Solvent-Free One-Pot Synthesis of Amidoalkyl Naphthols Catalyzed by Silica Sulfuric Acid[1])

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An efficient, inexpensive, and mild method for the synthesis of amidoalkyl naphthols, catalyzed by 'silica sulfuric acid' (SSA), was elaborated under solvent-free conditions at room temperature. Various amidoalkyl naphthols were synthesized in high yields from aromatic or aliphatic aldehydes, α- or β-naphthols, and amides or urea or thiourea.

Introduction. – There is current and general interest in heterogeneous systems because of their importance in industry and in the development of new technologies [1]. Heterogeneous-reagent systems have many advantages such as simple experimental procedures, mild reaction conditions, and minimum chemical wastes, when compared to analogous liquid-phase reactions [2]. Solid acid catalysts are easier to handle because they hold the acidity internally and are easily separated from products by simple filtration. Moreover, constraining a reaction to the surface of a solid habitually allows one to apply milder conditions.

Various methodologies based either on neat silica gel as catalyst [1] or on sulfuric acid (H_2SO_4)- and/or chlorosulfuric acid ($ClSO_3H$)-supported silica gel [3] have been developed. Chlorosulfuric acid reacts with silica gel (SiO_2) at ambient temperature to a material called 'silica sulfuric acid' (SSA): $[SiO_2] + ClSO_3H \rightarrow [SiO_2] - OSO_3H + HCl$. In this solid material, the acidic SO_3H moiety is immobilized on the SiO_2 surface by covalent-bond formation.

So far, a number of SSA-catalyzed reactions have been reported [4]. However, we wanted to find out if SSA is a suitable (or better) catalyst for one-pot multi-component reactions compared to other, homogeneous catalysts. Such reactions, including the *Biginelli* [5], *Passerini* [6], *Ugi* [7], or *Mannich* [8] transformations, have attracted considerable attention in recent years; and there is still a demand to develop new, elegant processes.

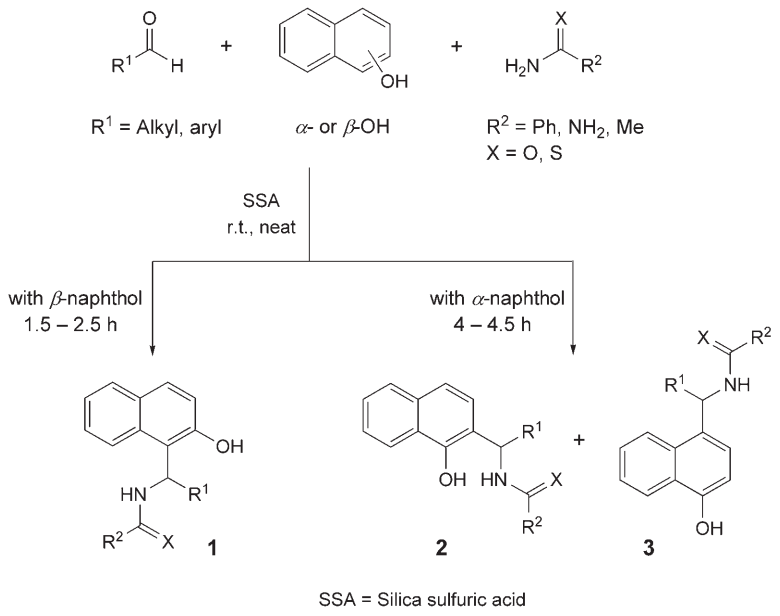
Our target compounds were amidoalkyl naphthols, which can be prepared from an aliphatic or aromatic aldehyde, a naphthol, and an amide, urea or thiourea. Amidoalkyl naphthols have been prepared with *para*-toluenesulfonic acid (TsOH), $Bi(OTf)_3$, $Zn(OTf)_2$, methanesulfonic acid (MsOH) [9], or iodine [10] as catalysts in organic solvents, elevated temperatures and prolonged reaction times often being required.

[1]) IICT Communication No. 070501.

Moreover, in all these reports, the reactions with aliphatic aldehydes were reported to suffer from low yields and harsh reaction conditions. Herein, we report a mild, simple, and efficient method for the one-pot three-component SSA-catalyzed synthesis of these compounds (see *Scheme* below).

Results and Discussion. – As shown in the *Scheme* and *Table*, the reaction was carried out by adding the three components, naphthol, alkyl or aryl aldehyde, and amide or (thio)urea to SSA. The mixture was stirred for 1.5 – 2.5 h (for β-naphthol) or for 4 – 4.5 h (for α-naphthol), which afforded the corresponding amidoalkyl naphthols of type **1** (79 – 92%) from β-naphthol, or a mixture of the regioisomers **2** (30 – 32%) and **3** (38 – 42%) from α-naphthol, respectively. In the reactions with α-naphthol, the isomers **2** and **3** were formed in similar proportions. The structures of all products were unequivocally confirmed spectroscopically (IR, ^{1}H- and ^{13}C-NMR) and by mass-spectrometric (MS) analysis (see *Exper. Part*).

Scheme



SSA = Silica sulfuric acid

Our procedure was found to be much more effective than those described in earlier reports [9][10]. In earlier reports, aliphatic aldehydes did not give satisfactory yields, and the corresponding products were not produced at all with thiourea. However, in the SSA-catalyzed reactions, the expected products were readily formed at room temperature under solvent-free conditions. All reactions proceed smoothly, without formation of by-products. No reactions were observed in the absence of the catalyst.

In conclusion, we have elaborated an efficient, simple, and mild procedure for the synthesis of a variety of different amidoalkyl naphthols. Since the SSA catalyst is

Table. *One-Pot Three-Component Reactions Catalyzed by Silica Sulfuric Acid* (SSA). Without solvent, at room temperature.

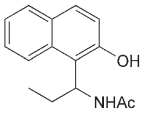
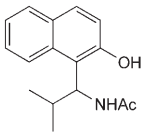
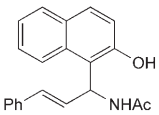
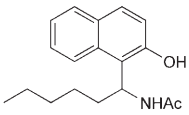
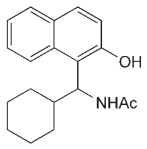
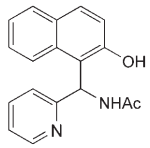
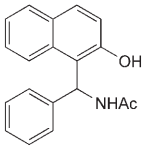
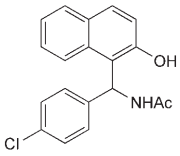
Series	Aldehyde	Amide or (thio)urea	Time [h]	Product(s)	Yield [%][a])
For β-naphthol:					
a	Propanal	$AcNH_2$	1.5		90
b	2-Methylpropanal	$AcNH_2$	1.5		92
c	Cinnamaldehyde	$AcNH_2$	1.7		90
d	Hexanal	$AcNH_2$	1.9		85
e	Cyclohexanecarbaldehyde	$AcNH_2$	2.0		90
f	Pyridine-2-carbaldehyde	$AcNH_2$	2.0		84
g	Benzaldehyde	$AcNH_2$	2.0		85
h	4-Chlorobenzaldehyde	$AcNH_2$	1.6		89

Table (cont.)

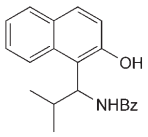
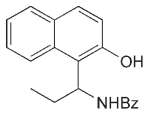
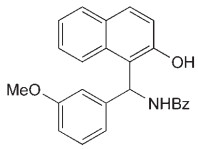
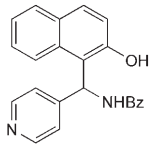
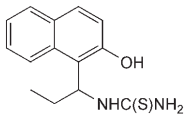
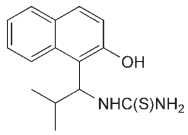
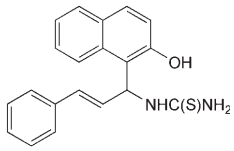
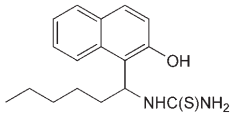
Series	Aldehyde	Amide or (thio)urea	Time [h]	Product(s)	Yield [%][a])
i	2-Methylpropanal	$BzNH_2$	1.9		83
j	Propanal	$BzNH_2$	2.0		85
k	3-Methoxybenzaldehyde	$BzNH_2$	2.5		82
l	Pyridine-4-carbaldehyde	$BzNH_2$	2.2		80
m	Propanal	Thiourea	1.8		83
n	2-Methylpropanal	Thiourea	1.5		82
o	Cinnamic aldehyde	Thiourea	1.8		80
p	Hexanal	Thiourea	1.8		81

Table (cont.)

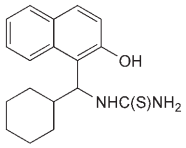
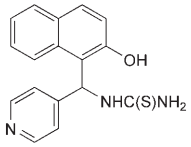
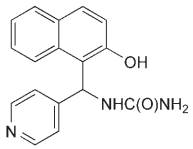
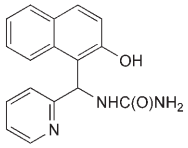
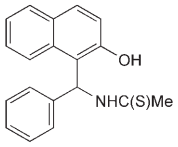
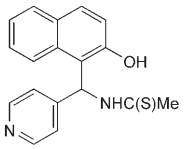
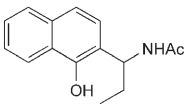
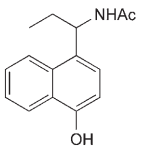
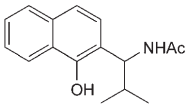
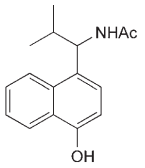
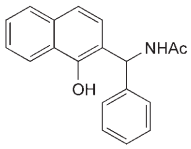
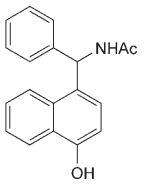
Series	Aldehyde	Amide or (thio)urea	Time [h]	Product(s)	Yield [%][a])
q	Cyclohexanecarbaldehyde	Thiourea	2.0		84
r	Pyridine-4-carbaldehyde	Thiourea	2.0		80
s	Pyridine-4-carbaldehyde	Urea	2.5		85
t	Pyridine-2-carbaldehyde	Urea	2.3		82
u	Benzaldehyde	$MeC(S)NH_2$	2.5		79
v	Pyridine-4-carbaldehyde	$MeC(S)NH_2$	2.2		82
For α-naphthol:					
w	Propanal	$AcNH_2$	4.0		32
					41

Table (cont.)

Series	Aldehyde	Amide or (thio)urea	Time [h]	Product(s)	Yield [%][a])
x	2-Methylpropanal	$AcNH_2$	4.2		35
					42
y	Benzaldehyde	$AcNH_2$	4.5		30
					38

[a]) After chromatographic purification.

inexpensive, easy to prepare and handle, and readily removable, our method seems to be suited also for large-scale operations.

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Experimental Part

General. IR-Spectroscopic data are reported in cm^{-1}. NMR-Spectroscopic chemical shifts δ are reported in ppm rel. to Me_4Si (=0 ppm). Mass-spectrometric (MS) data are given in *m/z*.

General Synthetic Procedure. A mixture of an aliphatic or aromatic aldehyde (1 mmol), α- or β-naphthol (1 mmol), an amide or (thio)urea (1.1 mmol), and a cat. amount of silica sulfuric acid (SSA; 20 mg) [3] was stirred at r.t. for the appropriate time (see *Table*). The reaction was monitored by TLC. After completion of the reaction, the mixture was purified by column chromatography (SiO_2; hexane/AcOEt 4:1). The IR, ^{1}H- and ^{13}C-NMR, and MS data of some representative compounds are given below.

N-*[1-(2-Hydroxynaphthalen-1-yl)hexyl]acetamide* (**1d**). IR (KBr): 3424, 1653, 1026, 1000, 826. ^{1}H-NMR (200 MHz, (D_6)DMSO): 9.85 (*s*, 1 H); 8.11 (*d*, J = 8.6, 1 H); 7.81–7.18 (*m*, 6 H); 5.80 (*q*, J = 7.8, 1 H); 2.02 (*m*, 2 H); 1.92 (*s*, 3 H); 1.40–1.21 (*m*, 6 H); 0.92–0.80 (*m*, 3 H). ^{13}C-NMR (75 MHz,

(D_6)DMSO): 168.37; 152.90; 132.22; 128.17; 125.90; 122.41; 122.06; 119.73; 118.48; 45.81; 33.62; 31.04; 25.89; 22.63; 21.93; 13.73. EI-MS: 285 (M^+), 215, 184, 173, 116, 44.

N-*[(2-Hydroxynaphthalen-1-yl)(3-methoxyphenyl)methyl]benzamide* (**1k**). IR (KBr): 3381, 1641, 1572, 1515, 1398, 1111, 693. ^{1}H-NMR (200 MHz, (D_6)DMSO): 9.87 (*s*, 1 H); 8.82 (*d*, *J* = 8.6, 1 H); 8.16 (*d*, *J* = 8.6, 1 H); 7.91 – 6.82 (*m*, 14 H); 6.65 (*d*, *J* = 7.8, 1 H); 3.71 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 168.03; 165.79; 159.19; 153.14; 143.62; 134.28; 134.20; 132.28; 131.43; 131.20; 129.37; 129.28; 128.49; 128.35; 128.17; 127.42; 127.07; 126.77; 122.68; 118.81; 118.66; 118.25; 112.96; 54.86; 49.22. LC/MS: 406 ($[M + Na]^+$), 383 (M^+).

1-[1-(2-Hydroxynaphthalen-1-yl)propyl]thiourea (**1m**). IR (KBr): 3413, 1626, 1545, 1514, 1265, 811, 750. ^{1}H-NMR (200 MHz, (D_6)DMSO): 9.80 (*s*, 1 H); 8.35 – 7.10 (*m*, 8 H); 6.33 (br., 2 H); 2.18 – 2.08 (*m*, 2 H); 0.83 (*t*, *J* = 7.3, 3 H). LC/MS: 283 ($[M + Na]^+$).

1-[(2-Hydroxynaphthalen-1-yl)(pyridin-4-yl)methyl]urea (**1s**). IR (KBr): 3405, 1615, 1510, 1135, 784. ^{1}H-NMR (200 MHz, (D_6)DMSO): 9.70 (*s*, 1 H); 8.41 (*d*, *J* = 5.9, 2 H); 7.93 – 7.10 (*m*, 8 H); 6.70 (*s*, 1 H); 6.48 (*s*, 1 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 154.44; 152.32; 149.12; 131.99; 129.31; 128.70; 128.15; 125.43; 124.85; 122.27; 120.64; 120.23; 117.99; 65.66. LC/MS: 316 ($[M + Na]^+$).

N-*[(2-Hydroxynaphthalen-1-yl)(phenyl)methyl]ethanethioamide* (**1u**). IR (KBr): 3420, 1628, 1514, 1441, 1379, 1267, 1212, 1170, 811, 747. ^{1}H-NMR (200 MHz, (D_6)DMSO): 9.82 (*s*, 1 H); 8.19 – 7.11 (*m*, 13 H); 2.62 (*s*, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 199.51; 153.51; 140.25; 132.57; 129.57; 128.44; 128.17; 128.00; 126.51; 126.25; 122.70; 122.41; 118.43; 116.89; 55.33; 32.90. LC/MS: 330 ($[M + Na]^+$).

N-*[1-(1-Hydroxynaphthalen-2-yl)propyl]acetamide* (**2w**). IR (KBr): 3390, 1617, 1575, 1540, 1460, 1377, 1079, 807. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.95 (*s*, 1 H); 8.35 (*d*, *J* = 7.8, 1 H); 7.68 (*d*, *J* = 7.8, 1 H); 7.40 (*m*, 2 H); 7.28 (*d*, *J* = 8.5, 1 H); 7.12 (*d*, *J* = 8.5, 1 H); 6.08 (*d*, *J* = 8.6, 1 H); 5.08 (*q*, *J* = 7.7, 1 H); 2.01 (*m*, 2 H); 1.95 (*s*, 3 H); 0.98 (*t*, *J* = 7.4, 3 H). LC/MS: 266 ($[M + Na]^+$).

N-*[1-(4-Hydroxynaphthalen-1-yl)propyl]acetamide* (**3w**). IR (KBr): 3401, 3275, 1644, 1583, 1542, 1384, 1276, 1054, 764. ^{1}H-NMR (200 MHz, (D_6)DMSO): 9.59 (*s*, 1 H); 8.22 (*d*, *J* = 7.8, 1 H); 8.05 (*d*, *J* = 7.8, 1 H); 7.72 (*d*, *J* = 8.6, 1 H); 7.52 – 7.20 (*m*, 3 H); 6.80 (*d*, *J* = 8.6, 1 H); 5.50 (*q*, *J* = 7.8, 1 H); 2.02 – 1.85 (*m*, 5 H); 0.95 (*t*, *J* = 7.8, 3 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 169.25; 152.38; 132.10; 129.60; 126.49; 124.95; 124.45; 123.69; 123.14; 122.79; 107.55; 50.79; 49.65; 22.75; 11.15. LC/MS: 266 ($[M + Na]^+$).

REFERENCES

[1] N. J. Turro, *Tetrahedron* **1987**, *43*, 1589.

[2] M. A. Zolfigol, M. Kiany-Borazjani, M. M. Sadeghi, I. Mohammadpoor-Baltork, H. R. Memarian, *Synth. Commun.* **2000**, *30*, 551; M. A. Zolfigol, M. Kiany-Borazjani, M. M. Sadeghi, H. R. Memarian, I. Mohammadpoor-Baltork, *Synth. Commun.* **2000**, *30*, 294; M. A. Zolfigol, S. E. Mallakpour, *Synth. Commun.* **1999**, *29*, 4061; M. A. Zolfigol, M. Kiany-Borazjani, S. E. Mallackpour, H. Nassr-Isfahani, *Synth. Commun.* **2000**, *30*, 2573; M. A. Zolfigol, S. E. Mallakpour, E. Ghaemi, E. Madrakian, *Synth. Commun.* **2000**, *30*, 1689; M. A. Zolfigol, E. Ghaemi, E. Madrakian, M. Kiany-Borazjani, *Synth. Commun.* **2000**, *30*, 2057.

[3] J. M. Riego, Z. Sedin, J. M. Zaldivar, N. C. Marziano, C. Tortato, *Tetrahedron Lett.* **1996**, *37*, 513; M. A. Zolfigol, *Tetrahedron* **2001**, *57*, 9509.

[4] M. A. Zolfigol, I. Mohammadpoor-Baltork, B. F. Mirjalili, A. Bamoniri, *Synlett* **2003**, 1877; P. Salehi, M. Dabiri, M. A. Zolfigol, M. A. Bodaghi Fard, *Tetrahedron Lett.* **2003**, *44*, 2889; P. Salehi, M. Dabiri, M. A. Zolfigol, M. Boghban Zadeh, *Synlett* **2005**, 1155; M. A. Zolfigol, B. Abdolhamid, *Synlett* **2002**, 1621; M. A. Zolfigol, F. Shirini, A. Ghorbani Choghawarani, I. Mohammadpoor-Baltork, *Green. Chem.* **2002**, *4*, 562.

[5] A. K. Bose, S. Pednekar, S. N. Ganguly, G. Chakraborthy, M. S. Manhas, *Tetrahedron Lett.* **2004**, *45*, 8351.

[6] T. A. Keating, R. W. Armstrong, *J. Am. Chem. Soc.* **1995**, *117*, 7842; H. Groger, M. Hatam, J. Martens, *Tetrahedron* **1995**, *51*, 7173; T. Yamada, Y. Omote, Y. Yamanaka, T. Miyazawa, S. Kuwata, *Synthesis* **1998**, 991.

[7] K. Kobayashi, Y. Matoba, I. Susumu, M. Takashi, O. Morikswa, H. Konishi, *Chem. Lett.* **1998**, 551; R. Bossio, S. Marcaccini, R. Pepino, T. Torrroba, *J. Chem. Soc., Perkin Trans. 1* **1996**, 229.
[8] T. Akiyama, K. Matsuda, K. Fuchibe, *Synlett* **2005**, 322; G. Zhao, T. Jiang, H. Gao, B. Han, J. Huang, D. Sun, *Green Chem.* **2004**, *6*, 75; N. S. Chowdari, D. B. Ramachary, C. Barbas, *Synlett* **2003**, 1906; T. Akiyama, J. Takaya, H. Kagohsima, *Tetrahedron Lett.* **1999**, *40*, 7831; M. Arend, B. Westermann, N. Risch, *Angew. Chem., Int. Ed.* **1998**, *37*, 1045.
[9] M. M. Khodaei, A. R. Khosropour, H. Moghanian, *Synlett* **2006**, 916.
[10] B. Das, K. Laxminarayana, B. Ravikanth, B. Ramarao, *J. Mol. Catal., Sect. A* **2006**, *261*, 180.

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