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Chiral atropisomeric diiodobiphenyls—enantiodifferentiation by the dirhodium method

Stefan Moeller,[a] Dieter Albert,[a] Helmut Duddeck,[a,*] András Simon,[b] Gábor Tóth,[b,*] Oleg M. Demchuk[c] and K. Michał Pietrusiewicz[c,d,*]

[a]*Hannover University, Institute of Organic Chemistry, Schneiderberg 1B, D-30167 Hannover, Germany*
[b]*Institute for General and Analytical Chemistry of the Budapest, University of Technology and Economics, Szent Gellért tér 4, H-1111 Budapest, Hungary*
[c]*Polish Academy of Sciences, Institute of Organic Chemistry, ul. Kasprzaka 44/52, PL-01-224 Warsaw, Poland*
[d]*Maria Curie-Sklodowska University, Department of Organic Chemistry, Gliniana 33, PL-20 615 Lublin, Poland*

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Abstract—Enantiodifferentiation of atropisomeric biphenyl diiodides can easily be accomplished by adding the enantiopure dirhodium complex **Rh*** as an NMR auxiliary, although iodine is only a weak donor in forming adducts with **Rh***. Further Lewis-base substituents X/X′ (e.g., NH_2 or SH) may dominate the adduct formation equilibria whereas others are hardly involved (e.g., Cl, OCH_3, NMe_2, and OH).

1. Introduction

Dirhodium complexes as well as their adducts, which are formed by adding ligands to the axial position(s), have been the focus of interest for many years.[1] They have been introduced as homogeneous catalysts in various reactions[2] and have even found medicinal applications.[3] Over the last decade, we have shown that the enantiomers of various soft-base ligands with low polarity can easily be differentiated by adding an equimolar amount of the dirhodium complex $Rh^{(II)}_2[(R)\text{-}(+)\text{-MTPA}]_4$ (**Rh***, MTPA-H = methoxytrifluoromethylphenylacetic acid ≡ Mosher's acid; see Scheme 1) to their $CDCl_3$ solution and monitoring the diastereomeric dispersion, $\Delta\nu$, of their NMR signals at room temperature ('dirhodium method' of chiral recognition).[4] It has turned out that the dirhodium method is complementary to the application of chiral lanthanide shift reagents (CLSR)[5] in that dirhodium adducts can be formed by such ligand functionalities, which are of low polarity (soft bases) and thereby fail to react with CLSR.

Iodine-containing natural products have been reported,[6] as well as iodine-containing intermediates, which are common in the synthesis of various target molecules including also atropisomeric biaryl ligands.[7] Thus, there is a need for an experimental method, which is capable of direct stereodifferentiation of nonpolar chiral iodohydrocarbons. Our preliminary experiment with 2-iodobutane[8] had shown that the dirhodium method is indeed successful. This prompted us to apply the dirhodium method to the aromatic biphenyl iodides **1**–**9** with chiral axes (Scheme 1).

2. Results and discussion

2.1. Signal assignments and parameters obtained by application of the dirhodium method

The assignment of the NMR signals of the free ligands **L** (**1**–**9**; see Scheme 1) is straightforward in most cases when routine NMR methods, such as DEPT, HMQC, HMBC, and various NOE techniques, are applied (Tables 1–4). Thereby, all ^1H, ^{13}C, and ^{31}P NMR signals could be identified. In the presence of **Rh*** however, the identification of the ligand signals was sometimes hampered by overlapping MTPA acid signals, particularly when aromatic signals are involved. It should be noted that in the cases of **1**–**4**, **6**, and **7**, it was not possible to state which sets of ^1H and ^{13}C signals belongs to

* Corresponding authors. Tel.: +49 511 762 4615; fax: +49 511 762 4616; e-mail: duddeck@mbox.oci.uni-hannover.de

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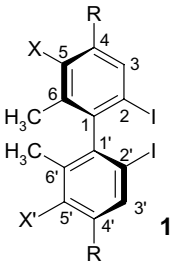
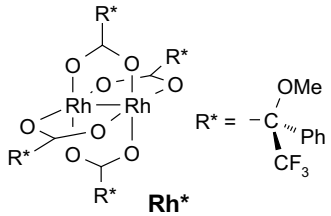




	1	2	3	4	5	6	7	8	9
R	H	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3	CH_3
X	H	H	OCH_3	Cl	NH_2	$N(CH_3)_2$	OH	SH	SH
X'	H	H	OCH_3	Cl	NH_2	$N(CH_3)_2$	OH	SH	H

Scheme 1. Structures of biphenyl derivatives **1**–**9** and the dirhodium complex **Rh***.

Table 1. ^1H and ^{13}C chemical shifts of the free ligands **1**–**7** (in ppm), recorded at room temperature

		CH_3-4	CH_3-6	1	2	3	4	5[a]	6
1	^1H		2.01			7.80	7.00	7.27	
	^{13}C		21.4	147.4	100.6	136.8	129.4	130.0	137.5
2	^1H	2.32	1.92			7.62		7.05	
	^{13}C	20.8	21.4	144.6	100.8	136.9	139.2	130.8	137.6
3	^1H	2.31	1.94			7.64			
	^{13}C	15.8	14.5	146.7	94.3	138.5	132.6	157.7	131.0
4	^1H	2.40	2.06			7.72			
	^{13}C	20.6	19.2	146.4	97.8	138.3	137.9	135.8	135.8
5	^1H	2.19	1.84			7.51			
	^{13}C	17.4	15.5	146.1	86.5	137.3	123.3	143.1	121.5
6	^1H	2.30	1.94			7.60			
	^{13}C	18.9	17.3	147.0	96.2	138.4	138.4	150.5	137.0
7	^1H	2.29	1.91			7.30			
	^{13}C	16.0	13.4	139.3	113.8	131.2	124.8	151.8	124.1
8	^1H	2.38	2.03			7.68			
	^{13}C	22.1	20.2	146.1	96.9	137.8	137.3	132.6	135.4

[a] Chemical shifts of the substituents at C-5/5′ (ppm). **3**, X = OCH_3: $\delta(^1H) = 3.73$, $\delta(^{13}C) = 60.0$; **5**, X = NH_2: $\delta(^1H) = 3.66$; **6**, X = $N(CH_3)_2$: $\delta(^1H) = 2.82$, $\delta(^{13}C) = 42.4$; **7**, X = OH: $\delta(^1H) = 5.69$; **8**, X = SH: $\delta(^1H) = 3.33$.

Table 2. ^1H and ^{13}C complexation shifts $\Delta\delta$ (in ppm) of **1**–**8** in the presence of an equimolar amount of **Rh***[a], recorded at room temperature

		CH_3-4	CH_3-6	1	2	3	4	5[b]	6
1	^1H		−0.01/−0.01			+0.01/+0.01	−0.01/−0.02	−0.01/−0.01	
	^{13}C		−0.1/−0.1	+0.0/+0.0	+0.1/+0.1	0.0/0.0	0.0/0.0	+0.1/+0.1	+0.2/+0.2
2	^1H	−0.03/−0.03	−0.02/−0.02			+0.02/+0.02		−0.01/−0.01	
	^{13}C	−0.0/−0.0	−0.1/−0.1	0.0/0.0	+0.1/+0.1	+0.1/+0.1	+0.1/+0.1	+0.0/+0.0	+0.1/+0.1
3	^1H	−0.02/−0.04	+0.01/+0.01			+0.03/+0.01			
	^{13}C	−0.1/−0.1	0.0/0.0	−0.1/−0.1	+0.6/+0.6	0.0/0.0	+0.5/+0.5	+0.1/+0.1	+0.4/+0.4
4	^1H	−0.04/−0.04	0.00/−0.02			+0.03/+0.03			
	^{13}C	−0.1/−0.1	0.0/0.0	−0.1/−0.1	+0.2/+0.2	0.0/0.0	+0.2/+0.2	+0.1/+0.1	+0.1/+0.1
5	^1H	−0.02/−0.05	+0.08/+0.07			−0.03/−0.06			
	^{13}C	−0.2/−0.3	−0.3/−0.3	−0.1/−0.1	+5.5/+5.5	+0.6/+0.5	+5.0/+5.2	−1.8/−1.8	+4.8/+4.5
6	^1H	−0.07/−0.07	−0.06/−0.06			−0.06/−0.06			
	^{13}C	−0.2/−0.2	−0.1/−0.1	−0.1/−0.1	+0.3/+0.3	−0.2/−0.2	+0.1/+0.1	+0.4/+0.4	−0.2/−0.2
7	^1H	−0.01/−0.01	0.00/0.00			0.00/0.00			
	^{13}C	−0.0/−0.0	0.0/0.0	0.0/0.0	+0.1/+0.1	0.0/0.0	0.0/0.0	0.0/0.0	0.0/0.0
8	^1H	−0.04/−0.06	0.00/−0.05			−0.03/−0.05			
	^{13}C	−0.6/−0.6	−0.2/−0.4	+0.2/+0.2	+1.9/+2.0	+0.8/+0.8	+1.1/+1.0	−3.3/−3.3	+1.0/+1.0

[a] ^1H and ^{13}C signal sets for each enantiomer cannot be assigned unequivocally due to the small chemical shift difference, except for **5** and **8** (see text).
[b] Complexation shifts $\Delta\delta$ in the substituents at C-5/5′ (in ppm). **3**, X = OCH_3: ^1H, +0.17/+0.15, ^{13}C, +0.8/+0.7; **5**, X = NH_2: ^1H, +1.44; **6**, X = $N(CH_3)_2$: ^1H, −0.06, ^{13}C, −0.1; **7**, X = OH: ^1H, −0.07/−0.08; **8**, X = SH: ^1H, +2.06/+2.00.

Table 3. Diastereomeric ^{1}H and ^{13}C dispersions $\Delta\nu$ (in Hz) of **1**–**8** in the presence of an equimolar amount of **Rh***, recorded at room temperature

		CH_3-4	CH_3-6	1	2	3	4	5[a]	6
1	^{1}H		<1			<1	1.9	<1	
	^{13}C		≈0	≈0	≈0	≈0	≈0	≈0	≈0
2	^{1}H	<1	≈0			<1		<1	
	^{13}C	≈0	≈0	≈0	≈0	≈0	≈0	≈0	≈0
3	^{1}H	7.2	<1			9.9			
	^{13}C	≈0	0.6	0.8	1.1	3.1	≈0	1.7	1.9
4	^{1}H	≈0	6.0			≈0			
	^{13}C	≈0	1.5	1.0	0.8	≈0	1.5	1.5	1.0
5[b]	^{1}H	+12.0	+6.8			+12.0			
	^{13}C	+6.0	+5.0	<1	<1	+6.0	−12.1	<1	+28.2
6	^{1}H	<1	<1			<1			
	^{13}C	≈0	≈0	≈0	≈0	≈0	≈0	≈0	≈0
7	^{1}H	<1	≈0			<1			
	^{13}C	≈0	≈0	≈0	<1	≈0	≈0	<1	≈0
8[b]	^{1}H	+8.8	+17.2			+10.0			
	^{13}C	+2.0	+17.1	−2.0	−2.0	3.0	+3.0	<+1	≈0

[a] Diastereomeric dispersions $\Delta\nu$ (in Hz) of the substituents at C-5/5′. **3**, X = OCH_3: $\Delta\nu(^{1}H) = 10.0$, $\Delta\nu(^{13}C) = 6.9$; **5**, X = NH_2: $\Delta\nu(^{1}H) < 1$; **6**, X = $N(CH_3)_2$: $\Delta\nu(^{1}H) < 1$, $\Delta\nu(^{13}C) \approx 0$; **7**, X = OH: $\Delta\nu(^{1}H) = 1.6$; **8**, X = SH: $\Delta\nu$ (^{1}H) = +23.2.

[b] In contrast to the others, ^{1}H and ^{13}C signal sets for each enantiomer of **5** and **8**, respectively, can be assigned. Since, however, the absolute configurations are not known, the signs of the $\Delta\nu$-values are arbitrary.

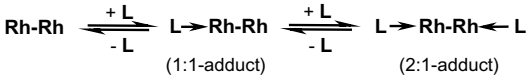
Table 4. ^{1}H and ^{13}C chemical shifts of the free ligands **9**, complexation shifts $\Delta\delta$ (in ppm) and diastereomeric dispersions $\Delta\nu$ (in Hz) in the presence of an equimolar amount of **Rh***[a]

	Compound **9**					
	$\delta(^{1}H)$	$\delta(^{13}C)$	$\Delta\delta(^{1}H)$	$\delta(^{13}C)$	$\Delta\nu(^{1}H)$	$\Delta\nu(^{13}C)$
CH_3-4	2.38	22.1	+0.00/−0.07	−0.7/−0.7	28.0	<1
CH_3-6	2.05	20.1	+0.18/+0.15	−0.2/−0.2	11.2	3.0
CH_3-4′	2.34	20.6	−0.03/−0.04	0.0/0.0	6.0	<1
CH_3-6′	1.95	21.5	−0.21/−0.22	−0.3/−0.3	4.4	2.0
1		145.6		+0.7/+0.7		2.0
2		97.0		+2.5/+2.4		6.0
3	7.68	137.8	+0.05/0.03	+0.7/+0.6	30.4	8.1
4		137.2		+1.5/+1.4		8.1
5		132.5		−3.5/−3.6		5.0
6		135.4		+1.2/+1.1		3.0
1′		145.1		−0.5/−0.5		2.0
2′		100.9		0.0/0.0		1.0
3′	7.64	137.2	−0.01/−0.02	0.0/0.0	5.6	2.0
4′		139.4		+0.2/+0.2		<1
5′	7.08	131.0	−0.05/−0.07	0.0/0.0	10.8	<1
6′		137.2		+0.2/+0.1		3.0

[a] The SH proton resonates at $\delta = 3.32$ ppm; the corresponding signal in the presence of **Rh*** is shifted by $\Delta\delta = +2.44$ ppm; no dispersion detectable.

one enantiomer and which to the other. This was due to the small chemical shift differences of respective atoms in the diastereomeric adducts (see below: diastereomeric dispersion), which could not be discerned by 2D NMR correlation methods. The situation was better for **5** and **8** with their larger δ-value differences, while there was no longer a problem in the case of the unsymmetrical monothiophenol **9**. As compounds **1**–**9** have been used in their racemic or nearly racemic forms, the discussion herein is restricted to the determination of enantiomeric ratios.

As indicated in Scheme 2, ligand molecules **L** form 1:1- and 2:1-adducts depending on the relative molar ratio of **L** versus **Rh***. Since we used equimolar amounts of the two adduct components in the standard experiment, 1:1-adducts prevail although a certain amount of free



Scheme 2. Equilibria between the free components and the adducts; the dirhodium complex **Rh*** is symbolized by **Rh**–**Rh** for a clearer representation of the adducts formed.

L and of 2:1-adducts cannot be ignored. All adducts, except those of phosphine ligands,[4a,9] are kinetically labile so that room-temperature NMR signals are averaged. When compared to free ligand NMR signals, the averaged adduct signals revealed two important parameters. First, the NMR signals can be shifted to some extent. In general, such complexation shifts $\Delta\delta$ are too small and can only be detected if the complexation site is closeby, because the inductive effect of the ligand's functional

group is enhanced. Such effects are deshielding ranging up to ca. 0.5 ppm for ^{1}H and a few ppm for ^{13}C and heavier nuclei. Thus, complexation shifts are good indicators of the preferred complexation site if the donor is strong enough. Secondly, if the ligand molecule is chiral, the ligand signals split into two due to the formation of diastereomeric adducts; the distance (in Hz) between the individual lines in such duplicated signals is the diastereomeric dispersion $\Delta\nu$, and their relative intensities reflect the enantiomeric composition of the ligand. Conformational differences within each partner in the diastereomeric adducts (**L** and **Rh***) and for both partners, with respect to each other, are held responsible for the signal dispersion effects in the adducts.

In this paper, the intensities within duplicated signals are 1:1 because most ligands are racemic mixtures (except for **8**, see below). There is no differentiation between respective atoms in the two identical parts of the biphenyls. That means that the ligands are either still symmetrical in the adduct(s), or that they display symmetrical averages. Tables 2–4 list all $\Delta\delta$- and $\Delta\nu$-values observable for **1**–**9** in the presence of an equimolar amount of **Rh***.

An alternative explanation for the above mentioned signal duplications may be a differentiation of the two phenyl rings by adduct formation involving a binding of only one single atom/group, so that the ligand molecules lose their C_2 symmetry in the adduct. This argument, however, can be rejected by considering the fact that at room temperature, the adducts are expected to be kinetically labile and ligand exchange is fast on the NMR time scale (for further arguments see below).

Deubel has communicated a theoretical study (based on DFT calculations) on the donor–acceptor interactions contributing to the binding energy in the adducts of dirhodium(II) tetraformate and a representative choice of strong and weak ligands (e.g., methylene carbene vs benzene).[10] As a result, attractive contributions are a blend of electrostatic and HOMO–LUMO interactions, the former always dominating.[10] We have recently shown that the steric repulsion between **L** and the bulky **Rh*** plays a significant role during adduct formation, as well.[4b,c]

Beside demonstrating the successful application of the dirhodium method for the enantiodifferentiation of iodides, the compound series of this study us allows to compare the relative donor properties of various functionalities: I, NR_2, OH, and SH.

2.2. Ligands without further donor functionalities—2,2′-diiodo-6,6′-dimethyl-1,1′-biphenyl 1 and 2,2′-diiodo-4,4′,6,6′-tetramethyl derivatives 2–4

We have found in all previous applications of the dirhodium method that benzene rings, ether–oxygen, and chlorine atoms are extremely weak donors with **Rh*** and do not produce significant complexation shifts and signal dispersions by adduct formation.[4,8,9,11–14] Thus, only the iodine atoms are expected to be complexation sites in biphenyls **1**–**4**. In fact, ^{1}H adduct formation shifts $\Delta\delta$ and even those of ^{13}C nuclei are negligible in all these compounds (Table 2) indicating that the iodine atoms are weak donors. Nevertheless, adducts as defined in Scheme 2 do exist even for such nonpolar compounds, as proven by the fact that significant dispersion effects $\Delta\nu$ can be identified for some NMR signals (except for **2**; Table 3). This is exemplified in Figure 1 for the methyl signals of ligand **3**.

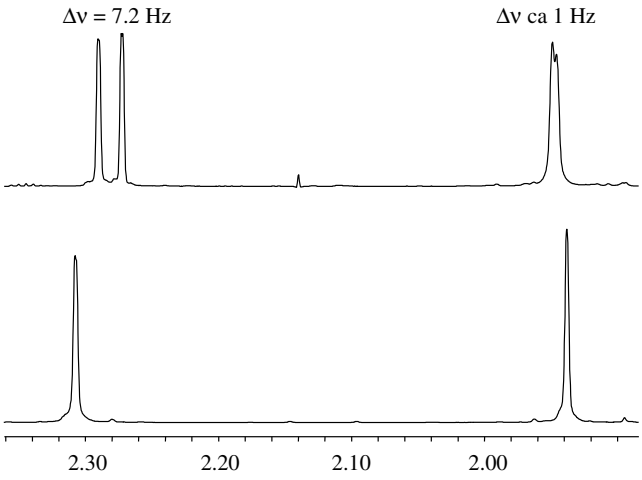


Figure 1. ^{1}H NMR signals of the 4/4′-methyl (left) and 6/6′-methyl protons in **3** and their duplication due to diastereomeric dispersion; bottom: in the free ligand, top: in the presence of 1 mol equiv of **Rh***.

The low donor ability of iodine in **Rh***-adducts can also be proven by inspecting the MTPA methoxy ^{1}H signal in the samples containing equimolar amounts of the ligand and of **Rh*** recorded at room temperature: it appears at $\delta = 3.163$ for **1**, $\delta = 3.158$ for **2**, $\delta = 3.107$ for **3**, and $\delta = 3.158$ for **4**, values which are very similar to that of pure **Rh*** ($\delta = 3.175$) indicating that the equilibria depicted in Scheme 2 are shifted to the left, that is, toward the free components **L** and **Rh***. This contrasts with the respective observation when stronger donors such as Se in Ph–Se–R,[14] P═S, P═Se, etc.[4c,11] are involved; here its ^{1}H chemical shift appears around $\delta = 2.9$–3.0, and the equilibria prefer the adducts.

Two binding modes of the 2,2′-diiodobiphenyls **1**–**4** to **Rh*** are conceivable on the basis of Deubel's interpretation:[10] (a) orbital interaction via the HOMO of the ligand (Fig. 2, left) creating a direct I···Rh contact, and/

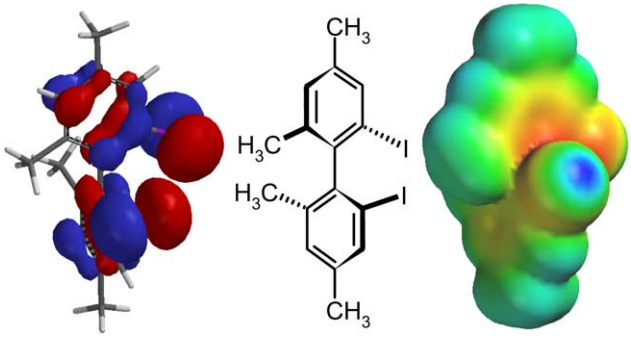


Figure 2. PM3-calculated geometry of **2**; left: HOMO, right: electrostatic potential surface (red: negative charge; blue: positive charge).

or (b) electrostatic interaction. The highest electrostatic potential is located in the center of the molecule (Fig. 2, right: area of red color code), that is, at the central C–C bond between the phenyl residues and the adjacent bonds. Both interactions lead to nearly the same adduct geometry because they are on the same side of the biphenyl molecule. Due to the lability of the adducts however, it is impossible to state whether or not any of the two contributions is dominant, inferior or even absent.

A clear difference emerges on comparing complexation shifts and dispersion effects of the biphenyls **1**–**4** (Tables 2 and 3) with those of 2-iodobutane.[8] We repeated the earlier experiment with racemic 2-iodobutane under the standard dirhodium method conditions (400 MHz ^{1}H frequency, equimolar amount of **Rh***, two to three drops of acetone-d_6; see Section 4) and found the following $\Delta\nu$-values: 6.8 Hz for H-1, 3.0 Hz for H-2, 3.2 Hz for H-3a, 2.6 Hz for H-3b, and 8.0 Hz for H-4. The complexation shifts are ca. 0.3 ppm for H-2 (geminal to iodine) and between 0 and 0.09 ppm for the other protons. A comparison of these values with those of **1**–**4** (Tables 2 and 3) led us to the conclusion that aliphatic iodides are significantly better donors than aromatic iodides. In order to understand this phenomenon, we calculated total charges at iodine atoms and the HOMOs in various model compounds, for example, iodobutanes, iodocyclohexanes, iodobenzene, etc., as well as **1**–**9**. The result supports that both mechanisms of interaction with **Rh***[10] should be weaker in the aromatic than in the aliphatic system. First, the total iodine charge in aromatic iodides is always positive (+0.02 to +0.11; compare Fig. 2, right: blue color code) whereas it is negative in aliphatic iodides (−0.02 to −0.09) leading to a stronger electrostatic attraction in the latter series. Secondly, the HOMO is extended into the π system of the aromatic iodides (π-type conjugation; compare Fig. 2, left) whereas any significant delocalization with other atomic orbitals does not exist in the aliphatic iodides.

2.3. Ligands with Lewis-basic functionalities as potential competitors in adduct formation, 2,2′-diiodo-4,4′,6,6′-tetramethyl-1,1′-biphenyl derivatives 5–9

Diiodobiphenyls **5** and **6** possess amino groups attached to the aromatic rings. Here, competition between the different donor atoms/groups is to be expected. Looking at the $\Delta\delta$-values of bis-aniline derivative **5**, it is immediately apparent that this compound has donors stronger than iodine, namely the two amino groups.[15] There is no doubt that the electrostatic attraction of the nitrogen atoms with their partially negative charge prevails over I···Rh HOMO–LUMO interaction. Due to the stronger adduct formation with **Rh***, we found more and stronger dispersion effects ($\Delta\nu$) for this compound. This is demonstrated in Figure 3 for the signals of H-3 and the methyl carbon atoms in **5** (Fig. 3a and c, respectively).

At first glance, it is surprising that the dimethylamino derivative **6** completely fails in displaying any significant complexation shifts and signal dispersions (Tables 2 and 3). Apparently, the bulky methyls in the *N*-dimethyl groups protect the negative charge at the nitrogen atoms from a close approach to a rhodium atom so that the electrostatic attraction is too weak over the long distance. Moreover, the lower polarity of this ligand molecule (according to PM3 calculations) seems even to prevent a rhodium approach to the iodine atoms on the backside of the molecule; the negative charge around the central bond is much weaker than in **1**–**4**. Thus, on the whole, there is hardly any electrostatic attraction between the ligand and a rhodium atom so that adducts of **6** are extremely weak if existing at all. This situation is similar to a previous study using an ytterbium salt as NMR shift reagent for the investigation of the ligand properties in 4-substituted adamantane-2,6-diones.[16] It has been shown that a dimethylamino substituent at C-4 does not contribute to the complexation of that ligand to the lanthanide ion but acts exclusively as a bulky repulsive group; binding takes place only at the carbonyl oxygens in this molecule.[16]

The difference in the stabilities of the two **Rh*** adducts with amino **5** and dimethylamino **6** derivatives is further proven by ROESY measurements of equimolar mixtures with **Rh***. The experiment with **5** reveals a number of strong cross-peaks indicating an intimate spatial contact between atoms of the two components in the adducts: OCH_3 (MTPA) with H-3/3′ and both types of methyl groups of **5** as well as *ortho*- and *meta*-protons of the MTPA phenyl group with both types of methyl groups of **5**. On the other hand, such inter-component ROESY peaks were completely missing in adducts with **6** whereas cross-peaks of protons inside each component were visible.

Surprisingly, bis-phenol **7** was another example to show no complexation shifts $\Delta\delta$ and dispersion effects $\Delta\nu$ for the proton and carbon signals in the diiodotetramethylbiphenyl system. Only the OH proton signal was somewhat shifted by adduct formation ($\Delta\delta = -0.07/-0.08$) and slightly split ($\Delta\nu = 1.6$ Hz; compare Fig. 3b). The oxygen atoms in water or in alcohols/phenols are hard bases and, therefore, not well suited for complexation to a rhodium atom in **Rh***, which itself is a soft acid. This is in accordance with our previous observation that in the presence of dirhodium tetramandelate even a 40-fold excess of methanol (added for better solubility) cannot compete with the soft base sulfur of methylphenylsulfoxide.[17] Moreover, each of the hydroxy groups of **7** is flanked by two methyl groups preventing a close approach of **7** and **Rh*** being essential for a significant electrostatic interaction. Finally, the polarity of the molecule does not even allow a weak Rh···I contact, for analogous arguments as described above for **6**.

The complexation shifts and dispersion effects observed for the bis-thiophenol **8** are analogous to those of the diamino derivative **5** discussed above; significant values were found at the signals of more or less the same hydrogen and carbon atoms. Since **8** is a nonracemic sample, the signals for each duplicated resonance were not equal in their intensities, another argument against the alternative interpretation of signal duplication mentioned

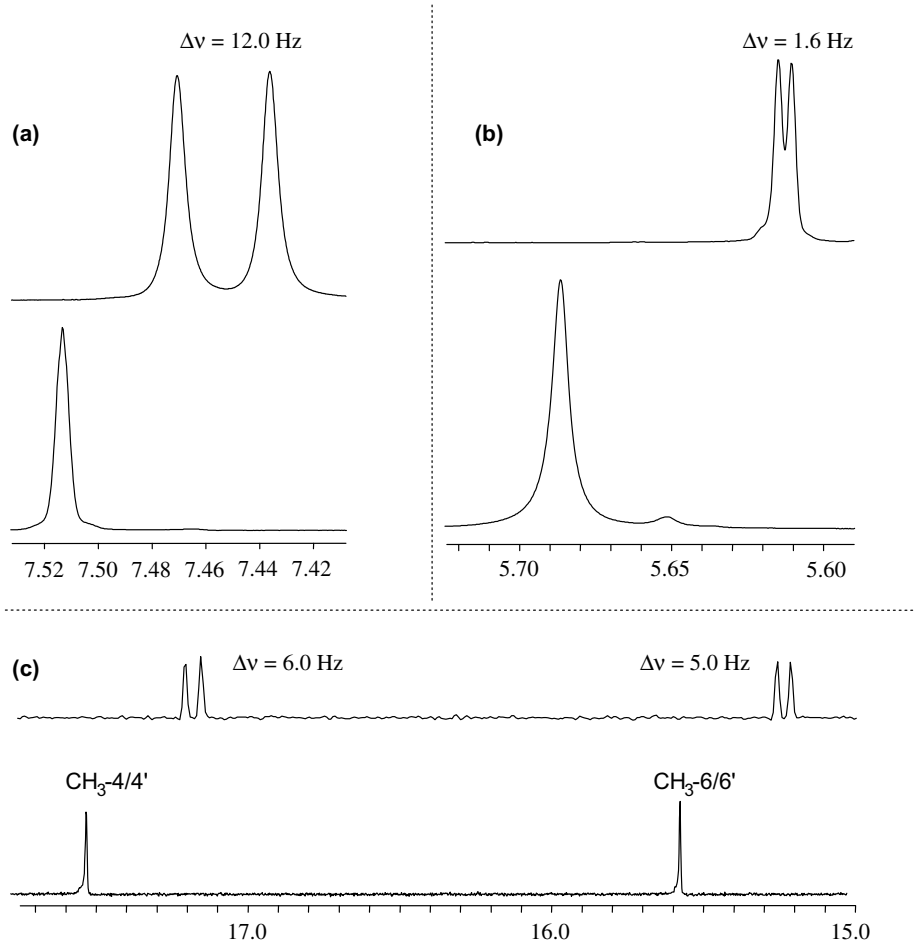


Figure 3. (a) Dispersion effects observed for the signals of H-3/3′ of **5**; (b) for the OH proton signal in **7**, and (c) for the methyl carbon atoms in **5**; in each instance, the lower trace refers to the free ligand, the upper trace to an equimolar mixture of ligand and **Rh***.

above. This proves the existence of a strong S···Rh contact in the adduct(s), although sulfur is in contrast to nitrogen not a strongly electronegative element and the C–S bond is not a strong dipole. Such an observation confirms that the HSAB principle is an important feature in the **Rh***-adduct; see also the fact that—as mentioned above, the sulfur atom is the complexation site in sulfoxides, not the oxygen.[17]

The structurally related thiophenol compound **9** can be regarded as a mono-SH-substituted derivative of **2** so that the C_2 symmetry is broken. Both phenyl groups are different and each of them gives rise to a separate set of ^{1}H and ^{13}C NMR signals (Table 4). An inspection of the $\Delta\delta$-values in this molecule immediately reveals that only the sulfur-substituted ring is close to the binding site. The complexation shifts in the second phenyl group (dashed numbers, Scheme 1) are negligible, similar to those of **2**. Signal dispersions, however, occur all over the molecule, and are more pronounced for signals of the SH-containing ring. Once a firm contact between the two partners in the adduct has been established (S···Rh), all atoms in the ligand (not only those of the thiophenol ring) are subjected to the anisotropy effects of the four MTPA acid residues with their wide range and strong directional dependence. The similarities in the $\Delta\delta$- and $\Delta\nu$-effects observed for the NMR signals of **8** and those of the thiophenol ring in **9** suggest a tentative interpretation of the general adduct structures of **5** and **8** in the equilibria: only one single atom is the binding site of the bidentate ligands **5** or **8** with identical donor groups (Fig. 4).

Whether a binding site exchange (X vs X′) occurs under spatial separation of the components as suggested in Scheme 2 or not, can be decided by inspecting the slow-exchange regime by low-temperature NMR spectroscopy. If there is no ligand site exchange during the life time of an adduct, the low-temperature spectrum shows signals of a bisphenyl derivative without C_2 symmetry, that is, with two different phenyl ring moieties (further signal duplication). If the X versus X′ exchange is faster than the ligand exchange, signal averaging precludes this second signal duplication. Unfortunately, the barrier of ligand exchange in **8** is too low; even at 213 K one finds signals, which are still approaching coalescence (Fig. 5), and the slow exchange regime cannot be reached. They same is valid for **5**. Therefore, we are unable to make a decision about this mechanism. On the other hand, these experiments indeed prove that the adduct system is on the rapid exchange side and all NMR signals are averaged, as anticipated above in arguing against the

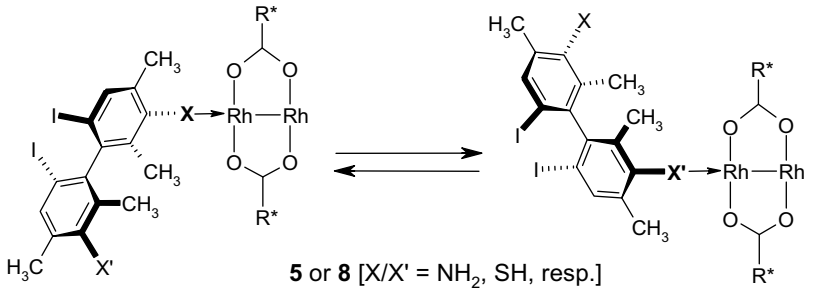


Figure 4. Tentative adduct structure and donor group exchange; only two carboxylate residues R* of **Rh*** are depicted for sake of clarity.

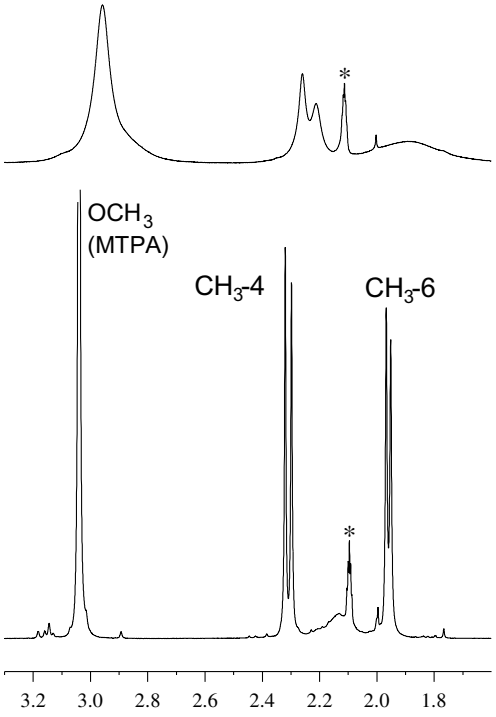


Figure 5. Section of the ^{1}H NMR spectrum of **8** in the presence of 1 molequiv of **Rh***; lower trace recorded at room temperature, upper trace at 213 K. Asterisked signal belongs to acetone-d_5.

alternative explanation of signal duplication. This holds for all compounds **1**–**9** because **5** and **8** are the strongest donors in this series.

In the series **5**–**9**, the different donor abilities of the pertinent functionalities (I or X/X′, respectively) are also reflected in the ^{1}H chemical shifts of the MTPA methoxy groups, which indicate the balance of the equilibria shown in Scheme 2 (compare for **1**–**4** above in Section 2.2): they appear at $\delta = 2.891$ for **5** (strong donor), $\delta = 3.138$ for **6** (very weak donor), $\delta = 3.163$ for **7** (very weak donor); $\delta = 3.000$ for **8** (moderately strong donor) and $\delta = 3.072$ for **9** (moderately strong donor).

3. Conclusion

Aromatic iodides are very weak donors in adduct formation with dirhodium tetracarboxylates, and even weaker than aliphatic iodides. Nevertheless, enantiodifferentiation of atropisomeric iodobiphenyls devoid of any further donor group (**1**–**4**) is still possible when using **Rh*** as a chiral NMR auxiliary, although not in all cases.

Amino groups, for example, NH_2 in **5**, are better donors. However, steric hindrance by *N*-substitution may completely prevent any approach of the adduct partners close enough for effective electrostatic interaction, for example, **6** with NMe_2. This difference in adduct stabilities is further proven by ROESY experiments. Whereas hydroxyl groups in **7** prove to be ineffective in adduct formation despite of their high polarity, the thiol groups in **8**—as soft bases—are good donors and dominate the adduct formation. This is a consequence of the HSAB principle being a decisive factor in donor selection in the dirhodium method. Monothiophenol derivative **9** can form stable adducts in a similar way as bis-thiophenol **8** proving that there is no principle difference between mono- and difunctional derivatives of **2** in the way how adducts are composed.

4. Experimental

4.1. Substances

The synthesis of **Rh*** has been described by us earlier.[18] Most of the diiodobiphenyl compounds used here were racemates (except **8** with ca. 10% ee) and were available from another study[19] where they were synthesized by a general procedure based on 2,2′-diiodo-4,4′,6,6′-tetramethyl-5,5′-diaminobiphenyl **5** as the common precursor. Diiodide **1** was an exception because the preparation procedure used, was reported before.[7f]

4.2. NMR spectroscopy

Room temperature ^{1}H (400.1 MHz) and ^{13}C (100.6 MHz) NMR measurements were performed on a Bruker Avance DPX-400 spectrometer. Chemical shift standards were internal tetramethylsilane ($\delta = 0$) for ^{1}H and ^{13}C. Signal assignments were assisted by selective 1D NOESY, COSY, HMQC, HMBC, and ROESY (standard BRUKER software). Digital resolutions were 0.14 Hz/point in the ^{1}H and 0.24 Hz/point in the ^{13}C and 0.22 Hz/point. Two to three drops of acetone-d_6

were added to each NMR sample before measurement in order to increase the solubility of **Rh***.[17]

Variable temperature ^{1}H (500.1 MHz) spectra were recorded in the presence of **Rh*** on a Bruker Avance DRX-500 spectrometer.[4c] Temperatures varied from 203 to 333 K and were read from the instrument panel; no further measures for more precise temperature determinations were taken.

4.3. Calculations

Semiempirical (PM3) calculations of the free ligands were performed using SPARTAN'04 of the Wavefunction® software package. Hartree–Fock ab initio calculations were carried out additionally in a few cases resulting in geometries and relative energies very similar to those obtained from PM3.

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