±SYNTHESIS OF (±)-1-ACETAMIDO-2, 3-ANHYDRO-4, 5, 6-TRI-O-ACETYL-1-DEOXY-*MYO*-INOSITOL FROM PURE (±)-(1,3/2,4)-1,2,3-TRI-O-ACETYL-4-AZIDO-5-CYCLOHEXENE-1, 2, 3-TRIOL

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Résumé

Les deux composés (±)–(1,3/2,4) et (±)–(1,3,4/2)-1,2,3-tri-O-acétyl-4-bromo-5-cyclohexène-1,2,3-triols ***3*** et ***4*** ont été synthétisés par réaction du HBr sur le composé tétraacétate conduritol-B-selon les données de la littérature [1]. Les produits obtenus sont séparés, pour la première fois, purifiés et caractérisés. La réaction de ces derniers par le triphényl phosphine dans le THF anhydre conduit aux amines (±)–(1,3,4/2)-1,2,3-tri-O-Acétyl-4-amino-5-cyclohexène-1,2,3-triol ***6*** et (±)–(1,3/2,4)-1,2,3-tri-O-Acétyl-4-amino-5-cyclohexène-1,2,3-triol ***8***. Ce dernier est obtenu par un auto réarrangement interne du composé; le transfert du groupement acétyl de l'atome d'oxygène vers l'atome d'azote conduit au produit (±)–(1,3/2, 4)-1,2,3-di-O-Acétyl-4-acétamido-5-cyclohexène-1,2,3-triol ***9***. L'hydrolyse du composé (±)–(1, 3/2, 4)-1,2,3-tri-O-Acétyl-4-azido-5-cyclohexène-1,2,3-triol ***7*** conduit à l'azide (±)–(1, 3/2, 4)-1,2,3-azido-5-cyclohexène-1,2,3-triol ***10***. La réduction à l'aide de triphényl phosphine conduit au composé (±)–(1, 3/2, 4)-1,2,3-azido-5-cyclohexène-1,2,3-triol ***10*** et donne le produit (±)–(1, 3/2, 4)-4-amino-5-cyclohexène-1,2,3-triol ***11***. L'acétylation du composé ***11*** à l'aide de l'acide acétique anhydride conduit à la formation de (±)–(1, 3/2, 4)-1,2,3-tri-O-acétyl-4-acétamido-5-cyclohexène-1,2,3-triol ***12*** qui donne par oxydation le (±)–1-Acétamido-2,3-anhydro-4,5,6-tri-O-acétyl-1-déoxy-myo-inositol ***13***.

Mots clés: *Azide-coduritol-B; Deoxy-myo-Inositol; Synthèse; O-N acyle migration; ^{1}H-NMR.*

Abstract

(±) –(1, 3/2, 4) - and (±)-(1,3, 4/2) -1, 2, 3-tri-O-acetyl-4-bromo-5-cyclohexene-1, 2, 3-triols ***3*** and ***4*** have been prepared by treating conduritol-B-tetraacetate ***1*** with HBr according to literature [1], and isolated in pure state and characterised. Treatment of these bromides with tetra-n-butylammoniumazide yielded the corresponding azides ***5*** and ***7*** respectively. Reducing these azides with triphenylphosphine in dry THF gave the corresponding amines ***6*** and ***8***. The latter has underwent a spontaneous O-N acetyl migration to give ***9***. Azide ***10*** was obtained by de-O-acetylation of ***7*** and was reduced with triphenylphosphine to give (±)-(1, 3/2, 4)-4-amino-5-cyclohxene- 1, 2, 3-triol ***11***. Acetylation of ***11*** with acetic anhydride led to (±)(1,3/2,4)-1,2,3-O-tri-O-acetyl-4-acetamido-5- cyclohexene-1,2,3-triol ***12*** which on oxidation gave a single product (±)-1- acetamido –2,3-anhydro-4, 5, 6-tri-O-acetyl-1-deoxy-*myo*-inositol ***13***.

Keywords: *Azido-coduritol-B; Deoxy-myo-Inositol; Synthesis; O-N acyl migration; ^{1}H-NMR.*

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ملخص

المركبان (±)-(4,2/3,1) و (±)-(2/4,3,1)- 3,2,1- ثلاثي- 0- أسيتيل-4- بروموـ-5- هكسين حلقي -3,2,1- ثلاثي أول ***3*** و ***4*** قد حضرا نتيجة لمعاملة المركب رباعي أسيتات كوندوريتول-B مع HBr وحسب الأدبيات الكيميائية [1] , ومن ثم فصلا لأول مرة بصورة نقية وتم تشخيصهما. وعند معاملة هذه البروميدات مع رباعي – n - بيوتيل ازيد الأمونيوم، كان الناتج هو ألازيدات المقابلة وهي ***5*** و ***7*** على التوالي. وبعدها تم اختزال تلك ألازيدات بواسطة ثلاثي فنيل الفوسفين في الجاف لتعطي ألامينات المقابلة ***6*** و ***8***. المركب الأخير خضع الى تفاعل انتقال تلقائي لمجموعة ألاسيتيل من الذرة 0 إلى الذرة N المجاورة لها ليعطي ألازيد ***9*** . أما الأزيد ***10*** فقد تم الحصول عليه بواسطة تفاعل ألاماهة للتخلص من مجاميع ألاسيتال في المركب ***7*** و بعدها تم اختزال هذا الأخير بواسطة ثلاثي فنيل الفوسفين ليعطي (±)-(4,2/3,1)- 4- أمينو -5-هكسين حلقي-3,2,1- ثلاثي أول ***11***. أستلة المركب ***11*** بواسطة الخليك ألالمائي أدى إلى تكوين (±)-(4,2/3,1)- 3,2,1- ثلاثي -0-أسيتيل أسيت أمايدو -5- هكسين حلقي-3,2,1-ثلاثي أول ***12*** و الذي عند أكسدته أعطى ناتجا واحدا و هو (±)-1- أسيتيل أمايدو-3,2- انهيدرو-6,5,4- ثلاثي-0- أسيتيل-1- دي أوكسي-مايو- أينوسيتول ***13***.

الكلمات المفتاحية: *أسيتات كوندوريتول-B، دي أوكسي- مايو- أينوسيتول، ^{1}H-NMR.*

Most of the conduritols and their derivatives act as inhibitors of D-glycosidases and almost all of the synthetic and inhibition works have done on stereoisomers and/or racemic mixtures [1→4], only few enantiomerical controlled and pure stereoselective syntheses have been reported [5].

The stereocontrolled synthesis, the separation of pure isomers and the determination of exact configuration of each isomer are of great importance to the biological work.

The following work describes the synthesis of (±)-1-acetamido-2, 3-anhydro-1, 5, 6-tri-O-acetyl-1-deoxy-*myo*-inositol ***13*** based on purely separated and characterised (±)-(1, 3, 4/2)-1, 2, 3-tri-O-acetyl-4-bromo-5-cyclohexene-1, 2, 3-triol ***8*** and (±)-(1, 3/2, 4)-1, 2, 3-tri-O-acetyl-4-azido-5-cyclohexene-1, 2, 3-triols ***7*** (see scheme 1).

RESULTS AND DISCUSSION

The reaction of conduritol-B-tetraacetate ***1***♦ with hydrobromic/acetic acids mixture has received a lot of attention but the results reported were rather contradictory concerning the percentages of yield of the monobromo conduritols resulted by this method (see ref., 1a and 2 particularly).

The treatment of conduritol-B-tetraacetate ***1*** with mixtures of HBr/HOAc of different concentrations 20 % and 30% has shown that 68 % of ***1*** has been converted into a mixture of dibromo-diacetates ***2***, monobromo-triacetates ***3*** (3.5 %) and ***4*** (42.5 %) which was separated

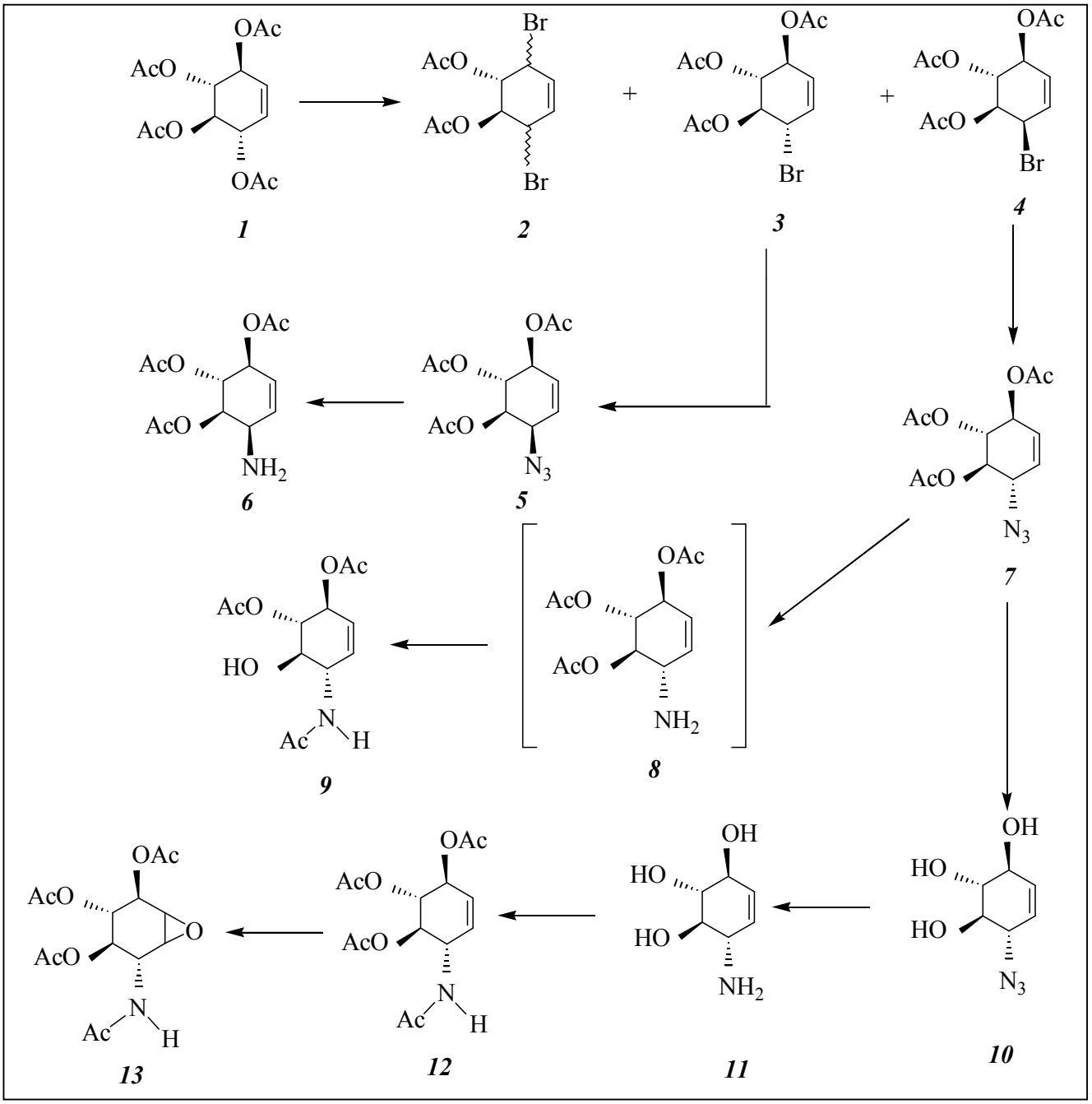
♦ The starting material is racemic and therfore all compounds synthesized are racemic too.

by column chromatography. The high percentage of inversion of configuration at C4 (45 %) in reaction of ***1*** with hydrobromic acid in

acetic acid is probably due to SN2 reaction and some SN1 reaction enhanced with the adjacent double bond and acetoxy group at C3.

The ^{1}H NMR spectrum [see table 1] of the monobromide of Rf 0.28 showed a signal ddd at δ 4.66ppm for H-4 with coupling constant $J_{3,4}$ of magnitude 8.25 Hz and $J_{4,5}$ of 3.5 Hz which indicates that H-4 and H-3 are pseudo diaxially disposed and therefore structure ***3*** was assigned to it. While the H-4 signal of the less mobile monobromide of Rf 0.20 appeared as dd at δ 4.86 ppm with a coupling constant $J_{3,4}$= 4.5 Hz which indicated that C-4 must have the inverted configuration which is consistent with structure ***4*** [1]. The acetates groups of compounds ***2-4*** appeared as three singlets between 2.01—2.15 ppm.

Having (±)–(1,3, 4/2)-1, 2, 3-tri-O-acetyl-4-bromo-5-cyclohexene-1, 2, 3-triol ***4*** of Rf 0.20 being separated in pure state it was treated with freshly prepared tetra-n-butyl ammonium azide in methylene chloride at room temperature [6]. The result was a single product as indicated by TLC, Rf 0.19. ^{1}H NMR spectrum of this azide [see table 1] has shown a signal at δ 4.18ppm as *ddd* with coupling constant $J_{3,4}$ of the magnitude 7.5Hz and $J_{4,5}$ = 2.5 Hz. This suggests that C4 has been inverted in configuration during the reaction and H-4 and H-3 are now diaxially oriented as in structure ***7***. Similarly when the (±) –(1,3/2,4)-1, 2, 3-tri-O-acetyl-4-bromo-5-cyclohexene-1,2,3-triol ***3*** was treated with tetra-n-butylamminum azide it gave the azide ***5*** which undergone an inversion in configuration



Scheme 1: Synthesis pathway of ***13*** from conduritol-B-tetraacetate ***1.***

Table 1: ^{1}H NMR Data chemical shifts in δ ppm and coupling constants in Hz.

Compound	H-1	H-2	H-3	H-4	H-5	H-6
2 R_f 0.39	5.59(dd)	5.34 (dd) overlapped		5.59 (dd)	5.59 overlapped	
3 R_f 0.28 3.5 %	5.63 (m) overlapped with H-5	5.19 (dd) $J_{1,2}$=8 Hz $J_{2,3}$=10 Hz	5.48 (dd) $J_{2,3}$=10.5 Hz $J_{3,4}$=8.5 Hz	4.66 (ddd) $J_{3,4}$=8.25 Hz $J_{4,5}$=3.5 Hz	5.95 (dt) $J_{4,5}$=2.25 Hz $J_{5,6}$=10.5 Hz	5.95 (dt) $J_{1,6}$=3 Hz $J_{5,6}$=10.5 Hz
4 R_f 0.20 42.5 %	5.627 (m) overlapped		4.935 (dd) $J_{2,3}$=6.5 Hz $J_{3,4}$=4.5 Hz	4.86 (dd) $J_{3,4}$=4.5 Hz	6.033 (ddd) $J_{4,6}$=7.5 Hz $J_{4,5}$=5 Hz	5.627 (m) overlapped with H-1
5 R_f 0.24	5.48 (m) overlapped		5.112 (ddd) $J_{2,3}$=5.5 Hz $J_{3,4}$=3.3 Hz	4.35 (t) $J_{3,4}$=4.5 Hz	5.79 (m) $J_{4,5}$=1.5 Hz $J_{5,6}$=10.5 Hz	5.862 (ddd) $J_{1,6}$=6 Hz $J_{5,6}$=10.5 Hz
7 R_f 0.19	5.56 (ddd) $J_{1,2}$=7.5Hz $J_{1,6}$=2.5Hz		5.26 (m) overlapped	4.18 (ddd) $J_{3,4}$=7.5 Hz $J_{4,5}$=2.5 Hz	5.75 (m) overlapped	5.862 (ddd) $J_{1,6}$=6 Hz $J_{5,6}$=10.5 Hz

at C4 ($J_{3,4}$=4.5 Hz) similar to ***4***, $J_{3,4}$=4.5 Hz.

Reduction of the azide ***5*** with triphenylphosphine [6] gave the amine ***6***. IR spectrum showed a broad band at 3450 cm^{-1} attributed to free and bonded N-H and an absorption at 1740cm^{-1} for the acetate groups. NMR spectrum showed three single signals at δ 2.02 ; 2.1; 2.05 ppm for 3×$OCOCH_3$. Reduction of the azide ***7*** with triphenylphosphine in a similar manner, TLC has shown the diminishing of azide spot Rf 0.19 but giving rise to a single spot of Rf 0.5 which did not respond to ninhydrine spray. IR showed weak and broad bands absorptions at region 4000-3500 cm^{-1} for free and bonded OH and NH and sharp and medium absorptions at 1730 and 1680cm^{-1} for CO and CON stretchings respectively. These observations suggest that the product ***8*** might have converted to ***9*** by spontaneous O-N acetyl migration [7]. To avoid such migration, the acetate groups of the azide ***7*** have been removed by alkaline hydrolysis to give rise to the azide ***10*** free of acetates. The latter was reduced with triphenylphosphine to give the corresponding amine ***11***. Acetylation of ***11*** with acetic anhydride gave tri-O-acetyl-4-acetamido conduritol-B ***12*** .

Epoxidation of the : (±) –(1,3 / 2,4) -1, 2, 3 – tri – O – acetyl - 4 - acetamido – 5 - cyclohexene - 1,2,3 - triol ***12*** with metachloroperbenzoic acid [8,9] gave a single product. IR spectrum showed the following characteristic bands at γ max 1725cm^{-1} for acetate groups; 1670cm^{-1} for acetamido group and 850cm^{-1} for the epoxide [10]. ^{1}H NMR spectrum showed one singlet signal at 1.8 ppm integrated for 3H attributed to CH_3 of acetamido group and three single signals integrated for 9H at δ 2.20; 2.25; 2.27 ppm for three acetate groups and a triplet at 3.2 ppm for one proton attributed to H2 based on $J_{2,1}$ and $J_{2,3}$ = 4.3 Hz and at 3.65 ppm as multiplet for one proton attributed to H3. This suggested that the direction of epoxidation was taken place almost entirely *cis* to the acetamido group .

EXPERIMENTAL

TLC was carried out on DC-Alufolian Kiesel- gel 60, Art.5553 produced by Merk. ^{1}H NMR spectra were recorded (internal Me_4Si) in $CDCl_3$ at 300 MHz unless stated otherwise. Melting points were recorded by Büch; 510 melting point apparatus and they are uncorrected.

REACTION OF (±) –CONDURITOL-B-TETRAACETATE 1 WITH HYDROBROMIC ACID:

(±) –Conduritol-B-tetraacetate ***1*** (200mg,0.6 mmole) was dissolved in hydrobromic acid /acetic acid 30 % (1.5 ml,10 mmole) and the reaction mixture was set aside in dark at room temperature for 18 hours. Proceeding of reaction was followed by TLC eluted with CCl_4/MeOH 9:1, (detected by alkaline potassium permanganate). Four spots were developed during the time of reaction of Rf :0.64; 0.59; 0.54 and 0.42. Toluene (1ml) was added followed by gradual addition of solid $NaHCO_3$ to the reaction mixture aided with magnetic stirring until evolution of gases seized. Saturated solution of $NaHCO_3$ was then added dropwise with continuous stirring to neutrality. Two layers were separated and the toluene layer was then washed with brine, then dried on anhydrous $MgSO_4$, filtered off to give clear yellow filtrate. The filtrate was evaporated to dryness on a warm water bath (50°) to give a brown syrup (162 mg, 81 %).

SEPARATION OF (±) -1,4 - DIBROMO-2, 3-DI-O-ACETYL - CONDURITOLS **2** ; (±) –(1,3/2,4)- 1,2,3-TRI-O-ACETYL-4-BROMO-5-CYCLOHEXENE-1,2,3-TRIOL **3** and (±)-(1,3,4/2)-1,2,3- TRI-O- ACETYL -4- BROMO-5-CYCLOHEXENE-1,2,3-TRIOL **4**:

The crude reaction mixture of bromoconduritols ***2***,***3*** and ***4*** (0.85 g) was adsorbed into column of silica gel of the kind (TLC 10-40 μm) (302 g) packing and elution were done by aid of pumping air from above the column and connecting the column from below to a moderate vacuum. Column was eluted with n-hexane/EtOAc 3:7, small fractions were collected (1ml every minute). Six groups of fractions were collected based on Rf values:

*Fraction one of Rf 0.39 for (±) -1,4Dibromo-2, 3-di-O-acetyl-Conduritols **2**:* (117 mg, 11.8 %) as colorless crystalline, m.p. 170-175°C recrystallized from methanol-hexane to give colorless crystals m.p., 170-173 °C, γmax

1740 cm^{-1} (Ac), ^{1}HNMR (see table1), (Found: C, 34.54 %; H, 3.57 %. Calculated for $C_{10}H_{12}O_4Br_2$: C, 34.74 %; H, 3.40 %).

Fraction two of Rf 0.39 and 0.28 attributed to a mixture of compounds ***2*** + ***3*** (3.4 mg, ~ 3.4 %) as a brownish syrup, γmax 1740 cm^{-1}.

Fraction three of Rf 0.28 attributed to (±) –(1,3 / 2,4)-1, 2, 3-tri-O-acetyl-4-bromo-5-cyclohexene-1, 2, 3-triol ***3*** (34.7 mg, 3.5 %) as colorless crystalline product m.p. 65-68°C. IR has shown a relatively strong absorption at γmax 1740 cm^{-1}. ^{1}H NMR (see table1). (Found: C, 42.83 %; H, 4.45 %. Calc. for $C_{12}H_{15}O_6Br$: C, 43.01 %; H, 4.51 %).

Fraction four of Rf 0.28 and 0.2 attributed to the mixture of compounds ***3*** and ***4*** (65.7 mg, 6.65 %) as a brownish solid recrystallised from n-hexane to give colorless crystalline (53.2 mg, 6.5 %) mp 76-81°C. IR, γmax 1740 cm^{-1}. (Ac). (Found: C, 43.51 %; H, 4.69 %. Calc. for $C_{12}H_{15}O_6Br$: C, 43.01 %; H, 4.51 %).

Fraction five of Rf 0.2 attributed to (±) –(1,3, 4/2)-1, 2, 3-tri-O-acetyl-4-bromo-5-cyclohexene-1, 2, 3-triol ***4*** (420mg, 42.5 %) as colorless crystalline m.p.120-123 °C, recrystallized from methanol/n--hexane to give colorless crystalline solid m.p., 120 °C. IR has shown an absorption at γmax 1740 cm^{-1} (Ac) in a similar intensity as for ***3***. ^{1}HNMR (see table1). (Found: ; C, 42.82 %; H, 4.51 %.Calc. for $C_{12}H_{15}O_6Br$: C, 43.01 %; H, 4.51 %).

*Fraction six of Rf 0.13 for starting conduritol-B-tetraacetate **1*** : (200mg, 23 %) colorless crystalline solid m.p.95,5°C IR, γmax 1740cm^{-1} (Ac) very strong.

(±)–(1,3/2,4)-1,2,3-TRI-O-ACETYL-4-AZIDO-5-CYCLOHEXENE-1, 2, 3-TRIOL **7**:

Compound ***4*** (60 mg, 0.2 mmole) was added to a solution of freshly prepared tetra-n-butylammonium azide (1.23 g, 4.5 mmole) in methylene chloride (1 ml) and set aside at room temperature until TLC (eluted with n-hexane/EtOAc 3:7) showed the development of new spot of Rf 0.24 at the expense of disappearing of ***4***. Water (10 ml) was added and the mixture was extracted with ether (20 ml). The ethereal layer was dried over anhydrous $MgSO_4$, filtered and evaporated to near dryness under vacuum*. The rest of ether was allowed to evaporate to dryness under atmospheric pressure at room temperature to give colorless crystalline ***7*** (43.2 mg; 72 %), m.p. 125-129 °C, recrystallized from methanol/n-hexane to give colorless crystalline m.p. 125-127 °C. IR, γmax 2100 cm^{-1} (N3 stretching) and 1740 cm^{-1} (Ac). ^{1}H NMR (see table1) . (Found: C, 49.05%; H, 5.4 %.; N, 13.6 %. Calc. for $C_{12}H_{15}O_6N_3$: C, 48.49 %; H, 5.09 %, N, 14.14 %).

(±)–(1,3,4/2)-1,2,3-TRI-O-ACETYL-4-AZIDO-5-CYCLOHEXENE-1,2,3-TRIOL**5** :

Compound ***3*** (60mg, 0.2 mmole) was treated with tetra-n-butylammonium azide as with procedure of preparation of *9* gave (±) –(1,3, 4/2)-1, 2, 3-tri-O-acetyl-4-azido-5-cyclohexene-1, 2, 3-triol ***5*** (40.8 mg, 60 %) m.p. 120°C. IR showed a moderately strong band at γmax 2100 cm^{-1} (N_3 stretching) and 1740cm^{-1}. (Ac). ^{1}H NMR (see table1) . (Found: C, 49.06 %; H, 5.38 %; N, 13.6 %. Calc. for $C_{12}H_{15}O_6N_3$: C, 48.49 %; H, 5.09 %, N, 14.14 %).

(±)–(1,3,4/2)-1,2,3-TRI-O-ACETYL-4-AMINO -5-CYCLOHEXENE-1, 2, 3-TRIOL **6** :

The azide ***5*** (20 mg, 0.07 mmole) was dissolved into dry THF (2 ml), Ph_3P (60 mg, 0.23 mmole) was added and the reaction mixture was allowed to stand at room temperature. The progress of the reaction was monitored by TLC and IR. Each sample of TLC was spotted on two plates , both were eluted with toluene/methanol 7:3, one plate was detected as normal with alkaline potassium permanganate to show the diminishing of the spot of Rf 0.19 responsible for the starting azide ***5***. The second plate was detected with ninhidrine spray to show the development of the amine ***6*** as a pink spot of Rf 0.22. The reaction can be also followed by IR spectroscopy by means of taking one drop sample directly from the reaction mixture and spotting it on an NaCl disc. IR spectra showed the growing absorption band at 1660 cm^{-1} for N=P of the complex formation while the band at 2100 cm^{-1} for N_3 was diminishing. When all azide ***5*** was consumed, water (2 drops) was added and the reaction mixture was heated on a warm water bath at 50 °C for 12 hours to break down the reaction complex. Water (5 ml) was added and the mixture was extracted several times with ether. The ethereal extracts were combined and dried over anhydrous $MgSO_4$, then filtered and evaporated to dryness to yield white crystalline solid (47 mg) of a mixture of (±) –(1,3, 4/2)-tri-O-acetyl-4-amino-5-cyclohexene-1, 2, 3-triol ***6*** and some Ph_3P. The mixture was separated by column chromatography packed with silica gel (10-40μm for TLC) in the ratio of 1:350 (reaction mixture : silica gel) eluted with benzene/MeOH 7:3 using moderate pressure to aid flow of solution. Ph_3P was collected as a white crystalline (14.6 mg) and (±) –(1,3, 4/2)-tri-O-acetyl-4-amino-5-cyclohexene-1, 2, 3-triol ***6*** as white crystalline (13 mg; 65 %) m.p. 76-79 °C. IR spectrum showed the following characteristic bands at 3450 cm^{-1} (broad) for (free and bonded NH2), 1740 cm^{-1} for (OAc). ^{1}H NMR (90 MHz) spectrum showed: 2.02; 2.05; 2.15 ppm, 3s(3×OAc); and 5.83m (H5×H6). (Found: C, 53.41 %; H, 6.16 %.; N, 4.13 %. Calc. for $C_{12}H_{17}NO_6$: C, 53.13 %; H, 6.27 %, N, 5.17 %).

(±)–(1,3/2,4)-1,2,3-TRI-O-ACETYL-4-AMINO-5-CYCLOHEXENE-1,2,3-TRIOL **8** and (±)– (1,3/ 2,4)-1,2,-DI-O-ACETYL-4-ACETAMIDO-5-CYCLOHEXENE-1,2,3-TRIOL **9** :

The azide *7* (20mg, 0.07 mmole) was treated with Ph_3P as above.Separation achieved by column chromatography to give a white crystalline material (12mg) m.p. 136-140°C, attributed to (±) –(1,3/2,4)-1, 2, 3-tri-O-acetyl-4-amino-5-cyclohexene-1, 2, 3-triol ***8*** and (±) –(1,3/ 2,4)-1, 2, -di-O-acetyl-4-acetamido-5-cyclohexene-1, 2, 3-triol ***9*** which_did not react towards ninhydrin spray.

IR spectrum has shown a weak broad absorption at 4000-3500 cm^{-1} (free and bonded OH and NH); 1730 cm^{-1} (OAc) and 1680 cm^{-1} (N-Ac).

* Caution: Several cases of explosions had occured during evaporation to dryness under vacuum on a warm water bath.

(±) –(1,3/2,4)- 4-AZIDO-5-CYCLOHEXENE-1, 2, 3-TRIOL **10**:

The azide *7* (64mg, 0.22 mmole) was dissolved in methanol (3 ml). Two drops of methanolic solution of sodium methoxide were added and the reaction mixture allowed to stand in dark at room temperature for 12 hours. TLC eluted with n-butanol/H_2O/HOAc 4:1:1 showed the development of one spot Rf 0.41. Few drops of diluted acetic acid in methanol were added until neutralization. The mixture was evaporated to dryness to give white crystalline solid. THF (5 ml) was added to dissolve the organic material and filtered off. The filtrate dried over anhydrous $MgSO_4$, filtered off and evaporated to dryness under vacuum to give a syrup (±) –(1,3, 2/4)- 4-azido-5-cyclohexene-1, 2, 3-triol ***10*** (61mg, 93.7 %). IR showed bands at 3400-3100cm^{-1} broad band (free and bonded OH), 2100 cm^{-1} (N_3). ^{1}H NMR (90 MHz), 5.74S (2H, H5 and H6). (Found: C, 41.93 %; H,5.35 %.; N, 24.66 %. Calc. for $C_6H_9N_3O_3$: C, 42.11 %; H, 5.26 %, N, 24.56 %) .

(±)–(1,3/2,4)-4-AMINO-5-CYCLOHEXENE-1,2,3-TRIOL. [4-AMINO-4-DEOXY CONDURITOL-B], **11**:

The azide ***10*** (400 mg, 2.3 mmole) was dissolved into anhydrous THF; Ph_3P (600 mg, 2.3 mmole) was added and the reaction mixture allowed to stand at room temperature for 48 hours. The proceeding of the reaction was monitored by TLC and IR as described earlier in preparation of 11. Water (10 drops) was added and the reaction mixture was heated on a warm water bath at 50 °C for 72 hours. The mixture was extracted continually with chloroform, the extract was dried over anhydrous $MgSO_4$, filtered off, and evaporated under vacuum to give a brownish semi-solid compound (720 mg). A small amount of methanol was added to dissolve the amine and filtered off, evaporated to dryness to give semi solid (±) –(1,3/2,4)- 4-amino-5-cyclohexene ***11*** (286mg; 67%). IR spectrum showed a broad band in the region 3500-3200 cm^{-1} (free and bonded OH and NH_2). (Found: C, 50.01 %; H, 7.62 %.; N, 9.43 %. Calc. for $C_6H_{11}NO_3$: C, 49.66 %; H, 7.59 %, N, 9.65 %.

(±)–(1,3/2,4)-1,2,3-TRI-O-ACETYL-4-ACETAMIDO-5-CYCLOHEXENE -1,2,3-TRIOL **12**:

The amine ***11*** (200 mg, 2.1 mmole) was dissolved in acetic anhydride (9ml), anhydrous pyridine (2drops) and chloroform (2 ml) were added. The reaction mixture was allowed to stand at room temperature for 30 minutes. TLC eluted with pet ether (60-80)/EtOAc 4:6 showed three spots, Rfs 0.42; 0.18; 0.14. The reaction mixture was evaporated to dryness to give brownish semi-solid substance (300 mg). The crude product (200 mg) was adsorbed into column chromatography packed with silica gel for TLC (GF60) in a ratio of 1:300 eluted with pet-ether (60-80)/EtOAc 4:6, gave compound ***12*** (100 mg; 50 %) m.p.133-135 ^oC. IR spectrum showed bands at 1725 cm^{-1}(CO-acetate) and at 1670 cm^{-1}(CO-amide).^{1}H NMR (90MHz),1.8s($CONH_3$); 2.04s, 2.05s, 2.07s(3xOAc); 5.84 t(H-5);5.87 t(H-6). (Found: C,53.77 %; H,6.29 %; N, 3.97 %. Calc. for $C_{14}H_{19}NO_7$: C,53.67 %; H,6.07 %; N,4.47 %.

(±)–1-ACETAMIDO-2,3-ANHYDRO-4,5,6-TRI-O-ACETYL-1-DEOXY -MYO-INOSITOL **13**:

To compound ***12*** (20 mg, 0.07 mmole) in CH_2Cl_2 (60 ml), m-chloroperbenzoic acid (27 mg, 0.2 mmole) was added, the mixture was heated under reflux in darkness for two hours. Aqueous saturated solution of: $NaHCO_3$ (25 ml) was added gradually with vigorous stirring until neutrality. The organic layer was washed with an aqueous saturated solution of $Na_2S_2O_3.5H_2O$, then washed again with $NaHCO_3$ followed with water. The organic layer dried over anhydrous $MgSO_4$, filtered and evaporated to dryness to give solid substance which extracted with ether; The ether extract showed one spot on TLC eluted with toluene/MeOH 7:3, Rf 0.35 which was detected by molybdatophosphoric acid. The ether extract dried over $MgSO_4$, filtered and evaporated to dryness to give semi solid (±) –1-acetamido-2,3-anhydro-4,5,6-tri-O-acetyl-1-deoxy-myo-inositol ***13*** (12 mg),crystallized by standing at room temperature, m.p. 148-154 °C. IR γmax 1725 cm^{-1} (OAc), 1670 cm^{-1} (N-Ac) and 850 cm^{-1} (epoxide). ^{1}H NMR (90MHz), 3.2 t(1H,H2,$J_{2,1}$= 4.3 Hz, $J_{2,3}$= 4.3 Hz),3.65 m (1H,H3),2.20, 2.25, 2.27 3s(3×O-$COCH_3$); 1.8s (N-$COCH_3$), Anal. Found: C, 50.83%; H, 5.55 %; N, 4.46 %. Calc. for $C_{14}H_{19}NO_8$: C, 51.06 %; H, 5.77 %, N, 4.26 %,

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