STEREOSELECTIVE 1,2-ASYMMETRIC INDUCTION OF CHIRAL α-(METHOXYMETHYL)OXY CARBONYL COMPOUNDS. APPLICATION TO SYNTHESIS OF NATURAL PRODUCTS HAVING PYRROLIDINE RING

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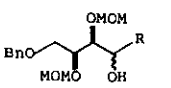
Biologically active natural products containing the pyrrolidine ring have been synthesized using 4-O-benzyl-2,3-O-bis(methoxymethyl)-L-threose (1), readily available from L-tartaric acid. The key feature of the synhtesis is 1,2-asymmetric induction of chiral α-(methoxymethyl)oxy carbonyl compounds based on α-chelation control.

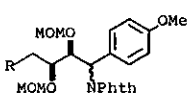
A diastereomeric mixture of the alcohols 2, derived from 1, was subjected to the Mitsunobu reaction, affording a 1:1 mixture of the syn and anti phthalimides 3. The less polar component, syn-3, was converted to the aldehyde 4 which on treatment with the Grignard reagent exclusively gave the threo alcohol 5. Transformation of 5 into (+)-codonopsinine (6) was achieved in 5 steps which established the absolute configuration of the natural product to be 2S,2R,4R,5R.

On the other hand, the L-threo-franose derivative 7, prepared by debenzylation of 1, was converted to the ketone 8, which afforded erythro-9 as a virtually sole product on reduction with zinc borohydride. Further steps resulted in the formation of deacetyl anisomycin which after N-protection underwent selective silylation to provide 10. The subsequent sequence involving acetylation-deprotection (two times) yielded optically pure (-)-anisomycine (11).



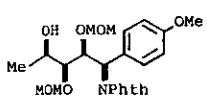
2 R = p-MeOC$_6$H$_5$

9 R = p-MeOC$_6$H$_4$CH$_2$



3 R = BnOCH$_2$

4 R = CHO



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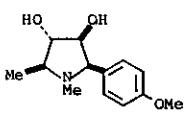

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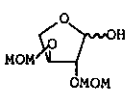

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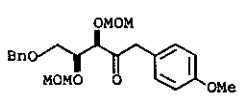

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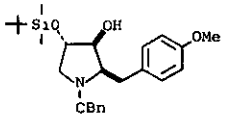

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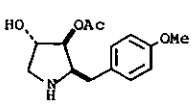

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