Monatsh Chem (2013) 144:1871–1876
DOI 10.1007/s00706-013-1066-8

ORIGINAL PAPER

Synthesis of a novel piperidine-functionalized poly(ethylene glycol) bridged dicationic ionic liquid and its application in one-pot synthesis of substituted 2-amino-2-chromenes and 3,4-dihydropyrano[3,2-*c*]chromenes in aqueous media

Yinglei Wang · Jun Luo · Tantan Xing · Zuliang Liu

Received: 16 October 2012 / Accepted: 17 July 2013 / Published online: 16 August 2013

Abstract A novel piperidine-functionalized poly(ethylene glycol) bridged dicationic ionic liquid was prepared and identified. It was used as a recyclable catalyst for the synthesis of substituted 2-amino-2-chromenes and 3,4-dihydropyrano[3,2-*c*]chromenes with excellent yields through a one-pot three-component reaction of aromatic aldehydes, malononitrile, and activated phenols in aqueous media. This environmentally benign protocol was found to be fairly efficient and offer wide substrate flexibility. The basic ionic liquid could be reused several times without any obvious loss of catalytic activity.

Keywords Poly(ethylene glycol) · Functionalized ionic liquid · Multicomponent condensation · Chromenes · Aqueous media · Recycability

Introduction

Multicomponent reactions (MCRs), involving domino processes with at least three components, have emerged as a powerful strategy in synthetic organic chemistry. Compared with conventional multistep linear synthetic protocols, MCRs exhibit high levels of efficiency and diversity because they offer rapid and convergent construction of complex molecular skeletons from simple starting materials in one-pot operations, and these reactions avoid the isolation and purification of intermediates and diminish waste generation [1–4]. Water is the most widely available and nontoxic reaction medium, which makes it an ideal solvent for green chemistry protocols [5–9]. Therefore, the development of MCRs in water or an aqueous medium is an active research area.

2-Amino-2-chromenes and 3,4-dihydropyrano[3,2-*c*]chromenes comprise an important class of heterocycles due to their biological and pharmacological properties, and are widely used in cosmetics and pigments [10], are potential biodegradable agrochemicals [11–13], and are employed in pharmaceuticals [14–16]. The conventional straightforward synthesis of this heterocyclic system involves multicomponent reactions of an aromatic aldehyde, malononitrile, and activated phenol in the presence of a basic catalyst in organic solvent. Recently, several modified catalysts have been employed to accomplish this transformation such as tetrabutylammonium bromide (TBAB) [17], hexadecyltrimethylammonium bromide (HTMAB) [18], DABCO [19], DBU [20], diammonium hydrogenphosphate (DAHP) [21], 4-(dimethylamino)pyridine (DMAP) [22], CuO nanoparticles [23], Ru(II) complexes bearing tertiary phosphine ligands [24], a (2-aminomethyl)phenol moiety supported on HAp-encapsulated-γ-Fe_2O_3 (γ-Fe_2O_3@HApSi-$(CH_2)_3$-AMP) [25], sodium dodecyl sulfate (SDS) [26], a heteropolyacid (HPA) [27, 28], and high-surface-area MgO [29]. At the same time, several methods of promoting this reaction have been reported, including the use of microwave irradiation [30–36], ultrasonic irradiation [37], and grinding [38, 39]. However, some of these methods suffer from one or more drawbacks, such as the use of volatile organic solvents, a long reaction time, unsatisfactory yields, the need for special equipment, difficulties in recycling the catalyst, and a laborious workup procedure.

Electronic supplementary material The online version of this article (doi:10.1007/s00706-013-1066-8) contains supplementary material, which is available to authorized users.

Y. Wang · J. Luo (✉) · T. Xing · Z. Liu
School of Chemical Engineering, Nanjing University of Science and Technology, Nanjing 210094, China
e-mail: luojun@njust.edu.cn

Ionic liquids (ILs) are considered to be among of the most promising novel reaction media due to their unique properties, such as their negligible volatility, high thermal and chemical stability, wide liquid range, excellent solubility, and ease of recovery and reuse [40–44]. Moreover, functionalized ionic liquids (FILs)—so-called task-specific ionic liquids (TSILs), which incorporate additional groups into the cation and/or anion—have attracted increasing attention from researchers in various fields due to their adjustable physical and chemical properties [45–48]. FILs have been used as alternative green solvents as well as reagents and/or catalysts in synthetic organic chemistry. Among them, basic ionic liquids exhibit unique advantages over traditional bases owing to their adjustable basicity and solubility, which gives them high catalytic efficiency and makes them easy to recover. Indeed, basic ionic liquids such as *N*,*N*,*N*′,*N*′-tetramethylguanidinium trifluoroacetate (TMGT) [49], 1-butyl-3-methylimidazolium hydroxide ([Bmim][OH]) [50, 51], (*N*,*N*-dimethylaminoethyl)benzyldimethylammonium chloride ($[PhCH_2Me_2N^+CH_2CH_2NMe_2][Cl^-]$) [52], 3-hydroxypropanaminium acetate (HPAA) [53], triethylenetetraammonium trifluoroacetate ([TETA][TFA]) [54], and 2-hydroxyethylammonium formate [55] have been successfully used as catalysts for the synthesis of 2-amino-2-chromenes and/or 3,4-dihydropyrano[3,2-*c*]-chromenes.

Due to the wide-ranging applications of these heterocyclic compounds and the advantages of basic ionic liquids, the further development of catalysts that are recyclable simply and efficiently is a desirable goal. In our continuous research on the synthesis and applications of poly(ethylene glycol)-bridged dicationic acidic ionic liquids in synthetic organic chemistry [56, 57], we prepared a novel piperidine-functionalized poly(ethylene glycol)-bridged dicationic ionic liquid PEG_{800}-DPIL(Cl) and applied it as an efficient and recyclable catalyst in a three-component condensation that was performed to prepare 2-amino-2-chromenes and 3,4-dihydropyrano[3,2-*c*]chromenes in an aqueous medium. That work is described in this paper.

Results and discussion

The synthetic route to piperidine-functionalized poly(ethylene glycol)-bridged dicationic ionic liquid is illustrated in Scheme 1. It was readily prepared through a convergence-style procedure from commercially available starting materials and reagents in good yields [64]. PEG_{800}-DPIL(Cl) has good thermal stability and does not decompose below about 250 °C. In addition, the solubility of PEG_{800}-DPIL(Cl) was determined at room temperature. In general, it is immiscible with heptane, cyclohexane, diethyl ether, toluene, and ethyl acetate, and miscible with dichloromethane, acetone, isopropanol, methanol, ethanol, *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and water.

PEG_{800}-DPIL(Cl) was then used to catalyze a one-pot three-component condensation that was performed to prepare 2-amino-2-chromenes and 3,4-dihydropyrano[3,2-*c*]chromenes from aromatic aldehydes, malononitrile, and activated phenols in water. Firstly, to evaluate the catalytic efficiency of this catalyst, benzaldehyde, malononitrile, and 1-naphthol were selected as model substrates for the preparation of 2-amino-2-chromenes. Selected results from our screening experiments are summarized in Table 1. When PEG_{800}-DPIL(Cl) was used as both catalyst and solvent, the yield was only 72 %, possibly because the high

Scheme 1

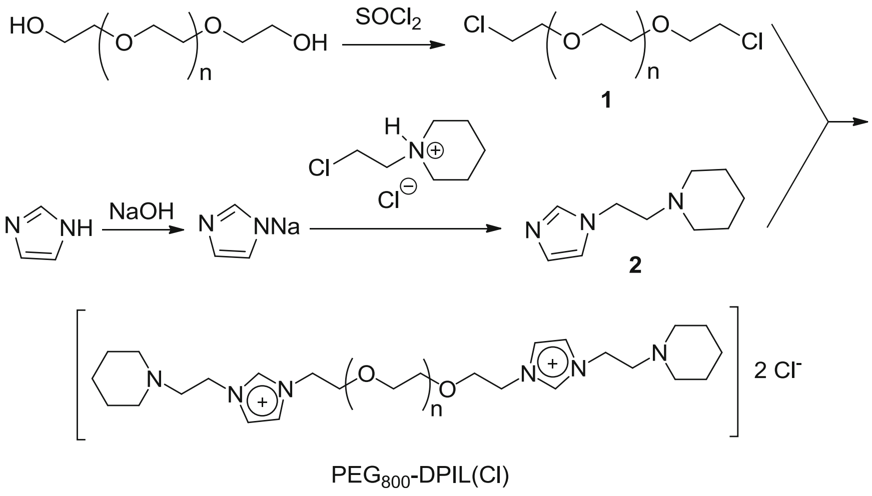
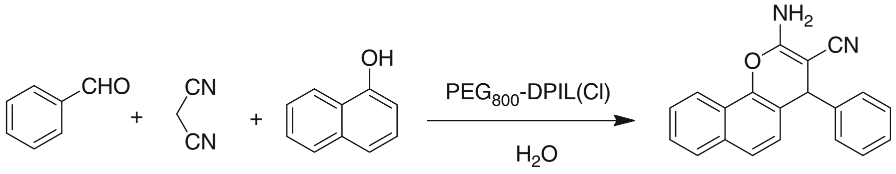


Table 1 Optimization of the reaction conditions



Entry	Amount of catalyst/%	Temp./°C	Solvent	Time/min	Yield/%[a]
1	10	100	–	20	72
2	–	100	H_2O	20	–
3	1	100	H_2O	20	45
4	3	100	H_2O	20	78
5	5	100	H_2O	20	90
6	7	100	H_2O	20	90
7	10	100	H_2O	20	91
8	5	80	H_2O	30	81
9	5	90	H_2O	20	87

Reaction conditions: 2 mmol benzaldehyde, 2 mmol malononitrile, 2 mmol 1-naphthol, 2 cm^3 water

[a] Isolated yield

viscosity of the ionic liquid blocked the mass transfer (Table 1, entry 1). However, none of the desired product was detected when the reaction was carried out in water under reflux for 20 min in the absence of PEG_{800}-DPIL(Cl) (Table 1, entry 2). The reaction was subsequently carried out in the presence of various amounts of catalyst in water. The results indicated that the optimal amount of catalyst was 5 mol% (Table 1, entries 3–7). Adding more catalyst did not improve the results at all. Furthermore, low temperatures decelerated the reaction and led to lower yields (Table 1, entries 8, 9).

The recyclability of the catalyst was also investigated using the above model reaction. After separating out the product by filtration, the filtrate containing the catalyst was reused for the next run without further purification. Fresh starting materials of benzaldehyde, malononitrile, and 1-naphthol in the appropriate stoichiometric ratio were charged into the filtrate and stirred under the same conditions. The results are depicted in Fig. 1. It is apparent that the reaction system could be reused five times without suffering any significant decrease in yield.

Using the optimized reaction conditions, the scope and efficiency of the reaction for the synthesis of a wide variety of 2-amino-2-chromenes with various aromatic aldehydes were explored. The results are summarized in Table 2. The substituents of the aromatic aldehyde and the position of the hydroxyl on the naphthol dramatically influence the reaction. When aromatic aldehydes bearing electron-donating groups (such as methyl, hydroxy, methoxy) (Table 2, entries 2–5) were employed, longer reaction times were required and lower yields were obtained than those bearing electron-withdrawing groups (such as halide, nitro) (Table 2, entries 6–14). It is worth noting that *ortho* and *meta* substituents did not significantly hamper the condensation reaction (Table 2, entries 6–8 and entries 11–13). Furthermore, the activity of 2-naphthol was lower than that of 1-naphthol owing to an electronic effect (Table 2, entries 16–18).

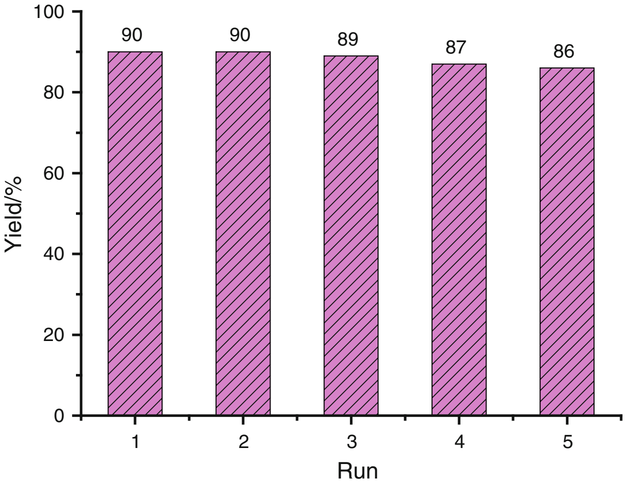
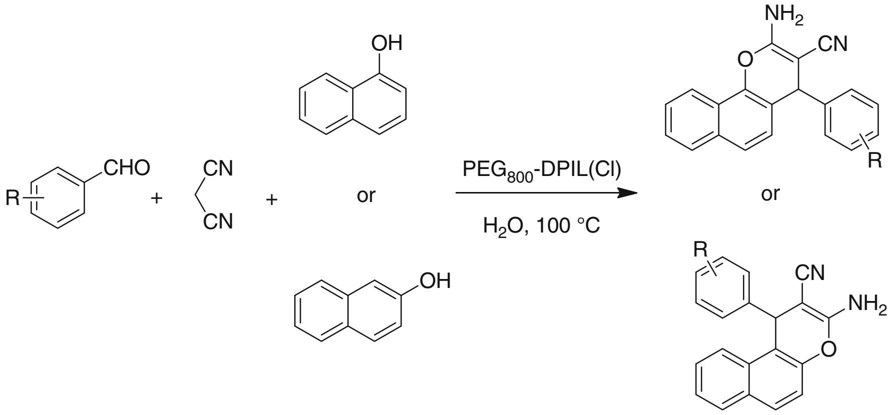


Fig. 1 The reusability of the PEG_{800}-DPIL(Cl)/H_2O system

The generality and versatility of this basic ionic liquid was further investigated by utilizing it in a one-pot condensation of an aromatic aldehyde, malononitrile, and 4-hydroxycoumarin to prepare 3,4-dihydropyrano[3,2-

Table 2 Synthesis of 2-amino-2-chromene derivatives by PEG_{800}-DPIL(Cl) in water



Entry	R	Naphthol	Time/min	Yield/%[a]	M.p./°C	Lit. m.p./°C
1	H	1-Naphthol	20	90	215–216	215–217 [19]
2	4-CH_3	1-Naphthol	30	86	207–208	206–207 [50]
3	4-OH	1-Naphthol	25	86	249–250	250–252 [32]
4	4-CH_3O	1-Naphthol	30	88	189–190	190–192 [52]
5	3-CH_3O-4-OH	1-Naphthol	40	85	214–215	215–218 [32]
6	2-Cl	1-Naphthol	12	92	248–249	248–250 [38]
7	3-Cl	1-Naphthol	10	92	228–229	228–230 [18]
8	4-Cl	1-Naphthol	8	94	247–248	245–248 [19]
9	4-Br	1-Naphthol	10	95	243–244	241–243 [19]
10	4-F	1-Naphthol	12	94	231–233	232–233 [50]
11	2-NO_2	1-Naphthol	10	93	207–209	208–210 [32]
12	3-NO_2	1-Naphthol	8	95	219–220	217–219 [19]
13	4-NO_2	1-Naphthol	8	96	213–214	210–212 [58]
14	2,4-Cl_2	1-Naphthol	15	94	223–224	222–224 [18]
15	2-Furyl	1-Naphthol	20	89	167–169	169–171 [52]
16	H	2-Naphthol	30	84	291–292	290–292 [59]
17	4-CH_3	2-Naphthol	40	81	273–275	270–272 [38]
18	4-Cl	2-Naphthol	20	86	222–223	222–224 [38]

Reaction conditions: 2 mmol aromatic aldehyde, 2 mmol malononitrile, 2 mmol 1-naphthol, 0.1 mmol PEG_{800}-DPIL(Cl), 2 cm^3 water, 100 °C

[a] Isolated yield

c]chromenes in aqueous media under reflux. As can be seen from Table 3, aromatic aldehydes with electron-donating as well as electron-withdrawing groups were transformed into the corresponding products in good to excellent yields within 10–20 min. The electronic and steric effects are in accord with the above condensations.

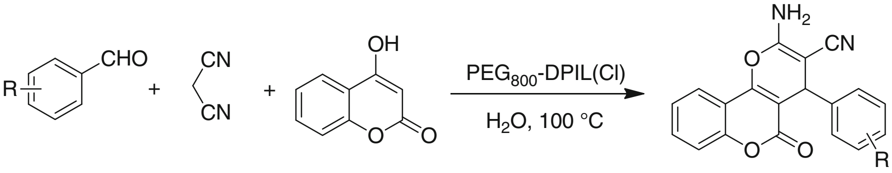
In summary, a novel piperidine-functionalized poly(ethylene glycol)-bridged dicationic ionic liquid was successfully prepared and used as an efficient and recyclable catalyst for the synthesis of substituted 2-amino-2-chromenes and 3,4-dihydropyrano[3,2-*c*]chromenes via one-pot three-component condensations of aromatic aldehydes, malononitrile, and activated phenols in water. Advantageously, this novel catalytic system is environmentally friendly, requires only mild reaction conditions and short reaction times, produces high yields, has a simple work-up procedure, and exhibits good reusability.

Experimental

All of the reagents and solvents were purchased from commercial suppliers and used without further purification. The synthesis of piperidine-functionalized poly(ethylene glycol)-bridged dicationic ionic liquid PEG_{800}-DPIL(Cl) was described previously [64].

All melting points were determined on a digital melting-point apparatus. ^1H NMR and ^{13}C NMR were recorded on

Table 3 Synthesis of 3,4-dihydropyrano[3,2-*c*]chromene derivatives by PEG_{800}-DPIL(Cl) in water



Entry	R	Time/min	Yield/%[a]	M.p./°C	Lit. m.p./°C
1	H	15	91	265–266	265–267 [60]
2	4-CH_3	20	88	249–251	250–251 [23]
3	4-OH	15	86	266–267	266–267 [20]
4	4-CH_3O	20	89	233–234	233–236 [23]
5	3-CH_3O-4-OH	25	85	250–251	252–253 [62]
6	4-NMe_2	30	87	223–224	224–225 [20]
7	2-Cl	8	93	274–275	273–274 [55]
8	3-Cl	8	93	248–249	246–248 [26]
9	4-Cl	6	94	264–265	263–265 [21]
10	4-Br	6	95	255–257	254–256 [63]
11	4-F	8	94	264–265	263–264 [23]
12	2-NO_2	8	93	253–255	254–256 [51]
13	3-NO_2	6	94	265–266	263–265 [29]
14	4-NO_2	6	96	277–278	278–280 [61]
15	2,4-Cl_2	15	93	244–246	245–247 [55]
16	3,4-Cl_2	15	94	243–244	243–244 [63]

Reaction conditions: 2 mmol aromatic aldehyde, 2 mmol malononitrile, 2 mmol 4-hydroxycoumarin, 0.1 mmol PEG_{800}-DPIL(Cl), 2 cm^3 water, 100 °C

[a] Isolated yield

a Bruker (Rheinstetten, Germany) Avance III 500, and tetramethylsilane (TMS) was used as internal standard. Mass spectra were taken on an Agilent (Santa Clara, CA, USA) liquid chromatography–mass spectrometry (LC-MS) 1100 series instrument in the electrospray ionization (positive electrospray ionization (ESI)) mode. IR spectra were recorded from KBr disks with a Shimadzu (Kyoto, Japan) IRPrestige-21 FT-IR spectrometer.

General procedure for the synthesis of 2-amino-2-chromenes or 3,4-dihydropyrano[3,2-c]chromenes and recycling of the catalyst

Aromatic aldehyde (2 mmol), malononitrile (2 mmol), phenol (2 mmol), and PEG_{800}-DPIL(Cl) (0.1 mmol) were added to 2 cm^3 H_2O. The reaction mixture was heated to 100 °C and stirred for a certain period of time. TLC was used to monitor for the end of the reaction. After the reaction had compleed, the mixture was cooled to room temperature and the precipitated solid was broken up, filtered off, and washed with water. The crude products were purified by recrystallization from methanol. All of the products are known and the data used to identify them were found to be in accord with those reported in literature. The solution of PEG_{800}-DPIL(Cl) in water was reused in the next reaction without any treatment.

Acknowledgments This project was financially sponsored and supported by the National Natural Science Foundation of China (No. 21002050), the Doctoral Fund of the Ministry of Education of China for New Teachers (No. 200802881029), the Zijin Star Project and the Excellence Initiative Project of NUST.

References

1. Posner GH (1986) Chem Rev 86:831
2. Trost BM (1995) Angew Chem Int Ed Engl 24:259
3. Touré BB, Hall DG (2009) Chem Rev 109:4439
4. Wessjohann LA, Rivera DG, Vercillo OE (2009) Chem Rev 109:796
5. Kobayahi S, Manabe K (2002) Acc Chem Res 35:209
6. Akiya N, Savage PE (2002) Chem Rev 102:2725
7. Li CJ (2005) Chem Rev 105:3095
8. Blackmond DG, Armstrong A, Coomber V, Wells A (2007) Angew Chem Int Ed 46:3798
9. Minakata S, Komatsu M (2009) Chem Rev 109:711
10. Ellis GP (1977) The chemistry of heterocyclic compounds: chromenes, chromanes, and chromones. Wiley, New York

11. Galil A, Riad FM, Sherif BY, Elnagdi SM (1982) Chem Lett 11:1123
12. Hafez EA, Elnagdi MH, Elagamey AG, Taweel FM (1987) Heterocycles 26:903
13. Sofan MA, Taweel FM, Elnagdi MH (1989) Liebigs Ann Chem 95:935
14. Andreani LL, Lapi E (1960) Bull Chim Farm 99:583
15. Foye WO (1991) Principi di chemico farmaceutica. Piccin, Padova, p 416
16. Bonsignore L, Loy G, Secci D, Calignano A (1993) Eur J Med Chem 28:517
17. Khurana JM, Kumar S (2009) Tetrahedron Lett 50:4125
18. Jin TS, Zhang JS, Liu LB, Wang AQ, Li TS (2006) Synth Commun 36:2009
19. Balalaie S, Ramezanpour S, Bararjanian M, Gross JH (2008) Synth Commun 38:1078
20. Khurana JM, Nand B, Saluja P (2010) Tetrahedron 66:5637
21. Abdolmohammadi S, Balalaie S (2007) Tetrahedron Lett 48:3299
22. Khan AT, Lal M, Ali S, Khan MM (2011) Tetrahedron Lett 52:5327
23. Mehrabi H, Mireki MK (2011) Chin Chem Lett 22:1419
24. Tabatabaeian K, Heidari H, Mamaghani M, Mahmoodi NO (2012) Appl Organomet Chem 26:56
25. Khoobi M, Ma'mani L, Rezazadeh F, Zareie Z, Foroumadi A, Ramazani A, Shafiee A (2012) J Mol Catal A Chem 359:74
26. Mehrabi H, Abusaidi H (2010) J Iran Chem Soc 7:890
27. Heravi MM, Jani BA, Derikvand F, Bamoharram FF, Oskooie HA (2008) Catal Commun 10:272
28. Heravi MM, Sadjadi S, Haj NM, Oskooie HA, Bamoharram FF (2009) Catal Commun 10:1643
29. Seifi M, Sheibani H (2008) Catal Lett 126:275
30. Kidwai M, Saxena S (2006) Synth Commun 36:2737
31. Pasha MA, Jayashankara VP (2007) Indian J Chem Sect B 46:1328
32. Patra A, Mahapatra T (2008) J Chem Res 7:405
33. Surpur MP, Kshirsagar S, Samant SD (2009) Tetrahedron Lett 50:719
34. Mekheimer RA, Sadek KU (2009) J Heterocycl Chem 46:149
35. Mekheimer RA, Sadek KU (2009) Chin Chem Lett 20:271
36. Mobinikhaledi A, Moghanian H, Sasani F (2011) Synth React Inorg Met Org Chem 41:262
37. Jin TS, Xiao JC, Wang SJ, Li TS (2004) Ultrason Sonochem 11:393
38. Jin TS, Xie H, Xue YP, Li TS (2008) Asian J Chem 20:5145
39. Zhou D, Ren ZJ, Cao WG, Chen J, Deng HM (2008) J Heterocycl Chem 45:1865
40. Welton T (1999) Chem Rev 99:2071
41. Dupont J, Souza RF, Suarez PAZ (2002) Chem Rev 102:3667
42. Bourbigou HO, Magna L, Morvan D (2010) Appl Catal A Gen 373:1
43. Hallett JP, Welton T (2011) Chem Rev 111:3508
44. Yue CB, Fang D, Liu L, Yi TF (2011) J Mol Liq 163:99
45. Lee S (2006) Chem Commun 10:1049
46. Pucheault M, Vaultier M (2009) Top Curr Chem 290:83
47. Giernoth R (2010) Angew Chem Int Ed 49:2834
48. Sawant AD, Raut DG, Darvatkar NB, Salunkhe MM (2011) Green Chem Lett Rev 4:41
49. Shaabani A, Samadi S, Badri Z, Rahmati A (2005) Catal Lett 104:39
50. Gong K, Wang HL, Fang D, Liu ZL (2008) Catal Commun 9:650
51. Gong K, Wang HL, Fang D, Liu ZL (2009) J Heterocycl Chem 46:1145
52. Chen L, Huang XJ, Li YQ, Zhou MY, Zheng WJ (2009) Monatsh Chem 140:45
53. Shaterian HR, Oveisi AR (2011) J Iran Chem Soc 8:545
54. Zheng J, Li YQ (2011) Mendeleev Commun 21:280
55. Shaterian HR, Arman M, Rigi F (2011) J Mol Liq 158:145
56. Zhi HZ, Lv CX, Zhang Q, Luo J (2009) Chem Commun 10:2878
57. Zhi HZ, Luo J, Feng GA, Lv CX (2009) Chin Chem Lett 20:379
58. Jamal MRN, Mashkouri S, Sharifi A (2010) Mol Divers 14:473
59. Davoodnia A, Nishaburi AT, Behmadi H, Hoseini NT, Attar P (2010) Asian J Chem 22:7978
60. Shaabani A, Samadi S, Rahmati A (2007) Synth Commun 37:491
61. Karimi AR, Eslami C (2011) Lett Org Chem 8:150
62. Aziz AS, Agrody AM, Bedair AH, Corkery TC, Ata A (2004) Heterocycles 63:1793
63. Shi DQ, Wu N, Zhuang QY (2008) J Chem Res 9:542
64. Luo J, Xin T, Wang Y (2013) New J Chem 37:269