89. Stereoselectivity in Reactions of Metal Complexes IV[1])

Asymmetric Synthesis of (2R, 7S, 10R)- and (2R, 7R, 10R)-2,10-diamino-5,5,7-trimethyl-4,8-diazaundecanenickel(II) by Stereoselective Hydrogenation of (2R, 10R)-2,10-diamino-5,5,7-trimethyl-4,8-diaza-7-undecenenickel(II)

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Summary. The catalytic hydrogenation of (2R,10R)-2,10-diamino-5,5,7-trimethyl-4,8-diaza-7-undecenenickel(II) yields two products when the reaction is performed in the presence of ethylenediamine, but only one, when ethylenediamine is absent. The stereochemistry of the reaction is discussed and a proposal for the absolute configuration of the two diastereomeric complexes and the free ligands is given on the base of CD.- and NMR.-spectra.

Linear optically active tetramines have found increased interest in the last years because of their stereoselective reactions in the formation of coordination compounds [1]. In metal complexes of such ligands the secondary nitrogen atoms represent two new centers of chirality, so that five geometric forms are possible, four of which may exist as pairs of enantiomers [2]. By adequate choice of substituents on the carbon chain of the ligand it is possible to isolate examples of all of these geometric forms as inert Co(III)complexes [3]. Not only the conformation of the different chelate rings and the configuration of the secondary nitrogen atoms may be determined in this way, but also the absolute configuration of the whole complex.

Derivatives of 1,9-diamino-3,7-diazanonane (2,3,2-tet) form complexes with two five- and one six-membered chelate rings. Ligands of this type prefer a square
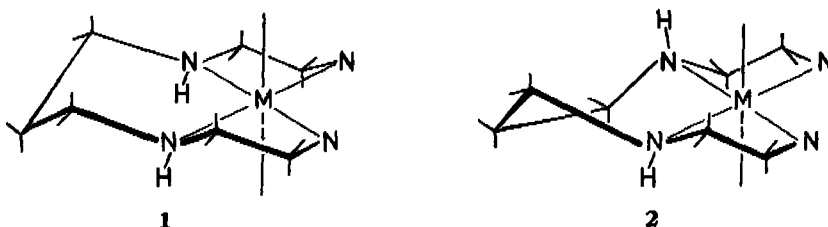

1   **2**

Fig. 1. *Structures of* trans-(2,3,2-tet)-*complexes with* R,S- (**1**), *and* R,R-*configuration* (**2**) *at the secondary nitrogen atoms*

planar structure. *Alexander et al.* [4] showed that in agreement with the greater stability of the chair-conformation of the six-membered chelate ring the complexes with an (R,S)-configuration at the nitrogen atoms (**1**) are more stable than the diastereomeric forms with R,R or S,S-configuration (**2**).

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[1]) Part III: see [7].

The relative stability of these diastereomeric forms may greatly change by the introduction of substituents. The formation of trans-[Co((S,S)-Me$_2$-2,3,2-tet)Cl$_2$]$^+$ (Me$_2$-2,3,2-tet — 2,10-diamino-4,8-diazaundecane) is for example stereospecific, only the product with structure **2** having the nitrogen atoms in R,R-configuration is formed [5]. In this product the two methyl-groups are placed in a favorable equatorial position. *Busch* and his coworkers have described the stereochemistry of cobalt(III) complexes of (4S)-methyl-1,9-diamino-3,7-diazanonane, the only example so far studied of a 2,3,2-tet-complex with a substituent in the central chelate ring [6]. Complexes with substituents in both, the five- and the six-membered ring, are not known.

Recently we described the stereospecific hydrogenation of a macrocyclic nickel(II) complex [7]. The present work shows, that such a stereospecific hydrogenation is also possible with nickel(II) complexes of open-chain *Schiff*-base type ligands. We first studied the reduction of a complex synthesized by *Ito & Fujita* [8], ((2R,10R)-2,10-diamino-5,5,7-trimethyl-4,8-diaza-7-undecene)-nickel(II)perchlorate ([Ni(R,R-C$_{12}$H$_{28}$N$_4$)](ClO$_4$)$_2$ (3) which is obtained by the reaction of [Ni(R-pn)$_3$] (ClO$_4$)$_2$ with acetone. In the reaction **4** is formed as a by-product. By catalytic hydrogenation **3** should be transformed to **5**.

3   4   5

Fig. 2

Experimental Part

1. Synthesis. · 1.1. ((2R,10R)-2,10-diamino-5,5,7-trimethyl-4,8-diaza-7-undecene) (ethylenediamine)nickel(II)perchlorate, [Ni(C$_{12}$H$_{28}$N$_4$) (en)](ClO$_4$)$_2$. The procedure given by *Ito & Fujita* [8] is modified as follows: 8.7 g of [Ni(R-pn)$_3$](ClO$_4$)$_2$ are dissolved in about 200 ml of acetone and the solution is refluxed for 24 h. By this procedure the two complexes **3** and **4** are obtained in a ratio of 3:1, whereas the reaction at room temp. gives the two products in about equal amounts. The reaction mixture is evaporated to dryness, dissolved in water and the diluted solution passed through a cation exchange column in Na$^+$-form. The column is then washed with water, until the washwater showed no further alcaline reaction. By elution with a 5% NaCl solution two yellow bands are formed which are collected separately. The eluate of the two bands is concentrated to a small volume and the precipitated NaCl filtered off. Addition of NaClO$_4$ to the solution of the first band yields the yellow macrocyclic complex **4** (ClO$_4$)$_2$. From the solution of the second band the violet [Ni(C$_{12}$H$_{28}$N$_4$) (en)] (ClO$_4$)$_2$ is precipitated by NaClO$_4$ and drop wise addition of ethylenediamine. Total yield of the two complexes: 85%.

1.2. ((2R,10R)-2,10-diamino-5,5,7-trimethyl-4,8-diaza-7-undecene)nickel(II)perchlorate monohydrate, [Ni(C$_{12}$H$_{28}$N$_4$)] (ClO$_4$)$_2$ · H$_2$O. The compound is obtained from [Ni(C$_{12}$H$_{28}$N$_4$) (en)] (ClO$_4$)$_2$ as indicated in [8].

1.3. ((2R,7S,10R)- and ((2R,7R,10R)-2,10-diamino-5,5,7-trimethyl-4,8-diazaundecane)nik-kel(II)perchlorate, [Ni(R, S, R-$C_{12}H_{30}N_4$)](ClO$_4$)$_2$ and [Ni(R, R, R-$C_{12}H_{30}N_4$)](ClO$_4$)$_2$. The reduction of [Ni($C_{12}H_{28}N_4$)]$^{2+}$ was performed under various conditions (cf. table 1). A typical example is as follows: 2 g of [Ni($C_{12}H_{28}N_4$) (en)](ClO$_4$)$_2$ are dissolved in 250 ml of water and reduced at 50° with PtO$_2$ as catalyst and a hydrogen pressure of about 4.5 atm. The hydrogenation was stopped, when the absorption band due to the C=N-group at 265 nm had completely disappeared; reaction time was about three days. After filtration of the catalyst, the solution is introduced to a small cation exchange column and aboundly washed with water to remove the ethylenediamine. The yellow band is then quantitatively eluted with 10% NaCl and the eluate is freed from most of the NaCl by repeated evaporation and addition of ethanol. After evaporation to dryness, the yellow solid is dissolved in a small volume of water and the solution introduced in a column filled with Sephadex G-15. Elution with water gives two bands E-1 and E-2, which are collected separately. The two solutions are concentrated to a small volume and the complexes are obtained as yellow [Ni($C_{12}H_{30}N_4$)](ClO$_4$)$_2$ by addition of an excess NaClO$_4$ and cooling or as violet [Ni($C_{12}H_{30}N_4$)-(en)](ClO$_4$)$_2$ by dropwise addition of ethylenediamine to the two solutions containing an excess of NaClO$_4$. Total yield: 75%. Calculated for [Ni($C_{12}H_{30}N_4$) (en)](ClO$_4$)$_2$:

		C	30.6	H	6.95	N	15.35%
Found for	E-1	C	29.6	H	6.68	N	15.40%
	E-2	C	29.8	H	6.80	N	15.35%

1.4.   (2R,7S,10R)-   and   (2R,7R,10R)-2,10-diamino-5,5,7-trimethyl-4,8-diazaundecane, $C_{12}H_{30}N_4$. – Procedure a): A solution of 0.55 g of [Ni($C_{12}H_{30}N_4$)](ClO$_4$)$_2$ obtained from E-1 is rendered strongly basic by KOH. 4.3 g of KCN is added and the free ligand extracted during several days by diisopropyl ether/benzene 1:1. The extraction is continued until the organic phase shows no more optical activity. The combined extracts are carefully evaporated and the remaining oil is distilled in a ball tube under reduced pressure at 90° (Büchi, Glass tube oven GKR-50). Titration with hydrochloric acid gives a mol. weight of 266 ± 2, corresponding to the dihydrate $C_{12}H_{30}N_4 \cdot 2$ H$_2$O. $[\alpha]_D^{25} = -6.8°$ ($c = 0.5$, EtOH) corresponding to $[\alpha]_D^{25} = -7.8°$ for the anhydrous compound.

Procedure b): The anhydrous tetramines can be obtained by the method of Love & Powell [9]. [Ni($C_{12}H_{30}N_4$)] Cl$_2$ is dissolved in absolute ethanol, four equiv. of NaCN are added and the solution stirred for 2 h. K$_2$Ni(CN)$_4$ and KCl are quantitatively precipitated by addition of absolute ether and filtered off. The filtered solution is evaporated and the residual oil distilled as indicated in procedure a).

$C_{12}H_{30}N_4$ from E-1 $[\alpha]_D^{25} = -7.7°$; $[\alpha]_{436}^{25} = -17.4°$

$C_{12}H_{30}N_4$ from E-2 $[\alpha]_D^{25} = -12,5°$; $[\alpha]_{436} = -27,5°$

The two diastereomeric tetramines are further characterized by NMR.- and mass-spectra.

2. Measurements: See [7].

Table 1. Relative yields of [Ni(R, S, R-$C_{12}H_{30}N_4$)]$^{2+}$ (E-1) and [Ni(R, R, R-$C_{12}H_{30}N_4$)]$^{2+}$ (E-2) by catalytic hydrogenation of [Ni(R, R-$C_{12}H_{28}N_4$)]$^{2+}$

[Ni(R, R-$C_{12}H_{28}N_4$)](ClO$_4$)$_2$ (mol/l)	equivalent ethylenediamine	t°C	% E-1	% E-2
0.016	0	50	100	–
0.016	1	50	85	15
0.016	1,3	50	82	18
0.016	2	50	76	24
0.027	1	50	63	37
0.036	1	35	57	43

Discussion. – For the unsaturated complex [Ni(R, R-$C_{12}H_{28}N_4$)](ClO$_4$)$_2$ obtained from |Ni(R-pn)](ClO$_4$)$_2$ the structure 6 with the greatest number of substituents in an equatorial or pseudo-equatorial position have been proposed [8]. The

proposition is based on the known absolute configuration of the asymmetric centers in the terminal chelate rings, and the comparison of the CD.-spectra with that of the macrocyclic complex **4**. The structure of **4** is known from X-ray diffraction [10]
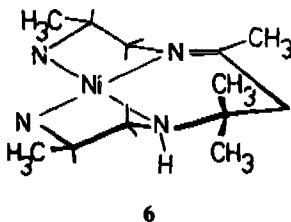

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Fig. 3. *Absolute configuration of* $[Ni(R, R-C_{12}H_{28}N_4)](ClO_4)_2$

Fig. 4 shows the CD.-spectra of the unsaturated complex (a) and of the two products obtained by hydrogenation (b)[2]).
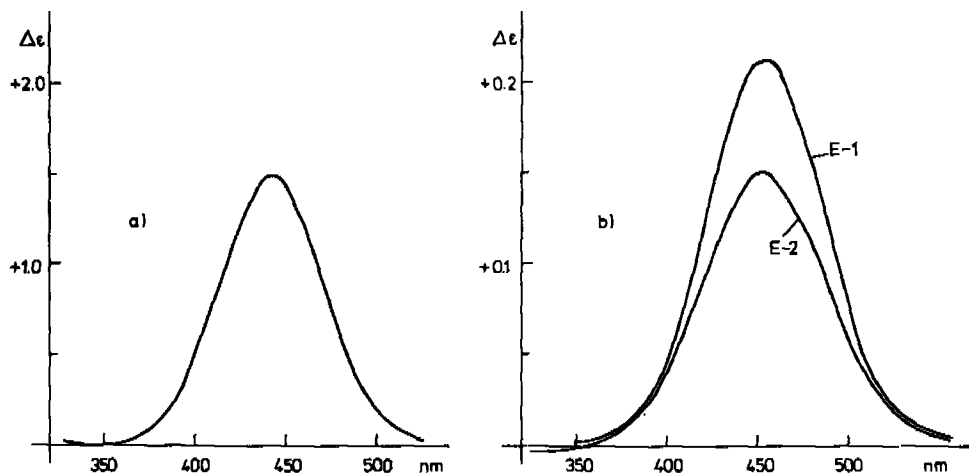

Fig. 4. *CD.-spectra of a)* $[Ni(R, R-C_{12}H_{28}N_4)]^{2+}$ *and of b)* $[Ni(R, S, R-C_{12}H_{30}N_4)]^{2+}$ *(E-1) and*
$[Ni(R, R, R-C_{12}H_{30}N_4)]^{2+}$ *(E-2)*

The most interesting feature is the great resemblance of the spectra of the two reduced diastereomeric compounds, which show, that the two chromophores should be very similar. The hypothesis, that the two complexes contain the same structural elements is further confirmed by the NMR.-spectra, of the two compounds. These spectra, reproduced in Fig. 5, are practically superimposable. This means that in both diastereoisomeric complexes all the substituents are found in a similar chemical environment. This excludes structure **2** with both secondary nitrogen atoms in the same absolute configuration so that the methyl group in the six-membered ring in one of the two diastereoisomers **7** and **8** must necessarily adopt an axial position (Fig. 6)

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[2]) The spectrum of E-2 was obtained from a solution containing one equivalent of ethylendiamine. The CD.-intensity may be somewhat reduced by the presence of some complex in the octahedral form, the contribution of which to net CD.-intensity should be negligible at 450 nm.
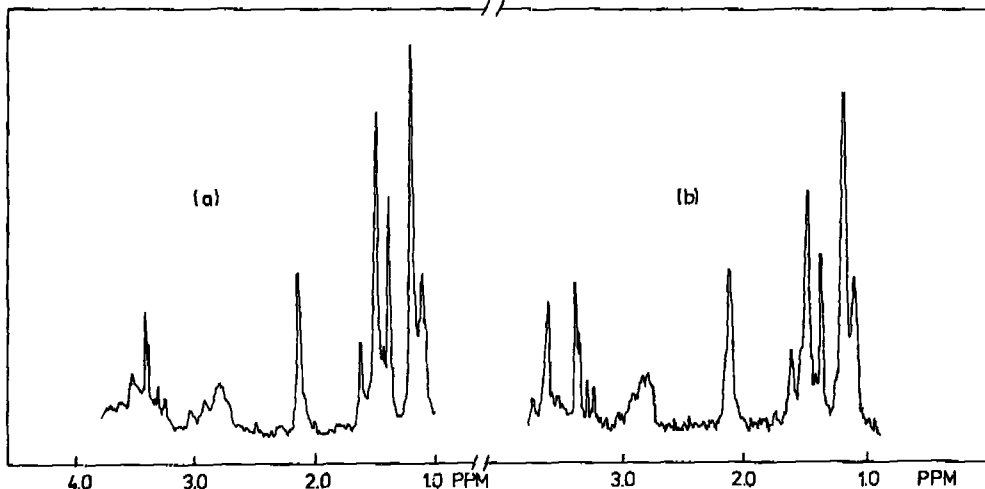
Fig. 5. *NMR.-spectra of a)* [Ni(R, S, R-$C_{12}H_{30}N_4$)]$^{2+}$ *and b)* [Ni(R, R, R-$C_{12}H_{30}N_4$)]$^{2+}$

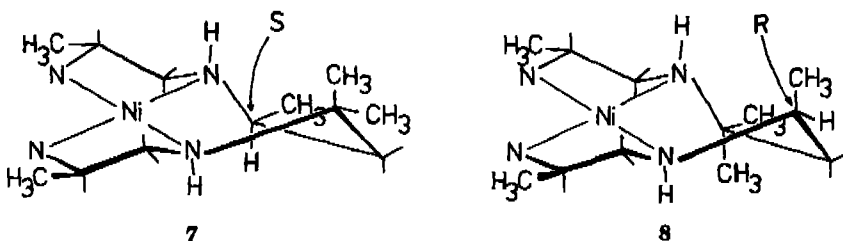
7   8

Fig. 6

Such a difference should clearly show up in NMR.-spectra. An equatorial position
in both cases is only possible, when the two secondary nitrogen atoms have opposite
(R,S) absolute configuration; that means, the central chelate ring must adopt a
chair conformation. Such a chair conformation is also suggested by comparison of
the NMR.-spectra with those of analogous macrocyclic compounds [11]. For the
five-membered chelate rings two possibilities exist: a) both rings adopt *gauche* con-
formation – one of the methyl substituents takes an axial position, b) both methyl
substituents are in equatorial position – one of the chelate rings takes an envelope
conformation. In the NMR.-spectra the two methyl groups show only one doublet,

9   10
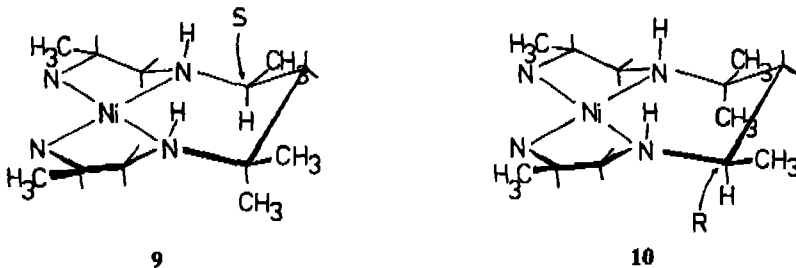
Fig. 7. *Probable structures of* [Ni(R, S, R-$C_{12}H_{30}N_4$)]$^{2+}$ **(9)** *and* [Ni(R, R, R-$C_{12}H_{30}N_4$)]$^{2+}$ **(10)**

so that the structures indicated in Fig. 7 seem the most probable. The basic chirality of the framework of (9) and (10) is identical; diastereoisomerism is given by the exchange of the substituents of the central chelate ring with respect to the conformations of the five-membered chelate rings. This confirms, that for five-membered diamine-chelate rings an equatorial position of methyl substituents is more important than chelate ring conformation. Examples of five-membered chelate rings with envelope conformation in complexes with open-chain tetramine ligands are known so far only for two cobalt(III) complexes with substituted triethylenetetramine ligands [3] [12].

The fact that the hydrogenation of the unsaturated complex in absence of ethylenediamine gives only one of the two diastereoisomeric complexes suggest that the reaction is stereospecific in a similar manner as described for macrocyclic nickel(II) complexes [7]. When the absolute configuration of the starting material is known by the defined structure of propylenediamine used in the synthesis, a proposition can be made for the absolute configuration of the product on the base of reaction mechanism. Assuming that the hydrogen molecule approaches from the side opposite to the axial methyl group, hydrogenation of the square planar R,R-complex yields only the product containing the ligand with R,S,R-configuration (Fig. 8). For the
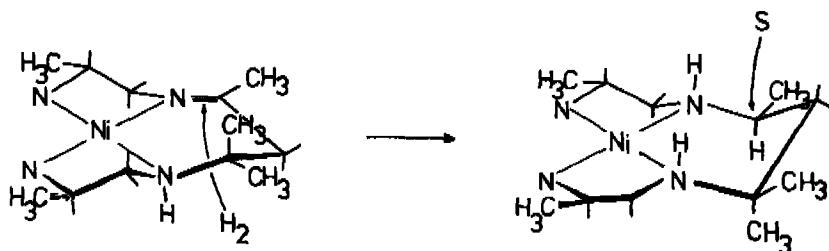

Fig. 8. *Stereochemistry of hydrogenation of planar* $[Ni(\mathrm{R},\mathrm{R}\text{-}C_{18}H_{28}N_4)]^{2+}$

octahedral complex four possibilities with cis-β-topography may exist, two with Λ- and two with Δ-configuration[3]). The pairs 11a/11b and 12a/12b in Fig. 9 are conformational isomers, the difference lies essentially in the orientation of the axial methyl group (circled in Fig. 9) in the central chelate ring. In 12a and 11b this methyl group is found near the polar chelate ring of the tetradentate ligand, whereas it points to the chelate ring of ethylenediamine in 11a and 12b. Investigation of molecular models shows, that the side opposite to this axial methyl group is clearly more favorable for the attack of a hydrogen molecule. From Fig. 9 it is seen that the diastereoisomeric forms 11a and 12a yields the complex with the ligand in R,S,R-configuration, which is the only product obtained by the hydrogenation of the planar complex.

The R,R,R-product must be formed by hydrogenation of 11b or 12b respectively. By analogy with the CD.-spectra of $[Ni(R,R\text{-}C_{18}H_{28}N_4)(R\text{-}pn)](ClO_4)_2$ and $[Ni(R\text{-}pn)_3](ClO_4)_2$ in acetonitrile it has been concluded that the former complex exhibits Λ-configuration [8], so that it may be proposed, that $[Ni(R,R,R\text{-}C_{12}H_{30}N_4)]^{2+}$

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[3]) The absolute configuration about the central metal ion is described as Λ and Δ according to [13] and is inversed with respect to [8].
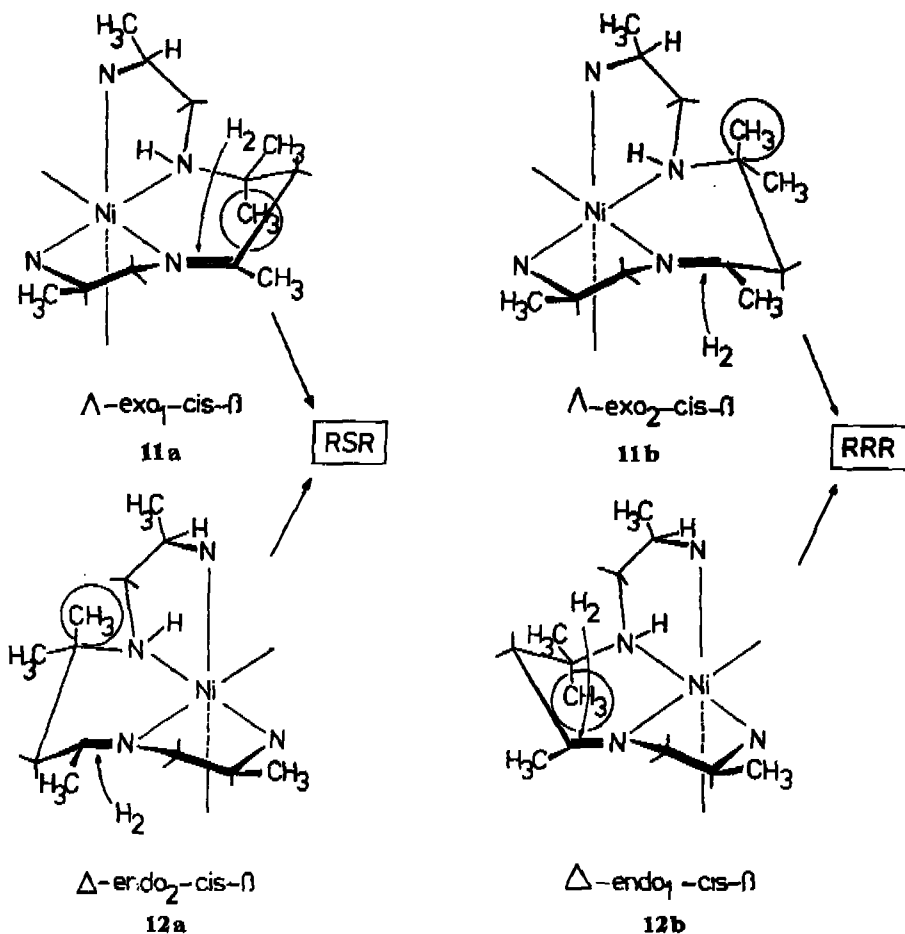
Fig. 9. *Stereochemistry of hydrogenation of the possible isomers of octahedral* $[Ni(R, R\text{-}C_{12}H_{28}N_4)\,(en)]^{2+}$ (ethylenediamine not indicated in the figures)

is obtained by hydrogenation of $[Ni(R, R\text{-}C_{12}H_{28}N_4)(en)]^{2+}$ in the $\varLambda\text{-}exo_2\text{-}cis\text{-}\beta$ configuration.

The attribution of absolute configuration to the two diastereomeric complexes is further confirmed by the specific rotation of the free tetramine ligands. The new asymmetric carbon atom obtained by hydrogenation of the C=N-bond carries four substituents very similar to those of propylenediamine, so that the contribution of this center to optical rotation should be of the same sign as that of propylenediamine with the same chirality. In the ligand with R, S, R-configuration the contribution of the S-center should be of opposite sign with respect to the contribution of the two R-propylenediamine units, whereas in the R, R, R-compound the contributions should be additive and give a negative rotation of a distinct higher value. This is confirmed by experimental data.

Clearly all the propositions of absolute configuration should be confirmed by X-ray structural analysis. Such a determination has been accomplished for $[Ni(R, S, R\text{-}C_{12}H_{30}N_4)](ClO_4)_2$ and will be published elsewhere [14].

The results given in this work show, that coordination compounds with 'frozen' ligand conformation may serve as examples to illustrate the *Auwers-Skita* rule concerning the stereochemistry of heterogeneous catalytic hydrogenation [15].

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90. Considerations on the Interpretation of Mass Spectra via Learning Machines

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(16. I. 75)

Summary. The application of learning machine techniques to the interpretation of mass spectra is investigated. An attempt to improve the characteristic ratio of the number of training points to the number of adjustable parameters is made by the use of reduced spectra. The ensuing results are corrected for the unequal representation of the different substances in the data bank. Reasonable performance is obtained for spectra of simple (monofunctional) substances, but predictive abilities are poor for more complicated substances.

Introduction. – The automated interpretation of mass spectra has been attempted by a variety of methods including library matching [1], artificial intelligence [2], nearest neighbour techniques [3] and learning machines [4]. The association of the first two methods has also been advanced in [5] and a review of the latter two methods, as well as some related techniques appears in [6].

Library matching requires a large bank of spectra if there is to be a reasonable probability of correct structure elucidation. Substantial memory requirements and access time are disadvantages here.

Computer times remain an important factor with artificial intelligence methods and, as with library matching, moderate size computers are necessary. Nearest neigh-