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Publisher *Taylor & Francis*

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## 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>

## The Quest for $\beta$ -Thiolactam Antibiotics

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**To cite this Article** Schaumann, Ernst , Nieschalk, Jens , Isecke, Rainer , Spanka, Carsten , Mrotzek, Herbert and Förster, Wolf-Rüdiger(1997) 'The Quest for  $\beta$ -Thiolactam Antibiotics', *Phosphorus, Sulfur, and Silicon and the Related Elements*, 120: 1, 349 — 350

**To link to this Article:** DOI: 10.1080/10426509708545543

**URL:** <http://dx.doi.org/10.1080/10426509708545543>

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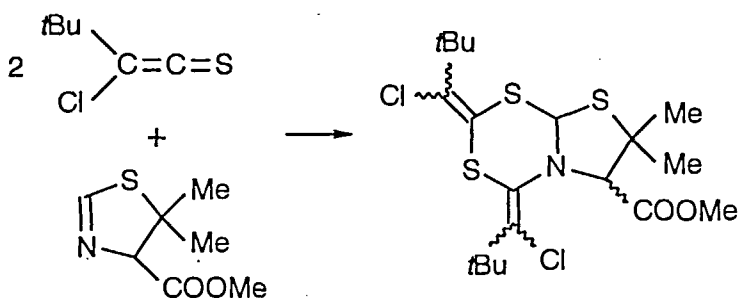
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## The Quest for $\beta$ -Thiolactam Antibiotics

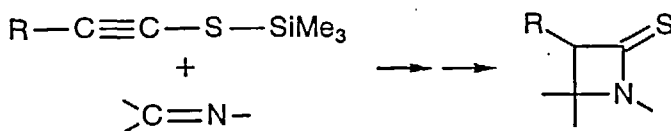
ERNST SCHAUMANN, JENS NIESCHALK, RAINER ISECKE,  
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Thioketenes or thioketene equivalents give  $\beta$ -thiolactams in the reaction with C=N systems, but problems arise in the synthesis of highly functionalized derivatives. Therefore to obtain the thione analog of a bactam a thionation approach was chosen.

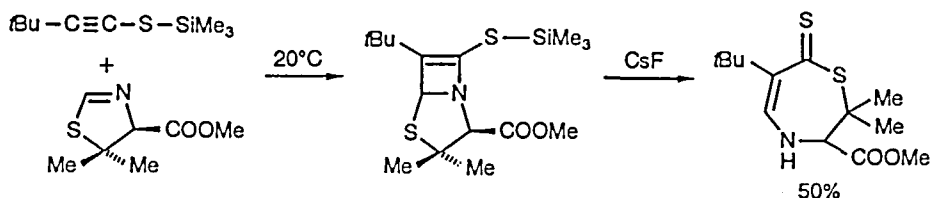
Modifications of natural  $\beta$ -lactams are a promising synthetic target. As to  $\beta$ -thiolactams, the obvious use of thioketenes in a cycloaddition approach with C=N systems is possible, but is limited to sterically hindered thioketenes. More reactive examples, e.g. tert.butyl(chloro)thioketene, tend to give 2:1 cycloadducts with azomethines or thioimides,<sup>1</sup> e.g.:



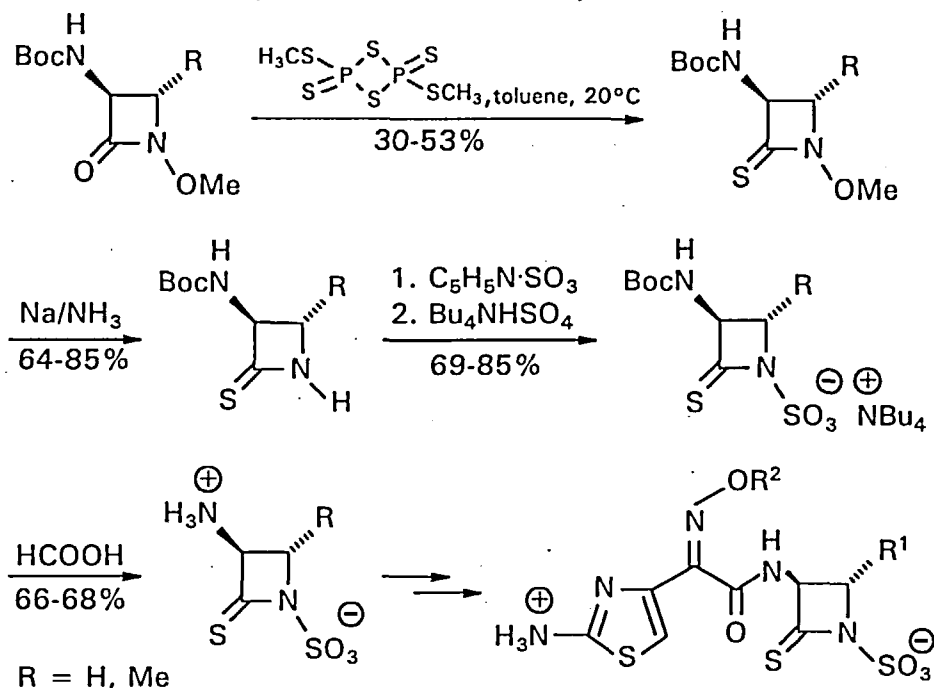
Recently, we found that alkynyl silyl sulfides are a convenient substitute for thioketenes. Interestingly, they give  $\beta$ -thiolactams, in the reaction with C=N systems:



Yields are variable, but can be significantly improved, if Lewis acid catalysis is employed. However, the catalysis fails if thioimides are reaction partners. Here, a competing ring-enlargement in the desilylation step can usually not be suppressed:<sup>2</sup>



Therefore, to obtain a true thione analogue of a natural  $\beta$ -lactam, we had recourse to a thionation approach.<sup>3</sup> As direct thionation of  $\beta$ -lactam antibiotics is known to be problematic,<sup>4</sup> the thionation was carried out in an early stage of the synthesis. This allowed access to the thione analogues of monobactams including the antibiotic aztreonam ( $\text{R} = \text{CH}_3$ ,  $\text{R}^2 = \text{CMe}_2\text{COOH}$ ):



## REFERENCES

1. E. Schaumann, *Tetrahedron* **44**, 1827 (1988).
2. E. Schaumann, W.-R. Förster und G. Adiwidjaja, *Angew. Chem.* **96**, 429 (1984); *Angew. Chem. Int. Ed. Engl.* **23**, 439 (1994).
3. J. Nieschalk, E. Schaumann, *Liebigs Ann.* **1996**, 141.
4. P.W. Wojtkowski, J.E. Dolfini, O. Kocy, C.M. Cimarusti, *J. Am. Chem. Soc.*, **97** 5628 (1975). - B.P. Murphy, R.F. Pratt, *Biochem. J.* **256**, 669 (1988).