Catalytic synthesis of new pyrazolo[3,4-b] pyridine via a cooperative vinylogous anomeric-based oxidation

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In this study, a novel nano-magnetic metal–organic frameworks based on Fe₃O₄ namely Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ was synthesized and fully characterized. The prepared sample was used as catalyst in the synthesis of pyrazolo[3,4-b] pyridines as convenient medicine by condensation reaction of aldehydes, 5-(1H-Indol-3-yl)-2H-pyrazol-3-ylamine and 3-(cyanoacetyl)indole via a CVABO. The products were obtained with high yields at 100 °C and under solvent-free conditions.

Nowadays, rational design, synthesis and catalytic systems is an important topic in the research and development (R&D) of the chemical industries. Nanoarchitectonics are methods for introducing nanoporous materials such as magnetic-based ones with high surface area. Metal–organic frameworks (MOFs) as nanoporous materials have been widely applied in magnetic resonance imaging (MRI), catalysis, biotechnology, gas separation, adsorption, purification, drug delivery, etc. The heterogeneous materials based on metallic nanoparticles can play a crucial role in organic synthesis, and have unique properties such as high surface area, easy separation and support for liquid tags materials. Therefore, metal–organic frameworks (MOFs) are one of the basic materials for the catalytic preparation of many important molecules in organic synthesis. Recently, the synthesis of Fe₃O₄ nanomagnetic-based metal–organic frameworks (MOFs) gained attention. Because these nanomagnetic-based MOFs catalytic systems have no limitations such as tedious separation and purification.

In recent years, many quests have been proceeded to investigate the biological and pharmaceutical properties of the nucleus with indole moieties. We have reviewed the reported methodologies for the synthesis of bis- and trisindolylmethanes. Shiri has comprehensively reviewed the application of indoles in the multicomponent processes. In this regard, fused N-heterocycles such as pyridines containing of indole moieties may be suitable candidates for biological and pharmacological chemistry investigations. Because, N-heterocycles have been used as a drug candidate for antimicrobial, cancer, malaria, anticonvulsant, antifungal, HIV, anti-tumor, antioxidant, antihypertension and urinary incontinence treatment. Furthermore, pyridine structure kernels are present in pharmaceutical materials and natural products. Among the N-heterocycle compounds, pyrazolo[3,4-b] pyridine scaffold is the valuable scaffold of material drugs and KDR kinase inhibition. Recent research in material chemistry confirmed that pyrazolo[3,4-b] pyridine compounds are key intermediates in industry, semiconductors and organic light-emitting diodes.

Anomeric effect (AE) as a fundamental example of stereoelectronic interaction has a great educational and research importance. It was discovered in 1955 by J. T. Edward in his studies of carbohydrate chemistry. Historically, this phenomenon was introduced to explain unusual conformational preferences in carbohydrates where the presence of endocyclic oxygen in a glycoside leads to an “abnormal” axial conformational preference for certain substituents at the anomeric carbon. In an extension of the classic anomeric effect, a vinyl heteroatom is able to donate electron density from its lone pair through an adjacent π orbital and into the accepting σ* orbital on the other end of the double bond (Fig. 1a).

The anomeric effect can be used as a powerful tool for the justification and interpretation of unusual molecular activities. For example, the forced alignment of three nitrogen non-bonding orbitals with the central antibonding

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σ*C–H orbital within the ortho formamide and cooperative anomeric effect weakens the bond and leads to an “unusual” hydride transfer under acidic conditions (Fig. 1b)\(^58–61\).

Recently the term ABO has been introduced\(^62,63\) and reviewed\(^64,65\). A famous example of ABO is the Cannizzaro reaction via the addition of hydroxide (OH\(^-\)) to the carbonyl group of aldehydes which do not have α-hydrogen (Fig. 1c), both of the lone pair’s electrons of oxygen atoms within the tetrahedral carbon sharing their electrons into the anti-bonding orbital of C–H bond (\(n_\pi \rightarrow \sigma^*_{C–H}\)) and weakened it. The resulting labile hydride acts as a powerful nucleophile that attacks to the second molecule of aldehyde. Finally, this reaction produced equal amounts of the corresponding alcohol and acid.

According to the strategy of expanding compounds with biological activities, we have introduced a novel Fe\(_3\)O\(_4\)@MIL-101(Cr)-N(CH\(_2\)PO\(_3\))\(_2\) as a catalyst. This magnetic metal–organic framework was used in the

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**Figure 1.** (a) Anomeric effect versus the vinylogous anomeric effect. (b) A (CABO) leads to hydride transfer in the mechanism of the Cannizzaro reaction. (c) Hydrogen releasing supported via a cooperative anomeric effect in the orthoformamide (perhydro-3a,6a,9a-triazaphenalene).
synthesis of novel mono, bis and tris pyrazolo[3,4-b] pyridines with both indole and pyrazole moieties at 100 °C in solvent-free conditions (Fig. 2).

### Experimental

**Synthesis of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ as catalyst.** According to the previously reported methods, MIL-101(Cr)-NH₂ and MIL-101(Cr)-N(CH₂PO₃H₂)₂ were synthesized. Then a mixture of MIL-101(Cr)-N(CH₂PO₃H₂)₂ (1.3 g) and Fe₃O₄ (1 g) were dispersed in toluene at 80 °C for 12 h. After cooling the reaction mixture, the nano-magnetic metal–organic framework Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ was separated by an external magnet and washed with ethanol for several times (Fig. 3).

**General method for the preparation of pyrazolo[3,4-b] pyridines.** Firstly, the raw materials 3-(cyanoacetyl) indole and 5-(1H-Indol-3-yl)-2H-pyrazol-3-ylamine were synthesized according to the previously literature reported procedures (Fig. 2). Then, a mixture of aldehyde derivatives (1 mmol), 5-(1H-Indol-3-yl)-2H-pyrazol-3-ylamine (0.198 g, 1 mmol), 3-(cyanoacetyl) indole (0.184 g, 1 mmol) and nano-magnetic metal–organic frameworks Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ as catalyst (20 mg) were mixed and stirred at 100 °C. Progress of the reaction was followed by applying the TLC technique. After completing the reaction, the reaction system was cooled to 25 °C. Then, hot ethanol was added to the reaction mixture, and the catalyst was removed from the reaction mixture with an external magnet. The ethanol was evaporated, and finally, the pyrazolopyridine product was purified by plate chromatography (EtOAc/n-hexane:1/1). ¹H NMR (400 MHz, DMSO-d₆), ¹³C NMR (100 MHz, DMSO-d₆), FT-IR (KBr, cm⁻¹) and melting point analysis were used for all synthesized molecules.

### Result and discussion

Nowadays, synthesized molecules bearing pyridine-based scaffolds with indole moieties are attracted the attention of pharmaceutical chemistry researchers due to their building block’s ability in pharmaceuticals and modern drug design approaches. So, there is still a great demand for the introducing of more practical and facile procedures and catalytic systems for multicomponent reactions in the organic synthesis field. On the other hand, the joining of indole, pyridine, and pyrazole moieties within a single molecule is our main research proposal in this investigation. We think that the combination of above-mentioned units in a single structure can open up a new and promising insight in the course of rational design, synthesis and applications of drug candidate compounds.

According to our recent findings, we believed that the stereoelectronic effect has a major role in the last step of the proposed mechanism. To the best of our knowledge and literature surveys, there is no report on the synthesis of described pyridines. Therefore, herein we wish to report the first catalytic and multicomponent method for the preparation of new pyridines with both pyrazole and indole aromatic moieties via CVABO.

In order to extend the field of magnetic metal–organic frameworks catalysts, our research group has presented and synthesized a novel MIL-101(Cr)-N(CH₂PO₃H₂)₂ connected to Fe₃O₄ tags (Fig. 2). The structure of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ as a magnetic metal–organic frameworks catalyst was characterized by FT-IR, XRD,
SEM, EDX, SEM-elemental mapping, TG, DTG and $N_2$ adsorption–desorption isotherm (BET analysis). Then, the magnetic metal–organic frameworks catalyst was applied for the preparation of novel pyrazolo[3,4-b]pyridine derivatives as biological candidates.

The FT-IR spectra of Fe$_3$O$_4$@MIL-101(Cr)-N(CH$_2$PO$_3$)$_2$ as the catalyst, MIL-101(Cr)-N(CH$_2$PO$_3$H$_2$)$_2$ and MIL-101(Cr)-NH$_2$ were shown in Fig. 4. The broadband at 2600–3500 cm$^{-1}$ is related to OH of PO$_3$H$_2$ functional groups in MIL-101(Cr)-N(CH$_2$PO$_3$H$_2$)$_2$. The peaks P–O and P=O bond stretching are shown in 1000 cm$^{-1}$, 1068 cm$^{-1}$ and 1121 cm$^{-1}$ respectively. Also, the absorption peaks at 2920 and 1626 cm$^{-1}$ are related to aromatic C–H and C=C stretching bands. Furthermore, the peak at 582 cm$^{-1}$ is related to the stretching vibrational modes of Fe–O groups in Fe$_3$O$_4$. The FT-IR difference between starting materials and Fe$_3$O$_4$@MIL-101(Cr)-N(CH$_2$PO$_3$)$_2$ as catalyst verified the scaffold of the catalyst.

The particle size and phase of Fe$_3$O$_4$@MIL-101(Cr)-N(CH$_2$PO$_3$)$_2$ as catalyst and MIL-101(Cr)-N(CH$_2$PO$_3$H$_2$)$_2$ were investigated by XRD at the range of 5–80°, Fig. 5. The XRD patterns demonstrated diffraction lines of high crystalline nature at 2θ = 18.0°, 30.3°, 35.5°, 43.6°, 54.0°, 57.3°, 62.7° and 74.6° correspond to the Fe$_3$O$_4$ diffraction lines (111), (220), (311), (400), (422), (511), (440) and (533) (Fig. 5)$.79$ Also, the Scherer equation...
and Bragg equation were used for the averaged inter planer distance and sizes of crystal, which are determined 5.1–26.4 nm (Table 1).

For further verification of the scaffold and elemental analysis in the prepared catalyst, the energy dispersive X-ray analysis (EDX) analysis was used (Fig. 6a). The constituents of the catalyst were verified with the existence of Fe, N, Cr, O, C and P atoms. Figure 6b shows that the elemental of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ are distributed uniformly.

In another study, the particle size and morphology of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ as catalyst were studied by scanning electron microscope (SEM) (Fig. 7). As shown in Fig. 7 the particles have spherical shape in the nanoscale size.

The N₂ adsorption/desorption isotherms were utilized to analyze the textural features of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ (Fig. 8a). A hysteresis loop is observed, indicating the presence of mesopores in the structure of the sample. The calculated surface area (BET) and the total pore volume are 100.03 m² g⁻¹ and 0.518 cm³ g⁻¹, respectively. The plot of the pore size distribution of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ obtained by the BJH method is presented in (Fig. 8a). This plot reveals that the catalyst possesses both micropores (size < 2 nm) and mesopores (2 < size < 50 nm), however, the radius of most of the pores is less than 10 nm. Figure 8b depicts the magnetic measurements of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ and Fe₃O₄. The vibrating sample magnetometer (VSM) of Fe₃O₄ and Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ were compared, the vibrating sample magnetometer of pure Fe₃O₄ reduced from 64.5 up to 53.5 mug⁻¹ for the Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂. Therefore, this reduction is for the coating of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ onto the surface of Fe₃O₄.

The thermal and behavioral stability of nano-magnetic metal–organic frameworks Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ were studied by thermal gravimetric (TG) and derivative thermal gravimetric (DTG) techniques (Fig. 9). The first step is the weight loss, which took place between 25 and 100 °C, associated with the removal of solvents (organic and water). The main stage of weight loss, disrupts the structure of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂, took place at 380 °C, and includes about 35% weight loss. Therefore, this catalyst can be used up to 300 °C.

Table 1. XRD data of catalyst.

| Entry | 2θ  | Peak width (degree) | Size [nm] | Inter planer distance [nm] |
|-------|-----|---------------------|----------|------------------------|
| 1     | 8.20| 0.30                | 26.4     | 1.074                  |
| 2     | 23.15| 0.55               | 14.6     | 0.383                  |
| 3     | 26.80| 0.55               | 14.7     | 0.331                  |
| 4     | 30.55| 1.6                | 5.1      | 0.291                  |
| 5     | 35.70| 1.15               | 7.2      | 0.251                  |
| 6     | 43.40| 0.67               | 12.6     | 0.208                  |
| 7     | 57.55| 1                  | 9.0      | 0.160                  |
| 8     | 63.05| 1                  | 9.2      | 0.147                  |
After the synthesis and characterization of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂, it was used for the synthesis of new pyrazolo-[3,4-b] pyridine derivatives with indole and pyrazole tags. The mentioned compounds were prepared by reaction of 4-chloro benzaldehyde (0.141 g, 1.0 mmol), 5-(1H-Indol-3-yl)-2H-pyrazol-3-ylamine (0.198 g, 1 mmol) and 3-(cyanoacetyl) indole (0.184 g, 1 mmol) as a suitable model for the optimization the reaction conditions. The results are assembled in Table 2, the best option for the preparation of compound C₂ was achieved in the presence of 20 mg Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ in solvent-free conditions (Table 2, entry 2). The target reaction was also examined by using several solvents such as DMF, CH₃CN, MeOH, H₂O, EtOH, CH₂Cl₂, CHCl₃, and EtOAc (5 mL) in the presence of 20 mg of catalyst. The reaction results did not improve (Table 2, entries 9–17). These interesting results encouraged us to synthesis a wide range of pyrazolo-[3,4-b] pyridine compounds in solvent-free conditions.

As above-mentioned, after optimizing the reaction conditions, catalyst (20 mg) is used for the preparation of new biomolecules products using widespread aldehydes such as bearing electron-donating, electron-withdrawing groups, iso-trephetaldehyde and tris-aldehyde, 5-(1H-Indol-3-yl)-2H-pyrazol-3-ylamine and 3-(cyanoacetyl) indole. The results can be seen in Table 3, the obtained results show that the prepared catalyst is suitable for the synthesis of mono, bis and tris products with high yields (70–90%) and short reaction time (35–60 min).

In the suggested mechanism, the catalyst activates the carbonyl group of aldehyde. Firstly, intermediate (I) as a Michael acceptor is produced by the reaction of activated aldehyde and 3-(cyanoacetyl)indole. In the next step, intermediate (II) is prepared from reactions of 5-(1H-Indol-3-yl)-2H-pyrazol-3-ylamine and intermediate (I). In the third step, intermediate (III) is obtained by cyclization and losing one molecule of H₂O. Then, intermediate (III) via interaction of lone pair electrons of N atoms from C≡C bonds causes the release hydride

Figure 6. Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂: (a) EDX analysis. (b) Elemental mapping of C (red), O (blue), N (green), Fe (yellow), P (purple) and Cr (gray) atoms.
and H₂. Finally, the 1,4-dihydropyridines convert to their corresponding pyrazolo [3,4-b] pyridine derivatives via a CVABO and release a hydrogen molecule (–H₂)⁸⁰,⁸¹. The optimization of model reaction under argon and N₂ atmospheres are also verified the desired product (Fig. 10). To investigate the activation of aldehyde by catalyst, p-chloro benzaldehyde was activated with Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ at room temperature. Then the FT-IR spectra of the reaction mixtures were examined. The absorption band of C=O of the p-chloro benzaldehyde at 1708 cm⁻¹ was changed to 1702, 1698, 1698 cm⁻¹ in the presence of MIL-101(Cr)-N(CH₂PO₃)₂, MIL-101(Cr)-NH₂ and Fe₃O₄ (Fig. 11).

To compare the efficiency of the synthesized catalyst in the preparation of pyrazolo [3,4-b] pyridine derivatives, the model reaction (compound C2) was tested using various inorganic and organic catalysts under optimal conditions (Table 4). As Table 4 shows, nano-magnetic metal–organic frameworks Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ is the best catalyst for the preparation of the desired product. Also, to investigate the heterogeneous nature of the protocols and palladium leaching, ICP/MS results proved that no Fe and Cr leaching was detected in the filtrate (Fe: 2.5 × 10⁻⁶ and Cr: 1.9 × 10⁻⁵ mol g⁻¹ respectively) upon reaction completion, which indicates the high stability of the prepared catalyst.

Finally, for the reusability of the nano-magnetic metal–organic frameworks Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ in the synthesis of pyrazolo[3,4-b] pyridine, this catalyst was examined in 3-(cyanoacetyl) indole (0.184 g, 1 mmol), 4-chloro benzaldehyde (0.141 g, 1 mmol) and 5-(1H-Indol-3-yl)-2H-pyrazol-3-ylamine (0.198 g, 1 mmol) (compound C2) as model reactions. The results show that the prepared catalyst can be reused up to 7 times without noticeable reduction (Fig. 12).
Conclusion

In summary, a magnetic metal–organic frameworks Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ as nano-catalyst was designed and synthesized and identified by various techniques such as FT-IR, XRD, SEM, EDX, Mapping, BET and VSM analysis. This catalyst was tested for the preparation of novel pyrazolo[3,4-b]pyridines according to (CVABO) concept. The advantages of this work include, synthesis of new pyrazolo[3,4-b]pyridines as biological candidates, short reaction time, clean profile of the reaction and catalyst recyclability.

Figure 8. Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂: (a) BET and BJH isotherms, (b) VSM.
Figure 9. Thermal gravimetric (TG) and derivative thermal gravimetric (DTG) analysis of Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂.

Table 2. Optimization parameter on the synthesis C2 compound.

| Entry | Solvent | Catalyst (mg) | Temp. (°C) | Time   | Yield (%) |
|-------|---------|---------------|------------|--------|-----------|
| 1     | –       | 20            | 110        | 60 (min) | 80        |
| 2     | –       | 20            | 100        | 60 (min) | 87        |
| 3     | –       | 20            | 90         | 60 (min) | 82        |
| 4     | –       | 20            | 50         | 60 (min) | 10        |
| 5     | –       | 20            | 25         | 60 (min) | –         |
| 6     | –       | 30            | 100        | 60 (min) | 85        |
| 7     | –       | 100           | 100        | 60 (min) | 56        |
| 8     | –       | 5             | 100        | 60 (min) | 25        |
| 9     | DMF     | 20            | Reflux     | 7 (h)   | 83        |
| 10    | DMF     | 20            | 100        | 8 (h)   | 82        |
| 11    | CH₃CN   | 20            | Reflux     | 10 (h)  | 38        |
| 12    | MeOH    | 20            | Reflux     | 8 (h)   | 15        |
| 13    | H₂O     | 20            | Reflux     | 9 (h)   | 10        |
| 14    | EtOH    | 20            | Reflux     | 10 (h)  | 45        |
| 15    | CH₃Cl   | 20            | Reflux     | 12 (h)  | –         |
| 16    | CH₂Cl₂  | 20            | Reflux     | 12 (h)  | –         |
| 17    | EtOAc   | 20            | Reflux     | 10 (h)  | –         |
Table 3. Synthesis of pyrazolo[3,4-<i>b</i>] pyridine derivatives (C1–C22) using Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ as a catalyst.
Figure 10. Proposed mechanism for the synthesis of pyrazolo[3,4-b]pyridine derivatives using Fe₃O₄@MIL-101(Cr)-Ni(CH₂PO₃)₂ as catalyst.
Figure 11. FT-IR spectra of p-Cl-benzaldehyde in percent of Fe₃O₄, MIL-101(Cr)-NH₂, MIL-101(Cr)-N(CH₂PO₃H₂)₂ and Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃).

Table 4. Compare of various catalyst for the synthesis of pyrazolo[3,4-b]pyridine derivatives in comparison with Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃).

| Entry | Catalyst | (Mol %) | (Time/min.) | Yield (%) |
|-------|----------|---------|-------------|-----------|
| 1     | FeCl₃    | 10      | 120         | –         |
| 2     | [PVI-SO₃H][FeCl₄] | 10 mg | 120 | 48 |
| 3     | CF₃SO₃H | 10      | 120         | 15        |
| 4     | H₂SO₄   | 10      | 120         | 42        |
| 5     | [Py-SO₃H][Cl] | 10 mg | 120 | 36 |
| 6     | Fe₃O₄   | 10 mg   | 120         | –         |
| 7     | K₂CO₃   | 10      | 120         | –         |
| 8     | SSA⁸⁵,⁸⁶ | 10 mg   | 120         | 20        |
| 9     | Et₃N    | 10      | 120         | –         |
| 10    | NaOH     | 10      | 120         | –         |
| 11    | MIL-100(Cr)/NHEtN(CH₂PO₃H₂)₂ | 10 mg | 120 | 52 |
| 12    | p-TSA    | 10      | 120         | 25        |
| 13    | GTBSA⁸⁷  | 10      | 120         | 40        |
| 14    | MHMHPA⁵⁵ | 10      | 120         | 32        |
| 15    | Fe₃O₄@MIL-101(Cr)-N(CH₂PO₃)₂ (this work) | 20 mg | 60 | 87 |

Figure 12. Recyclability of catalyst for the synthesis of pyrazolo[3,4-b]pyridine derivatives.
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Data availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

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References

1. Vojodic, A. & Norskov, J. K. New design paradigm for heterogeneous catalysts. Natl. Sci. Rev. 2, 140–143 (2015).
2. Hu, X., Zhu, H., Sang, X. & Wang, D. Design and synthesis of zirconium-containing coordination polymer based on unsymmetric indolyl dicarboxylic acid and catalytic application on borrowing hydrogen reaction. Adv. Synth. Catal. 360, 4293–4300 (2018).
3. Rossi, R., Angelici, G., Casotti, G., Manzini, C. & Lessi, M. Catalytic synthesis of 1, 2, 5-tetratrasubstituted 1H-imidazole deriva-
tives: State of the art. Adv. Synth. Catal. 361, 2737–2803 (2019).
4. Wan, K. T. & Davis, M. E. Design and synthesis of a heterogeneous asymmetric catalyst. Nature 370, 449–450 (1994).
5. Li, F. & Xiu, C. Synthesis of α-oxazolidinone catalyzed by palladium and highly effective heterogeneous catalytic system for oxidative cyclonbonylation of β-aminoalcohols and 2-amino phenol. J. Catal. 227, 542–546 (2004).
6. Du, M. et al. An efficient and recyclable AgNO3/ionic liquid system catalyzed atmospheric CO utilization: Simultaneous synthesis of 2-oxazolidinones and a hydroxyl ketones. J. Catal. 393, 70–82 (2021).
7. Maspoch, D., Ruiz-Molina, D. & Veciana, J. Magnetic nanoporous coordination polymers. J. Mater. Chem. A 14, 2713–2723 (2004).
8. Torad, N. L. et al. Direct synthesis of MOF-derived nanoporous carbon with magnetic Co nanoparticles toward efficient water treatment. Small 10, 2096–2107 (2014).
9. Zhu, Y., Zhao, W., Chen, H. & Shi, J. A simple one-pot self-assembly route to nanoporous and monodispersed Fe3O4 particles with oriented attachment structure and magnetic property. J. Phys. Chem. C 111, 5281–5285 (2007).
10. Peller, M., Böll, K., Zimpel, A. & Wuttke, S. Metal-organic framework nanoparticles for magnetic resonance imaging. Inorg. Chem. Front. 5, 1760–1779 (2018).
11. Taylor, K. M., Rieter, W. J. & Lin, W. Manganese-based nanoscale metal-organic frameworks for magnetic resonance imaging. J. Am. Chem. Soc. 130, 14358–14359 (2008).
12. Zhu, L., Liu, X. Q., Jiang, H. L. & Sun, L. B. Metal-organic frameworks for heterogeneous basic catalysis. Chem. Rev. 117, 8129–8176 (2017).
13. Martin, N., Dusselier, M., De Vos, D. E. & Cirujano, F. G. Metal-organic framework derived metal oxide clusters in porous alumi-
nosilicates: A catalyst design for the synthesis of bioactive aza-heterocycles. ACS Catal. 9, 44–48 (2018).
14. Dang, H. V. et al. Copper-catalyzed one-pot domino reactions via C–H bond activation: Synthesis of 3-aryloylinolines from 2-
amino benzylalcoholos and propiophenones under metal–organic framework catalysis. RSC Adv. 8, 31455–31464 (2018).
15. Mirhosseini-Eshkevari, B., Esnaashari, M. & Ghasemzadeh, M. A. Novel brominated acidic ionic liquids confined in UiO-66 nanoc-
angs for the synthesis of dihydropyrazoles [2, 1-d]pyrimidine derivatives under solvent-free conditions. ACS Omega 4, 10548–10557 (2019).
16. Rechac, V. L., Cirujano, F. G., Corna, A. & Llabres I Xamena, F. X. Diastereoselective synthesis of pyranocoumarins on zirconium-
containing UiO-66 metal-organic frameworks. Eur. J. Inorg. Chem. 2016, 4512–4516 (2016).
17. Sepehrmansourie, H. Metal-organic frameworks (MOFs): As multi-purpose catalysts. Iran. J. Catal. 11, 207–215 (2021).
18. Kalthor, S. et al. Anodic electrosynthesis of MIL-53(Al)-N(CH3)2Cl2 as a mesoporous catalyst for synthesis of novel (N-methyl-
pyrrol)-pyrazolo [3, 4-b]pyridines via a cooperative vinlylogous amnonic based oxidation. Sci. Rep. 11, 19370 (2021).
19. Farhadi, S., Ghasemzadeh, M. A. & Aghaei, S. S. NiCoO4@Ni(BDC) nano-porous metal-organic framework as a novel catalyst for the synthesis of spiro[indenyle[1,2-d]pyrimidine-ones and investigation of their antimicrobial activities. ChemistrySelect 4, 729–736 (2019).
20. Truong, T., Nguyen, C. V., Truong, N. T. & Phan, N. T. Ligand-free N-arylation of heterocycles using metal-organic framework 
[Cu(INA)2] as an efficient heterogeneous catalyst. RSC Adv. 5, 107547–107556 (2015).
21. Liu, J. et al. Applications of metal-organic frameworks in heterogeneous supramolecular catalysis. Chem. Soc. Rev. 43, 6011–6061 (2014).
22. Rathor, R. A. & Siddiqui, Z. N. Silver phosphate supported on metal-organic framework (Ag3PO4@MOF-5) as a novel heterogene-
ous catalyst for green synthesis of indenoquinolinediones. Appl. Organommet. Chem. 33, e1576 (2019).
23. Tourani, H., Naimi-Jamal, M. R., Panahi, L. & Dekamin, M. G. Nanoporous metal-organic framework Cu3(BDC)1,2(DABCO) as an efficient heterogeneous catalyst for one-pot facile synthesis of 1, 2, 3-triazole derivatives in ethanol: Evaluating antimicrobial activity of the novel derivatives. Sci. Iran. 26, 1485–1496 (2019).
24. Ghasemzadeh, M. A., Mirhosseini-Eshkevari, B., Tavakoli, M. & Zamani, F. Metal-organic frameworks: Advanced tools for mul-
ticomponent reactions. Green Chem. 22, 7265–7300 (2020).
25. Huang, S., Kou, X., Shen, J., Chen, G. & Ouyang, G. “Armor-Plating” enzymes with metal-organic frameworks (MOFs). Angew. Chem. Int. Ed. 59, 8786–8798 (2020).
26. Li, J. R., Kuppler, R. J. & Zhou, H. C. Selective gas adsorption and separation in metal-organic frameworks. Chem. Soc. Rev. 38, 1477–1504 (2009).
27. Alhamami, N., Doan, H. & Cheng, C. H. A review on breathing behaviors of metal-organic frameworks (MOFs) for gas adsorp-
tion. Materials 7, 3198–3250 (2014).
28. Bedia, J. et al. A review on the synthesis and characterization of metal organic frameworks for photocatalytic water purification. Catalysts 9, 52 (2019).
29. Zheng, H. et al. One-pot synthesis of metal-organic frameworks with encapsulated target molecules and their applications for controlled drug delivery. J. Am. Chem. Soc. 138, 962–968 (2016).
30. Argyle, M. D. & Bartholomew, C. H. Heterogeneous catalyst deactivation and regeneration: A review. Catalysts 5, 145–269 (2015).
31. Maleki, A., Hajizaddeh, Z. & Salehi, P. Mesoporous halloysite nanotubes modified by CuFe2O4 spinel ferrite nanoparticles and study of its application as a novel and efficient heterogeneous catalyst in the synthesis of pyrazolopyridine derivatives. Sci. Rep. 9, 1–8 (2019).
32. Bhana, P., Modak, A. & Bhaumik, A. Supported porous nanomaterials as efficient heterogeneous catalysts for CO2 fixation reac-
tions. Chem. Eur. J. 24, 7278–7297 (2018).
33. Gunasekar, G. H., Shin, J., Jung, K. D., Park, K. & Yoon, S. Design strategy toward recyclable and highly efficient heterogeneous catalysts for the hydrogenation of CO2 to formate. ACS Catal. 8, 4346–4353 (2018).
34. Pascaru, V., Gonzalez Miera, G., Inge, A. K. & Martin-Matute, B. Metal-organic frameworks as catalysts for organic synthesis: A critical perspective. J. Am. Chem. Soc. 141, 7223–7234 (2019).
35. Dhakshinamoorthy, A., Alvaro, M. & Garcia, H. Metal-organic frameworks (MOFs) as heterogeneous catalysts for the chemoselect-
tive reduction of carbon-carbon multiple bonds with hydrazine. Adv. Synth. Catal. 351, 2271–2276 (2009).
36. Qi, C., Ramella, D., Wensley, A. M. & Luan, Y. A Metal-organic framework brensted acid catalyst: Synthesis, characterization and application to the generation of quinone methides for [4+2] cycloadditions. Adv. Synth. Catal. 358, 2604–2611 (2016).
37. Kang, Y. S. et al. Metal-organic frameworks with catalytic centers: From synthesis to catalytic application. Coord. Chem. Rev. 378, 262–280 (2019).
38. Timofeeva, M. N. et al. Metal-organic frameworks as efficient catalytic systems for the synthesis of 1, 5-benzodiazepines from 1, 2-phenylenediamine and ketones. J. Catal. 354, 128–137 (2017).
39. Kumar, G. et al. Covalently linked EONIS-Y in a Zr(IV) framework as visible-light mediated, heterogeneous photocatalyst for efficient CH functionalization of tertiary amines. J. Catal. 371, 298–304 (2019).
40. Wu, Y. et al. Metal-organic framework coated Fe3O4 magnetic nanoparticles with peroxidase-like activity for colorimetric sensing of cholesterol. Sens. Actuators B 249, 195–202 (2017).
41. Yin, L. L., Kong, X. Y., Zhang, Y. & Ji, Y. Q. Facile synthesis of the magnetic metal organic framework Fe3O4@UiO-66-NH2 for separation of strontium. Biomed. Environ. Sci. 31, 483–488 (2018).
42. Sepehrmansourie, H., Zarei, M., Zolfigol, M. A., Babae, S. & Rostamnia, S. Application of novel nanomagnetic metal–organic frameworks as a catalyst for the synthesis of new pyridines and 1, 4-dihydropyridines via a cooperative vinylogous anomic based oxidation. Sci. Rep. 11, 5279 (2021).
43. Gao, G., Di, J. Q., Zhang, H. Y., Mo, L. P. & Zhang, Z. H. A magnetic metal-organic framework material as a highly efficient and recyclable catalyst for synthesis of cyclohexenone derivatives. J. Catal. 387, 39–46 (2020).
44. Zhang, M., Liu, Y. H., Shang, Z. R., Hu, H. C. & Zhang, Z. H. Supported molybdenum on graphene oxide/Fe3O4: An efficient, magnetically separable catalyst for one-pot construction of spiro-oxadione dihydroxydipyrindines in deep eutectic solvent under microwave irradiation. Catal. Commun. 88, 39–44 (2017).
45. Chen, N. M., Mo, L. P., Cui, Z. S. & Zhang, Z. H. Magnetic nanocatalysts: synthesis and application in multicomponent reactions. Curr. Opin. Green Sustain. Chem. 15, 27–37 (2019).
46. Shiri, M., Zolfigol, M. A., Kruger, H. G. & Tanbakouchian, Z. Bis- and trisindolymethanes (BIMs and TIMs). Chem. Rev. 110, 2735–2793 (2010).
47. Shiri, M. Indoles in multicomponent processes (MCPs). Chem. Rev. 112, 3508–3549 (2012).
48. Arshad, M., Shoeb Khan, M., Asghar Nami, S. A. & Ahmad, D. Synthesis, characterization, computational, antimicrobial screening, and MITT assay of thiazolidinone derivatives containing the indole and pyridine moieties. Russ. J. Gen. Chem. 88, 2154–2162 (2018).
49. Desai, N. C. et al. Synthesis, biological evaluation and molecular docking study of some novel indole and pyridine based 1, 3, 4-oxadiazole derivatives as potential antitubercular agents. Bioorg. Med. Chem. Lett. 26, 1776–1783 (2016).
50. Grivsky, E. M., Lee, S., Sigel, C. W., Duchs, D. S. & Nichol, C. A. Synthesis and antitumor activity of 2, 4-diamino-6- (2, 5-dimethoxybenzyl)-5-methylpyrido [2,3-d] pyrimidine. J. Med. Chem. 23, 327–329 (1980).
51. Deb, M. L. & Bhuyan, P. J. Synthesis of novel classes of pyridine[2,3-d]pyrimidines, pyrano[2,3-d]pyrimidines, and pteridines. Synth. Commun. 36, 3085–3090 (2006).
52. Aliass, C., Grassot, J. M., Rodriguez, J. & Constantieux, T. Metal-free multicomponent syntheses of pyridines. Chem. Rev. 114, 10829–10868 (2014).
53. El-Borai, M. A., Rizk, H. F., Abd-Aal, M. F. & El-Deeb, I. Y. Synthesis of pyrazolo[3,4-b] pyridines under microwave irradiation in multi-component reactions and their antitumor and antimicrobial activities. Eur. J. Med. Chem. 48, 92–96 (2012).
54. Nikpassand, M., Fekri, L. Z. & Rahro, P. N. Catalyst-free grinding method: A new avenue for synthesis of 6-amino-3-methyl-4-hydroxy-1H-pyrazolo[3,4-b] pyridine-5-carbonitrile and DFT studies on the mechanistic pathway of this category of compounds. Res. Chem. Intermed. 45, 1707–1719 (2019).
55. Abdul-Malik, M. A., Zaki, R. M., KamalEl-Dean, A. M. & Radwan, S. M. A concise review on the synthesis and reactions of 3-amino-5-dimethoxybenzyl)-5-methylpyrido[2,3-d]pyrimidine. J. Med. Chem. 53, 1828–1833 (2010).
56. Iuardisti, E. & Cuebas, G. Recent studies on the anomic effect. Tetrahedron 48, 5019–5087 (1992).
57. Alabugin, I. V. et al. Stereoelectronic power of oxygen in control of chemical reactivity: The anomic effect is not alone. Chem. Soc. Rev. 50, 10253–10345 (2021).
58. Erhardt, J. M. & Wuest, J. D. Transfer of hydrogen from orthoaamides. Reduction of protons to molecular hydrogen. J. Am. Chem. Soc. 102, 6363–6364 (1980).
59. Atkins, T. J. Tricyclic trisaminomethanes. J. Am. Chem. Soc. 102, 6364–6365 (1980).
60. Erhardt, J. M., Grover, E. R. & Wuest, J. D. Transfer of hydrogen from orthoaamides. Synthesis, structure, and reactions of hexahydro-6bH-2a, 4a, 6a-triazacyclopenta[c]dentalenyl and perhydro-3a, 6a, 9a-triazaphelenalene. J. Am. Chem. Soc. 102, 6365–6369 (1980).
61. Brunet, P. & Wuest, J. D. Formal transfers of hydride from carbon-hydrogen bonds. Attempted generation of H2 by intramolecular protonolyses of the activated carbon-hydrogen bonds of dihydrobenzimidazoles. Can. J. Chem. 74, 689–696 (1996).
62. Zolfigol, M. A., Afsharnadery, F., Baghery, S., Salehzadeh, S. & Melki, M. Catalytic irradiation. Iran. J. Catal. 8, 79–83 (2017).
63. Karimi, F., Yarie, M. & Zolfigol, M. A. Synthesis and characterization of Fe3O4@SiO2(CH3)4NH(CH3)2O,P(OH)2, and its catalytic application in the synthesis of benzyl[4] quantum 4-carboxylic acids via a cooperative anomic based oxidation mechanism. Mol. Catal. 489, 110924 (2020).
64. Afsar, J. et al. Synthesis and application of melamine-based nano catalyst with phosphonic acid tags in the synthesis of (3-indoly) pyrazolo[3,4-b] pyridines via vinylogous anomic based oxidation. Mol. Catal. 482, 110666 (2020).
65. Jafari, M., Zarei, M., Zolfigol, M. A., Rostamnia, S. & Moosavi-Zare, A. R. SBA-15/PtN(CH2PO3H)3, as a novel and efficient mesoporous solid acid catalyst with phosphorous acid tags and its application on the synthesis of new pyrimido[4,5-b] quinolones and pyrido[2,3-d] pyrimidines via anomic based oxidation. Microporous Mesoporous Mater. 294, 109865 (2020).
Torabi, M.
Zolfigol, M. A.
Ghasemi, P., Yarie, M., Zolfigol, M. A. & Taherpour, A. A. Ionically tagged magnetic nanoparticles with urea linkers: Application for preparation of 2-aryl-quinoline-4-carboxylic acids via an anomic-based oxidation mechanism. *ACS Omega* **5**, 3207–3217 (2020).

Karimi, F., Yarie, M. & Zolfigol, M. A. A convenient method for synthesis of terpyridines via a cooperative vinylogous anomic based oxidation. *RSC Adv.* **10**, 25828–25835 (2020).

Dashteh, M. *et al.* Synthesis of cobalt tetra-2,3-pyridiniumporphyrinato with sulfonic acid tags as an efficient catalyst and its application for the synthesis of bicyclic ortho-aminocarbonitriles, cyclohexa-1, 3-dienamines and 2-amino-3-cyanopyridines. *RSC Adv.* **10**, 27824–27834 (2020).

Karimi, F., Yarie, M. & Zolfigol, M. A. FeO\(_2\)SiO\(_2\)(CH\(_2\))\(_3\)-urea-thiourea: a novel hydrogen-bonding and reusable catalyst for the construction of bipyridine-3-carbonitriles via a cooperative vinylogous anomic based oxidation. *Mol. Catal.* **489**, 111201 (2020).

Torabi, M. *et al.* Synthesis of new pyridines with sulfonamide moeity via a cooperative vinylogous anomic-based oxidation mechanism in the presence of a novel quinoline-based dendrimer-like ionic liquid. *RSC Adv.* **11**, 3143–3152 (2021).

Zolfigol, M. A. *et al.* A highly stable and active magnetically separable Pd nanocatalyst in aqueous phase heterogeneously catalyzed couplings. *Green Chem.* **15**, 2132–2140 (2013).

Babaei, S., Zolfigol, M. A., Zarei, M. & Zamanian, J. 10-Phenanthroline-based molten salt as a bifunctional sulfonic acid catalyst: Application to the synthesis of N-heterocycle compounds via anomic based oxidation. *ChemistrySelect* **3**, 8947–8954 (2018).

Kalhor, S. *et al.* Novel uric acid-based nano organocatalyst with phosphorous acid tags: Application for synthesis of new biologically-interest pyridines with indole moieties via a cooperative vinylogous anomic based oxidation. *Mol. Catal.* **507**, 111549 (2021).

Sepehrmansourie, H., Zarei, M., Taghavi, R. & Zolfigol, M. A. Mesoporous ionically tagged cross-linked poly(vinyl imidazole)s as novel and reusable catalysts for the preparation of N-heterocycle spiropyrans. *ACS Omega* **4**, 17379–17392 (2019).

Moosavi-Zare, A. R., Zolfigol, M. A., Zarei, M., Khakyzadeh, V. & Hasaninejad, A. Design, characterization and application of new ionic liquid 1-sulfopyridinium chloride as an efficient catalyst for tandem knoevenagel-michael reaction of 3-methyl-1-phenyl-1H-pyrazol-5(4H)-one with aldehydes. *Appl. Catal. A* **467**, 61–68 (2013).

Zolfigol, M. A. Silica sulfuric acid/NaNO\(_2\) as a novel heterogeneous system for production of thionitrites and disulfides under mild conditions. *Tetrahedron* **57**, 9509–9511 (2001).

Sepehrmansourie, H. Silica sulfonic acid (SSA): As a multipurpose catalyst. *Iran. J. Catal.* **10**, 175–179 (2020).

Sepehrmansourie, H. *et al.* Multilinker phosphorous acid anchored En/MIL-100(Cr) as a novel nanoporous catalyst for the synthesis of new N-heterocyclic pyrimido-[4,3-b]quinolines. *Mol. Catal.* **481**, 110303 (2020).

Zarei, M., Sepehrmansourie, H., Zolfigol, M. A., Karamian, R. & Moazzami Farida, S. H. Novel nano-size and crab-like biological-based glycoluril with sulfonic acid tags as a reusable catalyst: Its application to the synthesis of new mono-and bis-spiropyrans and their in vitro biological studies. *New. J. Chem.* **42**, 14308–14317 (2018).

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