ORGANIC LETTERS

2010
Vol. 12, No. 15
3288−3291

An Efficient One-Pot Synthesis of Symmetrical Diselenides or Ditellurides from Halides with CuO Nanopowder/Se^0 or Te^0/Base

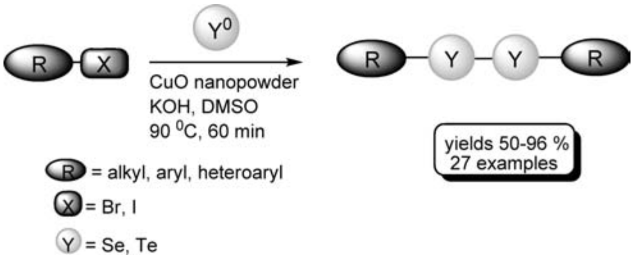
Devender Singh,[†] Anna M. Deobald,[†] Leandro R. S. Camargo,[†] Greice Tabarelli,[‡] Oscar E. D. Rodrigues,*[,†] and Antonio L. Braga*[,†,‡]

Departamento de Química, Universidade Federal de Santa Maria, 97105-900 Santa Maria, RS, Brazil, and Departamento de Química, Universidade Federal de Santa Catarina, 88040-970 Florianópolis, SC, Brazil

albraga@qmc.ufsc.br; rodriguesoed@smail.ufsm.br

Received March 16, 2010

ABSTRACT



A CuO nanopowder-catalyzed coupling reaction of aryl, alkyl, and heteroaryl iodides with elemental selenium and tellurium takes place in the presence of KOH at 90 °C in DMSO. A wide range of substituted symmetrical diselenides and ditellurides were afforded with good to excellent yields.

During the last few decades, organochalcogen (Se or Te) compounds[1] have emerged as important reagents and intermediates in organic synthesis.[2] Organodichalcogenides, the selenium or tellurium counterpart of organic peroxides, play an important role in organochalcogen chemistry since they are stable, easily handled, and reactive enough to produce electrophilic, nucleophilic, and radicophilic species.[3] Related derivatives in which one selenium or tellurium atom is replaced by oxygen or sulfur are also known and play crucial biological roles as antioxidants, antitumor agents, and apoptosis inducers, as well as in the degradation of hydroperoxides and in the chemoprevention of cancer in a variety of organs.[4] There are a

---

[†] Universidade Federal de Santa Maria.

[‡] Universidade Federal de Santa Catarina.

(1) For a comprehensive treatment of organoselenium chemistry, see: (a) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986. (b) Liotta, D. In *Organoselenium Chemistry*; John Wiley: New York, 1986. (c) Back, T. G. *Organoselenium Chemistry - A Practical Approach*; Oxford University Press: Oxford, 1999. (d) Devillanova, F. A. *Handbook of Chalcogen Chemistry - New Perspectives in Sulfur, Selenium and Tellurium*; The Royal Society of Chemistry: Cambridge, 2007.

(2) (a) Wirth, T. *Tetrahedron* **1999**, *55*, 1–28. (b) Wirth, T. *Organoselenium Chemistry - Modern Developments in Organic Synthesis*; Springer-Verlag: Heidelberg, 2000. (c) Wirth, T. *Angew. Chem.* **2000**, *112*, 3890–3900. (d) Freudendahl, D. M.; Santoro, S.; Shahzad, S. A.; Santi, C.; Wirth, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 8409.

(3) (a) Rheinboldt, H. Sulfur-, Selenium-, Tellurium-Compounds *Methoden Org. Chem. (Houben-Weyl)* **1967**, *9*. (b) Klayman, D. L.; Günther, W. H. H. *Organic Selenium Compounds: Their Chemistry and Biology*; Wiley & Sons: New York, 1973. (c) Paulmier, C.; Baldwin, J. E. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986; Vol. 5. (d) Patai, S.; Rappoport, Z. In *The Chemistry of Organic Selenium and Tellurium Compounds*; John Wiley & Sons: New York, 1987; Vol. 2. (e) Krief, A. Abel, E. W.; Stone, F. G. A.; Wilkinson, G.; McKillop, A. In *Comprehensive Organometallic Chemistry II*; Pergamon Press: Oxford, 1995, Vol. 11. (f) Wirth, T.; Crabtree, R. H.; Mingos, D. M. P. *Comprehensive Organometallic Chemistry III*; Elsevier: Oxford, 2006; Vol. 9.

(4) (a) Stadtman, T. C. *Annu. Rev. Biochem.* **1980**, *49*, 93–110. (b) Geiger, P. G.; Lin, F.; Girotti, A. W. *Free Radical Biol. Med.* **1993**, *14*, 251–266. (c) Krief, A.; Janssen, *Chim. Acta* **1993**, *11*, 10–11. (d) Nogueira, C. W.; Zeni, G.; Rocha, J. B. T *Chem. Rev.* **2004**, *104*, 6255.

10.1021/ol100558b

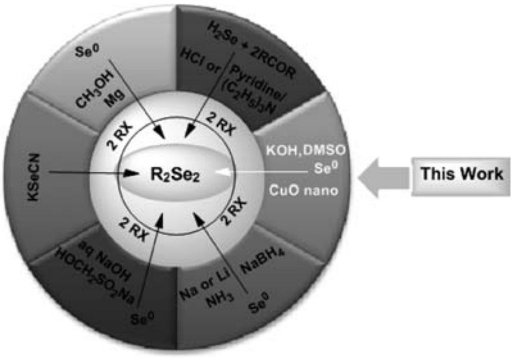
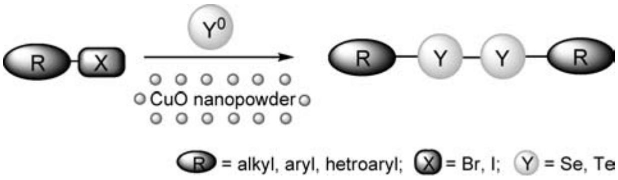


Figure 1. Various ways to prepare diselenides.

variety of methods reported to prepare organic diselenides or ditellurides (Figure 1). Most of them involve the reaction of metal diselenides or ditellurides with alkyl halides, dimerization with selenocyanates,[5−7] oxidation of selenols[8] or selenolates,[9] and reactions of aldehydes with sodium hydrogen selenide in the presence of an amine and sodium borohydride.[10,11] Sonoda et al. discovered that elemental selenium can be readily reduced by carbon monoxide and water in the presence of base to produce hydrogen selenide, which was successfully applied to the synthesis of aliphatic diselenides from both aliphatic ketones and aldehydes[12] or from alkyl chlorides and acyl chlorides,[13] respectively.

Despite the variety of methodologies, there are some drawbacks to these known methods of diselenide synthesis, such as the use of strong reducing agents, highly toxic gas, harsh reaction conditions, low yields, or complex manipulations. From a sustainable chemistry point of view, there is a need for new methods that are truly efficient, high yielding, responsive to mild reaction conditions, byproduct-free, and efficient in the presence of multifunctional groups. Organic reactions catalyzed by metallic nanostructures are currently an area of intensive research, with many reports in the literature.[14] Generally, catalysts in nanoscale afford a more effective process and allow a genuine advance in relation to traditional methodologies. The high surface area and reactive morphologies of nanomaterials allow them to be effective catalysts for organic synthesis.[15]

Scheme 1. General Scheme of Synthesis of Diselenides



In this new intensive area, CuO has emerged as a useful catalyst in several transformations.[16] As previously reported, CuO nanopowder shows an effective influence in the chalcogenide functionalizations, allowing the synthesis of organic selenides in high yields.[17] As part of our ongoing research into organochalcogen chemistry,[18] herein we disclose a new and efficient methodology to prepare symmetrical aryl and alkyl diselenides and ditellurides using CuO nanopowders as a catalyst, with good to excellent yields, as depicted in Scheme 1.

To the best of our knowledge, this is the first report of the use of a CuO nanoparticle-catalyzed reaction to prepare symmetrical organodichalcoganides.

In order to optimize the protocol and to understand the influence of different variables in this reaction, several components were studied. To this end, we carried out the reaction under standard conditions employing 4-iodotoluene

---

(5) (a) Gladysz, J.; Hornby, J.; Garbe, J. E. *J. Org. Chem.* **1978**, *43*, 1204–1207. (b) Syper, L.; Mlochowshi, J. *Tetrahedron* **1988**, 446119–6130. (c) Li, J. Q.; Bao, W. L.; Lue, P.; Zhou, X. J *Synth. Commun.* **1991**, *21*, 799–806. (d) Wang, J. X.; Cui, W.; Hu, Y. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2341–2343. (e) Krief, A.; Derock, M. *Tetrahedron Lett.* **2003**, *43*, 3083–3086.

(6) Krief, A.; Dumont, W.; Delmotte, C. *Angew. Chem., Int. Ed.* **2000**, *39*, 1669–1672.

(7) (a) Salama, P.; Bernard, C. *Tetrahedron Lett.* **1995**, *36*, 5711–5714. (b) Salama, P.; Bernard, C. *Tetrahedron Lett.* **1998**, *39*, 745–748.

(8) Prabhu, K.; Chandrasekaran, S. *Chem. Commun.* **1997**, 1021–1022.

(9) Krief, A.; De Mahieu, A. F.; Dumont, W.; Trabelsi, M. *Synthesis* **1988**, 131–133.

(10) (a) Krief, A.; Van Wemmel, T.; Redon, M.; Dumont, W.; Delmotte, C. *Angew. Chem., Int. Ed.* **1999**, *38*, 2245–2247. (b) Klayman, l. D; Griffin, T. S *J. Am. Chem. Soc.* **1973**, *95*, 197.

(11) (a) Lewicki, J. W.; Günther, W. H. H.; Chu, J. Y. C. *J. Chem. Soc., Chem. Commun.* **1976**, 552. (b) Lewicki, J. W.; Günther, W. H. H.; Chu, J. Y. C. *J. Org. Chem.* **1978**, *43*, 2672–2676.

(12) Huang, Z, Z.; Liu, F. Y.; Du, J. X.; Huang, X. *Org. Prep. Proced. Int.* **1995**, *27*, 492–494.

(13) Nishiyama, Y.; Hamanaka, S.; Ogawa, A.; Murai, S.; Sonoda, N. *Synth. Commun.* **1986**, *16*, 1059–1067.

(14) Nishiyama, Y.; Katsuura, A.; Negoro, A.; Hamanaka, S.; Miyoshi, N.; Yamana, Y.; Ogawa, A.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 3776–3780.

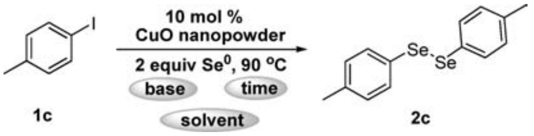
(15) (a) Reddy, V. P.; Kokkirala Swapna, A. V. K.; Rao, K. R *Org. Lett.* **2009**, *11*, 951. (b) Polshettiwar, V.; Baruwati, B; Varma, R. S *Chem. Commun.* **2009**, 1837. (c) Shibasaki, M.; Kanai, M. *Chem. Rev.* **2008**, *108*, 2853. (d) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952. (e) Jammi, S.; Sakthivel, S.; Rout, L.; Mukherjee, T.; Mandal, S.; Mitra, R.; Saha, P.; Punniyamurthy, T. *J. Org. Chem.* **2009**, *74*, 1971.

(16) (a) Su, F.-Z.; Liu, Y.-M.; Wang, L.-C.; Cao, Y.; He, H.-Y.; Fan, K.-N. *Angew. Chem., Int. Ed.* **2008**, *47*, 334. (b) Uozumi, Y.; Nakao, R. *Angew. Chem., Int. Ed.* **2003**, *42*, 194. (c) Hou, Z.; Theyssen, N.; Brinkmann, A.; Leitner, W. *Angew. Chem., Int. Ed.* **2005**, *44*, 1346. (d) Karimi, B.; Abedi, S.; Clark, J. H.; Budarin, V. *Angew. Chem., Int. Ed.* **2006**, *45*, 4776. (e) Mori, K.; Hara, T.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2004**, *126*, 10657. (f) Cassol, C. C.; Umpierre, A. P.; Machado, G.; Wolke, S. I; Dupont, J *J. Am. Chem. Soc.* **2005**, *127*, 3298. (g) Li, Y.; Hong, X. M.; Collard, D. M.; El-Sayed, M. A. *Org. Lett.* **2000**, *2*, 2385. (h) Son, S. U.; Jang, Y.; Park, J.; Na, H. B.; Park, H. M.; Yun, H. J.; Lee, J.; Hyeon, T. *J. Am. Chem. Soc.* **2004**, *126*, 5026. (i) Chung, M.-K.; Schlaf, M. *J. Am. Chem. Soc.* **2004**, *126*, 7386. (j) Cho, J. K.; Najman, R.; Dean, T. W.; Ichihara, O.; Muller, C.; Bradley, M. *J. Am. Chem. Soc.* **2006**, *128*, 6276. (k) Tamura, M.; Fujihara, H. *J. Am. Chem. Soc.* **2003**, *125*, 15742.

(17) (a) Singh, D.; Alberto, E. E.; Rodrigues, O. E. D.; Braga, A. L. *Green Chem.* **2009**, *11*, 1521. (b) Reddy, V. P.; Kokkirala Swapna, A. V. K.; Rao, K. R. *Org. Lett.* **2009**, *11*, 951. (c) Rout, L.; Jammi, S.; Punniyamurthy, T. *Org. Lett.* **2007**, *17*, 3397.

(18) For selected examples, see: (a) Braga, A. L.; Silva, S. J. N.; Lüdtke, D. S.; Drekener, R. L.; Silveira, C. C.; Rocha, J. B. T.; Wessjohann, L. A. *Tetrahedron Lett.* **2002**, *43*, 7329. (b) Braga, A. L.; Lüdtke, D. S.; Paixão, M. W.; Rodrigues, O. E. D. *Org. Lett.* **2003**, *5*, 2635. (c) Braga, A. L.; Lüdtke, D. S.; Alberto, E. E.; Sehnem, J. A. *Tetrahedron* **2005**, *61*, 11664. (d) Braga, A. L.; Sehnem, J. A.; Vargas, F.; Braga, R. C. *J. Org. Chem.* **2005**, *70*, 9021. (e) Braga, A. L.; Lüdtke, D. S.; Alberto, E. E. *J. Braz. Chem. Soc.* **2006**, *17*, 11. (f) Braga, A. L.; Schwab, R. S.; Alberto, E. E.; Salman, S. M.; Vargas, J.; Azeredo, J. B. *Tetrahedron Lett.* **2009**, *50*, 2309. (g) Narayanaperumal, S.; Alberto, E. E.; Andrade, F.M.d.; Lenardão, E. J.; Taube, P. S.; Braga, A, L. *Org. Biomol. Chem.* **2009**, *7*, 4647.

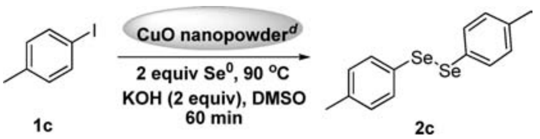
Table 1. Nano CuO Oxide-Catalyzed Cross-Coupling of Diphenyl Diselenide with 4-Methyl-1-iodobenzene



entry	solvent	base (2 equiv)	time (min)	yield[a] (%)
1	DMSO	KOH	60	96
2	DMF	KOH	60	90
3	CH_3CN	KOH	60	91
4	THF	KOH	60	
5	toluene	KOH	60	
6	dioxane	KOH	60	
7	CH_2Cl_2	KOH	60	
8	DMSO	Cs_2CO_3	60	85
9	DMSO	NaOH	60	86
10	DMSO	$NaHCO_3$	60	
11	DMSO	K_2CO_3	60	36
12	DMSO	KOH	30	64
13	DMSO	KOH	120	81
14	DMSO	KOH	240	45
15	DMSO	KOH	60	traces[b]
16[c]	DMSO		60	

[a] Yields determined by GC. [b] Reaction performed at room temperature. [c] No coupling reaction occurred without base.

Table 2. Optimization of Nano CuO Catalyst[a]



entry	nano CuO (mol %)	yield[b] (%)
1	2.0	70
2	5.0	89
3	10.0	96
4	20.0	96
5	0.0[c]	

[a] Reaction conditions: 4-iodotoluene (1.0 mmol), CuO nanoparticles, Se^0 (2.0 equiv), KOH (2.0 equiv), and DMSO (2.0 mL) were stirred under a nitrogen atmosphere at 90 °C for 60 min. [b] Yields determined by GC. [c] No coupling reaction occurred without nano CuO. [d] CuO nanopowder was purchased from Sigma-Aldrich, with an average of 30−40 nm as shown in technical support.

as a representative halide, 10 mol % of CuO nanopowder, elemental selenium (2.0 equiv), and KOH (2.0 equiv) in DMSO (2.0 mL) for 1 h, affording the corresponding diaryl selenide **2c** in 96% yield (Table 1, entry 1). In a first set of experiments, we studied the influence of different solvents (Table 1, entries 1−7). By analyzing Table 1, it can be observed that the desired product was not obtained in the solvents THF, 1,4-dioxane, and toluene (entries 4−6). However, the reaction was highly effective with polar aprotic solvents (entries 1−3). These results suggest that the success of the reaction depends on the polarity of the solvent. In this regard, DMSO was the most efficient solvent for this reaction affording the best yield for diselenide **2c** (entry 2).

The influence of different bases was the next variable studied. In this context, a number of bases, in DMSO, were used to afford M_2E_n reactive species. In this context, Cs_2CO_3, NaOH, and $NaHCO_3$ were compared to KOH (Table 1, entries 8, 9, and 10, respectively). Notably, KOH allowed the best performance among the screened bases, furnishing the desired product in excellent yield (Table 1, entry 1). As a result, KOH was selected as the optimum base to perform the subsequent reactions. Another important factor studied was the reaction time. This variable has an effective influence on the reaction course, with yields decreasing from 96 to 64% when the reaction time was reduced from 60 to 30 min (entries 1 and 12). Longer reaction times also have an influence on the product yields. When the reaction time was increased to 120 and 240 min, the product yields decreased to 81% and 45%, respectively (entries 13 and 14).

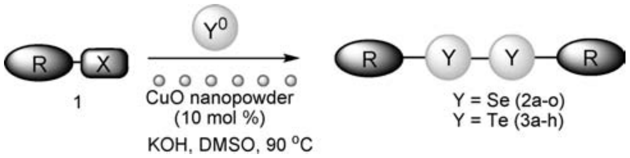
Finally, in order to optimize the protocol, the impact of the catalyst amount on the reaction efficiency was investigated. We found that this parameter had an effective influence on the reaction course. For instance, when the amount of CuO nanopowder was increased from 2.0 to 10 mol %, the yield of compound **2c** raised considerably (from 70% to 96%; Table 2, entries 1−3). Raising the amount of CuO nanopowder up to 20 mol % did not show a significant influence, affording the desired product at the same level of 96% (Table 2, entry 4). The product was not observed in the absence of catalyst; hence this component is required in order to perform the reaction (entry 5).

After the optimized reaction conditions were established, a number of halides were examined to explore the scope and limitations of this methodology. Under standard conditions, a series of reactions using different kinds of aryl, alkyl, and hetroaryl halides was performed to synthesize the symmetrical diselenides **2a−o** and ditellurides **3a−h** (Table 3).

As summarized in Table 3, both electron-rich and electron-deficient aryl iodides were effective in this process, giving the corresponding products in good to excellent yields. It is noteworthy that sterically hindered ortho and meta substrates also provided high yields of diselenides (Table 3, entries 3, 5, 6, and 9−12) and ditellurides (Table 3, entries 18, 20, and 22), respectively. One advancement associated with this methodology is that a wide range of functional groups are tolerated in this process, including methyl, methoxy, hydroxyl, aldehyde, amino, bromo, and heteroaryl moieties. Some of them are very sensitive, e.g., aldehyde, and the direct preparation of the related diselenides employing the described methodologies is not efficient for these kinds of substrates. Thus, we conclude that this method provides a general approach to preparing more complex diselenides and ditellurides.

Upon analysis of Table 3, it can be verified that, as expected, iodide was more reactive than bromides and chlorides. This result allowed the exploration of the regioselectivity of this reaction, with the preparation of selective bromo-and chlorodichalcogenides (Table 3, entries 4, 5, 7, and 19). Additionally, the electron-withdrawing groups attached to the aromatic ring afforded better yields than

Table 3. Synthesis of Diselenides via a One-Pot Coupling−Reduction Procedure[a]



entry	R	X	Y	product	yield[c] (%)
1	Ph	I (**1a**)	Se	**2a**	96
		Br (**1b**)	Se		52
2	4-MeC_6H_5	I (**1c**)	Se	**2b**	96
		Br (**1d**)	Se		71
3	2-MeC_6H_5	I (**1e**)	Se	**2c**	90
4	4-ClC_6H_5	I (**1f**)	Se	**2d**	89[b]
5	2-ClC_6H_5	I (**1g**)	Se	**2e**	90[b]
6	2-HOC_6H_5	I (**1h**)	Se	**2f**	72
7	4-BrC_6H_5	I (**1i**)	Se	**2g**	89[b]
8	4-$MeOC_6H_5$	I (**1j**)	Se	**2h**	80
		Br (**1k**)	Se		69
9	3-$MeOC_6H_5$	I (**1l**)	Se	**2i**	89
10	2-$MeOC_6H_5$	I (**1m**)	Se	**2j**	89
11	2,4-$MeOC_6H_4$	I (**1n**)	Se	**2k**	50
12	2-$NH_2C_6H_5$	I (**1o**)	Se	**2l**	87
13	3-Py	I (**1p**)	Se	**2m**	82
14	4-$OHCC_6H_5$	Br (**1q**)	Se	**2n**	72
15	C_7H_{15}	I (**1r**)	Se	**2o**	96
16	Ph	I (**1a**)	Te	**3a**	86
17	Ph	Br (**1b**)	Te		56
18	2-MeC_6H_5	I (**1e**)	Te	**3b**	88
19	4-ClC_6H_5	I (**1f**)	Te	**3c**	90[b]
20	2-HOC_6H_5	I (**1h**)	Te	**3d**	86
21	4-$MeOC_6H_5$	I (**1j**)	Te	**3e**	80
22	2-$NH_2C_6H_5$	I (**1o**)	Te	**3f**	82
23	3-Py	I (**1p**)	Te	**3g**	72
24	C_7H_{15}	I (**1r**)	Te	**3h**	84

[a] Reaction conditions: halide (1.0 mmol), CuO nanoparticles (10.0 mol %), Y^0 (2.0 equiv), KOH (2.0 equiv), and DMSO (2.0 mL) were stirred under a nitrogen atmosphere at 90 °C for 60 min. [b] Reaction complete in 30 min. [c] Yield of the isolated product.

donating groups (Table 3, entries 4 and 8). This can be explained by the easier insertion of copper into the more electron-deficient aromatic ring. In order to explore the versatility of the current methodology, more complex aromatic halides were employed. As depicted in Table 3, amino (entries 12, 13, 22, and 23), hydroxy (entries 6 and 20), and aldehyde (entry 14) groups were used, and in all cases the corresponding diselenide and ditelluride were obtained in good yields. Alkyl diselenide (entry 15) and ditelluride (entry 24) were obtained from the respective alkyl iodide, yielding 96 and 84%, respectively. Furthermore, diselenides were obtained in high yield, without the use of protection groups or an excess of reagents.

On the basis of previous reports,[19] a plausible mechanism for the CuO nanopowder-catalyzed cross-coupling of halides with selenium and tellurium nucleophiles to obtain diselenides and ditellurides can be proposed, as depicted in Figure 2.

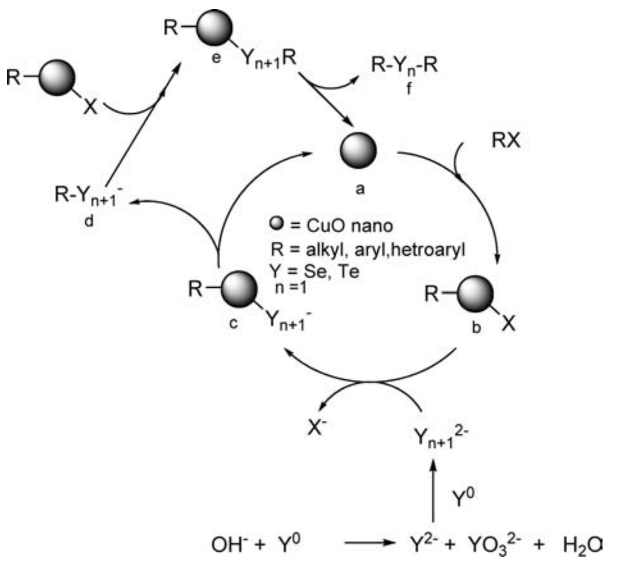


Figure 2. Plausible mechanism for organo dichalcogenide synthesis.

Selenium and tellurium may have behavior similar to that established for sulfur[19] in the presence of base, giving the chalcogenolate or dichalcogenolate anion. Using a superbasic DMSO−KOH system, a reductive dimsyl species is formed[20] which may selectively allow the preparation of the desired dichalcogenolate anion. We assume that this ion might serve as the active species in the catalytic cycle. The formation of the complexes **a** and **b** followed by the ligand exchange with the dichalogenolate anion might provide complex **c**, which could undergo reductive elimination to give the initial coupling product **d** and regenerate the CuO nanoparticles. The complex **d** would react with another complex **b** furnishing the complex **e**. Finally, a reductive elimination could afford the desired dichalcogenide **f** and release CuO nanoparticles for use in the catalytic cycle.

In conclusion, a simple, efficient, and straightforward procedure is described for the preparation of diselenides or ditellurides through cross-coupling of selenium and tellurium and aryl iodides using CuO nanopowder. This methodology is highly chemoselective, uses neutral conditions, and allows the preparation of a wide range of substituted symmetrical diselenides and ditellurides containing methoxy, hydroxyl, carboxylate, amino, aldehyde, and bromo groups in good to excellent yields.

Acknowledgment. We gratefully acknowledge CNPq (INCT-Catalise, INCT-NANOBIOSIMES) for financial support. D.S. thanks TWAS-CNPq for a Ph.D. fellowship.

Supporting Information Available: Detailed experimental procedures and copies of analytical data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL100558B

---

(19) (a) Jiang, Y.; Qin, Y.; Xie, S.; Zhang, X.; Dong, J.; Ma, D. *Org. Lett.* **2009**, *11*, 951.

(20) (a) Reddy, V. P.; Kumar, A. V.; Swapna, K.; Rao, K. R *Org. Lett.* **2009**, *11*, 951. (b) Trofimov, B. A.; Amosova, S. V.; Gusarova, N. K.; Musorin, G. K. *Tetrahedron* **1982**, *38*, 713.