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## Phosphorus, Sulfur, and Silicon and the Related Elements

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### The Synthesis of Chiral Myo-Inositol Trisphosphate Analogues

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## THE SYNTHESIS OF CHIRAL *MYO*-INOSITOL TRISPHOSPHATE ANALOGUES

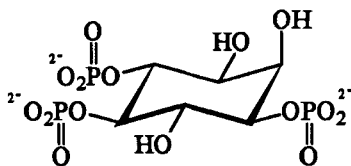
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 of Bath, Claverton Down, Bath BA2 7AY, UK.

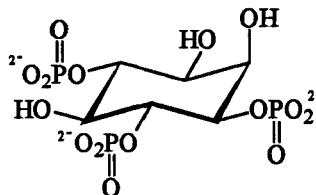
**Abstract** D- And L-Ins(1,4,6)P<sub>3</sub> and D-Ins(1,4,6)PS<sub>3</sub> were synthesised and evaluated for their ability to mobilise Ca<sup>2+</sup>.

D-*myo*-Inositol 1,4,5-trisphosphate [Ins(1,4,5)P<sub>3</sub>(1)] is a ubiquitous water soluble second messenger, which releases Ca<sup>2+</sup> from non-mitochondrial stores. It is generated by activation of GTP-binding proteins, which are coupled to phospholipase C-catalysed cleavage of the minor membrane lipid phosphatidylinositol 4,5-bisphosphate.

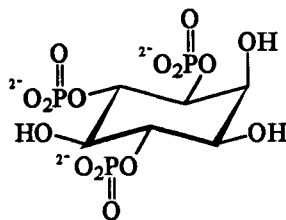
We have synthesised three chiral Ins(1,4,5)P<sub>3</sub> analogues. These include, D-Ins(1,4,6)P<sub>3</sub> (2), L-Ins(1,4,6)P<sub>3</sub> (3) and D-Ins(1,4,6)PS<sub>3</sub> (4). The latter (4) is a very low intrinsic partial agonist at the platelet Ins(1,4,5)P<sub>3</sub> receptor, releasing only 17% of the preloaded Ca<sup>2+</sup>. (2) Is a full agonist for Ca<sup>2+</sup> release, but (3) is essentially inactive.



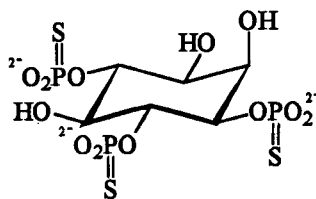
D-Ins(1,4,5)P<sub>3</sub> (1)



D-Ins(1,4,6)P<sub>3</sub> (2)



L-Ins(1,4,6)P<sub>3</sub> (3)



D-Ins(1,4,6)PS<sub>3</sub> (4)