Antimony(III) acetate an efficient catalyst for the synthesis of 1-amidoalkyl-2-naphthols

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Antimony(III) acetate was used in the one-pot three-component synthesis of multigram quantities of 1-amidoalkyl-2-naphthols from the condensation between aldehydes, 2-naphthol and acetamide under solvent-free conditions at ambient temperature. The present method has several advantages such as high yields, easy purification, mild reaction conditions, easy work-up, survival of different functional groups and very short reaction times.

Keywords: antimony(III) acetate, 2-naphthol, aldehydes, acetamide, 1-amidoalkyl-2-naphthols, solvent-free conditions

Multicomponent reactions (MCRs) are very important and efficient methods in organic synthesis to access complex structures from three or more reactions. Compounds bearing 1,3-amino-oxygenated functional groups are often found in various biologically important natural products and potent drugs, including nucleoside antibiotics and HIV protease inhibitors.[1] 1-Amidoalkyl-2-naphthol derivatives exhibit important cardiovascular, bradycardiac,[2] and hypertensive[3] activity. Previously some catalysts have been utilised in the synthesis of 1-amidoalkyl-2-naphthols.[4–27] Although many of the reported methods are effective, some of them suffer from disadvantages such as harsh reaction conditions, use of hazardous solvents, long reaction times, complex working and purification procedures, high catalyst loadings and moderate yields. Therefore, the development of a simple, mild and efficient method is still needed. In the present work, we used antimony(III) acetate as an efficient catalyst to overcome these limitations.

We have developed an efficient and very fast procedure for the one-pot synthesis of multigram quantities of 1-amidoalkyl-2-naphthols in high yields by the three-component condensation of 2-naphthol **1**, aldehydes **2**, and acetamide in the presence of antimony(III) acetate as a solid phase acidic catalyst, under solvent-free conditions at ambient temperature (Scheme 1).

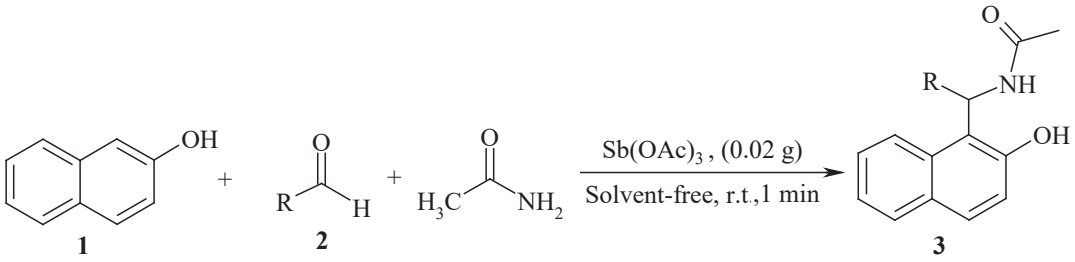
Results and discussion

Initially, the reaction of 2-naphthol **1** (1 mmol) with 4-nitrobenzaldehyde **2** (1 mmol) and acetamide (1 mmol) was chosen as a model system (Scheme 2).

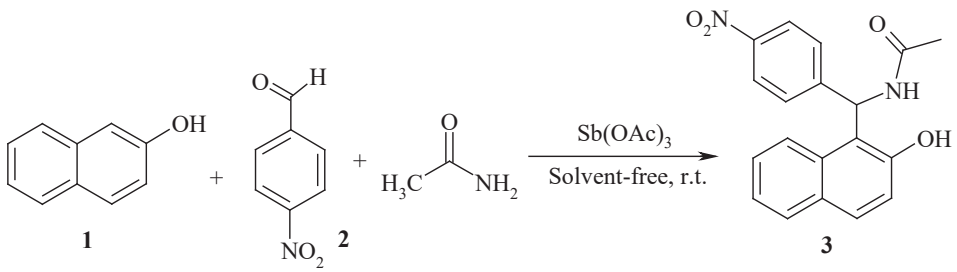
In order to determine the optimum quantity of $Sb(OAc)_3$, the reaction of 2-naphthol (1 mmol) with 4-nitrobenzaldehyde (1 mmol) and acetamide (1 mmol) using $Sb(OAc)_3$ was carried out at room temperature using varying quantities of $Sb(OAc)_3$ (Table 1). $Sb(OAc)_3$ (0.02 g) gave an excellent yield in 1 min (Table 1, entry 3).

In order to establish the better catalytic activity of $Sb(OAc)_3$, we have altered the catalyst and run the reaction under the same conditions (Table 2). Initially a control experiment confirmed that the reaction did not proceed in the absence of a catalyst (Table 2, entry 1). The results show that $Sb(OAc)_3$ is a more efficient catalyst with respect to the reaction time and exhibits broad applicability giving products in a similar or better yield (Table 2, entry 13).

Also to show the merit of the present work in comparison with reported results in the literature, we compared results using $FeCl_3.SiO_2$,[18] $HClO_4$-SiO_2,[19] iodine,[15] $Ce(SO_4)_2$,[14] $Al(H_2PO_4)_3$[21] and $NaHSO_4 \cdot H_2O$[20] in the synthesis 1-amidomethyl-2-naphthol



Scheme 1 Synthesis of 1-amidoalkyl-2-naphthols in the presence of antimony(III) acetate as catalyst.



Scheme 2 Synthesis of *N*-[(4-nitrophenyl)(2-hydroxynaphthalen-1-yl)methyl]acetamide in the presence of antimony(III) acetate as catalyst.

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Table 1 Optimisation of catalyst mass for the synthesis of 1-amidoalkyl-2-naphthols

Entry	Catalyst	Time/min	Yield/%[a]
1	0.04	1	96
2	0.03	1	96
3	0.02	1	96
4	0.01	1	70

[a]Isolated yield.

Table 2 Evaluation of the activity of different catalysts for the synthesis of 1-amidoalkyl-2-naphthols

Entry	Catalyst	Time/min	Yield/%[a]
1	None	1	0
2	$Ce(SO_4)_2$	1	10
3	I_2	1	18
4	K10 clay	1	20
5	$K_5CoW_{12}O_{40}\cdot 3H_2O$	1	24
6	$FeCl_3\cdot SiO_2$	1	15
7	$HClO_4\text{-}SiO_2$	1	26
8	$NaHSO_4\cdot H_2O$	1	20
9	$Al(H_2PO_4)_3$	1	16
10	*p*-TSA	1	30
11	Sulfamic acid	1	18
12	Silica sulfuric acid	1	22
13	$Sb(OAc)_3$	1	96

[a]Isolated yield.

Table 3 Comparison of $Sb(OAc)_3$ with $FeCl_3.SiO_2$,[18] $HClO_4\text{-}SiO_2$,[19] iodine,[15] $Ce(SO_4)_2$,[14] $Al(H_2PO_4)_3$[21] and $NaHSO_4\cdot H_2O$[20] in the synthesis of amidoalkyl naphthols

Entry	Catalyst	Time	Yield/%[a]
1	$FeCl_3\cdot SiO_2$ (0.025 g)	6 min	90
2	$HClO_4\text{-}SiO_2$ (0.024 g)	10 min	91
3	I_2 (5 mol%)	6 h	88
4	$Ce(SO_4)_2$ (100 mol%)	24 h	68
5	$Al(H_2PO_4)_3$ (0.075 g)	18 min	94
6	$NaHSO_4\cdot H_2O$ (0.045 g)	3 min	90
7	$Sb(OAc)_3$ (0.020 g)	1 min	96

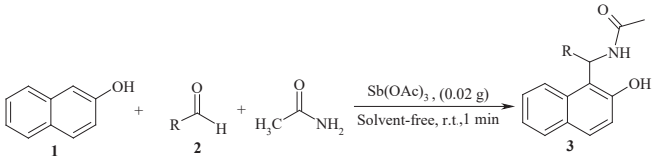
[a]Isolated yield.

Table 4 Effect of the solvent on the reaction between 2-naphthol with 4-nitrobenzaldehyde and acetamide using $Sb(OAc)_3$

Entry	Solvent	Temperature/ °C	Yield/%[a]
1	$CHCl_3$	Reflux	0
2	EtOH	Reflux	0
3	$CHCl_3$	25	0
4	EtOH	25	0
5	EtOAc	25	10
6	EtOAc	Reflux	15
7	Solvent-free	25	96

[a]Isolated yield.

Table 5 Reaction between 2-naphthol, aldehydes and acetamide catalysed by $Sb(OAc)_3$ (0.02 g) under solvent-free conditions



			M.p. (°C)	
3	R	%Yield*	Found	Reported[Ref.]
a	$2\text{-}NO_2C_6H_4$	95	260–262	263–265[28]
b	$3\text{-}NO_2C_6H_4$	96	254–256	252–256[29]
c	$4\text{-}NO_2C_6H_4$	96	243–245	242–243[30]
d	$3\text{-}ClC_6H_4$	92	238–240	237–238[29]
e	$4\text{-}ClC_6H_4$	90	228–230	226–228[29]
f	$2\text{-}OHC_6H_4$	90	214–216	215–217[30]
g	$3\text{-}CH_3OC_6H_4$	91	208–210	206–208[31]
h	$4\text{-}OH\text{-}3\text{-}CH_3OC_6H_3$	88	213–214	212[32]
i	Me	82	211–213	212[33]
j	$2\text{-}OH\text{-}3\text{-}CH_3OC_6H_3$	90	157–159	–
k	$4\text{-}CO_2CH_3C_6H_4$	90	220–222	–
l	$4\text{-}NHCH_3C_6H_4$	85	121–123	–

*Yields refer to the pure isolated products

derivatives. As shown in Table 3, $Sb(OAc)_3$ acts as an effective catalyst with respect to reaction times and yields of the obtained products. Thus, the present protocol with $Sb(OAc)_3$ catalyst is convincingly superior to other recently reported catalytic methods. Furthermore, $Sb(OAc)_3$ provides products of high purity in a short reaction time and is also eco-friendly.

The above reaction was also examined in various solvents (Table 4). The results indicated that different solvents affected the efficiency of the reaction. Most solvents required a longer reaction time and gave moderate yields, the highest yield was obtained when solvent-free conditions were used (Table 4, entry 7).

To study the scope of the reaction, a series of aldehydes, 2-naphthol and acetamide catalysed by $Sb(OAc)_3$ as catalyst were examined. The results are shown in Table 5. In all cases, aldehydes substituted with either electron-donating or electron-withdrawing groups underwent the reaction smoothly and rapidly to give products in excellent yields.

The compounds **3a**–**i** were characterised by ^1H, ^{13}C NMR and IR spectroscopy and elemental analyses.[28–33]

Compounds **3j**–**l** have not been previously synthesised and their structures were deduced by elemental and spectral analysis. The mass spectrum of compound **3j** showed the molecular ion peak at 337. The ^1H NMR spectrum of **3j** exhibits two sharp peaks at δ 2.02 and 3.73 ppm for the methyl protons. The methine proton (δ 6.16) and NH proton couple with each other and a doublet is observed for the NH proton at 8.00 ppm which disappears after addition of some D_2O to the DMSO-d_6 solution of **3j**. Multiplets are observed between 7.04 and 7.74 ppm which are associated with aromatic protons. The ^{13}C NMR spectrum of compound **3j** shows 20 distinct signals and is consistent with the proposed structure. The IR spectrum of compound **3j** also supported the suggested structure and showed absorption bonds at 3347, 3321 and 1635 cm^{-1}.

The method can be scaled up to a multigram scale. For example, the reaction of 2-naphthol (10 mmol, 1.44 g) with 4-nitrobenzaldehyde (10 mmol, 1.51 g) and acetamide (10 mmol, 0.59 g) in the presence of antimony(III) acetate (0.02 g) afforded a total amount of 2.6 g (96%) of 1-amidomethyl-2-naphthols, and further runs of this reaction using 15 mmol and 20 mmol of reactants similarly afforded good yields of products. Thus an efficient one-step, solvent-free synthesis of 1-amidomethyl-2-naphthols was achieved in the presence of antimony(III) acetate as a solid phase acidic catalyst.

In conclusion, we have developed a mild, highly efficient method for synthesis of multigram quantities of 1-amidoalkyl-2-naphthols. The method requires a simple work-up and very short reaction times, gives excellent yields and is inexpensive.

Experimental

All chemicals were purchased from commercial suppliers and were used without any purification. All products were identified by their spectra and physical data. Melting points were measured by using

the capillary tube method with an Electrothermal 9100 apparatus. Elemental analyses were performed using a Heraeus CHN–O–Rapid analyser. IR spectra were recorded on a Shimadzu spectrometer 883 (KBr pellets, Nujol mulls, 4000–400 cm^{-1}). ^1H NMR spectra were recorded on a Bruker-Avance DRX 400 spectrometer using TMS as an external standard.

Preparation of 1-amidoalkyl-2-naphtols catalysed by antimony(III) acetate

A mixture of 2-naphthol (1 mmol, 0.144 g), 4-nitrobenzaldehyde (1 mmol, 0.151 g), acetamide (1 mmol, 0.059 g) and antimony(III) acetate (0.02 g) was ground in a mortar for 1 min under solvent-free conditions at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the crude solid product was dissolved in CH_2Cl_2. The mixture was filtered to separate the catalyst. The catalyst was washed with CH_2Cl_2 (2 × 5 mL). The recovered catalyst was dried *in vacuo* and used in subsequent catalytic runs. The product was washed with cold diethyl ether (10 mL) and recrystallisation from MeOH afforded pure products.

N-*[(2-hydroxy-3-methoxyphenyl)(2-hydroxynaphthalen-1-yl) methyl]acetamide* (**3j**): Yellow powder; m.p. 157–159 °C; IR (ν_{max}/cm^{-1}) KBr: 3347, 3321, 1635; Anal. calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15; found: C, 71.38; H, 5.54; N, 4.29%; MS (*m/z*, %): 337 (6); ^1H NMR (400 MHz, DMSO-d_6): δ 2.02 (3H, s, CH_3), 3.73 (3H, s, OCH_3), 5.11 (1H, broad s, OH), 6.16 (1H, d, $^3J_{HH}$ = 8 Hz, NCH), 7.04–7.74 (9H, m, ArH), 8.00 (1H, d, $^3J_{HH}$ = 8 Hz, NH), 9.53 (1H, broad s, OH). ^{13}C NMR (100.6 MHz, DMSO-d_6): δ 21.4 (CH_3), 37.2 (CH), 55.2 (OCH_3), 112.1, 115.3, 118.7, 119.6, 121.0, 122.0, 123.9, 126.3, 128.3, 129.2, 129.4, 130.1, 133.0, 143.0, 151.8, 152.1, 173.0.

Methyl 4-[acetylamino(2-hydroxynaphtalen-1-yl)methyl]benzoate (**3k**): Pale brown powder; m.p. 220–222 °C; IR (ν_{max}/cm^{-1}) KBr: 3343, 3310, 1743, 1641; Anal. calcd for $C_{21}H_{19}NO_4$: C, 72.19; H, 5.48; N, 4.01; found: C, 72.01; H, 5.34; N, 4.23%; MS (*m/z*, %): 349 (3); ^1H NMR (400 MHz, DMSO-d_6): δ 2.10 (3H, s, CH_3), 3.79 (3H, s, OCH_3), 6.24 (1H, d, $^3J_{HH}$ = 8 Hz, NCH), 6.73–7.86 (10H, m, ArH), 8.13 (1 H, d, $^3J_{HH}$ = 8 Hz, NH), 9.55 (1 H, broad s, OH); ^{13}C NMR (100.6 MHz, DMSO-d_6): δ 23.3 (CH_3), 48.6 (CH), 51.4 (OCH_3), 115.4, 117.5, 118.8, 119.3, 122.1, 122.5, 123.2, 126.3, 128.1, 128.8, 130.4, 133.3, 147.2, 153.4, 167.9, 171.3.

N-*[(2-hydroxynaphthalen-1-yl)(4-methylaminophenyl)methyl] acetate* (**3l**): Brown powder; m.p. 121–123 °C; IR (KBr) (ν_{max}/cm^{-1}): 3350, 3345, 1681; Anal. calcd for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74; found: C, 75.13; H, 6.41; N, 8.90%; MS (*m/z*, %): 320 (5); ^1H NMR (400 MHz, DMSO-d_6): δ 2.17 (3H, s, CH_3), 2.69 (3H, s, NCH_3), 3.90 (1H, broad s, NH), 6.23 (1H, d, $^3J_{HH}$ = 8 Hz, NCH), 6.85–7.64 (10H, m, ArH), 8.16 (1 H, d, $^3J_{HH}$ = 8 Hz, NH), 9.67 (1 H, broad s, OH); ^{13}C NMR (100.6 MHz, DMSO-d_6): δ 23.5 (CH_3), 29.6 (NCH_3), 48.5 (CH), 114.2, 115.3, 118.8, 121.9, 123.3, 126.8, 128.7, 128.9, 129.6, 133.5, 145.2, 131.3, 134.0, 153.2, 172.1.

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References

1 D. Seebach and J.L. Matthews, *Chem. Commun*., 1997, 2015.
2 A.Y. Shen, C.T. Tsai and C.L. Chen, *Eur. J. Chem*., 1997, **34**, 877.
3 X.H. Cai. H. Guo and B. Xie, *Int. J. Chem.,* 2011, **3**, 119.
4 M.A. Zolfigol, A. Khazaei, A.R. Moosavi-Zare, A. Zare and V. Khaky-Zadeh, *Applied Catal. A: General,* 2011, **400**, 70.
5 A. Khazaei, M.A. Zolfigol, A.R. Moosavi-Zare, F. Abi, A. Zare, H. Kaveh, V. Khakyzadeh, K. Rostami, A. Parhami and H. Torabi-Monfared, *Tetrahedron*, 2013, **9**, 212.
6 A. Zare, S. Akbarzadeh, E. Foroozani, H. Kaveh, A.R. Moosavi-Zare, A. Hasaninejad, M. Mokhlesi, M.H. Beyzavi and M.A. Zolfigol, *J. Sulfur Chem.,* 2012, **23**, 259.
7 A. Zare, A. Hasaninejad, E. Rostami, A.R. Moosavi-Zare, N. Pishahang, M. Roshankar and M. Khedri, *E-J. Chem.,* 2010, **7**, 1162.
8 A.R. Hajipour, Y. Ghayeb, N. Sheikhan and A.E. Ruoho, *Tetrahedron Lett.,* 2009, **50**, 5649.
9 A.R. Supale and G.S. Gokavi, *J. Chem. Sci.,* 2010, **122**, 189.
10 B. Adrom, N. Hazeri, M.T. Maghsoodlou and M. Mollamohammadi, *Res. Chem. Intermed.,* 2015, **41**, 4741.
11 N. Hazeri, M.T. Maghsoodlou, S.M. Habibi-Khorassani, J. Aboonajmi and M. Safarzaei, *Chem. Sci. Trans.,* 2013, **2(S1)**, S330.
12 M. Kamali, *Der Pharma Chem.,* 2015, **7**, 318.
13 M. Hajjami, A. Ghorbani-Choghamarani and F. Gholamian, *Bulgar. Chem. Commun.,* 2015, **47**, 119.
14 N.P. Selvam and P.T. Perumal, *Tetrahedron Lett.*, 2006, **47**, 7481.
15 B. Das, K. Laxminarayana, B. Ravikanth and B.R. Rao, *J. Mol. Catal. A: Chem.,* 2007, **261**, 180.
16 S. Kantevari, S.V.N. Vuppalapati and L. Nagarapu, *Catal. Commun*., 2007, **8**, 1857.
17 L. Nagarapu, M. Baseeruddin, S. Apuri and S. Kantevari, *Catal. Commun*., 2007, **8**, 1729.
18 H.R. Shaterian and H. Yarahmadi, *Tetrahedron Lett.,* 2008, **49**, 1297.
19 H.R. Shaterian, H. Yarahmadi and M. Ghashang, *Tetrahedron,* 2008, **64**, 1263.
20 H.R. Shaterian and H. Yarahmadi, *Arkivoc,* 2008, **(ii)**, 105.
21 H.R. Shaterian, A. Amirzadeh, F. Khorami and M. Ghashang, *Synth. Commun*., 2008, **38**, 2983.
22 M.M. Khodaei, A.R. Khosropour and H. Moghanian, *Synlett,* 2006, 916.
23 S.B. Patil, P.R. Singh, M.P. Surpur and S.D. Samant, *Ultrason. Sonochem.,* 2007, **14**, 515.
24 G. Srihari, M. Nagaraju and M.M. Murthy, *Helv. Chim. Acta,* 2007, **90**, 1497.
25 H. Taghrir, M. Ghashang and M. Najafi Biregan, *Chin. Chem. Lett.,* 2016, **27**, 119.
26 A.R. Kiasat, L. Hemat-Alian and S.J. Saghanezhad, *Res. Chem. Intermed.,* 2016, 915.
27 Z. Karimi-Jaberi, M. Jokar and S.Z. Abbasi, *J. Chem.,* 2013, Article ID: 341649.
28 Q. Zhang, J. Luo and Y. Wei, *Green Chem.,* 2010, **12**, 2247.
29 J. Luo and Q. Zhang, *Monatsh. Chem.,* 2011, **142**, 923.
30 B.F. Mirjalili, A. Bamoniri and L. Rahmati, *Arab. J. Chem.,* 2016, DOI:10.1016/j.arabjc.2014.12.026.
31 S. Habibzadeh and H. Ghasemnejad, *J. Chin. Soc.,* 2012, **59**, 193.
32 B. Datta and M.A. Pasha, *Ultrason. Sonochem.,* 2010, **18**, 624.
33 M.M. Heravi, N. Tavakoli-Hoseini and F.F. Bamoharram, *Synth. Commun.,* 2011, **41**, 298.