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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>

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To cite this Article Jaeggi, K. A. and Winkler, T.(1990) 'A Novel Rearrangement in the Series of *GEM*-Bisphos-Phonic Acids', Phosphorus, Sulfur, and Silicon and the Related Elements, 51: 1, 287

To link to this Article: DOI: 10.1080/10426509008040821

URL: <http://dx.doi.org/10.1080/10426509008040821>

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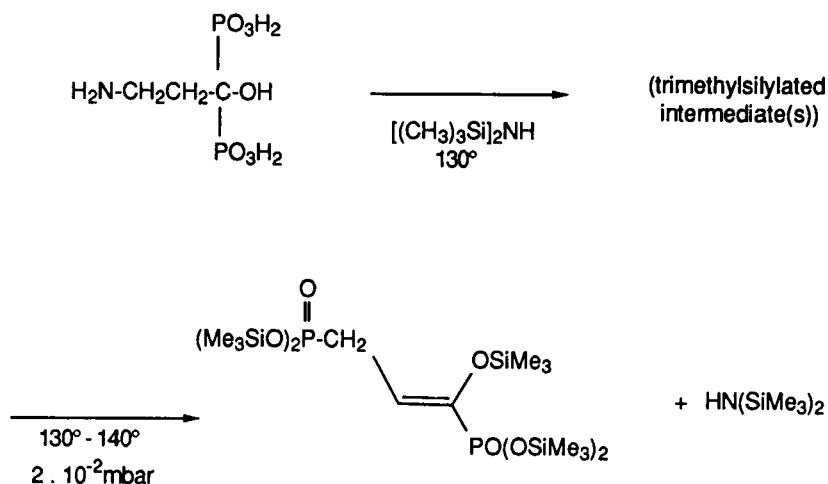
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A NOVEL REARRANGEMENT IN THE SERIES OF *GEM*-BISPHOSPHONIC ACIDS

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Some bisphosphonic acids containing basic side chain substituents are compounds of pharmaceutical interest which are undergoing clinical investigation as agents for the treatment of various bone diseases. 3-Amino-propane-1-hydroxy-1,1-bisphosphonic acid (pamidronic acid, APD) is a well known member of this series (1). When APD was subjected to trimethylsilylation and subsequent distillation at low pressure, a novel rearrangement was observed:



The main fraction of the distillation was an olefinic product identified as the E-isomer. No trace of the Z-olefin was observed.

The mechanism of this rearrangement may be rationalised by invoking a sequence of known reactions. Some bisphosphonic acids of similar structure were subjected to the rearrangement conditions in order to determine the scope. The olefinic product is easily accessible by the above procedure. It exhibits structural features of a polyvalent synthon which may be used for a variety of chemical reactions, e.g. the Wittig-Horner reaction. Some examples of the chemical reactivity of this compound are also described.

(1) F. Krueger, L. Bauer, W. Michel, Ger. Offen. 2 130 794 (Benckiser, J.A. GmbH)