Chemical Methodologies 4(2020) 400-407

Chemical Methodologies

Journal homepage: http://chemmethod.com

Original Research article

N,N,N′,N′-Tetramethyl-*N,N′*-bis(sulfo)ethane-1,2-Diaminium Mesylate as a Highly Effective and Dual-functional Catalyst for the Synthesis of 1-Thioamidoalkyl-2-naphthols

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ARTICLE INFORMATION

Received: 17 May 2019
Received in revised: 20 October 2019
Accepted: 19 December 2019
Available online: 01 July 2020

DOI: 10.33945/SAMI/CHEMM.2020.4.3

KEYWORDS

N,N,N′,N′-tetramethyl-*N,N′*-bis(sulfo)ethane-1,2-diaminium mesylate ([TMBSED][Oms]$_2$)
Thioacetamide
1-Thioamidoalkyl-2-naphthol
Multi-component reaction
Dicationic ionic liquid
Dual-functional catalyst

ABSTRACT

N,N,N′,N′-tetramethyl-*N,N′*-bis(sulfo)ethane-1,2-diaminium mesylate ([TMBSED][Oms]$_2$) is used as a highly efficient and dual-functional catalyst for the one-pot multi-component condensation of 2-naphthol with aryl aldehydes and thioacetamide under green, mild (70 °C), and solvent-free conditions. In this reaction, 1-thioamidoalkyl-2-naphthols are produced in high to excellent yields and in relatively short reaction times. In this reaction, products are identified by analysis of its ^{1}H NMR, ^{13}C NMR, and FT-IR data. Moreover, a plausible mechanism based on dual-functionality of the catalyst was proposed.

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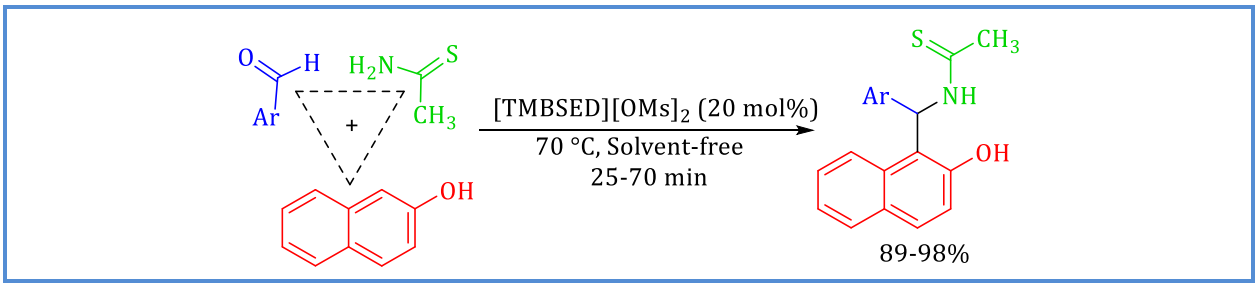
Graphical Abstract



Introduction

In multicomponent reactions (MCRs), three or more reactants are combined into a one-pot process. This may reduce the time and save the energy and the consumed raw materials. They are performed without isolating intermediates. MCRs offer the advantage of simplicity and synthetic efficiency over the conventional chemical reactions [1-8]. 1-thioamidoalkyl-2-naphthol derivatives are of importance as they can be easily hydrolyzed to the biologically interesting compounds. For example, one of the most important biologically active compounds, containing a 1-aminoalkyl-2-naphthol moiety in its structure which has been shown to have hypotensive, antipain, antibacterial, secretase inhibitory, notch-sparing, and bradycardic activities (Figure 1) [9-12, 17].

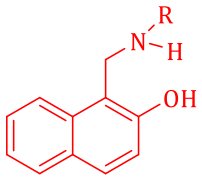


Figure 1. The general structures of 1-aminoalkyl-2-naphthols

The one-pot multi-component condensation of 2-naphthol with aldehydes and thioacetamide has been used as a practical synthetic route toward 1-thioamidoalkyl-2-naphthols [13-22]. Some catalysts have been applied for this transformation including, *p*-toluenesulfonic acid [13], $Fe(HSO_4)_3$ [14], 1,3-dibromo-5,5-dimethylhydantoin [15], 1,3-dichloro-5,5-dimethylhydantoin [16], 1,3,5-trichloro-1,3,5-triazinane-2,4,6-trione [16], trityl chloride [17], triethylaminium-*N*-sulfonic acid trifluoroacetate [18], *N*,2-dibromo-6-chloro-3,4-dihydro-2H-benzo[e][1,2,4]thiadiazine-7-sulfonamide 1,1-dioxide [19]. Saccharin sulfonic acid [20], tribromo-melamine [21], and P_2O_5-SiO_2 [22]. Ionic liquids (ILs) are generally composed of ions and solvent are considered unique. Ionic liquids have been widely studied due to their special properties such as high thermal stability, negligible vapor pressure, good solvation ability, high ionic conductivity, and the principles of green chemistry [23-26].

Another important practical technique in synthetic organic chemistry is carrying out reactions in solvent-free conditions. This technique has many advantages compared with solution conditions, which consist of compliance with green chemistry, higher yields, shorter reaction times, simplicity of reaction procedure, workup and purification, increment of selectivity, need for milder conditions, high effectiveness and minimization of by product/waste synthesis [27-29]. In this research study, we evaluated the one-pot multi-component condensation of 2-naphthol with aryl aldehydes and thioacetamide at the presence of catalytic amount of ([TMBSED][OMs]$_2$) under green and solvent-free conditions at 70 °C to produce 1-thioamidoalkyl-2-naphthols.

Experimental

All the chemicals were purchased from Merck, Fluka or Acros chemical companies. Monitoring progress of the reactions was achieved using the thin layer chromatography (TLC). The ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were performed using a Bruker avance DPX FT-NMR spectrometer; IR on Shimadzu IR-60; melting points were recorded using a Büchi B-545 apparatus in open capillary tubes.

Preparation of *N,N,N′,N′*-tetramethyl-*N,N′*-bis(sulfo)ethane-1,2-diaminium mesylate ([TMBSED][OMs]$_2$)

A solution of *N,N,N′,N′*-tetramethylethane-1,2-diamine (5 mmol, 0.581 g) in dry CH_2Cl_2 (20 mL) was added dropwise to a stirring solution of chlorosulfonic acid (10 mmol, 1.165 g) in dry CH_2Cl_2 (200 mL) over a period of 10 min at 10 °C. After that, the reaction mixture was allowed to heat to room temperature (accompanied by stirring), and stirred for another 4 h. The solvent was evaporated under reduced pressure, and the liquid residue was triturated with dry petroleum ether (3×2 mL), and dried under powerful vacuum at 90 °C to give [TMBSED][Cl]$_2$ [30]. Then, methanesulfonic acid (10 mmol, 0.96 g) was added dropwise to [TMBSED][Cl]$_2$ (5 mmol, 1.74 g) over a period of 3 min at room temperature under pressure of nitrogen gas (to remove the HCl produced during the reaction). The resulting mixture was stirred for 12 h at room temperature, and 2 h at 60 °C under a continuous flow of nitrogen gas to give [TMBSED][OMs]$_2$ as a viscous light-brown liquid in quantity yield [31].

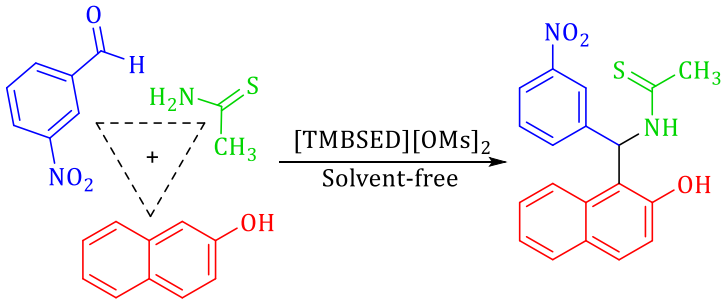
General procedure for the condensation of 2-naphthol with aryl aldehydes and thioacetamide

A mixture of 2-naphthol (1 mmol), aryl aldehyde (1 mmol), thioacetamide (1.2 mmol) and [TMBSED][OMs]$_2$ (0.20 mmol) was stirred mechanically at 70 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture

was allowed to cool down to room temperature, and the resulting solid was recrystallized from hot EtOH (95%) to give pure 1-thioamidoalkyl-2-naphthol (compounds **1-12**).

Results and discussion

At first, we selected the one-pot three-component condensation of 2-naphthol with 3-nitrobenzaldehyde and thioacetamide as model reaction to provide 1-thioamidoalkyl-2-naphthol **4**. The reaction was studied in the absence of catalyst under solvent-free conditions at 90 °C in which the product was obtained in 35% yield after 120 min. Afterward, the solvent-free reaction was examined in the presence of different amounts of $[TMBSED][OMs]_2$ (17-23 mol%) at range of 60-85 °C; the best results for were obtained when 20 mol% of $[TMBSED][OMs]_2$ was used at 70 °C (time: 35 min, yield: 98%).

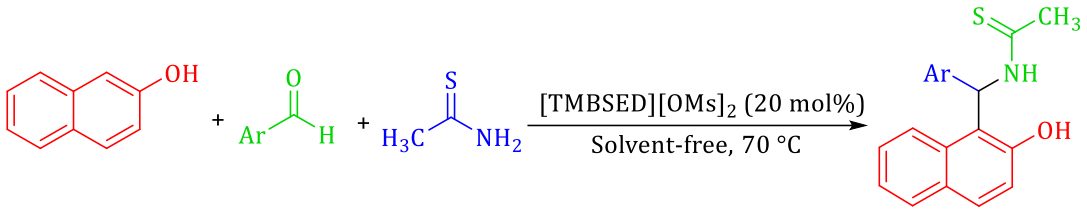


Scheme 1. The condensation of 2-naphthol with 3-nitrobenzaldehyde and thioacetamide

After choosing the best mol% of $[TMBSED][OMs]_2$ and temperature, these conditions were used for the condensation of 2-naphthol with different aromatic aldehydes and thioacetamide to show the efficiency and the generality of the method. The corresponding results are displayed in the Table 1. As seen in Table 1, all the aldehydes including, benzaldehyde and aryl aldehydes bearing various substituents on the *ortho*, *meta* and *para* positions, afforded the desired 1-thioamidoalkyl-2-naphthol derivatives in high to excellent yields (89-98%) within relatively short reaction times (25-70 min) (Table 1, compounds **1-12**). These observations confirmed that our method and catalyst are highly efficient.

To compare the efficiency of our method with the reported methods for the synthesis of 1-thioamidoalkyl-2-naphthols, we have tabulated the results of these methods to perform the condensation reaction between 2-naphthol, 3-nitrobenzaldehyde and thioacetamide in Table 2. As demonstrated in Table 2, compared to the previous studies, our approach revealed better performance in terms of the temperature, reaction time, and efficiency.

Table 1. The synthesis of 1-thioamidoalkyl-2-naphthols catalyzed by $[TMBSED][OMs]_2$ at 70 °C under solvent-free conditions



Product	Ar	Time (min)	Yield[a] (%)	M.p. °C (Lit.)
1	C_6H_5	55	91	192-194 (190-193) [17]
2	4-MeC_6H_4	55	92	181-183 (180-183) [17]
3	4-$O_2NC_6H_4$	45	95	245-247 (243-245) [14]
4	3-$O_2NC_6H_4$	35	98	232-234 (231-233) [18]
5	4-ClC_6H_4	35	89	244-246 (246-248) [14]
6	4-$MeOC_6H_4$	70	97	178-180 (181-182) [19]
7	2-$MeOC_6H_4$	55	90	214-215 (213-215) [13]
8	4-HOC_6H_4	45	94	238-240 (240-242) [15]
9	3-ClC_6H_4	45	91	257-259 (256-258) [19]
10	2,4-$Cl_2C_6H_3$	45	96	221-223 (219-221) [19]
11	2-$O_2NC_6H_4$	35	93	228-231 (228-231) [18]
12	2-FC_6H_4	25	95	238-240 (new)

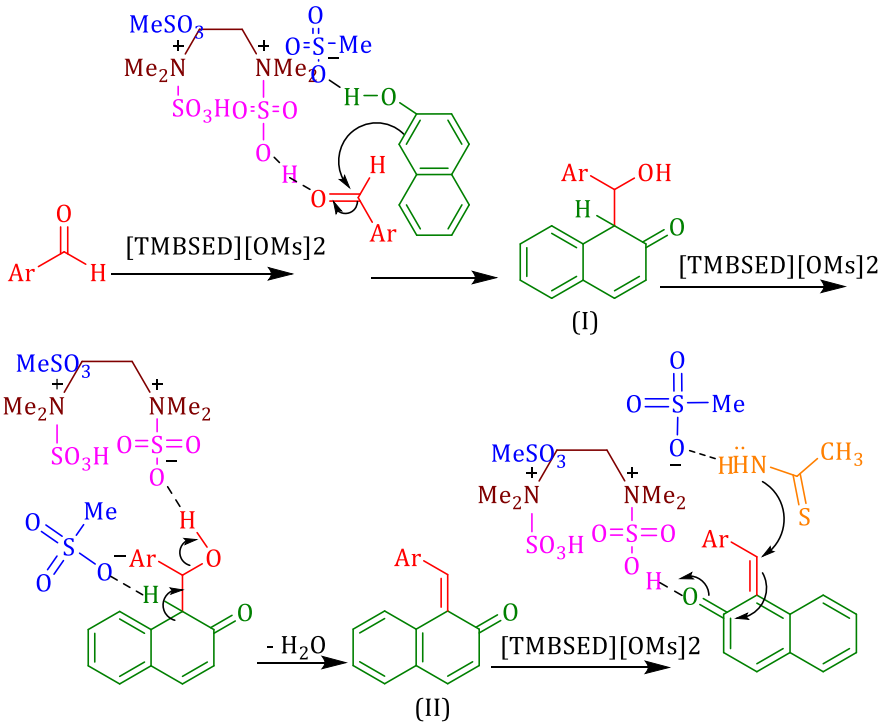
[a] Isolated yield

Table 2. Comparison of the results of the reaction of 2-naphthol with 3-nitrobenzaldehyde and thioacetamide using our method with those obtained by the reported methods

Catalyst	Temp. (°C)	Time (min)	Yield[a] (%)	Ref.
$[TMBSED][OMs]_2$	70	35	98	This work
SASA	70	40	75	[20]
p-TSA	100	60	90	[13]
DBH	130	150	93	[15]
TCCA	120	120	65	[16]
DCDMH	120	135	61	[16]
Trityl chloride	70	30	82	[17]
[TEASA][TFA]	100	15	96	[18]
DCDBTSD	80	30	78	[19]
Tribromo-melamine	130	180	95	[21]

In a plausible mechanism, ionic liquid is a dual-functional catalyst, as it has both acidic and basic sites (the SO_3H group is acidic and the mesylate is basic). Moreover, there are two acidic and basic sites in the catalyst. This issue is demonstrated in the reaction mechanism, Scheme 2. Two acidic and two basic sites of the ionic liquid can simultaneously catalyze the reaction. The proposed mechanism is supported by literature [13, 14, 19]. At first, the basic anion (mesylate) assists 2-naphthol for the addition to the activated aldehyde by the acidic hydrogen of $[TMBSED][OMs]_2$ to

produce the intermediate I. The removal of the H_2O molecule from I through the assistance of both the cation and anion in the IL gives the intermediate II. Finally, a Michael-type addition of thioacetamide to II affords the product, which is also accelerated by the acidic and basic sites of $[TMBSED][OMs]_2$.



Scheme 2. The proposed mechanism for the synthesis of 1-thioamidoalkyl-2-naphthol

Conclusions

In this work, we have introduced a new method for the one-pot three-component condensation of 2-naphthol with aromatioc aldehydes and thioacetamide using $[TMBSED][OMs]_2$ as an interesting SO_3H-containing catalyst in solvent-free conditions for synthesis of 1-thioamidoalkyl-2-naphthols. Advantages of this method include high efficiency, generality, relatively short reaction time, high yield, simplicity, ease of preparation and easy work-up and purification of the products. Furthermore, the catalytic system is environmentally benign and highly efficient, as well as being easy to prepare.

Acknowledgements

The authors would like to acknowledge the Research Council of Payame Noor University for providing the necessary research facilities and financial support for carrying out this work.

Conflict of Interest

We have no conflicts of interest to disclose.

References

[1] Devi I., Bhuyan P.J. *Tetrahedron Lett*., 2004, **45**:8625

[2] Mashraqui S.H., Patil M.B., Mistry H.D., Ghadigaonkar S., Meetsma A. *Chem. Lett*., 2004, **33**:1058

[3] Karami M., Gholami B., Hekmat-Zadeh T., Zare A. *Chem. Methodol.*, 2019, **3**:509

[4] Taghavi Fardood S., Ramazani A., Ayubi M., Moradnia F., Abdpour S., Forootan R. *Chem. Methodol.*, 2019, **3**:583

[5] Abshirini Z., Zare A. *Z. Naturforsc.*, 2018, **73b**:191

[6] Sujatha K., Vedula R.R. *J. Heterocyclic. Chem*., 2019, **56**:832

[7] Kumari S., Kumar D., Gajaganti S., Srivastava V., Singh S. *Synth. Commun*., 2019, **49**:431

[8] Kumari P., Bharti R., Parvin T. *Mol. Divers*., 2019, **23**:205

[9] Shen A.Y., Tsai C.T., Chen C.L. *Eur. J. Med. Chem*., 1999, **34**:877

[10] Gyémánt N., Engi H., Schelz Z., Szatmári I., Tóth D., Fülöp F., Molnár J., de Witte P.A.M., *Br. J. Cancer*, 2010, **103**:178

[11] Kidwai M., Chauhan R. *Asian J. Org. Chem*., 2013, **2**:395

[12] Wei H.X., Lu D., Sun V., Zhang J., Gu Y., Osenkowski P., Ye W., Selkoe D.J., Wolfe M.S., Augelli-Szafran C.E. *Bioorg. Med. Chem. Lett*., 2016, **26**:2133

[13] Hassanabadi A., Hosseini-Tabatabaei M.R. *J. Chem. Res*., 2012, **36**:510

[14] Eshghi H., Zohuri G.H., Damavandi S. *Synth. Commun*., 2012, **42**:516

[15] Ghorbani-Choghamarani A., Rashidimoghadam S. *Res. Chem. Intermed*., 2015, **41**:6271

[16] Khazaei A., Abbasi F., Moosavi-Zare A.R., Khazaei M., Beyzavi M.H. *J. Chin. Chem Soc.,* 2015, **62**:850

[17] Khazaei A., Zolfigol M.A., Moosavi-Zare A.R., Abi F., Zare A., Kaveh H., Khakyzadeh V., Kazem-Rostami M., Parhami A., Torabi-Monfared H. *Tetrahedron*, 2013, **69**:212

[18] Saadat A., Zare A., Jamadi F., Abdolalipour-Saretoli M. *Bull. Chem. React. Eng. Catal.*, 2018, **13**:204

[19] Khazaei A., Abbasi F., Moosavi-Zare A.R. *J. Sulfur Chem*., 2015, **36**:364

[20] Zare A., Kaveh H., Merajoddin M., Moosavi-Zare A.R., Hasaninejad A., Zolfigol M.A. *Phosphorus Sulfur Silicon Relat. Elem*., 2013, **188**:573

[21] Ghorbani-Choghamarani A., Rashidimoghadam S. *Chin. J. Catal*., 2014, **35**:1024

[22] Shaterian H.R., Azizi K., Fahimi N. *Res. Chem. Intermed*., 2014, **40**:2613

[23] Lang X.D., Li Z.M., He L.N. *Catal. Today*., 2019, **324**:167

[24] Ullah Z., Bustam M.A., Man Z., Khan A.S., Sarwono A., Muhammad N., Farooq N., Shah S.N., Ahmad, P., Haider S. *Int. J. Environ. Sci*., 2019, **16**:1269

[25] Keshapolla D., Srinivasarao K., Gardas R.L. *J. Chem. Therm.*, 2019, **133**:170

[26] Kanj A.B., Verma R., Liu M., Helfferich J., Wenzel W., Heinke L. *Nano Lett*., 2019, **19**:2114

[27] Kargar-Dolatabadi A., Zare A. *Chem. Methodol.*, 2019, **3**:655

[28] Zare A., Nasouri Z. *J. Mol. Liq*., 2016, **216**:364

[29] Reddy A.R., Farooq S., Dar B.A. *Chem. Methodol*., 2019, **3**:663

[30] Zare A., Sharif E., Arghoon A., Ghasemi M., Dehghani B., Ahmad-Zadeh S., Zarei F. *Iran. J. Catal.,* 2017, **7**:233

[31] Irannejad-Gheshlaghchaei N., Zare A., Sajadikhah S.S., Banaei A. *Res. Chem. Intermed*., 2018, **44**:6253

How to cite this manuscript: Navid Irannejad-Gheshlaghchaei*, Abdolkarim Zare, Alireza Banaei, Hamideh Kaveh, Nahid Varavi, *N,N,N′,N′*-Tetramethyl-*N,N′*-bis(sulfo)ethane-1,2-Diaminium Mesylate as a Highly Effective and Dual-functional Catalyst for the Synthesis of 1-Thioamidoalkyl-2-naphthols. Chemical Methodologies 4(4), 2020, 400-407. DOI:10.33945/SAMI/CHEMM.2020.4.3.