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GENERAL SYNTHESIS OF 1,4-DITHIINS FROM DIKETO SULFIDES

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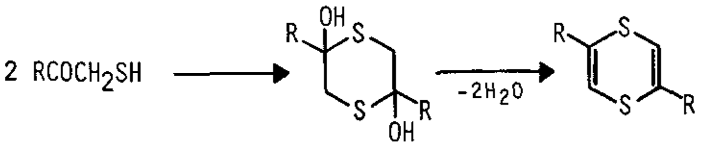
Abstract —— A variety of 1,4-dithiins are prepared in good yields by treatment of diketo sulfides (readily obtainable from α-haloketones and sodium sulfide) with phosphorus pentasulfide or Lawesson's reagent.

1,4-Dithiins constitute an interesting class of compounds possessing a cyclic 8 π structure. The most general synthesis of 1,4-dithiins including parent 1,4-dithiin involves acid-catalyzed self-condensation of α-mercaptoketones (Scheme 1).[1,2] The 1,4-dithiins obtainable by this method are inevitably restricted to those possessing the same substituents at 2- and 5-positions. Application of this method to α-mercaptocyclopentanone gives a mixture of the desired 1,4-dithiin and its isomer having an exocyclic double bond.[3] Synthesis of 2-alkyl-1,4-dithiins by reaction of ethynyl 1-alkynyl sulfides with hydrogen sulfide has recently appeared.[4] Preparation of the starting sulfides is laborious, however. Other methods either lack generality or need starting materials tedious to prepare, and hence are of limited use. Therefore, development of more general synthesis of 1,4-dithiins which permits introduction of a variety of substituents into the desired positions and uses easily accessible starting materials should be required.

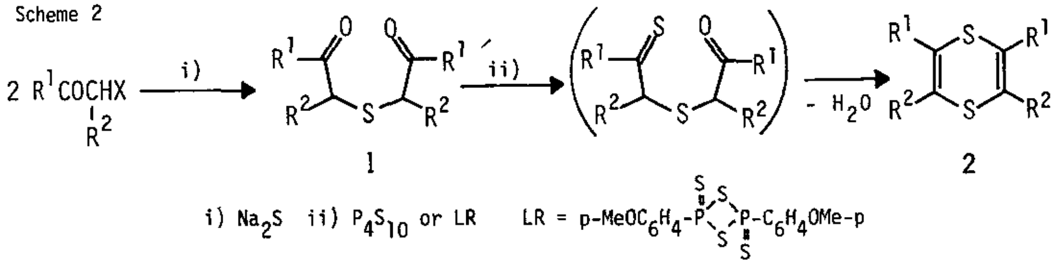


Scheme 1

We report here a general synthesis of 1,4-dithiins which enables us to introduce substituents into arbitrary positions (especially easily to 2- and 6-positions to whom introduction of substituents by other methods was hardly attained) of 1,4-dithiin nucleus.

Diketo sulfides (1) are easily obtainable in excellent yields by reaction of sodium sulfide with readily accessible α-haloketones.[5] We therefore planned preparation of 1,4-dithiins (2) by thionation of one of the carbonyl groups of (1) followed by cyclodehydration of the resulting monothiodiketones (Scheme 2).

Scheme 2



First, diphenacyl sulfide (1; R^1=Ph, R^2=H) is treated by phosphorus pentasulfide as thionating and dehydrating reagent. Thus, refluxing a mixture of diphenacyl sulfide (10 mmol) and phosphorus pentasulfide (20 mmol as P_4S_{10}) in toluene (100 ml) for 6.5 h satisfactorily afforded 2,6-diphenyl-1,4-dithiin (2; R^1=Ph, R^2=H) in 50% yield. However, this reaction unfortunately accompanied the formation of 2,5- and 3,4-diphenylthiophenes (20%) which arose from sulfur extrusion reaction of the resulting diphenyldithiin.[6,7] Since sodium bicarbonate is known to accelerate thionation reaction,[8] it was then used as the additive. The addition of sodium bicarbonate to the mixture resulted in the completion of the reaction by refluxing for 3 h and gave a better yield (78%) of the diphenyldithiin with markedly decreased yield (1%) of diphenylthiophenes.[9]

Lawesson's reagent (LR) is an another powerful thionating agent.[10] The reaction proceeded more rapidly with this reagent, and refluxing a mixture of diphenacyl sulfide (10 mmol) and LR (20 mmol) in toluene (100 ml) for 1.5 h afforded 80% yield of 2,6-diphenyl-1,4-dithiin along with a small amount of diphenylthiophenes.

We also tested hydrogen sulfide as a thionating reagent in boiling acetic acid. In this case, however, the yield of 2,6-diphenyl-1,4-dithiin from diphenacyl sulfide was low (12%).

In a similar way, a variety of diketo sulfides (1) were treated with LR or phosphorus pentasulfide using sodium bicarbonate as the additive. Results are summarized in Table. Generally speaking, LR is superior to phosphorus pentasulfide in that

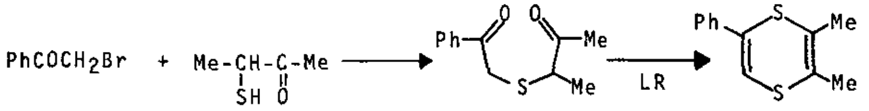
Table Preparation of 1,4-Dithiins (2) from Diketo Sulfides (1).[a]

R^1	R^2	thionating agent[b,c]	conditions[d] solvent	time (h)	yield of (2, %)	mp of (2, °C)
C_6H_5	H	P_4S_{10}[e]	toluene	6.5	50	62-63
C_6H_5	H	P_4S_{10}	toluene	3	78	
C_6H_5	H	LR	toluene	1.5	80	
p-$CH_3C_6H_4$	H	LR	toluene	1	73	126-126.5
p-$CH_3OC_6H_4$	H	LR	toluene	0.5	79	125.5-127.5
p-BrC_6H_4	H	LR	toluene	1.5	76	158-159
2-naphthyl	H	LR	benzene	6	60	125-126
2-thienyl	H	P_4S_{10}	benzene	3	61	73.5-74
2-thienyl	H	LR	benzene	3	52	
C_6H_5	C_2H_5	P_4S_{10}	toluene	10	59	81.5-83
C_6H_5	C_2H_5	LR	toluene	4	40	

[a] All of the dithiins are new and gave supporting spectral data. [b] LR stands for Lawesson's reagent. [c] Unless otherwise stated, phosphorus pentasulfide was used in combination with sodium bicarbonate. [d] At reflux temperature. [e] Phosphorus pentasulfide alone was employed.

the reaction completes more quickly by the use of this reagent. However, both LR and phosphorus pentasulfide are equally sufficiently suitable for the preparation of a variety of 1,4-dithiins.

Finally it is worth noting that the method developed here can also be applicable to the preparation of unsymmetrically substituted 1,4-dithiin. Phenacyl bromide reacts with 3-mercapto-2-butanone to give 97% yield of the sulfide (3), which affords 2,3-dimethyl-5-phenyl-1,4-dithiin (4) in 50% yield on treatment with LR in refluxing toluene for 2 h (Scheme 3).



3

4

Scheme 3

In conclusion the synthesis of a series of 1,4-dithiins which are otherwise difficult to obtain was attained in two steps starting from readily available α-haloketones and using inexpensive reagents.

REFERENCES

1. For preparation of 1,4-dithiins, see a) W. E. Parham in 'Organic Sulfur Compounds,' Vol. 1, ed. N. Kharasch, Pergamon Press, New York, 1961, P. 248, b) D. S. Breslow and H. Skolnick in 'The Chemistry of Heterocyclic Compounds,' Vol. 25, Part 2, ed. A. Weissberger, Interscience, New York, 1966, p. 1112, and c) K. Kobayashi, *Yuki Gosei Kagaku Kyokaishi*, 1982, 40, 642.
2. Parent 1,4-dithiin is prepared starting from dimethyl mercaptoacetal (protected form of mercaptoacetaldehyde); W. E. Parham, H. Wynberg, and F. Ramp, *J. Am. Chem. Soc.*, 1953, **75**, 2065.
3. F. Asinger, M. Thiel, H. Usbeck, K. H. Gröbe, and Tränkner, *Justus Liebigs Ann. Chem.*, 1959, **634**, 144; R. Moriarty, C. C. Chien, and C. W. Jefford, *Tetrahedron Lett.*, 1973, 4429.
4. A. Zilberschoon, J. Meijer, P. Vermeer, and L. Brandsma, *Recl. Trav. Chim. Pays-Bas*, 1974, **94**, 163.
5. Y. Miyahara, *J. Heterocycl. Chem.*, 1979, **16**, 1147.
6. Böhme et al. reported that heating diphenacyl sulfide with phosphorus pentasulfide at 170 °C gives 2,5-diphenylthiophene; H. Böhme, H. Pfeifer, and E. Schneider, *Ber.*, 1942, **75**, 900. We re-examined the reaction under the conditions reported and found that chromatographic workup gives 2,6-diphenyl-1,4-dithiin (25%) and 2,5- and 3,4-diphenylthiophenes (25%).[7]
7. Refluxing a solution of 2,6-diphenyl-1,4-dithiin in *o*-dichlorobenzene for 1 h gives a good yield of 2,5- and 3,4-diphenylthiophenes in a ratio of 17:1. The regiochemistry of sulfur extrusion from 2,6-diaryl-1,4-dithiins yielding a mixture of 2,5- and 3,4-diarylthiophenes will be reported later.
8. J. W. Scheeren, P. H. J. Ooms, and R. J. F. Nivard, *Synthesis*, 1973, 149.
9. A mixture of diphenacyl sulfide (10 mmol), phophorus pentasulfide (20 mmol as P_4S_{10}), and sodium bicarbonate (20 mmol) in toluene (100 ml) was refluxed for 3 h.
10. B. S. Pederson, S. Scheibye, N. H. Nilsson, and L. -O. Lawesson, *Bull. Chem. Soc. Belg.*, 1978, **87**, 223.

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