Pergamon

Tetrahedron, Vol. 53, No. 49, pp. 16747-16766, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)10101-6

Stereoselective synthesis of 6-deoxy and 3,6-dideoxy-D-*myo*-inositol precursors of deoxy-*myo*-inositol phosphate analogues from D-galactose

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Abstract : The synthesis of chiral protected D-6-deoxy-*myo*-inositol derivatives from D-galactose is described. Ferrier rearrangement of hexenogalactopyranosides has been employed to produce the corresponding 6-deoxy-cyclohexanone polyols. The stereoselectivity of the carbocyclic transformation was discussed on the basis of the experimental data and a mechanism has been proposed. From deoxy-inososes, the access to a variety of 6-deoxy and 3,6-dideoxy-*myo*-inositol was performed to prepare suitable monool, diol and triol precursors for the synthesis of D-deoxy-*myo*-inositol phosphate analogues. © 1997 Elsevier Science Ltd.

Receptor mediated turn-over of inositol phospholipids and inositol phosphates has generated considerable effort toward the elucidation of cellular signal transduction mechanisms.[1] It was established that the second messenger D-*myo*-inositol 1,4,5-trisphosphate [Ins(1,4,5)P_3] was deactivated *via* two different pathways:[2] a) subsequent dephosphorylations by 5-phosphatase and unspecific phosphatases leading to D-*myo*-inositol 1,4-bisphosphate [Ins(1,4)P_2] and D-*myo*-inositol 4-monophosphate [Ins(4)P], b) selective phosphorylation by 3-kinase leading to D-*myo*-inositol 1,3,4,5-tetrakisphosphate [Ins(1,3,4,5)P_4] which is subsequently degraded to D-*myo*-inositol 1,4,5-trisphosphate [Ins(1,3,4)P_3] and then phosphatases give several inositol diphosphates and monophosphates. After the characterization of phosphoinositide metabolites and associated enzymes involved in this process,[1-3] the synthesis of natural derivatives and various analogues were envisaged.[4] Reported synthetic studies have mostly employed the racemic *myo*-inositol as inexpensive starting material and required an optical resolution to produce chiral compounds. Specific enzyme inhibitors of phosphatases, kinases and phospholipase C, are interesting tools to understand and modulate the inositol phosphates turn-over. The crucial role of the phosphate ester positions 1, 3, 4 and 5 of the *myo*-inositol nucleus in the "second messengers" Ins(1,4,5)P_3 and Ins(1,3,4,5)P_4 is well documented. Therefore, for the elaboration of analogues, alterations or modifications to the hydroxyl functions in the vicinity of the phosphate positions involved in cellular process seemed attractive.[4,5] In this context, one of the promising targets was deoxy analogues of *myo*-inositol metabolites.

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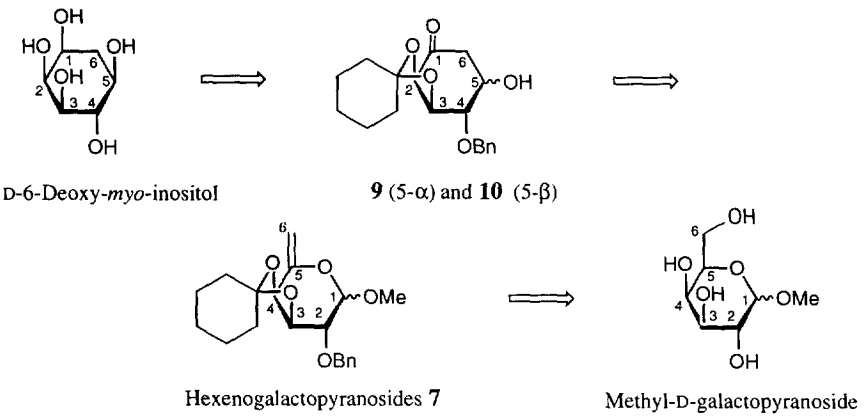
With this consideration in mind, we have initiated a synthetic program aimed at providing access to hitherto unknown protected deoxy-cyclitols, appropriate precursors of a variety of chiral deoxy-*myo*-inositol phosphates.

The two deoxy-inososes **9** and **10** were regarded as potential intermediates in our approach to deoxy-*myo*-inositol structures.[6] They could be obtained from hex-5-enopyranoside precursors **7** (α or β anomers), derived from methyl D-galactopyranoside, by the use of mercury(II) mediated carbohydrate-inosose Ferrier rearrangement[7] (**Retrosynthesis 1**).



Retrosynthesis 1

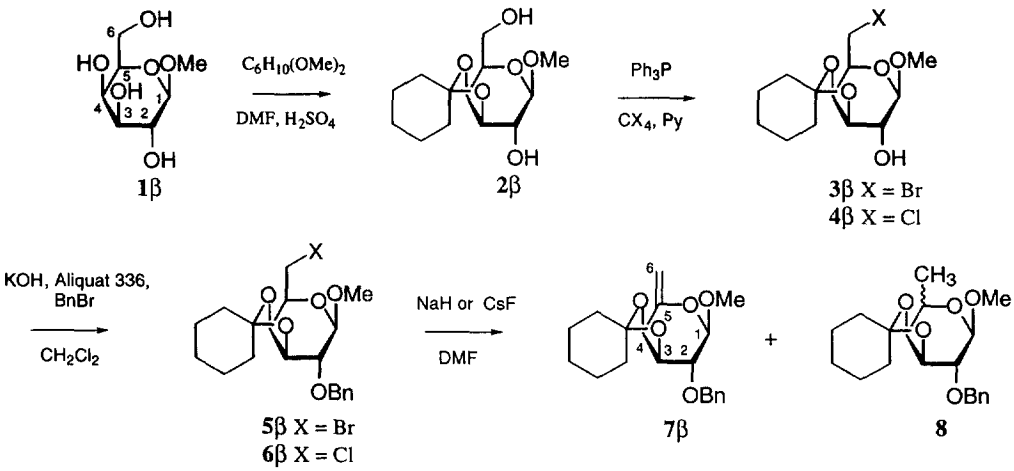
It was postulated that initial configurations at C_2, C_3 and C_4 centres of the galactopyranoside nucleus, corresponding to those at C_4, C_3 and C_2 respectively on the *myo*-inositol ring, will be retained during the carbocyclic transformation of the alkenes **7**. The introduction of two new stereogenic centres at the C_5 and C_1 positions of the carbocyclic inososes **9** and **10** would depend on the stereoselectivity of the hexenopyranoside rearrangements and on the subsequent reductions of the resulting exocyclic ketones respectively. For the synthesis of D-6-deoxy-*myo*-inositol nucleus an equatorial stereochemistry for the hydroxyl groups at C_1 and C_5 was required . While this work was under patent[8], further accounts of this strategy for the preparation of several other deoxy[9] and non deoxy[10] inositol phosphates have been reported from D-glucopyranoside.

RESULTS AND DISCUSSION

The synthesis of the hexenopyranoside derivatives **7** was carried out in an efficient four-step sequence from methyl D-galactopyranoside in 60% overall yield. As similar results were obtained starting from α or β anomers, the following discussion will be restricted to the preparation of olefin **7β** from the methyl β-D-galactopyranoside **1β** (**Scheme 1**).

Treatment of **1β** with 1,1-dimethoxycyclohexane in *N,N*-dimethylformamide (DMF) in the presence of a catalytic amount of sulfuric acid afforded the ketal **2β**.[11] Selective halogenation of the primary hydroxyl group using triphenylphosphine and carbon tetrabromide or carbon tetrachloride in pyridine[12] gave the bromide **3β** and the chloride **4β** in respectively 90% yields. Phase-transfer benzylation[13] of the halogenoalcohols **3β** and **4β** was performed in methylene chloride with benzyl bromide and benzyltriethylammonium chloride in the presence of solid potassium hydroxide affording the corresponding benzyl derivatives **5β** and **6β** respectively.

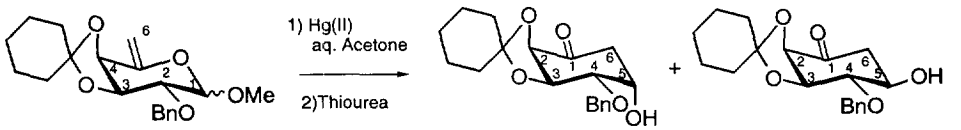
Initially, the access to the alkene **7β** was envisaged by dehydrohalogenation of compounds **5β** or **6β** using sodium hydride in DMF.[14] Under these conditions, the enol **7β** was produced in 90% yield from the bromo intermediate **5β**, however, the chloro derivative **6β** afforded a mixture of racemic 6-deoxy-galactopyranosides **8** isolated in 60% yield. Alternatively, **7β** could be obtained either from **5β** or **6β** in 85% yields by phase-transfer catalysis using caesium fluoride and benzyltriethylammonium chloride in DMF.[15]



Scheme 1

Following the similar reaction sequences, the anomeric hexopyranoside **7**α was isolated in the same overall yield from methyl α-D-galactopyranoside **1**α.

The carbocyclisation of the alkenes **7** (α or β) was attempted using the well known Ferrier reaction.[7,16] Unfortunately, under standard conditions [mercury(II) salt (1.1 eq.), acetone or dioxane-water (2:1), 40°C, 3 h.], **7** did not undergo the expected transformation. The metallic salt reacted efficiently with enol **7**, as monitored by TLC and ^{1}H NMR, but the subsequent ring closure of the resulting acyclic mercurial intermediates[17,18] seemed to be inhibited. This postulate was supported by a previous comment of Ferrier et al. who proposed the addition of hydrogen sulfide in the aqueous dioxane mercury solution to achieve at reflux the rearrangement of L-1,2;3,4-di-*O*-isopropylidene-6-deoxy-α-arabino-hex-5-enopyranose into the 2 (R)-(2,3/4,5)-2,3,4,5-tetrahydroxy-2,3-*O*-isopropylidene-cyclohexanone (40% yield).[19] In our case, the formation of the 6-deoxy-inososes **9** and **10** was achieved when the mercury aqueous-acetone solution of **7** was treated with an excess of thiourea (**Scheme 2**). The thio reagent was introduced in excess to the mixture (4 eq./**7**), at room temperature, 20 min. after the complete addition of the mercury (II) salt.



7 (α or β) **9** (5-α) **10** (5-β)

Scheme 2

When 1.1 eq./**7** of mercury(II) acetate was used, the efficient decomplexation of the organometallic complex intermediates[20] by thiourea, gave, in 70 % yield, a 3:1 mixture of the epimeric inososes **9** and **10** (see **table 1**, entry 1). No significant modification in the inososes ratio was observed using equal amounts of mercury sulphate, nitrate or chloride (entries 3, 5 and 7), whereas, the increase of organometallic salt concentration improved the formation of the 5-β epimer **10** (entries 2, 4, 6 and 8). At best, a 2/1 ratio of isomers **9** and **10** was obtained in 85 % yield using 1.7 eq. of mercury(II) chloride (entry 8). Under catalytic conditions, using mercury nitrate (0.1 eq. /**7**), the epimers **9** and **10** were also produced in the same ratio (entry 9). The use

of a larger amount of the mercury salt (entry 10), addition of sulphuric acid when catalytic conditions were used[21] (entry 11), or higher temperatures (entry 12), led to the partial hydrolysis of the ketal protecting group. Modifications of other experimental parameters such as dilution or changes in the nature of the metallic salt[22] were unable to improve the inososes ratio of the carbocyclic transformation (entries 13, 14 and 15).

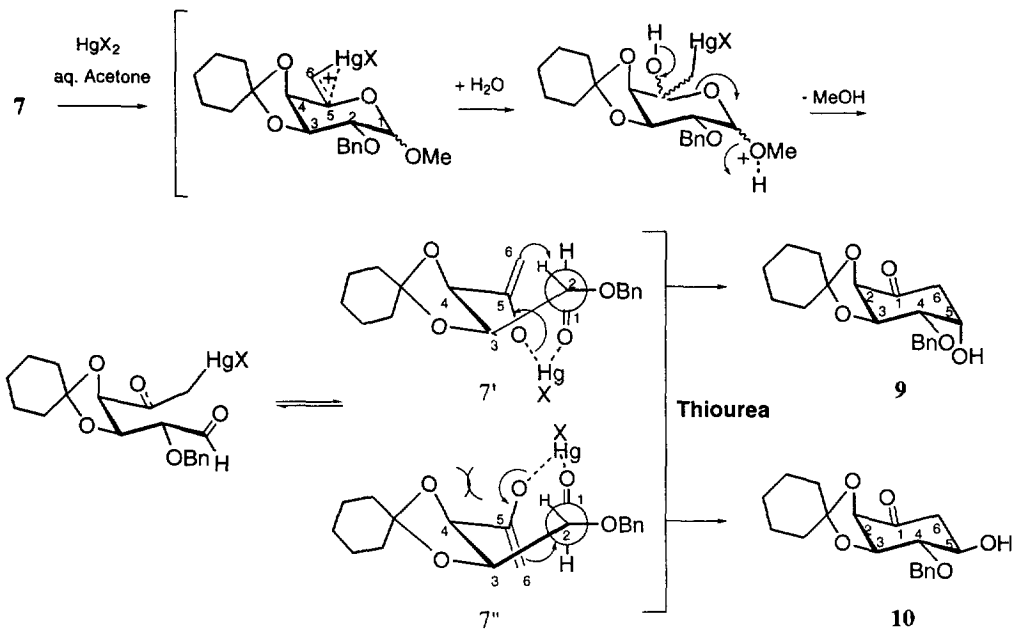
entry	metalic salt	eq./alkene **7**	T°C	% (**9**+**10**)	**9**(α) /**10** (β)
1	$Hg(OAc)_2$	1.1	25	70	3 / 1
2	$Hg(OAc)_2$	1.7	25	75	2 / 1
3	$HgSO_4$	1.1	25	65	3 / 1
4	$HgSO_4$	1.7	25	68	2 / 1
5	$Hg(NO_3)_2$	1.1	25	70	3 / 1
6	$Hg(NO_3)_2$	1.7	25	65	2 / 1
7	$HgCl_2$	1.1	25	75	3 / 1
8	$HgCl_2$	1.7	25	85	2 / 1
9	$Hg(NO_3)_2$	0.1 + HNO_3	25	75	2 / 1
10	$HgCl_2$	2	25	40	-
11	$HgCl_2$	0.2 + H_2SO_4	25	23	-
12	$HgCl_2$	1.7	reflux	18	-
13	$PdCl_2$	20%	25	-	-
14	$PdCl_2$	1,5	25	33	-
15	$NiCl_2$	20%	25	-	-

Table 1 : all experiments were run in aqueous/acetone 2/1 solution and the thiourea was introduced in excess 20 min. after the completion of the mercury salt addition.

Based on literature data and the related mechanism proposed by Machado et al.[18] for Ferrier rearrangements of hex-5-enopyranoside derivatives, the stereomer **9** (5-α) was expected to be the major (or the only) product of the transformation of **7** in a twist $^4C_1$ (D) conformation ($J_{H1\text{-}H2}$ = 2.6 Hz, $J_{H2\text{-}H3}$ = $J_{H3\text{-}H4}$ = 6.6 Hz for **7**α and $J_{H1\text{-}H2}$ = 7 Hz, $J_{H2\text{-}H3}$ = 6.5 Hz, $J_{H3\text{-}H4}$ = 6.6 Hz for **7**β).[18,21,23] The formation of the ketone **9** should result from the ring closure of the mercury enolate complex **7'** in thermodynamically favourable pseudo chair conformation (**Scheme 3**). Consequently, the presence of the epimer **10** should be predicted by the cyclisation of the less stable **7"** pseudo boat complex. The latter intermediates could derive from the ketoaldehyde precursor because of the extremely weak energy of the C-Hg bond. In our case, the presence of a cyclohexylidene substituent on the hexenopyranoside precursor should be taken into account to explain the unusual proportion of the 5-β epimer **10** obtained. The *syn-cis* aldolisation leading to **10** from the **7"** complex, occuring by the more hindered side of the C_4 chiral center, should be facilitated by a constriction ring at the transition state. The ketal group on **7** significantly affected the stereochemistry of the reaction as no 5-β inosose was reported from Ferrier rearrangement of methyl 2,3,4-tri-*O*-benzoyl-α-D-galacto-hex-5-enopyranoside analogue.[21]

Therefore, the minimization of the *cis* interaction between the C_4 and C_5 substituents on **7"** enolate derived from galactose structure, due to the presence of the ketal, should also influence the inososes ratio. The mercurial rearrangement of methyl 2,3,4-tri-*O*-benzyl-6-deoxy-α-D-xylo-hex-5-enopyranoside, reported by S. D. Gero et al.[23c], giving a 3/1 ratio of the corresponding inososes, could support this latter argument. Thus, the diaxal repulsion as a consequence of the equatorial configuration of the C_4 hydroxyl on the glucohexenopyranoside, should disfavour the mercurial precursor in pseudo-boat transition state and the obtention of a mixture of the both 5-epimers inososes could be anticipated.

Proposed mecanism for Ferrier rearrangement of the $^4C_1$ (D) hexenopyranosides **7**



Scheme 3

All these hypothesis correlate efficiently the inversion in the ketone ratio in favour of the 5-β stereomer during the Ferrier rearrangements of hexenopyranoside derivatives presenting a $^1C_4$ (D) conformation.[18,21,24]

Investigations by ^1H NMR (400MHz) to support the proposed reaction sequence were considered successful (**Fig 1**). The experiments were run in a D_2O:CD_3COCD_3 (2/1) solution of **7** (**Fig 1A**) and the ^1H NMR spectra were recorded after addition of 1.7 eq. of the mercury salt. The analysis of the spectrum reflected the hexenopyranoside ring transformation into the acyclic intermediates (**Fig 1B, 1C**), but the peak assigments remained too uncertain to identify unambiguously the proposed mercurial complex. Interestingly, the formation of the inososes **9** and **10** were clearly determined following the addition of thiourea (**Fig 1D, 1F** and **1G**). In the absence of this treatment, the ^1H NMR of the mixture showed two doublet signals at 2.45 and 2.75 ppm suggesting the presence of the keto aldehyde open chain organomercurial products which were unfortunatly unable to be properly purificated by chromatographic separation (**Fig 1E**). But, the absence of these corresponding signals in the ^1H NMR spectrum of the reactive intermediates even after 20 min. of experiment (**Fig 1C**) seemed to indicated that the cyclisation process is not initiated from keto aldehyde precursors and should support the existence of organomettalic enolate isomers.

How the concentration of mercury(II) salt affected the ratio of the rearrangement products from **7** was not clearly understood, apart from a participation in the complex stabilisation or in the pH of the medium. However, we believe that no predominent participation of the equatorial C_3 hydroxyl suggested by Làszlo et al.[25] is involved in the stereochemistry of the reaction. While the existence of a radical mechanism proposed by Kakinuma[26] leading to an sp^2 carbon cannot be completely ruled out at the final step of the reaction, the correlation between the stereoselectivity of the Ferrier reaction and the conformation of hexenopyranoside precursors would be not justified. Therefore, in our case, the role of the thiourea to achieve the mercury carbocyclisation of **7** would remain to be elucidated.

Fig **1** : ^{1}H-NMR (400 MHz) study of Ferrier rearrangement of compound 7α

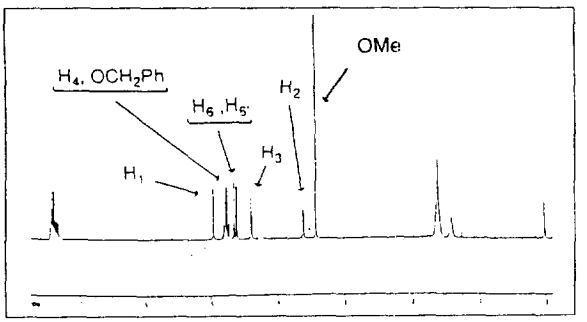
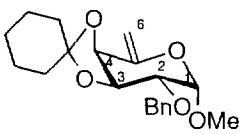


Fig **1A** : NMR structure of **7α**



$HgCl_2$

CD_3COCD_3
D_2O

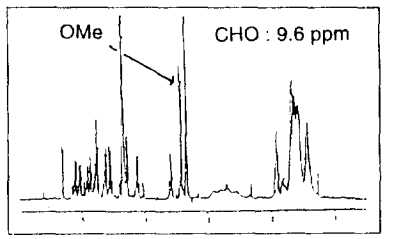


Fig **1B** : 3 mn after addition of $HgCl_2$

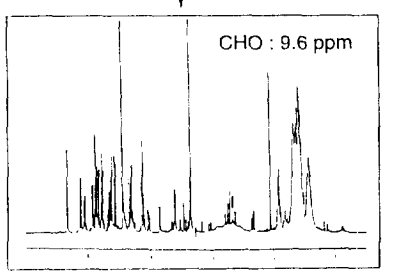


Fig **1C** : 20 mn after addition of $HgCl_2$

without thiourea treatment

evaporation to dryness and spectrum in $CDCl_3$

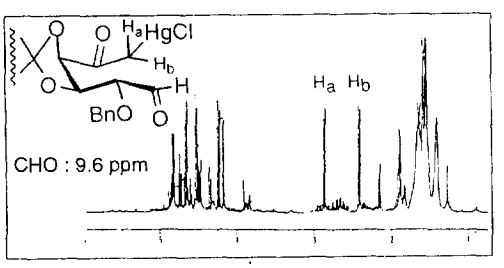


Fig **1E** : open-chain organomercurial intermediate

thiourea treatment

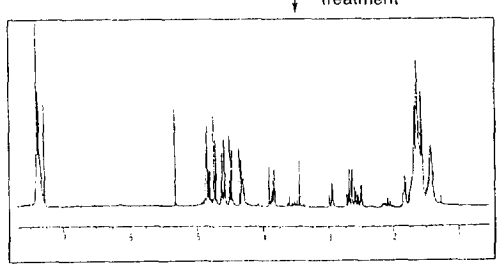
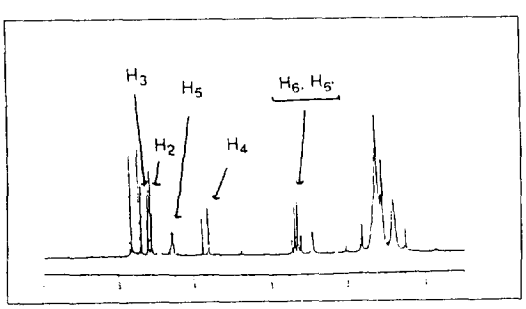


Fig **1D** : mixture of the ionososes **9** and **10**

purification



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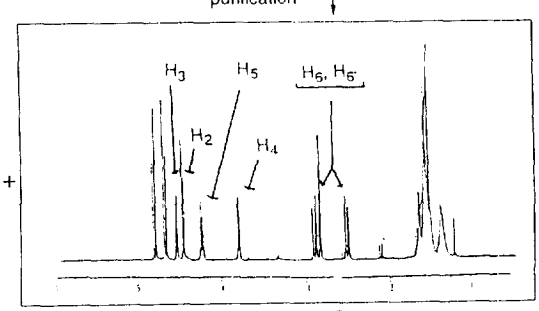


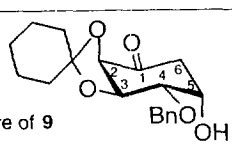


Fig **1F** : NMR structure of **9**

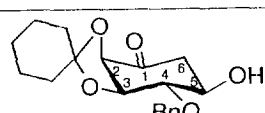
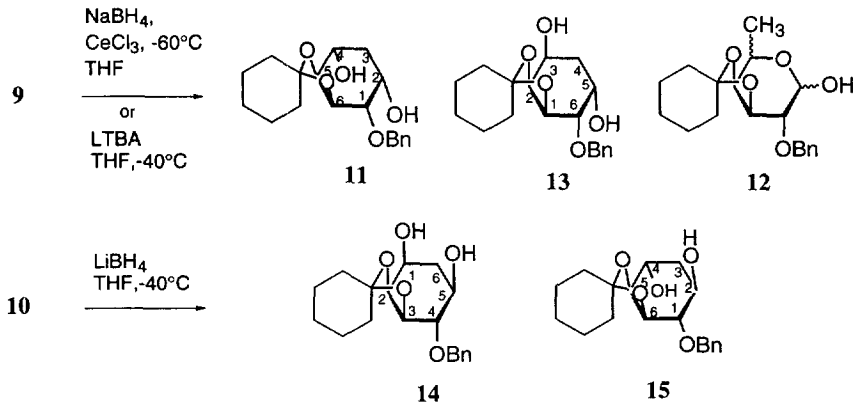


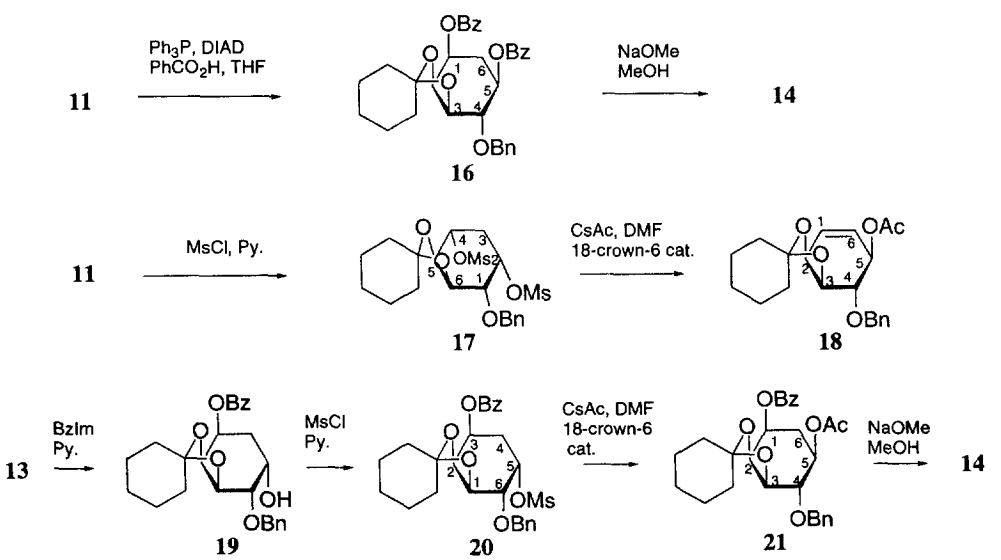
Fig **1G** : NMR structure of **10**

The stereoselective reduction of the ketones **9** and **10** was then under taken (**Scheme 4**). Cerium chloride ($CeCl_3$) mediated sodium borohydride reduction[27] of **9** in THF at -60°C resulted in the formation of L-1-*O*-benzyl-5,6-*O*-cyclohexylidene-3-deoxy-*chiro*-inositol **11** and D-6-*O*-benzyl-1,2-*O*-cyclohexylidene-4-deoxy-*neo*-inositol **13** in 68% and 16% yields respectively. Following similar experimental conditions, run at room temperature in methanol, **9** furnished a mixture of **11** and racemic retroaldols **12** isolated in 29% and 60% yields respectively. The use of hindered reagents such as lithium tri-terbutoxylaluminiumhydride, in THF at -40°C, gave a 3/1 ratio of deoxy-*chiro*- and deoxy-*neo*- inositols **11** and **13** obtained in 90% yields from **9**.



Scheme 4

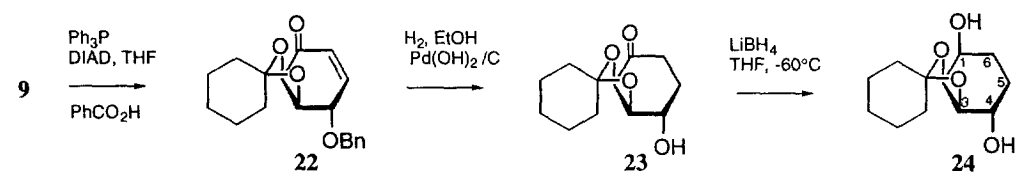
On the other hand, the 6-deoxy-inosose **10** was stereoselectively[28] reduced in 85% yield, with lithium borohydride in THF at -40°C, to give the D-4-*O*-benzyl-2,3-*O*-cyclohexylidene-6-deoxy-*myo*-inositol **14**. Attempts to produce **14** in better yield using various hydride reagents induced the unsuitable formation of the epimeric diol **15**.



Scheme 5

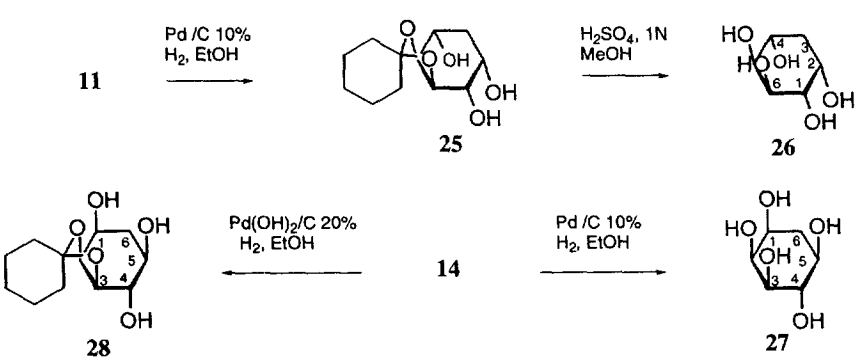
The transformation of the deoxy-cyclitols **11** and **13** into the epimeric 6-deoxy-*myo*-inositol **14** by the Mitsunobu epimerisation method[29] seemed attractive to improve the efficiency of our synthetic sequence (**Scheme 5**). The treatment of the diol **11** in THF with triphenylphosphine, benzoic acid and diisopropylazodicarboxylate (DIAD) under inert atmosphere yielded the 1,5-di-*O*-benzoyl-*myo*-inositol **16** in 70% yield. The transesterification of the latter with a catalytic amount of sodium methoxide in methanol led to the corresponding protected 6-deoxy-*myo*-inositol **14** in quantitative yield. Significant decrease in the yield of this double hydroxyl inversion on larger scale reaction[30] prompted us to consider an alternative approach *via* the 2,4-di-*O*-mesyl-*chiro*-inositol **17** easily produce from **11**. Unfortunately, the treatment of **17** in DMF with caesium acetate, in the presence of catalytic quantity of 18-crown-6,[31] mainly afforded the conduritol **18**. However, the efficient selective epimerisation with a similar procedure of the 3-*O*-benzoyl-5-*O*-mesylate **20**, prepared in two steps from the diol **13**, resulted in the formation of the 6-deoxy-*myo*-inositol **21** in 90% yield. Removal of the ester groups on **21** under basic conditions gave the target 6-deoxy-*myo*-inositol **14**.

The transformation of the ketone **9** (5-α) into the inosose **10** (5-β) was also envisaged using the Mitsunobu procedure. Despite the formation of **10**, in similar epimerisation conditions previously discussed, the cyclohexenone **22** was formed in 70% yield from **9** (**Scheme 6**). The selective reduction of **22**, under catalytic hydrogenation, afforded the 5,6-dideoxy-inosose **23** in 92% yield. Compound **23** was then stereoselectively converted to the corresponding 5,6-dideoxy-*myo*-inositol **24** in 85% yield using lithium borohydride in THF at -60°C. The diol **24** appeared to be a suitable precursor for the synthesis of 5,6-dideoxy-*myo*-inositol 1-mono and 1,4-bisphosphate analogues.



Scheme 6

As a result of our investigations, 6-deoxy-*myo*-inositol diol derivatives became available with stereocontrol from both inososes **9** and **10**. The selective deprotection of the cyclitols gave the access to a variety of D-6-deoxy-inositol 1,4,5-triols which are key intermediates for the synthesis of deoxy-inositol 1,4,5-trisphosphate analogues (**Scheme 7**). The hydrogenolysis of compound **11** using Pd/C 10% in ethanol (3.5 p.s.i) furnished the crystalline triol **25** in 97% yield. Complete deprotection of **25** by acidic hydrolysis gave the cyclohexane pentol **26**. Surprisingly under the same hydrogenation conditions, the diol **14** afforded the D-6-deoxy-*myo*-inositol pentol **27** in 90% yield. However, the treatment of **14** with $Pd(OH)_2/C$ 20% (Pearlman's catalyst) yielded the expected crystalline D-6-deoxy-*myo*-inositol 1,4,5-triol **28** in 95% yield.



Scheme 7

The structure of the cyclohexanols **14** and **25** were rigourously established by X-ray diffraction.[32] Compound **14** adopted a conventional $^4C_1$ (D) twist chair conformation, at solid state, but surprisingly, the cyclohexane triol **25** was organized as an unusual dimer crystal (**fig 2**). One of the monomers presents a $^4C_1$ (D) twist chair conformation associated with the second partner in a twist boat form. This original phenomena should be the consequence to the *cis*-configurations of the C_1 and C_4 hydroxyls and the ring constriction induced by the cyclohexylidene on the cyclitol.

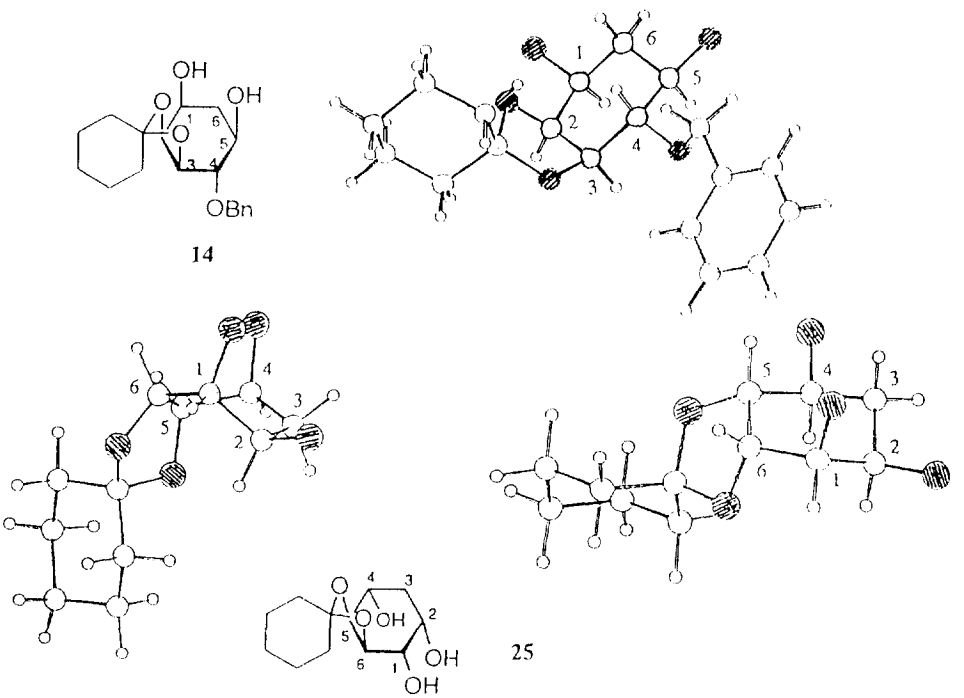
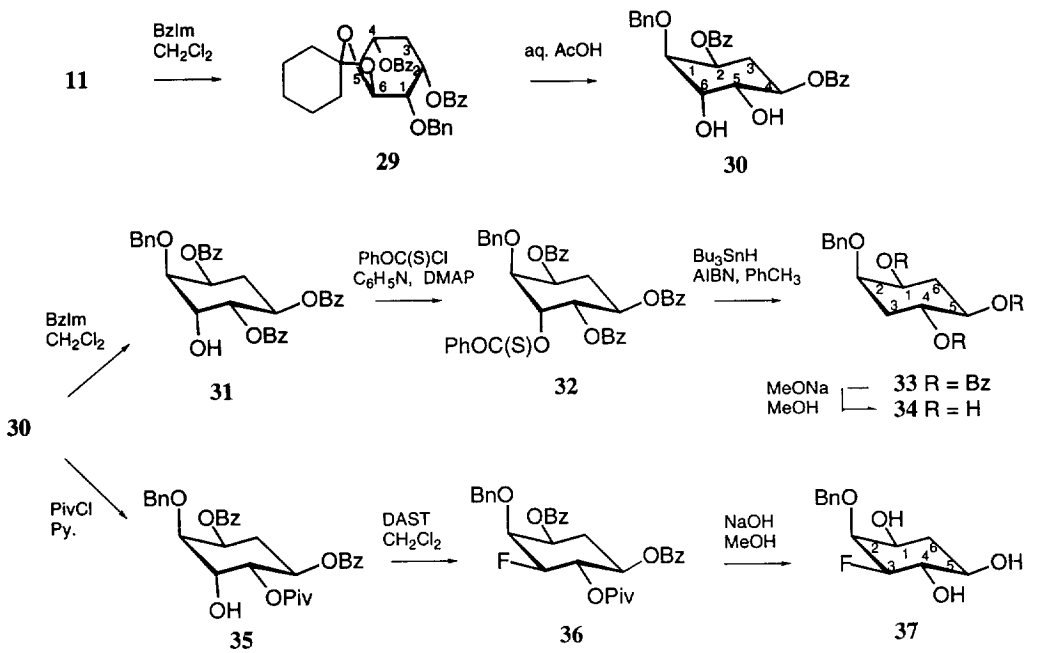


Figure 2 : O.R.T.E P. of cyclitols **14** and **25**.

We have extended our investigations to the preparation of two other dideoxy-cyclitols, 3,6-dideoxy and 3,6-dideoxy-3-fluoro-*myo*-inositols **33** and **37**, anticipating the influence of the deoxygenated position on the biological activity of the corresponding deoxy-inositol phosphate derivatives. Access to the analogues **33** and **37** was proposed from the diol precursor **30** (**Scheme 8**).

Benzoylation of the *chiro*-inositol **11** gave the dibenzoate **29** in 90% yield. Removal of the ketal on **29** led to the vicinal diol **30**. The selective esterification of the equatorial hydroxyl was performed in 78% yield using benzoylimidazole reagent (Bzlm). Deoxygenation of the resulting free hydroxyl position of **31** was possible following the Barton procedure *via* the thionoformate **32**.[33] The dideoxy-cyclitol **33** was isolated in 50% overall yield from **31**. Final deprotection of **33** with sodium methoxide in methanol, furnished the D-2-O-benzyl-3,6-dideoxy-*myo*-inositol 1,4,5-triol **34** in 70% yield.



Scheme 8

The D-3,6-dideoxy-3-fluoro-*myo*-inositol analogue **37** was synthetised in 60% overall yield from **30**. The pivaloyl intermediate **35**, obtained in 85% yield by selective esterification of the diol **30** using pivaloyl chloride in pyridine, was treated with the diethylaminosulphur trifluoride (DAST) to give the 3-fluoro-*myo*-inositol **36** in 70% yield. The saponification of the latter compound, achieved in 95% yield, led to the 2-O-protected 1,4,5-triol **37**.

CONCLUSION

D-6-deoxy-*myo*-inositol cyclitols are syntheticaly stereoselectively accesible from D-galactose. A key-step in the strategy was the Ferrier rearrangement of hexenogalactopyranoside derivates which yielded the corresponding 6-deoxy-cyclohexanones. The mercury (II) carbocyclic transformation of the alkenes **7** leading to the epimeric 6-deoxy-inososes **9** and **10**, was achieved by the decomplexation of the mercury enolate complexes by thiourea. The existence of stable acyclic intermediates was proposed following a mechanism taking into account the stereochemistry of the carbocyclisation. The preparation of D-6-deoxy-*myo*-inositol ring was then investigated from both cyclohexanones **9** and **10**. The strereoselective reductions of these ketones afforded a variety of isomeric protected 6-deoxy-cyclitols. The cyclohexane polyols derived from **9** were converted to the *myo*-inositol configuration by selective hydroxyl epimerisations.

The 6-deoxy-diols **14** and **24** have been considered for the synthesis of 6-deoxy analogues of *myo*-inositol 1-mono and 1,4-bisphosphates. The cyclohexane 1,4,5-triols **28, 34** and **37** are suitable precursors of D-6-deoxy and 3,6-dideoxy-*myo*-inositol 1,4,5-trisphosphate analogues. The phosphorylation procedures and their use to produce numbers of *myo*-inositol polyphosphates, phosphonates and phosphatidyl analogues will be presented in the next full paper. The biological activity of the deoxy-*myo*-inositol metabolites and thus of further isomers will also be revealed.

Acknowledgements : This work was funding by Bayer-AG Geschäftsbereich Pharma und Entwicklung Institut. Thanks to Drs. J. Lebreton and A. Guingant for faithful discussions.

EXPERIMENTAL PART

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker spectrometra WP 200, AC 200, AC 250, WM 400 or ARX 400 ; chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform (7.27 ppm). Coupling constants (J) are given in hertz (Hz). Multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet or complex). The $[\alpha]_D$ were recorded on Perkin-Elmer 241-MC sodium absorbtion at 20°C. Mass spectra (m/z (% base peak) were recorded on Atlas CH_4 or AEI MS9 spectrometra. Melting points were determined on a C. REICHERT microscope apparatus and are uncorrected. Elemental analyses were carried out at the "Laboratoire de Microanalyse de l'I.C.S.N." (CNRS, gif/yvette). All solvents were freshly distilled prior to use by standard methods[34]. Flash chromatography was performed on silica-gel Merck 60 230-400 mesh. Thin layer chromatography was performed on precoated plates of silica gel PF_{254} neutralised with sodium bicarbonate.

Methyl 3,4-*O*-cyclohexylidene-β-D-galactopyranoside 2β

A solution of methyl β-D-galactopyranoside **1β** (10 g, 51 mmol), 1,1-dimethoxycyclohexane (13 ml) and H_2SO_4 1M (0.7 ml) in dry DMF (40 ml) was stirred for 12h. at r.t.. $NaHCO_3$ (4 g) was added. The mixture was stirred for a further 2h. before being filtered through a pad of silicagel and the solid washed with AcOEt. The filtrate was evaporated to dryness and the residue was crystallized (AcOEt, hexane) to give white crystals of **2** (12.7 g, 90%); m.p. 120-121°C, $[\alpha]_D$ + 82° (c = 0.88, CH_3OH); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 4.20-4.00 (4H, m, H-1, H-3, H-5, H-6); 3.88 (2H, m, H-2, H-6'); 3.57 (3H, s, OCH_3); 3.53 (1H, m, H-4); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 111.1 (ketal); 103.4 (C-1); 78.7 (C-3); 74.1, 73.7, 73.6 (C-4, C-2, C-5); 62.6 (C-6); 57.1 (OCH_3); (Found C, 53.48; H, 8.0; $C_{13}H_{22}O_6$, 1/2 H_2O requires C, 53.40; H, 8.28%).

Methyl 3,4-*O*-cyclohexylidene-α-D-galactopyranoside 2α

Prepared by the same method from methyl α-D-galactopyranoside; syrup, $[\alpha]_D$ + 25° (c = 1.1, CH_3OH); ^1H NMR (400 MHz, $CDCl_3$) δ ppm : 4.75 (1H, d, J_{1-2}=3.7, H-1); 4.22 (1H, s, H-3); 4.00 (1H, d, J_{4-5}=1.7 H-4); 4.04 (1H, m, J_{5-4}=1.7, $J_{5-6'}$=4.2, J_{5-6}=6, H-5); 3.90 (2H, m, $J_{6-6'}$=11.7, H-6, H-6'); 3.80 (1H, m, H-2); 3.42 (3H, s, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 110.5 (ketal); 98.9 (C-1); 76.1 (C-3); 73.7 (C-4); 70.1 (C-2); 68.0 (C-5); 62.8 (C-6); 55.6 (OCH_3); (Found : C, 56.85; H, 8.17; $C_{13}H_{22}O_6$ requires C, 56.92; H, 8.08%).

Methyl 6-bromo-3,4-*O*-cyclohexylidene-6-deoxy-β-D-galactopyranoside 3β

PPh_3 (18 g, 70 mmol) then CBr_4 (18 g, 55 mmol) were added to a stirred solution of **2β** (13.7 g, 50 mmol) in dry pyridine (130 ml). The solution was stirred for 6h. at 60°C then cooled to r.t. before addition of MeOH (20 ml). Evaporation of solvent under reduced pressure gave a brown residue which was submitted to flash chromatography on silicagel. The bromide **3β** (13.5 g, 80%) was crystallized (AcOEt, hexane); m.p. 122-123°C; $[\alpha]_D$ + 21° (c = 1.01, CH_3OH); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 4.28 (1H, dd, J_{4-5}=1.7, J_{4-3}=5.5, H-4); 4.10 (1H, d, J_{1-2}=5.4, H-1); 4.08 (1H, m, H-3); 3.96 (1H, m, H-5); 3.64 (2H, m, H-6, H-6'); 3.56 (3H, s, OCH_3); 3.53 (1H, m, J_{2-1}=5.4, H-2); 1.70-1.40 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 111.0 (ketal); 103.3 (C-1); 78.4 (C-3); 73.9, 73.4, 73.0 (C-4, C-2, C-5); 57.0 (OCH_3); (Found : C, 46.16; H, 6.11; Br, 23.55. $C_{13}H_{21}BrO_5$ requires C, 46.29; H, 6.28; Br, 23.70%).

Methyl 6-bromo-3,4-*O*-cyclohexylidene-6-deoxy-α-D-galactopyranoside 3α

Prepared from **2α** as described for **3β**; syrup, $[\alpha]_D$ + 30° (c = 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ ppm : 4.77 (1H, d, J_{1-2}=3.9, H-1); 4.28 (1H, d, J_{4-5}=1.4, H-4); 4.27 (1H, s, H-3); 4.16 (1H, m, J_{5-4}=1.4, $J_{5-6'}$=5.7, J_{5-6}=7.5, H-5); 3.86 (1H, m, H-2); 3.59 (1H, dd, J_{6-5}=5.7, $J_{6-6'}$=10.4, H-6); 3.53 (1H, dd, $J_{6'-5}$=7.5, $J_{6-6'}$=10.4, H-6'); 3.50 (3H, s, OCH_3); 1.70-1.30 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 110.4 (ketal); 98.4 (C-1); 75.5 (C-3); 72.7 (C-4); 69.2, (C-2), 68.9 (C-5); 55.5 (OCH_3); (Found : C, 46.30; H, 6.15; Br, 23.86. $C_{13}H_{21}BrO_5$ requires C, 46.29; H, 6.28; Br, 23.70%).

Methyl 6-chloro-3,4-*O*-cyclohexylidene-6-deoxy-β-D-galactopyranoside 4β

PPh_3 (3 g, 35 mmol) and CBr_4 (15.4 g, 100 mmol) were added to stirred solution of **2β** (6.80 g, 25 mmol) in dry pyridine (60 ml). The mixture was maintained at 60°C for 8h. then cooled to r.t.. Evaporation of solvent under reduced pressure gave a residue submitted to flash chromatography on silicagel. The chloride **4β** was crystallized (AcOEt, hexane) (6.5 g, 90%); m.p. 100-101°C; $[\alpha]_D$ + 15 (c = 0.97, CH_3OH); ^1H NMR (200 MHz, $CDCl_3$) δ ppm: 4.27 (1H dd, J_{4-5}=1.2, J_{4-3}=4.3, H-4); 4.11 (1H, d, J_{1-2}=4.1, H-1); 4.04 (1H, m, H-3); 3.96 (1H, m, H-5); 3.7 (2H, m, H-6,H-6'); 3.56 (3H, s, OCH_3); 3.5 (1H, m, H-2); 1.70-1.30 (10H, m, C_6H_{10}); (Found : C, 53.50; H, 7.21; Cl, 12.10; $C_{13}H_{21}O_5Cl$ requires C, 53.33; H, 7.23; Cl, 12.11%).

Methyl 2-*O*-benzyl-6-bromo-3,4-*O*-cyclohexylidene-6-deoxy-β-D-galactopyranoside 5β

The bromide **3β** (13.5 g, 40 mmol) was dissolved in dry CH_2Cl_2 (200 ml). Powdered KOH (10 g, 178 mmol) and benzyltrimethylammonium chloride (1 g, 3.6 mmol) were added and the solution was vigorously stirred for 10 min. before addition of BnBr (10 ml, 84 mmol). After 12h., MeOH (10 ml) was added and stirring maintained for a additional hour. The solid salts were removed by filtration through a pad of celite. The filtrate was evaporated to dryness and the residue submitted to flash chromatography. Crystallization from hexane gave the product **5β** (13.7 g, 90%); m.p. 94-95°C; $[\alpha]_D$ + 46° (c = 1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 7.60-7.20 (5H, m, Ph); 5.00 (2H, m, CH_2Ph); 4.43 (1H, d, J_{1-2}=6.2, H-1); 4.40 (1H, dd, J_{4-3}=5.3, J_{4-5}=2.5, H-4); 4.33 (1H, dd, J_{3-4}=5.3, J_{3-2}=5, H-3); 4.06 (1H, m, H-5); 3.76 (2H, m, H-6, H-6'); 3.70 (3H, s, OCH_3); 3.53 (1H, dd, J_{2-1}=6.2, J_{2-3}=5, H-2); 1.70-1.20 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 110.7 (ketal); 104.0 (C-1); 79.7, 78.6, 78.0 (C-2, C-3, C-5); 73.5, 73.2 (OCH_2Ph), C-4); (Found : C, 56.33; H, 6.21; Br, 18.65. $C_{20}H_{27}BrO_5$ requires C, 56.21; H, 6.37; Br, 18.70%).

Methyl 2-*O*-benzyl-6-bromo-3,4-*O*-cyclohexylidene-6-deoxy-α-D-galactopyranoside 5α

Prepared from **3α** as described for **5β**; $[\alpha]_D$ + 50° (c = 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ ppm : 7.25-7.37 (5H, m, Ph); 4.72 and 4.82 (2H, 2d, CH_2Ph); 4.66 (1H, d, J_{1-2}=3.5, H-1); 4.35 (1H, dd, J_{3-4}=5.5, J_{3-2}=7.7, H-3); 4.25 (1H, dd, J_{4-5}=2.5, J_{4-3}=5.5, H-4); 4.12 (1H, m, J_{5-4}=2.5, $J_{5-6'}$=7.9, J_{5-6}=5.8, H-5); 3.53 (1H, dd, J_{6-5}=5.8, $J_{6-6'}$=10.5, H-6); 3.59 (1H, dd, $J_{6'-5}$=7.9, $J_{6-6'}$=10.5, H-6'); 3.50 (1H, dd. J_{2-1}=3.5 and J_{2-3}=7.7, H-2); 3.39 (3H, s, OCH_3); 1.70-1.20 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 110.0 (ketal); 98.6 (C-1); 76.4, 75;8 (C-2, C-3); 73.3, 72.5 (C-4, CH_2Ph); 68.0 (C-5); 55.7 (OCH_3); 30.6 (C-6); (Found : C, 56.32; H, 6.12; Br, 18.42. $C_{20}H_{27}BrO_5$ requires C, 56.21; H, 6.37; Br, 18.70%).

Methyl 2-*O*-benzyl-6-chloro-3,4-*O*-cyclohexylidene-6-deoxy-β-D-galactopyranoside 6β

6β was prepared from **4β** as described for preparation of **5β** from **3β**; m.p. 97-98°C; $[\alpha]_D$ + 38° (c = 1.23, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ ppm: 4.75 (2H, m, CH_2Ph); 4.63 (1H, d, J_{1-2}=5.9, H-1); 4.33 (1H, dd, J_{3-4}=5.5, J_{3-2}=7.5, H-3); 4.22 (1H, dd, J_{4-3}=5.5, J_{4-5}=2.6, H-4); 4.10 (1H, m, J_{5-4}=2.6, J_{5-6}=5.8, $J_{5-6'}$=8, H-5); 3.56 (2H, m, H-6, H-6'); 3.50 (1H, dd, J_{2-3}=7.5, J_{2-1}=5.9, H-2); 3.40 (3H, s, OCH_3); 1.70-1.20 (10H, m, C_6H_{10}); (Found : C, 62.83; H, 7.25; Cl, 9.55, $C_{20}H_{27}O_5Cl$ requires C, 62.73; H, 7.11; Cl, 9.26%).

Methyl L-2-*O*-benzyl-3,4-*O*-cyclohexylidene-6-deoxy-β-arabino-hex-5-enopyranoside 7β

a) 95% NaH (750 mg, 60 mmol) was added to a stirred solution of bromide **5β** (8.54 g, 20 mmol) in dry DMF (40 ml) . The suspension was stirred at 110°C during 3h. under argon. After cooling to r.t., MeOH (2 ml) was added. The mixture was diluted with water and extracted twice with CH_2Cl_2. The organic layer was washed with water, dried ($MgSO_4$) and evaporated to dryness. The residue was purified by chromatography on silicagel to give the olefin **7β** crystallized from pentane (6.2 g, 80% yield); m.p. 61-62°C; $[\alpha]_D$ - 55° (c = 1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 7.60-7.20 (5H, m, Ph); 4.67 (2H, m, CH_2Ph); 4.65 (2H, d, $J_{6-6'}$=12.7, H-6, H-6'); 4.60 (1H, d, J_{1-2}=7, H-1); 4.54 (1H, d, J_{4-3}=6.5, H-4); 4.20 (1H, dd, J_{3-4}=6.5, J_{3-2}=6.6, H-3); 3.50 (1H, dd, J_{2-1}=7, J_{2-3}=6.6, H-2); 3.47 (3H, s, OMe); 1.70-1.20 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 145.3 (C-5); 111.4 (ketal); 102.4 (C-1); 97.9 (C-6); 78.1 (C-2);

76.9 (C-3); 73.2, 72.4 (CH_2Ph, C-4); 56.3 (OCH_3); (Found : C, 56.33; H, 6.21; Br, 18.65; $C_{20}H_{27}BrO_5$ requires C, 56.21; H, 6.37; Br, 18.70%).

b) A mixture of **5β** (4.6 g, 10.8 mmol), dry CsF (3.3 g, 21.6 mmol), and benzyltriethylammonium chloride (492 mg, 2.16 mmol) dissolved in dry DMF (5 ml) was stirred for 4h. at 110°C. The cold solution was diluted with water and extracted twice with CH_2Cl_2. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The olefin **7β** was crystallized from pentane (3.2 g, 85%).

c) 95% NaH (94 mg, 3.9 mmol) was added under argon to a solution of chloride **6β** (500 mg, 1.3 mmol) in dry DMF (5 ml). The suspension was stirred for 3h. at 110°C. After cooling to r.t. and addition of MeOH (0.5 ml), the mixture was diluted with water and then extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was separated by chromatography on silicagel. The first eluted product was the retroaldol compound **8** isolated in 60% yield. Then the olefin **7β** (135 mg, 30%) was isolated.

Methyl L-2-*O*-benzyl-3,4-*O*-cyclohexylidene-6-deoxy-α-arabino-hex-5-enopyranoside 7α

Prepared from **5α** as described for **7β**; syrup, $[\alpha]_D$ - 42° (c = 1.09, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ ppm : 7.60-7.20 (5H, m, Ph); 4.80 (1H, d, J_{1-2}=2.6, H-1); 4.84 and 4.71 (2H, 2d, CH_2Ph); 4.74 (1H, d, J_{4-3}=6.6, H-4); 4.62 (2H, d, $J_{6-6'}$=12.8, H-6, H-6'); 4.43 (1H, dd, J_{3-4}=6.6, J_{3-2}=6.6, H-3); 3.50 (1H, dd, J_{2-1}=2.6, J_{2-3}=6.6, H-2); 3.43 (3H, s, OCH_3); 1.65-1.40 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 153.5 (C-5); 111.0 (ketal); 99.2 (C-1); 95.6 (C-6); 77.1, 76.0 (C-2, C-3); 72.4 (C-4), 72.1 (CH_2Ph); 56.0 (OCH_3); (Found : C, 69.32; H, 7.29; $C_{20}H_{26}O_5$ requires C, 69.34; H, 7.57%).

L-1-*O*-benzyl-5,6-*O*-cyclohexylidene-3-deoxy-*chiro*-4-inosose 9 [(2R)-(2,3/4,5)-2,3-dihydroxy-4-benzyloxy-2,3-O-cyclohexylidenecyclohexanone] and D-4-*O*-benzyl-2,3-*O*-cyclohexylidene-6-deoxy-*myo*-1-inosose 10 [(2R)-(2,3,5/4)-2,3-dihydroxy-4-benzyloxy-2,3-*O*-cyclohexylidenecyclohexanone]

a) With mercury (II) chloride : alkene **7β** (500 mg, 1.44 mmol) was dissolved in a mixture of CH_3COCH_3:water (2:1, 18 ml). $HgCl_2$ (665 mg, 2.45 mmol) was added whith stirring over a 20 min. period before addition of thiourea (745 mg). After 2h., the mixture was filtrated through celite, washed with CH_3COCH_3 and the filtrate was concentrated under reduced pressure. The residue was then extracted with AcOEt (four times). The organic layers were combined, dried ($MgSO_4$) and evaporated to dryness. The ketones **9** and **10** were separated by chromatography on silicagel. Ketone **9** was eluted first (204 mg, 42.6%); syrup, $[\alpha]_D$ + 10° (c = 1.03, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ ppm : 7.35 (5H, m, Ph); 4.84 and 4.71 (2H, 2d, CH_2Ph); 4.61 (1H, dd, J_{3-2}=6.9, J_{3-4}=4.3, H-3); 4.55 (1H, d, J_{2-3}=6.9, H-2); 4.28 (1H, m, H-5); 3.81 (1H, dd, J_{4-5}=2.3, J_{4-3}=4.3, H-4); 2.70 (2H, dd, $J_{6'-5}$=6.1, $J_{6'-6}$=16.9, H-6'), 2.61 (2H, dd, J_{6-5}=4.9, $J_{6'-6}$=16.9, H-6); 1.70-1.40 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 205.6 (C1); 11.4 (ketal); 80.0 (C2); 78.9 (C4); 78.7 (C3); 72.3 (CH_2Ph); 68.0 (C5); 42.9 (C6); (Found : C, 68.54; H, 7.43; O, 24.02; $C_{19}H_{24}O_5$ requires C, 68.65; H, 7.28; O, 24.07%). Ketone **10** was eluted second (203 mg, 42.3%) and crystallized from pentane; m.p. 79-80°C; $[\alpha]_D$ - 6° (c = 1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ ppm : 7.37 (5H, m, Ph); 4.84 and 4.71 (2H, 2d, CH_2Ph); 4.58 (1H, dd, J_{3-2}=6.5, J_{3-4}=4.1, H-3); 4.58 (1H, d, J_{2-3}=6.5, H-2); 4.28 (1H, m, H-5); 3.85 (1H, dd, J_{4-5}=6.6, J_{4-3}=4.1, H-4); 2.96 (1H, dd, $J_{6'-5}$=5.2, $J_{6-6'}$=16.3, H-6'); 2.89 (1H, d, J=5.9, OH), 2.57 (1H, dd, J_{6-5}=6.6, $J_{6-6'}$=16.3, H-6); 1.70-1.30 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 205.3 (C1); 111.9 (ketal); 78.8 (C2), 78.1 (C3, C4); 72.8 (CH_2Ph); 68.5 (C5); 43.2 (C6); (Found : C, 68.50; H, 7.28; O, 24.24; $C_{19}H_{24}O_5$ requires C, 68.65; H, 7.28; O, 24.07%).

b) With mercury (II) acetate (780 mg, 2.45 mmol), instead of mercury (II) chloride, in similar conditions described in a) the ketones **9** and **10** were isolated in 50 and 25% yields respectively.

c) Catalytic method with mercury (II) nitrate : alkene **7β** (5.54 g, 16 mmol) was dissolved in a mixture of CH_3COCH_3 and 0.05N aqueous solution of HNO_3 (2/1, 100 ml), then $Hg(NO_3)_2$ (545 mg, 1.6 mmol) was added and the solution was stirred over 1 h. at r.t. before addition of thiourea (380 mg, 5 mmol). After 2 h. the solution was concentrated under reduced pressure and extracted with AcOEt (four times). The organic layers were combined, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by chromatography on silicagel to give **9** (50%) and **10** (25%).

L-1-*O*-benzyl-5,6-*O*-cyclohexylidene-3-deoxy-*chiro*-inositol 11

a) Cerium (III) chloride heptahydrate (1.24 g, 2.26 mmol) in anhydrous MeOH (20 ml) was added quickly to a stirred solution of inosose **9** (1.46 g, 4.4 mmol) dissolved in anhydrous THF (30 ml) and cooled to - 60°C. Then a solution of $NaBH_4$ (201 mg, 5.3 mmol) in absolute EtOH (30 ml) was added dropwise. After 1 h. at - 60°C, the mixture was allowed to warm to r. t. and brine (30 ml) was added while stirring overnight. The solvents were evaporated under reduced pressure. The residue was diluted with isopropanol (10 ml) and the mixture concentrated to dryness (repeated three times). The residue was treated with hot AcOEt (50 ml) and the solid was removed by filtration through a pad of celite and washed three times with hot AcOEt (50 ml). The filtrate was concentrated under reduced pressure and submitted to flash chromatography. The derivative **11** was eluted first (1.16 g, 68%) and crystallized from pentane; m.p. 95-96°C, $[\alpha]_D$ + 48° (c = 0.95, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ ppm : 7.60-7.20 (5H, m, Ph); 4.75 (2H, m, CH_2Ph); 4.37 (1H, dd, $J_{6\text{-}5}$=4.5, $J_{6\text{-}1}$=6.6, H-6); 4.32 (1H, dd, $J_{5\text{-}4}$=6.5, $J_{5\text{-}6}$=4.5, H-5); 4.17 (1H, m, H-4); 4.05 (1H, m, $J_{2\text{-}1}$=2.9, $J_{2\text{-}3'}$=4.2, $J_{2\text{-}3}$=5.7, H-2); 3.45 (1H, dd, $J_{1\text{-}6}$=6.6, $J_{1\text{-}2}$=2.9, H-1); 2.12 (1H, m, H-3'); 1.84 (1H, m, H-3); 1.70-1.20 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 109.7 (ketal); 80.1 (C-5); 78.8 (C-6); 76.2 (C-1); 72.0 (CH_2Ph); 69.4, 68.0 (C-2, C-4); 31.2 (C-3); (Found : C, 68.44; H, 7.83; $C_{19}H_{26}O_5$,1/2H_2O requires C, 68.45; H, 7.93%).

The minor product, **D-6-*O*-benzyl-1,2-*O*-cyclohexylidene-4-deoxy-neoinositol 13** was eluted latter (273 mg, 16%); syrup, $[\alpha]_D$ 0° (c = 1.1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 7.60-7.20 (5H, m, Ph); 4.76 (2H, m, CH_2Ph); 4.36 (1H, m, H-2); 4.33 (1H, m, H-1); 4.25 (1H, m, $J_{5\text{-}4}$=4, H-5); 4.10 (1H, m, $J_{3\text{-}4}$=7, H-3); 3.45 (1H, m, H-4); 2.00 (1H, m, H-6ax); 1.90 (1H, m, H-6eq); 1.70-1.20 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 110.6 (ketal); 79.8 (C-2); 77.5 (C-1); 75.7 (C-6); 71.7 (CH_2Ph); 67.0 (C-3); 64.6 (C-5); 33.2 (C-4); (Found : C, 68.62; H, 7.80; $C_{19}H_{26}O_5$, 1/2H_2O requires C, 68.45; H, 7.93%).

b) The reduction of **9** (730 mg, 2.2 mol) in dry THF (30 ml) at -40°C with lithium tri-terbutylaluminohydride (763 mg, 3 mmol) provided, following the same experimental procedure describe above, **11** (436 mg, 60%) and **13** (219 mg, 30%).

D-4-*O*-benzyl-2,3-*O*-cyclohexylidene-6-deoxy-*myo*-inositol 14

Lithium borohydride (142 mg, 6.5 mmol) was added in one portion to a stirred solution of ketone **10** (1 g, 3 mmol) dissolved in dry THF (20 ml) and cooled to - 40°C under argon. The stirring was maintained during 1h. at - 40°C and the reaction was warmed up to r. t. Brine (20 ml) was added and the mixture was stirred overnight. After evaporation of the solvents under reduced pressure, the residue was dissolved in isopropanol (10 ml) and the solvent was removed to dryness (repeated three times). The residue was treated with hot AcOEt (50 ml) and the solid was filtrated through a pad of celite and washed three times with hot AcOEt (50 ml). The filtrate was concentrated under reduced pressure and the cyclitol **14** was crystallized (AcOEt, pentane) (868 mg, 85%); m.p. 124-125°C; $[\alpha]_D$ - 5° (c = 0.9, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ ppm : 7.60-7.20 (5H, m, Ph); 4.83 (2H, m, CH_2Ph); 4.33 (1H, dd, $J_{2\text{-}1}$=4.2, $J_{2\text{-}3}$=6, H-2); 4.05 (1H, dd, $J_{3\text{-}2}$=6, $J_{3\text{-}4}$=6.6, H-3); 3.95 (1H, m, $J_{1\text{-}2}$=4.2, $J_{1\text{-}6ax}$=10, H-1); 3.55 (1H, dd, $J_{4\text{-}3}$=6.6, $J_{4\text{-}5}$=9, H-4); 3.50 (1H, m, $J_{5\text{-}6'}$=4.7, $J_{5\text{-}6}$=10, H-5); 2.16 (1H, dd, $J_{6'\text{-}5}$=4.7, $J_{6'\text{-}6}$=12.8, H-6'); 1.82 (1H, dd, $J_{6\text{-}5}$=10 and $J_{6\text{-}6'}$=12.8, H-6); 1.70-1.20 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 110.4 (ketal); 84.5 (C-2); 79.1 (C-3); 76.4 (C-5); 73.0 (CH_2Ph); 67.9 (C-4); 66.3 (C-1); 34.2 (C-6); (Found : C, 66.62; H, 7.80; $C_{19}H_{26}O_5$,1/2H_2O requires C, 66.45; H, 7.93%).

From mother-liquors, the minor syrupy component **L-1-*O*-benzyl-5,6-*O*-cyclohexylidene-3-deoxy-*chiro*-inositol 15** can be separated by thin-layer chromatography on silicagel (AcOEt , heptane) (80 mg, 8%); $[\alpha]_D$ + 20° (c = 1.1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 7.60-7.20 (5H, m, Ph); 4.70 (2H, m, CH_2Ph); 4.33 (1H, dd, $J_{2\text{-}1}$=5, H-2); 4.06 (1H, m, $J_{1\text{-}6'}$=4, $J_{1\text{-}2}$=5, H-1); 3.96 (1H, m, $J_{3\text{-}4}$=6, H-3); 3.86 (1H, m, $J_{5\text{-}6'}$=4 and $J_{5\text{-}6}$=8, H-5); 1.80 (1H, m, $J_{6'\text{-}5}$=8, $J_{6'\text{-}6}$=10, H-6'); 1.65 (1H, m, H-6); 1.60-1.30 (10H, m, C_6H_{10}); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 109.5 (ketal); 80.0 (C-5); 78.6 (C-6); 76.1 (C-1); 71.8 (CH_2Ph); 69.21 (C-4); 67.8 (C-2); 31.0 (C-3); (Found: C, 68.21; H, 7.95; O, 24.24; $C_{19}H_{26}O_5$ requires C, 68.24; H, 7.84%).

D-1,5-di-*O*-benzoyl-4-*O*-benzyl-2,3-*O*-cyclohexylidene-6-deoxy-*myo*-inositol 16

PPh_3 (740 mg, 2.8 mmol), benzoic acid (341 mg, 2.8 mmol) then a solution of diisopropyl azodicarboxylate (0.55 ml, 2.8 mmol) in dry THF (10 ml) were added under argon to a solution of diol **11** (476 mg, 1.4 mmol) in dry THF (25 ml). After 4 h., the solvent was evaporated under reduced pressure and the residue was dissolved in AcOEt. Heptane was then added and the mixture was stored at 0°C for 12 h.. The precipitate was discarded by filtration through celite and the filtrate was concentrated to dryness. The residue was purified by preparative thin-layer chromatography on silicagel (AcOEt, heptane) to give the dibenzoate **16** (488 mg, 70%) as syrup; $[\alpha]_D$ - 45° (c = 1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 7.60-7.20 (5H, m, Ph); 6.06 (1H, d, J_{1-2}=3.9, $J_{1-6'}$=5.2, J_{1-6}=10, H-1); 5.90 (1H, m, $J_{5-6'}$=4, J_{5-6}=9.7, J_{5-4}=10.2, H-5); 5.00 (2H, dd, CH_2Ph); 4.63 (1H, dd, J_{2-1}=3.9, J_{2-3}=6, H-2); 4.50 (1H, t, J_{3-2}=6, J_{3-4}=6, H-3); 3.90 (1H, dd, J_{4-3}=6, J_{4-5}=10.2, H-4); 2.43 (1H, m, $J_{6'-1}$=5.2, $J_{6'-5}$=4, $J_{6'-6}$=12.3, H-6'); 2.26 (1H, m, J_{6-1}=10, J_{6-5}=9.7, $J_{6'-6}$=12.3, H-6); 1.70-1.30 (10H, m, C_6H_{10}); (Found: C, 73.01; H, 6.40; $C_{33}H_{34}O_7$ requires C, 73.04; H, 6.32%).

L-1-*O*-benzyl-5,6-*O*-cyclohexylidene-3-deoxy-2,4-di-*O*-mesyl-*chiro*-inositol 17

MesylChloride (0.23 ml, 3 mmol) was added to a stirred solution of diol **11** (334 mg, 1 mmol) dissolved in dry pyridine (10 ml) at 0°C. After 3h., the solution was diluted with water and extracted twice with CH_2Cl_2. The organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash chromatography on silicagel (AcOEt, heptane). The mesylate **17** (440 mg, 90%) was crystallized from pentane; m.p. 56-58°C, $[\alpha]_D$ - 40° (c = 1; $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ ppm : 5.00 (1H, m, H-4); 4.70 (3H, m, H-2, CH_2Ph); 4.30 (2H, m, H-1, H-6); 4.00 (1H, m, H-5); 3.15 (3H, s, CH_3SO_2); 3.00 (3H, s, CH_3SO_2); 2.40 (2H, m, H-3', H-3); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm : 79.5 (C-4); 76.2, 75.8, 75.5 (C-1, C-2, C-5, C-6); 73.4 (CH_2Ph); 38.8, 38.7 ($2CH_3SO_2$);
(Found : C, 48.81; H, 6.42; S, 12.39; $C_{21}H_{30}O_9S_2$ requires C, 48.73; H, 6.42; S, 12.39%).

D-5-*O*-acetyl-4-*O*-benzyl-2,3-*O*-cyclohexylidene-1,6-ene-*myo*-inositol 18

A solution of **17** (270 mg, 0.5 mmol) and anhydrous caesium acetate (384 mg, 2 mmol) in dry DMF (10 ml) was stirred at reflux for 24h.. The solvent was then evaporated under reduced pressure and the residue submitted to flash chromatography on silicagel (AcOEt, heptane) to give **18** (138mg, 70%) as syrup, $[\alpha]_D$ + 4° (c = 1.9, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ ppm : 5.80 (1H, m, H-1); 5.60 (1H, d, J_{6-1}=12, H-6); 5.30 (1H, m, H-5); 4.65 (2H, dd, CH_2Ph); 4.55 (1H, m, H-2); 4.20 (1H, dd, J_{3-2}=7.2, J_{3-4}=10, H-3); 3.55 (1H, t, J_{4-3}=10, J_{4-5}=10, H-4); 2.00 (3H, s, CH_3CO); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm : 170.5 (CH_3C=O); 130.6 (C-1); 125.2 (C-6); 78.7, 77.4, 73.8, 72.0 (C-2, C-3, C-4, C-5, CH_2Ph); 21.1 (CH_3CO); (Found : C, 70.21; H, 7.46; O, 22.13; $C_{21}H_{26}O_5$ requires C, 70.37; H, 7.31; O, 22.32%).

D-3-*O*-benzoyl-6-*O*-benzyl-1,2-*O*-cyclohexylidene-4-deoxy-5-*O*-mesyl-*neo*-inositol 20

A solution of benzoylchloride (0.14 ml, 1.2 mmol) in dry pyridine (10 ml) was added dropwise at 0°C to a stirred solution of **13** (330 mg, 1 mmol) in dry pyridine (10 ml). After 2hrs., mesylchloride (0.12 ml, 1.5 mmol) was added to the **D-6-*O*-benzyl-3-*O*-benzoyl-1,2-*O*-cyclohexylidene-4-deoxy-neoinositol 19** formed in the medium, and the stirring maintained for 2h. at r. t.. The mixture was diluted with water and extracted with CH_2Cl_2. Drying the organic layer ($MgSO_4$) and evaporation of solvent under reduced pressure gave a residue, submitted to flash chromatography on silicagel (AcOEt, heptane). A small amount of the **D-6-*O*-benzyl-1,2-*O*-cyclohexylidene-4-deoxy-3,5-di-*O*-benzoyl-*neo*-inositol** was eluted first (54 mg, 10%), and crystallized in pentane; m.p. 49-51°C; $[\alpha]_D$ + 7.7° (c = 1.7, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 5.80 (2H, m, H-3, H-5); 4.82 (2H, dd, CH_2Ph); 4.75 (1H, dd, J_{2-1}=4.1, J_{2-3}=5.9, H-2); 4.55 (1H, dd, J_{1-2}=4.1, J_{1-6}=6, H-1); 3.85 (1H, dd, J_{6-5}=3.2, J_{6-1}=6, H-6); 2.40 (2H, m, H-4', H-4); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 77.1; 76.5 (C-1, C-6); 73.6 (C-2); 71.8 (CH_2Ph); 68.0 (C-3, C-5); 29.3 (C-4); (Found : C, 63.12; H, 6.24; S, 6.20; $C_{27}H_{32}O_8S$ requires C, 62.77; H, 6.24; S, 6.21%). Then the compound **20** (407mg, 80%) was isolated and crystallized from heptane; m.p. 127-128°C; $[\alpha]_D$ + 14° (c = 0.5, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ ppm : 5.55 (1H, m, H-3); 5.10 (1H, m, H-5); 4.70 (2H, s, CH_2Ph); 4.50 (1H, m, H-2); 4.30 (1H, m, H-1); 3.65 (1H, m, H-6); 2.95 (3H, s, CH_3SO_2); 2.30 (2H, m, H-4', H-4); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm: 165.4 (C=O); 77.4 (C-1, C-6); 76.5 (C-5);

72.4 (CH_2Ph); 67.3 (C-3); 39.0 (CH_3SO_2); 30.6 (C-4); (Found : C, 63.12; H, 6.24; S, 6.20; $C_{27}H_{32}O_8S$ requires C, 62.77; H, 6.24; S, 6.21%).

D-5-*O*-acetyl-1-*O*-benzoyl-4-*O*-benzyl-2,3-*O*-cyclohexylidene-6-deoxy-*myo*-inositol 21

A solution of **20** (230 mg, 0.45 mmol) and anhydrous caesium acetate (192 mg, 1 mmol) in dry N,N-dimethylformamide (10 ml) was stirred at 60°C for 8h.. The solvent was evaporated under reduced pressure and compound **21** (202mg, 95%) was isolated by flash chromatography on silicagel and crystallized from hexane; m.p. 124-125°C, $[\alpha]_D$ - 39° (c = 1.6, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ ppm : 5.43 (1H, m, J_{1-2}=4, J_{1-6}=3.8, $J_{1-6'}$=10.1, H-1); 5.00 (1H, m, H-5); 4.85 (2H, dd, CH_2Ph); 4.50 (1H, dd, J_{2-1}=4, J_{2-3}=6.1, H-2); 4.35 (1H, t, J_{3-2}=6.1, J_{3-4}=6.1, H-3); 3.82 (1H, dd, J_{4-3}=6.1, J_{4-5}=9.9, H-4); 2.20 (2H, m, H-6', H-6); 2.00 (3H, s, CH_3CO); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 170.2 (CH_3C=O); 165.7 (PhC=O); 79.0 (C-3); 74.2 (C-2); 73.1 (CH_2Ph); 70.1 (C-5); 68.0 (C-1); 29.8 (C-6); 21.2 (CH_3C=O); (Found : C, 69.54; H, 6.24; S, 6.72; O, 23.03; $C_{28}H_{32}O_7$ requires C, 69.98; H, 6.71; O, 23.30%).

(2R)-(2,3/4)-2,3-dihydroxy-4-benzyloxy-2,3-*O*-cyclohexylidenecyclohex-5-enone 22

PPh_3 (790 mg, 3 mmol), benzoic acid (365 mg, 3 mmol) then a solution of diisopropyl-azodicarboxylate (0.6 ml, 3 mmol) in dry THF (10 ml), were added under argon to a stirred solution of ketone **9** (500 mg, 1.5 mmol) in dry THF (25 ml). After 4 h., the solvent was evaporated under reduced pressure and the residue was dissolved in AcOEt. Heptane was then added and the mixture was stored at 0°C for 12 h.. The precipitate was discarded by filtration through celite and the filtrate was concentrated to dryness. The residue was purified by preparative thin-layer chromatography on silicagel (AcOEt, heptane) to give the unsaturated ketone **22** (330 mg, 70%); $[\alpha]_D$ + 62° (c = 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ ppm : 6.80 (1H, dd, J_{5-4}=4, J_{5-6}=10.3, H-5); 6.05 (1H, d, J_{6-5}=10.3, H-6); 4.70 (2H, dd, CH_2Ph); 4.55 (1H, dd, J_{3-4}=3.8, J_{3-2}=6, H-3); 4.40 (1H, d, J_{2-3}=6, H-2); 4.30 (1H, m, H-4); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm : 194.0 (C=O); 146.6 (C-6); 129.2 (C-5); 111.2 (C-2); 74.4, 73.2 (C-3, C-4); 72.5 (CH_2Ph); (Found : C, 70.84; H, 7.17; $C_{19}H_{22}O_4$,1/2H_2O requires C, 70.57; H, 7.17%).

(2R)-(2,3/4)-2,3-dihydroxy-4-benzyloxy-2,3-*O*-cyclohexylidenecyclohexanone 23

The ketone **22** (310 mg, 1 mmol) dissolved in a mixture of AcOEt (5 ml) and EtOH (5 ml) was hydrogenated for 4h. at r.t. in the presence of $Pd(OH)_2$ on carbon 20% at 5 psi. The catalyst was removed by filtration and the ketone **23** was isolated after evaporation of the organic solvents under reduced pressure (205 mg, 92%); $[\alpha]_D$ - 27° (c = 0.8; $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ ppm : 4.45 (2H, m, H-2, H-3); 4.20 (1H, m, H-4); 3.35 (1H, s, OH); 2.70 (1H, m, H-6); 2.35 (1H, m, H-6'); 2.10 (2H, m, H-5, H-5'); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm : 208.6 (C=O); 111.3 (O-C-O); 80.5 (C-2); 77.6 (C-3); 67.5 (C-4); 36.8 (C-6); 35.0 (C-5); (Found : C, 61.29; H, 7.81; O, 30.74; $C_{12}H_{18}O_4$,1/2H_2O requires C, 61.26; H, 8.14; O, 30.60%).

D-2,3-*O*-cyclohexylidene-5,6-dideoxy-*myo*-inositol 24

$LiBH_4$ (100 mg, 4.6 mmol) was added to a solution of **23** (450 mg, 2 mmol) in dry THF (20 ml) at - 60°C under argon. After 1h., brine was added at r. t. and stirring was maintained for 2h.. The solution was evaporated under reduced pressure and the residue diluted with AcOEt and filtered through celite. The diol **24** was crystallized (AcOEt, pentane) (385 mg, 85%); m.p. 91-93°C, $[\alpha]_D$ + 55° (c = 1, pyridine); ^1H NMR (250 MHz, $CDCl_3$) δ ppm : 4.40 (1H, t, J_{2-1}=3, J_{2-3}=3, H-2); 4.00 (1H, dt, J_{1-2}=4.5, J_{1-6}=4.5, $J_{1-6'}$=10, H-1); 3.90 (1H, dd, J_{3-2}=3, J_{3-4}=7.9, H-3); 3.70 (1H, m, H-4); 1.90-1.20 (14H, m, H-5, H-5', H-6, H-6' and C6H_{10}); ^{13}C NMR (62.9 MHZ, D_2O) δ ppm : 111.0 (O-C-O); 80.2 (C-3); 76.3 (C-2); 71.8 (C-4); 67.8 (C-1); 27.3, 25.8 (C-5, C-6); (Found : C, 62.72; H, 8.84; $C_{12}H_{20}O_4$ requires C, 63.13; H, 8.84%).

L-3-deoxy-*chiro*-inositol 26

Hydrogenation of diol **11** (350 mg, 1.05 mmol) in 95% ethanol (20 ml) in the presence of $Pd(OH)_2$ on carbon 10% (350 mg) at 3 psi for 1h. at r.t., filtration of the mixture and evaporation of the filtrate under reduced pressure, gave a residue which was crystallized from chloroform to give the **L-5,6-O-cyclohexylidene-3-deoxy-*chiro*-inositol 25** (250 mg, 97%); m.p. 136-137°C; $[\alpha]_D$ - 38° (c = 0.8,

CH_3OH); (Found : C, 58.91; H, 8.32; $C_{12}H_{20}O_5$ requires C, 59.00; H, 8.25%).-The triol **25** (315 mg, 1.29 mmol) was dissolved in a 2M H_2SO_4 methanolic solution (10 ml) while stirring. After 2h., amberlite IRC50 (2 g) was added for neutralization. The solid was discarded by filtration, and the filtrate was concentrated under reduced pressure to give **26** (210 mg, 99%); $[\alpha]_D$ - 0.4° (c = 1, H_2O); (Found : C, 43.91; H, 7.39; $C_6H_{12}O_5$ requires C, 43.90; H, 7.37%).

D-6-deoxy-*myo*-inositol 27

The diol **14** (740 mg, 2.2 mmol) dissolved in 95% ethanol (10 ml) was hydrogenated at r.t. in the presence of Pd on carbon 10% (740 mg) at 5 psi for 12h.. Filtration of the suspension and evaporation of the organic solvent under reduced pressure gave the pentol **27**, crystallized from $CHCl_3$ (326 mg, 90%); m.p. 197-199°C; $[\alpha]_D$ + 7° (c = 1.37, H_2O); ^1H NMR (200 MHz, D_2O) δ ppm : 3.99 (1H, t, $J_{2\text{-}1}$=2.7, $J_{2\text{-}3}$=2.7, H-2); 3.78 (1H, d, $J_{1\text{-}2}$=2.7, H-1); 3.48 (1H, dd, $J_{4\text{-}5}$=6.3, $J_{4\text{-}3}$=10.2, H-4); 3.47 (1H, m, $J_{5\text{-}6}$=3.5, $J_{5\text{-}6'}$=11.5, H-5); 3.41 (1H, dd, $J_{3\text{-}2}$=2.7, $J_{3\text{-}4}$=10.2, H-3); 1.96 (1H, dd, $J_{6\text{-}1}$=4, $J_{6\text{-}6'}$=12, H-6); 1.75 (1H, dd, $J_{6'\text{-}1}$=12.2, $J_{6'\text{-}6}$=12, H-6'); ^{13}C NMR (50 MHz, D_2O) δ ppm : 77.0 (C-3); 75.4 (C-1); 74.4 (C-5); 71.8 (C-4); 69.1 (C-2); 36.5 (C-6); (Found: C, 43.89; H, 7.28; $C_6H_{12}O_5$ requires C, 43.90; H, 7.28%).

D-2,3-*O*-cyclohexylidene-6-deoxy-*myo*-inositol 28

The hydrogenation of diol **14** (334 mg, 1 mmol) in 95% ethanol (20 ml) in the presence of palladium hydroxide on carbon 20% (150 mg), as described for the preparation of **27**, gave the triol **28**, crystallized from chloroform (232 mg, 95%); m.p. 134°C; $[\alpha]_D$ + 42° (c = 1.3, CH_3OH); ^1H NMR (200 MHz, CD_3OD) δ ppm : 4.30 (1H, dd, $J_{2\text{-}1}$=4, $J_{2\text{-}3}$=6, H-2); 4.05 (1H, dd, $J_{3\text{-}2}$=6, $J_{3\text{-}4}$=6.6, H-3); 3.95 (1H, m, $J_{1\text{-}2}$=4, $J_{1\text{-}6'}$=4.6, $J_{1\text{-}6}$=10, H-1); 3.55 (1H, dd, $J_{4\text{-}3}$=6.6, $J_{4\text{-}5}$=9, H-4); 3.50 (1H, m, $J_{5\text{-}4}$=9, $J_{5\text{-}6'}$=4.7, $J_{5\text{-}6}$=10, H-5); 2.14 (1H, m, $J_{6'\text{-}6}$=12, H-6'); 1.82 (1H, m, $J_{6\text{-}6'}$=12, H-6); (Found: C, 58.78; H, 8.31; $C_{12}H_{20}O_5$ requires C, 59.00; H, 8.25%).

L-2,4-di-*O*-benzoyl-1-*O*-benzyl-5,6-*O*-cyclohexylidene-3-deoxy-*chiro*-inositol 29

Imidazoyl benzoate (7.74 mg, 4.5 mmol), prepared from imidazole (612 mg, 9 mmol) and benzoyl chloride (0.53 ml, 4.5 mmol) in dry CH_2Cl_2, was added to a solution of diol **11** (370 mg, 1.1 mmol) in dry CH_2Cl_2 (20 ml). The solution was stirred at 60°C for 12h.. The cold solution was washed with water, dried ($MgSO_4$) and evaporated to dryness. The dibenzoate **29** (540 mg, 90%) was crystallized (AcOEt, pentane); m.p 110°C; $[\alpha]_D$ - 16° (c = 1.1, CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 5.56 (1H, m, $J_{2\text{-}1}$=2.1, $J_{2\text{-}3}$=6, $J_{2\text{-}3'}$=6, H-2); 5.40 (1H, m, H-4); 4.48 (1H, dd, $J_{6\text{-}5}$=4.3, $J_{6\text{-}1}$=6, H-6); 4.37 (1H, dd, $J_{5\text{-}6}$=4.3, $J_{5\text{-}4}$=6, H-5); 3.92 (1H, dd, $J_{1\text{-}2}$=2.1, $J_{1\text{-}6}$=6, H-1); 2.26 (2H, m, H-3, H-3'); (Found : C, 72.91; H, 6.34; $C_{33}H_{34}O_7$ requires C, 73.04; H, 6.32%).

L-2,4-di-*O*-benzoyl-1-*O*-benzyl-3-deoxy-*chiro*-inositol 30

A solution of dibenzoate **29** (790 mg, 1.45 mmol) dissolved in a mixture of acetic acid and water (20 ml/30 ml) was stirred at 60°C for 2h.. The solvents were evaporated under reduced pressure, and the residue was submitted to flash chromatography on silicagel and **30** was crystallized (CH_2Cl_2, heptane) (647 mg, 89%); m.p. 114-115°C; $[\alpha]_D$ - 6° (c = 1.1, CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 5.70 (1H, m, H-2); 5.37 (1H, m, $J_{4\text{-}5}$=5.8, $J_{4\text{-}3}$=7, $J_{4\text{-}3'}$=7, H-4); 4.32 (1H, m, H-6); 4.25 (1H, m, H-5); 4.02 (1H, dd, $J_{1\text{-}2}$=2, $J_{1\text{-}6}$=7.2, H-1); 2.40 (2H, m, H-3, H-3'); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ ppm : 77.3 (C-1); 71.2, 72.0 (C-2, C-4); 70.0, 69.9 (C-5, -6C); 28.9 (C-3).

L-2,4,5-tri-*O*-benzoyl-1-*O*-benzyl-3-deoxy-*chiro*-inositol 31

Imidazoyl benzoate prepared as described for **29** (241 mg, 1.4 mmol) in dry CH_2Cl_2 was added to a solution of **30** (586 mg, 1.26 mmol) in dry CH_2Cl_2 (10 ml). The solution was stirred at 60°C for 12h. then washed, dried ($MgSO_4$) and concentrated to dryness. The residue was submitted to flash chromatography on silicagel and **31** was crystallized (AcOEt, heptane) (526 mg, 78%); m.p. 135-136°C; $[\alpha]_D$ - 19.5° (c = 1.03, CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 5.75 (3H, m, H-5, H-4, H-2); 4.58 (1H, m, H-6); 4.13 (1H, dd, $J_{1\text{-}2}$=3, $J_{1\text{-}6}$=7.8, H-1); 2.50 (2H, m, H-3, H-3'); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 77.1 (C-1);

73.5 (C-6); 68.8 (C-5); 68.5, 67.8 (C-2, C-4); 29.6 (C-3); (Found : C, 72.29; H, 5.22; $C_{34}H_{30}O_8$ requires C, 72.07; H, 5.35%).

L-2,4,5-tri-*O*-benzoyl-1-*O*-benzyl-3-deoxy-6-*O*-phenoxythiocarbonyl-*chiro*-inositol 32

Dry DMAP (415 mg, 3.4 mmol), dry pyridine (0.27 ml, 3.4 mmol) and phenyl chlorothionoformate (0.23 ml, 1.69 mmol) were added to a cold solution (0°C) of **31** (190 mg, 0.34 mmol) in dry CH_3CN (5 ml). After 3 h., the stirred solution was diluted in CH_2Cl_2. The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. The residue was separated by preparative thin-layer chromatography on silicagel. Compound **32** (200 mg, 84%) was obtained as syrup; $[\alpha]_D$ - 13° (c = 1.4, CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ ppm: 6.32 (1H, m, H-6); 6.00 (1H, dd, J_{5-6}=3.6, J_{5-4}=8, H-5); 5.65 (1H, m, H-2); 5.60 (1H, m, H-4); 4.36 (1H, m, H-1); 2.54 (2H, m, H-3, H-3'); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 194.1 (C=S); 78.5 (C-6); 73.2, 70.1, 68.8 (4C, C-1, C-2, C-4, C-5); (Found : C, 70.06; H, 4.89; O, 20.42; $C_{41}H_{34}O_9S$ requires C, 70.19; H, 4.88; O, 20.51%).

D-2-*O*-benzyl-3,6-dideoxy-1,4,5-tri-*O*-benzoyl-*myo*-inositol 33

A stirred solution of **32** (480 mg, 0.68 mmol) in dry toluene (27 ml) was heated to 110°C under argon. Bu_3SnH (0.36 ml, 1.36 mmol) and azobis-2-methylpropionitrile (13 mg) were added. After 15 min., the solvent was evaporated to dryness and the residue separated by chromatography on RP18 silicagel (water/MeOH : 2/8). **33** was crystallized (ethyl acetate, pentane) (224 mg, 60%); m.p. 133-134°C; $[\alpha]_D$ - 43° (c = 0.7, CH_2Cl_2); ^1H NMR (200 MHz, $CDCl_3$) δ ppm: 5.76 (1H, m, H-4); 5.45 (1H, m, J_{5-6}=4, J_{5-4}=8.9, $J_{5-6'}$=10, H-5); 5.33 (1H, m, J_{1-2}=4.1, J_{1-6}=4.5, $J_{1-6'}$=10.5, H-1); 4.12 (1H, m, J_{2-1}=4.1, J_{2-3}=4, $J_{2-3'}$=11, H-2); 2.70 (1H, m, J_{3-2}=4.5, J_{3-4}=4.5, $J_{3-3'}$=14, H-3); 2.55 (1H, m, $J_{6'-5}$=10, $J_{6'-1}$=10.5, $J_{6'-6}$=14, H-6'); 2.45 (1H, m, J_{6-5}=4, J_{6-1}=4.5, $J_{6-6'}$=14, H-6); 1.80 (1H, m, $J_{3'-4}$=10, $J_{3'-2}$=11, $J_{3'-3}$=14, H-3'); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 73.2 (C-2); 71.0 (C-1, C-4, C-5); 30.4 (C-3); 29.8 (C-6); (Found : C, 74.34; H, 5.43; O, 20.07; $C_{34}H_{30}O_7$ requires C, 74.17; H, 5.49; O, 20.34%).

D-2-*O*-benzyl-3,6-dideoxy-*myo*-inositol 34

The benzoate **33** (100 mg, 0.2 mmol) was dissolved in a 0.5N methanolic solution of MeONa and stirred for 12h. at r. t.. The solution was neutralized by addition of Amberlite IRN77, filtered and the filtrate was concentrated to dryness. The residue was washed three times with dry ethyl ether then **34** was crystallized (AcOEt, pentane) (32 mg, 70%); m.p. 96-97°C; $[\alpha]_D$ - 18° (c = 1.38, EtOH); ^1H NMR (250 MHz, $CDCl_3$) δ ppm: 4.05 (1H, m, H-2); 4.00 (1H, m, H-1); 3.90 (1H, m, H-4); 3.70 (1H, m, J_{5-6}=6, J_{5-4}=15, $J_{5-6'}$=15, H-5); 2.40 (1H, m, J_{3-2}=4.5, J_{3-4}=7.5, $J_{3-3'}$=17, H-3); 2.16 (1H, m, H-6); 1.90 (1H, m, $J_{6'-5}$=15, $J_{6'-1}$=18, $J_{6'-6}$=18, H-6'); 1.46 (1H, m, $J_{3'-2}$=6, $J_{3'-4}$=15, $J_{3'-3}$=17, H-3'); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 78.2 (C-2); 73.7, 71.6, 71.0 (C-1, C-4, C-5); 36.5 (C-3); 33.8 (C-6); (Found : C, 65.11; H, 7.42; O, 27.09; $C_{13}H_{18}O_4$ requires C, 65.33; H, 7.61; O, 26.86%).

L-2,4-di-*O*-benzoyl-1-*O*-benzyl-3-deoxy-5-*O*-pivaloyl-*chiro*-inositol 35

Pivaloyl chloride (0.08 ml, 0.5 mmol) was added to a solution of **30** (230 mg, 0.5 mmol) in dry pyridine (10 ml) at r. t. and the stirring was maintained for 8h.. The solution was diluted with cold water, extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$) and concentrated to dryness. The residue was submitted to flash chromatography and **35** was crystallized from heptane (230 mg, 85%), m.p. 139°C; $[\alpha]_D$ - 6° (c = 2, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ ppm : 5.75 (2H, m, H-2); 5.60 (2H, m, H-4, H-5); 4.75 (2H, q, CH_2Ph_2); 4.45 (1H, m, H-6); 4.10 (1H, m, H-1); 2.45 (2H, m, H-3, H-3'); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 177.4 , 165.8, 165.6 (C=O); 76.9 (C-1); 73.0 (CH_2Ph); 72.3 (C-6); 68.9, 68.8 (C-4, C-5); 39.0 [$C(CH_3)_3$]; 29.5 (C-3); 27.2 [$(CH_3)_3$]; (Found : C, 70.26; H, 6.29; $C_{32}H_{34}O_8$ requires C, 70.31; H, 6.27%).

D-1,5-di-*O*-benzoyl-2-*O*-benzyl-3,6-dideoxy-3-fluoro-4-*O*-pivaloyl-*myo*-inositol 36

A stirred solution of **35** (218 mg, 0.4 mmol) in dry CH_2Cl_2 (10 ml) was treated under argon with diethylaminosulphotrifluoride (DAST) (0.08 ml, 0.6 mmol) and stirred at r. t. for 4hrs.. Methanol (5 ml) was added and the solution was diluted with water and extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$)

and concentrated to dryness. The residue was submitted to flash chromatography on silicagel and **36** was crystallized (AcOEt, pentane) (153 mg, 70%); m.p. 163-164°C; $[\alpha]_D$ - 18° (c = 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 4.55 (1H, q, J_{4-3}=10, J_{4-5}=10, H-4); 4.3 (1H, dd, J_{2-1}=3.1, J_{2-3}=2.9, H-2); 4.22 (1H, m, H-1, H-6); 4.18 (1H, m, H-5); 4.12 (15H, m, CH_2O); 3.70 (1H, dd, J_{3-2}=2.9, J_{3-4}=10, H-3); 1.65 (12H, m, CH_2CH_2O); 1.40 (12H, m, CH_2CH_3); 0.90 (18H, m, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm : 80.5, 79.3 (C-4, C-6); 77.4, 77.1, 70.9, 70.6 (C-1, C-2, C-3, C-5); 68.7, 68.2 (CH_2O); 32.4 (CH_2CH_2O); 18.7 (CH_2CH_3); 13.7 [6*$CH_3(CH_2)_3$]; (Found: C, 70.17; H, 6.33; F, 3.16; $C_{32}H_{33}O_7F$ requires C, 70.06; H, 6.06; F, 3.46%).

D-2-*O*-benzyl-3,6-dideoxy-3-fluoro-*myo*-inositol 37

NaOH (200 mg) in MeOH (10 ml) was added to a stirred solution of **36** (165 mg, 0.3 mmol) dissolved in AcOEt (5 ml). After 4h., the mixture was concentrated under reduced pressure and the residue filtered through a pad of silicagel (AcOEt). The solvent was evaporated to dryness and **37** (73 mg, 95%) was crystallized from pentane; m.p. 94-96°C; $[\alpha]_D$ + 3° (c = 1.8, CH_3OH); ^1H NMR (200 MHz, $CDCl_3$) δ ppm: 4.95 (1H, ddd, J_{3-2}=3, J_{3-4}=8.1, J_{3-F}=48, H-3); 4.65 (2H, dd, $C\underline{H}_2Ph$); 4.10 (2H, m, H-2, H-4); 3.85 (1H, m, H-5); 3.50 (1H, s, OH); 2.80 (1H, s, OH); 2.30 (1H, s, OH); 1.95 (2H, m, H-6, H-6'); ^{13}C NMR (50 MHz, C_5D_5N) δ ppm : 93.9, 91.9 (C-3, J_{C3-F}=142); 79.0, 78.6 (C-4, J_{C4-F}=17); 73.3 (CH_2Ph), 73.1, 72.8 (C-2, J_{C2-F}=13); 69.8, 68.0 (C-1, C-5); 35.1 (C-6); (Found: C, 59.64; H, 6.94; F, 6.97; $C_{13}H_{17}O_7F$,1/4H_2O requires C, 59.87; H, 6.77; F, 7.28%).

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(*Received in Belgium* 30 *June* 1997; *accepted* 19 *September* 1997)