optimum conditions, aliphatic ketones gave a product yield in the range of 87%–94% after 45 min, which depended on the nature of the ketone. Cyclic ketones such as cyclohexanone, cycloheptanone, and cyclopentanone (Table 5, entries 4–6) also produced the corresponding fused-ring benzodiazepines in good yields but after a longer time (~120 min) as compared to the aliphatic ketones (Table 5, entries 1–3).

The condensation activity of acetophenones and its derivatives was found to be better than that of cyclic ketones. The reactivity depended on the substituent on the benzene. In the presence of electron withdrawing groups such as –OH, –Br, and $–NO_2$, the condensation reaction proceeded smoothly to give good yields of benzodiazepines (Table 5, entries 10–12). Whereas the presence of electron releasing groups such as methyl and methoxy groups on the benzene nucleus of acetophenone only gave poor yields (Table 5 entries 8 and 9) of benzodiazepines even after long reaction times.

Table 4 Synthesis of benzodiazepines using FeAlP-550 as an efficient and reusable catalyst

Cycle	Yield[a] (%)	Yield[b] (%)
1	96	94
2	90	88
3	43	85
4	20	69

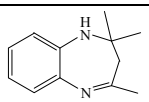
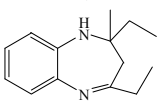
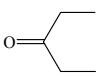
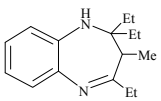
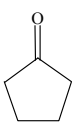
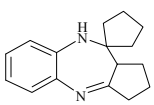
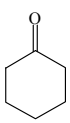
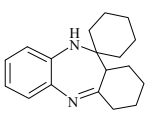
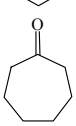
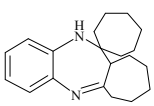
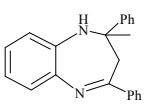
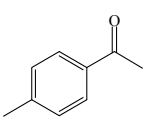
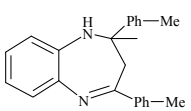
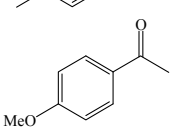
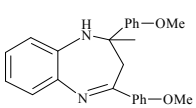
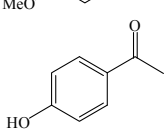
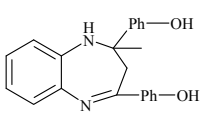
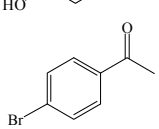
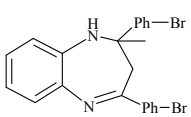
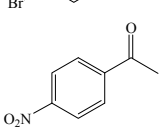
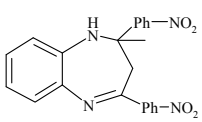
[a]Isolated yield in the absence of solvents. Reaction conditions: diamine 1 mmol, ketone 2.5 mmol, catalyst 0.3 g, 80 °C.
[b]Isolated yield in the presence of solvent (ethanol). Reaction conditions: diamine 1 mmol, ketone 2.5 mmol, catalyst 0.2 g in 5 ml ethanol, 80 °C.

2.6 Mechanism for the condensation of OPDA and ketones over FeAlP-550 catalyst

From the above observations on the reactivity of various ketones in the presence of FeAlP-550 as the catalyst, we propose the reaction mechanism shown in Scheme 2. The catalyst FeAlP-550 has surface acid sites. The oxygen atom of the ketones is adsorbed through its lone pair electrons on the surface acid sites of the catalyst, and the amino groups of OPDA attack the carbonyl group of the ketone to give the intermediate diimine (A and B). A 1,3-hydrogen shift to the attached methyl group then occurred to form an isomeric enamine, which cyclizes to afford the seven-member ring. An alternative mechanism involving the aldol condensation of ketones to give α,β-unsaturated carbonyl compound which subsequently undergoes 1,4-addition was ruled out because such an aldol condensation does not occur in ketones with a α-hydrogen in the presence of FeAlP. The reaction conditions are mild and no side products or decomposition of the products were observed.

The better catalytic activity of FeAlP-550 over that of the other catalysts reported may be attributed to its mesoporous texture and amorphous nature, which gave a higher concentration of active acid sites on its surface [30]. We have previously reported a correlation between the textural/structural properties and catalytic activity of these materials in organic transformations like transesterification and alkylation reactions [28, 29]. Since larger crystallites have only a small percentage of the reactive sites on the surface, smaller crystallites or amorphous materials possess a much higher surface concentration of sites, and it is this morphological difference that makes FeAlP an efficient catalyst.

Table 5 Condensation of OPDA and ketones catalyzed by FeAlP-550 catalyst under different reaction conditions

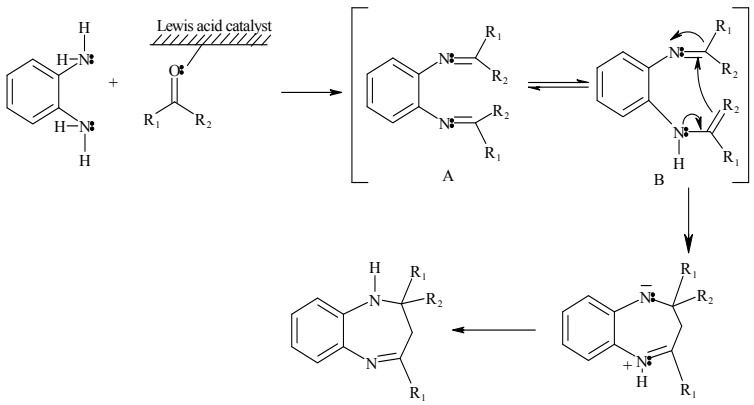
Entry	Ketone	Diazepine derivative	Time (min)	Yield[a] (%)	Yield[b] (%)	Melting point (°C)	
						Expt.	Reported
1		**a** 	45	94	94	140	137–139
2		**b** 	45	95	88	140	137–138
3		**c** 	45	90	87	140	144–145
4		**d** 	120	89	81	137	138–139
5		**e** 	120	94	96	139	137–139
6		**f** 	120	83	68	135	136–137
7		**g** 	75	92	90	152	151–152
8		**h** 	120	89	87	99	143
9		**i** 	120	85	84	117	114–116
10		**j** 	80	84	81	217	219–220
11		**k** 	80	83	85	146	145–146
12		**l** 	80	86	85	157	156–158

Reaction conditions: diamine 1 mmol, ketone 2.5 mmol, catalyst 0.3 g in 5 ml ethanol or 0.2 g in solvent-free conditions, 80 °C.

[a]In the presence of ethanol. [b]Under solvent free conditions.

2.7 Advantages of the FeAlP-550 catalyst

The catalyst preparation is simple and involves readily available non-hazardous and inexpensive reagents. The separation of the product from the reaction mixture does not require any tedious workup procedure. The recovered catalyst can be reused at least four to five times (Table 4) without any significant loss in activity. Thus, the present data showed the efficient reusability of the catalyst. As compared to other acid catalysts reported in the literature, iron aluminophosphate was superior in terms of a higher conversion, short reaction time, and small amount of catalyst needed. Also, this method does not require any expensive reagents or special care to exclude moisture from the reaction medium.



Scheme 2. Mechanism for the condensation of OPDA and ketones over a FeAlP-550 catalyst.

3 Conclusions

Iron aluminophosphate was a highly efficient heterogeneous, recyclable catalyst for the synthesis of 1,5-benzodiazepines by the condensation of OPDA with a wide variety of ketones. This method has easy workup, solvent-free conditions, fast reaction rate, good yields, and high selectivity, which make it attractive for large scale operations. This method is effective for the preparation of 1,5-benzodiazepines from both electron-rich and electron-deficient ketones and *o*-phenylenediamine derivatives under mild reaction conditions. The activity of the catalyst was attributed to its amorphous mesoporous nature and surface acid sites that allowed the reaction to be completed in a short time with high yield and 100% selectivity for the desired product.

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