# *The Synthesis and Configurational Analysis of 2-Amino-1,3-cyclohexanediol*

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Interest in inosamine and inosadiamine has been stimulated by their occurrence in certain antibiotics. The previous studies of 2-amino-cyclohexanol derivatives[1,2] have stimulated our interest in the synthesis of alicyclic compounds which have three neighboring groups. An attempt to prepare 2-amino-1, 3-cyclohexanediol was abandoned by McCasland et al. because of the poor yield of a corresponding nitrodiol.[3] Very recently, however, Lichtenthaler[4] synthesized two diastereomeric 2-amino-1, 3-cyclohexanediols (trans and DL-isomers) through the nitrodiol obtained by the cyclization of glutaraldehyde with nitromethane.

In the present paper, synthetic routes to another diastereomeric 2-amino-1, 3-cyclohexanediol (cis isomer) will be described, and its structure assignment will be made by means of the proton magnetic resonance spectrum of its acetyl derivative.

The cyclization of glutaraldehyde with nitromethane in the presence of sodium carbonate gave 2-nitro-1, 3-cyclohexanediol (IV).[4] Hydrogenation with Raney nickel, T4,[5] gave 2$\alpha$-amino-1$\beta$, 3$\beta$-cyclohexanediol (Ia) in a 63% yield. In order to establish the configurational purity of Ia, paper chromatography was employed. The compound, Ia, consumed 1.91 mol. of the periodate in an aqueous solution in 20 hr., showing a single spot ($R_f$ 0.59) in 1-butanol-ethanol-water (2 : 1 : 3), and also a single spot ($R_f$ 0.45) in 1-butanol-acetic acid-water (4 : 1 : 5). These data provide strong, if not conclusive, evidence that Ia is a single isomer.

The acetylation of IV with acetic anhydride and a small amount of concentrated sulfuric acid gave di-*O*-acety-2-nitro-1, 3-cyclohexanediol (VI).[4] VI was hydrogenated with Raney nickel, T4,[5] to give 2$\alpha$-acetamido-*O*-aecty-1$\beta$, 3$\beta$-cyclohexanediol (VII) in a 75% yield; this might be obtained through the O→N migration of an acetyl group[6] during the course of reduction. VII was further acetylated to give the triacetyl derivative of Ia, Ib, in a 83% yield. Under Kunz's conditions,[7] Ib was selectively deacetylated; this showed the presence of two hydroxyl groups. The *N*-acetyl derivative Ic was recovered from the neutralized solution of Kunz's hydrolysis. Ic did not consume any periodate in an aqueous methanol solution in 50 hr. These data are consistent with a cyclic structure with one acetamido group between two hydroxyl groups.

To obtain the other diastereomers of Ia, an inversion reaction of its mesyl derivative was employed. When a cyclohexane ring containing vicinal mesyloxy and acylamido groups in the trans position was treated with sodium acetate in refluxing aqueous 2-methoxyethanol, the replacement of the mesyloxy group takes place with Walden inversion through an intermediary oxazolinium ion to give *cis*-acylamido alcohol.[8] On the other hand, when vicinal mesyloxy and acylamido groups are in the cis position, the replacement of the mesyloxy group takes place at a considerably slower rate.[9]

1) T. Suami, S. Ogawa and S. Umezawa, This Bulletin, **35**, 474 (1962).
2) T. Suami, S. Ogawa and S. Umezawa, ibid., **36**, 459 (1963).
3) G. E. McCasland, T. J. Matchett and M. Hollander, *J. Am. Chem. Soc.*, **74**, 3429 (1952).
4) F. W. Lichtenthaler, *Chem. Ber.*, **96**, 845 (1963).
5) S. Nishimura, This Bulletin, **32**, 61 (1959).
6) G. Fordor and J. Kiss, *J. Am. Chem. Soc.*, **72**, 3495 (1950).
7) A. Kunz and C. S. Hudson, ibid., **48**, 1982 (1926).
8) S. Winstein and R. E. Buckles, ibid., **64**, 2787 (1942); G. E. McCasland, R. K. Clark, Jr., and H. E. Carter, ibid., **71**, 637 (1949); S. Winstein, L. Goodman and R. Boschan, ibid., **72**, 2311 (1950); T. Taguchi and M. Nakayama, ibid., **73**, 5679 (1951); B. R. Baker and R. E. Schaub, *J. Org. Chem.*, **19**, 646 (1954); B. R. Baker, R. E. Schaub and J. H. Williams, *J. Am. Chem. Soc.*, **77**, 7 (1955); R. W. Jeanloz, ibid., **79**, 2591 (1957); A. C. Richardson and H. O. L. Fischer, ibid., **83**, 1132 (1961).
9) S. Winstein, E. Grunwald, R. E. Buckles and C. Hanson, ibid., **70**, 816 (1948).

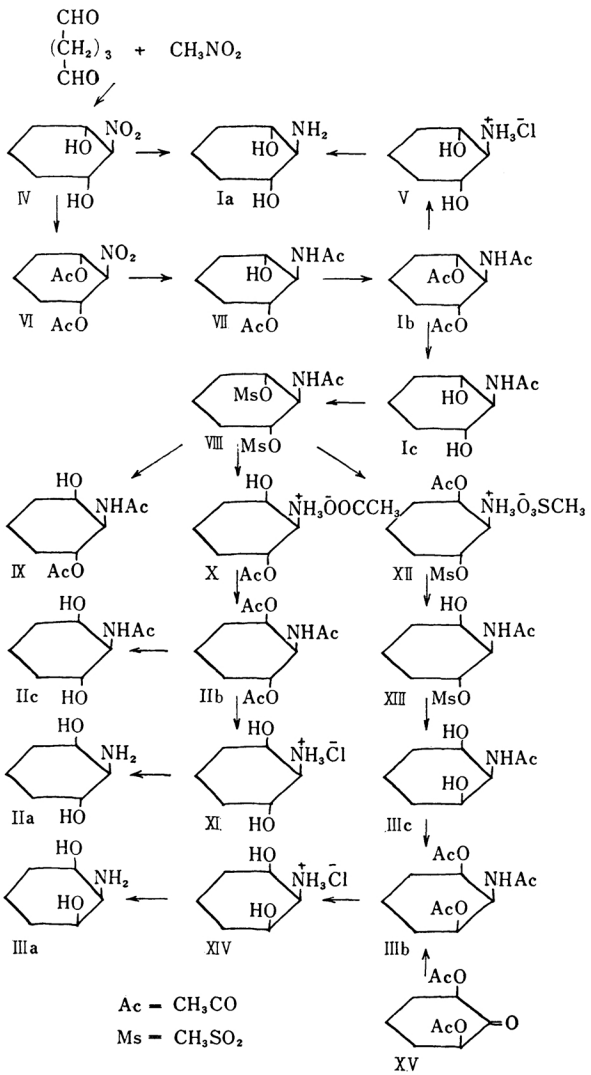
The compound, Ic, gave a dimesyl derivative (VIII) by reaction with mesyl chloride in pyridine.[4] The displacement of both mesyloxy groups of VIII gave DL-*O*-acetyl-2$\alpha$-amino-1$\alpha$, 3$\beta$-cyclohexanediol acetate (X) when the reaction with two moles of sodium acetate was carried out in boiling water for 1 hr. The fact that the replacement of two mesyloxy groups in VIII took place at a considerably higher rate showed that the C-1 and C-3 mesyloxy groups were both situated in the trans position to the C-2 acetamido group.[9] X gave a triacetyl derivative IIb melting at 146°C in a 74% overall yield, after acetylation. Studies of a detailed reaction mechanism in this reaction are in progress.

When IIb was hydrolyzed with 6 N hydrochloric acid, DL-2$\alpha$-amino-1$\alpha$,3$\beta$-cyclohexanediol hydrochloride (XI) melting at 117°C was obtained. The free base IIa melting at 113°C was recovered from XI with a sodium hydroxide solution. A paper chromatography of IIa showed a single spot ($R_f$ 0.49) in 1-butanol-acetic acid-water (4 : 1 : 5).

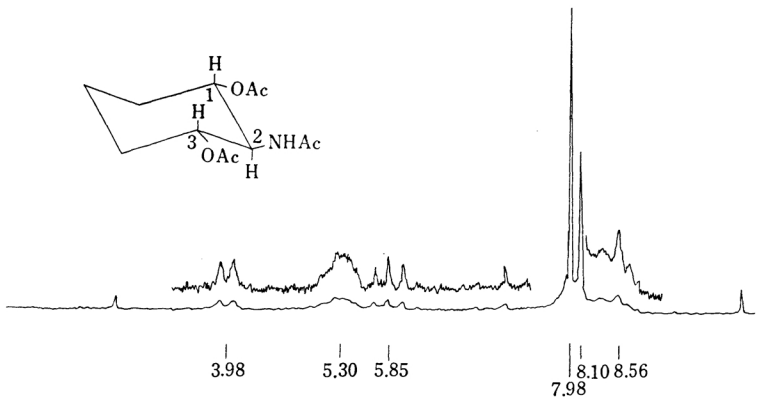
When VIII was refluxed in water for a few minutes, without adding any sodium acetate, DL-*O*-acetyl-*O*-mesyl-2$\alpha$-amino-1$\alpha$, 3$\beta$-cyclohexanediol methanesulfonate (XII) was produced in a 74% yield. In this reaction, the replacement of the mesyloxy group yielded an oxazolinium ion which was attacked by water to give *cis*-acetamido alcohol as usual. Then the acetyl group could migrate from nitrogen to oxygen in an acidic medium to yield XII, which could not have a further inversion because of the lack of an acetamido group adjacent to the mesyloxy group.

When treated with sodium hydroxide solution, XII gave DL-2$\alpha$-acetamido-*O*-mesyl-1$\alpha$, 3$\beta$-cyclohexanediol (XIII) in a 73% yield. Accordingly, it must involve the O→N migration of the acetyl group.[6] Since XIII had the mesyloxy group situated in the trans position to the vicinal acetamido group, a further inversion was expected. XIII was refluxed in 95% aqueous 2-methoxyethanol for 5 hr. to yield the *N*-acetyl derivative IIIc melting at 121.5°C with an inversion of the configuration. IIIc was acetylated to give the triacetyl derivative IIIb melting at 179°C.

IIIb was also obtained via a different synthetic route starting from *cis*-2, 6-diacetoxycyclohexanone (XV). XV was prepared by the oxidation of cyclohexanone with lead tetraacetate in boiling benzene.[10] The structure and configuration of XV were established by converting it to 1$\alpha$, 2$\alpha$, 3$\alpha$-cyclohexanetriol of a known configuration.[11] Anderson and Lardy[12] found that the primary amine obtained from the phenylhydrazone or oxime of *scyllo*-inosose practically consisted of a single isomer, when glacial acetic acid was used as a solvent and Adams platinum oxide, as a catalyst. Therefore, the reduction of *cis*-2, 6-diacetoxycyclohexanone oxime was carried out using the procedure of Anderson and Lardy.[12] Then the crude reduction product was treated with acetic anhydride in pyridine to obtain the compound, which was identical with IIIb. However, the yield was unexpectedly low. Since the starting material, XV, had a known configuration, the only point requiring to be clarified was the configuration of the newly-introduced amino group. The steric selectivity of the reduction condition employed in this

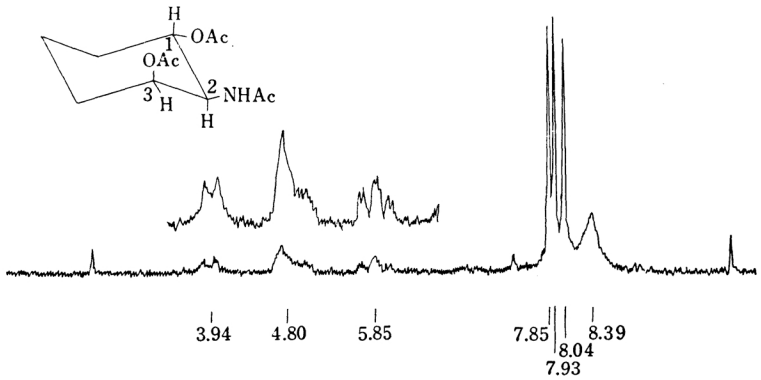



10) G. W. K. Cavill and D. H. Solomon, *J. Chem. Soc.*, **1955**, 4427.
11) T. Posternak and F. Ravenna, *Helv. Chim. Acta*, **80**, 441 (1947).
12) L. Anderson and H. A. Lardy, *J. Am. Chem. Soc.*, **72**, 3141 (1950).



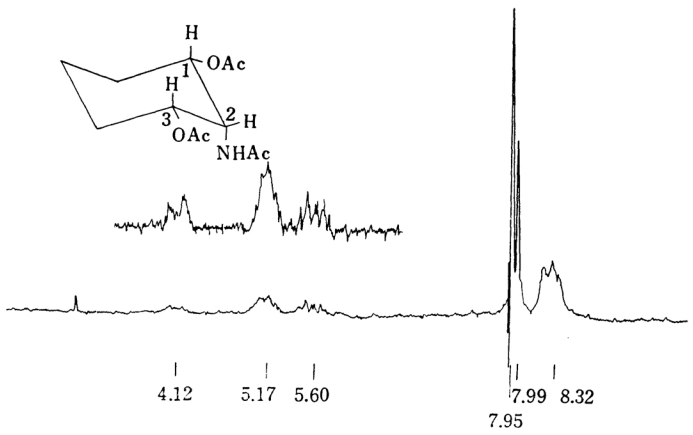

p. p. m., $H \rightarrow$

Fig. 1-A.




p. p. m., $H \rightarrow$

Fig. 1-B.




p. p. m., $H \rightarrow$

Fig. 1-C.

Fig. 1. NMR spectra in deuteriochloroform at 60 Mc.
Peak positions are given in $\tau$-values.

synthesis seemed ample enough to enable us to assign IIIb as all-cis configuration.

IIIb was hydrolyzed with 6 N hydrochloric acid to give 2α-amino-1α, 3α-cyclohexanediol hydrochloride (XIV) melting at 161.5°C. The free base IIIa melting at 128°C was obtained from XIV by an ordinary method. A paper chromatography of IIIa showed a single spot ($R_f$ 0.44) in 1-butanol-acetic acid-water (4 : 1 : 5).

The above consideration of the configuration of IIIb has been fully substantiated by means of its proton magnetic resonance spectra, as will be described below.

The protons of the acetoxy and acetamido groups of Ib and IIb have already been assigned by Lichtenthaler.[4] In the present study, the NMR spectrum of the compound, IIIb, gave two sharp signals of a 2 : 1 relative intensity (cf. Fig. 1-C), as was to be expected from the two equatorial acetoxy groups ($\tau$ of 7.95) and the axial acetamido group ($\tau$ of 7.99).

Lemieux et al.[13] assigned the configurations of two diastereomeric 2-acetoxy-1, 3-dimethoxycyclohexanes on the basis of the fine structure of an axial proton on C-2 in their NMR spectra. In the present experiments, the axial proton on C-2 of Ib was coupled with the two axial protons on the neighboring carbon atoms (C-1 and C-3) ; the signal for this proton should be a triplet with an intensity of 1 : 2 : 1 ($J_{aa}$=8~11.5 c.p.s.).[14] As Fig. 1-A shows, Ib was readily recognized as a trans isomer by the triplet centered at 5.85 with a 1 : 2 : 1 relative intensity (observed $J$=10.5 c.p.s.). In the case of IIb, the proton on C-2 was coupled with an axial proton (C-1 or C-3) and an equatorial proton (C-3 or C-1). Since the coupling between an equatorial proton and an axial proton was considerably weaker than that between two axial protons, the signal for the proton on C-2 could be anticipated to be a quartet. However, the sextuplet at 5.85 in the observed spectrum of IIb shown in Fig. 1-B could not be interpreted without counting the spin-spin coupling between the proton on C-2 and the proton on the nitrogen atom.[15] The spin-spin coupling constant between the proton on C-2 and the proton on the nitrogen atom in the trans orientation was about 9.0 c.p.s. (observed value) ; this value was close to that of the observed $J_{aa}$.

Also in the case of IIIb, it could be distinguished from the others by its lack of an axial proton on C-2. In Fig. 1-C, the signal for the proton on C-2 appears in a lower field (centered at 5.60) ; it can be recognized that this proton is in an equatorial position.

The signal of the protons on C-1 and C-3 was not well resolved, but the width of the signal presented some information on the configurations. The spin-spin coupling constant was greater between two axial protons than between axial-equatorial, or two equatorial protons.[16] Therefore, the most narrow peak width observed in Fig. 1-C was consistent with the assigned configuration of IIIb. The peak widths are listed in Table I.

Table I. Chemical shifts expressed in τ-values

| Protons (C-1 and C-3) | | Peak width c.p.s. |
|---|---|---|
| Ib | 5.30 | 30 |
| IIb | 4.80 | 30 |
| IIIb | 5.17 | 17 |

The other six protons showed a signal at 8.32~8.56, as was expected from the ring protons of cyclohexane in the chair conformation.[17]

As a result of these considerations of the NMR spectra and the chemical evidence, it has been concluded that the compound IIIb (m. p. 179°C) has the cis configuration, and Lichtenthaler's assignmets for the Ib and IIb compounds have been further confirmed. All three predicted diastereomers of 2-amino-1, 3-cyclohexanediol have now been synthesized.

## Experimental

All melting points are corrected, and unless noted otherwise, they were measured in a liquid bath. The melting points marked with asterisks were measured on a Mitamura-Riken micro hot stage. The NMR spectra of all the acetyl derivatives were determined at a frequency of 60 Mc. with a Japan Electron Optics instrument JNM-C-60 in deuteriochloroform containing tetramethylsilane as an internal reference. The peak positions are given in τ-values. The infrared spectra were recorded in potassium bromide pellets.

**2α-Nitro-1β, 3β-cyclohexanediol (IV).** — By the method of Lichtenthaler,[4] the cyclization of glutaraldehyde with nitromethane gave IV in a 59.5% yield ; m. p. 161.5~163.5°C (recrystallized from ethyl acetate). (Reported m. p. 159~161°C).[4] (Found : C, 44.92 ; H, 6.70 ; N, 8.71%).

**2α-Amino-1β, 3β-cyclohexanediol (Ia).**—A mixture of 5.0 g. of IV and 50 ml. of absolute ethanol was hydrogenated at room temperature under 40 p. s. i. g. of initial hydrogen pressure with a Raney

13) R. U. Lemieux, R. K. Kullnig and R. Y. Moir, ibid., **80**, 2237 (1958).
14) W. F. Trager, F. F. Vincenzi and A. G. Huitric, *J. Org. Chem.*, **27**, 3006 (1962).
15) J. A. Pople, W. G. Schneider and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill, New York (1959), pp. 366~371 ; L. H. Piette, L. D. Ray and R. A. Ogg, *J. Mol. Spectroscopy*, **2**, 66 (1958).
16) S. Brownstein and R. Miller, *J. Org. Chem.*, **24**, 1886 (1959).
17) F. R. Jensen, D. S. Noyce, C. H. Sederholm and A. J. Berlin, *J. Am. Chem. Soc.*, **84**, 386 (1962).

nickel T4 catalyst,[5] obtained from 7.0 g. of Raney nickel alloy, in a Parr shaker-type hydrogenation apparatus for 1 hr. After the catalyst had been removed by filtration, the filtrate was evaporated under reduced pressure. The residue was recrystallized from absolute ethanol to yield 2.3 g. (56%) of needles melting at 190.5~193.5°C (decomp.). The second crop of the product (0.25 g.) was obtained from the mother liquor. The total yield was 62.5%. Recrystallization from ethanol gave an analytically pure sample melting at 191.5~193.5°C (decomp).

Found: C, 54.77; H, 9.72; N, 10.74. Calcd. for $C_6H_{13}NO_2$: C, 54.94; H, 9.99; N, 10.68%.

*Paper Chromatography.* — 1-Butanol-ethanol-water (2 : 1 : 3) gave a single spot of $R_f$ 0.59 ($R_f$ of D-glucosamine hydrochloride : 0.33) in ascending development at 23°C. The spot was developed with ninhydrin. Both the pure crystals and the crude product gave a single spot in the same $R_f$ region, and no other spot was observed.

Also, an upper layer of 1-butanol-acetic acid-water (4 : 1 : 5) gave one spot of $R_f$ 0.45 in acending development at 25°C ($R_f$ of D-glucosamine hydrochloride : 0.14).

*Periodate Oxidation.*—A mixture of 100 mg. of Ia was treated with 100 ml. of a 0.1 M sodium metaperiodate solution at 24°C. Iodometric titrations with sodium arsenite[18] revealed that 1.91 mol. of periodate had heen consumed per mole of Ia in 20 hr.

**Di-*O*-acetyl-2α-nitro-1β, 3β-cyclohexanediol (VI).**—The acetylation of IV with a mixture of acetic anhydride and a small amount of concentrated sulfuric acid gave a crude product in a 79% yield.[4] (Found: C, 49.02; H, 6.05; N, 5.60%).

***N*, *O*-Diacetyl-2α-amino-1β, 3β-cyclohexanediol (VII).**—A mixture of 10 g. of VI and 120 ml. of absolute ethanol was hydrogenated, as described in the hydrogenation of IV, to yield 6.6 g. (75.2%) of pale yellow crystals. The crude product was recrystallized from benzene to yield 5.4 g. (61.6%) of colorless needles melting at 126~130°C. An analytical sample was further recystallized from benzene; it melted at 130.5~131.5°C.

Found: C, 55.62; H, 8.24; N, 6.63. Calcd. for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51%.

IR: 3420 (OH), 1626, 1566 (amide) and 1745 (ester) $cm^{-1}$.

**Triacetyl-2α-amino-1β, 3β-cyclohexanediol (Ib).**—A 2.0 g. portion of the crude product of VII was acetylated with 20 ml. of acetic anhydride and 20 ml. of pyridine at room temperature overnight. The mixture was then evaporated under reduced pressure. The product was recrystallized from ethanol to give 1.98 g. (83.0%) of needles melting at 152~152.5°C.

Found: C, 56.17; H, 7.20; N, 5.56. Calcd. for $C_{12}H_{19}NO_5$: C, 56.02; H, 7.44; N, 5.44%.

The product was identified with the triacetyl derivative[4] on the basis of a mixed melting point determination and infrared spectra.

**2α-Acetamido-1β, 3β-cyclohexanediol (Ic).** — Ib gave 2.15 mol. of acetic acid on hydrolysis under Kunz's conditions.[7]

18) J. M. Bobbitt, "Advances in Carbohydrate Chem.," Vol. XI, Academic Press, Inc., New York (1956), pp. 1—41.

The neutralized hydrolyzate was evaporated in vacuo and the residue was extracted with acetone. The combined acetone extract was evaporated to yield a crude product of *N*-acetyl derivative Ic. The product was recrystallized from ethanol to yield 48 mg. (28.2%) of crystals melting at 208.5~210°C. (Found: C, 55.60; H. 8.64; N, 8.31%). A mixed melting point determination with an authentic sample[4] was undepressed.

The porduct (200 mg.) did not consume any periodate in 50 hr. in a mixture of 40 ml. of a 0.1 M sodium metaperiodate solution and 10 ml. of methanol at 26°C.

**2α-Amino-1β, 3β-cyclohexanediol Hydrochloride (V).**—A mixture of 200 mg. of Ib and 10 ml. of 6 N hydrochloric acid was refluxed for 6 hr. The hydrolyzed solution was evaporated under reduced pressure to dryness, the residue was dissolved in 2 ml. of absolute ethanol, and 6 ml. of absolute ether was added. The mixture was stored in a refrigerator to yield 100 mg. (77%) of needles melting at 143.5~145.5°C. The mixed melting point determination with an authentic sample[4] was undepressed.

The free base, Ia, was regenerated from V by dissolving a 374 mg. portion of V in 30 ml. of a 0.5 N sodium hydroxide solution. The mixture was evaporated, and the residue was extracted with absolute ethanol to yield 217 mg. (74%) of crystals melting at 188.5~190.5°C (decomp.)., the melting point being undepressed upon adimxture with Ia.

**2α-Acetamido-di-*O*-mesyl-1β, 3β-cyclohexanediol (VIII).**—Ic gave VIII by a reaction with mesyl chloride in pyridine[4] in an 80% yield. Recrystallization from 95% ethanol afforded colorless needles melting at *153~154°C (Found: C, 36.86; H 5.96; N, 4.27; S, 19.43%).

**DL-*N*,*O*-Diacetyl-2α-amino-1α, 3β-cyclohexanediol (IX).**—VIII was refluxed with sodium acetate and 95% aqueous 2-methoxyethanol for 6 hr. to yield IX in a 36% yield.[4] The crude product was recrystallized from ethanol-ether to yield colorless plates melting at *148~152°C (Found: C, 55.96; H, 7.98; N, 6. 43%).

**DL-*O*-Acetyl-2α-amino-1α, 3β-cyclohexanediol Acetate (X).**—A mixture of 5.0 g. of VIII, 2.75 g. of anhydrous sodium acetate, and 100 ml. of water was refluxed for 1 hr. Then the mixture was evaporated under reduced pressure to dryness. The residue was extracted with boiling acetone repeatedly. The combined acetone extract was evaporated under reduced pressure to yield a crystalline residue. The residue was washed with a small amount of cold acetone to give 1.3 g. (20%) of colorless needles melting at 104~113°C. Recrystallization from acetone afforded needles melting at 130.5~132°C; these were shown by infrared spectrum and elementary analysis to be DL-*O*-acetyl-2α-amino-1α, 3β-cyclohexanediol acetate.

Found: C, 51.33; H, 8.44; N, 6.14. Calcd. for $C_{10}H_{19}NO_5$: C, 51.49; H, 8.21; N, 6.01%.

IR: 3200 (OH), 1725 (ester), 1638 ($NH_3^+$), 1547 and 1403 ($COO^-$) $cm^{-1}$.

**DL-Triacetyl-2α-amino-1α, 3β-cyclohexanediol (IIb).**—A mixture of crude X, obtained from 5.0 g. of VIII, 25 ml. of acetic anhydride, and 25 ml.

of pyridine, was left to settle at room temperature overnight and then heated at 80°C for 1 hr. The mixture was evaporated under reduced pressure and the residue was dissolved in 100 ml. of chloroform. The chloroform solution was washed with cold water, dried over anhydrous sodium sulfate, and then evaporated in vacuo to dryness. Crystallization of the residue with a mixture of benzene and petroleum ether gave 2.9 g. (74%) of the product melting at 140.5~143.5°C. Recrystallization from benzene afforded colorless crystals melting at 144.5~146.5°C.

Found: C, 55.81; H, 7.35; N, 5.39. Calcd. for $C_{12}H_{19}NO_5$: C, 56.02; H, 7.44; N, 5.44%.

**DL-2α-Acetamido-1α, 3β-cyclohexanediol (IIc).**—IIb was treated with methanol saturated by ammonia to give the crude product in a 74% yield.[4] (Found: C, 55.65; H, 8.37; N, 8.46%).

**DL-2α-Amino-1α, 3β-cyclohexanediol Hydrochloride (XI).**—A mixture of 0.3 g. of IIb and 15 ml. of 6 N hydrochloric acid was refluxed for 7 hr. The mixture was evaporated under reduced pressure to dryness. The residue was dissolved in 4 ml. of absolute ethanol, and absolute ether was added. The mixture was kept in a refrigerator to yield 0.13 g. (67%) of crystals melting at 111~117°C. The product was recrystallized from absolute ethanol-ether to yield needles melting at 115~117°C after sintering at 110°C.

Found: C, 42.89; H, 8.40; N, 8.18; Cl, 21.33. Calcd. for $C_6H_{14}NClO_2$: C, 42.99; H, 8.42; N, 8.36; Cl, 21.15%.

**DL-2α-Amino-1α, 3β-cyclohexanediol (IIa).**—A 517 mg. portion of XI was treated, as described in the regeneration of Ia from V, to yield 400 mg. (98%) of a crude product which crystallized gradually in a vacuum desiccator. The crude product was recrystallized from absolute ethanol-ether to give hygroscopic crystals melting at *112~113°C.

Found: C, 54.81; H, 10.01; N, 10.89. Calcd. for $C_6H_{13}NO_2$: C, 54.93; H, 9.99; N, 10.68%.

*Paper Chromatography.*—A nupper layer of 1-butanolacetic acid-water (4 : 1 : 5) gave a single spot of $R_f$ 0.49 in ascending development at 25°C.

**DL-*O*-Acetyl-*O*-mesyl-2α-amino-1α, 3β-cyclohexanediol Methanesulfonate (XII).**—A mixture of 5.0 g. of VIII and 70 ml. of water was refluxed for a few minutes to give a clear acidic solution (pH 1.0). After standing ovenight, the solution was evaporated under reduced pressure. The residue was recrystallized from ethanol to yield 3.6 g. (68%) of crystals melting at *173~174°C. A second crop of the product (0.3 g.) was obtained from the mother liquor. The total yield of the crude product was 74%. The product was recrystallized from ethanol to yield needles melting at *174.5~175°C.

Found: C, 34.80; H,6.23; N, 3.97; S, 18.11. Calcd. for $C_{10}H_{21}NO_8S_2$: C, 34.57; H, 6.09; N, 4.03; S, 18.46%.

IR: 1740 (ester) 1622 ($NH_3^+$), 1355, 1170 (mesyloxy), 1200 and 1045 ($SO_3^-$) $cm^{-1}$.

**DL-2α-Acetamido-*O*-mesyl-1α, 3β-cyclohexanediol (XIII).** A 2.0 g. portion of XII was dissolved in 6 ml. of water, and the pH was adjusted with a 10% potassium hydroxide solution to 11. Then the solution was cooled in an ice bath to give a white crystalline precipitate. After cooling at 0°C for 1 hr., the product was collected by filtration, washed with ethanol, and dried to yield 1.05 g. (72.5%) of crystals melting at *118~119°C. A sample was recrystallized from ethanol for analysis; it melted at *118~118.5°C.

Found: C, 43.17; H, 7.07; N, 5.61; S, 12.69. Calcd. for $C_9H_{17}NO_5S$: C, 43.01; H, 6.82; N, 5.58; S, 12.78%.

IR: 3540 (OH), 1643, 1542 (amide), 1340, 1175 (mesyloxy) and 960 (cyclohexane) $cm^{-1}$.

**2α-Acetamido-1α, 3α-cyclohexanediol (IIIc).**—a) A mixture of 0.55 g. of XIII, 0.6 g. of anhydrous sodium acetate, 0.5 ml. of water, and 10 ml. of 2-methoxyethanol was refluxed for 5 hr. The mixture was evaporated under reduced pressure to dryness. After drying, the residue was extracted with 10 ml. of boiling acetone five times, and the combined acetone extract was evaporated under reduced pressure to give an oily residue. Trituation of the residue with a mixture of ethanol and ether gave 0.30 g. (79%) of crystals melting at *118~120°C. Two recrystallizations from acetone afforded colorless needles melting at *120~123°C.

Found: C, 55.21; H, 8.97; N, 8.31. Calcd. for $C_9H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09%.

b) A 203 mg. portion of IIIb was added to 10 ml. of methanol saturated with ammonia. The mixture was kept at room temperature overnight and evaporated under reduced pressure to obtain a crystalline residue. The product was recrystallized from ethanol to yield 117 mg. (85.6%) of crystals melting at 119~123°C. A mixed melting point determination with an authentic sample was undepressed.

**Triacetyl-2α-amino-1α, 3α-cyclohexanediol (IIIb).**—a) The crude IIIc, obtained from 2.2 g of XIII, was treated with a mixture of 20 ml. of acetic anhydride and 20 ml. of pyridine for 24 hr. The mixture was evaporated in vacuo, and the residue was recrystallized from benzene to give 1.6 g. (71%) of colorless needles melting at 175.5~177.5°C. An analytical sample was obtained by recrystallization from benzene; m. p. 177.5~179°C.

Found: C, 56.23; H, 7.56; N, 5.45. Calcd. for $C_{12}H_{19}NO_5$: C, 56.02; H, 7.44; N, 5.44%.

b) A starting material, *cis*-2, 6-diacetoxycyclohexanone (XV), was prepared by the method of Cavill and Solomon.[10] A mixture of 2.97 g. of XV and 70 ml. of methanol was added to a mixture of 1.49 g. of hydroxylamine hydrochloride, 2.58 g. of sodium hydroxide, and 13 ml. of water under ice cooling. The mixture was kept in a refrigerator overnight and then evaporated. The residue was added to ethanol, and an insoluble salt was removed by filtration. The filtrate was evaporated in vacuo, and the residue was dissolved in 50 ml. of glacial acetic acid. The mixture was shaken with 0.57 g. of an Adams platium catalyst under an atmospheric pressure of hydrogen for 130 min. The crude hydrogenated product was then heated with pyridine and acetic anhydride for 3 hr. at 100°C. The crude product was dissolved in ethanol, and ether was added to give 0.53 g. (14.8%) of crystals melting at 170~176°C. The product was recrystallized twice from ethanol-ether to yield 0.33 g. (9.3%) of needles melting at 176.5~178°C.

A mixed melting point determination with an authentic sample was undepressed. The infrared spectrum of the product was superimposable on that of an authentic sample.

**2α-Amino-1α, 3α-cyclohexanediol Hydrochloride (XIV).**—A mixture of 2.0 g. of IIIb and 100 ml. of 6 N hydrochloric acid was refluxed for 6 hr. The mixture was then evaporated under reduced pressure to yield 1.21 g. (93%) of crystals melting at 156.5~160°C. The crude product was recrystallized from absolute ethanol-absolute ether to give needles melting at 160.5~161.5°C.

Found: C, 42.67; H, 8.46; N, 8.41; Cl, 21.38. Calcd. for $C_6H_{14}NClO_2$: C, 42.99; H, 8.42; N, 8.36; Cl, 21.15%.

**2α-Amino-1α, 3α-cyclohexanediol (IIIa).**—A 1.02 g. portion of the crude XIV was treated, as described in the regeneration of Ia from V, to yield 743 mg. (93%) of crystals melting at 78~83°C. The product was recrystallized from absolute ethanol-absolute ether to yield 322 mg. (40.5%) of crystals melting at 126~128°C.

Found: C, 54.65; H, 9.97; N, 10.84. Calcd. for $C_6H_{13}NO_2$: C, 54.93; H,9.99; N, 10.63%.

*Paper Chromatography.* — An upper layer of l-butanol-acetic acid-water (4 : 1 : 5) gave a single spot of $R_f$ 0.44 in ascending development at 25°C.

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