ICC
Iranian Chemical Communication
Original Research Article
Payame Noor University http://icc.journals.pnu.ac.ir

1,3-Disulfonic acid imidazolium hydrogen sulfate {[Dsim]HSO_4} as a highly efficient, recyclable and green catalyst for the preparation of α,α´-bis(arylidene)cycloalkanones

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Received: 5 April 2015, Accepted: 14 September 2015, Published: 14 September 2015

Abstract

A highly efficient and simple method for the preparation of α,α´-bis(arylidene)cycloalkanones under solvent-free conditions has been developed. The crossed-aldol condensation of cycloalkanones (Eq. 1) with arylaldehydes (Eq. 2) in the presence of 2.5 mol% of ionic liquid 1,3-disulfonic acid imidazolium hydrogen sulfate {[Dsim]HSO_4} afforded the title compounds in high yields and short reaction times. The catalyst has dual-functions and it is so because of possessing three acidic functional groups with different Brønsted acidic and basic sites. High catalytic activity and low loading of the catalyst can be attributed to its dual-functions.

Keywords: α,α´-Bis(arylidene)cycloalkanone; 1,3-disulfonic acid imidazolium hydrogen sulfate {[Dsim]HSO_4}; acidic ionic liquid; crossed-aldol condensation; cycloalkanone; arylaldehyde.

Introduction

α,α´-Bis(arylidene)cycloalkanones are of importance as they have different biological activities, such as quinine reductase inducer [1], cholesterol-lowering [2], antiangiogenic [3], and cytotoxic [4] properties. The use of these compounds as precursor for synthesis of pyrimidine derivatives has been also reported [5]. The crossed-aldol condensation reaction of cycloalkanones (Eq. 1) with arylaldehydes (Eq. 2) has been applied as the best synthetic route toward α,α´-

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bis(arylidene)cycloalkanone derivatives. Several catalysts have been used to promote this transformation [6-16]; nevertheless, most of these methods are associated with some disadvantages, including the use of expensive, unavailable and toxic catalysts, application of sealed ampoules or tubes, moderate yields, performing unwanted side reactions, long reaction times, the use of volatile organic solvents, application of an additional energy (microwave or ultrasonic), harsh conditions, and poor agreement with the green chemistry protocols. Thus, it is desirable to develope a highly efficient catalyst for the preparation of α,α´-bis(arylidene)cycloalkanones not accompanied by the above drawbacks.

In recent years, ionic liquids (ILs) have emerged as useful alternatives for conventional organic solvents or catalysts; because they have various particular properties, such as low vapor pressure, chemical and thermal stability, non-flammability, controlled miscibility, high boiling point, ability to solve a wide range of organic and inorganic compounds, and recyclability. Moreover, their polarity can be varied in wide range depending on the nature of both anions and cations; thus, they can be used as preferable solvents or catalysts for organic transformations [17-27]. Among the various kinds of ILs, Brønsted acidic ones have been especially applied as efficient, green, recyclable and selective catalysts in organic synthesis [21-27].

In many organic reactions, the use of volatile and toxic organic solvents as reaction media is unavoidable, and this subject is environmentally unacceptable from green chemistry view point. One of the most efficient techniques to solve this problem is solvent-free conditions, which makes synthesis simpler, saves energy and prevents solvent waste, hazards, and toxicity [28-30]. Consequently, it is noteworthy that the combination of safe catalysts accompanied by the application of solvent-free technique represents a suitable way toward the so-called “ideal synthesis” [28-30].

In this work, we report a highly efficient, green and recyclable catalyst with dual-functions, namely 1,3-disulfonic acid imidazolium hydrogen sulfate {[Dsim]HSO_4} for the solvent-free synthesis of α,α´-bis(arylidene)cycloalkanones by the crossed-aldol condensation reaction between cycloalkanones (Eq. 1) and arylaldehydes (Eq. 2). It is noteworthy that this method has none of the above-mentioned drawbacks at all.

Experimental

General

All chemicals were purchased from Merck or Fluka Chemical Companies. All known compounds were identified by comparison of their melting points and spectral data with those reported in the literature. Progress of the reactions was monitored by TLC using silica gel SIL G/UV 254 plates. The ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) were run on a Bruker Avance DPX, FT-NMR spectrometer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

Preparation of [Dsim]HSO_4

To a round-bottomed flask (100 mL) containing imidazole (0.340 g, 5 mmol) in dry CH_2Cl_2 (50 mL), chlorosulfonic acid (1.1885 g, 10.2 mmol) was added dropwise over a period of 20 min at room temperature. After the addition was completed, the reaction mixture was stirred for 12 h under pressure of nitrogen gas, then stood for 5 min, and finally the CH_2Cl_2 was decanted. The residue was washed with dry CH_2Cl_2 (3×50 mL), and dried under vacuum to give 1,3-disulfonic acid imidazolium chloride {[Dsim]Cl} as a viscous pale yellow oil in 95% yield. Then, sulfuric acid (99.99%) (0.49 g, 5 mmol) was added dropwise to [Dsim]Cl (1.63 g, 5 mmol) over a period of 5 min at room temperature under pressure of nitrogen gas (to remove the produced HCl during the reaction). The resulting mixture was stirred for 24 h at 60 °C under continuous flow of nitrogen gas to give [Dsim]HSO_4 as a viscous yellow oil in 99% yield [25-27].

General procedure for the synthesis of α,α´-bis(arylidene)cycloalkanones

A mixture of cycloalkanone (2 mmol), arylaldehyde (4.2 mmol) and [Dsim]HSO_4 (0.016 g, 2.5 mol%) in a test tube, was stirred magnetically at 80 °C, and after solidification of the reaction mixture, it was stirred with a small rod at the same temperature. After completion of the reaction, as monitored by TLC, the reaction mixture was cooled to room temperature, $CHCl_3$ (50 mL) was added, heated and stirred for 2 min, and stood for 2 min. The product was separated from the catalyst by decanting (the product is soluble in warm $CHCl_3$, but the catalyst isn't soluble in this solvent). Then, the $CHCl_3$ was evaporated, and the solid residue was recrystallized from ethanol (95%) to afford the pure product. The recovered catalyst was washed with $CHCl_3$ (10 mL), and used for next run. [Dsim]HSO_4 was re-used for two times without significant loss of its catalytic activity.

Selected spectral data of the products 2,6-Bis(3-chlorobenzylidene)cyclohexanone (3)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.69 (quintet, *J* = 5.7 Hz, 2H), 2.78 (t, *J* = 5.7 Hz, 4H), 7.30-7.37 (m, 6H), 7.41 (s, 2H), 7.62 (t, *J* = 1.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 23.7, 27.9, 126.3, 127.9, 129.3, 130.4, 130.9, 133.2, 135.8, 137.8, 188.9.

2,6-Bis(2 chlorobenzylidene)cyclohexanone (4)

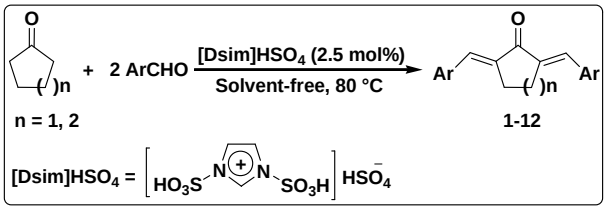
^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.75 (quintet, *J* = 5.8 Hz, 2H), 2.78 (t, *J* = 5.8 Hz, 4H), 7.28 (m, 4H), 7.34 (d, *J* = 3.4, 2H), 7.45 (d, *J* = 3.3 Hz, 2H), 7.89 (t, *J* = 1.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 23.2, 28.7, 126.8, 130.8, 130.9, 131.0, 134.5, 135.0, 135.5, 138.3, 189.2.

2,5-Bis(3-chlorobenzylidene)cyclopentanone (12)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.01 (s, 4H), 7.29-7.33 (m, 4H), 7.39-7.42 (m, 2H), 7.43 (s, 2H), 7.51 (t, *J* = 1.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 27.0, 128.6, 129.6, 130.5, 130.7, 132.5, 135.3, 137.1, 138.6, 196.0.

Results and discussion

In this work, 1,3-disulfonic acid imidazolium hydrogen sulfate was used as a highly efficient, green, inexpensive and recyclable catalyst for the preparation of α,α'-bis(arylidene)cycloalkanones *via* the condensation of arylaldehydes (Eq. 2) with cycloalkanones (Eq. 1) at 80 °C in the absence of solvent (Scheme 1).



Scheme 1. The synthesis of α,α'-bis(arylidene)cycloalkanones.

At first, the solvent-free condensation of 3-nitrobenzaldehyde (4.2 mmol) with cyclohexanone (2 mmol) was selected as a model reaction, and studied in the presence of different molar ratios of $[Dsim]HSO_4$ at range of 70-85 °C (Scheme 1). The results are summarized in Table 1. As the data in Table 1 show, 2.5 mol% of the catalyst was sufficient to catalyze the reaction efficiently. Moreover, the optimal temperature for the reaction was 80 °C. Increasing the amount of $[Dsim]HSO_4$ or the temperature didn't improve the results.

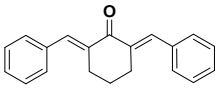
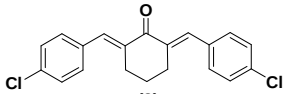
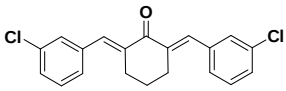
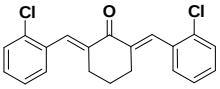
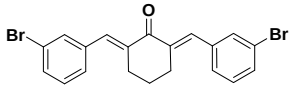
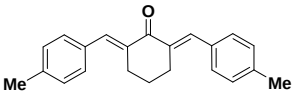
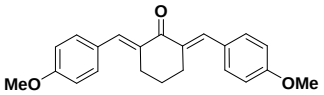
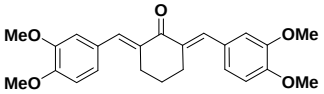
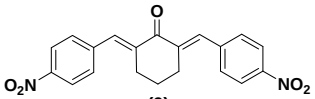
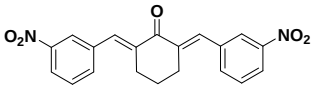
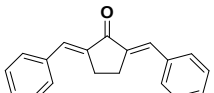
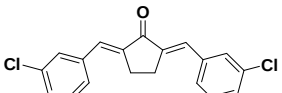
Table 1. Effect of the catalyst amount and temperature on the reaction of 3-nitrobenzaldehide with cyclohexanone

Entry	Mol% of $[Dsim]HSO_4$	Temp. (°C)	Time (min)	Yield[a] (%)
1	-	80	60	Trace
2	1.5	80	15	72
3	2.5	80	15	87
4	4	80	15	87
5	2.5	70	20	83
6	2.5	85	15	87

[a]Isolated yield

After optimization of the reaction conditions, the generality and the efficacy of the method were explored by studying the reaction of different arylaldehydes with cycloalkanones; the corresponding results are summarized in Table 2. As Table 2 indicates, all arylaldehydes (bearing halogens, electron-withdrawing and electron-releasing substituents on their aromatic rings) afforded the desired α,α'-bis(arylidene)cycloalkanones in high to excellent yields and in short reaction times. Thus, the method was highly efficient and general.

Table 2. The synthesis of α,α'-bis(arylidene)cycloalkanones using [Dsim]HSO_4

Product	Time[a]/ Yield[b]	M.p. °C (Lit.)
 (1)	20/92	115-117 (113-115) [7]
 (2)	20/97	144-146 (143-145) [7]
 (3)	20/95	106-108 (108-110) [8]
 (4)	20/93	103-105 (103-105) [8]
 (5)	20/92	118-120 (119-120) [12]
 (6)	20/95	172-174 (169-171) [8]
 (7)	20/93	161-163 (160-162) [14]
 (8)	20/97	164-166 (162-164) [8]
 (9)	15/93	155-157 (156-158) [8]
 (10)	15/87	183-185 (184-186) [7]
 (11)	20/89	187-189 (188-189) [14]
 (12)	20/93	174-176 (174-176) [7]

[a]Reaction time in min

[b]Isolated yield in %

[Dsim]HSO_4 has three acidic groups with different Brønsted acidic and basic sites (Fig. 1); thus, a few amount of it (2.5 mol%) was sufficient to promote the crossed-aldol reaction efficiently.

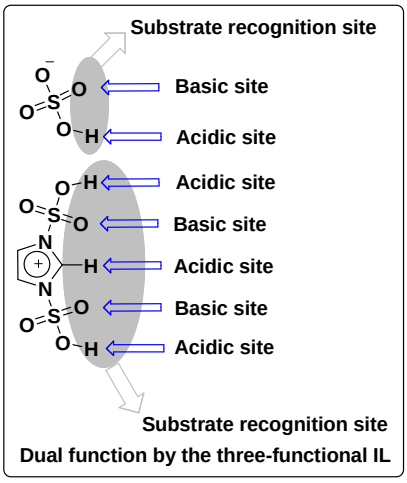
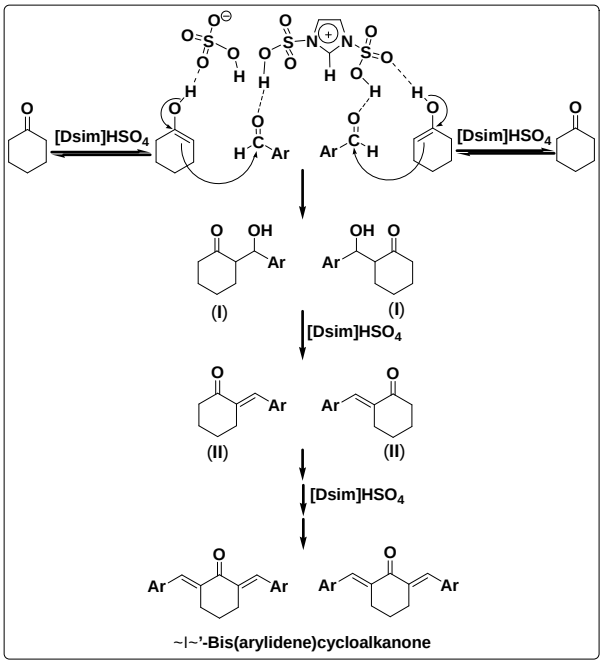


Figure 1. The structure of [Dsim]HSO_4

In a plausible mechanism (Scheme 2), we suggest that at first cycloalkanone is converted to its enol form using [Dsim]HSO_4. On the other hand, the acidic site of the catalyst activates the carbonyl group of aldehyde to accept nucleophilic attack. Afterward, the activated enol (by the basic site of the catalyst) reacts with the activated aldehyde to afford intermediate I. Removing one molecule H_2O from I using [Dsim]HSO_4, gives intermediate II. The same steps are applied to afford the desired α,α´-bis(arylidene)cycloalkanone. The mechanism is confirmed by the literature [7,9,12]. In fact, the catalyst not only activates the carbonyl group of aldehyde and the hydroxyl group of enol form of cycloalkanone, it also can collect and arrange two molecules of each starting materials by forming hydrogen-bond via its different acidic and basic sites. For these reasons, a few amount of [Dsim]HSO_4 (2.5 mol%) was sufficient to catalyze the reaction efficiently.

Conclusion

In summary, we have showed that 1,3-disulfonic acid imidazolium hydrogen sulfate could efficiently catalyze the crossed-aldol condensation of arylaldehydes with cycloalkanones. The promising points for the presented protocol are simple and clean reaction profile, efficiency, generality, low catalyst loading, high yields, performing the reaction in solvent-free media without side reactions, non-toxicity as well as low cost of the catalyst, and good compliance with the green chemistry protocols, which makes it an attractive procedure for the synthesis of α,α´-bis(arylidene)cycloalkanones as an important class of organic compounds.



Scheme 2. The mechanism for the synthesis of α,α´-bis(arylidene)cycloalkanones

Acknowledgments

The authors gratefully acknowledge financial support of this work by the Research Affairs Office of Payame Noor University.

References

[1] A.T. Dinkova-Kostova, C. Abeygunawardana, P. Talalay, *J. Med. Chem.*, **1998**, *41*, 5287-5296.

[2] C. Piantadosi, I.H. Hall, J.L. Irvine, G.L. Carlson, *J. Med. Chem.*, **1973**, *16*, 770-775.

[3] T.P. Robinson, R.B. Hubbard, T.J. Ehlers, J.L. Arbiser, D.J. Goldsmith, J.P. Bowen, *Bioorg. Med. Chem.*, **2005**, *13*, 4007-4013.

[4] A. Modzelewska, C. Pettit, G. Achanta, N.E. Davidson, P. Huang, S.R. Khan, *Bioorg. Med. Chem.*, **2006**, *14*, 3491-3495.

[5] J. Deli, *Pharmazie*, **1984**, *39*, 539-540.

[6] M. Vashishtha, M. Mishra, S. Undre, M. Singh, D.O. Shah, *J. Mol. Catal. A: Chem.*, **2015**, *396*, 143-154.

[7] A. Zare, M. Merajoddin, A. Hasaninejad, A.R. Moosavi-Zare, V. Khakyzadeh, *C. R. Chim.*, **2013**, *16*, 380-384.

[8] A. Hasaninejad, A. Zare, L. Balooty, H. Mehregan, M. Shekouhy, *Synth. Commun.*, **2010**, *40*, 3488-3495.

[9] G. Mohammadi Ziarani, A. Badiei, A. Abbasi, Z. Farahani, *Chin. J. Chem.*, **2009**, *27*, 1537-1542.

[10] A. Allahresani, M.A. Nasseri, B. Zakeri Nasab, *Iran. Chem. Commun.*, **2015**, *3*, 93-102.

[11] S.F.P. Braga, É.V.P. Alves, R.S. Ferreira, J.R.B. Fradico, P.S. Lage, M.C. Duarte, T.G. Ribeiro, P.A.S. Júnior, A.J. Romanha, M.L. Tonini, M. Steindel, E.F. Coelho, R.B. de Oliveira, *Europ. J. Med. Chem.*, **2014**, *71*, 282-289.

[12] F. Shirini, S. Sarvi Beigbaghlou, S. V. Atghia, *Iran. J. Catal.*, **2012**, *2*, 157-163.

[13] A. Lahyani, M. Chtourou, M.H. Frikha, M. Trabelsi, *Ultrason. Sonochem.*, **2013**, *20*, 1296-1301.

[14] M. Zhang, L. Wang, J. Shao, Q. Zhong, *Synth. Commun.*, **1997**, *27*, 351-354.

[15] A. Amoozadeh, E. Tabrizian, S. Rahmani, *C. R. Chim.*, in press (doi: 10.1016/j.crci.**2014**.11.003).

[16] Y. Riadi, R. Mamouni, R. Azzalou, R. Boulahjar, Y. Abrouki, M.E. Haddad, S. Routier, G. Guillaumet, S. Lazar, *Tetrahedron Lett.*, **2010**, *51*, 6715-6717.

[17] H. Olivier-Bourbigou, L. Magna, D. Morvan, *Appl. Catal. A: Gen.*, **2010**, *373*, 1-56.

[18] P. Wasserscheid, T. Welton, *Ionic Liquids in Synthesis*, Wiley-VCH, Weinheim, **2008**.

[19] P. Hapiot, C. Lagrost, *Chem. Rev.*, **2008**, *108*, 2238-2264.

[20] S.C. Azimi, K. Rad-Moghadam, *Iran. Chem. Commun.*, **2015**, *3*, 363-373.

[21] A.R. Hajipoura, N. Sheikhan, M.A. Alaei, A. Zarei, *Iran. J. Catal.*, **2015**, *5*, 231-236.

[22] K. Zhuo, Q. Du, G. Bai, C. Wang, Y. Chen, J. Wang, *Carbohydr. Polym.*, **2015**, *115*, 49-53.

[23] H. Ren, B. Girisuta, Y. Zhou, L. Liu, *Carbohydr. Polym.*, **2015**, *117*, 569-576.

[24] A. Ying, Z. Li, Y. Ni, S. Xu, H. Hou, H. Hu, *J. Indust. Engin. Chem.*, **2015**, *24*, 127-131.

[25] F. Shirini, A. Yahyazadeh, K. Mohammadi, N. Ghaffari Khaligh, *C. R. Chim.*, **2014**, *17*, 370-376.

[26] A. Zare, F. Abi, A.R. Moosavi-Zare, M.H. Beyzavi, M.A. Zolfigol, *J. Mol. Liq.*, **2013**, *178*, 113-121.

[27] M.A. Zolfigol, A. Khazaei, A.R. Moosavi-Zare, A. Zare, Z. Asgari, V. Khakyzadeh, A. Hasaninejad, *J. Indust. Engin. Chem.*, **2013**, *19*, 721-726.

[28] K. Tanaka, *Solvent-free Organic Synthesis*, Wiley-VCH, GmbH and KGaA, Weinheim, **2004**.

[29] E. Abbaspour-Gilandeh, S.C. Azimi, *Iran. Chem. Commun.*, **2015**, 3, 218-231.

[30] R. Hajinasiri, S. Rezayati, *Iran. Chem. Commun.*, **2015**, *3*, 159-165.