ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Highly Efficient, One-Pot, Solvent-Free Synthesis of Amidoalkyl Naphthols Using a Caro's Acid- Silica Gel as Solid Acid Catalyst

Montazeri N[1*], Pourshamsian K[1], Ghorchibeigi M[1], Fouladi M[2]

[1]Department of Chemistry, Tonekabon Branch, Islamic Azad University, Tonekabon, Iran.
[2] Islamic Azad University, Tonekabon Branch, Young Researchers Club, Tonekabon, Iran.

ABSTRACT

Amidoalkyl naphthol derivatives were efficiently synthesized by the reaction of appropriated aromatic aldehydes, 2-naphthol, and an amide in the presence of caro's acid- silica gel (CA-SiO_2) as an effective solid acid catalyst under solvent-free conditions. The significant features of this procedure are high yields of the products, shorter reaction times, and simple procedure with an easy work- up.

Keywords: Amidoalkyl Naphthols, Solvent-free Conditions, Caro's Acid Silica Gel, Aromatic aldehydes.

Corresponding author
Email: Montazer50@Toniau.ac.ir

ISSN: 0975-8585

INTRODUCTION

Aminoalkyl naphthols have attracted strong interest to their useful biological and pharmacological properties such as adrenoceptor blocking, antihypertensive, and Ca^{2+} channel blocking activities [1-5].

Amidoalkyl naphthols are also important synthetic building blocks and are used as precursors for the synthesis of 1-aminomethyl-2-naphthol derivatives, which exhibit important cardiovascular activity [6]. The hypotensive and bradycardiac affects of these compounds have been evaluated [7].

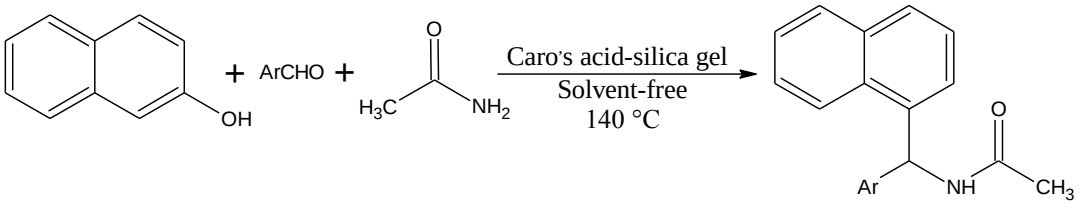
Multicomponent reaction (MCRs) have manifested as a powerful tool for the rapid introduction of molecular diversity. MCRs contribute to the requirements of an environmentally friendly process by reducting the number of synthetic steps, energy consumption, and waste production. One such reaction is the synthesis of amidoalkyl naphthols [8-10].

Amidoalkyl naphthols are generally synthesized via one-pot three-component reaction of an aryl aldehyde, 2-naphthol and an amide in the presence of several catalysts such as heteropoly acids[11], montmorillonite K10 clay[12], sulfamic acid[13], $K_5CoW_{12}O_{40}$.$3H_2O$[14], Iodine[15], $Ce(SO_4)_2$[16], $H_3MoO_{40}P$[17], 1-butyl-3-methyl imidazolium hydrogen sulphate[18], cation-exchanged resin[19], zircon(IV) chloride[20], PPA-SiO_2[21], silica sulfuric acid[22], $H_3PW_{12}O_{40}$[23], $NaHSO_4$-SiO_2[24], thiamine hydrochloride[25], $H_4SiW_{12}O_{40}$[26], oxalic acid [27], $Fe(HSO_4)_3$[28], copper p-toluenesulfonate[29], P_2O_5[30], $Sr(OTf)_2$[31], HPMo[32], $Yb(OTf)_3$ in ionic liquid[33], TMSCl/NaI[34], Al_2O_3-$HClO_4$[35], $InCl_3$[36], and 2,4,6-trichloro-1,3,5-triazine[37]. However, some of the reported methods are not entirely satisfactory and suffer from long reaction time, expensive reagents, low yields of products or tedious workup, and the use of additional microwave or ultrasonic irradiation.

These problems prompted us towards further investigation in search for a new catalyst, which will carry out the synthesis of amidoalkyl naphthols under simpler experimental set up, faster, and eco-friendly conditions.

In continuation of our efforts to develop novel synthetic routes using reusable catalysts in organic reactions, and due to our interest in the synthesis of heterocyclic compounds [38-42], herein we wish to report an efficient and solvent-free synthesis of amidoalkyl naphthols by reaction of aryl aldehydes, 2-naphthol, and an amide using Caro's acid-silica gel (CA-SiO_2) as a solid acid catalyst (Scheme 1).

ISSN: 0975-8585



1 2 3 4a-h

MATERIALS AND METHODS

All chemicals were available commercially and used without additional purification. Melting points were recorded on Electrothermal type 9100 melting point apparatus. The FT-IR spectra were obtained on a 4300-Shimadzu spectrophotometer in KBr disks. The ^{1}H NMR(500MHz) spectra were recorded on a Bruker-Ac-500 spectrometer. The catalyst was synthesized according to the literature[43].

EXPERIMENTAL

General procedure for the preparation of catalyst (CA-SiO_2)

Potassium persulfate(4.5g) was added in small portions to ice-cooled 98% sulfuric acid(4.7g) with stirring; to this were added crushed ice(13g) and water(4g). The temperature was kept below 15 ^{o} C. Silica gel(5g, TLC grade, kieselgel 60 G, particle size 15µm) was added in portions to the mixture, and the mixture was stirred for 4h in an ice-water bath. The mixture was then filtered under suction and dried in a desiccators to give a white, free-flowing powder[43].

General procedure for the synthesis of amidoalkyl naphthols(4a-h).

A mixture of 2-naphthol **1** (1mmol), aromatic aldehyde **2** (1mmol), acetamide **3** (1.1mmol), and Caro's acid-silica gel (CA-SiO_2) (35mg) as catalyst was heated at 140^{o}C with stirring for 2-6 min, and the solid product gradually formed. The progress of the reaction was monitored by TLC. After completion of the reaction, hot acetone was added and the mixture stirred for 2 min. The solid catalyst was filtered off, and the filtrate was evaporated and then washed with n-hexane, dried at 60^{o}C under vacuum for 1h. For further purification, it was crystallized with ethanol to afford the pure product. The structures of the products were confirmed by ^{1}H NMR, FT-IR spectra, and comparison with authentic samples prepared by reported methods.

RESULTS AND DISCUSSION

The use of solid acids as heterogeneous catalysts has received considerable interest in different areas of organic synthesis[44]. The heterogeneous solid acids are advantageous over conventional homogeneous acid catalyst as they can be easily recovered from the reaction mixture by simple filtration and can be reused after activation or without activation, thereby

ISSN: 0975-8585

making the process economically viable[11]. In many cases, heterogeneous catalysts can be recovered with only minor change in activity so that they can be conveniently used in continuous flow reactions[11]. The one-pot synthesis of amidoalkyl naphthol **1** , aromatic aldehydes **2** , and amides **3** in presence of CA-SiO_2 as a cheap, nontoxic, and inexpensive catalyst under solvent-free conditions(Scheme 1). Initially, the synthesis of compound **4a** was selected as a model reaction to determine suitable reaction conditions. The reaction was carried out by heating a mixture of 2-naphthol(1mmol), 2-nitrobenzaldehyde(1mmol), and acetamide(1.1mmol) in the presence of CA-SiO_2 under various amount of the catalyst and at different temperatures under solvent-free conditions(Table 1). It was found that the yield of compound **4a** was strongly affected by the catalyst amount and reaction temperature. No product was obtained in the absence of the catalyst(Entry 1), or in the presence of the catalyst at room temperature(Entry 2), indicating that the catalyst and temperature are necessary for the reaction. Increasing the amount of the catalyst and reaction temperature up to 35mg and 140^{o}C, respectively(Entry 10), increased the yield of the product **4a**, where as further increase in both catalyst amount and temperature was found to have an inhibitory effect on formation of the product(Entries 11-14).

Table 1: Effect of CA-SiO_2 amount and temperature on the model reaction[a]

Entry	Catalyst (mg)	T (^{o}C)	Time (min)	Yield (%)[b]
1	-	140	10	-
2	25	r.t.	10	-
3	25	120	6	80
4	25	140	3	86
5	25	160	3	85
6	30	120	4	82
7	30	140	4	83
8	30	160	3	81
9	35	120	3	86
10	35	140	2	95
11	35	160	3	88
12	40	120	4	84
13	40	140	2	87
14	40	160	2	85

[a] 1mmol 2-naphthol, 1mmol 3-nitrobenzaldehyde, and 1.1mmol acetamide under solvent-free conditions. [b] Isolated yields.

The model reaction was also examined in various solvents such as ethanol, methanol, acetonitrile, dichloromethane, and chloroform under reflux and under solvent-free conditions in the presence of 35mg catalyst at 140^{o}C . The yield of the reaction under solvent-free conditions was the highest and the reaction time was shortest. In order to evaluate the generality of the process, several examples illustrating the present method for the synthesis of amidoalkyl naphthols **4** were studied(Table 2). In all cases, aromatic aldehydes with substituents carrying either electron-donating or electron-withdrawing groups reacted

ISSN: 0975-8585

successfully and gave the products in high yields. No significant substituent effect was observed on the yields of the products (Table 2, Entries 1-8).

Table 2- CA-SiO_2 catalyzed synthesis of amidoalkyl naphthols 4a-h [a]

Entry	Ar	Products[b]	Time (min)	Yields (%)[c]	Melting point (^oC)	
					Found	Reported[Ref]
1	3-$NO_2C_6H_4$	4a	2	95	239-242	238-240[11]
2	C_6H_5	4b	3	87	232-235	228-230[18]
3	4-$NO_2C_6H_4$	4c	3	91	243-246	245-246[11]
4	4-ClC_6H_4	4d	4	85	227-229	224-226[11]
5	4-MeC_6H_4	4e	2	88	218-221	220-223[11]
6	2-MeC_6H_4	4f	4	92	202-204	201-203[18]
7	2-ClC_6H_4	4g	3	90	198-200	197-199[18]
8	4-$MeOC_6H_4$	4h	4	82	182-184	180-182[11]

[a] 1mmol 2-naphthol, 1mmol aromatic aldehydes, 1.1mmol acetamide, and (35mg) CA-SiO_2 at 140^{o}C under solvent-free conditions. [b] All products were characterized by FT-IR, and ^{1}H NMR spectral data and comparison of their melting points with those of authentic samples. [c] Isolated yields.

CONCLUSION

In summary, we have demonstrated a new and important catalytic activity of Caro's acid-silica gel(CA-SiO_2) as an inexpensive, effective, and non-corrosive catalyst for the synthesis of amidoalkyl naphthols in high yields. Other advantages of this protocol are short reaction time, simple experimental procedure combined with the easy work up, and omitting any volatile and hazardous organic solvents.

ACKNOWLEDGEMENT

The authors are thankful to Islamic Azad University, Tonekabon Branch (IAUT) for financial support.

REFERENCES

[1] Jim KF, and Matthews WD. J Pharmacol Exp Ther 1985; 234:161-165.
[2] Atwal KS, Reilly BCO, Ruby EP, and et al. J Med Chem 1987; 30:627-628.
[3] Grundke M, Himnel HM, Wettwer E et al. J Cardiovasc Pharmacol 1991; 18:918-925.
[4] Wang YF, Izawa T, Kobayashi S, and Ohno M. J Am Chem 1982; 104:6465-6466.
[5] Seebach D and Matthews JL. J Chem Soc Chem Commun 1997; 2015-
[6] Shen AY, Tsai CT, and Chen CL. Eur J Med Chem 1999; 34:877-882.
[7] Khodaei MM, Khosropour AR, and Moghanian H. Synlett 2006; 916-920.
[8] Domling A, and Ugi I. Angew Chem Int Ed 2000; 39:3168-3220.
[9] Bienayme H, Hulme C, Oddon G, and Schmitt P. Chem Eur J 2000; 6:3321-3329.
[10] Orru RVA, and De Greef M. Synthesis 2003; 10:1471-1499.
[11] Khabazzadeh H, Saidi K, and Seyedi N. J Chem Sci 2009; 121(4):429-433.

[12] Kantevari D, Vuppalapati SVN, and Nagarapu L. Catal Commun 2007; 8:1857-1862.
[13] Patil SB, Singh PR, Surpur MP, and Samant SD. Ultrason Sonochem 2007; 14:515-518.
[14] Nagarapu L, Baseeruddin M, Apun S, and Kantevari S. Catal Commun 2007; 8:1729-1734.
[15] Das B, Laxminarayana K, Ravikanth B, and Rao BR. J Mol Catal A: Chem 2007; 261:180-3.
[16] Selvam NP and Perumal PT. Tetrahedron Lett 2006; 47:7481-7483.
[17] Gawand P, Deokar H, Langi B, Yadav A and Chaskar A. Synth Commun 2009; 39:4171-
[18] Suryakant BS, Kiran FS, Balaji RM, Bapurao BS, and Murlidhar SS. Bull Korean Chem Soc 2009; 30(12):2887-2889.
[19] Patil SB, Singh PR, Surpur MP, and Samant SD. Synth Commun 2007; 37:1659-1664.
[20] Nagawade RR and Shinde DB. Acta Chim Solv 2007; 54:642-646.
[21] Shaterian HR, Hosseinian A and Ghashang M. Synth Commun 2008; 38:3375-3389.
[22] Srihari G, Nagaraju M, and Muthy MM. Helve Chem Acta 2007; 90:1497-1504.
[23] Dorehgiraee A, Khabazzadeh H, and Saidi K. Arkivoc 2009; 7:303-310.
[24] Shaterian HR, Hosseinian A, and Ghashang M. Tetrahedron Lett 2008; 49:5804-5806.
[25] Lei M, Ma L, and Hu L. Tetrahedron Lett 2009; 50:6393-6397.
[26] Amit RS, and Gavisiddappa SG. J Chem Sci 2010; 122(2):189-192.
[27] Ansari SAMK, Sangshetti JN, Kokare ND, Wakte PS, and Shinde DB. I J Chem Tech 2010; 17:71-73.
[28] Shaterian HR, Yarahmadi H, and Ghashang M. Bioorg Med Chem Lett 2008; 18:788-792.
[29] Min W and Yan L. Monatsh Chem 2011; 142:153-157.
[30] Nandi GC, Samai S, Kumar R, and Singh MS. Tetrahedron Lett 2009; 50:7220-7222.
[31] Su WK, Tang WY, and Li JJ. J Chem Res 2008; 123-128.
[32] Jiang WQ, An LT, and Zou JP. Chin J Chem 2008; 26:1697-1701.
[33] Kumar A, Rao MS, Ahmad I, and Khungar B. Can J Chem 2009; 87:714-719.
[34] Sabitha G, Arundhathi K, Sundhakar K, Sastry BS, and Yadav JS. J Heterocyclic Chem 2010; 47:272-275.
[35] Hamid Reza S, Fahimeh K, Azita A, and Majid G. Chin J Chem 2009; 27:815-820.
[36] Chavan NL, Naik PN, Nayak SK, and Kusurkar RS. Synth Commun 2010; 40:2941-2947.
[37] Zhang P and Zhang ZH. Monatsh Chem 2009; 140:199-203.
[38] Montazeri N. Asian J Chem 2010; 22:7432-7434.
[39] Montazeri N, Pourshamsian K, Khoddadi M and Khoddadi k. Oriental J Chem 2011; 27(3):1023- 1027.
[40] Montazeri N, and Rad-Moghadam K. Chin Chem Lett 2008; 19:1143-1146.
[41] Montazeri N, Khaksar S, Nazari A, Alavi SS, Vahdat SM and Tajbakhsh M. J Fluorine Chem 2011; 132:450-452.
[42] Montazeri N, and Rad-Moghadam K. Phosphorus, Sulfur and Silicon 2004; 179:2533-36.
[43] Movassagh B, Lakouraj MM and Ghodrati K. Synth Commun 1999; 29:3597-3603.
[44] Seitz WJ, Saha AK, and Hossain MM. Organometallics 1993; 12:2604-2608.