Bulgarian Chemical Communications, Volume 46, Number 2(pp. 397 – 400) 2014

Methanesulfonic acid catalyzed one-pot synthesis of pyrano[2,3-c] pyrazole derivatives in water

M. M. Heravi * [1], N. Javanmardi [1], H. A. Oskooie [1], B. Baghernejad [2]

[1]*Department of Chemistry, School of Science, Alzahra University, Tehran, Iran*
[2]*Department of Chemistry, School of Sciences, Payame Noor University(PNU), 19395-3697, i.r. of Iran*

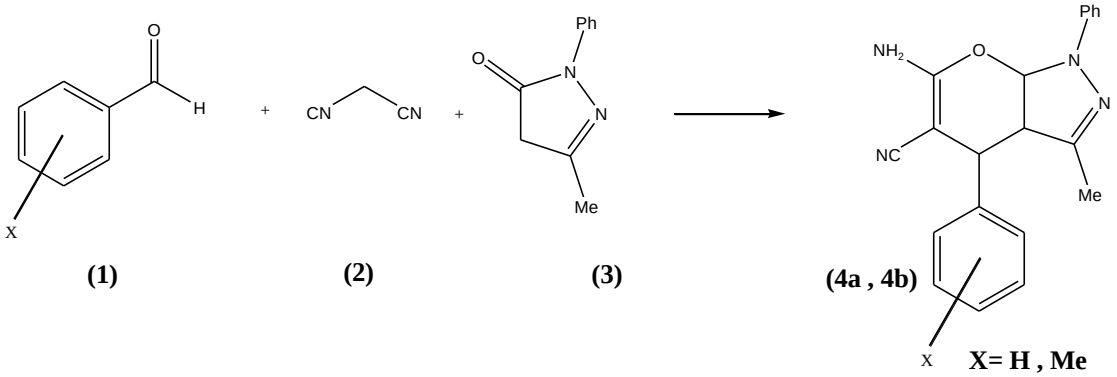
Received May 12, 2013; Revised September 3, 2013

A simple and efficient synthesis of 1,4-Dihydropyrano[2,3-c] pyrazoles was achieved via a one-pot three-component reaction of an aromatic aldehyde, malonitrile and 3-methyl-1-phenyl-2-pyrazolin-5-one using methanesulfonic acid as a catalyst in good yields.

Key words: methanesulfonic acid, 1,4-Dihydropyrano[2,3-c] pyrazole, one-pot synthesis.

INTRODUCTION

It is well known that 4H-pyran and its derivatives are very useful compounds. Substituted pyrano [2,3-c] pyrazoles have been synthesized in a search for new physiologically active compounds, drugs, pesticides, and other compounds of practical significance [1,2]. 2-Amino-3-cyano-4H-pyrans possesses photochemical activity [3]. Poly functionalized 4H-pyrans are a common structural unit in a number of natural products [4]. The 4H-pyran ring can be transformed to pyridine systems, which relate to pharmacologically important calcium antagonists of the DHP type [5, 6]. There are a lot of procedures to synthesis of these compounds but most of them are toxic. The need to reduce the amount of toxic waste and by-products arising from chemical processes requires increasing emphasis on the use of less toxic and environmentally compatible materials in the design of new synthetic methods. One of the most promising approaches is using water as reaction media. Recently, a great attention has been focused on the use of water as green solvent in various organic transformations. Water is a desirable solvent for chemical reactions because it is safe, non-toxic, environmentally friendly, readily available, and cheap compared to organic solvents [7-9]. Since the pioneering studies on Diels–Alder reactions by Breslow [10,11], there has been increasing recognition that organic reactions can proceed well in aqueous media and offer advantages over those occurring in organic solvents, such as rate enhancement and insolubility of the final products that facilitates their isolation. Herein, we would like to report one-pot synthesis of 1,4-dihydropyrano [2,3-c] pyrazole derivatives by three-component reaction of an aromatic aldehyde, malonitrile and 3-methyl-1-phenyl-2-pyrazolin-5-one using methanesulfonic acid as a catalyst in aqueous media (Scheme 1).



Scheme 1. Preparation rout of the compounds (4a, 4b)

* To whom all correspondence should be sent:
E-mail: mmh1331@yahoo.com

EXPERIMENTAL

Material and Equipment

All products are known compounds and were characterized by m.p., IR, ^{1}H-NMR and GC/MS. All melting points are uncorrected and taken with an Electrothermal melting point apparatus (Electrothermal Eng. Ltd, Essex, UK). The ^{1}H-NMR spectrums of the synthesized compounds were measured in DMSO-d_6 solution and TMS as the internal standard using a Bruker AQS AVANCE-300 MHz instrument. IR spectra were recorded from KBr disk on the FT-IR Bruker Tensor 27. GC/MS spectra were recorded on an Agilent Technologies 6890 network GC system and an Agilent 5973 network Mass selective detector. Thin layer chromatography (TLC) on commercial aluminum-backed plates of silica gel, 60 F254 was used to monitor the progress of reactions. All products were characterized by spectra and physical data.

General procedure for the synthesis of 1,4-dihydropyrano[2,3-c] pyrazole

A mixture of the aromatic aldehydes **(1)** (1 mmol), malononitrile **(2)** (1 mmol), 3-methyl-1-phenyl-2-pyrazolin-5-one **(3)** (1 mmol), and MSA (0.1 mL) in H_2O (10 mL) was refluxed for 45-55 min, and then cooled to room temperature. The crystalline powder formed was collected by filtration, washed with water, and re-crystallized from ethanol to give pure product **(4a, 4b)** (Scheme 1).

4a: ^{1}H-NMR (DMSO-d_6, δ/ppm): 1.93 (s, 3H, CH_3), 4.68 (s, 1H,), 4.75 (s, 2H, NH_2), 7.16-7.32 (m, 10H, Ph); IR (KBr, cm^{-1}): 3472, 3320, 2195, 1660, 1590, 1264, 1125, 1027, 753. MS (%), *m/z*: 330 (100) $[M]^+$, 331 (24) $[M+H]^+$.

4b: ^{1}H-NMR (DMSO-d_6, δ/ppm): 1.78 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 4.62 (s, 1H), 6.96 (s, 2H, NH_2), 7.02-7.78 (m, 9 H, Ph); IR (KBr, cm^{-1}): 3414, 3314, 2178, 1658, 1594, 1398, 1258, 1128, 1026, 754. MS (%), *m/z*: 344 (100) $[M]^+$, 345 (23) $[M+H]^+$.

4e: ^{1}H-NMR (DMSO-d_6, δ/ppm): 1.78 (3H, s, CH_3), 4.91 (s, 1H), 7.02 (s, 2H, NH_2), 7.32–7.98 (m, 9 H, Ph); IR (KBr, cm^{-1}): 3431, 3348, 2189, 1665, 1595, 1517, 1394, 1352, 1126, 1054, 831, 753.

4f: ^{1}H-NMR (DMSO-d_6, δ/ppm): 1.81 (3H, s, CH_3), 4.83 (s, 1H), 7.08 (s, 2H, NH_2), 7.22–7.88 (m, 9 H, Ph); IR (KBr, cm^{-1}): 3459, 3325, 2202, 1661, 1594, 1518,1491, 1444, 1391, 1262, 1127, 1089, 1066, 1015, 831, 804, 751, 686.

4g: ^{1}H-NMR (DMSO-d_6, δ/ppm): 1.77 (3H, s, CH_3), 3.78 (3H, s, CH_3O), 4.77 (s, 1H), 7.02 (s, 2H, NH_2), 7.12–7.68 (m, 9 H, Ph); IR (KBr, cm^{-1}): 3391, 3322, 2192, 1660, 1596, 1514, 1456, 1394, 1250, 1173, 1128, 1073, 1027, 813, 759, 692.

RESULTS AND DISCUSSION

Methanesulfonic acid (MSA) is an alkylsulfonic acid, which has numerous applications, for example, as an esterification or alkylation catalyst, as a polymer solvent, in the electroplating and electrochemistry industry, etc. MSA also is an effective reagent for the conversion of alcohols into corresponding amides [12], Fries-rearrangement [13], Beckmann rearrangement [14], hydration of nitriles into amides [15], monoesterification of diols [16], N-nitrosation of secondary amines [17], and aromatization of 1,4-dihydropyridines [18]. MSA is a strong acid (p*K*a= -1.9), which is almost completely ionized at 0.1 M in an aqueous solution and has a low tendency to oxidize organic compounds. It is, however, far less corrosive and toxic than other mineral acids. Under normal conditions, aqueous solutions evolve no dangerous volatiles, making it safe to handle. Finally, it is readily biodegradable within 28 days, only forming CO_2 and sulfate, making them an environmentally benign material [19]. Furthermore, it has the advantage, as will be shown that it can be separated readily from the reaction mixture and reused. As part of our program aimed at developing new selective and environmentally friendly methodologies for the preparation of fine chemicals,[20] then we decided to use this catalyst for the synthesis of 1,4-dihydropyrano[2,3-c]pyrazoles. In a typical procedure, benzaldehyde (1 mmol), malonitrile (1 mmol) with 3-methyl-1-phenyl-2-pyrazolin-5-one (1 mmol) in the presence of a catalytic amount of MSA in water at reflux temperature afforded the desired 1,4-dihydropyrano[2,3-c]pyrazole (4a) in 87% yield (Entry **1**, Table 1). The reaction then was applied to a variety of aromatic aldehydes in good yields. (As shown in Table 1) All aromatic aldehydes containing electron- withdrawing groups 3 (such as nitro group, halide) or electron-donating groups (such as hydroxyl group, alkoxyl group) were

Table1. Synthesis of 1,4-dihydropyrano[2,3-c]pyrazole derivatives catalyzed by MSA.

Entry	X	Time (min)	Product	m.p. (°C)		Yield(%)[a]
				Observed	Reported	
1	H	55	4a	172	170-171 [21]	87
2	4-Me	50	4b	177	177-178 [21]	80
3	4-OH	45	4c	213	210-212 [21]	90
4	3-NO_2	45	4d	191	190-191 [21]	95
5	4-NO_2	45	4e	195	195-196 [21]	95
6	4-Cl	50	4f	175	175-176 [21]	94
7	4-OMe	45	4g	173	171-172 [21]	90

[a] Isolated yields

Table 2. Synthesis of **3a** with MSA in the presence of different solvent

Entry	Solvent	Temperature	Time(min)	Yield(%)[a]
1	Water	reflux	55	87
2	Ethanol	reflux	70	80
3	dichloromethane	reflux	120	65
4	chloroform	reflux	120	66
5	Solvent-free	reflux	100	60

[a] Yield of isolated products

employed and reacted well to give the corresponding product **(4)** in good to excellent yields under these reaction conditions, so we conclude that no obvious effect of electron and nature of substituents on the aromatic ring were observed. We also found that the reaction did not proceed in the case in which aliphatic aldehyde was used. The reason we think this is the activity of aliphatic aldehydes is less than that of aromatic aldehyde. We performed the effect of various solvents on the synthesis of 4a. This reaction was carried out in various solvents such as water, chloroform, Ethanol, dichloromethane and solvent-free condition. As shown in Table 2, the best results in terms of yield and time obtained in water.

CONCLUSION

In conclusion, we have described a highly efficient procedure for the preparation of pyrano[2,3-c] pyrazole derivatives by a three component condensation using MSA as a catalyst. All the proposed reactions allowed the preparation of products in good yield without further purification. The reaction products were prepared in moderate to 5 average yields, even with different substituted aldehydes. No harmful organic solvents are used. Moreover, the procedure offers several advantages including high yields, operational simplicity, cleaner reaction, minimal environmental impact, and low cost, which make it a useful and attractive process for the synthesis of these compounds.

REFERENCES

1. (a) R. Varala, R. Enugala, *Chem. Pharm. Bull.*, **55**, 1254 (2007); (b) J. Ebrahimi, A. Mohanndi, V. Pakjoo, E. Bahramzadeh, A. Habibi, *J. Chem. Sci.*, **124**, 1013 (2012); (c) J. M. Khurana, A. Chaudhary, *Green Chem. Lett. Rev.*, **5**, 633 (2012); E.C. Witte, P. Neubert, A Roesoh, *Ger. Offen*. DE 3427985, *Chem. Abstr*.**, 104**, 224915f (1986).
2. (a) T. Hyama, H. Saimoto, *Jpn. KoKai Tokkyo Koho, JP*. 62181276, *Chem.* (1987) (b) J.L. Wang, D. Liu, Z.J. Zhang, S. Shan, X. Han, S.M. Srinivasula, C.M.Croce, E. S. Alnemri, Z. Huang, *Proc. Natl. Acad. Sci.*, **97**, 7124 (2000).
3. D. Armetso, W.M. Horspool, N. Martin, A. Ramos, C. Seaone, *J. Org. Chem*., **54**, 3069 (1989).
4. L.N. Martin, M. Quinteiro, C. Seoane, J.L. Soto, *Liebigs. Ann. Chem*., **1**, 101 (1990).
5. N. Martin, G. Martin, A.C. Secoane, J.L. Marco, A. Albert, F.H. Cano, *Liebigs. Ann. Chem*., **7**, 801 (1993).
6. J.L. Maco, N. Martin, A.M. Grau, C. Seoane, A. Albert, F. H. Cano, *Tetrahedron*, **50**, 3509 (1994).
7. C.J. Li, T.H. Chan, *Organic Reactions in Aqueous Media*; Wiley: New York. (1997).
8. P.A. Grieco, *Organic Synthesis in Water*, Ed.; Thomson Science, Glasgow: Scotland. (1998).
9. C. J. Li, *Chem. Rev*., **105**, 3095 (2005).
10. R. Breslow, *Acc. Chem. Res*., **24**, 159 (1991).
11. R. Breslow, *Acc. Chem. Res*., **37**, 471 (2004).
12. H. Sharghi, K. Niknam, *Iran. J. Chem. &Chem. Eng*., **18**, 36 (1999).
13. H. Sharghi, B. Kaboudin, *J. Chem. Res*. (S), 629 (1998).
14. H. Sharghi, M. Hosseini Sarvari, *J. Chem. Res*. (S), 446 (2001).

15. H. Sharghi, M. Hosseini Sarvari, *Synth. Commun*., **33**, 205 (2003).
16. H. Sharghi, M. Hosseini Sarvari, *Tetrahedron.*, **59**, 3627 (2003).
17. K. Niknam , M.A. Zolfigol, *Synth. Commun*., **36**, 2311 (2006).
18. K. Niknam, M.A. Zolfigol, S.M. Razavian, I. Mohammadpoor-Baltork, *J. Heterocycl. Chem*., **43**, 199 (2006).
19. M.D. Gernon, M. Wu, T. Buszta, P. Janney, *Green Chem*., **3**, 127 (1999).
20. (a) F.F. Bamoharram, M.M. Heravi, M. Roshani, A. Gharib, M. Jahangir, *Applied Catal.*, **302**, 42 (2006). (b) M.M. Heravi, R. Hekmatshoar, L. Pedram, *J. Mol. Catal. A: Chem.*, **89**, 231 (2005).
21. J.F. Zhou, S. J. Tu, Y. Gao, M. Ji, *J. Org. Chem*., **21**, 742 (2001).

МЕТАНСУЛФОНОВА КИСЕЛИНА КАТАЛИЗИРАЩА ЕДНОСТАДИЙНА СИНТЕЗА НА ПИРАНО [2,3-С] ПИРАЗОЛНИ ПРОИЗВОДНИ ВЪВ ВОДА

М. М. Херави[*1], Н. Джаванмарди [1], Х. А. Оскойе [a], Б. Багернаджад [2]

[1] *Департамент по химия, Научнен факултет, Университет Алзахра, Техеран, Иран*
[2] *Департамент по химия, Научен факултет, Университет Паям Нуур, 19395-3697, Иран*

Постъпила на 12 май 2013 г.; коригирана на 3 септември 2013 г.

(Резюме)

Прост и ефективен начин при добър добив за синтез на 1,4-дихидропирано[2,3-c] пиразоли е постигнат чрез едностадийна, трикомпонентна реакция на ароматен алдехид, малонитрил, и 3-метил-1-фенил-2-пиразолин-5-он прии използване на метансулфонова киселина като катализатор