Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: X. Zhang, T. Wang, X. Liu, X. Wang and Z. Quan, *Org. Biomol. Chem.*, 2019, DOI: 10.1039/C8OB02971G.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/C8OB02971G

Journal Name

ARTICLE

Received 00th January 20xx,

Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Solvent-Controlled Chemoselective Construction of C-S/S-S Bonds via Michael reaction/Thiol Coupling of Quinoline-2-thiones

Xi Zhang,[‡ a] Tong-Lin Wang,[‡ a] Xiao-Jun Liu,[a] Xi-Cun Wang,[a] Zheng-Jun Quan [*a]

K_2CO_3-catalyzed thio-Michael addition using quinoline-2-thiones and α,β-unsaturated carbonyl compounds was used to assess chemoselective construction of C-S and S-S bonds under mild reaction conditions in different solvents. The C-S bond showed a better chemoselective constructing in EtOH whereas the S-S bond showed a better chemoselective constructing in 1,4-dioxane. The corresponding products, generated from the reaction, presented a significant solvent-controlling effect.

Introduction.

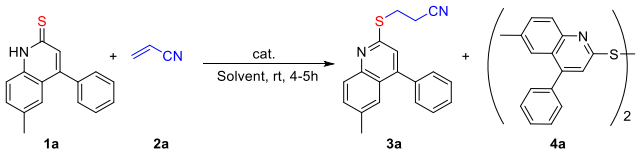
As a unique nitrogen-containing heterocyclic compound, the quinoline skeleton plays an essential role in the field of optoelectronic functional materials,[1,2] medical field[3,4] and organic synthesis.[5,6] Recently, Substituted quinoline compounds have attracted the attention of more and more chemical researchers.

Sulfur, it is an active non-metallic element that is ubiquitous, especially in nature and in living organisms. Thioether and disulfide are important unique moiety in drugs, agrochemicals,[7] materials science,[8] and many functional molecules.[9] The development of a gentle and versatile method for the formation of C-S and S-S bonds has received considerable attention, although many synthetic methods have been reported.[10] Some of these methods have significant limitations and require the implementation of metal-ligand combinations or highly pre-functionalized precursors. Therefore, an important task of chemical researchers is to find simple ways to form C-S bonds and S-S bonds.

It is well known that the Michael addition reaction is an essential reaction in organic chemistry, an important primary method for constructing C-C,[11] C-N,[12] and C-S bonds,[13] However, the strategy for constructing C-S remains the interest of chemists The thia-Michael addition reaction is a simple and effective method for forming C-S bonds and is widely used in organic synthesis.[13]

Herein, based on our previous work,[14] we reported the solvent-controlled selective construction of C-S and S-S bonds on the quinoline skeleton by using K_2CO_3 as a catalyst under mild conditions. The C=S bond in quinoline-2-thione were selectively converted into C-S bond in EtOH and S-S bond in dioxane without any additives except the air at room temperature.

Table 1. Optimization of Reaction Conditions [a]



1a 2a 3a 4a

Entry	Base	Solvent (mL)	Yield (%)[b] **3a**	Yield (%)[b] **4a**
1	K_2CO_3 (1 eq.)	DCE	trace	30
2	K_2CO_3 (1 eq.)	Acetone	10	35
3	K_2CO_3 (1 eq.)	EtOAc	trace	25
4	K_2CO_3 (1 eq.)	1,4-Dioxane	trace	83
5	K_2CO_3 (1 eq.	1,3-Dioxolane	trace	76
6	K_2CO_3 (1 eq.)	Dibutyl ether	trace	72
7	K_2CO_3 (1 eq.)	THF	12	53
8	K_2CO_3 (1 eq.)	DME	15	62
9	K_2CO_3 (1 eq.)	PEG-400	67	10
10	K_2CO_3 (1 eq.)	EtOH	92	trace
11	K_2CO_3 (1 eq.)	MeOH	85	trace
12	K_2CO_3 (1 eq.)	DMF	88	trace
13	**K_2CO_3 (20%)**	**EtOH**	**90**	**trace**
14	**K_2CO_3 (20%)**	**1,4-Dioxane**	**trace**	**80**
15[c]	K_2CO_3 (20%)	1,4-Dioxane	trace	13
16	DBU (20%)	EtOH	88	trace
17	Et_3N (20%)	EtOH	42	15
18	DABCO (20%)	EtOH	45	18
19	NaOH (20%)	EtOH	73	13
20	Cs_2CO_3 (20%)	EtOH	76	10
21	K_3PO_4 (20%)	EtOH	53	26
22	Na_2S (20%)	EtOH	47	31

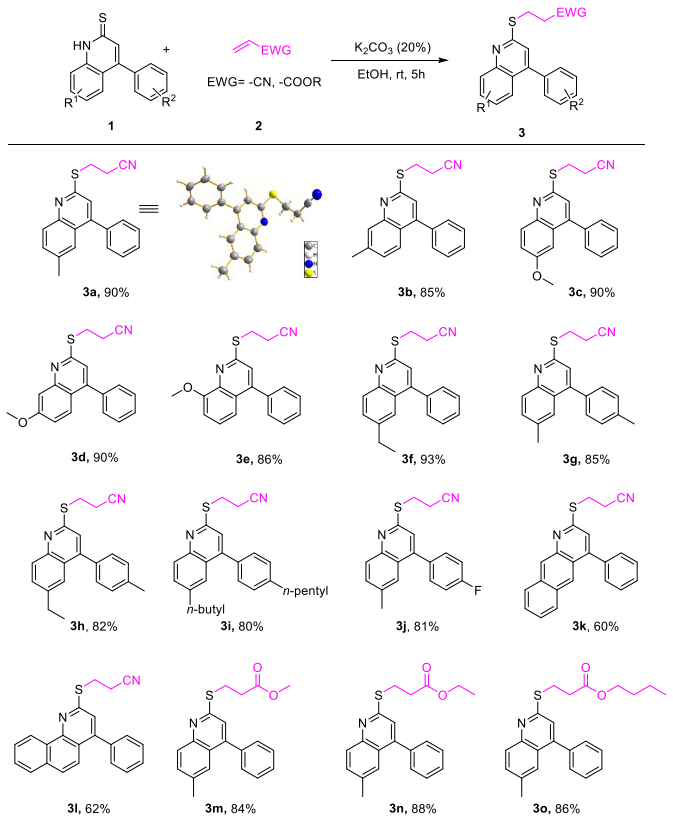
[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), K_2CO_3 (20 mol%), EtOH (2 mL), rt., 5 hours. [b]Isolated yield. [c] Under N_2 atmosphere.

[a]Gansu International Scientific and Technological Cooperation Base of Water-Retention Chemical Functional Materials, College of Chemistry and Chemical Engineering, Northwest Normal University, Lanzhou, Gansu 730070, People's Republic of China. E-mail: quanzhengjun@hotmail.com; Fax: +86-931-7972626

‡ These authors contributed equally to this work.

Electronic Supplementary Information (ESI) available: See DOI:10.1039/x0xx00000x

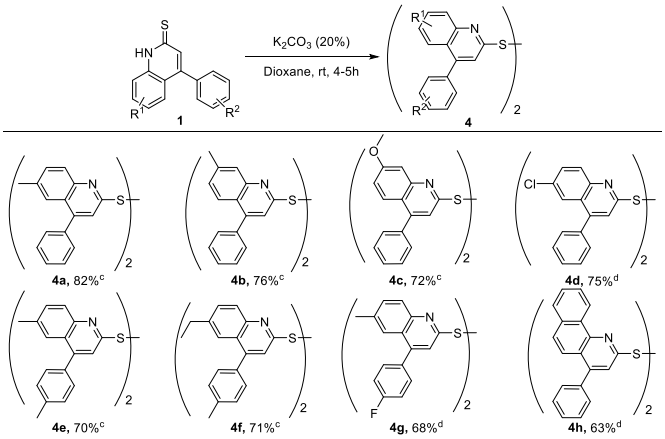
Results and discussion



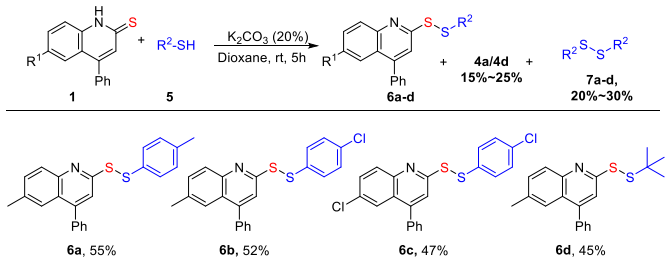
Scheme 1. Substrate scope of 4-arylquinoline-2(1H)-thione.

Our investigation was initiated by using quinoline-2-thione **1a** and acrylonitrile **2a** as the model substrates. First, we screened a series of solvents in the presence of 1 equivalent of K_2CO_3 as the base (**Table 1**, entries 1-12). When a common polar aprotic solvent was used (**Table 1**, entries 1-8), the target Michael addition product **3a** was obtained in a low yield, while the thiol coupling product **4a** was separated in moderate to a good yield, especially in ether solvents (**Table 1**, entries 4-8). 1,4-dioxane yielded a disulfide **4a** in 83% yield. The reaction in 1,3-dioxolane and dibutyl ether were able to give **4a** in 76% and 68% yield, and trace amounts of **3a** were detected (**Table 1**, entries 5-6). **4a** was obtained in a yield of 53% and 62% in THF or DME as a solvent, while a low yield of compound **3a** (**Table 1**, entries 7-8) was isolated. Next, we tested the common polar protic solvents (**Table 1**, entries 9-12) which showed that both polar protic solvents (EtOH, MeOH) and polar inert protic solvents (PEG-400, DMF) delivered compound **3a** in a moderate to good yield. Based on these results, we indicated that disulfide **4a** selectively obtained in a polar aprotic solvent, while the thia-Michael addition product **3a** can be advantageously obtained in a polar protic solvent. Finally, we screened the amount and type of base(**Table 1**, entries 16-22). The target products **3a** and **4a** were still obtained in 90% and 80% yields when a catalytic amount of K_2CO_3 (20 mol%) was used (**Table 1**, entries 13-14). Although DBU, NaOH, Cs_2CO_3 and some other bases gave target compound **3a** in moderate yield, K_2CO_3 remained the best one and **4a** has isolated only in a yield of 13%, when the dioxane that excluded oxygen was used (**Table 1**, entry 15), indicating that the process of forming **4a** required oxygen to participate. Thus, we got the optimal conditions: K_2CO_3 (20%) was used as base at room temperature. When EtOH was used as a solvent, the compound **3a** was isolated in a yield of 90% by reacting for 5 hours (**Table 1,** entry 13). Meanwhile, in the case of using dioxane as the solvent, **4a** can be obtained in an 80% yield after 5 hours (**Table 1,** entry 14).

With the optimized conditions in hand, we firstly studied the Michael addition range of differential quinoline-2-thiones **1** and acrylonitrile **2a** (**Scheme 1**). The results indicate that when acrylonitrile is used as a receptor, both electron-donating and electron-withdrawing substitution at the 2-position, 3-position, 4-position of the aromatic ring provided moderate to good yields of the thia-Michael addition products (**3a-3o**). The halide (-F) substituent was well tolerated under these conditions. However, it is unsatisfactory that the yield of naphthyl quinoline-2-thiones (**3k, 3l**) is relatively low. This may be caused by the high electron-withdrawing nature of the naphthyl group. Acrylates were also tested in this reaction, where both methyl acrylates **(3m)** and butyl esters **(3o)** gave addition products in good yields. This shows that the chain length of the acrylate does not affect the yield. The structure of **3a** was clearly determined by single crystal X-ray diffraction.[15]



Scheme 2. Substrate scope of the symmetric disulphide. [a] Reaction conditions: **1** (0.2 mmol), K_2CO_3 (20 mol%), dioxane (2 mL), rt., 4-5 hours. [b] Isolated yield. [c] 4h, [d] 5h.

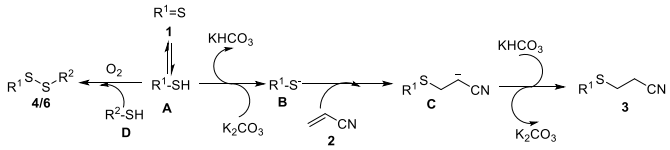


Scheme 3. Substrate scope of the asymmetric disulphide. [a] Reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), K_2CO_3 (20 mol%), Dioxane (2 mL), rt., 5 hours. [b] Isolated yield.

In view of the optimum conditions (**Table 1**, entry 17), we tested the coupling reaction of a series of quinolin-2-thiones. As shown in **Scheme 2**, a variety of disulfides were obtained in good yields and the functional groups are well-tolerated, and

the position of the substituent does not influence the yield. Based on our previous work, [17] asymmetric heterocyclic disulfides have different reaction sites, so we tried to synthesize asymmetric disulfides with quinoline-2-thione and simple thiols (**Scheme 3**). It was found that asymmetric disulfide compounds can be obtained in about 50% yield. And that the symmetric disulfides (**4a, 4d**) were obtained in a yield of 15% to 25%, and about 30% yield of the simple disulfides **7a-d** was isolated.

The possible reaction mechanism was obtained by comparing with the literature precedent (**Scheme 4**).[13,16] Initially, owing to the substrate has higher activity in this reaction, a thio intermediate **A** is formed by tautomerization of **1**. [18] Next, K_2CO_3 captures the protons in thiol **A** to generate $KHCO_3$ and sulfur-anion intermediates **B**. Usually, Michael reaction is carried out in a protic solvent,[19a] hydrogen bond formation among solvent (EtOH) and substrates increased the electrophilicity of **2** and nucleophilicity of **1**, thus, simultaneous activation of the **1** and **2**. [13] So, in a protic solvent the addition reaction of an intermediate **B** to an unsaturated carbonyl compound produces a carbon anion intermediate **C**. Finally, **C** obtained the proton in $KHCO_3$, generating the target product **3** and K_2CO_3 which was continued to enter the catalytical cycle. Meanwhile, it is more favourable that in a aprotic solvent **A** can be oxidized by O_2 (air) to form a disulfide **4** or **6**. [19b-d]



Scheme 4. Proposed mechanism.

Conclusions

In summary, we have reported a solvent-dependent selectively construction of C-S and S-S bonds in good yields under mild conditions. The thioether compounds could be obtained in high yields in EtOH with high efficiency. Particularly interesting is that the reaction could also produce the symmetric or asymmetric disulfides product in dioxane with chemical selectivity.

Experiment

Synthesis of quinoline-2-thiones *1a-1o*

Under an atmosphere of air, 2-(1-phenylvinyl) aniline (0.5 mmol, 0.0095 g), CS_2 (1.2 eq. 0.6 mmol, 0.0046 g), DBU (5 mol%, 0.00018 g) were added to a tube. DMF (3.0 mL) was added by dropper and the mixture was stirred for 8 h at 140 ℃ and the reaction was monitored by TLC analysis. Then, 2.0 mL ammonium chloride were added to the mixture to quench the reaction and extracted with ethyl acetate (3×25 mL). The combined organic layers were washed with saturated aq. NH_4Cl and brine, dried over $MgSO_4$, filtered, and the volatiles were removed in vacuum. The residue was purified by recrystallization (EtOH) to give the quinoline-2-thiones.

Typical Procedure for the Synthesis of *3a*

The mixture of quinoline-2-thione **1a** (0.2 mmol, 50 mg), acrylonitrile **2a** (0.24 mmol, 13 mg) and K_2CO_3 (20%, 6 mg) in EtOH (2 mL) was stirred at room temperature for 5 hours under air atmosphere. After the reaction was complete according to TLC detection, 2.0 mL of saturated aq. NH_4Cl was added to the mixture to quench the reaction. The mixture was extracted with ethyl acetate (3×25 mL). The organic layer was washed with aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and the volatiles were removed in vacuum. Then the mixture was purified by using silica gel column chromatography with a different eluent (ethyl acetate: petroleum ether = 1:30) thus yielding a pure **3a** was obtained as a white solid (55 mg, 90% yield).

Typical Procedure for the Synthesis of *6a*

The mixture of quinoline-2-thione **1a** (0.2 mmol, 50 mg), thiophenol **5a** (0.3 mmol, 13 mg) and K_2CO_3 (20%, 6 mg) in 1,4-dioxane (2 mL) was stirred at room temperature for 5 hours under air. After the completion of the reaction monitored by TLC detection, 2.0 mL of saturated aq. NH_4Cl was added to the mixture to quench the reaction and extracted with ethyl acetate (3×25 mL). The organic layer was washed with aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and the volatiles were removed in vacuum. Then, the mixture was purified by using silica gel column chromatography with different eluent (ethyl acetate: petroleum ether = 1:30) thus yielding a pure **6a** as a colourless oil (40 mg, 55% yield).

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We are thankful for the financial support from the National Nature Science Foundation of China (No. 21562036) and the Scientific and Technological Innovation Engineering program of Northwest Normal University (NWNU-LKQN-15-1).

References and notes

1 (a) J. P. Michael, *Nat. Prod. Rep.,* 2008, **25**, 166; (b) A. P. Gorka, A. de Dios and P. D. Roepe, *J. Med. Chem.,* 2013, **56**, 5231; (c) M. Rouffet, C. A. F. de Oliveira,Y. Udi, A. Agrawal, I. Sagi, J. A. McCammon and S. M. Cohen, *J. Am. Chem. Soc.,* 2010, **132**, 8232; (d) S. Andrews, S. J. Burgess, D. Skaalrud, J. X. Kelly and D. H. Peyton, *J. Med. Chem.,* 2010, **53**, 916.

2 (a) V. Bhalla, V. Vij, M. Kumar, P. R. Sharma and T. Kaur, *Org. Lett.,* 2012, **14**, 1012; (b) M. Velusamy, C. H. Chen, Y. S. Wen, J. T. Lin, C. C. Lin, C. H. Lai and P. T. Chou, *Organometallics.,* 2010, **29**, 3912; (c) S. Tao, L. Li, J. Yu, Y. Jiang, Y. Zhou, C. S. Lee, S. T. Lee, X. Zhang and O. Kwon, *Chem. Mater.,* 2009, **21**, 1284; (d) J. L. Kim, I. S.

Shin and H. Kim, *J. Am. Chem. Soc.,* 2005, **127**, 1614; (e) H. Xu, R. Chen, Q. Sun, W. Lai, Q. Su, W. Huang and X. Liu, *Chem. Soc. Rev.,* 2014, **43**, 3259; (f) A. Danel, E. Gondek and I. Kityk, *Opt. Mater.,* 2009, **32**, 267.

3 (a) S. S. Zhu, W. Y. Lin and L. Yuan, *Dyes Pigm.,* 2013, **99**, 465; (b) C. J. Fahrni and V. V. O' Halloran, *J. Am. Chem. Soc.,* 1999, **121**, 11448; (c) V. R. Solomon and H. Lee, *Curr. Med. Chem.,* 2011, **18**, 1488; (d) K. Kaur, M. Jain, R. P. Reddy and R. Jain, *Eur. J. Med. Chem.,* 2010, **45**, 3245; (e) R. Musiol, M. Serda, S. Hensel-Bielowka and J. Polanski, *Curr. Med. Chem.,* 2010, **17**, 1960; (f) J. P. Michael, *Nat. Prod. Rep.,* 2008, **25**, 166; (g) X. Z. Yang, Y. J. Feng, S. Duffy, V. M. Avery, D. Camp, R. J. Quinn and R. A. Davis, *Planta Med*., 2011, **77**, 1644; (h)B. Leon, J. C. N. Fong, K. C. Peach, W. R. Wong, F. H. Yildiz and R. G. Linington, *Org. Lett.,* 2013, 15, 1234; (i)D. A. Ibrahim, D. A. Abou El Ella, A. M. El-Motvvally and R. M. Aly, *Eur. J. Med. Chem.,* 2015, **102**, 115; (j) K. Gopaul, S. A Shintre and N. A Koorbanally, *Anti-Cancer Agents Med Chem.*, 2015, **15**, 631; (k) M. Orhan Puskullu, B. Tekiner and S. Suzen, *Mini. Rev. Med. Chem.*, 2013, **13**, 365.

4 (a) S. S. Zhu, W. Y. Lin and L. Yuan, *Dyes Pigm.,* 2013, **99**, 465; (b) C. J. Fahrni and V. V. O' Halloran, *J. Am. Chem. Soc.,* 1999, **121**, 11448; (c) V. R. Solomon and H. Lee, *Curr. Med. Chem.,* 2011, **18**, 1488; (d) K. Kaur, M. Jain, R. P. Reddy and R. Jain, *Eur. J. Med. Chem.,* 2010, **45**, 3245; (e) R. Musiol, M. Serda, S. Hensel-Bielowka and J. Polanski, *Curr. Med. Chem.,* 2010, **17**, 1960; (f) J. P. Michael, *Nat. Prod. Rep.,* 2008, **25**, 166; (g) X. Z. Yang, Y. J. Feng, S. Duffy, V. M. Avery, D. Camp, R. J. Quinn and R. A. Davis, *Planta Med*., 2011, **77**, 1644; (h)B. Leon, J. C. N. Fong, K. C. Peach, W. R. Wong, F. H. Yildiz and R. G. Linington, *Org. Lett.,* 2013, **15**, 1234; (i) D. A. Ibrahim, D. A. Abou El Ella, A. M. El-Motvvally and R. M. Aly, *Eur. J. Med. Chem.,* 2015, **102**, 115; (j) K. Gopaul, S. A Shintre and N. A Koorbanally, *Anti-Cancer Agents Med Chem.*, 2015, **15**, 631; (k) M. Orhan Puskullu, B. Tekiner and S. Suzen, *Mini. Rev. Med. Chem.*, 2013, **13**, 365.

5 (a) J. P. Michael, *Nat. Prod. Rep.,* 2007, **24**, 223; (b) J. P. Michael, *Nat. Prod. Rep.,* 2008, **25**, 166; (c) T. Eicher, S. Hauptamann and A. Speicher in *The Chemistry of Heterocycles*, II ed. Wiley-VCH: 2003; (d) Q. A. Zou, H. L. Duan, M. M. Ning, J. Liu, Y. Feng, L. M. Zhang, J. J. Zhu, Y. Leng and J. H. Shen, *Eur. J. Med. Chem.,* 2011, **46**, 3639; (e) P. Dziedzic, J. A. Cisneros, M. J. Robertson, A. A. Hare, N. E. Danford, R. H. G. Baxter and W. L. Jorgensen, *J. Am. Chem. Soc.,* 2015, **137**, 2996.

6 (a) R. Y. Zhu, T. G. Saint-Denis, Y. Shao, J. He, J. D. Sieber, C. H. Senanayake and J. Q. Yu, *J. Am. Chem. Soc.,* 2017, **139**, 5724; (b) P. X. Shen, X. C. Wang, P. Wang, R. Y. Zhu and J. Q. Yu, *J. Am. Chem. Soc.,* 2015, **137**, 11574; (c) G. Rouquet and N. Chatani, *Angew. Chem. Int. Ed.,* 2013, **52**, 11726; *Angew. Chem*., 2013, **125**, 11942; (d) M. Corbet and F. De Campo, *Angew. Chem. Int. Ed.,* 2013, **52**, 9896; *Angew. Chem*., 2013, **125**, 10080; (e) Y. Zhang and M. S. Sigman, *J. Am. Chem. Soc*., 2007, **129**, 3076; (f) M. M. Biddle, M. Lin and K. A. Scheidt, *J. Am. Chem. Soc.,* 2007, **129**, 3830.

7 (a) A. Casini, J. Y. Winum, J.-L. Montero, A. Scozzafava and C. T. Supuran, Bioorg. *Med. Chem. Lett*., 2003, **13**, 837; (b) M. Mellah, A. Voituriez and E. Schulz, *Chem. Rev*., 2007, **107**, 5133; (c) H. Haruki, M. G. Pedersen, K. I. Gorska, F. Pojer and K. Johnsson, *Science.*, 2013, **340**, 987; (d) A. Natarajan, H. Aktas, M. Chorev and J. A. Halperin, *J. Med. Chem*., 2004, **47**, 4979; (e) D. C. Cole, G. Zhang, J.Coupet and L. E. Schechter, *J. Med. Chem*., 2005, **48**, 353; (f) M. Banerjee, A. Poddar, G. Mitra, A. Surolia, T. Owa and B. Bhatta-charyya, *J. Med. Chem*., 2005, **48**, 547.

8 (a) H. K. Cui, Y. Guo, Y. He, F. L. Wang, H. N. Chang, Y. J. Wang, F. M. Wu, C. L. Tian and L. Liu, *Angew. Chem. Int. Ed.,* 2013, **52**, 9558; (b) H. Grönbeck, A. Curioni and W. Andreoni, J. *Am. Chem. Soc.,* 2000, **122**, 3839; (c) S. P. Stratton, E. R. Sharlow, A. Baker and , T. Dragovich, *Clin. Cancer Res*., 2007, **13**, 2109; (d) A. R. Murphy and J. M. J. Fre´chet, *Chem. Rev*., 2007, **107**, 1066.

9 (a) J. X. Gong, X. Shen, L. G. Yao, H. Jiang, K. Krohn and Y. W. Guo, *Org. lett*., 2007, **9**, 1715; (b) C. S. Jiang, W. E. G. Müller, H. C. Schröder and Y. W. Guo, *Chem. Rev.,* 2012, **112**, 2179; (c) S. A. Caldarelli, M. Hamel, J. F. Duckert, M. Ouattara, M. Calas, M. Maynadier, S. Wein, C. Périgaud, A. Pellet, H. J. Vial and S. Peyrottes, *J. Med. Chem*., 2012, **55**, 4619; (d) S. S. Mansy and J. A. Cowan, *Acc. Chem. Res*., 2004, **37**, 719; (e) N. S. Li, J. K. Frederiksen and J. A. Piccirilli, Acc. Chem. Res., 2011, 44, 1257; (f) P. Chauhan, S. Mahajan and D. Enders, *Chem. Rev.,* 2014, **114**, 8807; (g) J. S. Yu, H. M. Huang, P. G. Ding, X. S. Hu, F. Zhou and J. Zhou, *ACS Catal.,* 2016, **6**, 5319; (h) C. Shen, P. F. Zhang, Q. Sun, S. Q. Bai, T. S. A. Hor and X. G. Liu, *Chem. Soc. Rev.,* 2015, **44**, 291; (i) Z. Huang, D. Zhang, X. Qi, Z. Yan, M. Wang, H. Yan and A. Lei, *Org. Lett*., 2016, **18**, 2351; (j) K. L. Dunbar, D. H. Scharf, A. Litomska and C. Hertweck, *Chem. Rev*., 2017, **117**, 5521; (k) C.-F. Lee, Y.-C. Liu and S. S. Badsara, *Chem. Asian J.,* 2014, **9**, 706.

10 (a) C. Shen, and X. G. Liu, *Chem. Soc. Rev*., 2015, **44**, 291; (b) E. Schaumann, *Top. Curr. Chem*., 2007, **274**, 1; (c) D. Uraguchi, N. Kinoshita, D. Nakashima and T. Ooi, *Chem. Sci.*, 2012, **3**, 3161; (d) X. Wu, Y. Chen, M. Li, M. Zhou and S. K. Tian, *J. Am. Chem. Soc*., 2012, **134**, 14694; (e) A. Sakakura, H. Yamada and K. Ishihara, *Org. Lett.*, 2012, **14**, 2972; (f) J. F. Hartwig, *Nature*., 2008, 314; (g) Y. M. Xi, J. L. Petersen and X. D. Shi, *Angew. Chem. Int. Ed*., 2014, **53**, 4657; (h) Q. Q. Lu, and A. W Lei, *J. Am. Chem. Soc.*, 2013, **135**, 11481; (i) Q. Lu, J. Zhang, and A. W. Lei, *Angew. Chem., Int. Ed*., 2013, **52**, 7156; (j) M. Arisawa, K. Fujimoto, S. Morinaka and M. Yamaguchi, *J. Am. Chem. Soc*., 2005, **127**, 12226; (k) X. Xiao, M. H. Feng, X. F. Jiang, *Angew. Chem. Int. Ed*., 2016, **55**, 14121; (l) F. Dénès, M. Pichowicz, G. Povie and P. Renaud, *Chem. Rev*., 2014, **114**, 2587.

11 R. Yeab, F. F. Faucher and G. A. Somorjai, *Mol. Catal.*, 2018, **447**, 65.

12 (a) R. S. Varma and R. K. Saini, *Synlett.,* 1997, **7**, 857; (b) T. K. Roy, B. Parhi and P. Ghorai, *Angew. Chem. Int. Ed.,* 2018, **57,** 9397.

13 (a) S. Lauzon, M. Li, H. Keipour and T. Ollevier, *Eur. J. Org. Chem*., 2018, **2018**, 4536; (b) C. Berthonneau, F. Buttard, M. A. Hiebel, F. Suzenet and J. F. Brière, *Adv. Synth. Catal*., 2017, **359**, 4106; (c) P. Wadhwa and A. Sharma, *Asian J. Org. Chem.,* 2018, **7**, 634; (d) E. H. Krenske, R. C. Petter, Z. D. Zhu and H. K. N, *J. Org. Chem.,* 2011, **76**, 5074; (e) J. R. Christopher, H. K. Elizabeth, H. K. N and W. Peter., *Org. Lett*., 2013, **15**, 1076; (f) L. K. Gopal, K. Raj and K. C. Asit, *Org. Lett*., 2006, **8**, 6433; (g) F. H. Rosemarie and D. R. Seth, *J. Org. Chem*., 2006, **71**, 6342; (h) A. C. Valeria van, B. Fernando, D. C. Antonella, M. Luigi, R. Ivan and S. Luca, *J. Org. Chem*., 1999, **64**, 8122.

14 (a) T. L. Wang, X. J. Liu, C. D. Huo, X. C. Wang and Z. J. Quan, *Chem. Commun*., 2018, **54**, 499; (b) X. Zhang, T. L. Wang, C. D. Huo, X. C. Wang and Z. J. Quan, *Chem., Commun*. 2018, **54**, 3114.

15 The structure of **3a** was determined by X-ray crystallographic. CCDC No. CCDC 1877268.

View Article Online
DOI: 10.1039/C8OB02971G

16 (a) S. Lauzon, H. Keipour, V. Gandon and T. Ollevier, *Org. Lett.,* 2017, **19**, 6324; (b) F. Hampel, and S. B. Tsogoeva *Chem. Eur. J.,* 2018, **24**, 6551.
17 (a) K. J. Wei, Z. J. Quan and X. C. Wang, *Org. Biomol. Chem.*, 2016, **14**, 2395; (b)K. J. Wei, Z. J. Quan and X. C. Wang, *RSC Adv.*, 2016, **6**, 78059; (c)K. J. Wei, Z. J. Quan and X. C. Wang, *Synlett.*, 2016, **27**, 1743.
18 T. Y. Yang, Z. J. Quan and X. C. Wang, *Synlett*., 2017, **28**, 847.
19 (a) D. J. Macquarrie, *Tetrahedron Lett*., 1998, **39**, 4125; (b) M. Oba, K. Nishiyama and W. Ando, *J. Org. Chem*., 2011, **76**, 4173; (c) A. Dhakshinamoorthy, M. Alvaroa and H. Garcia, *Chem. Commun.*, 2010, **46**, 6476; (d) S. Song, J. Z. Liu and N. Jiao., *Angew. Chem. Int. Ed*. 2017, **56**, 1.

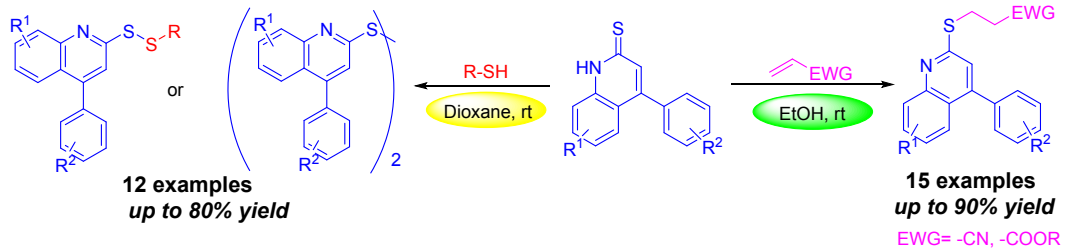
View Article Online
DOI: 10.1039/C8OB02971G

Table of contents entry

Solvent-Controlled Chemoselective Construction of C-S/S-S Bonds via Michael reaction/Thiol Coupling of Quinoline-2-thiones

Xi Zhang,[‡a] Tong-Lin Wang,[‡a] Xiao-Jun Liu,[a] Xi-Cun Wang,[a] Zheng-Jun Quan*[ab]

Solvent-controlled selectively constructing C-S and S-S bonds containing quinoline skeleton under mild conditions from quinoline-2-thione.



Keywords: Solvent-controlled; Thio-Michael addition; Quinoline-2-thione; C-S and S-S; Thioether; Symmetric/asymmetric disulfide.