An environmentally benign three component one-pot synthesis of amidoalkyl naphthols using $H_4SiW_{12}O_{40}$ as a recyclable catalyst

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Abstract.   One pot synthesis of amidoalkyl naphthol by condensation of aromatic aldehydes, 2-naphthol and amide/urea using silicotungstic acid as a catalyst is reported. The reaction was carried out under solvent-free reaction conditions. The method gave good yields of amidoalkyl naphthols in short reaction time compared with previous methods. The catalyst is recycled for five consecutive times without loss of activity.

Keywords.   Silicotungstic acid; amidoalkyl naphthols; multicomponent reaction; heterogeneous catalysis; solvent free conditions.

1. Introduction

One pot multicomponent reactions (MCR's), sometimes also called as zipper reactions, link several transformations in a single step. In recent decades, MCR's have gained wide applicability in the field of synthetic organic chemistry as they increase the efficiency of the reaction and decrease the number of laboratory operations along with quantities of solvent and chemicals used. They also reduce the reaction time considerably and facilitate the yield of products than the normal multiple step methods. MCR's are an important tool in reactions such as Biginelli,[1] Ugi[2] and Mannich.[3] Therefore, due to increased environmental responsibility and to develop more efficient catalytic systems in synthetic organic chemistry attempts have always been made to improve the known protocols. Such developments lead to prevail over one or more difficulties encountered in already reported systems.

1-amidoalkyl-2-naphthols are important intermediates which can be easily converted into biologically active 1-aminoalkyl-2-naphthols derivatives by amide hydrolysis. The hypertensive and bradycardiac effects of these compounds have been evaluated.[4,5] Various Brøonsted or Lewis acid catalysts have been utilized for the preparation of 1-amidoalkyl-2-naphthols.[6–10] However, some of the catalysts used suffer drawbacks such as long reaction time, toxicity, cost, unavailability and reusability of the catalyst. Therefore, there is still need for a green catalyst which can overcome one or more drawbacks and also an environmentally benign procedure to synthesize amidoalkyl naphthols.

Heteropoly acids due to their unique physico-chemical properties are widely used as homogeneous and heterogeneous catalysts[11] for redox and acid catalysed processes. The catalytic properties of heteropoly compounds have been associated with the characteristics of anionic units and the nature of elements contained in them. Among them, the compounds of Keggin structure are known for their good thermal stability, high acidity and high oxidizing capability and are used for various organic transformations.[12] Their significantly higher Brønsted acidity as compared with that of other traditional solid acids increased their importance in catalytic applications.[13] In continuation of our efforts to apply the properties of polyoxometalates in various organic transformations[1,14,15] we report here the catalytic activity of silicotungstic acid ($H_4SiW_{12}O_{40}$) for three component condensation of aldehyde, 2-naphthol and amide/urea to form 1-amidoalkyl-2-naphthols. The thermal condensation is carried out under solvent-free condition as shown in scheme 1.

2. Experimental

All the products have been reported previously and were characterized by comparison of their physical

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and spectral data. ^{1}H NMR was recorded on Bruker Avance 300 MHz spectrometer. Mass spectra were recorded on Shimadzu GCMS-QP2010. Melting points were determined on an open capillary and are uncorrected. IR was recorded on Perkin Elmer. Heteropoly acids and aldehydes, ethyl acetate were purchased from SD Fine chemicals (Mumbai, India) and used without further purification. All yields refer to isolated yields.
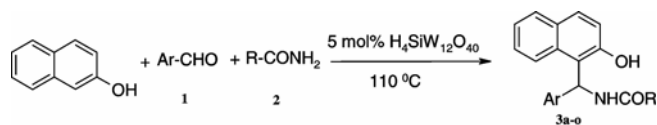
2.1 *General procedure for synthesis of amidoalkyl naphthols*

2-naphthol (1 mmol, 0·144 g), aldehyde (1 mmol), amide/urea (1·2 mmol) and catalyst (5 mol%) were taken in round-bottom flask. The reaction mixture was stirred at 110°C in oil bath. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled and ethyl acetate was added to it. The resulting solution was filtered off to separate catalyst. The filtrate was washed with aqueous $Na_2S_2O_3$. The organic layer was dried on anhydrous Na_2SO_4 which was concentrated to get the required product. The products were further recrystallized from 15% ethanol–water mixture.

Reusability of catalyst: After completion of the reaction, silicotungstic acid was separated by simple filtration. The separated catalyst was washed with ethyl acetate and dried at 100°C. This was reused further for five times without loss in its activity.

2.2 *Spectral data of selected compounds*

2.2a *Table 3, Entry 1* **(3a)** *– M.p. 242–244°C:* IR (KBr) 3400, 3249, 2924, 1640, 1583, 1515, 1437, 1373, 1338, 1278, 1210, 1160, 1029, 987, 932, 875, 839, 808, 743 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) $\delta = 9·98$ (*s*, 1H), 8·45–8·42 (*d*, 1H), 7·84–7·74 (*m*, 3H), 7·37–7·11 (*m*, 9H), 1·97 (*s*, 3H). MS *m/z*: 292 M$^+$ (17%), 248 (3%), 231 (100%), 202 (15%), 127 (3%), 115 (7%), 104 (6%), 77 (4%), 43 (8%).

Scheme 1. Acid catalysed synthesis of amidoalkyl naphthols.

2.2b *Table 3, Entry 2* **(3b)** *– M.p. 241–243°C:* IR (KBr) 3375, 3222, 2924, 2849, 1648, 1578, 1524, 1438, 1374, 1350, 1317, 1205, 1167, 1110, 1065, 1035, 1001, 925, 807, 741, 710 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10·13 (*s*, 1H), 8·63–8·60 (*d*, 1H), 8·05–8·001 (*m*, 2H), 7·83–7·78 (*m*, 3H), 7·56–7·40 (*m*, 2H), 7·30–7·25 (*m*, 1H), 7·19–7·15 (*m*, 3H), 2·01 (*s*, 3H). MS *m/z*: 337 M$^+$ (5%), 336 (23%), 319 (69%), 293 (5%), 276 (46%), 260 (45%), 247 (13%), 230 (100%), 218 (5%), 202 (44%), 189 (7%), 172 (7%), 145 (8%), 127 (10%), 115 (9%), 101 (7%), 43 (3%).

2.2c *Table 3, Entry 3* **(3c)** *– M.p. 202–204°C:* IR (KBr) 3376, 3193, 2926, 2824, 1742, 1647, 1610, 1581, 1518, 1438, 1369, 1339, 1308, 1279, 1234, 1154, 1104, 1060, 946, 856, 818, 751 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9·97 (*s*, 1H), 8·43 (*d*, 1H), 7·81–7·73 (*m*, 3H), 7·36 (*m*, 1H), 7·25–7·096 (*m*, 4H), 6·72 (*m*, 3H), 3·65 (*s*, 3H), 1·97 (*s*, 3H). MS *m/z*: 322 M$^+$ (8%), 321 (32%), 278 (5%), 261 (50%), 247 (15%), 231 (100%), 218 (13%), 202 (7%), 189 (10%), 134 (9%) 115 (12%), 109 (4%) 43 (14%).

2.2d *Table 3, Entry 4* **(3d)** *– M.p. 183–185°C:* IR(KBr) 3396, 3062, 3002, 2967, 2832, 2787, 2704, 2614, 1627, 1581, 1515, 1438, 1378, 1334, 1304, 1279, 1255, 1177, 1088, 1065, 1043, 983, 930, 880, 848, 822, 814, 8020, 745 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10 (*s*, 1H), 8·4 (*d*, 1H), 7·80–7·73 (*m*, 4H), 7·35–7·04 (*m*, 6H), 2·5 (*s*, 3H), 1·953 (*s*, 3H). MS *m/z*: 322 M$^+$(5%), 321 (20%), 278 (6%), 261 (98%), 247 (35%), 231 (100%), 218 (14%), 202 (5%), 189 (10%), 192 (7%), 144 (24%), 134 (19%), 115 (16%), 77 (6%), 43 (21%).

2.2e *Table 3, Entry 5* **(3e)** *M.p. 248–250°C:* IR(KBr) 3391, 3072, 1640, 1602, 1524, 1439, 1352, 1281, 1246, 1167, 1066, 1093, 983, 935, 883, 855, 825, 734, 750 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10·11 (*s*, 1H), 8·59–8·56 (*d*, 1H), 8·14–8·12 (*m*, 2H), 7·83–7·79 (*m*, 3H), 7·41–7·38 (*m*, 3H), 7·28–7·16 (*m*, 2H), 2·02 (*s*, 3H). MS *m/z*: 337 M$^+$ (8%), 336 (31%), 293 (8%), 276 (19%), 260 (72%), 247 (8%), 230 (100%), 202 (28%), 189 (6%), 145 (7%), 115 (13%), 43 (23%).

2.2f *Table 3, Entry 7* **(3g)** *– M.p. 166–168°C:* IR (KBr) 3429, 3393, 3377, 3193, 2925, 2849, 1726, 1655, 1601, 1527, 1476, 1439, 1350, 1315, 1267, 1206, 1142, 1095, 1040, 926, 812, 740 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10·11 (*s*, 1H), 8·05–

8·03 (*m*, 2H), 7·86–7·79 (*m*, 3H), 7·54–7·46 (*m*, 3H), 7·31–7·01 (*m*, 3H), 5·94 (*s*, 2H). MS *m/z*: 337 M$^+$ (7%), 336 (29%), 276 (18%), 260 (70%), 230 (100%), 202 (28%), 189 (6%), 145 (7%), 115 (13%), 43 (23%).

2.2g   *Table 3, Entry 8* (**3h**) – *M.p. 242–244°C*:   IR (KBr) 3481, 3405, 3377, 3179, 3062, 2924, 2849, 1716, 1655, 1600, 1517, 1439, 1346, 1257, 1140, 1109, 1018, 853, 825, 746 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9·957 (*s*, 1H), 7·82–7·73 (*m*, 3H), 7·41–7·27 (*m*, 1H), 7·24–7·11 (*m*, 3H), 6·89 (*m*, 2H), 6·75–6·72 (*m*, 3H), 5·82 (*s*, 2H), 3·65 (*s*, 3H). MS *m/z*: 322 M$^+$ (7%), 320 (30%), 276 (38%), 260 (65%), 230 (100%), 202 (55%), 189 (8%), 144 (34%), 127 (19%), 115 (37%), 101 (27%), 88 (16%), 77 (18%), 63 (12%), 51 (13%).

2.2h   *Table 3, Entry 12* (**3l**) – *M.p. 255–257°C*:   IR (KBr) 3374, 3277, 3090, 2972, 2916, 1634, 1578, 1531, 1522, 1509, 1480, 1439, 1347, 1308, 1280, 1207, 1171, 1093, 1070, 963, 928, 856, 815, 733 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10·42 (*s*, 1H), 9·15–9·13 (*d*, 1H), 8·11–8·08 (*m*, 4H), 7·90–7·82 (*m*, 5H), 7·73–7·71 (*m*, 2H), 7·61–7·38 (*m*, 6H). MS *m/z*: 398 M$^+$ (12%), 381 (49%), 276 (27%), 260 (35%), 246 (6%), 230 (53%), 202 (24%), 115 (11%), 105 (100%), 77 (54%), 51 (8%).

3.   Results and discussion

To optimize reaction conditions benzaldehyde and acetamide were chosen as model compounds. The various concentrations of catalyst silicotungstic acid were employed and reaction was carried out at 110°C. As the catalyst concentration increases there is an increase in the product yield and decrease in the time required with maximum yield at 5 mol% of catalyst. Further increase in the concentration of catalyst up to 10 mol% decreases the yield within the same time period. It was observed that there is no change in yield and selectivity when the temperature was increased above 110°C. The results are summarized in table 1. The scope of the reaction was verified by taking various aldehydes and subjected to the reaction along with acetamide, benzamide and urea as their counterparts in the reaction. The results of preparation of various amidoalkyl naphthols are summarized in table 2.
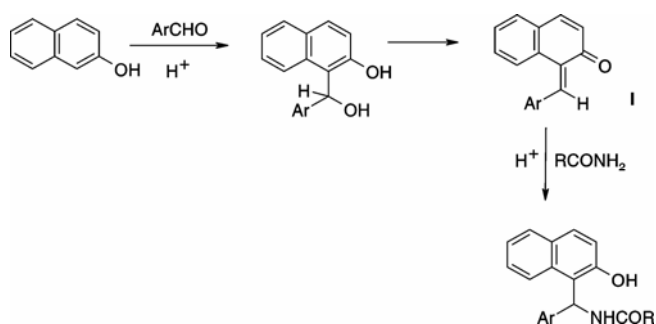
Aromatic aldehydes bearing electron donating substituents such as 3-methoxybenzaldehyde and electron withdrawing group such as 3-nitrobenzaldehyde gave good yields. The method gave various amidoalkyl naphthols in high yields (78–95%) within shortest time. Aliphatic aldehydes gave side products and hence required product could not be isolated. The probable mechanism is as shown in scheme 2.

It is known that reaction of 2-naphthol with aromatic aldehydes in the presence of acid catalyst give *othto*-quinone methides(*o*-QMs) (**I**) which reacted further, in presence of a catalyst, with amide/urea via conjugate addition to give 1-amidoalkyl-2-naphthols. After completion of the reaction, the reaction mixture was filtered off to get catalyst back. It was recycled for five times without loss in its activity (table 3).

4.   Conclusion

In summary, we have found that the silicotungstic acid is an extremely good heterogeneous acid catalyst for synthesis of amidoalkyl naphthols by condensation of aromatic aldehyde, 2-naphthol and amide/

Scheme 2.   Suggested mechanism for the formation of amidoalkyl naphthols via conjugate addition reaction.

Table 1.   Effect of catalyst concentration on the reaction[a].

Sr. no.	Catalyst (mol %)	Time (min)	Yield (%)[b]
1	0·1	100	48
2	1	80	60
3	2	75	80
4	3	40	85
5	4	30	88
6	5	15	92
7	10	12	92

[a]Reaction conditions: aldehyde (1 mmol), 2-naphthol (1 mmol) and amide/urea (1·2 mmol) and respective mol% $H_4W_{12}SiO_{40}$; [b]Isolated yield

Table 2. Preparation of amidoalkyl naphthols.

Entry	Product	Ar	R	Time (min)	Yield[b] (%)
1	**3a**	C_6H_5	CH_3	20	92
2	**3b**	$3\text{-}NO_2C_6H_5$	CH_3	15	95
3	**3c**	$3\text{-}OMeC_6H_5$	CH_3	35	88
4	**3d**	$4\text{-}OMeC_6H_5$	CH_3	40	80
5	**3e**	$4\text{-}NO_2C_6H_5$	CH_3	15	82
6	**3f**	C_6H_5	NH_2	35	90
7	**3g**	$3\text{-}NO_2C_6H_5$	NH_2	30	85
8	**3h**	$3\text{-}OMeC_6H_5$	NH_2	50	80
9	**3i**	$4\text{-}NO_2C_6H_5$	NH_2	30	85
10	**3j**	$4\text{-}OMeC_6H_5$	NH_2	50	80
11	**3k**	C_6H_5	Ph	20	88
12	**3l**	$3\text{-}NO_2C_6H_5$	Ph	15	91
13	**3m**	$3\text{-}OMeC_6H_5$	Ph	30	78
14	**3n**	$4\text{-}NO_2C_6H_5$	Ph	20	80
15	**3o**	$4\text{-}OMeC_6H_5$	Ph	40	80

[b]Pure isolated yield. All products have been reported previously and were characterized by comparison of IR, NMR and MS spectra with literature. Reaction condition – 5 mol% $H_4W_{12}SiO_{40}$, aldehyde(1 mmol), 2-naphthol (1 mmol) and amide/urea (1·2 mmol) at 110°C under solvent free condition

Table 3. Recyclability of catalyst.

Cycles	Yield[b]
Initial	92
1	92
2	92
3	90
4	88
5	85

[b]Pure isolated yield

urea. The reaction was carried out under solvent-free condition at 110°C. The method is environmentally benign and gives high yields of products after simple work-up procedure in short reaction time. The catalyst, silicotungstic acid, used was recycled for five times without any loss of activity.

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