

Synthesis of Aryl Disulfides by Bismuth(III) Triflate-mediated Coupling of Thiols

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Abstract: Disulfides are used in many organic procedures and play a very important role as vulcanizing agents and linkages for controlled drug delivery. As far as we know, no triflate-catalysed coupling of thiols has yet been reported. Metal triflates are classified as very selective catalysts. In view of previous reports on the successful use of Lewis acids in many organic procedures, the aim of this work was to check the activity of those catalysts in the coupling of thiols. A new method has been discovered to obtain symmetric disulfides with yields of up to 97% under mild conditions within a short time. Bismuth(III) triflate demonstrates the highest catalytic activity among all of the tested triflates. This versatile and highly efficient method opens up the way to synthesize aryl disulfides, that play a very important role as further reagents in many organic procedures. Mild conditions, low catalyst loading and the simplicity of the experimental technique are favourable features of this reaction.

REFERENCES

- [1] Nagy, P. Kinetics and mechanisms of thiol-disulfide exchange covering direct substitution and thiol oxidation-mediated pathways. *Antioxid. Redox Signal*, **2013**, *18*(13), 1623-1641.
- [2] Trivedi, M.V.; Laurence, J.S.; Sahaan, T.J. The role of thiols and disulfides in protein chemical and physical stability. *Curr. Protein Pept. Sci.*, **2009**, *10*(6), 614-625.
- [3] Zhou, N.E.; Kay, C.M.; Hodges, R.S. Disulfide bond contribution to protein stability: Positional effects of substitution in the hydrophobic core of the two-stranded alpha-helical coiled-coil. *Biochemistry*, **1993**, *32*(12), 3178-3187.
- [4] Wu, C.; Leroux, J.; Gauthier, M.A. Twin disulfides for orthogonal disulfide pairing and the directed folding of multicyclic peptides. *Nat. Chem.*, **2012**, *4*, 1044-1049.
- [5] Jacob, C.; Giles, G.I.; Giles, N.M.; Sies, H. Sulfur and selenium: The role of oxidation state in protein structure and function. *Angew. Chem. Int. Ed.*, **2003**, *42*, 4742-4758.
- [6] Black, S.P.; Sanders, J.K.M.; Stefankiewicz, A.R. Disulfide exchange: Exposing supramolecular reactivity through dynamic covalent chemistry. *Chem. Soc. Rev.*, **2014**, *43*, 1861-1872.
- [7] Mandal, B.; Basu, B. Recent advances in S-S bond formation. *RSC Adv.*, **2014**, *4*, 13854-13881.
- [8] Fernández-Salas, J.A.; Manzini, S.; Nolan, S.P. Efficient ruthenium-catalysed S-S, S-Si and S-B bond forming reactions. *Chem. Commun.*, **2013**, *49*, 5829-5831.
- [9] Abdel-Mohsen, H.T.; Sudheendran, K.; Conrad, J.; Beifuss, U. Synthesis of disulfides by laccase-catalyzed oxidative coupling of heterocyclic thiols. *Green Chem.*, **2013**, *15*, 1490-1495.
- [10] Xiao, X.; Feng, M.; Jiang, X. Transition-metal-free persulfuration to construct unsymmetrical disulfides and mechanistic study of the sulfur redox process. *Chem. Commun.*, **2015**, *51*, 4208-4211.
- [11] Chauhan, S.M.S.; Kumar, A.; Srinivas, K.A. Oxidation of thiols with molecular oxygen catalyzed by cobalt(II) phthalocyanines in ionic liquid. *Chem. Commun.*, **2003**, (18), 2348-2349.
- [12] Chauhan, D.; Kumar, P.; Joshi, C.; Labhsetwar, N.; Ganguly, S.K.; Jain, S.L. Photo-assisted oxidation of thiols to disulfides using cobalt "Nanorust" under visible light. *New J. Chem.*, **2015**, *39*, 6193-6200.
- [13] Bagi, N.; Kaizer, J.; Speier, G. Oxidation of thiols to disulfides by dioxygen catalyzed by a bioinspired organocatalyst. *RSC Adv.*, **2015**, *5*, 45983-45986.
- [14] Dhakshinamoorthy, A.; Alvaro, M.; Garcia, H. Aerobic oxidation of thiols to disulfides using iron metal-organic frameworks as solid redox catalysts. *Chem. Commun.*, **2010**, *46*, 6476-6478.
- [15] Kumar, R.; Sharma, N.; Sharma, U.K.; Shard, A.; Sinha, A.K. First metaland base-free selective oxidative coupling of thiols in neat ionic liquids: NMR probed "ambiphilic" character of neutral [hmim]Br towards atomefficient synthesis of disulfides. *Adv. Synth. Catal.*, **2012**, *354*(11-12), 2107-2112.
- [16] Tan, K.Y.D.; Teng, G.F.; Fan, W.Y. CpMn(CO)₃-catalyzed photoconversion

- of thiols into disulfides and dihydrogen. *Organometallics*, **2010**, *29*(20), 4459-4463.
- [17] Tan, K.Y.D.; Teng, H.T.; Fan, W.Y. Photocatalytic transformation of organic and water-soluble thiols into disulfides and hydrogen under aerobic conditions using Mn(CO)5Br. *Organometallics*, **2011**, *30*(15), 4136-4143.
- [18] Talla, A.; Driessen, B.; Straathof, N.J.W.; Milroy, L.G.; Brunsveld, L.; Hessel, V.; Noël, T. Metal-free photocatalytic aerobic oxidation of thiols to disulfides in batch and continuous-flow. *Adv. Synth. Catal.*, **2015**, *357*, 2180-2186.
- [19] Firouzabadi, H.; Iranpoor, N.; Samadi, A. One-pot synthesis of aryl alkyl thioethers and diaryl disulfides using carbon disulfide as a sulfur surrogate in the presence of diethylamine catalyzed by copper(I) iodide in polyethylene glycol (PEG200). *Tetrahedron Lett.*, **2014**, *55*, 1212-1217.
- [20] Joshi, A.V.; Bhusare, S.; Baidossi, M.; Qafisheh, N.; Sasson, Y. Oxidative coupling of thiols to disulfides using a solid anhydrous potassium phosphate catalyst. *Tetrahedron Lett.*, **2005**, *46*, 3583-3585.
- [21] Rajabi, F.; Kakeshpour, T.; Saidi, M.R. Supported iron oxide nanoparticles: Recoverable and efficient catalyst for oxidative S-S coupling of thiols to disulfides. *Catal. Commun.*, **2013**, *40*, 13-17.
- [22] Ghammamy, S.; Tajbakhsh, M. Oxidative coupling of thiols to disulfides in solution and under microwave radiation with tripropylammonium chlorochromate. *J. Sulfur Chem.*, **2005**, *26*(2), 145-148.
- [23] Firouzabadi, H.; Iranpoor, N.; Gorginpour, F.; Samadi, A. Dithioamide as an effective sulfur surrogate for odorless high-yielding carbon-sulfur bond formation in Wet PEG200 as an eco-friendly, safe, and recoverable solvent. *Eur. J. Org. Chem.*, **2015**, (13), 2914-2920.
- [24] Liu, Y.; Wang, H.; Wang, C.; Wan, J.P.; Wen, C. Bio-based green solvent mediated disulfide synthesis via thiol couplings free of catalyst and additive. *RSC Adv.*, **2013**, *3*, 21369-21372.
- [25] Li, Z.; Ke, F.; Deng, H.; Xu, H.; Xiang, H.; Zhou, X. Synthesis of disulfides and diselenides by copper-catalyzed coupling reactions in water. *Org. Biomol. Chem.*, **2013**, *11*, 2943-2946.
- [26] Iranpoor, N.; Zeynizadeh, B. Air oxidative coupling of thiols to disulfides catalyzed by Fe(III)/NaI. *Synthesis*, **1999**, *1*, 49-50.
- [27] Firouzabadi, H.; Karimi, B. Efficient deoxygenation of sulfoxides to thioethers and reductive coupling of sulfonyl chlorides to disulfides with tungsten hexachloride. *Synthesis*, **1999**, *3*, 500-502.
- [28] Kumar, V.; Kaushik, M.P. Efficient oxidative coupling of thiols into disulfides using N-tert-butyl-N-chlorocyanamide. *B. Chem. Soc. Jpn.*, **2008**, *81*, 160-162.
- [29] Fortman, G.C.; Kegl, T.; Hoff, C.D. Kinetic, thermodynamic, and mechanistic aspects of oxidative addition reactions of RE-ER (E = S, Se, Te) and transition metal complexes. *Curr. Org. Chem.*, **2008**, *12*(15), 1279-1297.
- [30] Guo, Y.; Quan, Z.J.; Da, Y.X.; Zhang, Z.; Wang, X.C. (2-chlorobenzoyloxy) copper(I) catalyzed C-S cross-coupling of di(hetero)aryl disulfides with aryl boronic acids under base-free conditions. *RSC Adv.*, **2015**, *5*, 45479-45483.
- [31] Chen, J.; Tang, Z.; Qiu, R.; He, Y.; Wang, X.; Li, N.; Yi, H.; Au, C.T.; Yin, S.F.; Xu, X. Cesium-catalyzed regioselective synthesis of trisubstituted heteroatom alkenes: A new strategy for the preparation of functional alkenes. *Org. Lett.*, **2015**, *17*(9), 2162-2165.
- [32] Wang, X.; Qiu, R.; Yan, C.; Reddy, V.P.; Zhu, L.; Xu, X.; Yin, S.F. Nickelcatalyzed direct thiolation of C(sp³)-H bonds in aliphatic amides. *Org. Lett.*, **2015**, *17*(8), 1970-1973.
- [33] Gholinejad, M.; Firouzabadi, H. One-pot odorless thia-Michael reaction by copper ferrite nanoparticle-catalyzed reaction of elemental sulfur, aryl halides and electron-deficient alkenes. *New J. Chem.*, **2015**, *39*, 5953-5959.
- [34] Quan, Z.J.; Lv, Y.; Jing, F.Q.; Jia, X.D.; Huo, C.D.; Wang, X.C. Chemoselective carbon-carbon cross-coupling via palladium-catalyzed coppermediated C-S cleavage of disulfides. *Adv. Synth. Catal.*, **2014**, *356*, 325-332.
- [35] Engels, H.W. In: *Ullmann's Encyclopedia of Industrial Chemistry 5th ed*; Elvers B.; Hawkins S.; Russey W.; Schulz G. ed.; Cambridge: New York, **1993**; A23, pp. 365-432.
- [36] Li, Y.; Shen, Y.; Wang, S.; Zhu, D.; Du, B.; Jiang, J. Disulfide cross-linked cholic-acid modified PEG-poly(amino acid) block copolymer micelles for controlled drug delivery of doxorubicin. *RSC Adv.*, **2015**, *5*, 30380-30388.
- [37] Madabhushi, S.; Vangipuram, V.S.; Mallu, K.K.R.; Chinthala, N.; Beeram, C.R. Europium(III) triflate-catalyzed trofimov synthesis of polyfunctionalized

- pyrroles. *Adv. Synth. Catal.*, **2012**, *354*, 1413-1416.
- [38] Yoon, M.Y.; Kim, J.H.; Choi, D.S.; Shin, U.S.; Lee, J.Y.; Song, C.E. Metal triflate-catalyzed regio- and stereoselective Friedel-Crafts alkenylation of arenes with alkynes in an ionic liquid: Scope and mechanism. *Adv. Synth. Catal.*, **2007**, *349*, 1725-1737.
- [39] Kuriyama, M.; Hamaguchi, N.; Onomura, O. Copper(II)-catalyzed monoarylation of vicinal diols with diaryliodonium salts. *Chem. Eur. J.*, **2012**, *18*(6), 1591-1594.
- [40] Zhang, L.J.; Lu, H.L.; Wu, Z.W.; Huang, Y.S. Ytterbium triflate: A versatile catalyst in organic synthesis. *Curr. Org. Chem.*, **2013**, *17*(23), 2906-2920.
- [41] Gaspard-Iloughmane, H.; Le Roux, C. Bismuth(III) triflate in organic synthesis. *Eur. J. Org. Chem.*, **2004**, (12), 2517-2532.
- [42] Kobayashi, S. Scandium triflate in organic synthesis. *Eur. J. Org. Chem.*, **1999**, *1*, 15-27.
- [43] Hreczycho, G.; Pawluć, P.; Marciniak, B. A new selective approach to unsymmetrical siloxanes and germasiloxanes via *O*-metalation of silanols with 2-methylallylsilanes and 2-methylallylgermanes. *New J. Chem.*, **2011**, *35*, 2743-2746.
- [44] Hreczycho, G.; Kuciński, K.; Pawluć, P.; Marciniak, B. Catalytic synthesis of linear oligosiloxanes and germasiloxanes mediated by scandium trifluoromethanesulfonate. *Organometallics*, **2013**, *32*(17), 5001-5004.
- [45] Hreczycho, G. Efficient catalytic approach for the synthesis of unsymmetrical siloxanes. *Eur. J. Inorg. Chem.*, **2015**, *1*, 67-72.
- [46] Kuciński, K.; Pawluć, P.; Hreczycho, G. Metal triflate-mediated coupling of allylgermanes with thiols: A facile route to thiogermanes. *Dalton Trans.*, **2015**, *44*, 10943-10946.
- [47] Kuciński, K.; Pawluć, P.; Marciniak, B.; Hreczycho, G. Highly selective hydrothiolation of unsaturated organosilicon compounds catalyzed by scandium(III) triflate. *Chem. Eur. J.*, **2015**, *21*, 4940-4943.
- [48] Kuciński, K.; Pawluć, P.; Hreczycho, G. Scandium(III) triflate-catalyzed anti-Markovnikov hydrothiolation of functionalized olefins. *Adv. Synth. Catal.*, **2015**, *357*, 3936-3942.
- [49] Capozzi, G.; Modena, G. In: *The Chemistry of the Thiol Group*; S. Patai, Ed.; John & Sons Ltd.: Chichester, **1974**; Vol. 2, pp. 785-839.
- [50] Bochmann, M.; Song, X.; Hursthouse, M.B.; Karaulov, A. Chalcogenolato complexes of bismuth and antimony. Syntheses, thermolysis reactions, and crystal structure of Sb(SC₆H₂Pri₃-2,4,6)₃. *J. Chem. Soc. Dalton Trans.*, **1995**, (10), 1649-1652.
- [51] Dreyer, D.R.; Jia, H.P.; Todd, A.D.; Geng, J.; Bielawski, C.W. Graphite oxide: A selective and highly efficient oxidant of thiols and sulfides. *Org. Biomol. Chem.*, **2011**, *9*, 7292-7295.
- [52] Li, Y.S.; Liang, X.R.; Su, W.K. A facile synthesis of disulfides by oxidation of thiols with bis(trichloromethyl)carbonate and triphenylphosphine oxide. *Org. Prep. Proced. Int.*, **2003**, *35*, 613-616.
- [53] Barba, F.; Ranz, F.; Batanero, B. Electrochemical transformation of diazonium salts into diaryl disulfides. *Tetrahedron Lett.*, **2009**, *50*, 6798-6799.
- [54] Vandavasi, J.K.; Hu, W.P.; Chen, C.Y.; Wang, J.J. Efficient synthesis of unsymmetrical disulfides. *Tetrahedron*, **2011**, *67*, 8895-8901.
- [55] Barrett, A.G.M.; Barton, D.H.R.; Colle, R. Acid-catalysed rearrangement of Bis-5,6-dihydro-4*H*-1,3-thiazin-2-yl and other disulphides and related reactions. *J.C.S. Perkin I*, **1980**, (0), 665-671.