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Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 17 (2006) 2358–2365

Interaction of amines with rhodium(II) tetracarboxylates in solution: formation of nitrogenous stereogenic center

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Received 2 August 2006; accepted 1 September 2006
Available online 26 September 2006

Abstract—The ^{1}H, ^{13}C, and ^{15}N NMR spectra of amines: *N*,*N*-dimethylisopropylamine, *N*-ethyl-*N*-methylbenzylamine, *N*,*N*-dimethyl-1-phenylethylamine and *N*-methyl-1-phenylethylamine in the presence of dirhodium(II) tetratrifluoroacetylate and a dirhodium(II) Mosher's acid derivative were measured in $CDCl_3$ as the solvent. Dirhodium(II) salts with amines form 1:1- and 1:2-adducts, respectively, depending on the amine and dirhodium salt molar ratio. The formation of the Rh–N bond slows down the nitrogen atom inversion process and causes either non-equivalency of the two methyl groups in $N(CH_3)_2$ or the formation of a nitrogenous stereogenic center in the molecule having an –NR′R″ group. The latter causes the formation of additional diastereoisomers in solution. Application of NMR spectroscopy at low temperature (253 K) allows us to observe separately the signals of all compounds in solution, despite ligand chemical exchange between species.

1. Introduction

Dirhodium(II) tetracarboxylates **1**–**3** are known to form complexes with one or two 'axially' bonded organic ligands[1] (Fig. 1). Aside from numerous applications in organic synthesis, the complexes of dirhodium(II) tetracarboxylates formed in situ in solution are applied as the auxiliary reagents in spectroscopy. The enantiomerically pure salt of Mosher's acid, $Rh_2[(CF_3)(OCH_3)(C_6H_5)CO_2]_4$ **3**, has been used as a chemical shift and chiral recognition reagent to determine the enantiomeric excess[2] and absolute configuration[2,3] of organic compounds by nuclear magnetic resonance (NMR) spectroscopy. Rhodium(II) tetraacetate **1** and tetratrifluoroacetate **2** have been applied as auxiliary chromophores to determine the absolute configuration by circular dichroism (CD) spectroscopy.[4]

In contrast to the solid phase, the composition of solutions containing rhodium(II) tetraacylate and the ligand is not well defined. Such a solution usually contains the equilibrium mixture of various complexes having different stoichiometries. The shape of the NMR spectrum depends on the ligand exchange rate. Fast ligand exchange (in the NMR time scale) averages the signal positions of all species. Consequently, only one set of averaged signals is visible on the spectrum; only titration NMR experiments and the analysis of signal chemical shift changes provide information on mixture composition. In contrast, slow ligand exchange allows us to observe the signals of all species existing in the solution.[5]

Our previous work comprises of the ^{1}H, ^{13}C, and ^{15}N NMR investigation of rhodium(II) complexes formed in situ in $CDCl_3$ solution with ligands having a nitrogen atom. The experiments covered mesoionic oxatriazoles, pyridine, picolines,[6] and amines.[7] This methodology was based on NMR titration experiments at a decreased temperature. In some cases, the reduced temperature allowed access to the slow exchange conditions and observing the signals of two adducts in the solution.

We decided to investigate the adducts of amines **4**, **5**, **7**, and **8** with rhodium(II) tetraacylates.[7] Amines generally form 1:1- and 1:2-adducts with $Rh_2(TFA)_4$ **2**. However, in case of racemic *N*-methyl-1-phenylethylamine **8** the signals of two 1:1-adducts and at least the signals of three 1:2-adducts have been observed in the NMR spectra. The chiral tertiary amines such as *N*,*N*-dimethyl-1-phenylethylamine **7** and *N*,*N*-dimethyl-*sec*-butylamine **4** form only one 1:1- and one 1:2-adduct with $Rh_2(TFA)_4$, but both $N(CH_3)_2$ methyl groups in these adducts are non-equivalent according to NMR. All the aforementioned phenomena can be explained tentatively by assuming either hindered rotation

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doi:10.1016/j.tetasy.2006.09.001

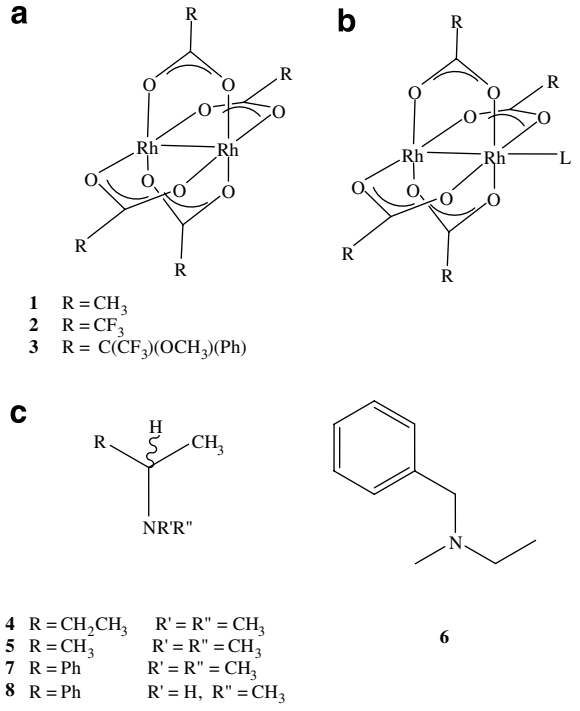

Figure 1. The compounds discussed in the present work: (a) dirhodium(II) dimeric tetraacylates: acetylate **1** ($Rh_2(OAc)_4$), trifluoroacetylate **2** ($Rh_2(TFA)_4$), and optically pure Mosher's acid derivative (4*R*)-**3** or (4*S*)-**3**. (b) An example of 1:1 'axial' adduct of dirhodium salt and organic ligand L; (c) amines used as the ligands; racemic and enantiomerically pure (*S*) amines **7** and **8** have been used.

around C–C or C–N bonds in the complex, or slow nitrogen inversion in the complex and formation of a nitrogenous stereogenic center. In contrast, no such phenomena have been observed in the case of rhodium(II) tetracetate adducts. Both amines **4** and **8** form with **1** only one 1:1-adduct; non-equivalency of the two $N(CH_3)_2$ methyl groups was not observed.

In principle, the amines of NRR′R″ type are chiral. However, these amines in solution form a racemic mixture, due to fast nitrogen inversion process. Only particular cyclic amines can exist as enantiomerically pure stable isomers. A slow down of structure inversion by complexation is expected to cause the phenomena associated with nitrogenous chirality. The application of NMR spectroscopy to gain insight into nitrogenous chirality in rhodium(II) tetracarboxylate-amine complexes is the main purpose of the present work.

2. Results and discussion

Amines with various structural properties have been used as model ligands: *N*,*N*-dimethylisopropylamine **5** without any stereogenic centers, *N*-ethyl-*N*-methylbenzylamine **6** with only a potential nitrogenous chiral atom; *N*,*N*-dimethyl-1-phenylethylamine **7** with stereogenic carbon atom and *N*-methyl-1-phenylethylamine **8** with both a carbon and potential nitrogenous stereogenic centers (Fig. 1). All combinations of the above amines with the two dirhodium salts, **2** and **3**, have been investigated as model systems. The NMR spectra have been interpreted by taking into account two factors: (i) enantiomers cannot be distinguished in achiral medium by a standard NMR experiment, whereas diastereomers may be recognized, (ii) two R groups such as H or CH_3 in a $–CR_2–$ unit are chemically non-equivalent in the vicinity of the stereogenic center in a molecule, so these groups produce two signals in the NMR spectra.[8] The application of decreased temperature to NMR experiments allowed to achieve slow exchange conditions. As a result, the signals of all species have been observed in the spectra. NMR titration experiments at low temperature have confirmed explicitly the presence of two adducts (1:1 and 1:2) for each dirhodium salt–amine system investigated.

Two parameters conveniently characterize adduct formation: the diastereomeric dispersion $\Delta\nu$ (Hz), and the complexation shift $\Delta\delta$ (ppm).[2] The $\Delta\nu$ is simply defined as the chemical shift difference between corresponding diastereomers, and obviously concerns only chiral adducts. The $\Delta\delta$ is defined as the chemical shift difference of the corresponding atoms in bonded and free (uncomplexed) ligand. The complexation shift for various adducts of amines with rhodium acetate **1** and trifluoroacetate **2** has been collected and discussed elsewhere.[7] The $\Delta\delta(^1H)$ and $\Delta\delta(^{13}C)$ parameters observed in the present work do not differ significantly from those previously observed. Generally, $\Delta\delta(^1H)$ values are positive and do not exceed 2 ppm. The greatest value was observed for a ^1H nucleus close to the binding site, for example, the CH hydrogen in **7** or **8**. In contrast, $\Delta\delta(^{13}C)$ is either negative or positive, and reaches an absolute value of a few ppm (Table 1).

The appearance of the NMR spectra depends on the individual combination of the amine and dirhodium salt.

2.1. Adducts with *N*,*N*-dimethylisopropylamine 5

The amine does not provide any chirality and forms only an achiral 1:1- and 1:2-complex with $Rh_2(TFA)_4$ **2**. The methyl groups of each adduct provide two ^1H signals: the singlet arising from the $N(CH_3)_2$ and the doublet of the $CH(CH_3)_2$. The corresponding ^{13}C signals appear as singlets.[7] In contrast, adducts of **5** with (4*R*)-**3** are chiral due to chiral dirhodium salt (Table 1). By definition, each adduct (1:1 or 1:2) exists as a single enantiomer (4*R*). The adduct chirality shows up as the chemical non-equivalence of two methyl group in each $C(CH_3)_2$ and $N(CH_3)_2$ pair. Hence, the 1:1-adduct produces four signals arising from methyl groups: two singlets, at 2.90 and 2.89 ppm, provided by the $N(CH_3)_2$, and two partially superposed doublets at 1.47 ppm from the $CH(CH_3)_2$ unit. The signals of the 1:2-adduct appear in a similar manner. Two non-equivalent groups attached to one nitrogen atom are an important feature of these adducts. Such an effect proves that the nitrogen inversion process is slow in NMR time scale. A comparison of both adducts (i.e., with **2** and **3**) also shows that differentiation of the methyl groups in the complex is caused by the stereogenic center in the molecule, and not by hindered rotation around either the C–C or N–C bonds.

Table 1. ^{1}H, ^{13}C (in parenthesis), and ^{15}N NMR chemical shifts for some amines and their adducts with dirhodium(II) tetraacylates

Atom	Ligand 303 K	1:1-Adduct 303 K	1:2-Adduct 273 K
5 *and* (4*R*)-**3** *adducts*			
CH	2.59m (54.7)	3.65m, br (n.o.)	3.38m (60.4)
CCH_3	1.01d (18.5)	1.46d, 1.48d (18.3)	1.29d, 1.32d (18.7)
NCH_3	2.23s (41.1)	2.89s, 2.90s (45.1)	2.76s, 2.79s (45.0)
OCH_3	3.18s (54.8)	3.08s	3.10s
	303 K	253 K [263 K]	253 K
6 *and* (4*R*)-**3** [**6** *and* **2**] *adducts*			
$PhCH_2$	3.50s (61.9)	4.52t,[a] 4.91d (61.0) [4.31d, 4.74d (62.3)]	4.41m, 4.77m (59.6, 61.1) [4.41d, 4.81d (61.4)]
NCH_2CH_3	1.10t (12.4)	1.41br (11.5) [1.24br (11.5)]	1.22m (12.0) [1.29t (11.6)]
NCH_2CH_3	2.46q (51.2)	3.31br (52.4) [3.15m, 3.27m (52.8)]	3.19br (51.7) [3.27m, 3.35m (52.0)]
NCH_3	2.21s (41.6)	2.85s, 2.88s (42.8) [2.75s (43.3)]	2.686s,[b] 2.706s[b] (42.2); 2.764s,[b] 2.777s[b] (43.4) [2.86s (42.8)]
NCH_3	−340.5	−358.9	−352.7, −353.0
OCH_3	3.18s (54.8)	3.03s (54.6)	3.043s,[c] 3.055s,[c] 3.071s[c] (54.0)
	303 K	253 K	253 K
7 *and* (4*R*)-**3** *adducts*			
CH	3.25 (65.9)	4.90q* (68.0), 4.99q# (67.9)	4.73[d] (67.1), 4.91[e] (67.0)
$CHCH_3$	1.38 (20.1)	1.767d,* 1.804d# (18.6)	1.551d, 1.558d* (18.8), 1.686d,# 1.718d (19.0)
NCH_3	2.20 (43.1)	2.660s,# 2.673* (49.6) 2.976s* 3.005s# (39.8)	2.575s,# 2.604s,[f] 2.632s* (48.7) 2.865s, 2.875s,# 2.892s,* 2.906s (39.2)
OCH_3		3.038s,# 3.044*s (54.8)	3.089s,* 3.105s, 3.122s# (54.7)
	303 K	253 K	253 K
(*S*)-**8** *and* (4*R*)-**3** [(*S*)-**8** *and* (4*S*)-**3**] *adducts*			
CH	3.64q (60.2)	4.59m (63.4), 5.09q (58.8) [4.67m (63.7), 5.17q (58.8)]	4.54m (62.9), 4.99m (58.6) [4.64m (62.8), 5.11m (58.5)]
$CHCH_3$	1.36d (23.8)	1.77d (23.1), 1.88d (13.2) [1.74d (23.2), 1.85d (13.2)]	1.68m (23.2), 1.80d (14.9) [1.58m (23.7), 1.76m (14.9)]
$NHCH_3$	2.31s (34.5)	2.67d (37.6), 2.92d (29.8) [2.68d (37.8), 2.92d (29.8)]	2.63d, 2.65d (37.1), 2.92t (30.3) [2.69m (37.5), 2.87m (30.3)]
$NHCH_3$	1.82br	5.17m, 5.30q [5.13m, 5.35m]	4.73m, 4.84m [4.71m, 4.92m]
OCH_3		3.03s, 3.05s [3.06s, 3.08s]	3.03s 3.09m

Asterisk (*) denotes the signals of the (*S*,4*R*) or (*S*,4*R*,*S*) isomer; the symbol # denotes the signals of the (*R*,4*R*) or (*R*,4*R*,*R*) isomer.
The signals of the main component of the mixture are underlined.
Abbreviations used in the table: n.o.—signal not observed, s—singlet, d—doublet, t—triplet, q—quartet, m—multiplet, br—broad signal. Although the accuracy of ^{1}H NMR chemical shifts does not exceed ca. 0.01 ppm, some values are given with three digits next to point in order to demonstrate the signal dispersion. The signals of Ph groups are omitted as they do not provide important structural information.
[a] Superposition of two doublets ($\Delta\nu = 13.5$ Hz).
[b] Superposition of four singlets; ^{1}H NMR chemical shifts and relative integral intensities (3:2:3:2) have been obtained from the deconvolution procedure.
[c] Broad triplet; ^{1}H NMR chemical shifts and relative integral intensities (35:50:15) have been obtained from deconvolution procedure.
[d] Superposition of two multiplets ($\Delta\nu = 16$ Hz); high frequency component has been identified as the signal of the (*S*,4*R*,*S*) isomer.
[e] Superposition of two multiplets ($\Delta\nu = 16$ Hz); low frequency component has been identified as the signal of the (*R*,4*R*,*R*) isomer.
[f] Superposition of two singlets.

2.2. Adducts with *N*-ethyl-*N*-methylbenzylamine 6

Only a potential nitrogenous stereogenic center is provided by **6**. The free (uncomplexed) ligand does not reveal any symptoms of chirality due to fast nitrogen inversion. However, assuming the inversion in the complex is prevented, **2** and **6** are expected to form two 1:1 (*R*) and (*S*) and three 1:2-adducts, (*R*,*R*), (*R*,*S*) and (*S*,*S*). The molecule chirality can be conveniently observed using the ^{1}H NMR signal of the benzyl CH_2 group: chemically non-equivalent two hydrogen atoms indicate the presence of a stereogenic center. Two enantiomeric 1:1-adducts of **6** with **2** are not differentiated by NMR, but the signal of the methylene group shows up as the AX quartet proving the presence of such a center (Fig. 2). The *R*,*R* (*S*,*S*) enantiomeric 1:2-adducts are expected to differ from the 1:2 *R*,*S* isomer, that is the

signals of three different molecules of the ligand should appear in NMR spectra. In fact, only one AX doublet has been found in the ^{1}H NMR spectrum. Such a result can be explained by small diastereomeric dispersion $\Delta\nu$ of signals, less than ^{1}H signal half width (ca. 6 Hz). In other words, one ligand molecule in the 1:2-adduct does not recognize the configuration of the second ligand.

Assuming that the nitrogen inversion slows down, the adducts of **6** with chiral salt (4*R*)-**3** are expected to be a combination of two chiral units, enantiomerically pure (4*R*) dirhodium salt and chiral amine molecule (*R* or *S*). As consequence, two 1:1- and three 1:2-adducts are expected in the solution: (*R*,4*R*), (*S*,4*R*), (*S*,4*R*,*S*), (*R*,4*R*,*R*) and (*R*,4*R*,*S*). All adducts of (4*R*)-**3** with **6** should, in principle, be differentiated by NMR.

The ^{1}H NMR spectrum of the 1:1-adducts contains two overlapped AX quartets of the benzyl CH_2 group (Fig. 3): a doublet, which consists of two overlapped signals ($\Delta\nu \approx 0$ Hz) and a pseudotriplet, composed from two doublets ($\Delta\nu = 13.5$ Hz). The corresponding signals of the 1:2-adduct show up as two multiplets. These multiplets have been analyzed using 2D *J*-resolved technique; the intersection of the 2D spectrum along the chemical shift axis (Fig. 3) has clearly demonstrated the presence of four signals in each multiplet. The distance between the individual ^{1}H signals in the multiplet varies from 3 to 14 Hz. Each multiplet correlates with only two ^{13}C signals, at 59.6 and 61.1 ppm. Since four ^{13}C signals are expected, the ^{13}C data imply that one diastereomeric dispersion $\Delta\nu(^{13}C)$ is equal

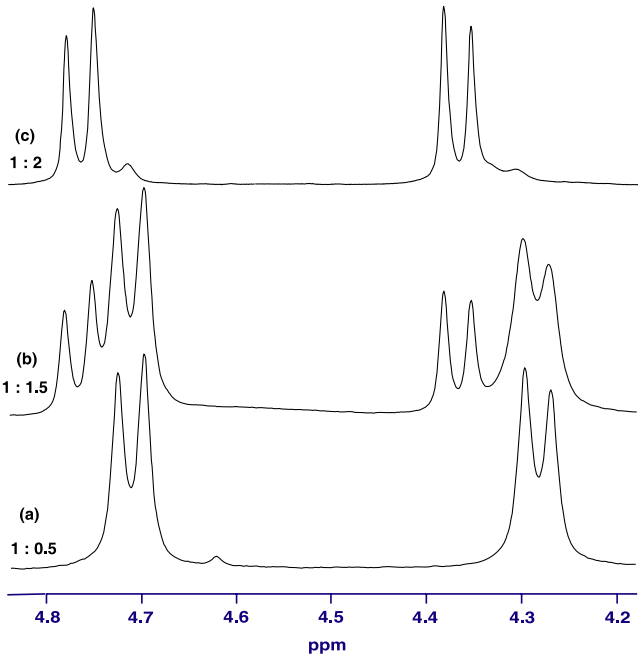

Figure 2. ^{1}H NMR spectra (263 K) of $Rh_2(TFA)_4$ **2** and *N*-ethyl-*N*-methylbenzylamine **6** mixtures in $CDCl_3$ (titration experiment); the CH_2 signals of benzyl group are shown. (a) The 1:0.5 mixture of **2** and **6**; the solution contains only 1:1-adducts; (b) the 1:1.5 mixture of **2** and **6**; the signals of both adducts (1:1 and 1:2) are visible; (c) the 1:2 mixture; only the signals of 1:2-adducts are present.

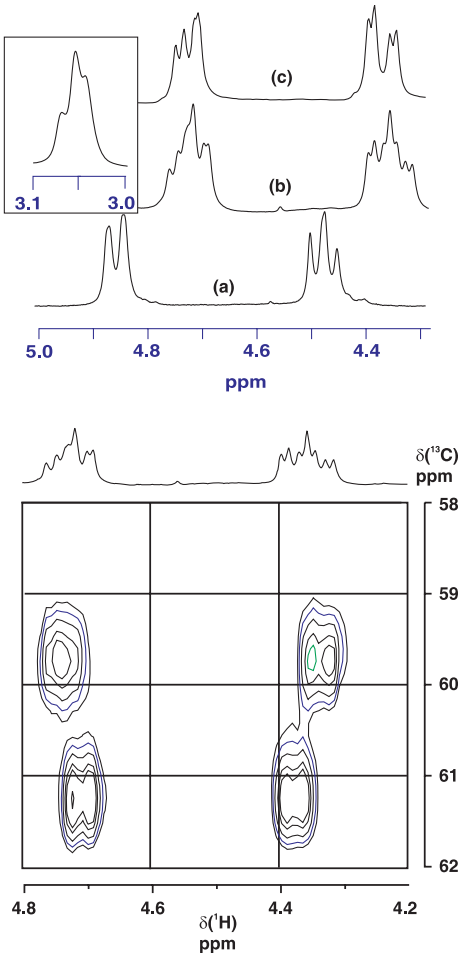

Figure 3. Top: ^{1}H NMR spectra (253 K) of enantiomerically pure dirhodium salt (4*R*)-**3** and *N*-ethyl-*N*-methylbenzylamine **6** mixtures (titration experiment); the CH_2 signals of benzyl group are shown. (a) The 1:0.5 mixture; only the signals of the 1:1-adduct are visible; (b) the 1:2 mixture; the signals of the 1:2-adduct are present; (c) intersection of 2D *J*-resolved spectrum of the 1:2-adduct. Inset: the OCH_3 signal of Mosher's acid residue of the 1:2-adduct. Bottom: Part of the ^{13}C, ^{1}H-HSQC correlation spectrum of the 1:2-adduct. See explanations in the text.

to ca. 190 Hz and the second is close to 0 Hz (or, strictly speaking, less than ^{13}C signal resolution of 2D spectrum). Similar relationships have been observed for the NCH_3 signals (Table 1).

The number of isomeric 1:2-adducts detected by NMR imply the mutual recognition of two ligands via a Rh–Rh chain: two amine molecules having the same configuration differ by NMR depending on the configuration of the second ligand molecule, at the opposite side of the dirhodium unit. As a consequence, three 1:2-adducts provide the signals of four ligand molecules (in contrast to the adducts of $Rh_2(TFA)_4$ **2**; see above).

The OCH_3 signal of the Mosher's acid residue appears as a broad triplet (Fig. 3). The deconvolution procedure has resolved the triplet into three signals with relative integral intensities of 35:50:15 (Table 1). Despite the approximated results of the broad signal deconvolution, the NMR spec-

tra clearly shows that the composition of 1:2 adduct mixture does not fit simple statistical ligand distribution (25:50:25), that is some preference in diastereomer formation occur.

The $\Delta\delta(^{15}N)$ complexation shift for the 1:1- and 1:2-adduct of (4*R*)-**3** and **6** are −18.4 and −12.4 ppm, respectively. These values are in agreement with those observed previously for amines.[6] Similarly to $\Delta\nu(^{13}C)$ discussed above, one value of diastereomeric dispersion is ca. 15 Hz, whereas the second one is close to 0 Hz. Considering the large range of ^{15}N chemical shifts observed for organic compounds, the ^{15}N NMR technique is relatively non-sensitive in this case.

2.3. Adducts with *N*,*N*-dimethyl-1-phenylethylamine 7

This ligand only provides a carbon stereogenic center. The adducts of $Rh_2(OAc)_4$ with *N*,*N*-dimethyl-1-phenylethylamine **7** have been investigated and discussed in the previous work.[6] The racemic amine **7** forms with **2** to give either a 1:1- or 1:2-adduct, depending on the reagent's molar ratio. The NMR spectrum of each adduct contains one set of signals, so the 1:2-adducts (*R*,*S*), (*R*,*R*) and (*S*,*S*) are not differentiated by the NMR. Two $N(CH_3)_2$ methyl groups giving two signals in the NMR spectrum are chemically non-equivalent, and prove the restricted inversion of the nitrogen atom.[6]

The ^1H NMR spectrum of the particular *N*,*N*-dimethyl-1-phenylethylamine molecule in a complex is expected to consist of four signals (omitting Ph group multiplets): the quartet of the CH group, two singlets of the two non-equivalent $N(CH_3)_2$ methyl groups and the doublet arising from the CCH_3 methyl group. In fact, the spectrum of **7** and (4*R*)-**3** in a 1:1 mixture shows up as the superposition of the two sub-spectra arising from (*R*,4*R*) and (*S*,4*R*) isomers. The spectrum of the 1:2 mixture consists of four sub-spectra produced by four non-equivalent ligand molecules from (*R*,4*R*,*R*), (*R*,4*R*,*S*) and (*R*,4*R*,*R*) diastereoisomers.

The signals of all the complexes have been identified with the use of enantiomerically pure reagents: (*S*)-*N*,*N*-dimethyl-1-phenylethylamine (*S*)-**7**, dirhodium salts (4*R*)-**3** and (4*S*)-**3**. Substrate (4*R*)-**3** forms with (*S*)-**7** two adducts (*S*,4*R*) and (*S*,4*R*,*S*); salt (4*S*)-**3** with (*S*)-**7** produces (*S*,4*S*) and (*S*,4*S*,*S*) complexes. According to NMR spectroscopy, the last two adducts are identical to (*R*,4*R*) and (*R*,4*R*,*R*) species. The signals of (*R*,4*R*,*S*) isomer have been identified by the simple NMR spectra comparison. Signals assignment has allowed calculating accurate diastereomeric dispersions $\Delta\nu$. For example, the $\Delta\nu(^1H)$ values produced by (*R*,4*R*) and (*S*,4*R*) diastereoisomers amount ca. 45 Hz for CH, 6.5 and 14.5 Hz for two signals of $N(CH_3)_2$, 18.5 Hz for CCH_3 and 3 Hz for OCH_3. The corresponding values of (*R*,4*R*,*R*) and (*S*,4*R*,*S*) isomers are 74, 28.5, 8.5, 64, and 16.5 Hz, respectively. There is no method for unambiguous ligand identification within the (*R*,4*R*,*S*) complex, that is, identification of which signals are produced by the (*R*) ligand, and which are produced by (*S*). However, one can calculate $\Delta\nu$ arising from both ligands within the complex: the $\Delta\nu(^1H)$ values are equal to 106 for CH, 20.5 and 0 for $N(CH_3)_2$ and 83.5 Hz for CCH_3 ($\Delta\nu$ for OCH_3 is zero by definition). It is interesting to note that $\Delta\nu(^1H)$ values in this case are noticeably greater than those observed for **6** having only a nitrogenous stereogenic center.

2.4. Adducts with *N*-methyl-1-phenylethylamine 8

NMR investigations on adducts of racemic **8** with $Rh_2(TFA)_4$ **2** have previously been described.[6] It has been found that **8** with **2** forms in $CDCl_3$ two 1:1-adducts differentiated by ^1H and ^{13}C NMR spectroscopies. Since enantiomers are not recognizable by NMR, such a result has been explained by the presence of two stereogenic centers in the ligand molecule, and by the formation of two pairs of the 1:1-adducts: (*R*,*R*), (*S*,*S*) and (*R*,*S*), (*S*,*R*). It has been also proven that the mixture of 1:2-adducts contains at least four non-equivalent ligand molecules.[6]

Assuming two stereogenic centers are in **8** and considering the adduct structure, one can expect the formation of 10 different 1:2 stereoisomers of $Rh_2(TFA)_4$ adducts. According to the standard NMR experiment, some of them are identical, and only six species are potentially detectable. In fact, only two isomers were seen in the ^1H NMR spectrum, and it became an aim to determine which two. As part of the work herein, ^1H NMR measurements on the adduct of (*S*)-*N*-methyl-1-phenylethylamine (*S*)-**8** with $Rh_2(TFA)_4$ **2** were carried out. The experiments revealed that the spectrum of adducts formed from both racemic and enantiomerically pure **8** were practically identical. Two 1:2-adducts of (*S*)-**4** differ in the configuration of the nitrogen atoms only, so the NMR technique just needed to recognize the nitrogenous chirality in the $Rh_2(TFA)_4$ adduct. Diastereomeric dispersion arising from the carbon stereogenic atom was non-detectable in the experimental conditions.

Application of enantiomerically pure dirhodium salt (4*R*)-**3** instead of achiral $Rh_2(TFA)_4$ **2** does not change the number of isomers, but increases the number of species recognizable by NMR. The 1:1-adduct was expected to consist of four isomers: (*R*,*S*,4*R*), (*R*,*R*,4*R*), (*S*,*R*,4*R*) and (*S*,*S*,4*R*). NMR differentiates all these species as diastereoisomers; so the corresponding ^1H NMR spectrum appeared as the superposition of four sub-spectra. The signals were identified with the use of enantiomerically pure (*S*)-**8** amine. The 1:0.5 molar mixture of (4*R*)-**3** and (*S*)-**8** has provided two set of signals assigned to (*S*,*S*,4*R*) and (*S*,*R*,4*R*) isomers (Fig. 4). Each set of signals includes two quartets (or multiplets) arising from NH and CH groups, two doublets from NCH_3 and two doublets from CCH_3 methyl group. The OCH_3 signals of Mosher's acid residue show up as three single lines: one produced by uncomplexed dirhodium salt, and two singlets attributed to two adducts (the signals of Ph groups do not provide useful information) The signals of the 1:1-adducts deriving from (*R*)-**8** amine were identified using (*S*)-**8** amine and (4*S*)-**3** dirhodium salt. According to the NMR spectroscopy, (*S*,*R*,4*S*) and (*S*,*S*,4*S*) complexes are identical to (*R*,*S*,4*R*) and (*R*,*R*,4*R*) adducts.

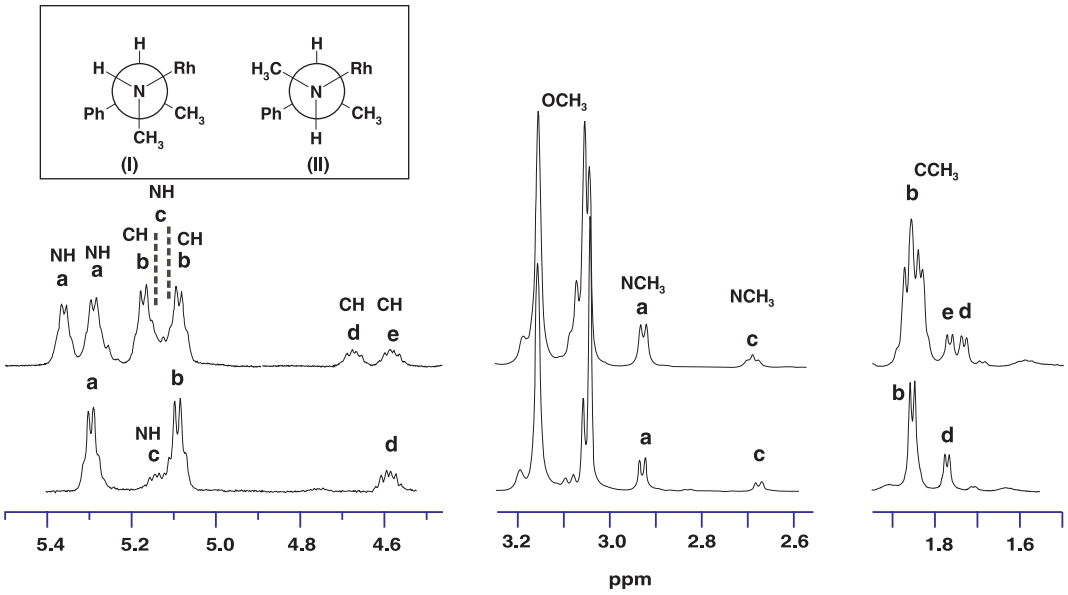

Figure 4. ^{1}H NMR spectra (253 K) of the 1:1-adducts of (4*R*)-**3** with racemic (upper raw) and optically pure (*S*)-*N*-methyl-1-phenylethylamine **8** (bottom row). The letters denote COSY correlations. Vertical scales of each part of the spectra are adjusted arbitrarily; the signals of Ph group are omitted. Inset shows possible ligand conformations in the complex; right Newman's structures (II) have been assigned to the minor component. See explanations in the text.

The molar ratio of the major to minor isomer in the mixture is ca. 2.5:1. The isomers have been tentatively identified on the basis of NH and CH signal shapes. Both signals in the major component show up as broad quartets, due to couplings with CH_3 groups, ^{3}J(NH,NCH_3) and ^{3}J(CH,CCH_3). In contrast, the corresponding signals in the minor component appear as multiplets, due to additional coupling ^{3}J(NH,CH), of 6 Hz. Greater ^{3}J(NH,CH) coupling constants are expected for the antiperiplanar position of both hydrogen atoms, in accordance with Karplus's law. Assuming the antiperiplanar position of the two bulky groups in the complex (Rh and Ph), the minor isomers have been identified as (*S*,*S*) or (*R*,*R*) compounds, whereas the major components have been identified as the compound having two stereogenic centers with an opposite configuration. On the other hand, rough analysis does not take into consideration the mutual influence of all the rotamers with Mosher's acid residues.

The experiment using enantiomerically pure (*S*)-**8** allows us to calculate the diastereomeric dispersions arising from the nitrogen atom configuration, for example, the $\Delta\nu(^{1}H)$ values for (*S*,*R*,4*R*) and (*S*,*S*,4*R*) diastereoisomers amount to 250 Hz for CH, 55 Hz for CCH_3, 125 Hz for NCH_3, 65 Hz for the NH hydrogen, and 10 Hz for OCH_3.

The 1:2 mixture of racemic **8** with (4*R*)-**3** includes 10 species, having in total 16 ligand molecules differentiated by the NMR. The ^{1}H spectrum of such a mixture having unresolved multiplets is difficult for analysis. In contrast, the mixture of (*S*)-**8** and (4*R*)-**3** containing only three isomers and having four different ligand molecules, has allowed some signal identification (Table 1). NMR data on next three isomers have been extracted using (*S*)-**8** and (4*S*)-**3** combinations.

2.5. Adducts of $Rh_2(OAc)_4$ 1 with 6, 7, and 8

The NMR studies on the interaction of various amines with dirhodium tetraacetate **1** have been presented elsewhere.[6] Generally, the adducts of **1** did not exhibit any effects related to slow nitrogen inversion, such as the non-equivalent two $N(CH_3)_2$ groups in **7**, or the presence of an additional nitrogenous $NH(CH_3)$ stereogenic center in **8**. Low temperature (253 K) NMR measurements of *N*-ethyl-*N*-methylbenzylamine **6** and **1** mixture yield the spectra having only broad signals. Such effects can be explained by fast ligand exchange in the NMR time scale, and ligand racemization over the course of it. The phenomena related to hindered nitrogen inversion did not appear in the NMR spectra in this case.

2.6. VIS experiments

Electronic absorption spectroscopy in the visible light (VIS) has previously been used for the examination of $Rh_2(OAc)_4$ **1** and $Rh_2(TFA)_4$ **2** adducts with some amines. The $CDCl_3$ solution of the 1:1-adduct is blue, whereas the 1:2-adduct solution adopts red color. As a result, VIS spectroscopy has turned out to be a good means of ligation monitoring.[6] Over the course of the present work, VIS titration experiments on the adducts of salt **3** with **5** and **6** have been carried out. The spectrum of the 1:1-adduct of **5** contained a signal at 629 nm (ε 482); whereas the signal of the 1:2-adduct appeared at 552 nm (ε 313). The corresponding signals of **6** appeared at 638 (ε 448) and 549 nm (ε 329).

3. Conclusions

The results of the NMR experiments lead to the following conclusions:

(i) In $CDCl_3$ solution, dirhodium salts **2** and **3** form with amines **5**–**8** two kinds of species, the 1:1- and 1:2-adducts, depending on the reagents molar ratio. NMR measurements at a decreased temperature allow us to observe the signals of both adducts.

(ii) The formation of the Rh–N bond slows down the nitrogen inversion process. Hindered inversion causes either non-equivalency of two $N(CH_3)_2$ methyl groups in a chiral complex, or the formation of nitrogenous stereogenic center in the case of amines having three different substituents (NRR′R″). The latter phenomenon causes the creation of the new optical isomers of certain adducts, or increases the adduct number. All diastereoisomers are, in principle, differentiated by standard NMR experiments. In particular, the mixture of stereoisomers can be analyzed by the 'dirhodium method'.[2]

(iii) An interesting point is the possibility of mutual recognition of two ligand molecules within the 1:2-adduct, that is do the NMR properties of two ligands having the same configuration differ depending on the second ligand configuration. In case of chiral salt **3**, two amine molecules have recognized each other; consequently, two adducts (*R*,4*R*,*R*) and (*R*,4*R*,*S*) have been differentiated by NMR. However, it is not the general feature; NMR does not differentiate the 1:2 diastereomeric adducts of achiral $Rh_2(TFA)_4$, for example, adducts of **2** with *N*-ethyl-*N*-methylbenzylamine **6**.

(iv) The aforementioned results point out the possibility of a complication arising from the application of the 'dirhodium method' to chiral compounds with a NRR′R″ group. As previously mentioned, whether the phenomena related to the hindered nitrogen inversion appear in NMR spectra or not, it depends on the ligand exchange rate and chemical shift differences between the species (here diastereomeric dispersion and complexation shift).[5] These phenomena, those not observed in NMR, are expected to be seen by techniques operating on a shorter time scale, such as electronic absorption spectroscopy. The 'hidden' nitrogenous stereogenic center can affect circular dichroism (CD) spectra. For example, the 1:1 mixture of (*S*)-*N*-methyl-1-phenylethylamine **8** with chiral dirhodium salt (4*R*)-**3** contains two diastereoisomers, (*S*,*S*,4*R*) and (*R*,*S*,4*R*), which are in thermodynamic equilibrium. The CD curve of such a mixture is expected to be a superposition of two curves. According to Boltzman's law, the molar ratio of both isomers should depend on the temperature. Consequently, the CD spectrum is expected to be temperature-dependent.

4. Experimental

Dirhodium(II) tetra-(*R*)- and tetra-(*S*)-α-methoxy-α-(trifluoromethyl)-phenylacetate dimer (4*R*)-**3** and (4*S*)-**3** have been prepared from dirhodium tetraacetate **1** and enantiomerically pure Mosher's acid (MTPA).[9] Tertiary *N*,*N*-dimethyl-1-phenylethyl **7** and (*S*)-*N*,*N*-dimethyl-1-phenylethylamine (*S*)-**7** have been obtained from the appropriate 1-phenylethylamine by the reaction with formic acid and formic aldehyde; the same procedure has been applied to the conversion of secondary *N*-ethylbenzylamine to tertiary *N*-ethyl-M-methyl-benzylamine **6**.[10] Secondary *N*-methyl-1-phenylethylamine **8** and (*S*)-*N*-methyl-1-phenylethylamine (*S*)-**8** have been obtained from suitable primary 1-phenylethylamine by the reaction with methyl chloroformate and by subsequent reduction with $LiAlH_4$.[11] All starting amines: racemic 1-phenylethylamine, (*S*)-1-phenylethylamine, *N*-ethylbenzylamine, (*R*) and (*S*) Mosher's acid (MTPA), rhodium(II) tetraacetate **1** and dirhodium(II) tetratrifluoroacetate are commercially available and have been purchased from Aldrich.

Amines were dried over KOH pellets and distilled. A weighed amount of amine (ca. 50 mg) was placed in the 1 cm^3 volumetric flask and dissolved in $CDCl_3$ (99.8% D atom, stabilized by Ag). A weighed amount of dirhodium salt (ca. 10 mg) was placed in the NMR tube and dissolved in 0.7 cm^3 of $CDCl_3$. A suitable volume of amine solution was added to dirhodium salt using a 25 μl syringe; the sample was then measured. All measurements of each amine-dirhodium salt combination were carried out using one NMR sample by the subsequent addition of amine solution. Typically, the solutions containing molar ratios of 1:0.5, 1:1, 1:1.5, 1:2, and 1:2.5 dirhodium salt to amine were used.

All NMR measurements were conducted on a Bruker DRX-500 spectrometer equipped with the XWIN NMR acquisition and processing software. Measurements were carried out using the 5 mm triple broadband inverse probe with *z*-gradient coil. The BVT 300 temperature unit was used for all variable temperature experiments. Temperatures were read directly from the instrument panel with no additional temperature correction.

^1H NMR spectra were gained with parameters acquisition time of 2.52 s, flip angle ca. 30°, relaxation delay 1 ms and spectral width ca. 13 ppm; 32–128 scans were acquired depending on the sample. Data points (32K) were used for data acquisition and processing, giving the spectral digital resolution of 0.2 Hz per point. The residual solvent peak was used as secondary reference, $\delta(^1H) = 7.26$ ppm with respect to TMS (0 ppm).

^{13}C NMR spectra of ligands were obtained with parameters acquisition time of 1 s, flip angle ca. 90°, relaxation delay 500 ms and spectral width 260 ppm; typically 64–200 scans were acquired depending on the sample. Data points (64K) were used for data acquisition and processing, giving the spectral digital resolution of 0.5 Hz per point. The signals were referred to $CDCl_3$ central signal, $\delta(^{13}C) = 77.0$ ppm with respect to TMS signal (0 ppm).

^1H,^1H COSY spectra were acquired using Bruker's 'cosygp' pulse program (homonuclear shift correlation using gradient pulse selection, magnitude mode), with parameters acquisition time of 0.13 s, relaxation delay 1 s,

spectral width 8 ppm and with 4 scans per experiment. A 1024×256 matrix, zero filled to 1024×1024 was used.

^{1}H *J*-resolved spectra were acquired using Bruker's 'jres' pulse program (magnitude mode), with parameters acquisition time of 0.26 s, relaxation delay 1.2 s, with 4 scans per experiment, and with sweep width 64 Hz (F_1) and 8 ppm (F_2 domain). A 2048×64 (2048×128) matrix was used, giving the spectral digital resolution 0.38 Hz (F_1) and ca.2 Hz (F_2 domain).

Due to low sample concentrations, ^{13}C chemical shifts of rhodium complexes were gained by means of inverse gradient ^{13}C,^{1}H correlation technique. ^{13}C,^{1}H HSQC ('invietgs' Bruker's pulse program: phase sensitive, E/A gradient selection with decoupling during acquisition) experiments were applied. Typically, a 512×2048 matrix, zero filled to 1024×2048 was used, with parameters acquisition time of 0.25 s, relaxation delay 1.2 s, and 8 scans per experiment. Spectral width of 160 ppm in the F_1 (^{13}C) domain and 8.3 ppm in the F_2 (^{1}H) domain were used giving spectral digital resolution of ca. 20 Hz per point (^{13}C) and 2 Hz per point (^{1}H), respectively. ^{13}C chemical shifts were referred to residual solvent peak, $\delta(CHCl_3) = 77.2$ ppm with respect to TMS signal (0 ppm).

^{15}N NMR chemical shifts were taken from 2D ^{15}N,^{1}H HMQC spectra (Bruker's 'inv4gplrnd' pulse program: gradient selection, magnitude mode, no decoupling during acquisition). A 256×1024 matrix, zero filled to 1024×1024 was used, giving digital spectrum resolution of ca. 5 Hz per point (^{15}N domain) and 2 Hz per point (^{1}H domain). The spectra were gained with parameter acquisition time 0.13 s, relaxation delay 1.5 s, a delay for evolution of long range $^nJ(^{15}N–^1H)$ coupling 75 ms, spectral width of 100 ppm in the F_1 (^{15}N) domain and 8 ppm in the F_2 (^{1}H) domain. Typically 16 scans per experiment were gained. The ^{15}N chemical shifts were referred to CH_3NO_2 signal (0 ppm).

Absorption measurements (VIS) were carried out on a Varian Cary IE spectrometer using $CDCl_3$ solvent, in order to retain the same experimental conditions as for NMR experiment. Extinction coefficient ε is expressed as $dm^3\ mol^{-1}\ cm^{-1}$.

Acknowledgements

This work was supported by the State Committee for Scientific Research under Grant No. 4 T09A 060 25.

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