

Tayebeh Jari, Mohammad Ali Amrollahi* and Zohreh Kheilkordi

ZrOCl₂·SiO₂-catalyzed synthesis of bis(indoles) via conjugate addition of indole with electron-deficient alkenes in water

Abstract: This report provides a description of an efficient and environmentally benign procedure for the synthesis of bis(indole) derivatives via reaction of indole with electron-deficient alkenes. The remarkable advantages of this method for obtaining bis(indoles) are the simplicity of the experimental procedure, short reaction times, and high yields with the green aspects by avoiding toxic catalysts and solvents.

Keywords: aqueous media; bis(indole); Michael addition; oxidative dehydrogenation; zirconium oxychloride.

DOI 10.1515/hc-2015-0014

Received December 13, 2014; accepted March 2, 2015; previously published online March 26, 2015

Introduction

Michael addition is one of the most important reactions for the construction of carbon-carbon bonds in organic reactions [1, 2]. Among the Michael acceptors, (arylmethylidene)malononitriles are attractive because nitrile moiety is an electron-withdrawing group that can be readily transformed into a range of different functionalities.

Bis(indole) derivatives have received much attention because of their synthetic as well as biological applications [3, 4]. The synthesis of this important class of nitrogen heterocycles has been reported via condensation reactions of indole with different carbonyl compounds. A variety of reagents such as I₂ [5, 6], hexamethylenetetramine-bromine [7], ZrOCl₂ [8], *p*-toluenesulfonic acid [9], [bnmim][HSO₄] [10], NH₄Cl [11], AlPW₁₂O₄₀ [12], TPA-ZrO₂ [13], Zr(DS)₄ [14], ZrCl₄ [15], trichloro-1,3,5-triazine [16], ZrOCl₂ silica gel [17], and N-bromosuccinimide [18] have been used to accomplish this transformation.

*Corresponding author: Mohammad Ali Amrollahi, Department of Chemistry, Yazd University, PO Box 89195-741, Yazd, Iran, e-mail: mamrollahi@yazd.ac.ir

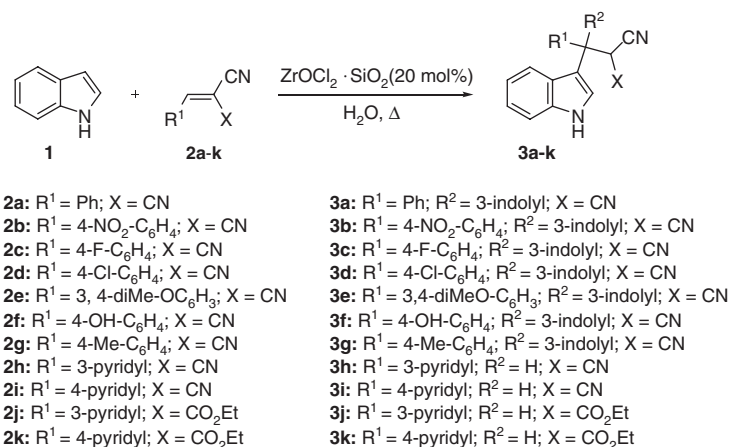
Tayebeh Jari and Zohreh Kheilkordi: Department of Chemistry, Yazd University, PO Box 89195-741, Yazd, Iran

Aqueous phase organic synthesis has attracted the attention of chemists as it overcomes the harmful effects associated with the organic solvents and is environmentally benign [19].

In recent years, zirconium salts have been used as catalysts in organic synthesis because these solid acids are relatively nontoxic, easy to handle, inexpensive, and possess good stability [20–23]. Among these, ZrOCl₂ has been reported to be an efficient catalyst for many important organic transformations [24–29]. In continuation of our previous work on the development of new synthetic methodologies [30, 31], we report the synthesis of bis(indole) derivatives via reaction of indole with electron-deficient alkenes in the presence of ZrOCl₂·SiO₂ in H₂O under reflux conditions (Scheme 1).

Results and discussion

For optimizing the experimental conditions, the reaction between **1** and **2a** was used as a model reaction. To find the best catalyst, several Lewis acids such as ZrCl₄, Ni(NO₃)₂, ZrOCl₂, P₂O₅, Cu(I)Cl, and Cu(OAc)₂ were used. The highest yield was achieved with ZrOCl₂. The formation of the product was more facile and proceeded in shorter time when the reaction was performed in the presence of ZrOCl₂·SiO₂. Similar reactions were then attempted in the presence of 10, 15, 20, and 25 mol% of ZrOCl₂·SiO₂. The results show that the use of 20 mol% of ZrOCl₂·SiO₂ at reflux in water is sufficient. Greater amounts of the catalyst had no significant influence on the reaction yield. To find the optimum temperature, the reaction was conducted with 20 mol% of ZrOCl₂·SiO₂ at room temperature, 60°C, and at reflux, which resulted in the isolation of product in a trace amount, 70 and 92% yields, respectively. In addition, CH₂Cl₂, CHCl₃, MeCN, and AcOEt were also tested as solvents. In all these cases, product **3a** was formed in lower yields. Solvent-free conditions at different temperatures did not accelerate the reaction. Thus, the reaction is optimally conducted in the presence of 20 mol% of ZrOCl₂·SiO₂ under reflux conditions.



Scheme 1

Bis(indole) derivatives **3a–g** were synthesized under the optimized conditions. It can be observed that the process tolerates both electron-donating and electron-withdrawing substituent R^1 in the substrates **2a–k**. In all cases, the reactions proceed efficiently at reflux in water under mild conditions to afford the corresponding products in high yields. All products were characterized by IR, ^1H - and ^{13}C -NMR spectra, and elemental analysis.

Under the optimized conditions, the treatment of (pyridylmethylene)malononitriles (**2h** and **2i**) and ethyl (pyridyl)acrylates (**2j** and **2k**) with indole does not yield bis(indole) derivatives. These reactions proceed smoothly, but the products contain only one indole moiety in the molecule. Changes in a molar ratio of the substrates (**1:2**=1:0.5 or 1:1) do not affect the final structural outcome.

Conclusion

Depending on the structure of electron-deficient alkenes, their addition reactions with indole in the presence of $\text{ZrOCl}_2 \cdot \text{SiO}_2$ give rise to bis(indole) or mono-indole adducts.

Experimental

Melting points were determined on a Büchi melting point B-540 B.V.CHI apparatus in open capillaries and are uncorrected. IR spectra were recorded in KBr pellets on a Bruker Equinox 55 spectrometer. ^1H - and ^{13}C -NMR spectra were obtained in CDCl_3 on a Bruker Avance 500 MHz spectrometer. Elemental analyses were conducted with a Costech ECS 4010 CHN analyzer. Column chromatography was performed on silica gel (230–400) mesh. Analytical thin-layer chromatography (TLC) was performed on precoated plastic sheets of silica gel G/UV-254 of 0.2 mm thickness. The catalyst $\text{ZrOCl}_2 \cdot \text{SiO}_2$ was prepared as previously reported [32].

General procedure for the synthesis of bis(indole) compounds **3a–g** and mono adducts **3h–k**

A mixture of indole (**1**, 1 mmol), an electron-deficient alkene [(**2a–g**, 0.5 mmol) or (**2h–k**, 1 mmol)], and the catalyst $\text{ZrOCl}_2 \cdot \text{SiO}_2$ (20 mol%) in water (8 mL) was heated under reflux until the reaction was completed, as monitored by TLC. After cooling, the mixture was filtered and the filtrate was concentrated. The residue was subjected to column chromatography eluting with chloroform/*n*-hexane, 9:1.

2-[Di(1H-indol-3-yl)(phenyl)methyl]malononitrile (3a) Yield 92%; red crystals; mp 89–90°C; IR: 3409, 3050, 2923, 2259, 1619, 1455 cm^{-1} ; ^1H -NMR: δ 5.94 (s, 1H, CH), 6.67 (s, 2H, CH), 7.07 (t, $J = 6.4$ Hz, 2H, ArH), 7.23 (t, $J = 6.4$ Hz, 2H, ArH), 7.27–7.35 (m, 7H, ArH), 7.45 (d, $J = 6.9$ Hz, 2H, ArH), 7.88 (s, 2H, NH); ^{13}C -NMR: δ 27.7, 40.6, 111.4, 112.6, 119.6, 120.1, 120.3, 122.3, 124.0, 126.5, 127.5, 128.6, 129.1, 137.1, 144.4. Anal. Calcd for $\text{C}_{26}\text{H}_{18}\text{N}_4$: C, 80.81; H, 4.69; N, 14.50. Found: C, 80.51; H, 4.49; N, 14.20.

2-[Di(1H-indol-3-yl)(4-nitrophenyl)methyl]malononitrile (3b) Yield 90%; yellow crystals; mp 243–245°C; IR: 3422, 3047, 2923, 2263, 1592, 1504, 1453, 1339 cm^{-1} ; ^1H -NMR: δ 5.93 (s, 1H, CH), 6.64 (s, 2H, CH), 6.92 (t, $J = 7.4$ Hz, 2H, ArH), 7.09 (t, $J = 7.4$ Hz, 2H, ArH), 7.26 (d, $J = 7.9$ Hz, 2H, ArH), 7.34 (d, $J = 8.1$ Hz, 2H, ArH), 7.46 (d, $J = 8.3$ Hz, 2H, ArH), 8.15 (d, $J = 8.3$ Hz, 2H, ArH), 9.45 (s, 2H, NH); ^{13}C -NMR: δ 32.0, 45.9, 111.0, 113.0, 113.8, 117.2, 119.8, 120.1, 122.0, 123.8, 124.0, 128.0, 132.4, 148.0, 149.1. Anal. Calcd for $\text{C}_{26}\text{H}_{17}\text{N}_5\text{O}_2$: C, 72.38; H, 3.97; N, 16.23. Found: C, 72.15; H, 3.65; N, 16.43.

2-[(4-Fluorophenyl)di(1H-indol-3-yl)methyl]malononitrile (3c) Yield 86%; pink crystals; mp 132–135°C; IR: 3408, 3052, 2923, 2252, 1601, 1416, 1217, 743 cm^{-1} ; ^1H -NMR: δ 5.90 (s, H, CH), 6.33 (s, 2H, CH), 7.00 (m, 2H, ArH), 7.19–7.27 (m, 4H, ArH), 7.30 (m, 2H, ArH), 7.80 (d, $J = 8.1$ Hz, 2H, ArH), 8.00 (d, $J = 7.9$ Hz, 2H, ArH), 9.30 (s, 2H, NH); ^{13}C -NMR: δ 39.9, 48.0, 112.0, 112.8, 113.0, 116.0, 119.0, 120.7, 121.2, 123.8, 128.4, 131.1, 136.8, 138.0, 159.1. Anal. Calcd for $\text{C}_{26}\text{H}_{17}\text{N}_4\text{F}$: C, 77.21; H, 4.24; N, 13.58. Found: C, 77.00; H, 4.60; N, 13.44.

2-[(4-Chlorophenyl)di(1H-indol-3-yl)methyl]malononitrile (3d) Yield 85%; viscous oil; IR: 3411, 3070, 2923, 2257, 1616, 1470, 744 cm^{-1} ; ^1H -NMR: δ 5.89 (s, 1H, CH), 6.66 (s, 2H, CH), 6.93–7.04 (m, 4H,

ArH), 7.21 (d, 2H, $J = 8.0$ Hz, ArH), 7.44 (d, 2H, $J = 7.3$ Hz, ArH), 7.80 (d, 2H, $J = 8.0$ Hz, ArH), 8.00 (d, $J = 7.3$ Hz, 2H, ArH), 8.60 (s, 2H, NH); $^{13}\text{C-NMR}$: δ 37.6, 50.0, 112.1, 113.2, 113.8, 118.5, 120.1, 121.5, 121.7, 125.5, 128.3, 130.1, 131.9, 138.1, 140.0. Anal. Calcd for $\text{C}_{26}\text{H}_{17}\text{N}_4\text{Cl}$: C, 74.19; H, 4.07; N, 13.31. Found: C, 74.42; H, 4.28; N, 13.55.

2-[(3,4-Dimethoxyphenyl)di(1H-indol-3-yl)methyl]malononitrile (3e) Yield 81%; light yellow crystals; mp 168–169°C; IR: 3309, 3055, 2926, 2250, 1593, 1580, 1455 cm^{-1} ; $^1\text{H-NMR}$: δ 3.80 (s, 3 H, CH_3), 3.89 (s, 3H, CH_3), 5.88 (s, 1H, CH), 6.67 (d, $J = 1.8$ Hz, 1H, ArH), 6.71 (s, 2H, CH), 6.81 (d, $J = 8.2$ Hz, 1H, ArH), 6.88 (dd, $J_1 = 8.2$ Hz, $J_2 = 1.8$ Hz, 1H, ArH), 7.05 (t, $J = 7.5$ Hz, 2H, ArH), 7.21 (t, $J = 7.5$ Hz, 2H, ArH), 7.4 (d, $J = 8.0$ Hz, 2H, ArH), 7.45 (d, $J = 8.0$ Hz, 2H, ArH), 7.96 (s, 2H, NH); $^{13}\text{C-NMR}$: δ 38.0, 50.0, 57.3, 57.4, 110.0, 112.0, 112.8, 115.0, 117.7, 119.7, 120.0, 122.0, 123.01, 123.7, 128.7, 133.0, 136.5, 148.0, 150.0. Anal. Calcd for $\text{C}_{28}\text{H}_{22}\text{N}_4\text{O}_2$: C, 75.32; H, 4.97; N, 12.55. Found: C, 75.52; H, 4.63; N, 12.22.

2-[(4-Hydroxyphenyl)di(1H-indol-3-yl)methyl]malononitrile (3f) Yield 80%; red crystals; mp 87–88°C; IR: 3407, 3055, 2922, 2273, 1611, 1509, 1455 cm^{-1} ; $^1\text{H-NMR}$: δ 5.30 (s, 1H, OH), 5.40 (s, 1H, CH), 6.67 (s, 2H, NH), 6.80 (d, $J = 8.2$ Hz, 2H, ArH), 7.00 (m, 2H, ArH), 7.14 (d, $J = 7.9$ Hz, 2H, ArH), 7.60 (m, 2H, ArH), 7.90 (d, $J = 8.2$ Hz, 2H, ArH), 7.97 (d, $J = 8.2$ Hz, 2H, ArH), 8.30 (s, 2H, NH); $^{13}\text{C-NMR}$: δ 39.0, 49.1, 111.2, 113.0, 116.1, 119.6, 121.1, 123.0, 128.2, 129.0, 129.3, 132.7, 136.5, 138.1, 155.5. Anal. Calcd for $\text{C}_{26}\text{H}_{18}\text{N}_4\text{O}$: C, 77.59; H, 4.51; N, 13.92. Found: C, 77.65; H, 4.71; N, 13.62.

2-[Di(1H-indol-3-yl)(p-tolyl)methyl]malononitrile (3g) Yield 82%; red crystals; mp 174–176°C; IR: 3380, 3030, 2923, 2267, 1610, 1475 cm^{-1} ; $^1\text{H-NMR}$: δ 2.54 (s, 3H, CH_3), 5.32 (s, 1H, CH), 6.80 (s, 2H, CH), 7.00–7.25 (m, 4H, ArH), 7.35 (d, $J = 7.3$ Hz, 2H, ArH), 7.49 (d, $J = 8.1$ Hz, 2H, ArH), 7.65 (d, $J = 7.3$, 2H, ArH), 7.95 (d, $J = 8.1$ Hz, 2H, ArH), 8.93 (s, 2H, NH); $^{13}\text{C-NMR}$: δ 21.4, 37.8, 55.7, 112.6, 113.4, 119.6, 120.1, 120.9, 122.3, 124.0, 126.5, 127.5, 128.6, 129.1, 137.1, 144.4. Anal. Calcd for $\text{C}_{27}\text{H}_{20}\text{N}_4$: C, 80.98; H, 5.03; N, 13.99. Found: C, 80.71; H, 4.69; N, 14.20.

2-[(1H-Indol-3-yl)(pyridine-3-yl)methyl]malononitrile (3h) Yield 92%; white crystals; mp 159–161°C; IR: 3407, 3075, 2902, 2258, 1618, 1494; $^1\text{H-NMR}$: δ 4.80 (d, $J = 6.9$ Hz, 1H, CH), 5.00 (d, $J = 6.9$ Hz, 1H, CH), 7.50–7.90 (m, 7H, ArH), 8.42 (s, 1H, CH), 8.61 (s, 1H, CH), 10.37 (s, 1H, NH); $^{13}\text{C-NMR}$: δ 29.5, 42.1, 110.9, 112.2, 112.9, 116.1, 118.6, 120.0, 122.8, 124.0, 127.9, 134.1, 136.1, 136.9, 141.4, 156.1, 165.7. Anal. Calcd for $\text{C}_{17}\text{H}_{12}\text{N}_4$: C, 74.98; H, 4.44; N, 20.58. Found: C, 74.55; H, 4.61; N, 20.55.

2-[(1H-Indol-3-yl)(pyridine-4-yl)methyl]malononitrile (3i) Yield 91%; white crystals; mp 165–166°C; IR: 3402, 3050, 2930, 2269, 1605, 1472 cm^{-1} ; $^1\text{H-NMR}$: δ 4.80 (d, $J = 6.9$ Hz, 1H, CH), 4.50 (d, $J = 6.9$ Hz, 1H, CH), 7.10 (s, 1H, ArH), 7.10–7.30 (m, 4H, ArH), 7.28 (d, $J = 7.7$ Hz, 2H, ArH), 8.61 (d, $J = 7.7$ Hz, 2H, ArH), 9.37 (s, 1H, NH); $^{13}\text{C-NMR}$: δ 49.5, 62.1, 110.9, 112.9, 116.1, 118.6, 119.8, 120.7, 123.3, 124.0, 127.3, 134.1, 136.9, 155.0, 163.1. Anal. Calcd for $\text{C}_{17}\text{H}_{12}\text{N}_4$: C, 74.98; H, 4.44; N, 20.58. Found: C, 74.65; H, 4.61; N, 20.65.

Ethyl 2-cyano-3-(1H-indol-3-yl)-3-(pyridine-3-yl)propanoate (3j) Yield 87%; light pink crystals; mp 147–148°C; IR: 3411, 3040, 2980, 2252, 1732, 1260 cm^{-1} ; $^1\text{H-NMR}$: δ 1.06 (t, $J = 7.1$ Hz, 3H, CH_3), 4.08 (q, $J = 7.1$ Hz, 2H, CH_2), 4.34 (d, $J = 6.1$ Hz, 1H, CH), 5.01 (d, $J = 6.1$ Hz, 1H, CH), 6.80–7.90 (m, 7H, ArH), 8.45 (d, $J = 3.9$ Hz, 1H, CH), 8.63 (s, 1H, CH), 10.04 (s, 1H, NH); $^{13}\text{C-NMR}$: δ 14.1, 38.0, 40.8, 63.4, 111.1,

112.9, 116.1, 118.6, 119.9, 122.1, 122.6, 123.0, 124.0, 133.2, 135.29, 136.9, 148.2, 149.9, 165.2. Anal. Calcd for $\text{C}_{19}\text{H}_{17}\text{N}_3\text{O}_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.16; H, 5.67; N, 13.36.

Ethyl 2-cyano-3-(1H-indol-3-yl)-3-(pyridine-4-yl)propanoate (3k) Yield 85%; viscous oil; IR: 3402, 3060, 2981, 2250, 1741, 1599, 1458 cm^{-1} ; $^1\text{H-NMR}$: δ 1.06 (t, $J = 7.1$ Hz, 3H, CH_3), 4.08 (q, $J = 7.1$ Hz, 2H, CH_2), 4.34 (d, $J = 6.2$ Hz, 1H, CH), 5.01 (d, $J = 6.1$ Hz, 1H, CH), 7.18 (m, 4H, ArH), 7.28 (d, $J = 8.0$ Hz, 2H), 8.46 (d, $J = 8.0$ Hz, 2H, ArH), 8.63 (s, 1H, CH), 10.04 (s, 1H, NH); $^{13}\text{C-NMR}$: δ 14.1, 38.1, 40.1, 63.4, 112.0, 117.4, 120.9, 121.7, 122.6, 123.2, 124.5, 124.7, 137.1, 141.0, 150.0, 153.4, 164.7. Anal. Calcd for $\text{C}_{19}\text{H}_{17}\text{N}_3\text{O}_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.23; H, 5.14; N, 13.54.

Acknowledgments: The authors thank the Research Council of Yazd University for financial support.

References

- [1] Yadav, J. S.; Abraham, S.; Reddy, B. V. S.; Sabitha, G. InCl_3 -catalysed conjugate addition of indoles with electron-deficient olefins. *Synthesis* **2001**, 14, 2165–2169.
- [2] Mariappan, J.; Kuppusamy, K.; Amarajothi, D.; Kasi, P. Michael addition of indoles to b-nitrostyrenes catalyzed by HY zeolite under solvent-free conditions. *Tetrahedron Lett.* **2014**, 55, 2061–2064.
- [3] Osawa, T.; Namiki, M. Structure elucidation of streptindole, a novel genotoxic metabolite isolated from intestinal bacteria. *Tetrahedron Lett.* **1983**, 24, 4719–4722.
- [4] Sadaphal, S. A.; Kattegaonkar, A. H.; Labade, V. B.; Shingare Murlidhar, S. Synthesis of bis(indolyl) methanes using aluminium oxide (acidic) in dry media. *Chinese Chem. Lett.* **2010**, 21, 39–42.
- [5] Ganguly, N. C.; Mondal, P.; Barik, S. K. Iodine in aqueous micellar environment: a mild effective eco-friendly catalytic system for expedient synthesis of bis(indolyl)methanes and 3-substituted indolyl ketones. *Green Chem. Lett. Rev.* **2012**, 5, 73–81.
- [6] Ji, S. J.; Wang, S.; Zhang, Y.; Loh, T. P. Facile synthesis of bis(indolyl)methanes using catalytic amount of iodine at room temperature under solvent-free conditions. *Tetrahedron* **2004**, 60, 2051–2055.
- [7] Bandgar, B. P.; Bettigeri, S. V.; Joshi, N. S. Hexamethylenetetraamine-bromine catalyzed rapid and efficient synthesis of bis(indolyl)methanes. *Monatsh. Chem.* **2004**, 135, 1265–1273.
- [8] Nagawade, R. R.; Shinde, D. B. Zirconyl(IV) chloride—catalysed reaction of indoles: an expeditious synthesis of bis(indolyl) methanes. *Acta Chim. Slov.* **2006**, 53, 210–213.
- [9] Pashas, M. A.; Jayashankara, V. P. p-Toluenesulfonic acid (p-TSA) catalyzed efficient synthesis of bis(indolyl)methanes under grindstone method. *J. Pharmacol. Toxicol. Sci.* **2006**, 1, 585–590.
- [10] Azizian, J.; Teimouri, F.; Mohammadizadeh, M. R. Ammonium chloride catalyzed one-pot synthesis of diindolylmethanes under solvent-free conditions. *Catal. Commun.* **2007**, 8, 1117–1121.
- [11] Firouzabadi, H.; Iranpoor, N.; Jafari, A. A. Aluminumdodecatungstophosphate ($\text{AlPW}_{12}\text{O}_{40}$), a versatile and a highly water tolerant green Lewis acid catalyzes efficient preparation of indole derivatives. *J. Mol. Catal. A. Chem.* **2006**, 244, 168–172.

- [12] Satam, J. R.; Parghi, K. D.; Jayaram, R. V. 12-Tungstophosphoric acid supported on zirconia as an efficient and heterogeneous catalyst for the synthesis of bis(indolyl)methanes and tris(indolyl)methanes. *Catal. Commun.* **2008**, *9*, 1071–1078.
- [13] Zolfigol, M. A.; Salehi, P.; Shiri, M.; Tanbakouchian, Z. A new catalytic method for the preparation of bis-indolyl and tris-indolyl methanes in aqueous media. *Catal. Commun.* **2007**, *8*, 173–178.
- [14] Li, W. J.; Lin, X. F.; Wang, J.; Lia, G. L.; Wang, Y. G. A mild and efficient synthesis of bis-indolylmethanes catalyzed by sulfamic acid. *Synth. Commun.* **2005**, *35*, 2765–2769.
- [15] Sharma, G. V. M.; Reddy, J. J.; Lakshmi, P. S.; Krishnal, P. R. A versatile and practical synthesis of bis(indolyl)methanes/bis(indolyl)glycoconjugates catalyzed by trichloro-1,3,5-triazine. *Tetrahedron Lett.* **2004**, *45*, 7729–7732.
- [16] Firouzabadi, H.; Iranpoor, N.; Jafarpour, M.; Ghaderi, A. $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ /silica gel as a new efficient and a highly water-tolerant catalyst system for facile condensation of indoles with carbonyl compounds under solvent-free conditions. *J. Mol. Catal. A. Chem.* **2006**, *253*, 249–251.
- [17] Firouzabadi, H.; Jafarpour, M. Some applications of zirconium(IV) tetrachloride (ZrCl_4) and zirconium(IV) oxydichloride octahydrate ($\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$) as catalysts or reagents in organic synthesis. *J. Iranian Chem. Soc.* **2008**, *5*, 159–183.
- [18] Kuo, C. W.; Wang, C. C.; Fang, H. L.; Raju, B. R.; Kavala, V.; Mujamil Habib, P.; Yao, C. F. An efficient method for the N-bromosuccinimide catalyzed synthesis of indolyl-nitroalkanes. *Molecules* **2009**, *14*, 3952–3963.
- [19] Kokkiral, S.; Sabbavarapu, N. M.; Yadavalli, V. D. N. β -Cyclodextrin-mediated synthesis of 1,8-dioxooctahydroxanthenes in water. *Eur. J. Chem.* **2011**, *2*, 272–275.
- [20] Lin, J.; Zhang, L. F. ZrCl_4 -catalyzed efficient synthesis of enamines and enamino esters under solvent-free conditions. *Monats. Chem.* **2007**, *138*, 77–81.
- [21] Singh, S.; Duffy, C. D.; Shah, S. T. A.; Guiry, P. J. ZrCl_4 as an efficient catalyst for a novel one-pot protection/deprotection synthetic methodology. *J. Org. Chem.* **2008**, *73*, 6429–6432.
- [22] Tocco, G.; Begala, M.; Meli, G.; Podda, G. InCl_3 and ZrCl_4 catalyzed regioselective reaction of 2,2'-dihydroxybiphenyl with terminal alkynes: synthesis of new dibenzo[*d,f*][1,3]dioxepines. *Tetrahedron* **2008**, *64*, 6755–6759.
- [23] Chakraborti, A. K.; Kondaskar, A. ZrCl_4 as a new and efficient catalyst for the opening of epoxide rings by amines. *Tetrahedron Lett.* **2003**, *44*, 8315–8319.
- [24] Babu, A. R. S.; Raghunathan, R. $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ mediated microwave induced [3+2] cycloaddition of azomethine ylides – a facile one-pot synthesis of novel dispiroheterocycles. *Tetrahedron Lett.* **2007**, *48*, 305–308.
- [25] Mirkhani, V.; Mohammadpoor-Baltork, I.; Moghadam, M.; Tangestaninejad, S.; Abdollahi-Alibeik, M.; Kargar, H. $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$: an efficient and reusable catalyst for the synthesis of imidazolines and bis-imidazolines under various reaction conditions. *Appl. Catal. A. Gen.* **2007**, *325*, 99–104.
- [26] Rodríguez-Domínguez, J. C.; Bernardi, D.; Kirsch, G. ZrCl_4 or ZrOCl_2 under neat conditions: optimized green alternatives for the Biginelli reaction. *Tetrahedron Lett.* **2007**, *48*, 5777–5780.
- [27] Bhagat, S.; Chakraborti, A. K. Zirconium(IV) compounds as efficient catalysts for synthesis of α -aminophosphonates. *J. Org. Chem.* **2008**, *73*, 6029–6032.
- [28] Shen, W.; Wang, L. M.; Feng, J. J.; Tian, H. Highly efficient synthesis of homoallylic alcohols and amines via allylation of aldehydes and imines catalyzed by $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ in water. *Tetrahedron Lett.* **2008**, *49*, 4047–4049.
- [29] Ghosh, R.; Maiti, S.; Maity, S. K.; Roy, S. $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ -catalyzed one-pot multicomponent synthesis of β' -acetamido- β -dicarbonyl compounds with special reference to pref-selective β' -acetamido- β -ketoesters. *Synth. Commun.* **2008**, *38*, 1958–1971.
- [30] Emtiazi, H.; Amrollahi, M. A.; Mirjalili, B. B. F. Nano-silica sulfuric acid as an efficient catalyst for the synthesis of substituted pyrazoles. *Arabian J. Chem.* in press **2015**.
- [31] Amrollahi, M. A.; Mirjalili, B. B. F.; Emtiazi, H. $\text{Mg}(\text{ClO}_4)_2$ catalyzed preparation of 1-amidoalkyl-2-naphthols under solvent-free conditions. *J. Chem. Sci.* **2013**, *125*, 561–566.
- [32] Karami, B.; Kiani, M. $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}/\text{SiO}_2$: an efficient and recyclable catalyst for the preparation of coumarin derivatives by Pechmann condensation reaction. *Catal. Commun.* **2011**, *14*, 62–67.