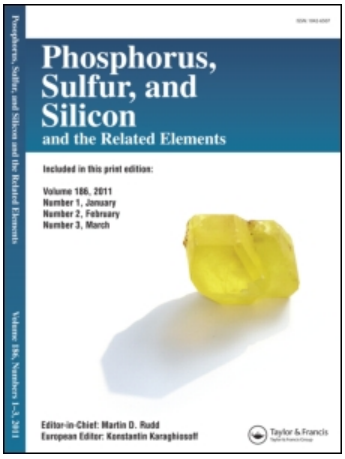


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Enzymatic Synthesis of Inositol Phosphodiesters Using Phosphatidylinositol-Specific Phospholipase C

Guan Zhiwen[a]; Karol S. Bruzik[a]
[a] Department of Medicinal Chemistry and Pharmacognosy, University of Illinois at Chicago, Chicago, IL

To cite this Article Zhiwen, Guan and Bruzik, Karol S.(1996) 'Enzymatic Synthesis of Inositol Phosphodiesters Using Phosphatidylinositol-Specific Phospholipase C', Phosphorus, Sulfur, and Silicon and the Related Elements, 111: 1, 69
To link to this Article: DOI: 10.1080/10426509608054698
URL: http://dx.doi.org/10.1080/10426509608054698

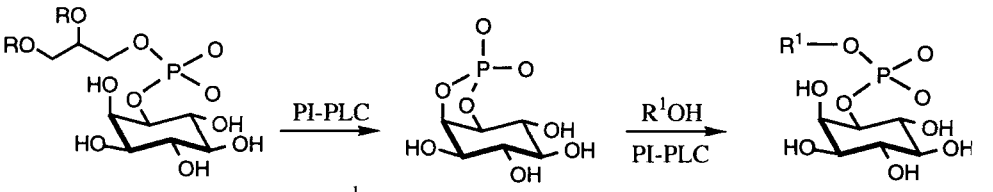
Phosphorus, Sulfur, and Silicon, 1996, Vol. 111, p. 69
Reprints available directly from the publisher
Photocopying permitted by license only

ENZYMATIC SYNTHESIS OF INOSITOL PHOSPHODIESTERS USING PHOSPHATIDYLINOSITOL-SPECIFIC PHOSPHOLIPASE C

GUAN ZHIWEN & KAROL S. BRUZIK*
Department of Medicinal Chemistry and Pharmacognosy, University of Illinois at Chicago, Chicago, IL 60612

Abstract Transesterication of inositol 1,2-cyclic phosphate with primary alcohols in the presence of phospholipase C produces alkyl inositol phosphates.

Cleavage of phosphatidylinositol (PI) by the specific phospholipase C (PI-PLC) produces inositol 1,2-cyclic phosphate (IcP) [1]. Bacterial PI-PLC further hydrolyze IcP into inositol 1-phosphate (IP) at low rates. We have found originally that incubation of IcP with PI-PLC in the presence of the Tris-HCl buffer and glycerol produced several by-products. These products were identified as acyclic diesters containing Tris and glycerol, respectively.



R = palmitoyl, R^1 = 1° alcohols, diols, aminoalcohols, alditols, serine

Application of other primary alcohols showed that this reaction is of a very general scope. Transesterification of IcP proceeded with a wide spectrum of alcohols such as primary alkanols and alkenols, diols, polyols and 2- and 3-amino alcohols, diacetyl glycerol and serine, but not with acyclic or cyclic secondary alcohols. The presence of the branching point at the carbon atom β- with respect to the hydroxyl group did not hamper the reaction. With polyols derived from monosaccharides only the primary hydroxyl groups participated, and the presence of inositol was inhibitory. The attempts at transesterification with long chain-, bromo-, epoxy- and mercapto- alcohols were unsuccessful. The reaction was completely nonstereospecific with respect to configuration of an alcohol, and thus both pro-*R* and pro-*S* hydroxyl groups of prochiral diols and *R*- and *S*-enantiomers of chiral diols reacted with equal rates. The obtained acyclic diesters undergo further transesterification in water to produce IcP. The final product of a prolonged incubation with PI-PLC was always IP, however, monitoring the reaction time courses by means of high performance anion exchange chromatography coupled with pulsed amperometric detection, or by ^{31}P NMR, allowed determination of the optimal point for stopping the transesterification process. The obtained yields were in the range 20-80% depending on the nature of an alcohol and its concentration. The starting IcP can be conveniently obtained in a single step by treatment of soybean phospholipid with small amounts of PI-PLC.

REFERENCES

1. For a review see K. S. Bruzik & M. -D. Tsai, Bioorg. Med. Chem. 2, 49 (1994).