

REACTIONS OF METAL COMPLEXES WITH CARBOHYDRATES:
SYNTHESIS AND CHARACTERIZATION OF NOVEL NICKEL(II) COM-
PLEXES CONTAINING GLYCOSYLAMINES DERIVED FROM A
MONOSACCHARIDE AND A DIAMINE. AN X-RAY CRYSTALLO-
GRAPHIC STUDY OF (ETHYLENEDIAMINE) {*N*-(2-AMINOETHYL)-D-
FRUCTOPYRANOSYLAMINE} NICKEL(II) · Cl₂ · CH₃OH

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ABSTRACT

Tris(ethylenediamine)- or tris(trimethylenediamine)-nickel(II) salts react with D-glucose, D-mannose, or D-fructose to give novel, octahedral, nickel(II) complexes containing glycosylamine(s) derived from the reaction of the monosaccharide with the diamine. The complexes have been characterized by elemental analysis, magnetic susceptibility, and electronic absorption, infrared, and circular dichroism spectra. The complexes from aldoses contain two sugar entities, and those from a ketose have one sugar unit. The X-ray crystal structure was determined of one of the products, in which *N*-(2-aminoethyl)-D-fructopyranosylamine and ethylenediamine are coordinated to a nickel ion. Crystal data for the compound: *a* = 12.348(5) Å, *b* = 18.478(8) Å, *c* = 8.464(4) Å, *Z* = 4, space group P2₁2₁2₁, 2348 unique observed reflections [*F*_o > 3σ(*F*_o)] used in the structure analysis, *R* = 0.068, *R*_w = 0.053. The sugar is coordinated to the nickel ion at three points, through the 1- and 3-hydroxyl groups and the nitrogen atom on C-2.

INTRODUCTION

The interaction of carbohydrates with metals is of current interest for various reasons: it has some application in analysis (in electrophoresis, chromatography, and n.m.r. shift reagents), industry (sequestration of metal ions), medicine, coordination chemistry, and biochemistry. The isolation and structure determination of metal complexes containing sugar derivatives should provide useful information to aid in the interpretation of this interaction.

Many crystalline complexes containing sugar units have been reported, but

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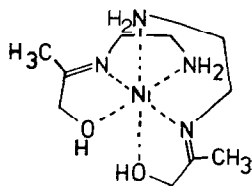


Fig. 1. A proposed structure for the blue Ni(II) complex derived from the reaction of $[\text{Ni}(\text{en})_3]^{2+}$ with 1-hydroxy-2-propanone (α -hydroxyacetone)⁶.

the complexes were mainly restricted to those of group IA and IIA metals; the structures of a dozen such complexes have been determined by X-ray crystallography¹. Literature on the complexation of sugars with transition metals and metals other than those in groups IA and IIA is much more recent² and less abundant. Thus, very little is known about the structure of these compounds, except for two preliminary reports, one on our present work³, and the other on a binuclear Mo(VI) complex containing D-lyxose⁴.

MacDermott and Busch⁵ reported that hydroxy ketones react with tris(ethylenediamine)nickel(II) salts to give blue, paramagnetic, bis(tridentate) nickel(II) complexes in which the ligand is the Schiff base formed from a hydroxy ketone and ethylenediamine (see Fig. 1)^{5,6}. Because ketoses are hydroxy ketones, we have developed a method in which sugars serve as ligands to transition-metal ions. We show herein the broad generality of the reaction of tris(diamine)-nickel(II) salts with some natural hexoses, to afford a novel type of nickel(II) complexes containing sugar moieties, and describe the results of the first X-ray crystal-structure determination on one of the products containing a glycosylamine derived from the reaction of ethylenediamine with D-fructose.

EXPERIMENTAL

Materials. — All reagents were of the highest commercial grade and were used without further purification. Tris(ethylenediamine)nickel(II) salts⁷ and tris(trimethylenediamine)nickel(II) salts⁸ were prepared by known methods. The following abbreviations are used: en, ethylenediamine; tn, 1,3-propanediamine (trimethylenediamine); D-Glc, D-glucose; D-Man, D-mannose; D-Fru, D-fructose; D-Glc-en, *N*-(2-aminoethyl)-D-glucosylamine; D-Glc-tn, *N*-(3-aminopropyl)-D-glucosylamine; D-Man-en, *N*-(2-aminoethyl)-D-mannosylamine; D-Man-tn, *N*-(3-aminopropyl)-D-mannosylamine; D-Fru-en, *N*-(2-aminoethyl)-D-fructosylamine; and D-Fru-tn, *N*-(3-aminopropyl)-D-fructosylamine.

General preparation of complexes. — To a stirred solution of $[\text{Ni}(\text{en})_3]\text{Cl}_2 \cdot 2 \text{H}_2\text{O}$ or $[\text{Ni}(\text{tn})_3]\text{Cl}_2 \cdot 2 \text{H}_2\text{O}$ (8.38 mmol) in methanol (50 mL) was added D-Glc, D-Man, or D-Fru (25.14 mmol). The solution was warmed to $\sim 70^\circ$, with stirring, until it became blue, evaporated to ~ 30 mL, loaded onto an LH-20 gel-permeation column, and eluted with methanol. The colored materials were thus separated into

a (major) blue band, and (minor) purple, yellow, and green ones. After evaporation of the blue-band fractions to a small volume, a second chromatographic separation was conducted. The purified blue-band fractions were concentrated to ~10 mL, and then the concentrate was kept at 5° in a refrigerator. Each blue compound thus obtained was recrystallized twice from the minimal volume of hot methanol. The crystals were collected, successively washed with ethanol and ether, and dried *in vacuo*.

Nonreaction of nickel(II) ions with monosaccharides in the absence of diamines. — Although $\text{NiCl}_2 \cdot 6 \text{H}_2\text{O}$ in methanol was boiled under reflux with an excess of each monosaccharide for several hours, no evidence of coordination of any of the sugars to nickel was observed.

Measurements. — Microanalyses were performed by Shonan Bunseki Center. Magnetic susceptibilities were determined at room temperature by the Faraday method, using a Shimazu MB-100 Model magnetic balance; diamagnetic corrections were calculated from tables of Pascal constants⁹. Infrared spectra were recorded for KBr pellets with a Shimazu IR-400 recording i.r. spectrophotometer. Electronic absorption spectra for solutions in methanol were obtained at room temperature with a Hitachi 340 recording spectrophotometer. Reflectance spectra were recorded with a Hitachi 340 instrument equipped with a reflectance attachment. Circular dichroism spectra were recorded with a JASCO J-500C recording spectropolarimeter.

Chromatography. — The gel-permeation column was prepared by pouring a slurry of LH-20 (200 g) into a column (4 cm × 80 cm). A concentrated solution of each reaction mixture was introduced onto the column, and eluted with methanol.

Recovery of sugars. — Each complex obtained was dissolved in water. The solution was made slightly acidic with 0.05M H_2SO_4 , and stirred for several hours. In order to remove the Ni(II) complexes, the reaction solution was passed through a column of Dowex-50W (Na^+) cation-exchange resin. It was confirmed that the solution contained monosaccharides by means of a TSK HLC-802 UR chromatographic system (Toyo Soda Kogyo Assoc.), which included a differential refractometer for monitoring sugars.

Crystal data for, and intensity measurements on, $[\text{Ni}(\text{en})(\text{D-Fru-en})]\text{Cl}_2 \cdot \text{CH}_3\text{OH}$.* — The sample was recrystallized several times from methanol. Weissenberg photographs indicated orthorhombic symmetry, with space group $\text{P2}_1\text{2}_1\text{2}_1$. A blue crystal (0.4 × 0.2 × 0.2 mm), sealed within a glass capillary tube, was mounted on the goniometer head of a Rigakudenki four-circle diffractometer equipped with a LiF monochromator and employing $\text{MoK}\alpha$ radiation (λ 0.7107 Å). The unit-cell parameters were obtained by least-squares refinement of high-angle

*Lists of observed and calculated structure factors and anisotropic thermal parameters have been deposited with, and can be obtained from, Elsevier Science Publishers, BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/316/*Carbohydr. Res.*, 142 (1985) 179–193.

reflections. The results were as follows: $a = 12.348(5) \text{ \AA}$, $b = 18.478(8) \text{ \AA}$, and $c = 8.464(4) \text{ \AA}$. With $Z = 4$ and the molecular weight of this complex, the calculated density is $1.522 \text{ g} \cdot \text{cm}^{-3}$, compared with a measured density of $1.525 \text{ g} \cdot \text{cm}^{-3}$ obtained by flotation in a dibromomethane–carbon tetrachloride mixture. Intensity data were measured by the $\theta - 2\theta$ scan method (θ up to 60°). Each reflection was measured with a scanning rate of $2^\circ/\text{min}$, and two background measurements for 15 s on each side of the reflection. Four standard reflections were monitored every 50 reflections, and no apparent decay intensities were detected. A total of ~ 2500 reflections was measured; of these, 2348 having $I > 3\sigma(I)$ were considered to be observed. Intensities were corrected for Lorentz and polarization effects. No absorption correction was made, as μ (13.0 cm^{-1}) was low.

Structure solution and refinement. — The structure was solved by heavy-atom methods. A three dimensional Patterson map was calculated, and the positions of the Ni and Cl atoms were determined. Careful peak selection coupled with bond-length calculations was used to locate all remaining, nonhydrogen atoms. Isotropic, followed by anisotropic, full-matrix least-squares refinement gave values of $R = \Sigma||F_o| - |F_c||/\Sigma|F_o| = 0.078$, and $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2} = 0.063$, where $w = 1/[\sigma(F_o)]^2$. Atomic scattering factors were taken from ref. 10. Because the complex had been prepared by the reaction between $[\text{Ni}(\text{en})_3]\text{Cl}_2 \cdot 2 \text{ H}_2\text{O}$ and D-fructose, the known absolute configurations of the asymmetric carbon atoms of the sugar unit were used as internal reference asymmetric centers in order to determine the absolute configuration of the complex. The effects of anomalous dispersion were included in Fc; values of f' and f'' for Ni, Cl, O, N, and C were taken from Cromer's tabulation¹¹. After including these anomalous-dispersion corrections, least-squares refinement, on assignment of anisotropic thermal parameters to all of the atoms except the hydrogen atoms, converged with $R = 0.077$ and $R_w = 0.062$. When the coordinates were inverted, in order to test the enantiomorphic structure, convergence was reached with $R = 0.084$ and $R_w = 0.066$, which are significantly higher than the corresponding values 0.077 and 0.062 for the final structure. This result agreed with the earlier assumption of the absolute configuration of the D-fructose unit. At this stage, idealized positions of the hydrogen atoms, except for those in hydroxyl groups and the *O*-methyl group of the methanol of crystallization, were calculated by assuming a tetrahedral coordination about carbon and nitrogen atoms, with a C–H distance of 1.08 \AA and an N–H distance of 1.03 \AA . Hydrogen-atom coordinates were recalculated prior to each refinement cycle. Scattering factors for hydrogen atoms were taken from Stewart *et al.*¹². On inclusion of fixed contributions from 22 hydrogen atoms with an isotropic thermal parameter $B = 3.0 \text{ \AA}^2$, further refinement of the nonhydrogen parameters converged with $R = 0.068$ and $R_w = 0.053$. A difference-Fourier synthesis showed no unusual features. The final positional parameters, along with their standard deviations, are listed in Table I. All calculations were performed on a HITAC 8700/8800 computer at the Computer Center of this University. The programs used were RSCL3 (lattice constants and their e.s.d. values), ANSFR-2 (Fourier

TABLE I

FINAL POSITIONAL PARAMETERS FOR $[\text{Ni}(\text{en})(\text{D-Fru-en})]\text{Cl}_2 \cdot \text{CH}_3\text{OH}^{\text{a,b}}$

| Atom | x | y | z |
|------|----------|-----------|------------|
| Ni | 373.6(6) | -477.3(3) | 1812.3(10) |
| N-1 | 301(3) | -1230(2) | 4(6) |
| N-2 | 1812(3) | -1000(2) | 2468(6) |
| N-3 | 132(3) | 277(2) | 3565(5) |
| N-4 | 1102(3) | 364(2) | 563(6) |
| O-1 | -530(3) | -1354(2) | 2988(5) |
| O-2 | -1149(3) | -2034(2) | -926(5) |
| O-3 | -1169(2) | -221(1) | 812(4) |
| O-4 | -2362(3) | 16(2) | -1960(5) |
| O-5 | -3069(3) | -1405(2) | -2375(5) |
| C-1 | -1013(4) | -1803(3) | 1818(8) |
| C-2 | -848(4) | -1495(3) | 183(8) |
| C-3 | -1574(4) | -805(2) | -139(7) |
| C-4 | -1628(5) | -574(4) | -1838(11) |
| C-5 | -1996(6) | -1209(4) | -2816(10) |
| C-6 | -1196(7) | -1845(4) | -2578(10) |
| C-7 | 1159(7) | -1792(4) | 290(13) |
| C-8 | 2126(6) | -1387(5) | 1081(13) |
| C-9 | 720(7) | 969(5) | 3054(12) |
| C-10 | 707(7) | 1032(4) | 1331(11) |
| O-6 | -1345(5) | 1315(3) | -1809(9) |
| C-11 | -530(8) | 1411(5) | -2933(13) |
| Cl-1 | 1279(1) | -324(1) | -3115(3) |
| Cl-2 | -1090(2) | 2612(1) | 395(3) |

^aValues are multiplied by 10⁴. ^bEstimated standard deviations in parentheses.

synthesis), FLS-4 (full-matrix, least-squares refinement), COSMO (distances, angles, and their e.s.d. values), and ORTEP II (thermal ellipsoid plotting program)[†].

RESULTS AND DISCUSSION

This work considers the reactions between the two types of hexose (aldose and ketose) and tris(diamine)nickel(II) salts.

When tris-(ethylenediamine)- or -(trimethylenediamine)-nickel(II) salts in methanol are refluxed for a short time with an excess of each sugar, the solution becomes blue. The blue-band fractions are purified by chromatography on an LH-20 gel-permeation column. A blue product separated as the purified, blue solution is concentrated and cooled. All of these complexes can be recrystallized from methanol without any evidence of decomposition. The products obtained are highly sensitive to the length of the reaction time. If the reaction solution is refluxed for a

[†]Computer illustrations were generated by means of¹³ ORTEP II.

long time, the color changes from violet, through green and reddish orange, to brown, and no blue compound can be obtained.

The complexes obtained by the reaction of sugars with tris(ethylenediamine)-nickel(II) ion are highly sensitive to moisture, except for the D-fructose complex.

When the length of the chain of the diamine is extended from ethylenediamine to trimethylenediamine, the sugars react with $[\text{Ni}(\text{tn})_3]^{2+}$ ions to give, in 10–30 min, good yields of the complexes as crystalline powders (see Table II). Interestingly, the small difference in the length of the diamine chain (as between tn and en) causes remarkable changes. The results suggest that trimethylenediamine is a suitable ligand to form nickel(II) complexes containing monosaccharide units.

In an acidic solution, all of the compounds obtained decompose into nickel(II) complexes of the diamine and the respective monosaccharides, which consist of the original sugar and a trace of another monosaccharide. Similar decomposition also gradually occurs in neutral aqueous solution.

The magnetic moments, and analyses, for the solid compounds are listed in Table II, which also includes yields of the compounds. Elemental analyses indicated that both the D-Glc and the D-Man complexes contain two monosaccharide units and two diamine units, and the D-fructose complexes have one sugar and two diamine units. The magnetic moments of the complexes fall within the range 2.9–3.4 μ_B reported¹⁴ for octahedral complexes of nickel(II).

In the infrared spectra of these compounds, C=N stretching bands (arising as a result of the Schiff-base formation between the sugars and the primary amines) are not observed. The results obtained suggest the cyclic, amino acetal nature of the sugar units in the coordination ligands.

The near-infrared-visible absorption spectra for solutions of the nickel(II)

TABLE II

ANALYTICAL DATA, MAGNETIC MOMENTS, AND YIELDS FOR THE Ni(II) COMPLEXES

| Complex | | Analysis | | | | μ_B | Yield (%) |
|--|-------|----------|-------|-------|--------|---------|-----------|
| | | C (%) | H (%) | N (%) | Cl (%) | | |
| [Ni(D-Glc-en) ₂]Cl ₂ · H ₂ O | found | 32.47 | 6.36 | 9.39 | 11.83 | 3.29 | 23 |
| | calc. | 32.46 | 6.47 | 9.46 | 11.98 | | |
| [Ni(D-Glc-tn) ₂]Cl ₂ | found | 35.90 | 6.96 | 9.46 | 11.79 | 3.04 | 72 |
| | calc. | 35.74 | 7.13 | 9.26 | 11.72 | | |
| [Ni(D-Man-en) ₂]Cl ₂ | found | 33.26 | 6.57 | 9.74 | 12.66 | 3.16 | 24 |
| | calc. | 33.48 | 6.32 | 9.76 | 12.35 | | |
| [Ni(D-Man-tn) ₂]Cl ₂ · 5 H ₂ O | found | 34.39 | 6.69 | 8.53 | 12.10 | 2.94 | 27 |
| | calc. | 34.36 | 6.89 | 8.91 | 11.27 | | |
| [Ni(en)(D-Fru-en)]Cl ₂ · CH ₃ OH | found | 29.25 | 6.38 | 12.64 | 15.94 | 3.17 | 11 |
| | calc. | 29.75 | 6.81 | 12.62 | 15.97 | | |
| [Ni(tn)(D-Fru-tn)]Cl ₂ · CH ₃ OH | found | 33.52 | 7.44 | 12.23 | 14.97 | 3.18 | 53 |
| | calc. | 33.08 | 7.26 | 11.87 | 15.02 | | |

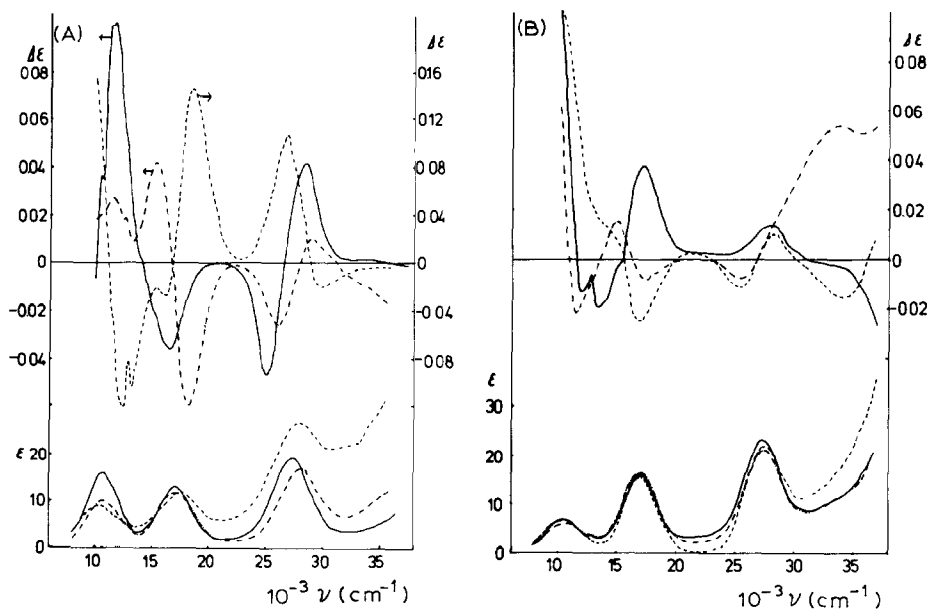


Fig. 2. Absorption (upper) and circular dichroism (lower) spectra of the complex ions. (A) (—) $[\text{Ni}(\text{D-Glc-en})_2]^{2+}$, (-----) $[\text{Ni}(\text{D-Man-en})_2]^{2+}$, (- · - · - ·) $[\text{Ni}(\text{en})(\text{D-Fru-en})]^{2+}$; (B) (—) $[\text{Ni}(\text{D-Glc-tn})_2]^{2+}$, (-----) $[\text{Ni}(\text{D-Man-tn})_2]^{2+}$, and (- · - · - ·) $[\text{Ni}(\text{tn})(\text{D-Fru-tn})]^{2+}$.

complexes in methanol are illustrated in Fig. 2, and representative spectral data and reflectance-spectral data are presented in Table III. No significant differences are observed between the spectra of the solid and the methanolic solution, except for the typically lower resolution obtained for the reflectance spectra; these show no gross changes in electronic or geometrical structures which might occur on dissolution.

Because the electronic spectra of these complexes are similar, the following discussion applies equally to all of the compounds. The solution spectra of these complexes in the near-infrared and visible regions consist of three principal bands (ν_1 , ν_2 , and ν_3), having comparatively low intensities, which are characteristic of octahedral nickel(II) complexes¹⁵. The energies represent the electronic transitions from the $^3A_{2g}$ (F) ground state to the successively higher excited states $^3T_{2g}$ (F), $^3T_{1g}$ (F), and $^3T_{1g}$ (P). Generally, the ratio ν_2/ν_1 of the frequencies of the first and second band maxima for most octahedral nickel(II) complexes lies between 1.5 and 1.7. The values of Dq found for octahedral nickel(II) vary between 640 and 1270 cm^{-1} , depending on the position of the ligand in the spectrochemical series. The usual value of β [the ratio of $B(\text{bound})/B(\text{free ion})$, where B is the Racah parameter] falls in the interval 0.7–0.9. Thus, the values of Dq , β , and ν_2/ν_1 for the present complexes fall within the ranges expected for octahedral complexes of nickel(II) (see Table IV).

The elemental analyses, coupled with the magnetic susceptibility and spectral

TABLE III

ABSORPTION, CIRCULAR DICHROISM, AND REFLECTANCE SPECTRA OF Ni(II) COMPLEXES

| Complex | Absorbance | C.d. | Reflectance |
|---|-------------------------------------|--|--------------------------|
| | $10^3 \nu_{\max}, \text{cm}^{-1}$ | $10^3 \nu_{\max}, \text{cm}^{-1}$ | $(10^2 \Delta \epsilon)$ |
| $[\text{Ni}(\text{D-Glc-en})_2]\text{Cl}_2 \cdot \text{H}_2\text{O}^a$ | 10.7(16.0), 12.7(6.4) ^{sh} | 10.5(+3.7) ^{sh} , 11.7(+10.3) | 10.6, 12.5 ^{sh} |
| | 17.1(13.1) | 16.4(-3.6) | 17.2 |
| | 27.3(19.2) | 25.1(-4.7), 28.3(+4.1) | 27.4 |
| | 10.5(6.9), 12.7(3.7) ^{sh} | 12.2(-1.3), 13.4(-2.0) | 10.5, 12.6 ^{sh} |
| $[\text{Ni}(\text{D-Glc-tm})_2]\text{Cl}_2^b$ | 17.1(16.1) | 17.1(+3.8) | 16.7 |
| | 27.4(23.0) | 27.8(+1.3) | 27.2 |
| $[\text{Ni}(\text{D-Man-en})_2]\text{Cl}_2^a$ | 10.3(8.9), 12.8(4.9) ^{sh} | 12.4(-12.1), 13.2(-10.4) | 9.6, 12.5 ^{sh} |
| | 17.5(11.5) | 16.0(-2.8), 18.6(+14.8) | 15.8 |
| | 27.8(26.3) | 26.9(+10.6), 29.9(-2.2) | 26.3 |
| | 10.5(6.7), 12.4(3.4) ^{sh} | 10.1(+10.0), 14.8(+1.3) ^{sh} | 10.4, 12.8 ^{sh} |
| $[\text{Ni}(\text{D-Man-tm})_2]\text{Cl}_2 \cdot 1.5 \text{H}_2\text{O}^a$ | 17.2(15.8) | 16.8(-2.5), 21.6(+0.2) | 17.0 |
| | 27.4(21.6) | 25.2(-1.1), 28.0(+1.5) | 27.4 |
| | | 33.8(-1.5) | |
| | 10.8(10.0), 12.8(4.7) ^{sh} | 11.5(+2.6), 12.6(+1.9) | 11.4, 12.7 ^{sh} |
| $[\text{Ni}(\text{en})(\text{D-Fru-en})]\text{Cl}_2 \cdot \text{CH}_3\text{OH}^a$ | 17.2(11.7) | 15.3(+4.2), 18.3(-6.0) | 17.1 |
| | 28.2(17.0) | 26.1(-2.6), 29.0(+1.0) | 27.8 |
| | 10.4(6.1), 12.6(3.7) ^{sh} | 10.4(-2.2) | 10.7, 12.7 ^{sh} |
| | 17.0(16.6) | 14.8(+1.5), 17.3(-0.86) | 17.1 |
| $[\text{Ni}(\text{tm})(\text{D-Fru-tm})]\text{Cl}_2 \cdot \text{CH}_3\text{OH}^a$ | 27.4(21.4) | 25.3(-0.84), 33.7(+5.4) | 27.4 |

^aIn methanol solution. ^bIn ethyleneglycol solution.

TABLE IV

SPECTRAL DATA FOR THE Ni(II) COMPLEXES

| <i>Complex ions</i> | ν_2/ν_1 | $Dq\ (cm^{-1})$ | $B\ (cm^{-1})$ | β |
|---------------------------|---------------|-----------------|----------------|---------|
| $[Ni(D-Glc-en)_2]^{2+}$ | 1.60 | 1070 | 820 | 0.788 |
| $[Ni(D-Glc-tn)_2]^{2+}$ | 1.63 | 1050 | 867 | 0.832 |
| $[Ni(D-Man-en)_2]^{2+}$ | 1.70 | 1030 | 960 | 0.922 |
| $[Ni(D-Man-tn)_2]^{2+}$ | 1.64 | 1050 | 873 | 0.839 |
| $[Ni(en)(D-Fru-en)]^{2+}$ | 1.59 | 1080 | 867 | 0.833 |
| $[Ni(tn)(D-Fru-tn)]^{2+}$ | 1.63 | 1040 | 880 | 0.845 |

data, and the results of the decomposition of the complexes in aqueous solution, substantiate that all of the compounds obtained are octahedral complexes of nickel(II) containing the original sugar and diamine units.

It is well known that the coordination of an optically active ligand to a metal ion induces optical activity into the d-d electronic transitions of the metal ion, and circular dichroism is observed. When a methanol solution of $NiCl_2 \cdot 6 H_2O$ and a monosaccharide was refluxed for several hours in the absence of diamine, no circular dichroism was observed in the d-d transition. On the other hand, all of the complexes derived from the reaction between sugars and $[Ni(diamine)_3]^{2+}$ ions show c.d. curves in the near-infrared-visible region. Therefore, this indicates that the diamine plays an important role on the ability of sugars to bind to the nickel atom. It is well known that cyclic sugars possessing a free reducing group are able to react with primary and secondary amines to give, under mild conditions, glycosylamines, derivatives in which the glycosidic hydroxyl group has been replaced by an amino group. This is generally accepted as being the first step in the "Maillard reaction" or nonenzymic browning¹⁶. Consequently, it may be predicted that D-Glc, D-Man, or D-Fru will react with one of the amine centers of $[Ni(en\ or\ tn)_3]^{2+}$, to form the corresponding glycosylamine.

From all these considerations, it was decided that the D-Glc and D-Man complexes contain two, tridentate glycosylamine ligands (*viz.*, D-Glc-en, D-Glc-tn, D-Man-en, D-Man-tn), and that the D-Fru complexes are made up of bidentate diamine and a tetradentate ligand of D-Fru-en or D-Fru-tn[†].

It is proposed that when the hydroxyl group adjacent to the glycosylated nitrogen atom of the glycosylamine ligand coordinates to the nickel atom, involving a favored, five-membered chelate ring, the D-fructose unit is attached to the metal at three points, namely through the hydroxyl groups on C-1 and C-3 and the nitrogen atom on C-2, and the D-glucose or D-mannose units bind to the nickel atom at two points, through the oxygen atom on C-2 and the nitrogen atom on C-1, as shown in Fig. 3. When the pyranoid ring of the D-Glc-en or D-Glc-tn has the usual β - 4C_1 form, the chelate ring taken by the sugar moiety adopts the λ -gauche

[†]See the Experimental section for ligand abbreviations.

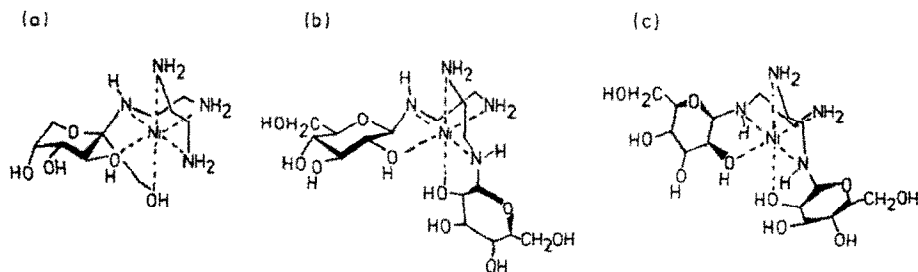


Fig. 3. Structures of the complex ions: (a) $[\text{Ni}(\text{en})(\text{D-Fru-en})]^{2+}$, (b) $[\text{Ni}(\text{D-Glc-en})_2]^{2+}$, and (c) $[\text{Ni}(\text{D-Man-en})_2]^{2+}$. The corresponding tn complexes would have analogous structures.

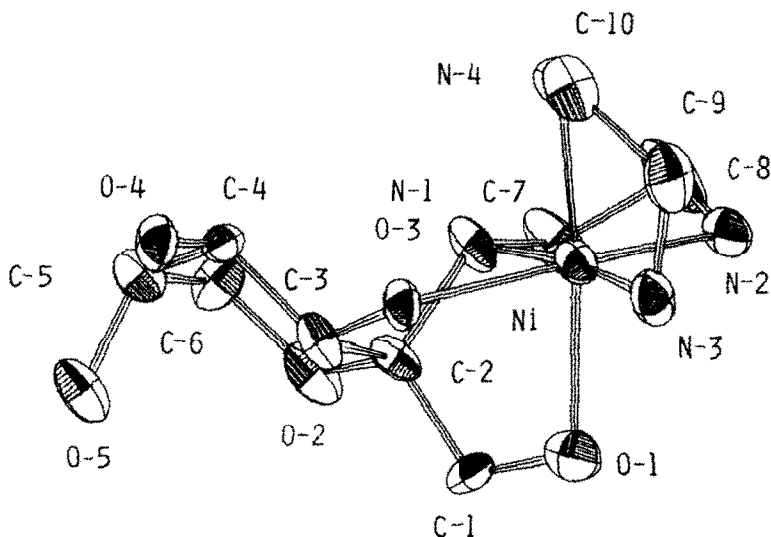


Fig. 4. Perspective drawing of the complex cation $[\text{Ni}(\text{en})(\text{D-Fru-en})]^{2+}$, and the numbering scheme for the atoms.

form, and the absolute configuration of the secondary nitrogen atom will be *S*. All of these environments are the inverse for the D-Man-en and D-Man-tn ligands; the chelate conformation of the sugar part is *δ-gauche*, and the absolute configuration of the secondary nitrogen atoms is *R*. These structural features are evident in the circular dichroism curves of the D-Glc and D-Man complexes, which are almost mirror images of the corresponding c.d. curves in the first absorption region (see Fig. 2).

X-Ray crystal structure of $[\text{Ni}(\text{en})(\text{D-Fru-en})]\text{Cl}_2 \cdot \text{CH}_3\text{OH}$. — A perspective view of the $[\text{Ni}(\text{en})(\text{D-Fru-en})]^{2+}$ cation is shown in Fig. 4. The coordination at the central atom of the cation is essentially octahedral, with the four coordination sites being occupied by a tetradentate glycosylamine ligand of D-Fru-en; the remaining two coordination sites are occupied by a bidentate ethylenediamine. The complex cation has the *cis*-(O-O)- $[\text{NiN}_4\text{O}_2]$ structure.

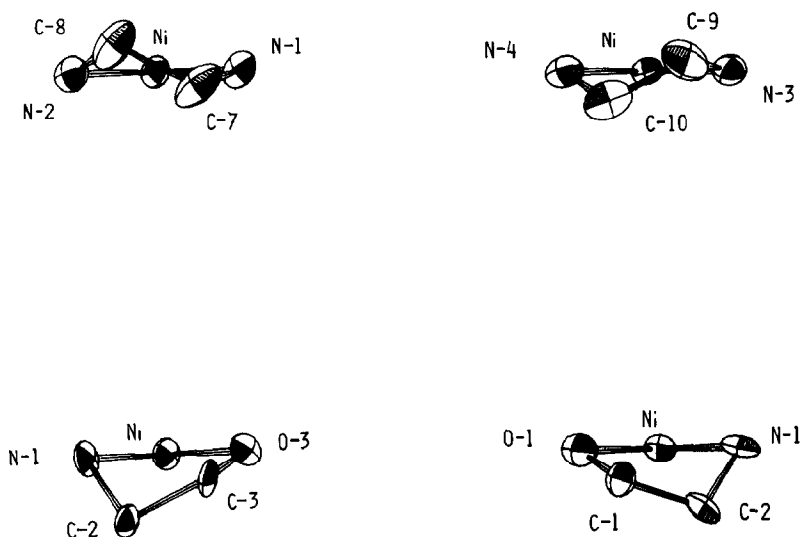


Fig. 5. Perspective drawings of the chelate rings.

As expected, one nitrogen atom of ethylenediamine binds to C-2 of D-fructose, forming the glycosylamine; this attaches to the nickel atom at four points, through the 1- and 3-hydroxyl groups and the two nitrogen atoms of the ethylenediamine residue. The configuration of the secondary nitrogen atom is found to be (*S*) in the notation of Cahn *et al.*¹⁷ Four five-membered chelate ring conformations are presented in Fig. 5. The bidentate ethylenediamine chelate ring has an unsymmetrical, λ -*gauche* conformation. In contrast, the other diamine chelate in the D-Fru-en takes the symmetrical δ -*gauche* form. Both of the five-membered chelate rings involving the sugar unit, Ni, N-1, C-2, C-3, O-3, and Ni, N-1, C-2, C-1, O-1 adopt the envelope forms which deviate from the ideal *gauche* conformation.

The pyranoid ring of the D-fructosyl group is in the β - 2C_5 conformation, with C-1, O-3, and O-4 in the equatorial orientation and O-5 and N-1 axial with respect to the pyranoid ring. The 2C_5 conformation is also adopted by β -D-fructopyranose in the free state¹⁸ and the calcium complexes of D-fructose^{1-(g),(h),(i)}.

The intramolecular distances and bond angles are given in Tables V and VI. The Ni-N distances range from 2.059(8) (Ni-N-3) to 2.098(8) Å (Ni-N-2). These values are normal for the Ni-N bond-distances in octahedral Ni(II) complexes. Ni-O distances of 2.205(8) (Ni-O-1) and 2.137(6) Å (Ni-O-3) are much longer than the sum of the covalent radii, 2.05 Å [octahedral Ni(II), 1.39 Å; O, 0.66 Å]^{19,20}. Thus, the sugar-oxygen to Ni bond is weakened.

For the bond angles around the nickel atom, deviations from ideal octahedral geometry are observed. The deviations from 180° occur for the *trans* angles: N-2-Ni-O-3, 164.1(3)°, N-1-Ni-N-3, 169.2(4)°, and O-1-Ni-N-4, 174.6(3)°. The ring

TABLE V

INTRAMOLECULAR DISTANCES FOR $[\text{Ni}(\text{en})(\text{D-Fru-en})]\text{Cl}_2 \cdot \text{CH}_3\text{OH}$

| <i>Bond</i> | <i>Bond distances^a (Å)</i> |
|-------------|---------------------------------------|
| Ni-N-1 | 2.070(8) |
| Ni-N-2 | 2.098(8) |
| Ni-N-3 | 2.059(8) |
| Ni-N-4 | 2.085(8) |
| Ni-O-1 | 2.205(7) |
| Ni-O-3 | 2.137(6) |
| N-1-C-2 | 1.510(13) |
| N-1-C-7 | 1.503(18) |
| N-2-C-8 | 1.428(19) |
| N-3-C-9 | 1.532(19) |
| N-4-C-10 | 1.477(18) |
| O-1-C-1 | 1.424(13) |
| O-2-C-2 | 1.419(13) |
| O-2-C-6 | 1.442(17) |
| O-3-C-3 | 1.436(12) |
| O-4-C-4 | 1.424(15) |
| O-5-C-5 | 1.424(16) |
| C-1-C-2 | 1.511(15) |
| C-2-C-3 | 1.582(14) |
| C-3-C-4 | 1.502(17) |
| C-4-C-5 | 1.506(20) |
| C-5-C-6 | 1.549(21) |
| C-7-C-8 | 1.561(23) |
| C-9-C-10 | 1.463(23) |
| O-6-C-11 | 1.396(22) |

^aEstimated standard deviations in parentheses.

angles at the nickel atom for the five-membered, chelate rings, namely, N-1-Ni-N-2, N-3-Ni-N-4, N-1-Ni-O-1, and N-1-Ni-O-3, are 85.5(3)°, 85.3(3)°, 79.5(3)°, and 79.5(3)°, respectively. The N-Ni-N bond-angles appear normal for Ni(II), five-membered, chelate rings. The significant deviations from the ideal angle (90°) occur for the angles contained in the N-Ni-O angles. Consequently, it is evident that some strain exists in the glycosylamine coordination system. This strain presumably comes from the elongation of the Ni-O bond-distances which can be compared with the Ni-N bond-distances.

It is often observed that the ring angles at the central metal atom for the six-membered, diamine rings are ~90°. The values are significantly larger than those (~85°) for the five-membered, diamine rings. It is evident that, in the complexes, the glycosylamine ligands containing trimethylenediamine are fairly strain-free as compared with those containing ethylenediamine. These structural features support the view that sugars react with $[\text{Ni}(\text{tn})_3]^{2+}$ to give good yields of the glycosylamine complexes in a short time. The C-C distances of β -D-fructose, except for the length of C-2-C-3, are quite similar to the usual carbon-carbon values for the keto- and aldo-hexoses. The C-C-C and C-C-O bond-angles are close to

TABLE VI

BOND ANGLES FOR $[\text{Ni}(\text{en})(\text{D-Fru-en})]\text{Cl}_2 \cdot \text{CH}_3\text{OH}$

| <i>Bonds</i> | <i>Bond angles^a (degrees)</i> |
|--------------|--|
| N-1-Ni-N-2 | 85.5(3) |
| N-1-Ni-N-3 | 169.2(4) |
| N-1-Ni-N-4 | 98.4(3) |
| N-1-Ni-O-1 | 79.5(3) |
| N-1-Ni-O-3 | 79.5(3) |
| N-2-Ni-N-3 | 104.1(3) |
| N-2-Ni-N-4 | 96.5(3) |
| N-2-Ni-O-1 | 88.3(3) |
| N-2-Ni-O-3 | 164.1(3) |
| N-3-Ni-N-4 | 85.5(3) |
| N-3-Ni-O-1 | 95.7(3) |
| N-3-Ni-O-3 | 90.4(3) |
| N-4-Ni-O-1 | 174.6(3) |
| N-4-Ni-O-3 | 91.1(3) |
| O-1-Ni-O-3 | 83.7(2) |
| Ni-N-1-C-2 | 100.6(4) |
| Ni-N-1-C-7 | 108.4(6) |
| C-2-N-1-C-7 | 115.0(9) |
| Ni-N-2-C-8 | 104.1(7) |
| Ni-N-3-C-9 | 107.1(6) |
| Ni-N-4-C-10 | 105.0(6) |
| Ni-O-1-C-1 | 109.1(4) |
| C-2-O-2-C-6 | 118.9(9) |
| Ni-O-3-C-3 | 111.5(4) |
| O-1-C-1-C-2 | 111.1(7) |
| N-1-C-2-O-2 | 114.0(6) |
| N-1-C-2-C-1 | 110.0(7) |
| N-1-C-2-C-3 | 104.8(6) |
| O-2-C-2-C-1 | 107.8(7) |
| O-2-C-2-C-3 | 107.6(6) |
| C-1-C-2-C-3 | 112.7(7) |
| O-3-C-3-C-2 | 108.1(6) |
| O-3-C-3-C-4 | 109.9(7) |
| C-2-C-3-C-4 | 114.8(8) |
| O-4-C-4-C-3 | 108.4(7) |
| O-4-C-4-C-5 | 111.4(8) |
| C-3-C-4-C-5 | 108.6(9) |
| O-5-C-5-C-4 | 109.6(8) |
| O-5-C-5-C-6 | 111.5(9) |
| C-4-C-5-C-6 | 109.1(10) |
| O-2-C-6-C-5 | 109.6(9) |
| N-1-C-7-C-8 | 106.1(9) |
| N-2-C-8-C-7 | 112.6(10) |
| N-3-C-9-C-10 | 110.1(9) |
| N-4-C-10-C-9 | 111.6(10) |

^aEstimated standard deviations in parentheses.

tetrahedral, as in free β -D-fructose¹⁸ and its calcium complex^{1-(g),(h),(i)}. The crystal packing of the unit-cell contents, projected along the *c* axis, is presented in Fig. 6. The unit cell consists of four discrete complex cations, eight chloride counter-ions, and four molecules of methanol of crystallization. Because recrystallization from solvents other than methanol gives a blue powder, the presence of the molecule of methanol of crystallization seems to be essential, in order to provide crystalline stability.

The present crystal structure suggests the general coordination pattern of the sugar unit in the glycosylamine ligands, which binds to the metal to form the five-membered chelate ring(s) by using the glycosylated nitrogen atom and the adjacent

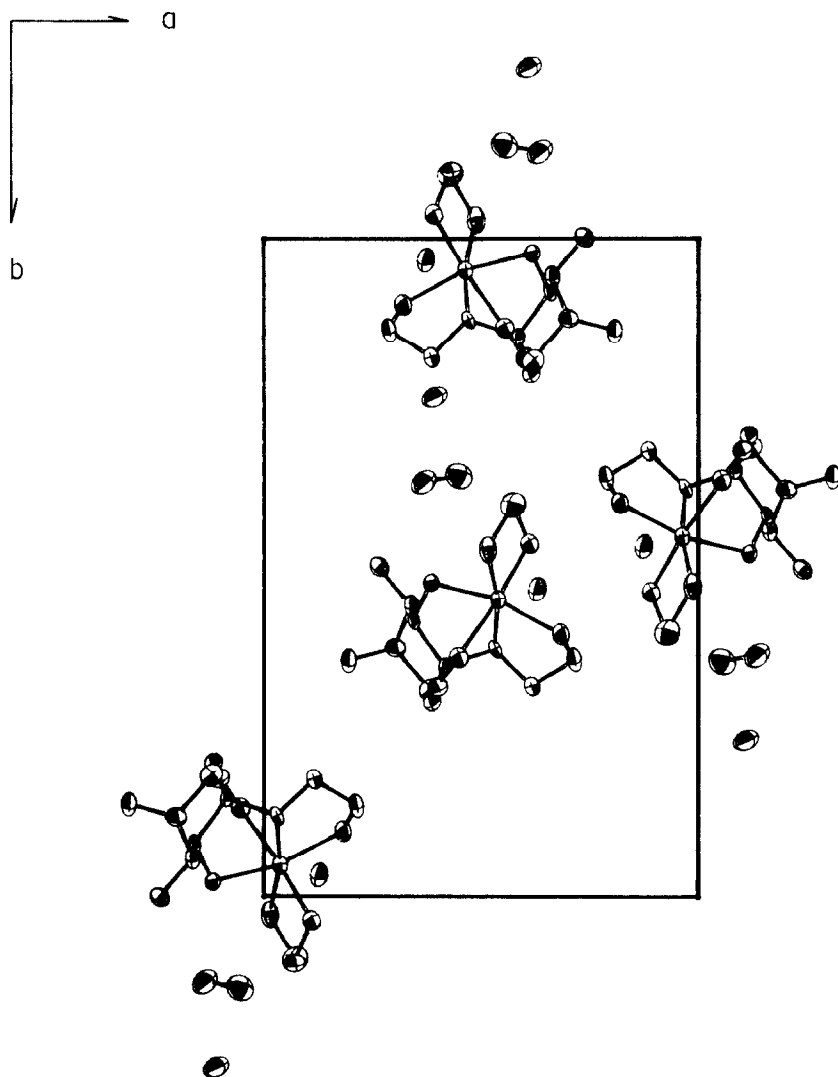


Fig. 6. Unit-cell contents viewed along the *c* axis.

hydroxyl group(s). Thus, the most important result from this study of the X-ray crystal structure is associated with the anchoring mode of the sugar part.

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