

SYNLETT Spotlight

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

2-Thioxothiazolidin-4-one (Rhodanine)

Compiled by Khadijeh Hajibabaei

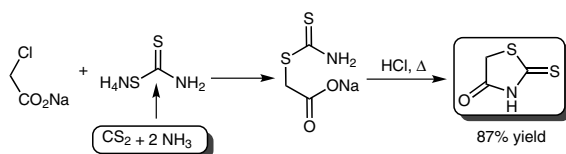
Khadijeh Hajibabaei was born in Isfahan, Iran in 1984 and received her B.Sc. degree in chemistry from the Kashan University in 2007 and her M.Sc. degree in organic chemistry in 2009 from the University of Isfahan. She is currently pursuing her Ph.D. under the supervision of Dr. H. Zali-Boeini at the University of Isfahan. Her research interests focus on the use of thiocarbonyl derivatives in the synthesis of organic compounds and on the preparation of novel chemosensors.

Department of Chemistry, University of Isfahan, P.O. Box 81746-73441, Isfahan, Iran
E-mail: KhadijehHajibabaei@yahoo.com



Introduction

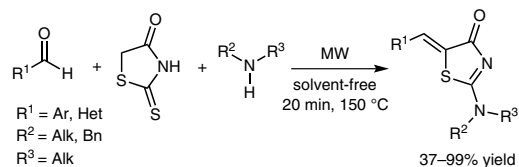
2-Thioxothiazolidin-4-one, commonly known as rhodanine, is an organic compound derived from thiazolidine. It is an interesting organic molecule with potential biological activities and pharmacological properties.^{1–3} However, the biological activity of compounds possessing a rhodanine moiety should be considered critically.⁴ Rhodanine is commercially available and has been synthesized by the reaction of carbon disulfide, ammonia, and chloroacetic acid (Scheme 1).⁵



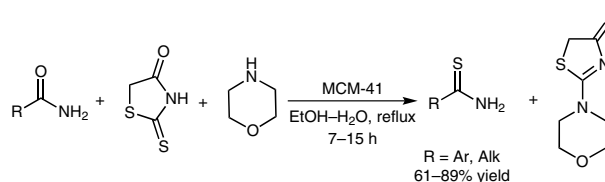
Scheme 1

Abstracts

(A) Anderluh et al. reported an efficient method for the synthesis of 2-amino-5-alkylidene-thiazol-4-ones in excellent yields via a microwave-mediated synthesis. The reaction involves the Knoevenagel condensation of aromatic aldehydes and rhodanine, followed by displacement of the thiocarbonyl sulfur with primary or secondary amines.⁶



(B) The rhodanine/secondary amine system was used for the interconversion of amides into thioamides. Diverse thioamides can be achieved through this simple and convenient method in the presence of MCM-41 as mesoporous silica acid catalyst with a high specific surface area, large pore sizes and pore volumes.⁷ The effect of different secondary amines on the yield of thioamide was also studied. Considerably better yields were observed with secondary cyclic amines. Hence, morpholine was selected as an effective additive in the reaction mixture to produce the corresponding thioamides in moderate to good yields (61–89%).



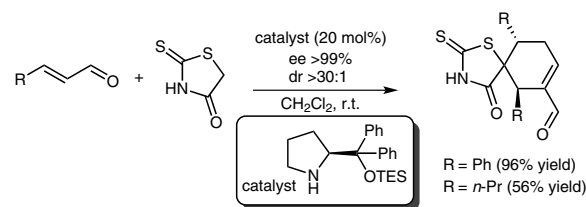
SYNLETT 2014, 25, 2083–2084

Advanced online publication: 31.07.2014

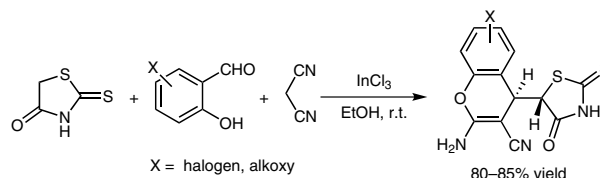
DOI: 10.1055/s-0033-1378268; Art ID: st-2014-v0485-v

© Georg Thieme Verlag Stuttgart · New York

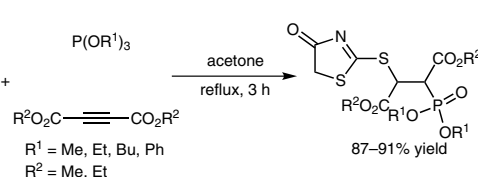
(C) Zhang and co-workers reported the thermal reaction of rhodanine with α,β -unsaturated aldehydes via a Michael addition–cyclization cascade, leading to structurally different fused thiopyrane scaffolds. The diverse spirorhodanines were produced from organocatalytic enantioselective three-component Michael–Michael–aldol cascade reactions of respective rhodanines with enals. This reaction was performed in short reaction times with good diastereoselectivity (3.9:1 to >30:1) and excellent enantioselectivities (>99% ee), despite relatively low yields (56–95%).⁸



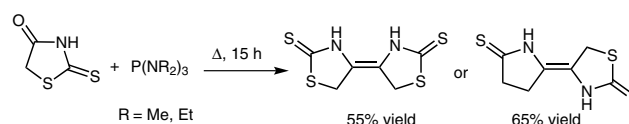
(D) Lakshmi et al. developed the synthesis of 2-amino-4-substituted 4*H*-chromenes by a multi-component reaction between salicylaldehyde, malononitrile, and rhodanine. In this reaction, indium trichloride was employed as an efficient catalyst.⁹ This reaction was investigated with a variety of substituted salicylaldehydes (including halogens and alkoxy groups). All reactions proceeded smoothly to provide 2-amino-4-(4-oxo-2-thioxo-thiazolidin-5-yl)-4*H*-chromenes in good yields (80–85%).



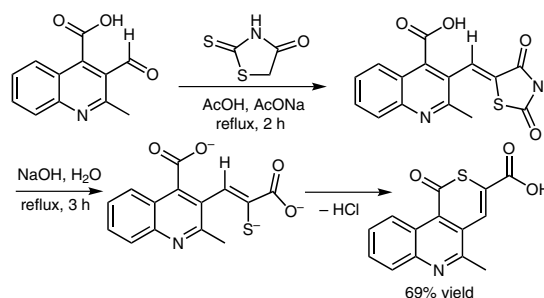
(E) The sulfur atom of rhodanine is highly activated and its nucleophilicity induces the Michael addition type reaction with α,β -unsaturated alkynes. Therefore, treatment of a variety of trialkyl(aryl) phosphites with dialkyl acetylenedicarboxylates and rhodanine led to diverse dialkyl 2-(dialkoxyphosphoryl)-3-(4-oxo-4,5-dihydrothiazole-2-yl)succinate derivatives in good yields.¹⁰



(F) Rhodanine was reacted with diverse tris(dialkylamino)phosphines under solvent-free conditions, obtaining different coupling products of rhodanine.¹¹ However, a mixture of *E* and *Z* isomers were produced.



(G) Pokhodylo et al. described a convenient method for the construction of a fused thiopyrane ring from the quinoline starting material. In this work, the authors used the condensation between quinolin-3-carboxaldehyde and rhodanine to produce fused thiopyrano[4,3-*c*]quinoline in 69% yield.¹²



References

- Andres, C. J.; Bronson, J. J.; D'Andrea, S. V.; Deshpande, M. S.; Falk, P. J.; Grant-Young, K. A.; Harte, W. E.; Ho, H. T.; Misco, P. F.; Robertson, J. G.; Stock, D.; Sun, Y.; Walsh, A. W. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 715.
- Baell, J. B.; Holloway, G. A. *J. Med. Chem.* **2010**, *7*, 2719.
- Tomašić, T.; Peterlin, M. L. *Expert Opin. Drug Discov.* **2012**, *7*, 549.
- Please see: http://pipeline.corante.com/archives/2012/05/23/another_vote_against_rhodanines.php, http://pipeline.corante.com/archives/2011/09/07/get_yer_rhodanines_here.php, http://pipeline.corante.com/archives/2011/12/06/riding_to_the_rescue_of_rhodanines.php
- Redemann, E. C.; Icke, R. N.; Alles, G. A. *Org. Synth. Coll.* **1935**, *3*, 763.
- Anderluh, M.; Jukič, M.; Petrič, R. *Tetrahedron* **2009**, *65*, 344.
- Ray, S.; Bhaumik, A.; Dutta, A.; Butcher, R. J.; Mukhopadhyay, C. *Tetrahedron Lett.* **2013**, *54*, 2164.
- Zhang, Y.; Wang, S.; Wu, S.; Zhu, S.; Dong, G.; Miao, Z.; Yao, J.; Zhang, W.; Sheng, C.; Wang, W. *ACS Comb. Sci.* **2013**, *15*, 298.
- Lakshmi, N. V.; Selvarangam, E. K.; Perumal, P. T. *Can. J. Chem.* **2013**, *6*, 479.
- Hassanabadi, A.; Mosslemin, M. H.; Salari, S.; Momeni, L. M. *Synth. Commun.* **2012**, *42*, 2309.
- Abdel-Malek, H. A. *Phosphorus Sulfur Silicon Relat. Elem.* **2012**, *187*, 506.
- Pokhodylo, N. T.; Matiychuk, V. S.; Obushak, N. D. *Chem. Heterocycl. Compd.* **2009**, *45*, 121.