Catal Lett (2008) 121:255–259
DOI 10.1007/s10562-007-9325-0

Synthesis of Coumarins via Pechmann Reaction in Water Catalyzed by Acyclic Acidic Ionic Liquids

Fang Dong · Cheng Jian · Gong Kai ·
Shi Qunrong · Liu Zuliang

Received: 16 July 2007 / Accepted: 22 October 2007 / Published online: 8 November 2007

Abstract Some recyclable acyclic SO_3H-functionalized ionic liquids have been used as catalysts for Pechmann condensation reaction. *N*, *N*, *N*-trimethyl-*N*-propanesulfonic acid ammonium hydrogen sulfate [TMPSA][HSO_4] has been proved to be the most active catalyst. The coumarins products could simply be separated from the catalyst by filtration and the catalyst could be recycled and reused for several times without noticeably decreasing the catalytic activity.

Keywords Pechmann reaction · Ionic liquid · Catalyst

1 Introduction

Coumarins and its derivatives have attracted great interest because of their importance in the synthetic organic and medicinal chemistry. They are widely used as additives in foods, perfumes, cosmetics, pharmaceuticals [1], and in the preparation of insecticides, optical brighteners [2] and dispersed fluorescent and laser dyes [3]. Coumarins have been synthesized by several methods including Pechmann [4], Perkin [5], Knoevenagel [6], Reformatsky [7], Wittig [8] reactions and by flash vacuum pyrolysis [9].

The Pechmann reaction is one of the most widely applied method for the synthesis of coumarins and its derivatives, which involves the condensation of phenols with β-ketoesters in the presence of a variety of acidic condensing agents. Several acid catalysts have been used in the conventional procedure, such as sulfuric acid [4], aluminum chloride [10], phosphorus pentoxide [11] or trifluoroacetic acid [12].

However, these catalysts have to be used in large excess, and they cannot be recovered or reused. The disposal of acidic waste leads to environmental pollution. Therefore, it is important to find the simple, cheap, and recoverable catalysts for the synthesis of coumarins. Nowadays cleaner and safer methods have been developed: using microwave irradiation [13], solid acids and Lewis acids as catalysts to prompt the Pechmann condensation [14], and the search for the new readily available and green catalysts is still being actively pursued.

Acidic task-specific ionic liquids (TSILs), which possess the advantageous characteristics of solid acids and mineral acids, are designed to replace traditional mineral liquid acids, such as sulfuric acid and hydrochloric acid. Potdar et al. synthesized coumarin in Lewis acidic chloroaluminate ionic liquid and neutral ionic liquids [15], Gu and coworkers reported Pechmann reaction in no-chloroaluminate acidic ionic liquids [16]. In fact, the use of Brønsted-acidic TSILs as catalysts is an area of ongoing activity; however, development and exploration of acidic TSILs are currently in the preliminary stage.

To date, research of some "greener" halogen-free ionic liquids with phosphate or octyl sulfate anions and the effects of the anion and toxicology have appeared in literature [17]. We are especially interested in developing the potential use of simple, inexpensive TSILs catalysts. In our previous work the novel and cheap SO_3H-functional halogen-free acidic ionic liquids that bear an alkane sulfonic acid group in an acyclic trimethylammonium cation

---

F. Dong · C. Jian · G. Kai · S. Qunrong · L. Zuliang (✉)
School of Chemical Engineering, Nanjing University of Science & Technology, Nanjing 210094, P.R. China
e-mail: liuzuliang302@163.com

F. Dong
Jiangsu Provincial Key Laboratory of Coastwetland Bioresources & Environment Protection, Yancheng 224002, P.R. China

have been synthesized, and their catalytic activity for acid-catalyzed reactions have also been investigated [18]. In continuation of our work in studying acid-catalyzed reactions in ionic liquids, we report here the synthesis of coumarin derivatives by the Pechmann condensation in halogen-free acidic ionic liquids.

2 Experimental

2.1 Materials and Methods

Melting points were determined on X-6 microscope melting apparatus and reported uncorrected. The IR spectra were run on a Nicolete spectrometer and expressed in cm^{-1} (KBr). ^{1}H NMR spectra were recorded on Bruker DRX300 (300 or 500 MHz) and ^{13}C NMR spectra on Bruker DRX300 (75.5 MHz) spectrometer. Mass spectra were obtained with automated FININIGAN Trace Ultra-Trace DSQ GC/MS spectrometer. All chemicals (AR grade) were commercially available and used without further purification.

2.2 Synthesis of SO_3H-functional Halogen-free Acidic Ionic Liquid (TSILs)

All used acyclic SO_3H-functionalized halogen-free acidic ionic liquids were synthesized according to our previous methods [18d]. The TSILs was analyzed by ^{1}H NMR, ^{13}C NMR and MS spectroscopies, and the spectral data agreed with their structures (Scheme 1).

The selected spectral data for SO_3H-functionalized halogen-free TSILs:

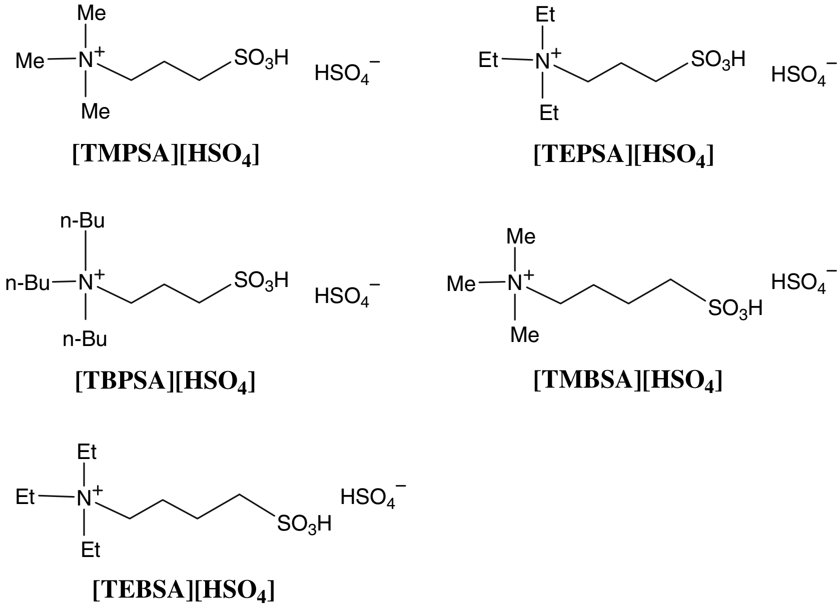
N, *N*, *N*-trimethyl-*N*-propanesulfonic acid ammonium hydrogen sulfate [TMPSA][HSO_4] ^{1}HNMR (300 Mz, D_2O): δppm 3.22 (*t*, $J = 7.2$ Hz, 2H, –N–CH_2–), 2.90 (s, 9H, –CH_3), 2.73 (*t*, $J = 7.8$ Hz, 2H, –CH_2–SO_3), 1.99 (m, 2H, –CH_2–). ^{13}CNMR (75.5 Mz, D_2O): δppm 65.00, 52.51, 47.89, 18.85. MS (m/z): 279.05 (M^+), 182.14 (100).

N, *N*, *N*-triethyl-*N*-propanesulfonic acid ammonium hydrogen sulfate [TEPSA][HSO_4] ^{1}HNMR (300 Mz, D_2O): δppm 3.22–3.05 (m, 8H, (6H + 2H), –N–CH_2–CH_3, –N–CH_2–C_2H_4–), 2.85 (*t*, $J = 7.2$ Hz 2H, –CH_2–SO_3), 1.97 (m, 2H, –CH_2–), 1.12 (*t*, 9H, –CH_3). ^{13}CNMR (75.5 Mz, D_2O): δppm 56.00, 52.95, 48.34, 18.93, 8.04. MS (m/z): 321.05 (M^+), 322.05, 320.15, 194.05 (100).

N, *N*, *N*-tributhyl-*N*-propanesulfonic acid ammonium hydrogen sulfate [TBPSA][HSO_4] ^{1}HNMR (500 Mz, D_2O): δppm 3.28 (*t*, 2H, $J = 4.0$ Hz, –N–CH_2–), 3.13 (*t*, 6H, $J = 8.5$ Hz, –N–CH_2–), 2.85 (*t*, 2H, $J = 7.0$ Hz, –CH_2–SO_3), 2.03 (m, 2H, CH_2–CH_2–CH_2), 1.56 (m, 6H, –CH_2–CH_2CH_3), 1.27 (m, 6H, –CH_2–CH_3), 0.84 (*t*, 9H, $J = 7.5$ Hz, –CH_3). ^{13}CNMR (75.5 Mz, D_2O): δppm 58.49, 50.66, 48.42, 23.93, 20.36, 19.16, 14.46. MS (m/z): 405.29 (M^+), 406.28, 404.28 (100).

N, *N*, *N*-trimethyl-*N*-butanesulfonic acid ammonium hydrogen sulfate [TMBSA][HSO_4] ^{1}HNMR (300 Mz, D_2O): δppm 3.24 (*t*, $J = 8.4$ Hz, 2H, –N–CH_2–), 2.99 (s, 9H, –CH_3), 2.85 (*t*, $J = 7.5$ Hz, 2H, –CH_2–SO_3), 1.82 (m, 2H, –CH_2–), 1.70 (m, 2H, –CH_2–). ^{13}CNMR (75.5 Mz, D_2O): δppm 66.15, 53.16, 50.31, 21.46, 19.93. MS (m/z): 293.36 (M^+), 196.39 (100).

N, *N*, *N*-triethyl-*N*-butanesulfonic acid ammonium hydrogen sulfate [TEBSA][HSO_4] ^{1}HNMR (300 Mz, D_2O): δppm 3.15 (q, $J = 7.2$ Hz, 6H, –N–CH_2–CH_3), 3.07 (*t*, $J = 8.4$ Hz, 2H, –N–CH_2– $C_3H_6SO_3$), 2.82 (*t*, $J = 7.2$ Hz,



Scheme 1 The halogen-free ionic liquids used in Pechmann condensation

2H, –CH_2–SO_3), 1.68 (m, 4H, –C_2H_4–CH_2SO_3), 1.11 (m, $J = 7.2$ Hz, 9H, –CH_3). ^{13}CNMR (75.5 Mz, D_2O): δppm 56.21, 52.85, 50.32, 21.50, 20.20, 6.90. MS (m/z): 335.35 (M^+), 208.36 (100).

2.3 General Procedure for the Pechmann Condensation Catalyzed by TSILs

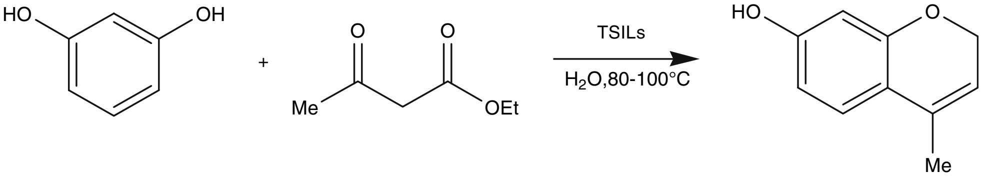
In a typical experiment, weighed 20 mmol phenols, 20 mmol ethyl acetoacetate, 1.0 mmol ionic liquid TSILs and 10 mL of water were mixed in a 25 mL round-bottom flask equipped with a distillation condenser. The reaction was typically allowed to proceed for a length of time (0.8–4 h) at 80 °C with the vigorous stirring. After the reaction (TLC monitored), the reaction mixture was cooled to room temperature then filtered, the crude product was then recrystallized form ethanol to give pure product as colorless prisms. The ionic liquids contained in the filtrate could be reused directly in the next run without further purification. The products were identified by ^{1}HNMR, and physical data (m.p.) with those reported in the literatures.

3 Results and Discussion

For the beginning of this study, resorcinol and ethyl acetoacetate were employed as the model reactants at 80 °C in water for a length of time to compare the catalytic performance of the TSILs.

As shown in Table 1, no reaction was observed in the absence of ionic liquids (entry 1), which indicated that the catalyst should be absolutely necessary for the Pechmann reaction. All the five TSILs proved to be very active, leading to 89–94% yield of 7-hydroxy-4-methylcoumarin within 60 min in the presence of 5% TSILs (entries 4, 10–13). In addition, ionic liquids containing the shorter length of alkyl chain are relatively cheaper. Hence, [TMPSA][HSO_4] should be the best catalyst for the Pechmann condensation among the five TSILs and the optimized reaction conditions went to entry 4 in Table 1. The prolonged reaction time and

Table 1 The Pechmann condensation between resorcinol and ethyl acetoacetate catalyzed by ionic liquids[a]



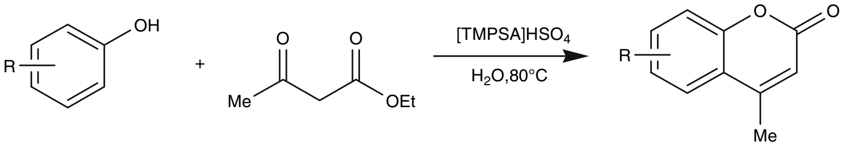
Entry	Catalysts	TSILs (%)[b]	Time (min)	T (°C)	Isolated yield (%)
1	0	0	120	100	0
2	[TMPSA][HSO_4]	5	15	80	47
3	[TMPSA][HSO_4]	5	30	80	71
4	[TMPSA][HSO_4]	5	60	80	93
4[c]	[TMPSA][HSO_4]				93
4[d]	[TMPSA][HSO_4]				91
4[e]	[TMPSA][HSO_4]				90
4[f]	[TMPSA][HSO_4]				90
4[g]	[TMPSA][HSO_4]				88
5	[TMPSA][HSO_4]	5	60	100	93
6	[TMPSA][HSO_4]	5	120	80	93
7	[TMPSA][HSO_4]	2	120	80	75
8	[TMPSA][HSO_4]	10	15	80	92
9	[TMPSA][HSO_4]	10	30	80	94
10	[TEPSA][HSO_4]	5	60	80	92
11	[TBPSA][HSO_4]	5	60	80	89
12	[TMBSA][HSO_4]	5	60	80	92
13	[TEBSA][HSO_4]	5	60	80	90

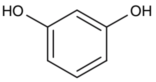
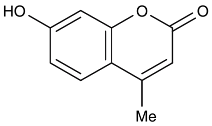
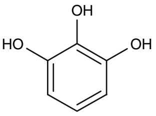
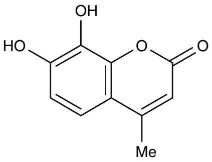
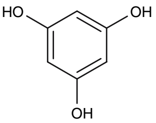
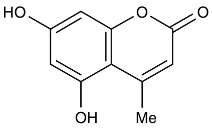
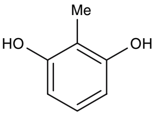
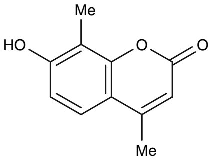
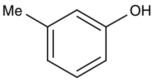
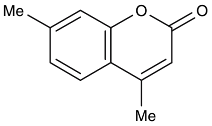
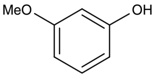
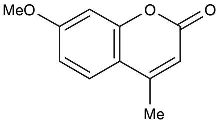
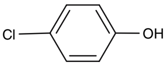
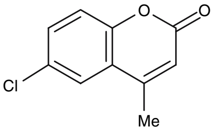
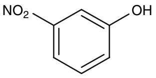
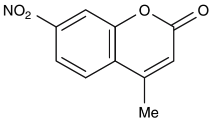
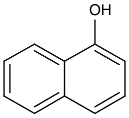
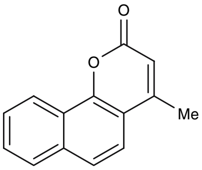
[a] 20 mmol resorcinol, 20 mmol ethyl acetoacetate

[b] Molar ratio of TSILs to phenol

[c–g] Run 1 to run 5 of entry 4

Table 2 Pechmann reactions between phenols and ethyl acetoacetate catalyzed by [TMPSA][HSO$_4$[a]]



Entry	Phenols	Products	Time (h)	Isolated yield (%)	M.p.(L) (°C)
1			1	93	182–184(183–186)[16]
2			0.8	92	234–237(236–239)[16]
3			1	91	280–283(282–284)[14f]
4			1.5	90	137–138(137–139)[16]
5			2	80	130–131(130–132)[16]
6			1	93	160–161(160–162)[16]
7			1	90	180–182(183–185)[14f]
8			1.5	87	176–178(177–179)[14f]
9			4	75	154–155(155–156)[16]

[a] 20 mmol resorcinol, 20 mmol ethyl acetoacetate, 1.0 mmol [TMPSA][HSO$_4$], 80 °C

higher amount of the catalyst did not improve the result to a greater extent (entries 6, 9).

The Pechmann condensation reaction of other phenols and ethyl acetoacetate in the presence of [TMPSA][HSO_4] was accomplished under the optimized reaction conditions described above and the results are presented in Table 2. It can easily be seen that the Pechmann condensation proceeded smoothly in water and gave reasonable to good yields ranged from 75% to 93%. Many phenols, such as resorcinol, pyrogallol, phloroglucinol, 3-methoxyphenol, 2-methylresorcinol, 4-chlorophenol and 3-nitrophenol could be converted to corresponding coumarins in good yields (entries 1–4, 6–8). The reactivities of 3-methylphenol and 1-naphthol seem to be inferior as compared with that of the former (entries 5, 9), only 80% and 75% of the yields were obtained, respectively. The starting materials, which could be separated from the product by recrystallization from ethanol, remained in the reaction mixture although the two condensations were carried out under the prolonged reaction time.

As an air and moisture stable ionic liquid, [TMPSA][HSO_4] was superior than chloroaluminate ionic liquids in the aspect of recycle and reuse. The recycling performance of [TMPSA][HSO_4] was then investigated in the reaction of resorcinol and ethyl acetate.

The results listed in Table 1 showed that the [TMPSA][HSO_4] could be reused five times with only a slightly lowering of the catalytic activity (entries 4^c–4^g). Compared with the traditional solvents and catalysts, which is complex and time and energy consuming and environmentally malign, the easy recycling performance is an attractive property of the TSILs for the environmental protection.

4 Conclusion

In conclusion, it was demonstrated that some readily available, economic task-specific ionic liquids have been used as recyclable catalysts for the benign Pechmann condensation of phenols with ethyl acetoacetate to synthesis coumarin derivatives. The merit of this methodology is that it is simple, efficient and eco-friendly.

Acknowledgment This work was financially supported by the Educational Committee of Jiangsu Province (07KJD530238), Jiangsu Provincial Key Laboratory of Coastwetland & Environment Protection and Nanjing University of Science & Technology (N0.2006001).

References

1. Kennedy O, Thornes RD (1997) Coumarins: biology, applications and mode of action. Wiley and Sons, Chichester
2. Zahradnik M (1990) The production and application of fluorescent brightening agents, Wiley and Sons
3. Murray RDH, Mendez J, Brown SA (1982) The natural coumarins: occurrence, chemistry and biochemistry. Wiley and Sons, New York
4. von Pechmann H, Duisberg C (1884) Chem Ber 17:929
5. Johnson JR (1942) Org React 1:210
6. (a) Jones G (1967) Org. React. 15:204; (b) Brufola G, Fringuelli F, Piermatti O, Pizzo (1996) F Heterocycles 43:1257
7. Shriner RL (1942) Org React 1:1
8. (a) Narasimahan NS, Mali RS, Barve MV (1979) Synthesis 906; (b) Yavari I, Hekmat-Shoar R, Zonouzi A (1998) Tetrahedron Lett 39:2391
9. Cartwright GA, McNab W (1997) J Chem Res (S) 296
10. Sethna SM, Shah NM, Shah RC (1938) J Chem Soc 228
11. (a) Simmonis H, Remmert P (1914) Chem Ber 47:2229; (b) Robertson A, Sandrock WF, Henry CB (1931) J Chem Soc 2426
12. Woods LL, Sapp J (1962) J Org Chem 27:3703
13. (a) de la Hoz A, Moreno A, Vazquez E (1999) Synlett 608; (b) Frere S, Thiery V, Besson T (2001) Tetrahedron Lett 42:791; (c) Singh V, Kaur S, Sapehiyia V, Singh J, Kad GL (2005) Catal Commun 6:57; (d) Manhas MS, Ganguly NS, Mukherjee S, Jain AK, Bose AK (2006) Tetrahedron Lett 47:2423; (e) Katkevics M, Kontijevskis A, Mutule I, Suna E (2007) Chem Heter Comp 43
14. (a) Selvakumar S, Chidambaram M, Singh AP (2007) Catal Commun 8:777; (b) Kumar BS, Kumar PS, Srinivasulu N, Rajitha B, Reddy YT, Reddy PN, Udupi RH (2006) Chem Heter Comp 42:6; (c) Bahekar SS, Shinde DB (2004) Tetrahedron Lett 45:7999; (d) Reddy BM, Patil MK, Lakshmanan P J (2006) Mol Catal A Chemical 256:290; (e) Dominguez JCR, Kirsch G (2006) Tetrahedron Lett 47:3279; (f) Hegedus A, Hell Z (2006) Catal Lett 112:105
15. (a) Potdar MK, Mohile SS, Salunkhe MM (2001) Tetrahedron Lett 42:9285; (b) Potdar MK, Rasalkar MS, Mohile SS, Salunkhe MM (2005) J Mol Catal A Chemical 235:249
16. Gu Y, Zhang J, Duan Z, Deng Y (2005) Adv Synth Catal 347:512
17. (a) Wasserscheid P, Hal R (2002) Green Chem 4:400; (b) Fraga-Dubreuil J, Bourahla K, Rahmouni M, Bazureau JP, Hamelin J (2002) J Catal Commun 3:185; (c) Garcia MT, Gathergood N, Scammells PJ (2005) Green Chem 7:9
18. (a) Fang D, Luo J, Zhou X, Liu Z (2007) Catal Lett 116:76; (b) Fang D, Luo J, Zhou X, Ye Z, Liu Z (2007) J Mol Catal A Chemical 274:208; (c) Fang D, Liu Z, Zhou X (2007) Chin Appl Chem 24:85; (d) Fang D, Luo J, Zhou X, Ye Z, Liu Z (2006) Ind Eng Chem Res 45:7982; (e) Fang D, Gong K, Shi Q, Liu Z (2007) Catal Commun 8:1463