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ORIGINAL PAPER

Synthesis of 14H-dibenzo xanthene derivatives using choline chloride/tin(II) chloride deep eutectic solvent and Fe_3O_4/ƛ-carrageenan/Zn(II)

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Abstract In this study, various xanthene derivatives have prepared efficiently through a simple method using choline chloride/tin(II) chloride ($ChCl·2SnCl_2$) deep eutectic solvent (DES), alone, or in the presence of Fe_3O_4/ƛ-carrageenan/Zn(II) magnetic bionanocatalyst. In the employed procedure, 2-naphthol derivatives have mixed with aromatic or aliphatic aldehydes and the reactions have been completed in the presence of DES at 90 °C in 1.5 h. In addition, using DES/Fe_3O_4/ƛ-carrageenan/Zn(II), the reaction time was reduced to 30 min. The employed DES has been recycled four times without important loss of its activity.

Keywords Condensation · DES · Nanocomposite · Catalyst · Xanthene

Introduction

Xanthene derivatives are important organic compounds, because they exhibit useful biological activities, such as antibacterial [1], anti-inflammatory [2], and antiviral activities [3]. In addition, these compounds have widely been used in the laser technology [4], functional materials for visualization of biomolecular assemblies [5], photodynamic therapy [6], and as antagonists [7]. Therefore, much attention has been focused on developing different methods for the synthesis of xanthene derivatives in the past decades. By reviewing the literatures, various methods, such as cycloacylation of carbamates [8], trapping of benzynes by phenols [9], condensation reaction between aryl oxymagnesium halides and triethyl ortho formate [10], reaction of 2-hydroxyaryl aldehydes with 2-tetralone [11], and many other reaction [12–16], have been reported for the synthesis of xanthene derivatives. Moreover, in these reactions, various catalysts have been developed, such as p-toluene sulfonic acid [17], molecular iodine [18], $K_5CoW_{12}O_{40}$ [19], LiBr under microwave irradiation [20], amberlyst-15 [21], cation-exchange resins [22], silica sulfuric acid [23], sulfamic acid [24], AcOH-H_2SO_4 [25], silica perchloric acid [26], heteropoly acids [27], cyanuric chloride [28], $BF_3.SiO_2$ [29], $Yb(OTf)_3$ [30], $In(OTf)_3$ [31], P_2O_5/Al_2O_3 [32], and Bu_4NBr under microwave irradiation [33]. However, the most of these methods suffer at least from one of some disadvantages, such as a long reaction time, expensive reagents, use of toxic solvents or catalysts, harsh reaction conditions, environmental problems, undesirable wastes, unsatisfactory yield, non-recyclable catalyst, and tedious work-up procedures. Therefore, the synthesis of this class of heterocyclic compounds is particularly significant for researchers and in continuation of our previous works on the use of DES in the synthesis of important compounds [34–38], we have decided to develop a new method for synthesis of xanthene derivatives.

In this report, we hope to present a simple and efficient method for the synthesis of xanthene derivatives by the reaction between 2-naphthols and aromatic or aliphatic aldehydes in the presence of DES, alone, or in the presence of Fe_3O_4/ƛ-carrageenan/Zn(II) nanocatalyst. The procedure of this synthesis and the obtained results will be discussed in the following sections.

Electronic supplementary material The online version of this article (doi:10.1007/s13738-016-0965-0) contains supplementary material, which is available to authorized users.

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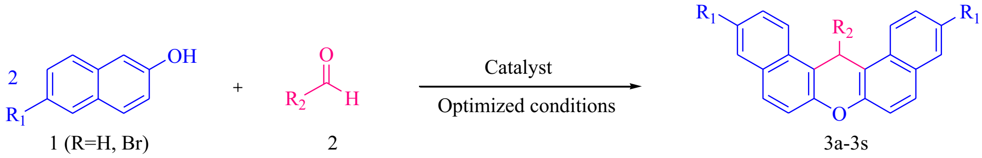


Scheme 1 General reaction for the synthesis of xanthene derivatives

Table 1 Optimization of reaction conditions for the model reaction

Entry	Cat. type	Cat (mol%)	*T* (°C)	Time (h)	Yield (%)[a]
1	ChCl·2SnCl$_2$	20	r.t.	5	0
2	ChCl·2SnCl$_2$	20	60	2	20
3	ChCl·2SnCl$_2$	20	90	30 min	25
4	ChCl·2SnCl$_2$	20	90	1	45
5	ChCl·2SnCl$_2$	20	90	1.5	94
6	ChCl·2SnCl$_2$	20	90	2	94
7	ChCl·2SnCl$_2$	20	120	2	94
8	ChCl·2SnCl$_2$	15	90	1.5	94
9	ChCl·2SnCl$_2$	10	90	1.5	94
10	ChCl·2SnCl$_2$	5	90	1.5	96
11	ChCl·2ZnCl$_2$	20	90	1.5	35
12	ChCl·2Urea	20	90	1.5	67

The model reaction: 2-naphthol (2 mmol), benzaldehyde (1 mmol)

[a] Isolated yield

Table 2 Optimization of reaction conditions for the model reaction

Entry	Fe_3O_4/ƛ-Carrageenan/Zn(II) (g)	*T* (°C)	Time (min)	Yield (%)[a]
1	0.1	r.t	120	0
2	0.1	60	30	35
3	0.1	90	30	96
4	0.1	120	30	75
5	0.05	90	30	60
6	0.01	90	30	50

The model reaction: 2-naphthol (2 mmol), benzaldehyde (1 mmol) in the presence of DES (5 mol%)

[a] Isolated yield

Experimental

Chemicals were purchased from Merckand Sigma-Aldrich companies. Melting points were measured using Gallen Kamp melting point instrument. IR spectra were recorded with KBr pellets on JASCO FT-IR spectrophotometers. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Ultrashield 400 MHz spectrometer in $CDCl_3$ solution. To prepare the employed DES, a mixture of choline chloride/tin (II) chloride with 1:2 ratio was heated with stirring until a clear and colorless liquid was obtained.

Preparation of Fe_3O_4/ƛ-carrageenan/Zn(II)

Fe_3O_4 nanoparticles were prepared by chemical co-precipitation of 2:1 of a molar ratio of $FeCl_3·6H_2O$ (1 g) and $FeSO_4·6H_2O$ (0.65 g). Both iron salts were dissolved in 50 mL of deionized water and stirred to produce a clear solution. This solution has been sonicated for 30 min. Then, NH_4OH solution (25 %) was added to the solution. When the pH of the solution was reached to 10, a dark solution was appeared, indicating the formation of magnetic nanoparticles. The solution was allowed to stir at 80 °C under N_2 atmosphere for 2 h and the nanomagnetite was separated by a magnet, washed with water and acetone, and dried by air. Then, ƛ-carrageenan (0.25 g) was dissolved into 50 mL of distilled water to get the homogenous solution, magnetite nanoparticles were added, and the solution was stirred for 18 h at room temperature. The resulting coated nanomagnetite was separated by a magnet, washed with water and acetone, and dried by air. Finally, Fe_3O_4/ƛ-carrageenan (1 g) was added to 25 mL aqueous solution of $ZnCl_2·6\ H_2O$ (0.5 g) and the mixture was gently stirred at room temperature for 24 h. The resulting catalyst (Fe_3O_4/ƛ-carrageenan/Zn(II)) was separated using external magnet, washed with water and acetone, and dried by air. All characterization analyses on this catalyst have been reported by our group in another manuscript.

General procedure for the synthesis of xanthene derivatives

2-Naphthol derivatives (2 mmol), aromatic or aliphatic aldehyde (1 mmol), and ChCl·2SnCl$_2$ (5 mol%) (in some reactions, in the presence of 0.1 g of Fe_3O_4/ƛ-carrageenan/Zn(II)) were mixed in a 25 mL round-bottom flask equipped with a condenser on the top. The reaction mixture has been stirred for 30 min, and during stirring, it was warmed slowly on the oil bath to 90 °C. The progress of the reaction was monitored by TLC (eluent phase = *n*-hexane:EtOAc = 3:1). After completion of the reaction, the mixture was diluted with water (5 mL) and Et_2O (2 × 5 mL) and shaken vigorously. The nanomagnetic catalyst was separated with magnet. The organic layer was separated from the aqueous layer (consisted of DES) by simple liquid–liquid extraction. The deep eutectic solvent was dried at 60–70 °C to remove water and reused. The organic layer was dried over $MgSO_4$ and its solvent was evaporated. The crude product was recrystallized in ethanol to give the pure product. All products were known compounds and their physical and spectroscopic data (mp, IR,

Table 3 Results for the synthesis of xanthene derivatives at optimized conditions

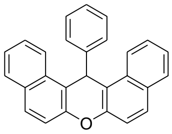
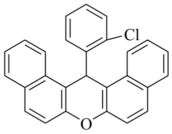
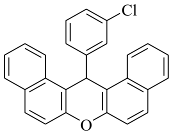
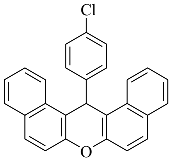
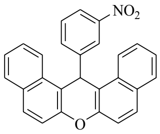
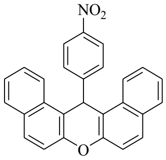
	R_1	R_2	Product	Yield (%)^a	mp (°C)	References
a	H	C_6H_5		96	181–183	[39]
b	H	2-Cl–C_6H_4		90	213–215	[40]
c	H	3-Cl–C_6H_4		91	209–211	[41]
d	H	4-Cl–C_6H_4		96	290–292	[40]
e	H	3-NO_2–C_6H_4		84	213–215	[40]
f	H	4-NO_2–C_6H_4		85	310–312	[39]

Table 3 continued

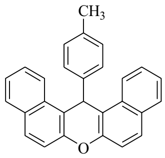
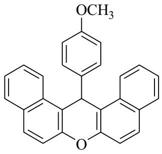
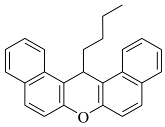
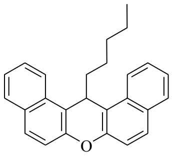
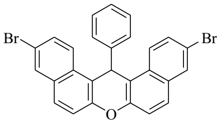
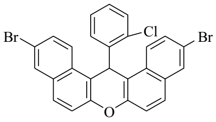
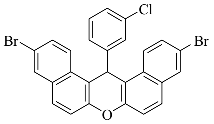
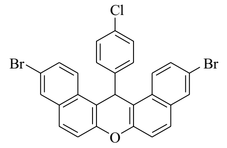
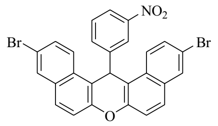
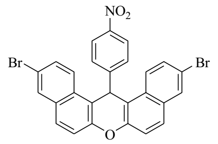
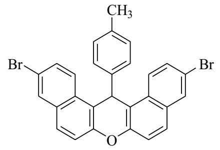
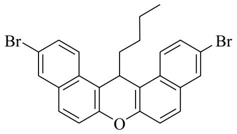
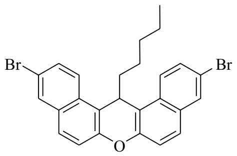
	R_1	R_2	Product	Yield (%)^a	mp (°C)	References
g	H	4-CH_3–C_6H_4		75	239–240	[39]
h	H	4-OCH_3-C_6H_4		85	203–205	[40]
i	H	C_4H_9		60	109–113	[42]
J	H	C_5H_{11}		63	102–104	[42]
k	Br	C_6H_5		88	247–250	[42]
l	Br	2-Cl–C_6H_4		85	218–220	[42]
m	Br	3-Cl–C_6H_4		81	266	[42]

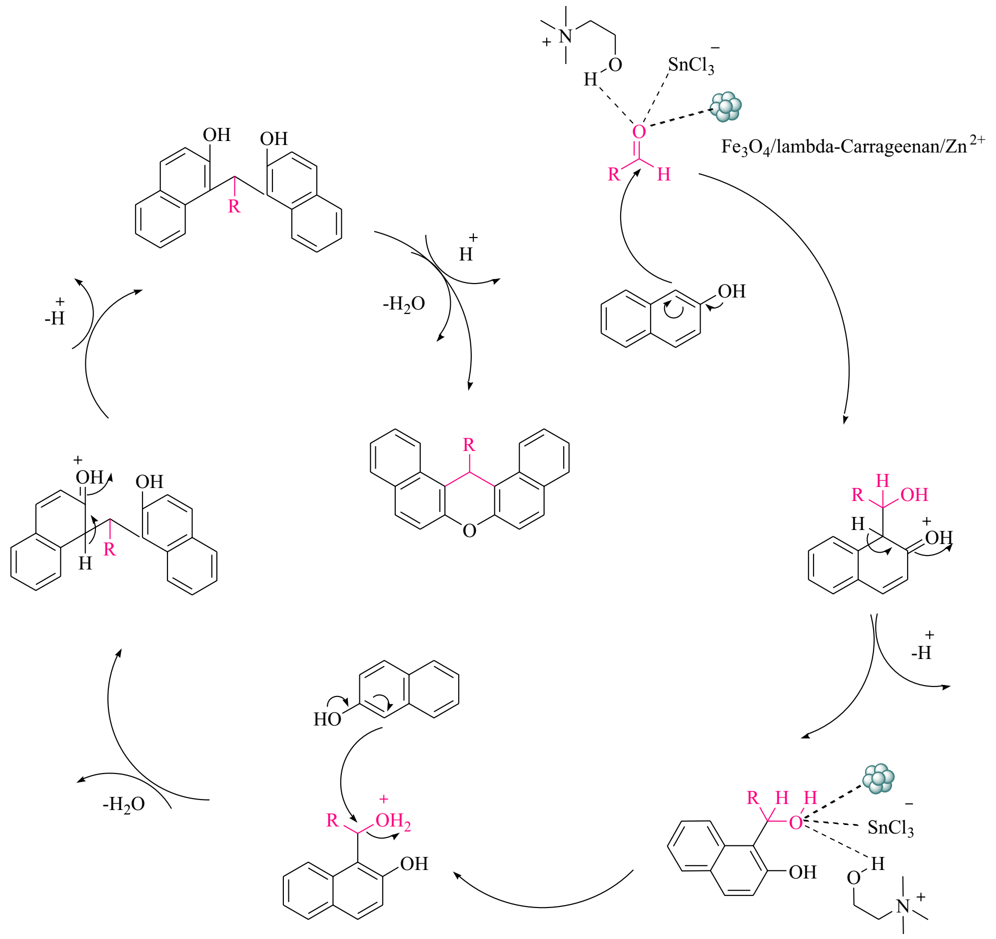
Table 3 continued

	R_1	R_2	Product	Yield (%)^a	mp (°C)	References
n	Br	4-Cl–C_6H_4		92	296–299	[42]
o	Br	3-NO_2–C_6H_4		80	159–161	[42]
p	Br	4-NO_2–C_6H_4		81	303–305	[42]
q	Br	4-CH_3–C_6H_4		70	247–251	[42]
r	Br	C_4H_9		58	138–140	[42]
s	Br	C_5H_{11}		56	Liquid	[42]

[a] Isolated yield

^1H NMR, ^{13}C NMR) were compared with those of authentic samples in the references [39–42]. The physical and spectroscopic data for selected compounds are as follows.

14-(4-Chlorophenyl)-14H-dibenzo-[a,j]-xanthenes (3d) White solid, mp = 295 °C, FT-IR (KBr): ν_{max} (cm^{-1}) = 3066, 1620, 1590, 1514, 1483, 1456, 1430, 1242, 1082, 960, 807, 743. ^1H



Scheme 2 Proposed mechanism for the synthesis of xanthenes catalyzed by ChCl·2SnCl$_2$/Fe$_3$O$_4$/ƛ-carrageenan/Zn(II)

Table 4 Result of the reusability of the DES in the model reaction

Entry	Cycle	Yield (%)
1	1st run	94
2	2nd run	90
3	3nd run	89
4	4nd run	86

NMR (400 MHz, CDCl$_3$): δ (ppm) = 8.21 (d, 2H, $J = 8$ Hz), 7.75 (d, 2H, $J = 8$ Hz), 7.71 (d, 2H, $J = 8$ Hz),7.49 (t, 2H, $J = 8$ Hz), 7.31–7.40 (m, 6H), 7.01 (d, 2H, $J = 8$ Hz), 6.37 (s, 1H).^{13}C NMR (125 MHz, CDCl$_3$): δ (ppm) = 148.7, 143.5, 131.3, 131.3, 131.1, 129.5, 129.1, 128.91, 128.6, 126.9, 124.4, 122.4, 118.0, 116.8, 37.4. Elemental analysis for $C_{27}H_{17}OCl$: C 82.56, H 4.33; found: C 81.80, H 3.82.

14-(4-Methoxyphenyl)-14H-dibenzo-[a.j]-xanthene (3h) Light pink solid, mp = 203–205 °C, FT-IR (KBr): ν_{max} (cm^{-1}) = 3071, 1590, 1509, 1458, 1398, 1248, 960, 809, 742. ^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) = 8.29 (d, 2H, $J = 8$ Hz), 7.73 (d, 2H,$J = 8$ Hz), 7.68 (d, 2H, $J = 8$ Hz), 7.50 (t, 2H, $J = 8$ Hz), 7.30–7.46 (m, 6H), 6.57 (d, 2H, $J = 8$ Hz), 6.35 (s, 1H), 3.51 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ (ppm) = 157.8, 148.7, 137.4, 131.4, 131.1, 129.2, 128.8, 128.7, 126.8, 124.2, 122.7, 118.0, 117.5, 113.8, 55.1, 37.1. Elemental analysis for $C_{28}H_{20}O_2$: C 86.60, H 5.15; found: C 82.03, H 4.54.

Results and discussion

Initially, we chose the model reaction between 2-naphthol and benzaldehyde in the presence of catalyst (DES or DES and nanomagnetic) to optimize the reaction parameters and obtain the best conditions (Scheme 1).

Different reaction conditions, such as the type of DES (ChCl·2SnCl$_2$, ChCl·2ZnCl$_2$ and ChCl·2Urea), the amount of DES (5, 10, 15 and 20 mol%), reaction temperature (r.t, 60, 90, 120 °C), and the reaction time (15 min, 0.5, 1, 1.5, 2, 5 h), have employed to obtain the best reaction conditions. The results were listed in Table 1 which showed that the best yield of the product has observed in the reaction at 90 °C in the presence of 5 mol% $ChCl{\cdot}2SnCl_2$ at 1.5 h. Moreover, to determine the catalytic or synergic effect of the prepared bionanocatalyst, different values of this catalyst were added to the reaction at its optimized conditions (Table 2) and the reaction time and its temperature has reoptimized. The results showed that this catalyst reduces the reaction time to 30 min.

The optimized conditions were employed for the synthesis of other xanthene derivatives to show the versatility of this method. The details of these experiments were shown in Table 3. According to this table, various aromatic aldehydes-containing electron withdrawing and electron-donating groups at different positions have used in addition to the use of 2-naphthol and 6-bromo-2-naphthol as another reactant.

The obtained yields show that the reactions with 2-naphtol have higher yields than those of 6-bromo-2-naphtol. In addition, aromatic aldehydes give more yields than aliphatic aldehydes and the best yields (96 %) have been observed in the reaction of 2-naphtol with benzaldehyde or 4-chlorobenzaldehyde. The role of employed catalyst is shown in the proposed mechanism, in Scheme 2.

At the final step of this study, the reusability of the employed DES has been explored in the model reaction. The result were listed in Table 4 which showed that the employed DES could be reused at least four times without any significant loss in the yield.

Conclusion

In summary, an environmentally friend and green approach has presented for the synthesis of xanthane derivatives via the reaction between 2-naphthol derivatives and aromatic or aliphatic aldehydes in the presence of $ChCl_2.SnCl_2$, alone, or in the presence of Fe_3O_4/ƛ-carrageenan/Zn(II). This method offers several advantages, including using DES instead of toxic organic solvents or catalysts (or both), high yields, short reaction times, simple work-up procedure, and reusability of DES.

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References

1. A.N. Dadhania, V.K. Patel, D.K. Raval, C. R. Chim. **15**, 378 (2012)
2. J.P. Poupelin, G.S. Ruf, O.F. Blanpin, G. Narcisse, G.U. Ernouf, R. Lacroix, Eur. J. Med. Chem. **9**, 67 (1978)
3. R. Tayebee, S. Tizabi, Chin. J. Catal. **33**, 962 (2012)
4. S.M. Menchen, S.C. Benson, J.Y.L. Lam, W. Zhen, D. Sun, B.B. Rosenblum, S.H. Khan, M. Taing, Tetrahedron Lett. **6**, 583 (2003)
5. A. Bekaert, J. Andrieux, M. Plat, Tetrahedron Lett. **33**, 2805 (1992)
6. R.M. Ion, D. Frackowiak, A. Planner, K. Wiktorowicz, Acta Biochim. Pol. **45**, 833 (1998)
7. G. Saint-Ruf, H.T. Hieu, J.P. Poupelin, Naturwissenschaen **62**, 584 (1975)
8. D. Quintas, A. Garcia, D. Dominguez, Tetrahedron Lett. **44**, 9291 (2003)
9. D.W. Knight, P.B. Little, J. Chem. Soc. **14**, 1771 (2001)
10. G. Casiraghi, G. Casnati, M. Cornia, Tetrahedron Lett. **14**, 679 (1973)
11. A. Jha, J. Beal, Tetrahedron Lett. **45**, 8999 (2004)
12. T.S. Rivera, M.N. Blanco, L.R. Pizzio, G.P. Romanelli, Green Chem. Lett. Rev. **5**, 433 (2012)
13. F. Shirini, M. Abedini, S. Akbari-Dadamahaleh, A. Rahmaninia, J. Iran. Chem. Soc. **11**, 791 (2014)
14. F. Shirini, M. Mamaghani, S.V. Atghia, J. Iran. Chem. Soc. **10**, 415 (2013)
15. A. Khalafi-Nezhad, F. Panahi, S. Mohammadi, H.O. Foroughi, J. Iran. Chem. Soc. **10**, 189 (2013)
16. B. Maleki, S. Barzegar, Z. Sepehr, M. Kermanian, R. Tayebee, J. Iran. Chem. Soc. **9**, 757 (2012)
17. A.R. Khosropour, M.M. Khodaei, H. Moghannian, Synlett **6**, 955 (2005)
18. B. Das, B. Ravikanth, R. Ramu, K. Laxminarayana, B.V. Rao, J. Mol. Catal. A Chem. **55**, 74 (2006)
19. L. Nagarapu, S. Kantevari, V.C. Mahankhali, Catal. Commun. **8**, 1173 (2007)
20. A. Saini, S. Kumar, J.S. Sandhu, Synlett **12**, 1928 (2006)
21. S. Ko, C.F. Yao, Tetrahedron Lett. **47**, 8827 (2006)
22. B. Patil, R.P. Bhat, S.D. Samant, Synth. Commun. **36**, 2163 (2006)
23. H.R. Shaterian, M. Ghashang, A. Hassankhani, Dyes Pigments **76**, 564 (2008)
24. B. Rajitha, B. Sunil Kumar, Y. Thirupathi Reddy, P. Narsimha Reddy, N. Sreeni-vasulu, Tetrahedron Lett. **46**, 8691 (2005)
25. R.J. Sarma, J.B. Baruah, Dyes Pigments **64**, 91 (2005)
26. M.A. Bigdeli, M.M. Heravi, G.H. Mahdavinia, J. Mol. Catal. A Chem. **275**, 25 (2007)
27. M.M. Amini, M. Seyyedhamzeh, A. Bazigir, Appl. Catal. A Gen. **323**, 242 (2007)
28. A.B. Mohammad, M.H. Majid, H.M. Gholam, Catal. Commun. **8**, 1595 (2007)
29. B.B.F. Mirjalili, A.H. Bamoniri, A. Akbari, Tetrahedron Lett. **49**, 6454 (2008)
30. W. Su, D. Yang, C. Jin, B. Zhang, Tetrahedron Lett. **49**, 3391 (2008)

31. S. Urinda, D. Kundu, A. Majee, A. Hajra, Heteroat. Chem. **20**, 232 (2009)
32. A. Zarei, A.R. Hajipour, L. Khazdooz, Dyes Pigments **85**, 133 (2010)
33. S. Kantevari, M.V. Chary, A.P.R. Das, S.V.N. Vuppalapati, N. Lingaiah, Catal. Commun. **9**, 1575 (2008)
34. H. Tavakol, S. Zakery, A. Heydari, J. Organomet. Chem. **692**, 1924 (2007)
35. A. Heydari, H. Tavakol, J. Azarnia, N. Ahmadi, Synthesis **2005**(5), 627 (2005)
36. F. Keshavarzipour, H. Tavakol, Catal. Lett. **145**, 1062 (2015)
37. F. Keshavarzipour, H. Tavakol, J. Iran. Chem. Soc. **13**, 149 (2016)
38. A. Heydari, M. Mehrdad, H. Tavakol, Synthesis **2003**(13), 1962 (2003)
39. S. Nagarapu Kantevari, V.C. Mahankhali, S. Apuri, Catal. Commun. **8**, 1173 (2007)
40. L. Khazdooz, A. Zarei, A.R. Hajipour, N. Sheikhan, Iran. J. Catal. **1**, 1 (2011)
41. X. Wang, M. Chen, F. Xie, M. Zhang, RSC Adv. **4**, 14744 (2014)
42. H. Eshghi, M. Bakavoli, H. Moradi, Org. Prep. Proc. Int. **43**, 302 (2011)