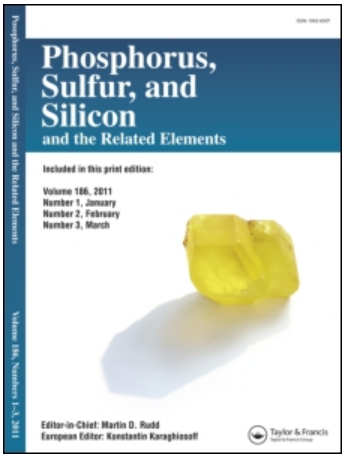

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

S-S Cleavage of Stable 1,2-Dithiolanes with Carbon Nucleophiles as Model for Enzyme Reductive Acylation of Lipoic Acid

Masato Tazaki

To cite this Article Tazaki, Masato(1999) 'S-S Cleavage of Stable 1,2-Dithiolanes with Carbon Nucleophiles as Model for Enzyme Reductive Acylation of Lipoic Acid', Phosphorus, Sulfur, and Silicon and the Related Elements, 153: 1, 419 — 420
To link to this Article: DOI: 10.1080/10426509908546500
URL: http://dx.doi.org/10.1080/10426509908546500

Phosphorus, Sulfur and Silicon, 1999, Vol. 153-154, pp. 419-420
Reprints available directly from the publisher
Photocopying permitted by license only

S-S Cleavage of Stable 1,2-Dithiolanes with Carbon Nucleophiles as Model for Enzyme Reductive Acylation of Lipoic Acid

MASATO TAZAKI

Department of Applied Chemistry, Kumamoto Institute of Technology
Ikeda 4–22–1, Kumamoto 860–0082, Japan

Coenzyme lipoic acid is bound covalently to pyruvate and 2-oxoglutarate dehydrogenase complexes and reductively acylated by the "active aldehydes" bound to thiamine diphosphate in Krebs cycle[1]. The mechanism for these acylations is controversial; redox and carbanion mechanisms have been proposed[2]. Owing to the intrinsic ring strain, 1,2-dithiolanes **2** have the polymerizability preventing the studies on their reactivity towards carbon nucleophiles **1**. We found substituents on the dithiolane ring reduced the polymerizability; 4,4-diethyl- and 4,4-pentamethylene-1,2-dithiolanes do not polymerize and are suitable to the model study[3]. The substituent effect was discussed in terms of the ceiling temperature *Tc*.

1 **2** **3**

The stable 1,2-dithiolanes **2** reacted with simple Grignard and lithium reagents to give the corresponding ring-opened products **3** in excellent yields[3]. Lithiated heterocycles such as thiophenes, furans, N-

methylpyrroles, 1,3-azoles, and methylpyridines can cleave the S-S bond in a quantitative manner[4]. The reaction provides a facile, chemoselective synthesis of mono-S-substituted 1,3-propanedithiol derivatives **3**. Acetylides[5] and sulfonium ylides[6] reacted similarly but the products further isomerized to cyclic compounds. The reactivity of 1,2-dithiolanes towards EtMgBr was compared with that of linear disulfide BuSSBu. The strain-assisted acceleration Ca. 10^4 was observed for the 1,2-dithiolanes, and that of Ca 10 for 1,2-dithiane[3]. Acetophenone enolates and indenyl anions as resonance-stabilized carbanions can cleave the S-S bond. No electron transfer process was detected so far except the case that sterically hindered dithiolanes were reacted with sterically hindered Grignard reagents.

The results are summarized as follows; polymerization resistant 1,2-dithiolanes are suitable to the simple models for the enzyme bound lipoic acid, since they are highly reactive towards carbon nucleophiles as expected for the lipoic acid. The reaction of polymerization resistant 1,2-dithiolanes proceeds via a simple SN2 mechanism on the sulfur in many cases in line with the carbanion mechanism proposed for the enzyme process.

References

[1] L. Teuber, *Sulfur Rep.*, **9**, 257 (1990); L. J. Reed, Acc. *Chem. Res.*, **7**, 40 (1973); N. Isenberg and M. Grdinic, *J. Chem. Educ.*, **49**, 392 (1972); U. Schmidt, P. Grafen, K. Altland, and H. W. Goedde, *Adv. Enzymol. Relat. Areas Mol. Biol.*, **32**, 423 (1969); L. J. Reed, *Organic Sulfur Compounds*, ed. N. Kharasch, Pergamon Press, 1961, pp 443.

[2] P. A. Frey, D. S. Flournoy, K. Gruys and Y.-S. Yang, *Ann. N.Y. Acad. Sci.*, **573**, 21 (1989); R. Bleslow, *Ann. N.Y. Acad. Sci.*, **98**, 445 (1962).

[3] M. Tazaki, et al, *J. Chem. Soc., Chem. Commun.*, 291 (1994); *Chem. Lett.*, 1339 (1988).

[4] M. Tazaki, et al, *Phosphorus Sulfur Silicon*, **88**, 189 (1994), **112**, 101 (1996); *Heteroatom Chemistry*, in press.

[5] M. Tazaki, et al, *J. Chem. Soc., Chem. Commun.*, 1763 (1995).

[6] M. Tazaki, et al, *Phosphorus Sulfur Silicon*, **106**, 227 (1995), **116**, 253 (1996).