

A NOTE ON : USE OF GLUCOSE AND GLUCOSE-TETRA-  
ACETATE IN THE RESOLUTION OF 1-AMINO-2-PROPANOL

BY

N. Sharaf El-Din

Department of Pharmaceutical Chemistry, Faculty of  
Pharmacy Tanta University ,Tanta , Egypt

Received : 13 - 9 - 1988

ABSTRACT

N-(2'R-hydroxy)propyl-1-deoxy-1-imino-glucose and N-(2'S-hydroxy)propyl-1-deoxy-1-iminoglucose, diastereoisomers (1 and 2 ) were prepared by reaction of the racemic 1- amino-2-propanol with D(+)-glucose. The same racemate gave with D(+)-glucose-tetraacetate two other diastereoisomers (3 and 4). The obtained diastereoisomers were separated from the suitable solvents by fractional crystallization. After acid hydrolysis for diastereoisomers the antipodes were produced in a good yield. The calculated optical purities for such antipodes, thereafter, were high enough.

The obtained diastereoisomers showed some chelating behaviour toward cupric ion. In addition, copper complexes exhibited some fungicidal and bactericidal properties.

INTRODUCTION

D(-)-1-Amino-2-propanol represents a constituent of vitamin B<sub>12</sub> and it has been isolated by hydrolysis of the

Delta J. Sci. 12 (3)1988

A Note on : Use of Glucose

vitamin (Cooley et al. 1953). So far, few procedures for the resolution of the racemic 1-amino-2-propanol have been known in the literature. The indirect and complexed method was published by Clark et al. (1954). Further, a partial resolution method via formation of diastereoisomeric salt of tartaric acid had been described by the Sullivan's patent (1958). Later, the racemic 1-amino-2-propanol was resolved via chromatographic separation for the diastereoisomers halfamide (Miljkovic et al. 1985) .

On the other hand, D(+)-glucose has used as resolving agent for racemic aminothiols where glucose was removed by an exchange reaction with benzaldehyde, then the optically active aminothiol was isolated by hydrolysis (Piper and Johnston 1964) . From the literature, D(+)-glucosetetraacetate can be used as a resolving agent, it was already utilized in resolution of the racemic  $\alpha$  - phenylethylamine ( Helferich and Portz 1959) . Also, compounds having azomethine linkage were suggested to be potential chelating agents (Akelah et al. 1985) . Therefore, study of chelating behaviour of the prepared compounds was found to be of interest. As the correlation between certain Schiff's bases and biological activities has been observed (Safwat et al. 1983,1988), as well as, the solution of  $\text{Cu}(\text{OH})_2$ , glucose and  $\text{NH}_4\text{OH}$  or amine was used as algicide and germicide composition (Kuchikata et al. 1980) , an attempt was conducted to

Delta J. Sci. 12 (3) 1988

Sharaf El-Din .

evaluate the fungicidal and bactericidal activity for these new compounds and their copper chelates.

The aim of the present work is to find simple and efficient method for the resolution of 1- amino-2-propanol.

#### RESULTS AND DISCUSSION

The racemic 1-amino-2-propanol was converted into a diastereoisomeric pair with an optically active naturally occurring D(+)-glucose and its derivative (+)-glucoacetate. Thus, from racemic 1-amino-2-propanol and D(+)-glucose in absolute alcohol at molar ratio 1:1 the diastereoisomers 1 and 2 were obtained (scheme 1). The two diastereoisomers were separated by fractional crystallization from absolute alcohol.

The IR spectral data show that the absorption band at  $1660\text{ cm}^{-1}$  represents  $\text{-C=N-}$  group (Silverstein et al 1967 ). The calculated specific rotation for both diastereoisomers was greater than that of the amine and glucose from which the diastereoisomers were prepared. These results agreed with those obtained by (Potapov et al. 1961 and Smith et al. 1971) who found that chelating of an internally asymmetric chromophore was the essential reason which caused a higher specific rotation of diastereoisomers than reactants.

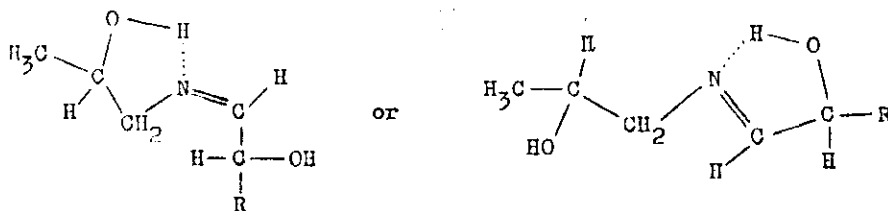
Delta J. Sci. 12 (3) 1988

A Note on : Use of Glucose

A smooth hydrolysis of compounds 1 and 2 were achieved by adding an amount of 4-N-HCl at room temperature. The solution was neutralized with  $\text{Na}_2\text{CO}_3$  and extracted with ether. The two antipodes were produced with optical purities of 91% and 76% for (+)- and (-)- isomers.

Further, the racemic 1-amino-2-propanol reacted with D(+)- glucosetetraacetate ( molar ratio 1:1) in absolute ether under the cold conditions producing diastereoisomers 3 and 4 (Scheme 1 ).

IR spectra of the diastereoisomers 3 and 4 show the strong bands at  $1660\text{ cm}^{-1}$  which attributed to (C=O) ester group. On the other hand, the bands at  $1660, 1650\text{ cm}^{-1}$  correspond to the C=N groups (Silverstein et al. 1967) . Furthermore, a broad absorption bands ( $3600\text{-}3400\text{ cm}^{-1}$ ) in IR spectra of the compounds revealed that the hydrogen bond was presented in structure of the compounds as shown below:-



Delta J. Sci. 12 (3) 1988

Sharaf El-Din

Also, from IR spectrum show that , each diastereoisomeric pair exhibited the same characteristic absorption bands but the position of these bands were differed with  $\sim 5-10 \text{ cm}^{-1}$  (Table 1).

The free (+)- and (-)- enantiomers were obtained by extracting the ethereal solution of each compound with cold 4-N-HCl . After neutralization of aqueous layer with 30% cold KOH, the solution was extracted with absolute ether. The optical purities were 98% and 68% for (+)- and (-)- isomers.

The diastereoisomers gave coloured complexes with aqueous solution of copper sulfate. However, the compounds and their complexes were tested against bacteria and fungi by agar diffusion method. It was found that the prepared copper chelates are active against the tested organisms, while the compounds themselves show no activity against the same tested organisms (Table 2 ) .

#### EXPERIMENTAL

IR were recorded with a Perkin Elmer 710 B. The UV/VIS spectra were measured using Beckman Du 24 spectrophotometer. The angles of rotation  $[\alpha]^{20}_D$  were recorded with a polarimeter Carl Zeiss Jena. The microanalysis were carried out in Microanalytical Unit, Cairo University.

1- Formation of diastereoisomers 1 and 2:-

D(+)-Glucose (0.1 mol) was added to the solution of (0.1 mol) racemic 1-amino-2-propanol in absolute alcohol (30 ml). The solution was heated in water bath to dissolve glucose. The mixture was left over night in a cold place at 8°C. The bulky, white crystalline product was separated.  
 mp 108 - 110°C [  $\alpha$  ]<sub>D</sub><sup>20</sup> = 100.3° (conc. 1.5 H<sub>2</sub>O )  
 IR spectrum : 3600 - 3450 cm<sup>-1</sup> (OH), 1665 cm<sup>-1</sup> (C=N), 1100, 1020 cm<sup>-1</sup> (C - O).

Microanalysis (C<sub>9</sub>H<sub>19</sub>NO<sub>6</sub>)

	C %	H %	N %
Found	45.8	7.8	6.1
Calc.	45.6	8.0	5.9

The filtrate was evaporated under vacuum to give oily clourles product which was unstable at room temperature for long time. Their colour change by time to brown, this brownness due to Maillard reaction which involves both C-C bond cleavag and subsequent recombination. [  $\alpha$  ]<sub>D</sub><sup>20</sup> = + 69° ( conc. 3, H<sub>2</sub>O)  
 IR spectrum : 3600-3400 cm<sup>-1</sup> (OH), 1660 cm<sup>-1</sup> (C=N), 1090, 1000 cm<sup>-1</sup> (C-O).

Microanalysis (C<sub>9</sub>H<sub>19</sub>NO<sub>6</sub>)

	C %	H %	N %
Found	45.4	8.2	5.8
Calc.	45.6	8.0	5.9

Delta J. Sci. 12 (3)1988

Sharaf El-Din

2- Hydrolysis of diastereoisomers 1 and 2 :-

Compound 1 (1 gr) was dissolved in 20 ml of 4-N-HCl and the mixture stirred at room temperature for 3 he. The reaction mixture was neutralized with 20 %  $\text{Na}_2\text{CO}_3$  , Then extracted several times with ether. The combined extracte was dried over KOH. After removal of solvent by vacuum the (+)-1-amino-2-propanol was obtained  $[\alpha]_D^{20} = + 24^\circ$  (conc.1, MeOH)

Compound 2 (1 gr) was dissolved in (20 ml)4 -N-HCl. After working up as previously described the (-)-1-amino-2-propanol was produced  $[\alpha]_D^{20} = -20^\circ$  (conc. 1, MeOH)

3- Preparation of glucose-tetraacetate :-

Glucose pentaacetate was prepared according to the method reported in literature ( Lugas 1949) then 0.1 mol of glucosepentaacetate and 0.3 mol of benzylamine were reacted in absolute ether (150 ml). The separated crystalline product was filtered off rapidly, then it was dissolved in chloroform and extracted with 4-N-HCl. The organic layer was washed with  $\text{Na}_2\text{CO}_3$  (10 %) and dried over anhydrous  $\text{CaCl}_2$ . The solvent was evaporated to give white crystalline product, mp.  $130^\circ\text{C}$   $[\alpha]_D^{20} = + 140^\circ$   
 IR spectrum :  $1760\text{ cm}^{-1}$  (C=O ),  $1250\text{ cm}^{-1}$  (C-O-C),  $1060\text{ cm}^{-1}$  (C-O)

4- Formation of diastereoisomers 3 and 4 :-

A solution of racemic 1-amino-2-propanol (0.1 mol) in absolute ether was added to the solution of glucosete-tetraacetate (0.1 mol) in absolute ether (150 ml). the solution was left at  $-30^{\circ}\text{C}$  for 2 hr . A white crystalline product was obtained. The product filtered off rapidly and washed with cold absolute ether.  $[\alpha]_{\text{D}}^{20} = + 90^{\circ}$  (conc. 1,  $\text{CHCl}_3$ ).  
IR spectrum:  $3600-3450$  (OH) ,  $1760 \text{ cm}^{-1}$ (C=O),  $1660 \text{ cm}^{-1}$   
(C=N),  $1260 \text{ cm}^{-1}$ (C-O-C),  $1040 \text{ cm}^{-1}$ (C-O)

The filtrate was collected and evaporated under vacuum. An oily colourless product was produced.  
IR spectrum :  $3600-3450 \text{ cm}^{-1}$ (OH),  $1745 \text{ cm}^{-1}$ (C=O),  $1250 \text{ cm}^{-1}$   
(C-C-C),  $1040 \text{ cm}^{-1}$ (C-O)

5- Hydrolysis of diastereoisomers 3 and 4 :-

Compound 3 (2gr) was dissolved in  $\text{CHCl}_3$ (15 ml). The solution was extracted with cold 4-N-HCl (20 ml), the cold KOH (30%) was added to make alkaline solution. The mixture was extracted with ether. The ethereal extract was dried over KOH and evaporated to give colourless oily product.  
 $[\alpha]_{\text{D}}^{20} = + 26^{\circ}$  (conc. 1, MeOH).

The cold filtrate was extracted with 4-N-HCl (30 ml). The extract was reextracted with  $\text{CHCl}_3$  (10 ml). The alkalinity of the aqueous layer was made by added cold 30 % KOH,



Delta J. Sci. 12 (3) 1988

Sharaf El-Din

then the alkaline aqueous layer extracted with ether. The solvent was dried over KOH and evaporated to yield oily colourless product.  $[\alpha]_D^{20} = +18^\circ$  (conc. 1, MeOH).

#### 6-Chelating properties of diastereoisomers:-

On the basis of the chelating characteristics of the synthesized compounds, it was found that compounds 1 and 2 reacted with  $\text{CuSO}_4$  in aqueous media to give yellowish green colour with max. absorbance at  $\lambda$  380 nm  $\epsilon$   $11.5 \times 10^3$ . The colour of complex was stable at room temperature for 48 hr. However, the chelating behaviour of the compounds is under investigation.

#### 7-Biological activity of the diastereoisomers and their copper complexes :-

Procedure of the agar diffusion method used to test the biological activities of these compounds was as follows: the discs of paper (6 mm) were immersed in the aqueous solution of compounds 1 and 2 and copper complexes separately. Another paper discs were immersed in the chloroform solution of either compound 3 or 4. The concentration used was 15 ppm, and each disc was repeated three times.

All the discs were left to dry and placed on the surface of agar plates, which previously seeded with the tested organisms. Plates were then maintained at  $37^\circ\text{C}$  for 24 hr.

Delta J. Sci. 12 (3) 1988

A Note on : Use of Glucose

Table 1 : Infrared absorption spectra of the compounds.

Compounds	C = O	C = N	C - O	OH
	(ester)	(azomethine)	C - N	
1	---	1665 1020	1100	3600-3450
2	---	1660	1090 1000	3600-3400
3	1760	1660	1260 1115-1045	3600-3400
4	1745	1650	1250 1040	3600-3450

Delta J. Sci. 12 (3) 1988

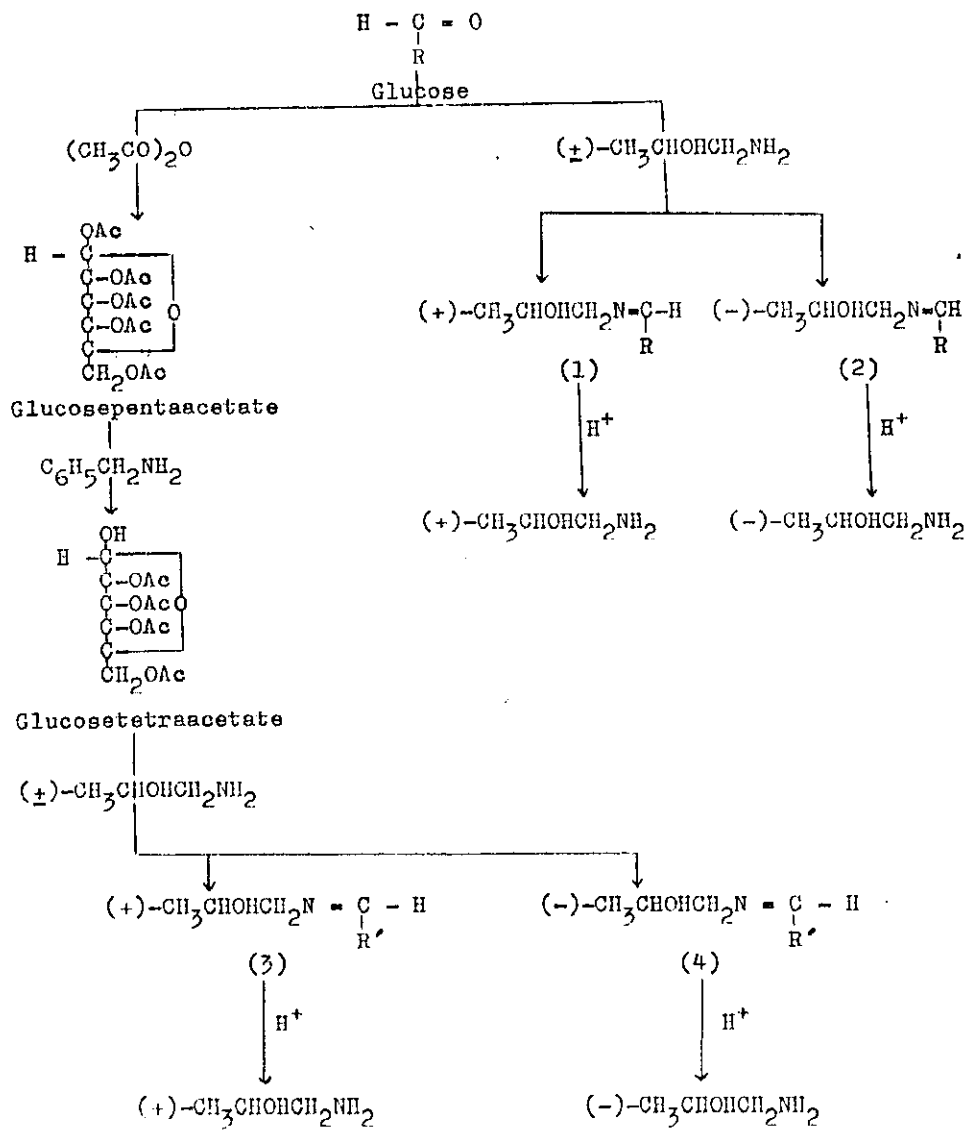
Sharaf El-Din

Table 2 : Antifungal, antibacterial activities of compounds

1 - 4

Organisms	Compounds				Cu comp- lexes	CuSO <sub>4</sub> only
	1	2	3	4		
Fungi :-	-	-	-	-	++	W
<u>Sacch.cerev.</u>	-	-	-	-	+	-
<u>penicil. not.</u>						
Bacteria :-						
<u>E. coli</u>	-	-	-	-	++	W
<u>Stap. aureus</u>	-	-	-	-	+	-
<u>B. subbtilis</u>	-	-	-	-	-	-
<u>con. jejuni</u>	-	-	-	-	+	-

Whereas, ++ = More active, + = Active, W = Weak



Where  $\text{R} = \text{-CHOH(CHOH)}_3\text{CH}_2\text{OH}$

$\text{R}' = \text{-(CHOAc)}_3\text{CHOHCH}_2\text{OAc}$

Scheme 1

REFERENCES

- Akelah, A., M., M. Abbasi and M.K.Awad, Delta J.Sci. 9,1,35 (1985)
- Akelah, A.,M. Massoud and S.Kandil, Delta J. Sci. 9, 1, 57 (1985)
- Clark, R.L., W.H. Jones, W.J.Raich and K.Folkers, J. Am. Chem. Soc.76, 3995, (1954)
- Cooly, G., M.T. Davies, B. Ellis, V. Petrow and B. Sturen, J.Pharm. Pharmacol. 5, 257 (1953)
- Helferich, B. and W. Portz, Chem. Ber. 86, 103 (1959)
- Kuchikata, Masuo, Nitta, Yoshihiro, Kuzan, Hiroshi, 19 Dec. 1979 Appl 78/67 246 C.A. 92, 175795 q (1980)
- Lugas, H.J., Principles and Practice Organic Chemistry, New York John Willy and Sons , 492 (1949)
- Miljkovic, D.A.N. Sharaf El-Din and K.Gasi, J.Serb. Chem. Soc. 50, 6, 277 (1985)
- Piper, J.B. and T.P. Johnaston, J.Org. Chem., 29,6, 1657 (1964)
- Potapov, V.M.,A.P.Terentiev and S.P.Spivak, Zhur. Obsch. Khim. 31, 8, 2415 (1961)
- Safwat, H.M., A.N. Milkhael and J.P.Dheyongera, Egypt J.Pharm. Sci. 24, 189 (1983)
- Safwat, H.M.,F.A. Ragab, N.M. Eid M.Abd-El-Gawad, Egypt J. Pharm. Sci., 29, 1-4, 99 (1988)
- Silverstein, R.M. and G.C. Bassler, Spectrometric Identification of Organic Compounds, John Wiley and Sons, Inc., New York, London, Sydney,97, (1967)

Delta J. Sci. 12 (3) 1988

Smith, H.E. and H.E. Ensley , Canada J. Chem., 49,  
17, 2902 (1971)

Sullivan, R.H., U.S., 3, 116 , 332, 31,1963, Appl.  
Oct. 17, 1958.

## استخدام جلو جوز تتراسيبتات فى فصل الشكل الراسيمى ١-امينو-٢- بروبانول

نبويه شرف الدين

قسم الكيمياء الصيدليه - كلية الصيدله - جامعه طنطا - مصر

تم تحضير الدياستيريوايزمير ١، ٢ [ ن - ( R٢ - هيدوكسى ) بروبييل  
- ١ - ديوكسى - ١ - امينو جلو جوز ، ن - ( S٢ - هيدوكسى ) بروبييل  
- ١ - ديوكسى - ١ - امينو جلو جوز ) بتفاعل الشكل الراسيمى ١-امينو-٢-  
بروبانول مع جلو جوز . وأيضا بتفاعل نفسى الشكل الراسيمى مع جلو جوز  
تتراسينات تم تحضير الدياستيريوايزمير ٣ و ٤ .

وقد فصلت هذه الدياستيريوايزوميرات بواسطة البلوره التجزيئيه  
من المذيب المناسب . وبعد تحليل هذه الدياستيريوايزوميرات نتج زوج  
الايزومير (+) و (-) ذات قوه نوعيه دورانيه عاليه .

وقد وجد أن لهذه الدياستيريوايزوميرات خواص مخلاييه تجاه  
عنصر النحاس بالاضافه الى أن المركبات المعقده مع النحاس لها تأثير  
ضد بعض أنواع من الفطريات و البكتريا .