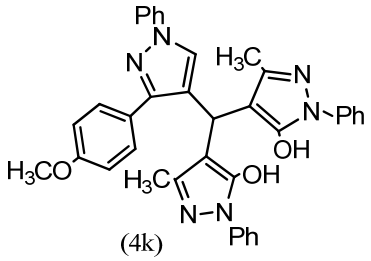
Table 2. Morpholinium glycolate catalyzed synthesis of bis(pyrazol-5-ol) derivatives (4a-k).[a]

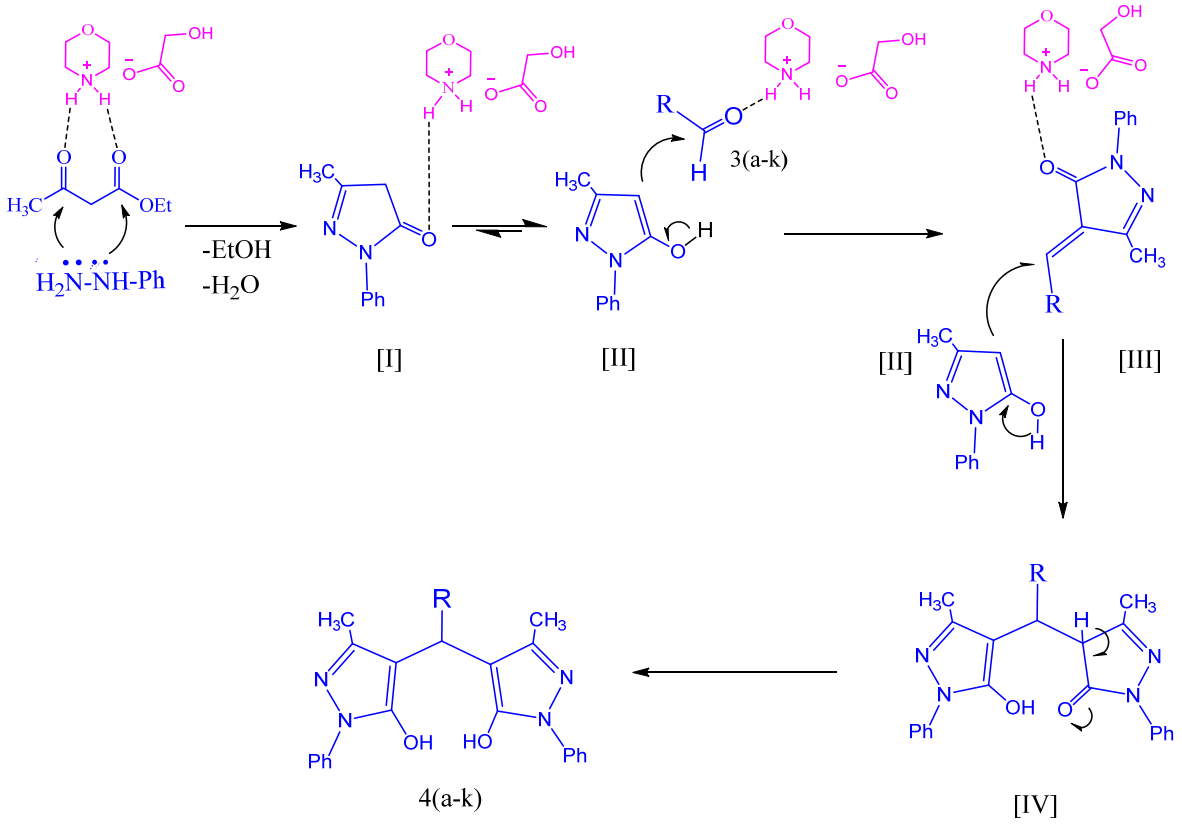
Entry	R	Product	Time (min)[b]	Yield (%)[c]	m.p. (°C)		Ref.
					Found	Reported	
1	C_6H_5	4a	10	90	170-172	171-172	[37]
2	4-ClC_6H_4	4b	5	96	208-210	207-209	[37]
3	2-ClC_6H_4	4c	8	91	234-236	236-237	[37]
4	4-$NO_2C_6H_4$	4d	6	96	229-231	230-232	[37]
5	3- $NO_2C_6H_4$	4e	9	92	149-150	148-150	[35]
6	4-$CH_3C_6H_4$	4f	10	90	200-202	201-202	[35]
7	4-$CH_3OC_6H_4$	4g	12	90	171-173	171-173	[43]
8	4-HOC_6H_4	4h	12	89	154-156	155-157	[38]
9	2-HOC_6H_4	4i	12	85	225-227	227-229	[38]
10	2-furyl-	4j	9	86	188-190	187-189	[43]
11	3k	 (4k)	10	92	198-200	New	This work

[a]Reaction conditions: Ethyl acetoacetate (2 mmol), phenyl hydrazine (2 mmol) and aldehydes (1mmol) catalyzed by 15 mol% morpholinium glycolate under solvent-free conditions at 80 °C.
[b]Reaction progress monitored by TLC.
[c]Isolated yield.

Table 3. Comparison of catalytic activity of Morpholinium glycolate with different ILs in the synthesis of (4a) under solvent-free conditions.

Entry	Ionic liquids as catalyst	Amount of catalyst (mol%)	Temp. (°C)	Time (min)	Yield (%)[a]	Ref.
1	N-Methylimidazolium perchlorate [MIm]ClO_4	5.4	50	37	90	[43]
2	1-(carboxymethyl)pyridinium chloride [cmpy]Cl	10	110	17	82	[42]
3	2-Hydroxy ethylammonium propionate (2-HEAP)	10	90	30	91	[45]
4	[Et_3NH]HSO_4	10	90	45	90	[41]
5	Na+-MMT-[pmim]HSO_4	5	100	14	91	[39]
6	Morpholinium glycolate	15	80	10	90	This work

[a]Isolated yield.



Scheme 3. The proposed mechanism for the synthesis of bis(pyrazol-5-ol) derivatives 4(a-k) using morpholinium glycolate as the catalyst.

3.3. Catalyst reusability

The reusability of morpholinium glycolate in the reaction of ethyl acetoacetate, phenyl hydrazine and benzaldehyde under the optimized reaction conditions was investigated for five runs. After completion of the reaction, 5 mL water was added, and the solid product was separated by simple filtration. The filtrate containing morpholinium glycolate was concentrated under reduced pressure. Then the recovered catalyst was washed with cyclohexane, dried and used directly for subsequent reaction with no considerable drop in its catalytic activity. (The yields for five runs were 91, 91, 90, 88 and 86 %, respectively).

4. Conclusions

In outline, the catalyst morpholinium glycolate was fabricated from the commercially available low-cost reagents. Further, their catalytic activity was explored for the synthesis of bis(pyrazol-5-ol) (**4a-k**) derivatives. The solvent-free conditions, utilization of homogeneous reusable catalyst, shorter reaction times, clean and straightforward work up, and excellent yields of the products are the notable features of the current protocol.

Acknowledgments

The authors are grateful to the principal of Maualna Azad College, Aurangabad for providing the laboratory facilities. We are also thankful to the SAIF Panjab University, Chandigarh and STIC Cochin University of Science & Technology, Cochin for spectral analysis.

References

[1] P.T. Anastas, J.C. Warner, Green Chemistry: Theory and Practice, Oxford University Press, Oxford, 1998.
[2] L.F. Tietze, A. Modi, Med. Res. Rev. 20 (2000) 304-322.
[3] I. Ugi, A. Domling, B. Werner, J. Heterocycl. Chem. 37 (2000) 647-658.
[4] K. Tanaka, G. Kaupp, Solvent-free organic synthesis, John Wiley & Sons, 2009.
[5] T. Welton, Chem. Rev. 99 (1999) 2071-2084.
[6] P. Walden, Bull. Acad. Imper. Sci. St. Petersburg 1800 (1914) 405-422.
[7] M.J. Earle, K.R. Seddon, Pure Appl. Chem. 72 (2000) 1391-1398.
[8] N.V. Plechkova, K.R. Seddon, Ionic Liquids: "Designer" Solvents for Green Chemistry, in: Methods and Reagents for Green Chemistry: An Introduction, 2007, pp. 103-130.
[9] P. Wasserscheid, W. Keim, Angew. Chem. Int. Ed. 39 (2000) 3773-3789.
[10] C.M. Gordon, Appl. Catal. A 222 (2001) 101-117.

[11] D. Zhao, M. Wu, Y. Kou, E. Min, Catal. Today 74 (2002) 157-189.
[12] V.I. Pârvulescu, C. Hardacre, Chem. Rev. 107 (2007) 2615-2665.
[13] K. Biswas, C.N.R. Rao, Chem. Eur. J. 13 (2007) 6123-6129.
[14] T. Ichikawa, M. Yoshio, A. Hamasaki, T. Mukai, H. Ohno, T. Kato, J. Am. Chem. Soc. 129 (2007) 10662-10663.
[15] P. Hapiot, C. Lagrost, Chem. Rev. 108 (2008) 2238-2264.
[16] F. van Rantwijk, R.A. Sheldon, Chem. Rev. 107 (2007) 2757-2785.
[17] H. Zhao, Chem. Eng. Commun. 193 (2006) 1660-1677.
[18] X. Han, D.W. Armstrong, Acc. Chem. Res. 40 (2007) 1079-1086.
[19] J.G. Huddleston, H.D. Willauer, R.P. Swatloski, A.E. Visser, R.D. Rogers, Chem. Commun. (1998) 1765-1766.
[20] H. Zhao, S. Xia, P. Ma, J. Chem. Technol. Biotechnol. 80 (2005) 1089-1096.
[21] J. Pernak, N. Borucka, F. Walkiewicz, B. Markiewicz, P. Fochtman, S. Stolte, S. Steudte, P. Stepnowski, Green Chem. 13 (2011) 2901-2910.
[22] J. Elguero, P. Goya, N. Jagerovic, A.M.S. Silva, Targets Heterocycl. Syst. 6 (2002) 52-98.
[23] E. McDonald, K. Jones, P.A. Brough, M.J. Drysdale, P. Workman, Curr. Top. Med. Chem. 6 (2006) 1193-1203.
[24] M.A. Zolfigol, A. Khazaei, F. Karimitabar, M. Hamidi, Appl. Sci. 6 (2016) 1-9.
[25] P.C. Lv, J. Sun, Y. Luo, Y. Yang, H.L. Zhu, Bioorg. Med. Chem. Lett. 20 (2010) 4657-4660.
[26] G. Mariappan, B.P. Saha, L. Sutharson, A. Haldar, Indian J. Chem. Sect. B: Org. Chem. Incl. Med. Chem. 49 (2010) 1671-1674.
[27] D.M. Bailey, P.E. Hansen, A.G. Hlavac, E.R. Baizman, J. Pearl, A.F. DeFelice, M.E. Feigenson, J. Med. Chem. 28 (1985) 256-260.
[28] G. Mariappan, B.P. Saha, L. Sutharson, A. Singh, S. Garg, L. Pandey, D. Kumar, Saudi Pharm. J. 19 (2011) 115-122.
[29] L.C. Behr, R. Fusco, C.H. Jarboe, The Chemistry of Heterocyclic Compounds, Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles, and Condensed Rings, A. Weissberger, (Ed.); Interscience, New York, 1967.
[30] D. Castagnolo, A. De Logu, M. Radi, B. Bechi, F. Manetti, M. Magnani, S. Supino, R. Meleddu, L. Chisu, M. Botta, Bioorg. Med. Chem. 16 (2008) 8587-8591.
[31] M. Londershausen, Pestic. Sci. 48 (1996) 269-292.
[32] D. Singh, D. Singh, J. Indian Chem. Soc. 68 (1991) 165-167.
[33] C. Pettinari, F. Marchetti, R. Pettinari, A. Drozdov, S. Troyanov, A.I. Voloshin, N.M. Shavaleev, J. Chem. Soc. Dalton Trans. (2002) 1409-1415.
[34] H. Banari, H. Kiyani, A. Pourali, Res. Chem. Intermed. 43 (2017) 1635-1649.
[35] S.J. Saghanezhad, M.H. Sayahi, I. Imanifar, M. Mombeni, S. Deris Hamood, Res. Chem. Intermed. 43 (2017) 6521–6536.
[36] A. Das Gupta, R. Pal, A.K. Mallik, Green Chem. Lett. Rev. 7 (2014) 404-411.
[37] W. Wang, S.X. Wang, X.Y. Qin, J.T. Li, Synth. Commun. 35 (2005) 1263-1269.
[38] S. Tayebi, K. Niknam, Iran. J. Catal. 2 (2012) 69-74.
[39] F. Shirini, M. Seddighi, M. Mazloumi, M. Makhsous, M. Abedini, J. Mol. Liq. 208 (2015) 291-297.
[40] E. Kolvari, N. Koukabi, M.M. Hosseini, J. Mol. Catal. A: Chem. 397 (2015) 68-75.
[41] Z. Zhou, Y. Zhang, J. Chil. Chem. Soc. 60 (2015) 2992-2996.
[42] A.R. Moosavi-Zare, M.A. Zolfigol, E. Noroozizadeh, O. Khaledian, B.S. Shaghasemi, Res. Chem. Intermed. 42 (2016) 4759-4772.
[43] N.G. Khaligh, S.B.A. Hamid, S.J.J. Titinchi, Chin. Chem. Lett. 27 (2016) 104-108.
[44] A. Khazaei, F. Abbasi, A.R. Moosavi-Zare, New J. Chem. 38 (2014) 5287-5292.
[45] Z. Zhou, Y. Zhang, Green Chem. Lett. Rev. 7 (2014) 18-23.
[46] D. Banerjee, R. Karmakar, U. Kayal, G. Maiti, Synth. Commun. 47 (2017) 1006-1012.
[47] M. Fatahpour, F. Noori Sadeh, N. Hazeri, M.T. Maghsoodlou, M. Lashkari, J. Iran. Chem. Soc. 14 (2017) 1945-1956.
[48] P.S. Mahajan, M.D. Nikam, V. Khedkar, P. Jha, P.V. Badadhe, C.H. Gill, J. Heterocycl. Chem. 54 (2017) 1109-1120.
[49] S. Sobhani, F. Zarifi, J. Skibsted, ACS Sustainable Chem. Eng. 5 (2017) 4598-4606.
[50] M. Xing, T.T. Zhao, Y.J. Ren, N.N. Peng, X.H. Yang, X. Li, H. Zhang, G.Q. Liu, L.R. Zhang, H.L. Zhu, Med. Chem. Res. 23 (2014) 3274-3286.
[51] S. Abed, S.M. Akmal, N. Ali, M. Farooqui, Chem. Sci. Int. J. 17 (2016) 1-8.