

This article was downloaded by:

On: 28 January 2011

Access details: Access Details: Free Access

Publisher Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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>

Pathways for the Production of Pharmaceutical Grade Synthetic Phospholipids

D. J. Harris^a; E. R. Lee^a; C. S. Siegel^a; I. R. Davison^a; C. B. Jackson^a; R. D. Brown^a; J. Beaumont^a; H. C. Pinkard^a; R. Probst^{ab}; H. Eibl^{ac}

^a Genzyme Corp., One Kendall Square, Cambridge, MA, USA ^b Sygena LTD., Liestal, Switzerland ^c Max-Planck-Institut für Biophysikalische Chemie, Göttingen, FRG

To cite this Article Harris, D. J. , Lee, E. R. , Siegel, C. S. , Davison, I. R. , Jackson, C. B. , Brown, R. D. , Beaumont, J. , Pinkard, H. C. , Probst, R. and Eibl, H.(1996) 'Pathways for the Production of Pharmaceutical Grade Synthetic Phospholipids', Phosphorus, Sulfur, and Silicon and the Related Elements, 111: 1, 74

To link to this Article: DOI: 10.1080/10426509608054703

URL: <http://dx.doi.org/10.1080/10426509608054703>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

PATHWAYS FOR THE PRODUCTION OF PHARMACEUTICAL GRADE SYNTHETIC PHOSPHOLIPIDS

D. J. HARRIS, E. R. LEE, C. S. SIEGEL, I. R. DAVISON, C. B. JACKSON, R. D. BROWN, J. BEAUMONT, H. C. PINKARD, R. PROBST* AND H. EIBL.**
Genzyme Corp., One Kendall Square, Cambridge, MA 02139, USA, *Sygena LTD.,
Eichenweg 1, CH-4410 Liestal, Switzerland and **Max-Planck-Institut für
Biophysikalische Chemie, D-37077 Göttingen, FRG.

Abstract Two routes are described for the synthesis of pharmaceutical grade phospholipids at the multi-kilogram scale.

Key Words: phospholipid synthesis, biocatalytic synthesis, asymmetric synthesis

In the past, kilogram and multi-kilogram amounts of phospholipids were only available by isolation from natural sources. Recently, developments in synthetic phospholipid chemistry have resulted in the creation of effective methods for the large scale production of lipid and phospholipid molecules well defined in structure and configuration.

The Sygena route was based on the work of H. Eibl [1] with D-mannitol as the source of chirality. The intermediate diacylglycerols were phosphorylated with phosphorous oxychloride and the resulting diacylglycerolphosphorous oxydichlorides were converted to the respective phospholipids by reaction with different alcohols (or protected alcohols) such as choline, ethanolamine, glycerol etc.

Genzyme [2] has developed a route based on the biocatalytic enantioselective phosphorylation of glycerol by glycerol kinase to give sn-glycerol-3-phosphate. Sn-glycerol-3-phosphate was then converted to a variety of phosphatidic acids via acylation with fatty acid anhydrides. The respective phosphatidylcholines were prepared by a chemical phosphate esterification step. Mixed chain phosphatidylcholines were prepared by the phospholipase A2 catalyzed preparation of lyso-phosphatidylcholines followed by acylation with the appropriate fatty acid anhydride. Phospholipids with other head groups were prepared from phosphatidylcholines via phospholipase D catalyzed transesterification. Both the Sygena and Genzyme pathways are being used to prepare a range of pharmaceutical grade phospholipids at the multi-kilogram or greater scale.

REFERENCES

1. H. EIBL, *Chem. Phys. Lipids*, **26**, 405, (1980).
2. A. E. WALTS, D. G. SCHENA, M. FOX, J. T. DAVIS and M. R. MISCHKE, *Chirality in Industry* (John Wiley & Sons, New York, 1992), Chap. 10, pp. 223-235.