Vietnam Journal of Catalysis and Adsorption
Tạp chí xúc tác và hấp phụ Việt Nam

http://chemeng.hust.edu.vn/jca/

Metal-organic framework-118 (MOF-118): A heterogeneous catalyst for effective synthesis of pyrroles from aryl amines and 2,5-hexanedione

Nguyen Van Chi,[1] Nguyen Thanh Tung,[2,3] Nguyen Thi Hong Huong,[4] Ca Thi Thuy, [2,3] and Phan Thanh Son Nam[2,3*]

[1] *Institute of Applied Science and Technology, Van Lang University, Vietnam.*
[2] *Faculty of Chemical Engineering, Ho Chi Minh City University of Technology (HCMUT), Vietnam*
[3] *Vietnam National University Ho Chi Minh City, Vietnam.*
[4] *Faculty of Medicine and Pharmacy, Van Lang University, Vietnam.*
**Email: ptsnam@hcmut.edu.vn*

ARTICLE INFO

Received: 31/7/2020
Accepted: 25/8/2020

Keywords:
Metal-Organic Frameworks, MOF-118; Pyrroles synthesis, 2,5-hexandione, p-anisidine, heterogeneous catalyst.

ABSTRACT

Metal-organic frameworks (MOFs) have been widely used in many applications, particularly catalysis. Here, we reported the synthesis and characteristics of metal–organic framework-118 (MOF-118), which was used for pyrroles synthesis via Paal-Knorr reaction between diketone and aryl amines. It was found that MOF-118 exhibited excellent activity in the reaction between p-anisidine and 2,5-hexanedione. The reaction parameters including catalyst concentrations, reaction temperatures, molar ratio of p-anisidine/2,5-hexadione, and solvents, were systematically investigated. Almost 100% conversion was achieved under the optimized reaction conditions. The reusability of MOF-118 catalyst was studied. Furthermore, we demonstrated that the functional groups on aryl amines have strongly effect on the reaction rate.

Introduction

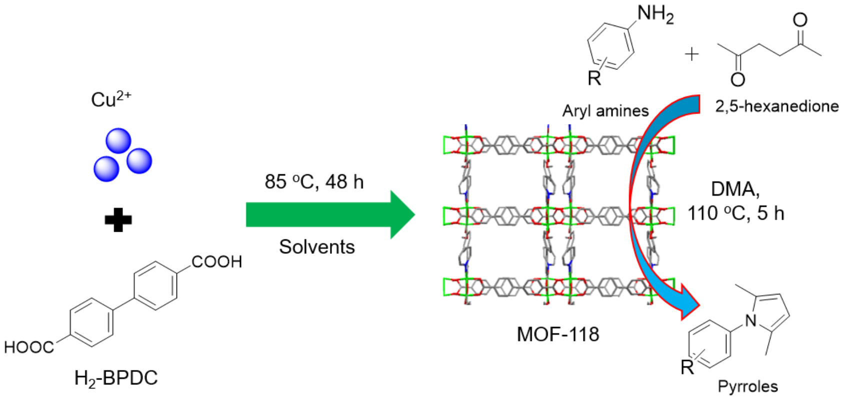
Pyrroles and their derivatives, an important class of heterocyclic compounds have been widely used in many applications such as polymer synthesis [1], optical molecules [2], and gas sensor [3]. In addition, they exhibited varieties of biological activities, including antibacterial [4], anti-inflammatory [5], and antioxidant activities [6]. Thus, the synthesis of pyrroles has been attracted intensive attentions. The general methods for pyrroles preparation included the Pall-Knorr [7], Hantszch [8], Knorr [9], aza-Witting reaction [10]. Among these methods, the Paal-Knorr reaction, a direct cyclocondensation of amines and γ-diketones, was commonly used for the synthesis of N-substituted pyrroles [11-13].

The Paal-Knorr reaction could be promoted via various acidity catalysts, including mineral acids [14], metal salts [15], metal oxides [16], zeolite [17], and montmorillonite [18]. In addition, this reaction was carried out in ion liquid media [7], or under assisting microwave [19] and ultrasonic [20]. Despite showing high catalytic activity, these catalytic systems require an excess amount of catalysts and reagents, which caused purification issues and generation a large amount metal-containing waste. Moreover, unsatisfactory yields, the used of costly solvent (i.e. ion liquids), microwave- or ultrasound-assisted, and prolonged reaction times were the drawbacks in the previous reports. Therefore, the development of efficient and reusable catalyst is still demanding.

https://doi.org/10.51316/jca.2020.061

Recently, metal-organic framework (MOFs), the class of highly porous materials, have attracted remarkable interests in catalysis applications due to their abundant and tunable catalytic active sites [21-23]. MOFs exhibited superior catalytic activities for many organic transformations, including the Fried-Crafts alkylation [24], Knoevenagel reaction [25], asymmetric alkylation of aldehydes [26], oxidation [27], coupling reaction [28], aza-Michael condensation [29], N-methylation of aromatic primary amines [30], epoxide ring-opening reaction [31]. In addition, facile separation from the reaction mixture and reusability potential make MOF become a promising heterogeneous catalyst for catalysis application.

In this work, we aim to investigate the synthesis and characterizations of MOF-118 and applied as heterogeneous catalyst for Paal-Knorr reaction between 2,5-hexanedione and aryl amines to form N-substituted pyrroles (Scheme 1). MOF-118 was synthesized by the reaction between copper nitrate and 4-4′-dicaboxylic acid in the solvothermal condition [32]. The physical and chemical properties of synthesized MOF-118 were characterized using XRD, FT-IR, TGA, SEM, N_2 adsorption/desorption, and AAS. The MOF-118 showed highly active for the pyrroles synthesis at mild reaction conditions.



Scheme 1: Illustration of MOF-118 synthesis and its catalytic activity for Paal-Knorr reaction

Materials and methods

Chemicals

$Cu(NO_3)_2.3H_2O$ (99%), Biphenyl 4-4′-dicaboxylic acid (H_2BPDC, 98%), N-N dimethylacetamide (DMA), dimethylformamide (DMF), dimethylsulfoxide (DMSO), p-xylene, p-anisidine (99%), 2,5-hexanedione (99%) were purchased from Arcos, Merck, and Sigma-Aldrich company. All chemicals were directly used without purification.

Instrumentations

The crystal structure of the samples was recorded using powder X-ray diffraction (XRD - Bruker AXS D8 Advantage). The FT-IR spectra was analysed on Bruker Optics Tensor37. The morphology of the samples was monitored by scanning electron microscopy (SEM, JEOL JSM- 7401F TEM). TGA analysis was performed in the N_2 gas with the heating rate of 10 °C/ min to 800 °C (NETZCH STA 409 P). The copper content in the MOF-118 was determined by atomic absorption spectroscopy (AAS). Gas chromatographic (GC, Shimadzu GC 2010-Plus) with a flame ionization detector (FID) and an SPB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 µm), was used to monitor the reaction.

Synthesis of MOF-118

MOF-118 was synthesized analogous to the previous report with slightly modification [32]. Typically, $Cu(NO_3)_2.3H_2O$ (0,026g, 0,11 mmol) and 4-4′-dicaboxylic acid (H_2BPDC, 0,027g, 0,11 mmol) were dissolved in DMA/methanol/pirydine (20.5 mL, 15:5:0.5 v/v). The mixture was heat at 85 °C for 48 h and then cooled at room temperature. The green solid was collected by washing with DMA (5 mL x 3) and dichloromethane (DCM, 5 mL x 2), then activated under vacuum at 100 °C in 5 h.

Catalytic studies

In a typical reaction, *p*-anisidine (0.12 g, 1 mmol), 2,5-hexanedione (0.24 mL, 2 mmol), and n-dodecane (0.15 mL) as internal standard were added to the three-neck flask containing 5 mL DMA and MOF-118 (3 %mol) as the solvent and catalyst, respectively. The catalyst concentration was calculated with respect to the copper/*p*-anisidine molar ratio. The reaction mixture was heated at 110 °C. The reaction conversion was

https://doi.org/10.51316/jca.2020.061

monitored by withdrawing aliquots from the reaction mixture at different time intervals. The withdrawn solution was diluted with diethyl ether, and dried with anhydrous Na_2SO_4 before gas chromatographic (GC) analysis. The products were confirmed by GC–MS.

Results and discussion

Characterization of MOF-118

As shown in Fig. 1a, the XRD pattern of as-synthesized MOF-118 displays diffraction peaks at 2θ = 5.9°, 6.2°, 10.14°, 12.4°, 18.7°, which was similar to those simulated from single crystal X-ray structure reported in the previous literature [32]. The sharp peak indicates the as-synthesized product with high purity. It is noticed that the XRD of as-synthesized MOF-118 also exhibited several extra peaks, resulting from polycrystalline structure of MOF-118. Interestingly, the diffraction peaks of MOF-118 are changed after activation (Fig. 1a). We suppose that this phenomenon could be caused by the removal of solvent out MOF-118, which can reveal the open-metal active site for catalytic performance [33]. The FT-IR spectrum of MOF-118 shown the C=O vibration frequency ($\upsilon_{C=O}$) at 1657 cm^{-1} while this values is 1689 cm^{-1} in the free H_2BPDC ligand, suggesting the bonding formation between Cu^{2+} and the carboxylic acid (Fig. 1b). Further, the TGA analysis was performed to determine the thermal stability of MOF-118. The TGA result shown that MOF-118 can be stable at temperature of 270 °C (Fig. 1c). SEM image revealed the rod-like morphologies of MOF-118 with the length of 200 µm and the width of 40 µm (Fig. 1d). The copper content in MOF-118 was detected by AAS, to be 21.9 wt%, which was similar to that of the theoretical calculation (i.e. 21.1 wt%). These results indicated that MOF-118 was successfully synthesized.

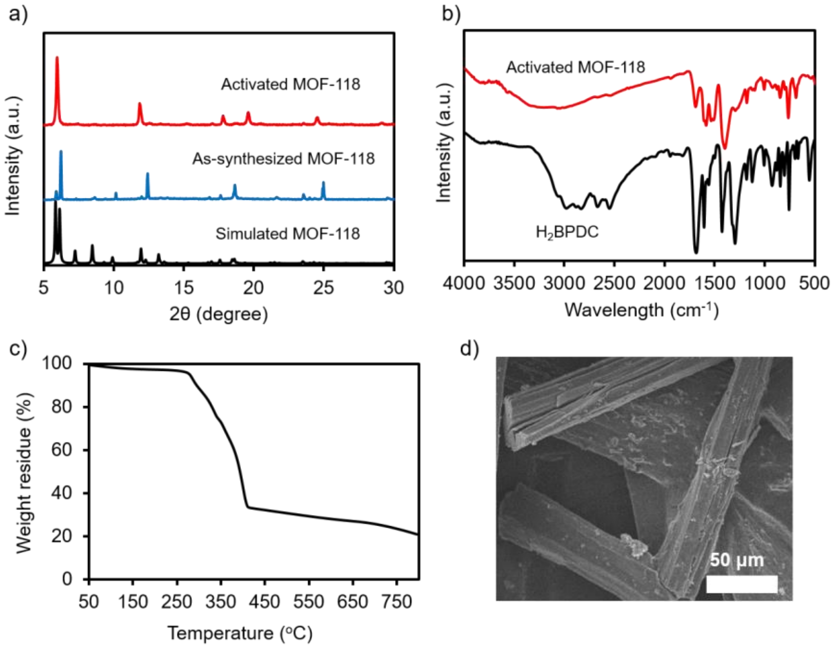
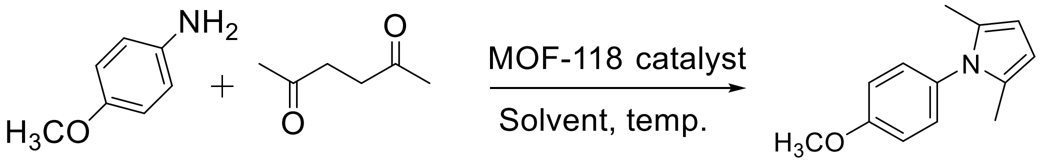


Fig. 1: a) XRD patterns, b) FT-IR spectra, c) TGA analysis, and d) SEM image of MOF-118

Catalytic studies

The Paal-Knorr reaction between p-anisidine and 2,5-hexanedione was carried out at different reaction conditions (Table 1). Extremely low p-anisidine conversion (2.1 %) was observed in the absence of catalyst (Table 1, Entry 1). As expected, MOF-118 was highly active for the reaction, the conversion significantly enhanced with 78.2 % in the presence of 1 mol% MOF-118 catalyst at 110 °C for 6 h (Table 1, entry 2). The reaction conversion was additionally increased, corresponding to increasing of MOF-118 concentration. The reaction conversion achieved 96.6% and 97.5% using 3 and 5 mol% catalyst, respectively (Table 1, entry 3-4). This result confirmed that MOF-118 played crucial role for the reaction. Moreover, the reaction conditions including reaction temperatures, time, and molar ratio of the reactant were scanned (Table 1, entry 6-11). The tested results indicated that an affordable conversion (96.6%) could be obtained using 3 mol% MOF-118 catalyst and DMF solvent, with the molar ratio of p-anisidine/2,5-hexanedione of 1:2 at 110 °C for 6 h. The obtained reaction parameters were in good agreement with the previous reports [16, 34].

Table 1: Paal-Knorr reaction between p-anisidine and 2,5-hexanedione over MOF-118 catalyst



Entry	Catalyst loading (mol%)	2,5-hexanedione (equiv)	Temperature (°C)	Time (h)	Conversion (%)
1	Non	2.0	110	6	2.1
2	1.0	2.0	110	6	78.2
3	3.0	2.0	110	6	96.6
4	5.0	2.0	110	6	97.5
5	3.0	2.0	100	6	81.4
6	3.0	2.0	90	6	37.0
7	3.0	2.0	80	6	28.1
8	3.0	2.0	110	4	81.0
9	3.0	2.0	110	2	44.0
10	3.0	1.1	110	6	54.4
11	3.0	1.15	110	6	90.0

Reaction condition: the reaction was carried out with 1 mmol p-anisidine over MOF-118 catalyst using 5 mL DMF and 0.15 mL n-dodecane as solvent and internal standard. The amount of MOF-118 catalyst was calculated based on the molar ratio of Cu/p-anisidine.

Further, we investigated the effect of solvents on the reaction of p-anisidine and 2,5-hexanedione. The solvent testing results displayed that the reaction was accelerated rapid in DMSO, DMA, and DMF than in p-xylene (Fig. 2). After reaction time of 3 h, the reaction conversion was observed to be 59.5%, 77.1%, 91.2%, and 100% in the solvent including p-xylene, *N,N'*-dimethylformamide (DMF), N-N dimethylacetamide (DMA), and dimethylsulfoxide (DMSO), respectively. Although, DMSO exhibited the highest effective for the Paal-Knorr reaction between p-anisidine and 2,5-hexanedione, the MOF-118 was collapsed during the reaction condition. In contrast, the MOF-118 structure still remained in the p-xylene, DMA and DMF solvent. In addition, 100% reaction conversion could achieve in the DMA solvent for 5 h reaction time. Thus, the DMA was the best solvent for the reaction.

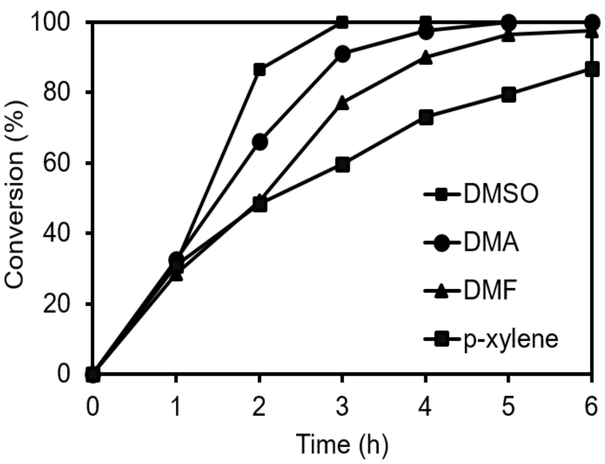


Fig. 2: The effect of solvent on the Pall-Knorr reaction. Reaction condition: p-anisidine (1 mmol), 2,5-hexanedione (2 mmol), 3 mol% MOF-118 catalyst, 110 °C, 5 mL solvent.

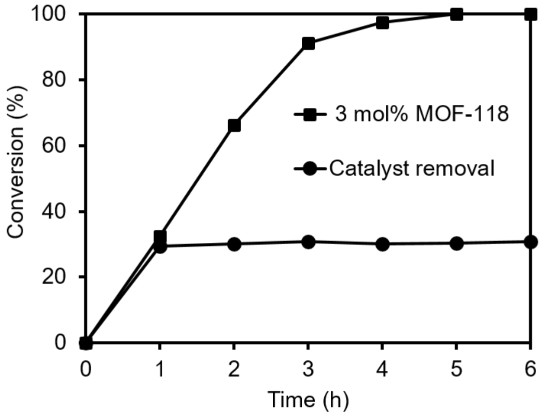


Fig. 3: Leaching test of the Pall-Knorr reaction over MOF-118 catalyst.

As for most liquid-phase organic transformations using solid catalysts, the active sites could be possibly leaked into the reaction mixture, causing purification issues and decrease catalytic activity in the next usage [25], thus, leaching test was conducted. The Pall-Knorr reaction between p-anisidine and 2,5-hexanedione was performed in DMA solvent at 110 °C, using 3 mol% MOF-118 catalyst and p-anisidine/2,5hexanedione molar ratio of 1:2. After 1 h reaction time, the solid catalyst was separated from the reaction mixture by simple centrifugation, then the organic phase was transferred to the new three-neck flash. The reaction mixture was stirred for additional 5 h at 110 °C. The aliquots were withdrawn at different time intervals, and analyzed by GC. As shown in Fig. 3, the p-anisidine conversion remained unchanged (29.5%) after removal of the MOF-118 catalyst. The result clearly confirmed that the reaction of *p*-anisidine and 2,5-hexanedione proceeded in the presence of the solid MOF-118 catalyst, and copper ions of the MOF-118 did not leak out in the liquid phase.

A great significance of using MOFs as solid catalyst was their facile recoverability and efficient reusability [27, 35]. Hence, we investigated the recyclability of MOF-118 catalyst in the Paal-Knorr reaction. After each catalysis run, the MOF-118 catalyst was centrifuged from the reaction mixture. The obtained solids were washed with known amounts of DMA and DCM to remove adsorbed reagents, dried at 100 °C under vacuum in 4 h. The catalyst was then reused in further catalysis runs under the identical reaction conditions. It can be seen that MOF-118 can be reused five times without a significant loss in catalytic activity (Fig. 3b). The XRD pattern of the reused MOF-118 catalyst was similar to that of the fresh MOF-118, indicating that MOF-118 was stable during the reaction conditions.

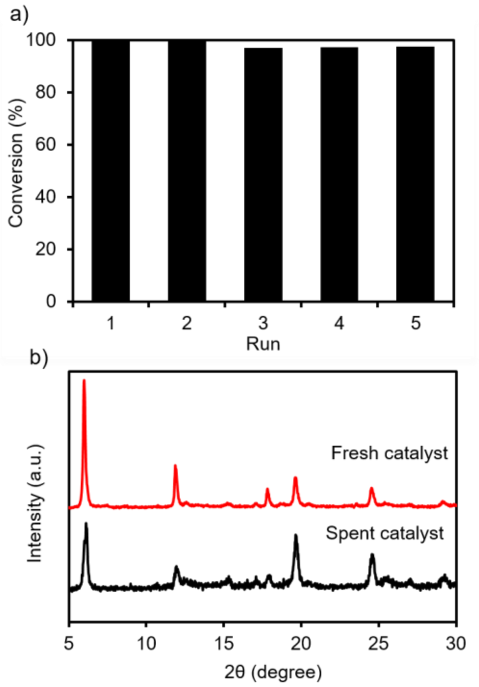


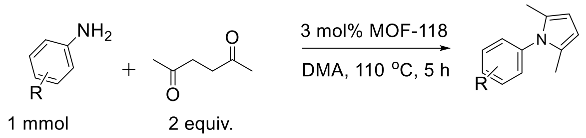
Fig. 4: a) Recycle testing of MOF-118 catalyst in the Pall-Knorr reaction; reaction condition: p-anisidine (1 mmol), 2,5-hexanedione (2 mmol), 5 mL DMA as solvent, 0.15 mL n-dodecane as internal standard, 3 mol% MOF-118. b) the XRD patterns of the fresh and spent MOF-118 catalyst.

For extensive study, we further conducted the Paal-Knorr reaction of 2,5-hexanedione with different aryl amines (such as p-anisidine, m-anisidine, o-anisidine, aniline, p-toluidine, 4-bromoaniline) using MOF-118 as catalyst (Table 2). It was found that the substitutional groups on aryl amines structure have strongly effect on the reaction conversion. Aryl amines containing electron-donating p-OCH_3 and p-CH_3 substituents exhibited the excellent conversion, achieving the reaction conversion of 100% and 95.1% for 5 h, respectively (Table 2, entries 1, 2). A lower conversion was observed for aryl amines with electron-withdrawing group and without substituent, to be aniline (50.9%) and 4-bromoaniline (21.2%) (Table 2, entries 3, 4). Our result was in good agreement with the previous reports [36, 37], showing that amines containing the electron-rich groups exhibited higher pyrroles yield, compared to the amines coupling with the electron-deficient groups. Interestingly, the positions of substituents in the aryl amines have significantly contributed to the Pall-Knorr reaction conversion. Aniline comprising the methoxy group (-OCH_3) at its *para* position enhanced noticeable reaction rate, with 100% conversion in 5 h (Table 2, entry 1). In contrast, the methoxy substituent at *meta*

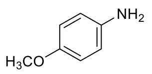
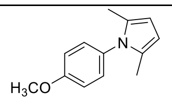
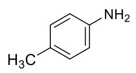
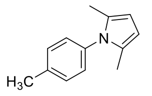
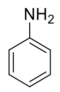
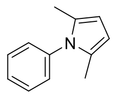
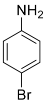
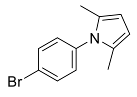
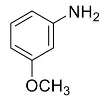
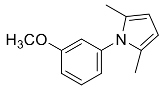
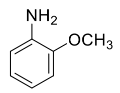
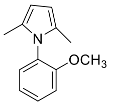
https://doi.org/10.51316/jca.2020.061

and *ortho* in aniline decreased significant conversion to 36.8% and 15.4% for m-anisidine and o-anisidine, respectively (Table 2, entries 5, 6).

Table 2: Substrate scope for the Pall-Knorr of amines with 2,5-hexanedione using MOF-118 as catalyst.



R = H, CH_3, NH_2, Br

Entry	Aryl amines	Products	Conversion (%)
1			100
2			95.1
3			50.9
4			21.2
5			36.8
6			15.4

Conclusion

In summary, we reported the synthesis of MOF-118 catalyst and studied its catalytic activity for the Paal-Knorr reaction. The crystalline porous MOF-118 was prepared by the reaction between copper (II) nitrate trihydrate and 4,4' biphenyldicarboxylic acid in DMA as solvent. Various characterizations, including XRD, SEM, FT-IR, TGA analysis, and AAS, were conducted for MOF-118. The MOF-118 exhibited the excellent catalytic activities for the Paal–Knorr reaction of p-anisidine with 2,5-hexanedione to form 2,5-dimethyl-1-phenyl-1H-pyrrole as the major product. Under the optimized conditions, the reaction conversion achieved to be 100% in the presence of 3 mol% MOF-118 using DMA as solvent at 100 °C in 5 h, with p-anisidine/2,5hexanedione molar ratio of 1:2. Moreover, the MOF-118 catalyst could be reused five times without a significant decrease in catalytic activity. Further, we extended to the Paal-Knorr reaction of 2,5-hexanedione with different substituents on the aryl amines. Our work contributed to catalysis application of the porous metal–organic frameworks (MOFs), which could be interested to the organic synthesis and heterogeneous catalysis.

Acknowledgments

The Viet Nam National Foundation for Science and Technology Development (NAFOSTED) is acknowledged for supporting this research under Project code 104.01-2019.340 (for Nam T. S. Phan).

References

1. C.-F. Lee, L.-M. Yang, T.-Y. Hwu, A.-S. Feng, J.-C. Tseng, and T.-Y. Luh, J. Am. Chem. Soc., 122 (2000) 4992-4993. https://doi.org/10.1021/ja0004736
2. R.M.F. Batista, S.P.G. Costa, E.L. Malheiro, M. Belsley, and M.M.M. Raposo, Tetrahedron, 63 (2007) 4258-4265. https://doi.org/10.1016/j.tet.2007.03.065
3. B.P.J.d.L. Costello, P. Evans, N. Guernion, N.M. Ratcliffe, and P.S. Sivanand, Synthetic Metals, 114 (2000) 181-188. https://doi.org/10.1016/S0379-6779(00)00250-2
4. G. Dannhardt, W. Kiefer, G. Kramer, S. Maehrlein, U. Nowe, and B. Fiebich, Eur. J. Med. Chem. , 35 (2000) 499-510. https://doi.org/10.1016/S0223-5234(00)00150-1
5. Y. Harrak, G. Rosell, G. Daidone, S. Plescia, D. Schillaci, and M.D. Pujol, Bioorg. Med. Chem., 15 (2007) 4876-4890. https://doi.org/10.1016/j.bmc.2007.04.050
6. J. Lehuede, B. Fauconneau, L. Barrier, M. Ourakow, A. Piriou, and J.-M. Vierfonf, Eur. J. Med. Chem., 34 (1999) 991-996. https://doi.org/10.1016/S0223-5234(99)00111-7
7. B. Wang, Y. Gu, C. Luo, T. Yang, L. Yang, and J. Suo, Tetrahedron Lett., 45 (2004) 3417-3419. https://doi.org/10.1016/j.tetlet.2004.03.012
8. V.F. Ferreira, M.C.B.V.d. Souza, A.C. Cunha, L.O.R. Pereira, and M.L.G. Ferreira, Org. Prep. Proced. Int. , 33 (2002) 411-454. https://doi.org/10.1080/00304940109356613
9. I. Elghamry, Synth. Commun., 32 (2002) 897-902. https://doi.org/10.1081/SCC-120002701
10. A.R. Katritzky, J. Jiang, and P.J. Steel, J. Org. Chem., 59 (1994) 4551-4555. https://doi.org/10.1021/jo00095a034
11. V. Polshettiwar and R.S. Varma, Tetrahedron, 66 (2010) 1091-1097. https://doi.org/10.1016/j.tet.2009.11.015
12. J.S. Yadav, B.V.S. Reddy, B. Eeshwaraiah, and M.K. Gupta, Tetrahedron Lett., 45 (2004) 5873–5876. https://doi.org/10.1016/j.tetlet.2004.05.152
13. B.C. Ranu and S.S. Dey, Tetrahedron Lett., 44 (2003) 2865-2868. https://doi.org/10.1016/S0040-4039(03)00439-8
14. S.E. Drewes and C.J. Hogan, Synth. Commun., 19 (1989) 2101-2107. https://doi.org/10.1080/00397918908052604

15. S.K. De, Heteroatom Chem, 10 (2008) 592-595. https://doi.org/10.1002/hc.20482
16. k.K. Pasha, V.S.V. Satyanarayana, A. Sivakumar, K. Chidambaram, and L.J. Kennedy, Chinese Chemical Letters 22 (2011) 891–894. https://doi.org/10.1016/j.cclet.2010.12.053
17. R. Sreekumar and R. Padmakumar, Synth. Commun., 28 (1998) 1661-1665. https://doi.org/10.1080/00397919808006870
18. M. Abid, A. Spaeth, and B. Török, Adv. Synth. Catal. , 348 (2006) 2191-2196. https://doi.org/10.1002/adsc.200606200
19. G. Minetto, L.F. Raveglia, A. Sega, and a.M. Taddei, Eur. J. Org. Chem., (2005) 5277–5288. https://doi.org/10.1002/ejoc.200500387
20. D. Bandyopadhyay, S. Mukherjee, J.C. Granados, J.D. Short, and B.K. Banik, Eur. J. Med. Chem. , 50 (2012) 209-215. https://doi.org/10.1016/j.ejmech.2012.01.055
21. J. Jiang and O.M. Yaghi, Chem. Rev., 115 (2015) 6966-6997. https://doi.org/10.1021/acs.chemrev.5b00221
22. X. Li, Y. Liu, J. Wang, J. Gascon, J. Li, and B.V.d. Bruggen, Chem. Soc. Rev., 46 (2017) 7124-7144. https://doi.org/10.1039/C7CS00575J
23. J.J.P. IV, J.A. Perman, and M.J. Zaworotko, Chem. Soc. Rev., 38 (2009) 1400-1417. https://doi.org/10.1039/B807086P
24. N.T.S. Phan, K.K.A. Le, and T.D. Phan, Applied Catalysis A: General, 382 (2010) 246-253. https://doi.org/10.1016/j.apcata.2010.04.053
25. U.P.N. Tran, K.K.A. Le, and N.T.S. Phan, ACS Catalysis, 1 (2011) 120-127. https://doi.org/10.1021/cs1000625
26. P. Wu, C. He, J. Wang, X. Peng, X. Li, Y. An, and C. Duan, J. Am. Chem. Soc., 134 (2012) 14991-14999. https://doi.org/10.1021/ja305367j
27. A. Dhakshinamoorthy, M. Alvaro, and H. Garcia, ACS Catalysis 1(2011) 48-53. https://doi.org/10.1021/cs1000703
28. T.A. To, C.B. Tran, N.T.H. Nguyen, H.H.T. Nguyen, A.T. Nguyen, A.N.Q. Phan, and N.T.S. Phan, RSC Advances, 8 (2018) 17477-17485. https://doi.org/10.1039/C8RA02389A
29. M. Savonnet, S. Aguado, U. Ravon, D. Bazer-Bachi, V. Lecocq, N. Bats, C. Pinel, and D. Farrusseng, Green Chem., 11 (2009) 1729-1732. https://doi.org/10.1039/B915291C
30. A. Dhakshinamoorthy, M. Alvaro, and H. Garcia, Appl. Catal. A, 378 (2010) 19-25. https://doi.org/10.1016/j.apcata.2010.01.042
31. K. Tanaka, S. Oda, and M. Shiro, Chem. Commun., 44 (2008) 820-822. https://doi.org/10.1039/B714083E
32. H. Furukawa, J. Kim, N.W. Ockwig, M. O'Keeffe, and O.M. Yaghi, J. Am. Chem. Soc. , 130 (2008) 11650-11661. https://doi.org/10.1021/ja803783c
33. Y. Li, L.-J. Wang, H.-L. Fan, J. Shangguan, H. Wang, and J. Mi, Energy Fuels, 29 (2015) 298-304. https://doi.org/10.1021/ef501918f
34. Z.-H. Zhang, J.-J. Li, and T.-S. Li, Ultrasonics Sonochemistry, 15 (2008) 673-676. https://doi.org/10.1016/j.ultsonch.2008.02.008
35. S.H. Doan, C.B. Tran, A.L.N. Cao, N.T.H. Le, and N.T.S. Phan, Catalysis Letters, 149 (2019) 2053-2063. https://doi.org/10.1007/s10562-019-02747-1
36. A. Rahmatpour, Appl. Organometal. Chem., 25 (2011) 585-590. https://doi.org/10.1002/aoc.1806
37. B.K. Banik, I. Banik, M. Renteria, and S.K. Dasgupta, Tetrahedron Lett., 46 (2005) 2643–2645. https://doi.org/10.1016/j.tetlet.2005.02.103