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K_2CO_3-mediated, direct C–H bond selenation and thiolation of 1,3,4-oxadiazoles in the absence of metal catalyst: An eco-friendly approach

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A eco-friendly, straightforward and high-yielding methodology for the synthesis of chalcogenyl oxadiazoles via the K_2CO_3-promoted direct C–H bond chalcogenation of 2-subsituted-1,3,4-oxadiazoles is described herein. The reaction was performed in the absence of metal catalyst and inert atmosphere using only a half equiv. of dichalcogenides and a low-cost base

Metal-free reactions can be applied in the functionalization of C−H bonds to access C−C and C−heteroatom bonds and this has become a rapidly developing area.[1] In this regard, one of the most important discoveries made in organic synthesis in recent years is that certain reactions which were thought to involve transition metal (TM) catalysis can, in fact, proceed without the requirement for a TM.[2] Reactions carried out under metal-free conditions are particularly attractive in the synthesis of pharmaceuticals.[3] Therefore, from the economic and environmental viewpoints, it would be advantageous and desirable to develop TM-free systems in the area of organic synthesis.

The synthetic versatility of organochalcogenides has been explored extensively in research articles,[4] reviews[5] and books.[6] This group includes the organoselenium compounds, which can be employed in certain reactions[7] as catalysts,[8] ionic liquids,[9] and synthetic intermediates in total synthesis.[5,6,10] Another important advancement in this context is the formation of C-Se bonds, which has contributed to the synthesis of a wide range of biologically active molecules[11] and functional materials.[12] A large number of organoselenides have been found to function as antioxidants, antinociceptive agents, antidepressant apoptosis inducers and chemopreventors in several organs, etc.[5d-e, 11]

Functionalization of the 1,3-4-oxadiazoles scaffold is an important synthetic task, since oxadiazoles are well established as "privileged scaffolds" and are widely used for pharmaceutical, biological and material applications.[13] They show a very broad spectrum of biological activity, being used, for instance, as inhibitors of various enzymes and as antimicrobial, analgesic, antiviral and antitumor agents.[14] Interestingly, few of the active compounds have a sulphur linkage at C-5.[14b] 1,3,4-Oxadiazole motifs are also of interest in material science and have been widely used to create novel materials.[15]

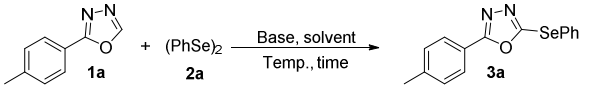
Many methods for the C-H functionalization of 1,3,4-oxadiazoles have been reported in the literature with the formation of C-alkyl,[16a] C-allyl,[16b] C-alkynyl,[16c] C-aryl,[16d] C-benzyl,[16e] C-N,[16f] C-S,[16g-h] etc. However, the disadvantages associated with many of these methodologies, owing to the use of TM catalysts, expensive reagents, harsh reaction conditions, hazardous materials, oxygen-free techniques or elaborate multi-stepped processes, have limited their synthetic scope.

Considering the significance of these compounds, the challenging task of developing new green routes for the syntheses of chalcogenides which provide high efficiency, through direct substitution with heteroacromatics and other organic moieties, is an important research area.[17] As part of our wider research program aimed at designing and developing eco-friendly processes,[18] herein we report for the first time a straightforward, mild, and environmentally benign protocol for the direct selenation of 1,3,4-oxadiazole, which is also applicable to disulphides. The functionalization of C_{sp2}-H bonds proceeded smoothly with half equivs. of different dichalcogenides and a low-cost base in the absence of a metal catalyst and in an inert atmosphere.

To identify the best reaction conditions, 2-(4-methylphenayl)-1,3,4-oxadiazole (**1a**) and diphenyl diselenide (**2a**) were initially used as standard substrates under different conditions, Table 1. Considering the need for a metal catalyst and base under inert atmosphere for C_{sp2}-H bond funtionalization,[17b] a preliminary experiment was performed using 1 equiv. of K_2CO_3 and 20 mol% of CuO-nanopowder under an inert atmosphere in DMSO (Table 1, entry 1),

affording the product **3a** in 56% yield. Notably, the yield was 58% under catalyst-free conditions (entry 2). However, there was a slight improvement in the yield under an open atmosphere (Table 1, entry 3). These results suggest that the use of TM-free and open atmosphere conditions is appropriate for the selenation of **2a**.

Table 1 Optimization of the reaction conditions[a]



Entry	Base	Solvent	Temp. (°C)	Time (h)	Yield[b] (%)
1 [c,d]	K_2CO_3	DMSO	100	18	56
2 [d]	K_2CO_3	DMSO	100	18	58
3	K_2CO_3	DMSO	100	18	63
4	K_2CO_3	DMSO	100	12	81
5	**K_2CO_3**	**DMSO**	**100**	**10**	**86**
6	K_2CO_3	DMSO	100	8	82
7	K_2CO_3	DMSO	120	10	59
8	K_2CO_3	DMSO	80	10	71
9	K_2CO_3	DMSO	rt	10	9
10 [e]	K_2CO_3	DMSO	100	10	85
11	K_2CO_3	DMSO-dry	100	10	84
12	K_2CO_3	DMF	100	10	67
13	K_2CO_3	H_2O	100	10	0
14	K_2CO_3	THF	100	10	0
15	K_2CO_3	EtOH	100	10	0
16	K_2CO_3	Toluene	100	10	11
17	K_2CO_3	Acetonitrile	100	10	12
18	K_2CO_3	1,4-dioxane	100	10	0
19	--	DMSO	100	10	0
20	Na_2CO_3	DMSO	100	10	59
21	Cs_2CO_3	DMSO	100	10	32
22	*t*-BuOK	DMSO	100	10	0
23	Et_3N	DMSO	100	10	0
24	KOH	DMSO	100	10	13
25 [f]	K_2CO_3	DMSO	100	10	82
26 [g]	K_2CO_3	DMSO	100	10	61
27 [h]	K_2CO_3	DMSO	100	10	41
28 [i]	K_2CO_3	DMSO-dry	100	10	85

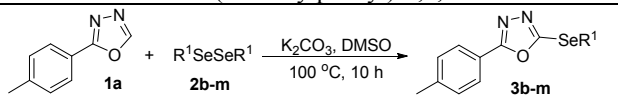
[a] *Reaction conditions*: **1a** (0.5 mmol), **2a** (0.26 mmol), base (0.5 mmol), solvent (1 ml) at a specific time under air. [b] Isolated yield based on **1a**. [c] CuO-nano (20 mol%). [d] Under argon atmosphere. [e] **2a** (0.5 mmol). [f] K_2CO_3 (2 equiv.). [g] K_2CO_3 (0.5 equiv.). [h] K_2CO_3 (30 mol%). [i] K_2CO_3 with 99.997% purity.

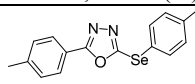
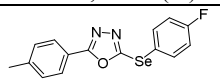
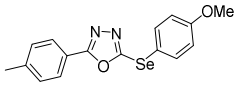
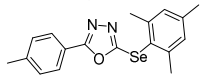
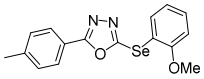
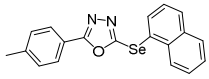
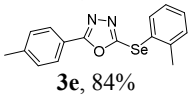
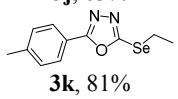
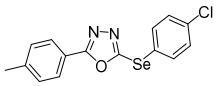
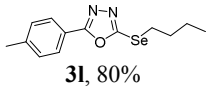
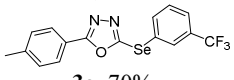
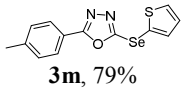
In the next step the reaction time and temperature were screened for this transformation (entries 4-9). Ideal conditions were found to be 10 h reaction time at 100 °C, resulting in **3a** with 86% yield (entry 5). It should be noted that increasing the stoichiometric amount of **2a** to 0.5 mmol did not affect the yield of **3a** (entry 10), while the unreacted **2a** was completely recovered using column chromatography. During the course of the reaction the formation of PhSePh, a common by-product, was not observed.

Subsequently, using freshly distilled and dried DMSO was found to be ineffective and the product was obtained in 84% yield (entry 11). Other solvents were also screened and they failed to provide a more favourable outcome (entries 12-18). No product was observed in the absence of base (entry 19). The influence of other bases was also investigated (entries 20-24), all giving poor results. An adverse effect on the yield was noted when the amount of base (K_2CO_3) varied from 1 mmol (entries 25-27). Finally, in order to eliminate any possibility of a catalytic effect due to trace metal contamination,[17b,19] a controlled experiment was carried out using K_2CO_3 with 99.997% purity, freshly distilled DMSO, new glassware and a new magnetic bar (entry 28). This experiment afforded **3a** with 85% yield and thus we can assume that a trace metal was not involved in these reactions.

After determining the ideal reaction parameters, we explored the efficiency and generality of our methodology by applying it to various diorganyl diselenides **2** under the optimized conditions (Table 2). The reaction worked well for several diselenides containing both electron-donating (R^1 = Me, OMe) and electron-withdrawing (R^1 = F, Cl, CF_3) groups as well as bulky groups, verifying the sensitivity and tolerance to electronic effects and steric effects of several different substituents. Generally, electron-donating groups at the phenyl ring of **2** afforded good results (entries 1-4 vs 5-7). There was a weaker influence on the yields due to steric hindrance of *ortho*-substituted aryl substrates (entries 1-2) as compared to the respective *para* derivatives (entries 3-4). Sterically-hindered substrates (R^1 = 2-napthyl) resulted in the desired product **3j** in 63% yield (entry 9), but dimesityldiselenide not only showed complete tolerance but afforded **3i** with 92% yield (entry 8). Normally, aliphatic diselenides are considered to be less reactive and give low yields due to *β*-selenoxide elimination.[17b] Gratifyingly, under our optimized conditions, aliphatic diselenides produced the corresponding products in very good yields (entries 10-11). We were also delighted to find that C-2 heteroaryl diselenide afforded the desired product **3m** with 79% yield (entry 12).

Table 2 Selenation of 2-(4-methylphenyl)-1,3,4-oxadiazole **1a**[a]



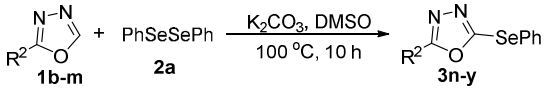
Entry	Product, Yield[b] (%)	Entry	Product, Yield (%)
1	 **3b**, 88%	7	 **3h**, 65%
2	 **3c**, 96%	8	 **3i**, 92%
3	 **3d**, 88%	9	 **3j**, 63%
4	 **3e**, 84%	10	 **3k**, 81%
5	 **3f**, 82%	11	 **3l**, 80%
6	 **3g**, 70%	12	 **3m**, 79%

[a] *Reaction conditions*: **1a** (0.5 mmol), **2** (0.26 mmol), K_2CO_3 (1 equiv.),

DMSO (1 ml), at 100 °C for 10 h under an open atmosphere. [b] Isolated yields based on **1a**.

To further extend the scope of the reaction in relation to the substrate, we tested various 2-subtituted 1,3,4-oxaidazoles **1** (Table 3). All of these substrates provided the desired product from good to excellent yields. The electronic and steric properties of the substituents in the benzene ring exerted a very limited influence on the reactivity (entries 1-9). Substrates with di- and tri-substitutions on the phenyl ring, participated effectively to give the desired product **3t-v**. These results encouraged us to examine the heteroaromatic and aliphatic groups at the C-2 position of oxadiazole and the desired products were also obtained in very good yields (Table 3, entries 10,11). Interestingly, in an attempt to use bis-1,3,4-oxaidzoel as the substrate, the selenated product **3y** was obtained in good yield (entry 12), a compound which is a potential candidate for use in material sciences.[20]

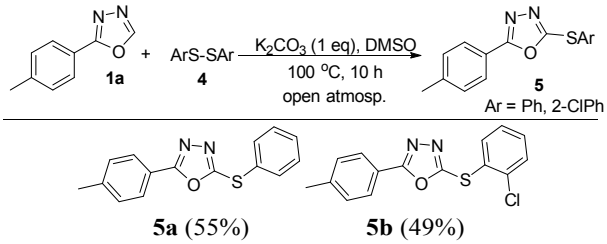
Table 3 Selenation of 2-(substituted)-1,3,4-oxadiazoles **1**[a]



Entry	Product, Yield[b] (%)	Entry	Product, Yield (%)
1	**3n**, 84%	8	**3u**, 89%
2	**3o**, 79%	9	**3v**, 92%
3	**3p**, 95%	10	**3w**, 82%
4	**3q**, 96%	11	**3x**, 84%
5	**3r**, 83%	12 [c]	**3y**, 61%
6	**3s**, 85%		
7	**3t**, 88%		

[a] *Reaction conditions*: **1a** (0.5 mmol), **2** (0.26 mmol), K_2CO_3 (1 equiv.), DMSO (1 ml), at 100 °C for 10 h under an open atmosphere. [b] Isolated yields based on **1a**. c 0.25 mmol of the oxadizole was used.

In order to further investigate the scope of this new methodology we extended our study to disulphides (Scheme 1), applying the optimal reaction conditions (Table 1, entry 5). Interestingly, the reaction of different diaryl disulphides **4a-b** with oxadiazole **1a** proceeded smoothly and afforded the corresponding C-5 thiolated oxadiazoles **5a** and **5b** in 55% and 49% isolated yield (Scheme 1). The decrease in the yield values can be explained by the stronger S–S bond of diaryl disulphides compared to the respective diselendies.



Scheme 1 Thiolation of oxadiazole

To demonstrate the synthetic utility of this new protocol, a series of reactions was carried out on different scales (Figure 1; up to 10 mmol). Oxadiazole **1a** and diselenide **2a** were selected as the test materials, affording **3a** with no major decrease in yield. Therefore, this method could be used as a practical method to synthesize biologically-relevant lead compounds

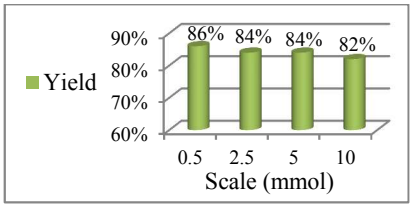
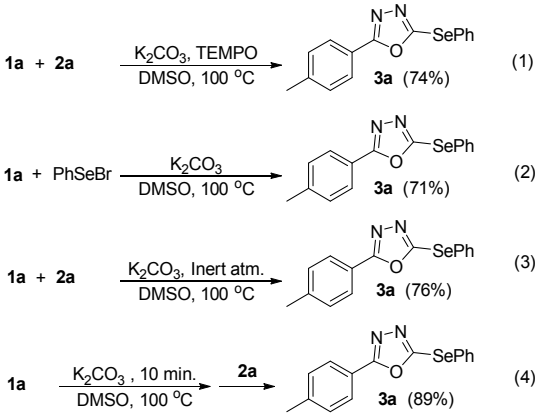


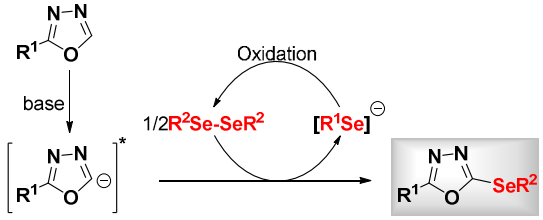
Figure 1 Results for the reaction at different scales

To elucidate the mechanism, some control experiments were conducted (Scheme 3). The radical inhibitor (TEMPO) did not hamper the reaction and **3a** was obtained in 74% yield [Eq 1], which excluded the possibility of a radical pathway. **3a** was obtained with 71% yield when phenyl selenium bromide was used instead of diphenyl diselenide **2a** [Eq 2], demonstrating that the reaction passes through a phenylselenium cation species. While under an inert atmosphere, the reaction afforded **3a** with 76% yield [Eq 3], indicating that although oxygen is not required it can facilitate the reaction. Subsequently, improvement in the yield of **3a** was observed when **2a** was added after 10 min under standard conditions [Eq 4], suggesting that deprotonation of the oxadiazole core is an important step in the reaction.



Scheme 3 Investigation of the mechanism

Based on these results, a plausible mechanism is proposed in Scheme 4 as follows. Initially, the K_2CO_3/base-promoted deprotonation of the oxadiazole core takes place at the C-5 position, generating an anion. Subsequently, the selenated product is formed through nucleophilic attack of the anion on diorganyldiselenide, while the organo-selenolated species (anionic) is oxidized back to diselenide.



Scheme 4 Proposed mechanism for the reaction

In conclusion, we developed an efficient, economical and greener K_2CO_3-promoted procedure for the synthesis of selenated and thiolated oxadiazoles through C_{sp2}-H bond functionalization, in the absence of metal catalyst. We prepared for the first time selenated oxadiazoles, compounds with potential for biological applications. Under mild conditions the reaction worked well in the presence of K_2CO_3, with a half equiv. of diorganyl dichalcogenides, without the exclusion of air and moisture, affording a wide range of chalcogenated oxadiazoles at the C5 position in good to excellent yields. The various substituents with different electronic effects and steric effects tolerated the optimized reaction conditions.

The chemistry described herein represents a feasible eco-friendly synthetic approach for the preparation of chalcogenated oxadiazoles through the C-S/Se bond. This novel method provides a complementary, environmentally benign, and easy-operation approach to accessing 5-chalcogenayloxadiazole derivatives.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Details on the experimental procedure and characterization, as well as the spectral data for all synthesized compound. See DOI: 10.1039/c000000x/

1 (a) Y. Xu, X. Tang, W. Hu, W. Wu and H. Jiang, *Green Chem.,* 2014, **16**, 3720;. (b) Y. Siddaraju, M. Lamani and K. R. Prabhu, *J. Org. Chem.,* 2014, **79**, 3856; (c) K. Matcha and A. P. Antonchick, *Angew. Chem., Int. Ed.,* 2013, **52**, 2082; (d) S. Wertz, D. Leifert and A. Studer, *Org. Lett.,* 2013, **15**, 928.

2 (a) J. Cuthbertson, V. J. Gray and J. D. Wilden, *Chem. Commun.,* 2014, **50**, 2575; (b) C.-L. Sun, H. Li, D.-G. Yu, M. Yu, X. Zhou, X.-Y. Lu, K. Huang, S.-F. Zheng, B. J. Li and Z.-J. Shi, *Nat. Chem.*, 2010, **2**, 1044; (c) M. Rueping, M. Leiendecker, A. Das, T. Poisson and L. Bui, *Chem. Commun.,* 2011, **47**, 10629.

3 (a) X.-Q. Chu, H. Meng, Y. Zi, X.-P. Xu and S.-S. Ji, *Chem. Commun.,* 2014, **50**, 9721; (b) X. Zhang, M. Wang, P. Lia and L. Wang, *Chem. Commun.*, 2014, **50**, 8006; (c) H. J. Kim, J. Kim, S. H. Cho and S. Chang, *J. Am. Chem. Soc.*, 2011, **133**, 16382.

4 (a) S. Thurow, F. Penteado, G. Perin, R. G. Jacob, D. Alves and E. J. Lenardão, *Green Chem.*, 2014, **16**, 3854; (b) D. S. Rampon, L. A. Wessjohann and P. H. Schneider, *J. Org. Chem.*, 2014, **79**, 5987; (c) C. Santi, B. Battistelli, L. Testaferria and M. Tiecco, *Green Chem.,* 2012, **14**, 1277; (d) V. G. Ricordi, C. S. Freitas, G. Perin, E. J. Lenardão, R. G. Jacob, L. Savegnago and D. Alves, *Green Chem.*, 2012, **14**, 1030; (e) C. S. Freitas, A. M. Barcellos, V. G. Ricordi, J. M. Pena, G. Perin, R. G. Jacob, E. J. Lenardão and D. Alves, *Green Chem.*, 2011,**13**, 2931

5 (a) B. Godoi, R. F. Schumacher and G. Zeni, *Chem. Rev.*, 2011, **111**, 2937; (b) G. Zeni, D. S. Lüdtke, R. B. Panatieri and A. L. Braga, *Chem. Rev.,* 2006, **106**, 1032; (c) G. Perin, E. J. Lenardão, R. G. Jacob and R. B. Panatieri, *Chem. Rev.*, 2009, **109**, 1277; (d) K. P. Bhabak and G. Mugesh, *Acc. Chem. Res.*, 2010, **43**, 1408; (e) C. W. Nogueira, G. Zeni and J. B. T. Rocha, *Chem. Rev.*, 2004, **104**, 6255.

6 (a) *The Chemistry of Organic Selenium and Tellurium Compounds*, ed. Z. Rappoport. Wiley & Sons, Ltd, Chichester, 2014, vol. **4**; (b) *Handbook of Chalcogen Chemistry: New Perspectives in Sulfur, Selenium and Tellurium*, ed. F. A. Devillanova and W.-W. du Mont, RSC, Cambridge, 2nd ed, 2013; (c) *Organoselenium Chemistry: Synthesis and Reactions,* ed. T. Wirth, Wiley-VCH, Weinheim, 2011;

7 (a) M. Godoi, M. W. Paixão and A. L. Braga, *Dalton Trans.*, 2011, **40**, 11347; (b) A. L. Braga, D. S. Lüdtke, J. A. Sehnem and E. E. Alberto, *Tetrahedron*, 2005, **61**, 11664; (c) Y. Nishiyama, A. Katsuura, A. Negoro and S. J. Hamanaka, *J. Org. Chem.,* 1991, **56**, 3776.

8 (a) E. E. Alberto, A. L. Braga and M. R. Detty, *Tetrahedron*, 2012, **68**, 10476; (b) F. V. Singh and T. Wirth, *Org. Lett.*, 2011, **13**, 6504.

9 (a) S. Thurow, N. T. Ostosi, S. R. Mendes, R. G. Jacob and E. J. Lenardão, *Tetrahedron Lett.*, 2012, **53**, 2651; (b) H. S. Kim, Y. J. Kim, H. Lee, K. Y. Park, C. Lee and C. S. Chin, *Angew. Chem., Int. Ed.*, 2002, **41**, 4300

10 (a) J.-D. Yu, W. Ding, G.-Y. Lian, K.-S. Song, D.-W. Zhang, X. Gao and D. J. Yang, *J. Org. Chem.*, 2010, **75**, 3232; (b) K. C. Nicolaour, D. J. Edmonds and P. G. Bulger, *Angew. Chem. Int. Ed.*, 2006, **45**, 7134; (c) C. C. Silveira, A. Machado, A. L. Braga and E. J. Lenardão, *Tetrahedron Lett.,* 2004, **45**, 4077.

11 A. L. Braga and J. Rafique, in *The Chemistry of Organic Selenium and Tellurium Compounds*, ed. Z. Rappoport. Wiley & Sons, Ltd, Chichester, 2014, vol. **4**, ch. 13-15, 989-1174.

12 (a) T. E. Frizon, D. S. Rampon, H. Gallardo, A. A. Merlo, P. H. Schneider, O . E. D. Rodrigues and A. L. Braga, *Liq. Crys.*, 2012, **39**, 769; (b) S. Haid, A. Mishra, M. Weil, C. Uhrich, M. Pfeiffer and P. Bäuerle, *Adv. Funct. Mater.*, 2012, **22**, 4322.

13 E. Maccioni, S. Alcaro, R. Cirilli, S. Vigo, M. C. Cardia, M. L. Sanna, R. Meleddu, M. Yanez, G. Costa, L. Casu, P. Matyus and S. Distinto, *J. Med. Chem.*, 2011, **54**, 6394.

14 J. Boström, A. Hogner, A. Llinàs, E. Wellner and A. T. Plowright, *J. Med. Chem.*, 2012, **55**, 1817; (b) C. S. Oliveira, B. F. Lira, V. S. F. Silva, J. P. Siqueira-Junior, J. M. Barbosa-Filho and P. F. Athayde-Filho, *Molecules*, 2012, **17**, 5095; (c) M. A. Khanfar, R. A. Hill, A. Kaddoumi and K. A. El Syed, *J. Med. Chem.*, 2010, **53**, 8535.

15 (a) J. Lü, Z. Ma, B. Meng, D. Sui, B. Zhang, Z. Xie, X. Jing, F. Wang, J. Ding and L. Wang, *Opt. Express*, 2011, **19**, A1241; (b) S. Varghese, N. S. S. Kumar, A. Krishna, D. S. S. Rao, S. K. Prasad and Suresh Das, *Adv. Funct. Mater.*, 2009, **19**, 2064; (c) S.-H. Hsiao and G.-S. Liou, *Polym. J.*, 2002, **34**, 917.

16 (a) L. Chu and F.-L. Qing, *J. Am. Chem. Soc.*, 2012, **134**, 1298; (b) B. Das , G. C. Reddy, P. Balasubramanyam and N. Salvanna, *Tetrahedron,* 2012, **68**, 300; (c) T. Kawano, N. Matsuyama, K. Hirano, T. Satoh and Masahiro Miura, *J. Org. Chem.*, 2010, **75**, 1764; (d) C. Li, P. Li, J. Yang and L. Wang, *Chem. Commun.*, 2012, **48**, 4214; (e) T. Mukai, K. Hirano, T. Satoh and Masahiro Miura, *Org. Lett.*,2010, **12**, 1360; (f) S. Wertz, S. Kodama and A. Studer, *Angew. Chem. Int. Ed.*, 2011, **50**, 11511; (g) S. H. Wunderlich and P. Knochel, *Angew. Chem. Int. Edi.*, 2007, **46**, 7685; (h) L.-H. Zou, J. Reball, J. Mottweiler and C. Bolm, *Chem. Commun.*, 2012, **48**, 11307.

17 (a) P. Sang, Z. Chen, J. Zou and Y. Zhang, *Green Chem.*, 2013, **15**, 2096; (b) A. R. Rosario, K. K. Casola, C. E. S. Oliveira and Gilson Zeni, *Adv. Synth. Catal.*, 2013, **355**, 2960.

18 (a) M. Godoi, E. W. Ricardo, G. V. Botteselle, F. Z. Galetto, J. B. Azerado and A. L. Braga, *Green Chem.*, 2012, **4**, 456; (b) M. Godoi, G. V. Botteselle, J. Rafique, M. S. T. Rocha, J. M. Pena and A. L. Braga, *Asian J. Org. Chem.*, 2013, **2**, 746.; (c) D. Singh, S. Narayanaperumal, K. Gul, M. Godoi, O. E. D. Rodriques and A. L. Braga, *Green Chem.*, 2010, **12**, 957.

19 N. E. Leadbeater, *Nat. Chem.*, 2010, **2**, 1007.

20 R. Cristiano, D. M. P O. Santos and H. Gallardo, *Liq. Crys.*, 2004, **32**, 7.