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$Bi(NO_3)_3$–Al_2O_3 CATALYZED THREE COMPONENT ONE POT SYNTHESIS OF 1,4-DIHYDROPYRANO[2,3-C]PYRAZOLE DERIVATIVES IN THE SOLID STATE

Deepali Mahajan* & Anil Kumar**
* Department of Chemistry, Government G.M Science College, Jammu & Kashmir
** Department of Chemistry, Government Degree College, Akhnoor, Jammu & Kashmir

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Abstract:

An efficient, $Bi(NO_3)_3$-Al_2O_3 catalyzed one pot three component synthesis of 6-amino-4-aryl-5-cyano-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazoles via a reaction between 3-methyl-1-phenyl-2-pyrazolin-5-one, aromatic aldehydes and malononitrile is described. This method provides advantages such as high yield, shorter reaction time, mild reaction conditions, easy work-up procedure and operational simplicity.

Key Words: $Bi(NO_3)_3$-Al_2O_3, 1,4-dihydropyrano[2,3-c]pyrazoles, One Pot Synthesis & Solid-State

Introduction:

Multicomponent reactions have advantages over multistep reactions, in terms of yield of the desired products, time of the reactions and raw materials required for the reaction[1-2]. Condensed pyrazoles are biologically active compounds[3]. Pyrano[2,3-c]pyrazoles have useful pharmacological and biological properties such as analgesic, anti-allergic and anti-tumour[4-6]. They also serve as potential inhibitor of human Chk1 kinase[7].

Numerous methods for the synthesis of pyranopyrazoles have been reported in literature by the reactions catalyzed by piperidine[8], triethylamine[9], L-proline/KF-alumina[10], trichloroacetic acid[11], Iodine[12], ionic liquid[13], amberlyst A21[14], nanosized MgO[15], silico tungstic acid[16], DABCO[17] etc. Some of these methods involve excess amount of the catalyst, long reaction time, tedious work up and low yield of products.

Surface mediated organic synthesis is investigated extensively now days because of their eco-friendly nature[18]. Bismuth nitrate is easily available in the pure form and has low toxicity[19] and high stability in air and moisture. This led us to evaluate the possible catalytic potential of Bi(III)nitrate immobilized on neutral alumina for the synthesis of nitrogen heterocycles. Bi(III) ions, being on the borderline of hard and soft acids[20], could bind efficiently to the surface of neutral alumina, prevent its restructing[21], synergize its catalytic activity[22] and initiate a reaction under mild conditions. Herein, one pot solid state synthesis of 6-amino-7-aryl-5-cyano-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazoles on $Bi(NO_3)_3$-Al_2O_3 is reported.

Results and Discussion:

The procedure involved the reaction between suitable aldehyde (1a-k), malononitrile (2), 3-methyl-1-ohenyl-2-pyrazolin-5-one(3) and $Bi(NO_3)_3$-Al_2O_3 in a thermostatically controlled hot air oven at 90 ± 5 °C for 2 to 3.5 hrs (Scheme-1). The resulting product mixtures were isolated with ethanol and separated by column chromatography to yield the products (4a-k) in (75-90%) yield (Table 1). The compounds (4a-k)were analyzed by spectral method, HREIMS, IR, ^{1}H NMR, ^{13}C NMR and the melting points of the known compounds were consistent with those of the references reported. Initially, the reaction was optimized by taking benzaldehyde. The reaction did not proceed in the forward direction in the absence of the catalyst even after prolonged heating. The amount of the catalyst was optimized and it was observed that 5 mol% catalyst was sufficient (Table 1).

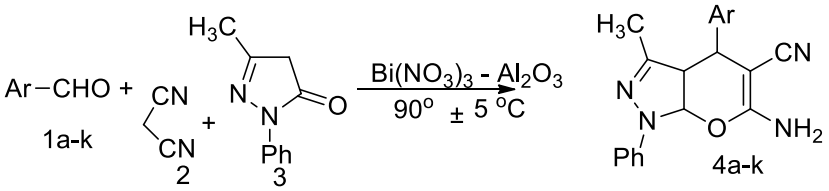

Table1: Optimization of amount of catalyst for the synthesis of 4a-k

Entry	Catalyst Mole%	Time (h)	Yield (%)
1	0	4	Trace
2	1	2	80
3	2	2	82
4	3	2	85
5	4	2	87
6	5	2	92
7	6	2	92

Table 2: Synthesis of pyrano [2, 3-c] pyrazoles in the presence of 5 mol% $Bi(NO_3)_3$-Al_2O_3

Entry	Ar	Product	Time (h)	Yield (%)	M.P(ºC)	
					Found	Reported
1	C_6H_5	4a	2	92	167	168
2	3-$NO_2C_6H_4$	4b	2.5	85	187	190
3	4-$NO_2C_6H_4$	4c	1.8	92	193	195
4	4-$CH_3C_6H_4$	4d	2.2	91	176	177
5	4-ClC_6H_4	4e	1.5	91	175	178
6	2,4,$Cl_2C_6H_3$	4f	2.5	92	182	183
7	3,4-$OCH_2OC_6H_3$	4g	3.0	90	175	176
8	3-ClC_6H_4	4h	2.5	88	157	159
9	4-OHC_6H_4	4i	3.0	82	207	209
10	4-$OCH_3C_6H_4$	4j	3.5	89	169	170
11	2-ClC_6H_4	4k	3.5	90	145	--

Experimental:

All the reagents were purchased from Merck, Fluka, Aldrich and used without purification melting points were recorded by capillary melting point apparatus and are uncorrected. All experiments were monitored by TLC. FTIR spectra were recorded on Perkin Elmer FTIR-1600 spectrophotometer. ^1H and ^{13}C NMR spectra (400MHz, 100 MHz) were recorded on a Brucker Advance DRX-400 spectrophotometer.

General Procedure for the Preparation of 4a-k:

A mixture of aldehyde (1 mmol), malononitrile (1 mmole), 3-methyl-1-phenyl-2-pyrazolin-5-one (1 mmol) and $Bi(NO_3)_3$-Al_2O_3 were grinded in a pestle mortar and the resulting mixture was put in a stoppered conical flask and kept in a hot air oven for the time period as mentioned in the Table 2. Progress of the reaction was monitored by TLC. After completion of the reaction, reaction mixture was extracted with ethanol in a soxhlet apparatus. This was then purified by column chromatography.

Spectral Data of Selected Compounds:

4a. 6-Amino-4-phenyl-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile.

IR: 3471, 3324, 2195, 1655, 1590, 1515, 1490, 1455, 1440, 1380, 1262, 1124, 1062, 1025, 752, 701, 632 cm^{-1}.

^1H NMR(DMSO-d_6, 400MHz): δ 1.78(s, 3H, CH_3), 4.68(s,1H,C-H), 7.20(s,2H,NH_2), 7.25-7.37(m, 6H, Ar-H), 7.48-7.51(m, 2H, Ar-H), 7.79(d, 2H, J = 8.8Hz, Ar-H). ^{13}C NMR(DMSO-d_6, 100 MHz): δ 9.70,36.23, 57.14, 78.57, 78.90,79.23, 97.97, 120.71, 126.61, 127.41, 128.32, 135.45, 144.35, 154.70, 160.75.

Anal. Calcd. For $C_{20}H_{16}N_4O$: C 73.15, H 4.94, N 17.06.

Found: C 73.27, H 5.03, N 17.31.

4b.6-Amino-4-(3-nitrophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile.

IR(KBr)υ_{max}: 3460, 3550, 2194, 1662, 1640, 1486, 1575, 1493, 1450, 1385, 1352, 836, 815, 775, 745 cm^{-1}.

^1H NMR(DMSO-d_6, 400 MHz)δ: 1.80(s, 3H, CH_3), 4.98(s, 1H, C-4), 7.32-7.52(m, 5H, NH_2, Ar-H), 7.66-7.70(m, 1H, Ar-H), 7.77-7.8(m, 3H, Ar-H), 8.15(d, 2H,J = 4.0 Hz, Ar-H).

^{13}C-NMR(DMSO-d_6, 100 MHz)δ: 9.69, 35.53, 56.70, 97.14, 120.63, 128.42, 129.30, 131.20, 135.63, 143.40,154.63, 160.85.

Anal. Calcd. for $C_{20}H_{15}N_5O_3$: C, 64.34; H,4.05; N, 18.76.

Found: C, 64.52; H, 3.87; N, 18.63.

4c.6-Amino-4-(4-nitrophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c] pyrazole-5-carbonitrile.

IR(KBr)υ_{max}: 3430,3345, 2186, 1664, 1593, 1516, 1393,1350, 1124, 1055, 828, 752 cm^{-1}.

^1H-NMR(DMSO-d_6, 400 MHz)δ: 1.78(s, 3H, CH_3), 4.93(s,1H, C-4),7.32-7.35(m, 1H,Ar-H), 7,38(s, 2H,NH_2), 7.48-7.52(m, 2H, Ar-H), 7.58(d, 2H,J = 8.8Hz, Ar-H), 7.79(d, 2H, J = 7.2 Hz, Ar-H),8.23(d, 2H, J = 8.4 Hz, Ar-H).

^{13}C-NMR(DMSO-d_6, 100MHz)δ: 9.68,35.82, 55.82, 96.50,120.45, 123.85, 128.78, 135.82,146.32,152.0, 154.61, 161.09.

Anal. Calcd. For $C_{20}H_{15}N_5O_3$: C, 64.34; H,4.05; N, 18.76.

Found: C, 64.25; H, 4.09; N, 18.92.

4d.6-Amino-4-(4-methylphenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c] pyrazole-5-carbonitrile.

IR(KBr)υ_{max}: 3465, 3344, 2183, 1645,1583, 1515, 1483, 1443, 1385, 1262,1180, 1125, 1071,1021, 835, 794,755, 690, 665cm^{-1}.

^1H-NMR(DMSO-d_6, 400 MHz)δ: 1.78(s, 3H, CH_3), 2.28(s, 3H, CH_3),4.62(s,1H, C-4),7.14-7.16(m, 6H, NH_2 and Ar-H), 7.31-7.33(m, 1H, Ar-H), 7.46-7.50(m, 2H, Ar-H), 7.78(d, 2H, J=8.0 Hz, Ar-H).

^{13}C-NMR(DMSO-d_6, 100 MHz)δ: 9.8, 20.7, 36.7,40.1,78.3,97.4, 120.7, 127.2, 128.6, 135.4, 140.9, 154.7, 160.4.

Anal. Calcd. For $C_{21}H_8N_4O$: C, 73.67; H, 5.30; N, 16.36.

Found: C, 73.81; H, 5.01; N,16.54.

4e.6-Amino-4-(4-Chlorophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c] pyrazole-5-carbonitrile.
IR(KBr)υ_{max}: 3450, 3324, 2201, 1660, 1595,1515, 1490,1443, 1390, 1260,1125, 1085, 1065, 1012, 830, 804, 751,685 cm^{-1}.
^{1}H-NMR(DMSO-d_6, 400 MHz)δ: 1.79(s, 3H, CH_3), 4.73(s, 1H, C-4), 7.25(s, 2H, NH_2), 7.29-7.34(m, 3H, Ar-H), 7.41(d, 2H, J=8.0 Hz, Ar-H), 7.47-7.51(m, 2H, Ar-H), 7.78(d, 2H, J = 8.0 Hz, Ar-H).
Anal. Calcd. For $C_{20}H_{15}ClN_4O$: C, 66.21, H 4.17; N, 15.44.
Found: C, 66.29; H, 3.96; N, 15.62.
4f.6-Amino-4-(2,4-dichlorophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c] pyrazole-5-carbonitrile.
IR(KBr)υ_{max}: 3455, 3324, 2199, 1661,1584, 1561, 1521,1494, 1471, 1458,1393, 1268, 1180, 1125, 1101, 1071, 904, 835, 814, 755, 690 cm^{-1}.
^{1}H-NMR: 1.78(s, 3H, CH3), 5.16(s, 1H, C-4), 7.31-7.44(m, 5H, NH_2, Ar-H), 7.48-7.52(m, 2H, ArH), 7.62(s, 1H, Ar-H),, 7.78(d, 2H, J = 8.0 Hz, Ar-H).
4g.6-Amino-4-(benzo[d][1,3]dioxol-6-yl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile.
IR(KBr)υ_{max}: 3400, 3321, 2199, 1660, 1595,1393, 1252, 1128, 1037, 788 cm^{-1}.
^{1}H-NMR(DMSO-d_6, 400 MHz)δ: 2.12(s, 3H, CH_3), 5.09(s, 1H, C-4), 5.95(s, 2H, OCH_2O), 6.92(s, 2H, NH_2), 7.02-7.12(m, 2H, Ar-H), 7.21(m, 1H, Ar-H), 7.26(d, 2H, J = 8.0 Hz, Ar-H).
Anal. Calcd. For $C_{21}H_{16}N_4O_3$: C, 67.73; H, 4.33; N, 15.05.
Found: C, 67/65; H, 4.30; N, 15.08.
4h.6-Amino-4-(3-Chlorophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c] pyrazole-5-carbonitrile.
IR(KBr) υ_{max}: 3461, 3317, 2191 1656, 1595, 1392, 1071, 758 cm^{-1}.
^{1}H NMR(DMSO-d_6)δ: 1.92(s, 3H, CH_3), 4.67(s, 1H, C-4), 4.74(s, 2H, NH_2), 7.19-7.37(m, 5H, Ar-H), 7.48(d, 2H, J = 8.0 Hz, Ar-H), 7.67(d, 2H, J =8.0 Hz, Ar-H),
Anal. Calcd. For $C_{20}H_{15}ClNO_4$: C, 66.21; H, 4.17; N, 15.44.
Found: C,66.13; H, 4.09; N, 15.35.
4i.6-Amino-4-(4-hydroxyphenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c] pyrazole-5-carbonitrile.
IR(KBr) υ_{max}: 3412, 3311, 2175, 1654, 1594, 1396, 1256, 1125, 1024, 752 cm^{-1}.
^{1}H NMR(DMSO-d_6)δ: 1.79(s, 3H, CH_3), 4.5(s, 1H, C-4), 6.72(d, 2H, J = 8.4 Hz, Ar-H), 7.04(d, 2H,J = 8.4 Hz, Ar-H), 7.12(s, 2H, NH_2), 7.29-7.33.
Anal. Calcd. For $C_{20}H_{16}N_4O_2$: C, 69.76; H, 4.68; N, 16.27.
Found: C, 69.68; H, 4.55; N, 16.14.

Conclusion:

This communication describes $Bi(NO_3)_3$-Al_2O_3 mediated efficient, eco-friendly and rapid synthesis of 1,4-dihydropyrano[2,3-c]pyrazole in excellent yield in the solid state. Bismuth nitrate adsorbed on neutral alumina acts as a green media for the reaction making this method cheaper, simple and environment friendly.

References

1. Indalkar K.S, Manisha S. P, Chaturbhuj G. U, Tetrahedron Letters, 2017, 10, 1016.
2. Khurana J. M, Magoo, D, Tetrahedron Lett., 2009, 50, 7300.
3. Elnagdi M. H, Elmoghayar M.R.H., Sadek, K. U., Adv. Heterocyclic Chem., 1990, 48, 223.
4. Kuo, S. G, Huang J and Nakamura H., J. Med. Chem., 1984,27, 539.
5. Wang J. L, Liu D., Zheng Z. J., Shan S, Hax X., Proc. Natl Acad. Sci. USA, 2009, 97, 7124-7129.
6. Zaki M.E.A, Saliman H. A., Hickal O. A., Rashed A. E. Z, Z. Natureforsch C, 2006, 61, 1-5.
7. Liu Z, Zhang R, Meng Q, Zhang X, Sun Y, Med. Chem. Common, 2016, 7, 1352.
8. Vasuki G, Kumaravel K, Tetrahedron Lett., 2008, 49, 5636.
9. Litvinov Y. M., Shestrpalov A. A, Rtinovskaya L. A., Shestopalov A. M., J. Comp. Chem., 2009, 11, 914.
10. Mecadon H, Rohman M. R., Kharbanger I., Laloo B. K., Kharkonger I, Rajbanjshi M, Myrboh B., Tetahedron Lett., 2011, 52, 3228.
11. Karimi-Jaberi, Z Sham, M. M. R., Poolrdian B, Acta Chim Slon. 2013, 60, 105.
12. Madhusudana Reddy M. B., Pasha M. A., Indian, J. Chem., 2012, 51B, 537.
13. Ebrahimi J, Mohammadi A, Pakjoo V, Bahrmzade E, Habibi A, J. Chemi. Sci., 2012, 124, 1013.
14. Bihani M, Bora P. P., Bez G, Askari H., ACS Sustain. Chem. Eng., 2013, 1, 440.
15. Babaie M, Seibani H, Arb. J. Chem., 2014, 4, 159.
16. Chavan H. V., Baba S. B., Hoval R. U., Bandgra B. P., Bull Korean Chem. Soc., 2011, 32, 3963.
17. Waghmare A. S., Pandit S. S., J. Saudi Chem. Soc., 2017, 21, 286.
18. Ravi P and Tewari S. P, Catalysis Communications, 2012, 19, 37.
19. Suzuki H., Ikegami T., Matano Y, Synthesis, 1997, 249.
20. March J. Advanced Organic Chemistry, 4th Ed. John Wiley and Sons NY, 121, 1999, P 262.
21. Sohlberg K, Pennycook S. J., Pantelides S. T., J. Am. Chem. Soc., 1999, 121, 10999.
22. Satterfield C. N., Heterogenous Catalysis in Practice, McGraw Hills, NY, 1980, Sect 4.5.