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Formation of chiral ionic liquids and imidazol-2-ylidene metal complexes from the proteinogenic aminoacid L-histidine

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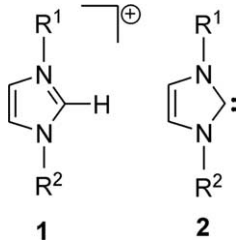
Abstract

Treatment of the amino acid derivative Bz-His-OMe with excess *n*-propyl bromide gave the corresponding histidinium salt [Bz-His(*n*-propyl)$_2$-OMe$^+$Br$^-$]. It features a melting point of 39 °C and may serve as a useful readily available optically active ionic liquid. Its subsequent treatment with silver oxide gave the corresponding L-histidine derived chiral N-heterocyclic carbene complex [''(carbene)$_2$Ag · AgBr$_2$'']. Transmetallation by treatment with Pd(CH$_3$CN)$_2$Cl$_2$ or [Rh(cod)Cl]$_2$ led to the formation of the respective chiral late metal imidazol-2-ylidene complexes [''(carbene)$_2$PdCl$_2$''] and [''(carbene)RhCl(cod)''], respectively. Four diastereomers of the square planar palladium system were observed. Due to the additional chirality center in the L-histidine-derived ''Arduengo-carbene ligand'' two diastereomers of the rhodium carbene complex were formed.

Keywords: Imidazolium salts; Arduengo-carbenes; Metal complexes; Bio-organometallic chemistry; Chiral ionic liquid

1. Introduction

N-Alkylated imidazolium salts (**1**) and imidazol-2-ylidenes (**2**) are chemically related [1]. The latter are usually derived from the former by a deprotonation reaction at carbon atom C2 of the heterocyclic ring system. Examples of both systems have found extensive use in organic synthesis, in organometallic chemistry and catalysis. Suitably substituted imidazolium salts (**1**) that are associated with the right counteranions have served as ionic liquids, which represent a class of very polar reaction media that is finding a rapidly increasing current interest [2]. The neutral stable carbenes **2** have found extensive use as strong σ-donating ligands in metal complex synthesis and in catalysis [3]. From both the families of the compounds **1** and **2** a limited number of enantiomerically enriched chiral variants has become known, among them surprisingly few examples that were derived from amino acids [4–6].



We have developed synthetic pathways to chiral derivatives of **1** based on L-histidine and found that some such systems featuring rather low melting points have a potential to serve as useful ionic liquids. Subsequent deprotonation makes L-histidine derived chiral imidazol-2-ylidene derivatives or their respective metal complexes available. Several examples that illustrate this synthetic development will be presented and discussed in this account.

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[1] X-ray crystal structure analyses.

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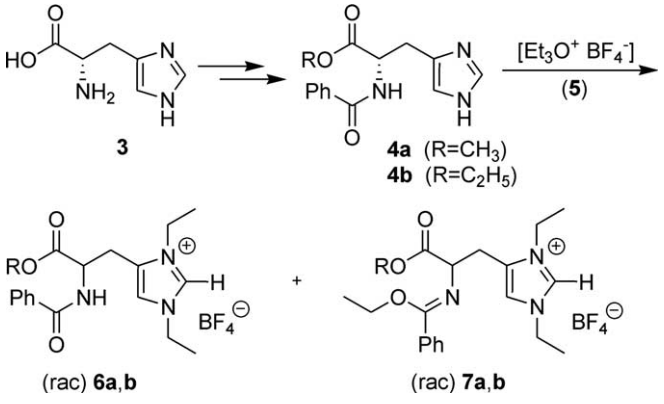
2. Results and discussion

2.1. Formation of L-histidine-derived imidazolium salts: new optically active ionic liquids

For this study, L-histidine (**3**) was O-protected by ester formation (methyl or ethyl ester) and then *N*-benzoyl (Bz) or *N*-*tert*-butoxycarbonyl (Boc) protected to give the starting materials **4** (see Scheme 1). Treatment with excess Meerwein's reagent $[Et_3O^+BF_4^-]$ (**5**) resulted in N- as well as O-alkylation [7]. Starting from Bz-His-OMe (**4a**) [8] we obtained a mixture of compounds (including transesterification products) from which the main component (**7a**) was isolated by chromatography and characterized by X-ray diffraction. The reaction of **4b** ($R = C_2H_5$) with **5** was less complicated. It gave a mixture of **6b** and **7b**, from which the *N*,*N*,*O*-tri-alkylated product **7b** was isolated in 43%. The imino-ester **7b** was also characterized by X-ray diffraction (see Fig. 1). Unfortunately, the products **7** were obtained racemized from these reactions. Apparently, (reversible) deprotonation at C_α of these histidine derivatives occurs too fast under the applied reaction conditions [9] to make these routes useful and, consequently, a different synthetic pathway was subsequently followed.

The problem was solved by treatment of Bz-His-OMe (**4a**) with *n*-propylbromide in acetonitrile. The N-selective di-alkylation [10] required 60 h at 65 °C to go to completion. Product isolation was facilitated by the high water solubility of **8**. It was isolated on a 150 g scale in >70% yield. The [Bz-His(*n*-propyl)$_2$-OMe$^+$Br$^-$] salt **8** was characterized by X-ray diffraction (see Fig. 2). The ^{1}H NMR spectrum of **8** shows the typical pairs of resonances for the two positionally differentiated *n*-propyl groups. The 2-H resonance of the imidazolium subunit is monitored at typical δ 9.62 (see Scheme 2).

Ionic liquids have per definition a melting point below 100 °C [2]. The new histidinium salt **8a** exhibits mp 39 °C. It is optically active ($[\alpha]^{20}(589) = -34$ ($CHCl_3$)). A test has shown that the ionic liquid **8a** does not lose its optical activity even if heated for 6 h at 110 °C in a two phase system with toluene. First, orientating experiments have shown that **8a** has typical features that may make it a



Scheme 1.

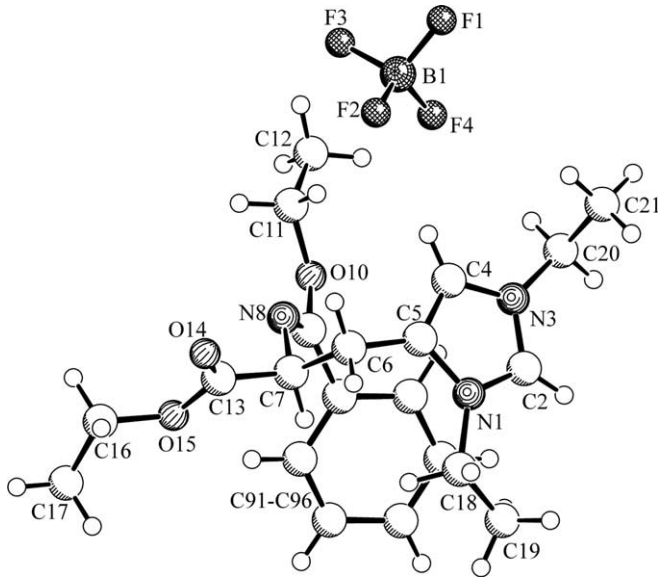


Fig. 1. A view of the molecular structure of *rac*-**7b** ($R = C_2H_5$). Selected bond lengths (Å) and angles (°): N1–C2 1.331(6), N1–C5 1.370(6), N1–C11 1.497(6), C2–N3 1.327(6), N3–C4 1.392(6), N3–C31 1.481(6), C4–C5 1.344(6), C4–C6 1.485(7), C6–C7 1.524(6), C7–C8 1.520(6), C8–O81 1.192(6), C8–O82 1.316(6), C7–N9 1.469(5), N9–C10 1.266(5), C10–O10 1.364(5); C2–N1–C5 108.1(4), C2–N1–C11 125.7(5), C5–N1–C11 126.1(4), N1–C2–N3 108.3(4), C2–N3–C4 109.4(4), C2–N3–C31 125.6(4), C4–N3–C31 124.9(4), N3–C4–C5 105.2(4), C5–C4–C6 129.6(4), N3–C4–C6 125.0(4), N1–C5–C4 108.9(4), C4–C6–C7 112.0(4), C6–C7–C8 111.2(4), C6–C7–N9 108.6(4), C8–C7–N9 106.8(4), C7–N9–C10 119.5(4), N9–C10–O10 119.9(4).

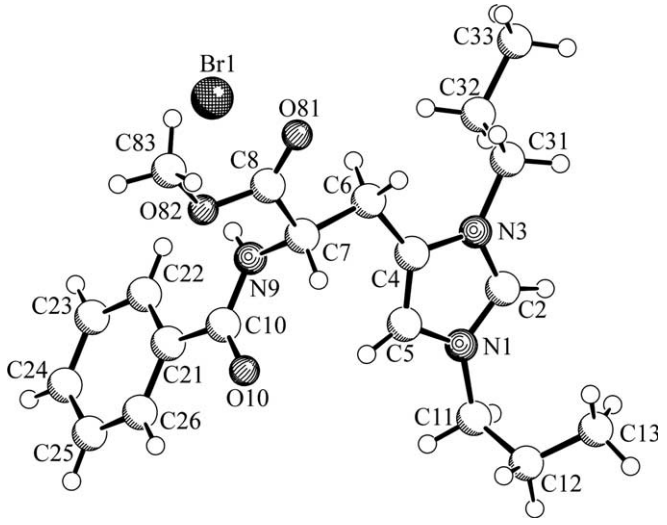
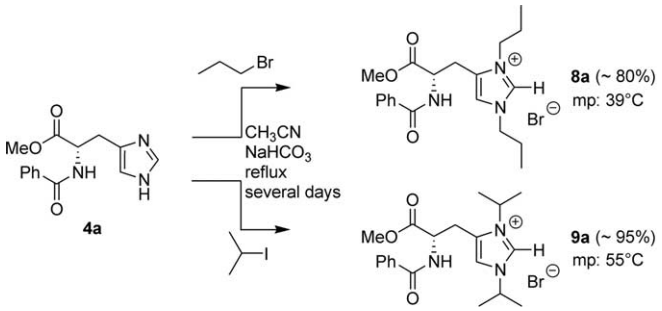


Fig. 2. Molecular structure of the L-histidine-derived chiral ionic liquid **8a**. Selected bond lengths (Å) and angles (°) for molecule A: N1–C2 1.320(6), N1–C5 1.387(6), N1–C11 1.478(6), C2–N3 1.337(6), N3–C4 1.402(5), N3–C31 1.470(6), C4–C5 1.347(6), C4–C6 1.492(5), C6–C7 1.524(5), C7–C8 1.538(6), C8–O81 1.194(5), C8–O82 1.328(5), C7–N9 1.459(6), N9–C10 1.334(6), C10–O10 1.228(5); C2–N1–C5 108.5(4), C2–N1–C11 125.1(4), C5–N1–C11 126.4(4), N1–C2–N3 109.1(4), C2–N3–C4 108.2(4), C2–N3–C31 124.1(4), C4–N3–C31 127.7(4), N3–C4–C5 106.2(4), C5–C4–C6 133.2(4), N3–C4–C6 120.6(4), N1–C5–C4 107.9(4), C4–C6–C7 111.8(3), C6–C7–C8 110.7(3), C6–C7–N9 112.3(3), C8–C7–N9 111.8(4), C7–N9–C10 121.3(4), N9–C10–O10 121.0(4).



Scheme 2.

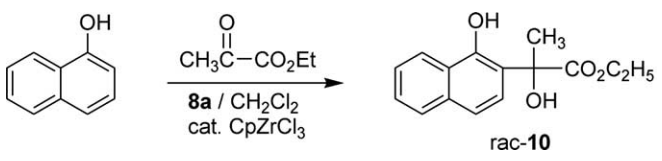
useful compound for ionic liquid applications. The hydroxyalkylation of α-naphthol with ethylpyruvate, catalyzed by the Lewis acid $CpZrCl_3$ (6 mol%) [11], was successfully carried out in a 1:2 mixture of [Bz-His(*n*-propyl)$_2$-OMe^+Br^-] (**8a**)/CH_2Cl_2 [12] at room temperature. Unfortunately, the isolated product (**10**, 60% yield) was racemic (Scheme 3).

Treatment of **4a** with iso-propyl iodide under the typical reaction conditions gave **9a** in excellent yield (see Scheme 2). The salt **9a** features a melting point of mp 55 °C. It, thus, may potentially serve as a chiral ionic liquid as well. We have similarly dialkylated the imidazol core of the related Boc-His-OMe starting materials to give the products **8b** and **9b**, respectively (see Scheme 4).

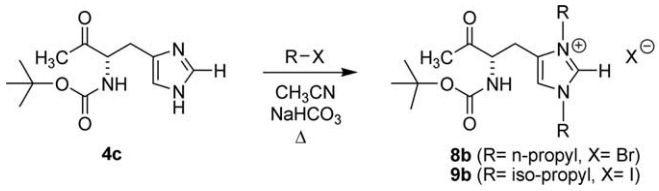
2.2. Histidine-based (imidazol-2-ylidene)metal complexes

The deprotonation at C2 of the imidazolium unit of the [Bz-His(*n*-propyl)$_2$-OMe^+Br^-] salt **8a** was effected by treatment with 0.5 molar equivalents of Ag_2O in dichloromethane [13] (in the presence of molecular sieves to remove the water that was formed in this reaction). The histidine-derived "Arduengo-carbene" complex **11a** was formed and isolated in close to quantitative yield. The formation of the carbene complex system is evident by the marked shift of the C2 ^{13}C NMR resonance [14] from δ 135.7 (**8a**) to δ 180.3 for the (carbene)$_2Ag \cdot AgBr_2$ complex **11a**. The [(carbene)$_2Ag^+$] subunit was identified by HR ESI MS, featuring a characteristic isotopic pattern (see Section 4). Complex **11a** was obtained optically active, as shown by its optical rotation. The Boc-protected analogue (**8b**) reacts analogously with silver oxide to yield **11b** [δ (C2): 181.2] (see Scheme 5).

The (carbene)$_2Ag \cdot AgBr_2$ complexes **11a** and **11b** were used as reagents for the transfer of the chiral imidazol-2-ylidende ligands to transition metals [15,16]. Two procedures



Scheme 3.

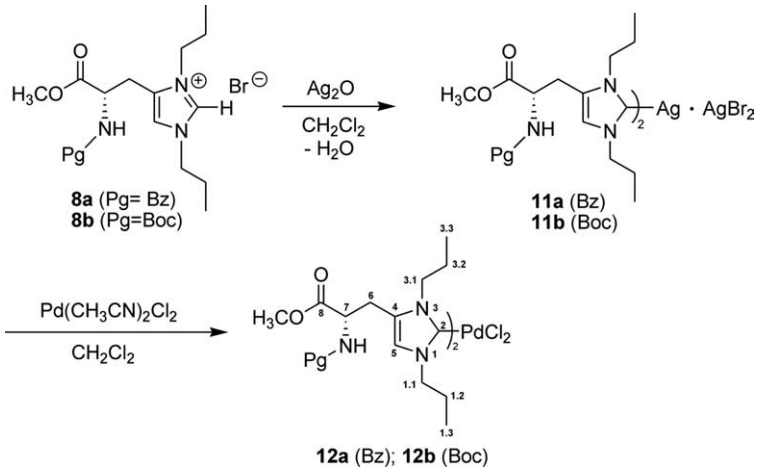


Scheme 4.

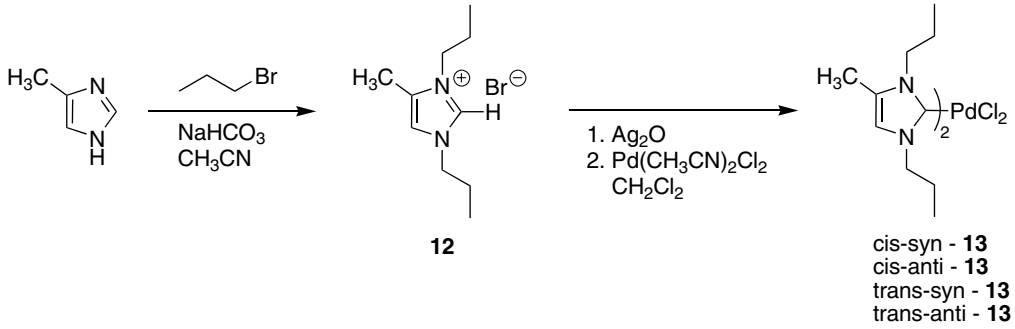
were followed, one involving the isolated Ag-carbene complexes **11** as reagents for the transmetallation step; alternatively, the systems **11** were in situ generated from the corresponding histidinium salts by treatment with silver oxide, and then $Pd(CH_3CN)_2Cl_2$ was added to effect the transmetallation. The formation of both the (carbene)$_2PdCl_2$ products **12a** (Bz) and **12b** (Boc) was practically quantitative. These two products were isolated in >90% (**12a**) or >80% (**12b**) yield, respectively. Optical activity is retained through the transmetallation step from Ag to Pd. However, in each case a mixture of four stereoisomers was formed. This was evident from a splitting of many of the NMR signals of these compounds into sets of four signals resulting from the presence of these isomers (e.g., the **12a**: C2 ^{13}C NMR resonance: δ 170.2, 169.99, 169.83, 169.77). We assume that we have here observed two pairs of *cis*- and *trans*-L_2PdCl_2. These are characterized by a *syn*- or *anti*-arrangement at the substituents at carbon atom C4 of the imidazol-2-ylidene ring in a situation where the heterocyclic ligand plane and the major plane of the square-planar L_2PdCl_2 framework are orthogonal *and* the rotation around the (imidazol-2-ylidene)–C2–Pd vector is frozen on the NMR time scale [15]. Although this can safely be assumed we have prepared an achiral closely related model system to support this likely interpretation.

For this purpose we alkylated 4-methylimidazol with *n*-propylbromide/$NaHCO_3$. The resulting imidazolium salt [16] was then deprotonated by treatment with silver oxide in dichloromethane and the resulting 4-methyl-imidazol-2-ylidene ligand system transmetallated to palladium. The resulting (carbene)$_2PdCl_2$ system **13** can again form a set of four isomers (*cis–syn*-, *cis–anti*, *trans–syn*- and *trans–anti*-**13**). A near to equimolar mixture of these four isomers was actually formed, as is evident from the observation of the respective "quadrupletts" of NMR signals (e.g., imidazol-2-ylidene C2 ^{13}C NMR resonances at δ 169.03, 169.00, 168.74 and 168.72). Heating of a sample of the four **13** isomers in d_2-tetrachlorethane showed the coalescence to the two pairs of C4 ^{13}C NMR (δ 129.31, 129.28, 129.20, 129.17) to a single pair of such signals (*cis*-**13**/*trans*-**13**) at ca. 90 °C, which emphasizes the rather large rotational barrier around the carbene–C2–Pd vector in these complexes (**13**) and their related chiral analogues **12** (see above) (see Scheme 6).

Single crystals of the *trans–anti*-**13** isomer that were suited for an X-ray crystal structure determination were obtained from dichloromethane. The structure of the complex is distorted square planar. The two halide ligands



Scheme 5.



Scheme 6.

(70% Cl and 30% Br because of some halide exchange) are in *trans*-positions as are the imidazol-2-ylidene ligand (see Fig. 3). The planes of the ''Arduengo-carbene'' ligands are oriented normal to the central N_2X_2Pd plane.

The C2–Pd bond length amounts to 2.047(5) Å, which is in a typical range [17]. In this general arrangement the methyl groups at C4 of the carbene ligands could be oriented on the same (*syn*) or different faces (*anti*) relative to

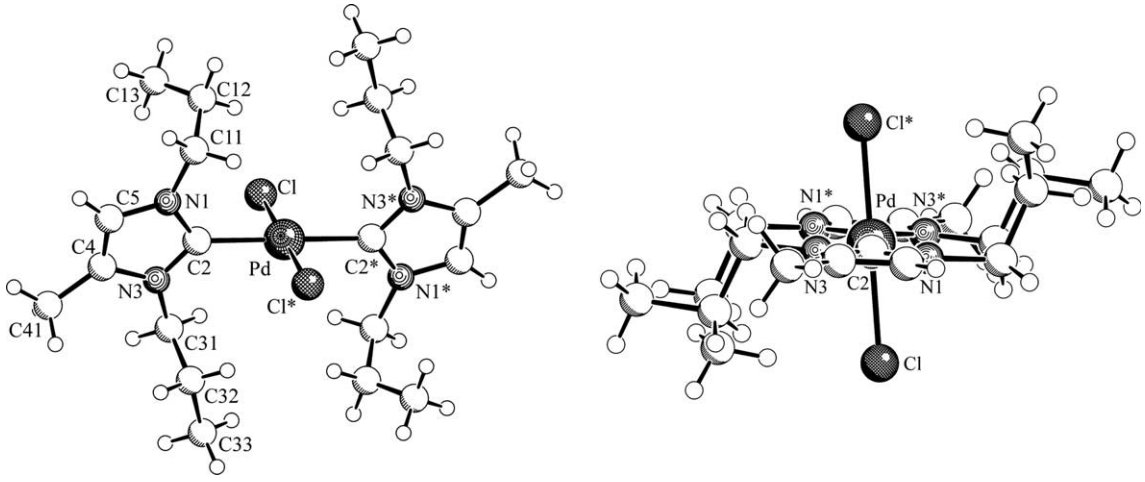
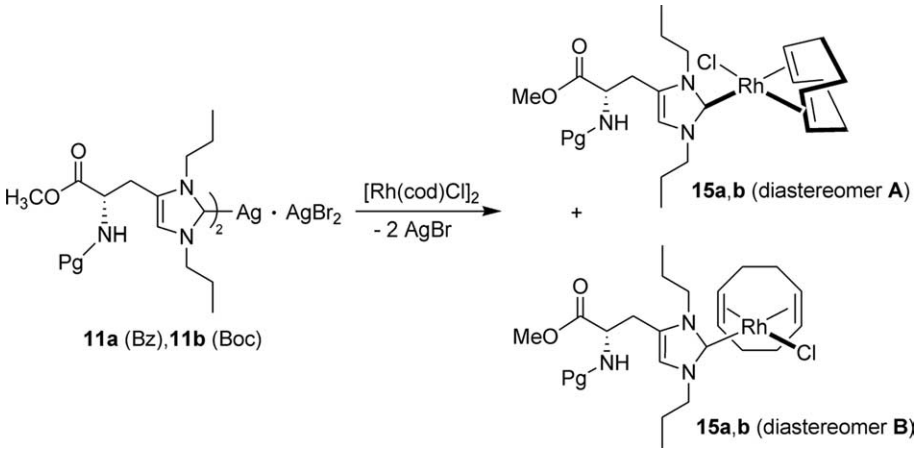


Fig. 3. Two views of the molecular structure of the *trans-anti*-**13** isomer. Selected bond lengths (Å) and angles (°):Pd–C2 2.047(5), Pd–Cl 2.311(14), Pd-Br 2.384(15), N1–C2 1.351(6), N1–C5 1.381(7), N1–C11 1.465(8), C2–N3 1.327(6), N3–C4 1.401(7), N3–C31 1.437(7), C4–C5 1.292(8), C4–C41 1.521(9); Cl–Pd–Cl* 180.0(5), Cl–Pd–C2 90.3(3), Pd–C2–N1 127.7(4), Pd–C2–N3 127.5(4), C2–N1–C5 110.1(5), C2–N1–C11 124.6(5), C5–N1–C11 125.3(5), N1–C2–N3 104.8(4), C2–N3–C4 110.4(5), C2–N3–C31 122.7(4), C4–N3–C31 126.9(5), N3–C4–C5 106.9(5), C5–C4–C41 131.0(6), N3–C4–C41 122.1(5), N1–C5–C4 107.8(5).



Scheme 7.

the central plane. In this structure they are anti-oriented at the *trans*-L_2PdX_2 framework.

We have also prepared two rhodium complexes of the L-histidine-derived carbene ligands. For that purpose the $(carbene)_2Ag \cdot AgBr_2$ reagents **11a**,**b** (see above) were each treated with $[Rh(cod)Cl]_2$ (**14**) [18]. Transmetallation gave the (carbene)RhCl(cod) complexes **15a** (Bz) and **15b** (Boc) in 65% and 73% yield, respectively. Each of the complexes was obtained as a ca. 1:0.8 mixture of two diastereoisomers. This became evident by the observation of the respective pairs of e.g., the carbene C2 ^{13}C NMR resonances of the isomers **15a-A** (δ 183.04) and **15a-B** (δ 182.98) each with a ^1J(Rh,C) coupling constant of ca. 51.5 Hz.

One may assume a distorted square planar geometry of the complexes **15** with the carbene ligand plane oriented normal to the major complex framework plane and a hindered rotation around the carbene ligand C2-Rh vector [19]. This orientations results in the presence of an element of axial chirality inside the framework. Together with the additional chirality center in the side chain of the L-histidine derived unsymmetrically substituted imidazol-2-ylidene ligand this gives rise to the occurrence of pairs of diastereomers of the compound **15**, as it is experimentally observed.

A consequence of this structure is that all four carbons of each pair of cod C=C double bonds become different. Consequently, sets of four cod C=C ^{13}C NMR signals were observed of each of the diastereomers **15a-A** and **15a-B** (**A**: δ 98.14, 97.74, 68.82, 68.08; **B**: δ 98.14, 97.78, 68.72, 67.97) (see Scheme 7).

3. Conclusion

This study has shown that L-histidine derived imidazolium salts, some of which have the potential to serve as useful chiral ionic liquids, and their related chiral imidazol-2-ylidene ligands and their metal complexes are readily available by the synthetic routes described in this article. It will be investigated if derivatives of such systems may become useful solvents, reagents or catalysts in reactions proceeding with transfer of their chirality features.

4. Experimental

4.1. General information

Solvents were dried and distilled under argon prior to use or purified by a chromatographic solvent purification system. Organometallic reactions were carried out under argon using Schlenk-type glassware or in a glovebox. For additional general information, including a list of instruments used for spectroscopic and physical characterization of the compounds see [20]. X-ray crystal structure analyses were done using Enraf Nonius CAD4 and Nonius Kappa-CCD diffractometers. For the programs used see [21]. Bz-His-OMe was synthesized according to the literature procedures [7]. NMR assignments were mostly secured by additional 2D NMR measurements.

4.2. Synthesis of rac-7*a*

A solution of Meerwein's reagent $[Et_3O^+BF_4^-]$ (15.7 g, 82.8 mmol) in dichloromethane was slowly added via syringe pump to a solution of the sodium salt of *N*-(α)-benzoyl-L-histidine methyl ester [Na(Bz-His-OMe)] (8.15 g, 27.6 mmol) in 50 ml of CH_2Cl_2 over 4 h at ambient temperature. After stirring overnight, the $NaBF_4$ precipitate was filtered off and the solvent removed in vacuo. The components of the mixture were separated by column chromatography (silicagel, CH_2Cl_2/MeOH/NH_3: 75/10/1 *rac*-**7a**: $R_f = 0.18$). The trialkylated product was obtained in 26% yield (3.2 g). mp 124 °C (DSC). ^1H NMR (600 MHz, 298 K, CD_3OD): $\delta = 8.83$ (s, 1H, 2-H); 7.52 (m, 1H, *p*-Ph); 7.44 (m, 2H, *m*-Ph); 7.31 (s, 1H, 5-H); 7.16 (m, 2H, *o*-Ph); 4.31 (m, 1H, 10-H); 4.26 (m, 1H, 7-H); 4.21 (m, 2H, 1.1-H); 4.20 (m, 1H, 10′-H); 4.05 (m, 1H, 3.1-H); 3.94 (m, 1H, 3.1′-H); 3.67 (s, 3H, O–CH_3); 3.18 (ddd, ^4J(H,H) = 0.6 Hz, ^3J(H,H) = 4.6 Hz, ^2J(H,H) = 15.4 Hz, 1H, 6-H); 3.11 (ddd, ^4J(H,H) = 0.6 Hz, ^3J(H,H) = 8.2 Hz,

^2J(H,H) = 15.4 Hz, 1H, 6′-H); 1.50 (t, ^3J(H,H) = 7.4 Hz, 3H, 1.2-H); 1.34 (t, ^3J(H,H) = 7.2 Hz, 3H, 3.2-H); 1.31 (t, ^3J(H,H) = 7.1 Hz, 3H, 11-H). $^{13}C\{^1H\}$ NMR (150 MHz, 298 K, CD_3OD): δ = 173.1 (C, C_8); 166.9 (C, C_9); 135.9 (C, C_2); 133.3 (C, C_4); 133.0 (C, *i*-Ph); 131.1 (CH, *p*-Ph); 129.8 (CH, *m*-Ph); 128.5 (CH, *o*-Ph); 121.7 (CH, C_5); 63.3 (CH_2, C_{10}); 62.0 (CH, C_7); 53.0 (CH_3, O–CH_3); 45.9 (CH_2, $C_{1.1}$); 43.3 (CH_2, $C_{3.1}$); 28.3 (CH_2, C_6); 15.6 (CH_3, $C_{1.2}$); 15.0 (CH_3, $C_{3.2}$); 14.6 (CH_3, C_{11}). HR-MS ($C_{20}H_{28}BF_4N_3O_3$, MW = 445.26) (ESI, *m*/*z*): calcd. 358.2131; found: 358.2123 $[C_{20}H_{28}N_3O_3]^+$ $[M - BF_4^-]^+$. IR (KBr): $\tilde{\nu}$ = 3487 (br), 3174 (w), 3135 (w), 3104 (vw), 2978 (w), 2943 (vw), 2904 (vw), 1748 (vs), 1648 (s), 1604 (w), 1556 (w), 1452 (w), 1374 (w), 1283 (s), 1204 (s), 1169 (s), 1060 (br), 1000 (w), 852 (w), 783 (w), 709 (w), 652 (w), 522 (w). $[\alpha]^{20}$ (λ) = 0 (589), 0 (578), 0 (546), 0 (436), 0 (365) (c = 8.1, $CHCl_3$).

4.3. X-ray crystal structure analysis of rac-7a

Formula $C_{20}H_{28}N_3O_3 \cdot BF_4$, MW = 445.26, colourless crystal 0.60 × 0.40 × 0.15 mm, a = 8.715(1) Å, b = 9.389 (1) Å, c = 31.953(1) Å, α = 81.61(1)°, β = 89.98(1)°, γ = 62.54(1)°, V = 2288.5(4) Å^3, ρ_{calc} = 1.292 g cm^{-3}, μ = 1.08 cm^{-1}, no absorption correction ($0.938 \leqslant T \leqslant 0.984$), Z = 4, triclinic, space group $P\bar{1}$ (No. 2), λ = 0.71073 Å, T = 198 K, ω and ϕ scans, 13 336 reflections collected ($\pm h, \pm k, \pm l$), $[(\sin\theta)/\lambda] = 0.59$ Å^{-1}, 7899 independent (R_{int} = 0.032) and 5251 observed reflections [$I \geqslant 2\sigma(I)$], 659 refined parameters, R = 0.064, wR_2 = 0.169, maximum (minimum) residual electron density 0.42 (−0.28) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms, anions heavily disordered and refined with split positions.

4.4. Preparation of rac-7b

The reaction of [Na(Bz-His-OEt)] (4.6 g, 14.87 mmol) with $[Et_3O^+BF_4^-]$ (9.89 g, 52.1 mmol) was carried out analogously as the reaction described above. The product *rac*-**7b** was isolated in 30% yield (2.08 g) after column chromatography (R_f = 0.14, silica gel, CH_2Cl_2/MeOH/NH_3: 75/10/1). mp 122 °C (DSC). ^{1}H NMR (400 MHz, 298 K, $CDCl_3$): δ = 8.93 (s, 1H, 2-H); 7.60 (m, 1H, *p*-Ph); 7.42 (m, 2H, *m*-Ph); 7.17 (m, 2H, *o*-Ph); 6.96 (s, 1H, 5-H); 4.3–4.1 (m, 8H, 1.1, 3.1, 9-H, 12-H); 4.02 (d, ^3J(H,H) = 7.6 Hz, 1H, 7-H); 3.03 (m, 1H, 6-H); 1.49, 1.48 (t, ^3J(H,H) = 7.2 Hz, each 3H (double bond isomers), 13-H); 1.40 (t, ^3J(H,H) = 7.2 Hz, 3H, 10-H); 1.31 (t, ^3J(H,H) = 7.2 Hz, 2× 3H (double bond isomers), 1.2-H); 1.23 (t, ^3J(H,H) = 6.8 Hz, 2× 3H (double bond isomers), 3.2-H). $^{13}C\{^1H\}$ NMR (100 MHz, 298 K, $CDCl_3$): δ = 170.9 (C, C_8); 165.5 (C, C_{11}); 132.9 (C, C_4); 132.8 (C, *i*-Ph); 135.3 (CH, C_2); 131.9, 131.4 (each CH (double bond isomers), *p*-Ph); 130.1, 129.5 (each CH (double bond isomers), *m*-Ph); 128.8, 128.3 (each CH (double bond isomers), *o*-Ph) 119.5 (CH, C_5); 61.7 (CH_2, C_{12}); 60.6 (CH_2, C_9); 62.3 (CH, C_7); 42.5 (CH_2, $C_{1.1}$); 45.1 (CH_2, $C_{3.1}$); 27.7 (CH_2, C_6); 14.9 (CH_3, C_{10}); 15.1 (CH_3, C_{13}); 14.2 (CH_3, $C_{3.2}$); 14.1 (CH_3, $C_{1.2}$). HR-MS ($C_{21}H_{30}BF_4N_3O_3$, MW = 459.29) (ESI, *m*/*z*): calcd. 372.2287; found: 372.2258 $[C_{21}H_{30}N_3O_3]^+$ $[M - BF_4^-]^+$. IR (KBr): $\tilde{\nu}$ = 3474 (w), 3165 (s), 3135 (s), 3100 (w), 2978 (s), 2943 (s), 2908 (s), 1734 (s), 1661 (s), 1600 (s), 1483 (s), 1443 (s), 1365 (s), 1287 (s), 1174 (s), 1061 (br), 856 (w), 774 (s), 713 (s), 657 (w), 522 (w). $[\alpha]^{20}$ (λ) = −1.5 (589), −1.6 (578), −1.8 (546), −3.1 (436) (c = 11.0, EtOH).

4.5. X-ray crystal structure analysis of rac-7b

Formula $C_{21}H_{30}N_3O_3 \cdot BF_4$, MW = 459.29, colourless crystal 0.30 × 0.20 × 0.03 mm, a = 8.709(2) Å, b = 9.245 (2) Å, c = 17.049(3) Å, α = 84.30(2)°, β = 81.44(1)°, γ = 62.97(2)°, V = 1208.4(4) Å^3, ρ_{calc} = 1.262 g cm^{-3}, μ = 8.89 cm^{-1}, empirical absorption correction via ψ scan data ($0.776 \leqslant T \leqslant 0.974$), Z = 2, triclinic, space group $P\bar{1}$ (No. 2), λ = 1.54178 Å, T = 223 K, $\omega/2\theta$ scans, 4385 reflections collected ($+h, \pm k, \pm l$), $[(\sin\theta)/\lambda] = 0.59$ Å^{-1}, 4085 independent (R_{int} = 0.041) and 1920 observed reflections [$I \geqslant 2\sigma(I)$], 331 refined parameters, R = 0.072, wR_2 = 0.254, maximum (minimum) residual electron density 0.35 (−0.24) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms, due to crystal size and form diffracting power was low.

4.6. Synthesis of [Bz-His(n-propyl)$_2$-OMe$^+$Br$^-$] (8a)

Compound [Bz-His-OMe] (**4a**) (133.6 g, 0.49 mol) and 164.7 g (1.69 mol, 4 equiv.) of $NaHCO_3$ were suspended in 1.2 l acetonitrile. 1-Bromopropane (600 ml, 12.3 mol, 25 equiv.) were slowly added and the suspension was stirred under argon for 60 h at 65 °C. The end of the reaction was monitored by ^{1}H NMR of samples taken. The mixture was allowed to cool to room temperature, filtered and the solvent removed in vacuo. The residue was dissolved in water (500 ml) and extracted with 400 ml of $CHCl_3$. The aqueous phase was stripped in vacuo and the product **8a** dried. The organic phase was extracted with water (3 × 150 ml). The water was removed and the product dried in vacuo. The product **8a** is hygroscopic. Combined yield 154.1 g (72%), mp 39 °C (DSC). Anal. Calc. for $C_{20}H_{28}BrN_3O_3$ (MW = 437.36): C, 54.80; H, 6.44; N, 9.59. Found: C, 54.33; H, 6.44; N, 9.62%. ^{1}H NMR (600 MHz, 298 K, $CDCl_3$): δ = 9.62 (s, 1H, 2-H); 8.77 (d, ^3J(H,H) = 7.8 Hz, 1H, N–H); 8.03 (m, 2H, *o*-Ph); 7.55 (s, 1H, 5-H); 7.43 (m, 1H, *p*-Ph); 7.35 (m, 2H, *m*-Ph); 4.94 (m, 1H, 7-H); 4.20 (m, 1H, 3.1-H); 4.10 (m, 1H, 3.1′-H); 4.06 (m, 2H, 1.1-H); 3.71 (m, 1H, 6-H); 3.71 (s, 3H, O–CH_3); 3.32 (dd, ^3J(H,H) = 4.1 Hz, ^2J(H,H) = 16.0 Hz, 1H, 6′-H); 1.87 (m, 2H, 3.2-H); 1.75 (m, 2H, 1.2-H); 0.91 (t, ^3J(H,H) = 7.3 Hz, 3H, 3.3-H); 0.77 (t, ^3J(H,H) = 7.3 Hz, 3H, 1.3-H). $^{13}C\{^1H\}$ NMR (150 MHz, 298 K, $CDCl_3$): δ = 170.8 (C, C_8); 167.5 (C, C_9); 135.7 (C, C_2); 132.6 (C, *i*-Ph); 132.0 (CH, *p*-Ph); 132.0 (C, C_4); 128.4 (CH, *m*-Ph); 127.8 (CH, *o*-Ph); 120.5 (CH, C_5); 52.9

(CH_3, O–CH_3); 48.8 (CH_2, $C_{3.1}$); 51.3 (CH_2, $C_{1.1}$); 51.0 (CH, C_7); 23.32 (CH_2, $C_{1.2}$); 23.27 (CH_2, $C_{3.2}$); 25.3 (CH_2, C_6); 10.8 (CH_3, $C_{3.3}$); 10.5 (CH_3, $C_{1.3}$). MS ($C_{20}H_{28}BrN_3O_3$, MW = 437.36) (ESI, *m/z*): 358.4 $[M - Br^-]^+$. IR (KBr): $\tilde{\nu}$ = 3208 (br), 2965 (br), 2874 (vs), 2352 (vw), 1748 (vs), 1656 (vs), 1600 (w), 1535 (vs), 1487 (s), 1443 (w), 1339 (s), 1304 (s), 1174 (s), 1087 (w), 1035 (w), 991 (w), 870 (w), 804 (w), 717 (s), 696 (s), 648 (w). $[\alpha]^{20}$ (λ) = −34 (589), −36 (578), −41 (546), −75 (436), −132 (365) (*c* = 9.9, $CHCl_3$). $[\alpha]^{20}$ (λ) = −16.6 (589), −17.4 (578), −20.0 (546), −36.9 (436), −66.2 (365) (*c* = 10.2, MeOH).

4.7. X-ray crystal structure analysis of **8a**

Formula $C_{20}H_{28}N_3O_3Br$, MW = 438.36, colourless crystal 0.20 × 0.15 × 0.06 mm, *a* = 11.920(1) Å, *b* = 13.670 (1) Å, *c* = 14.317(1) Å°, β = 111.31(1)°, *V* = 2173.4(3) Å^3, ρ_{calc} = 1.340 g cm^{-3}, μ = 19.15 cm^{-1}, empirical absorption correction (0.701 ⩽ *T* ⩽ 0.894), *Z* = 4, monoclinic, space group $P2_1$ (No. 4), λ = 0.71073 Å, *T* = 198 K, ω and ϕ scans, 14951 reflections collected ($\pm h, \pm k, \pm l$), [(sin θ)/λ] = 0.66 Å^{-1}, 9584 independent (R_{int} = 0.039) and 7394 observed reflections [$I \geqslant 2\ (I)$], 501 refined parameters, *R* = 0.050, wR_2 = 0.108, Flack parameter 0.001(9), maximum (minimum) residual electron density 0.51 (−0.49) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

4.8. Preparation of [Bz-His(iso-propyl)$_2$-OMe$^+$I$^-$] (**9a**)

In a Schlenk flask [Bz-His-OMe] (**4a**) (1.00 g, 3.66 mmol) and 1.20 g (14.0 mmol, 4 equiv.) $NaHCO_3$ were suspended in dry acetonitrile. iso-Propyliodide (9.15 ml, 92.0 mmol, 25 equiv.) was added and the mixture was refluxed at 65 °C for 3 d with stirring. After cooling the mixture was filtered. Solvent was removed in vacuo. The residue was dissolved in chloroform (30 ml) and extracted with water (5 × 10 ml). Water was removed in vacuo and the hygroscopic product dried. Yield of **9a**: 1.69 g (95%), mp 55 °C (DSC). Anal. Calc. for $C_{20}H_{28}IN_3O_3$ (MW = 438.36): C, 49.49; H, 5.81; N, 8.66. Found: C, 49.23; H, 5.66; N, 8.60%. ^{1}H NMR (600 MHz, 298 K, CD_3OD): δ = 9.15 (d, ^4J(H,H) = 1.7 Hz 1H, 2-H); 7.83 (m, 2H, *o*-Ph); 7.56 (m, 1H, *p*-Ph); 7.56 (s, 1H, 5-H); 7.47 (m, 2H, *m*-Ph); 5.03 (d, ^3J(H,H) = 5.0 Hz, 1H, 7-H); 4.74 (sep., ^3J(H,H) = 6.8 Hz, 1H, 3.1-H); 4.60 (sep., ^3J(H,H) = 6.8 Hz, 1H, 1.1-H); 3.80 (s, 3H, O–CH_3); 3.51 (dd, ^3J(H,H) = 5.0 Hz, ^2J(H,H) = 16.0 Hz, 1H, 6-H); 3.32 (dd, ^3J(H,H) = 10.1 Hz, ^2J(H,H) = 16.0 Hz, 1H, 6′-H); 1.64 (d, ^3J(H,H) = 6.8 Hz, 3H, 3.2-H); 1.56 (d, ^3J(H,H) = 6.8 Hz, 3H, 3.2′-H); 1.48 (d, ^3J(H,H) = 6.8 Hz, 3H, 1.2-H); 1.46 (d, ^3J(H,H) = 6.8 Hz, 3H, 1.2′-H). $^{13}C\{^1H\}$ NMR (150 MHz, 298 K, CD_3OD): δ = 172.0 (C, C_8); 169.9 (C, C_9); 134.4 (C, *i*-Ph); 134.0 (C, C_2); 133.3 (CH, *p*-Ph); 132.6 (C, C_4); 129.7 (CH, *m*-Ph); 128.5 (CH, *o*-Ph); 119.8 (CH, C_5); 54.7 (CH, $C_{1.1}$); 51.9 (CH, $C_{3.1}$); 52.5 (CH, C_7); 53.4 (CH_3, O–CH_3); 26.8 (CH_2, $C_{6'}$); 23.6 (CH_3, $C_{3.2}$); 23.2 (CH_3, $C_{3.2'}$); 23.0 (CH_3, $C_{1.2}$); 23.0 (CH_3, $C_{1.2'}$). MS ($C_{20}H_{28}IN_3O_3$, MW = 438,36) (ESI, *m/z*): 358.4 $[M - I^-]^+$. IR (KBr): $\tilde{\nu}$ = 2978 (w), 1743 (s), 1648 (vs), 1600 (w), 1526 (vs), 1483 (w), 1439 (w), 1296 (w), 1183 (w), 1130 (w), 804 (w), 717 (w), 687 (w), 643 (w). $[\alpha]^{20}$ (λ) = −5.7 (589), −5.8 (578), −6.9 (546), −12.8 (436), −23.0 (365) (*c* = 13.35, MeOH).

4.9. Preparation of [Boc-His(n-propyl)$_2$-OMe$^+$Br$^-$] (**8b**)

Analogously as described above Boc-His-OMe (**4c**) (2.98 g, 11.1 mmol) was reacted with 25.4 ml *n*-propyl bromide (271 mmol) in the presence of 3.75 g (44.6 mmol) of $NaHCO_3$ in acetonitrile (8 d, 65 °C) to yield 4.46 g (92%) of **8b** after the usual aqueous workup, mp 198 °C (decomp., DSC). Anal. Calc. for $C_{18}H_{32}BrN_3O_4 \cdot 1/2H_2O$ (MW = 452.37): C, 47.79; H, 7.58; N, 9.29. Found: C, 48.36; H, 7.47; N, 9.37%. ^{1}H NMR (600 MHz, 298 K, CD_3OD): δ = 9.21 (s, 1H, 2-H); 7.55 (s, 1H, 5-H); 7.24 (ABMX, ^3J(H,H) = 9.4 Hz, 1H, N–H); 4.52 (ABMX, ^3J(H,H) = 4.9 Hz, ^2J(H,H) = 9.4 Hz, 1H, 7-H); 4.23 (m, 2H, 3.1-H); 4.23 (m, 2H, 1.1-H); 3.77 (s, 3H, O–CH_3); 3.33 (ABMX, ^3J(H,H) = 4.9 Hz, ^2J(H,H) = 15.8 Hz, 1H, 6-H); 3.17 (ABMX, ^3J(H,H) = 9.4 Hz, ^2J(H,H) = 15.8 Hz, 1H, 6′-H); 1.94 (m, 2H, 3.2-H); 1.94 (m, 2H, 1.2-H); 1.41 (s, 9H, $C(CH_3)_3$); 1.02 (t, ^3J(H,H) = 7.5 Hz, 3H, 3.3-H); 0.96 (t, ^3J(H,H) = 7.5 Hz, 3H, 1.3-H). $^{13}C\{^1H\}$ NMR (150 MHz, 298 K, CD_3OD): δ = 172.4 (C, C_8); 157.5 (C, C_9); 132.9 (C, C_4); 137.0 (C, C_2); 121.9 (CH, C_5); 80.8 (C, $C(CH_3)_3$); 53.5 (CH_3, O–CH_3); 53.3 (CH, C_7); 49.6 (CH_2, $C_{3.1}$); 52.3 (CH_2, $C_{1.1}$); 26.8 (CH_2, C_6); 28.5 (CH_3, C(CH_3)$_3$); 24.4 (CH_2, $C_{3.2}$); 24.2 (CH_2, $C_{1.2}$); 11.1 (CH_3, $C_{3.3}$); 11.0 (CH_3, $C_{1.3}$). HR-MS ($C_{18}H_{32}BrN_3O_4$, MW = 434.37) (ESI, *m/z*): calc.: 354.2393; found: 354.2392 $[C_{18}H_{32}N_3O_4]^+$ $[M - Br^-]^+$. IR (KBr): $\tilde{\nu}$ = 3235 (br), 3130 (s), 2965 (br), 2874 (s), 1748 (vs), 1700 (vs), 1608 (w), 1565 (s), 1513 (vs), 1452 (s), 1365 (s), 1256 (s), 1169 (s), 1048 (s), 1013 (s), 861 (w), 791 (w), 648 (w), 626 (w), 465 (w). $[\alpha]^{20}$ (λ) = −15.6 (589), −16.1 (578), −18.4 (546), −32.0 (436), −52.2 (365) (*c* = 10.65, MeOH).

4.10. Preparation of [Boc-His(iso-propyl)$_2$-OMe$^+$I$^-$] (**9b**)

Analogously as described above the reaction of 2.00 g (7.43 mmol) of Boc-His-OMe (**4c**) with 16.8 ml (58.2 mmol) of iso-propyl iodide and 2.50 g (29.8 mmol) of $NaHCO_3$ gave 2.47 g (69%) of **9b**, mp 55 °C (DSC). ^{1}H NMR (600 MHz, 298 K, CD_3OD): δ = 9.27 (d,^4J-(H,H) = 1.6 Hz, 1H, 2-H); 7.58 (s, 1H, 5-H); 4.72 (sep., ^3J(H,H) = 6.8 Hz, 1H, 1.1-H); 4.69 (sep., ^3J(H,H) = 6.7 Hz, 1H, 3.1-H); 4.54 (ABX, ^3J(H,H) = 5.0 Hz, 1H, 7-H); 3.77 (s, 3H, O–CH_3); 3.36 (ABX, ^3J(H,H) = 5.0 Hz, ^2J(H,H) = 15.8 Hz, 1H, 6-H); 3.16 (ABX, ^3J(H,H) = 9.7 Hz, ^2J(H,H) = 15.8 Hz, 1H, 6′-H); 1.63 (d, ^3J(H,H) = 6.7 Hz, 3H, 3.2-H); 1.62 (d, ^3J(H,H) = 6.7 Hz, 3H, 3.2′-H);

1.58 (d, ^3J(H,H) = 6.7 Hz, 3H, 1.2-H); 1.58 (d, ^3J(H,H) = 6.7 Hz, 3H, 1.2′-H); 1.41 (s, 9H, C(CH_3)$_3$). $^{13}C\{^1H\}$ NMR (150 MHz, 298 K, CD_3OD): δ = 172.4 (C, C_8); 157.6 (C, C_9); 133.9 (C, C_2); 132.6 (C, C_4); 119.7 (CH, C_5); 80.9 (C, $C(CH_3)_3$); 54.6 (CH, $C_{3.1}$); 51.8 (CH, $C_{1.1}$); 53.5 (CH, C_7); 53.3 (CH_3, O–CH_3); 28.7 (CH_3, C(CH_3)$_3$); 27.2 (CH_2, C_6); 23.6 (CH_3, $C_{3.2}$); 23.4 (CH_3, $C_{3.2'}$); 23.2 (CH_3, $C_{1.2}$); 23.1 (CH_3, $C_{1.2'}$). HR-MS ($C_{18}H_{32}IN_3O_4$, MW = 481.37): calc.: 354.2393; found: 354.2405 [$C_{18}H_{32}N_3O_4^+$] [M − I^-]$^+$. IR (KBr): $\tilde{\nu}$ = 3421 (vw), 3061 (vs), 2982 (vs), 2312 (vw), 1743 (w), 1704 (w), 1496 (w), 1439 (w), 1365 (w), 1156 (w), 896 (w), 778 (s), 717 (s), 461 (s). $[\alpha]^{20}$ (λ) = −13.3 (589), −14.0 (578), −15.9 (546), −27.7 (436), −44.7 (365) (c = 10.4, CH_3OH).

4.11. Reaction of **8a** with silver oxide, preparation of **11a**: general procedure

Ag_2O (0.52 molar equiv.) are added to a solution of the respective histidinium salt in abs. dichloromethane at room temperature. The mixture is then stirred in the dark for 2 h. The solution is then decanted from the precipitate. Solvent is removed in vacuo and the product dried in vacuo. In some reactions activated molecular sieves were added to remove the reaction water. In this case the mixture was not stirred but only shaken to avoid mechanical decomposition of the mol. sieve pellets.

According to this procedure, 2.00 g (2.29 mmol) of **8a** were reacted with 0.63 g (2.71 mmol) of Ag_2O to give 1.98 g (97%) of **11a**, mp 57 °C, decomp.: 182 °C (DSC). Anal. Calc. for $C_{40}H_{54}Ag_2Br_2N_6O_6$ (MW = 1090.44): C, 44.06; H, 4.99; N, 7.71. Found: C, 45.21; H, 5.03; N, 7.76%. ^1H NMR (600 MHz, 298 K, CD_2Cl_2): δ = 7.94 (m, 2H, *o*-Ph); 7.46 (m, 1H, *p*-Ph); 7.37 (m, 2H, *m*-Ph); 7.12 (s, 1H, 5-H); 7.10 (d, ^3J(H,H) = 3.7 Hz, 1H, N–H); 4.97 (m, 1H, 7-H); 4.08 (m, 1H, 3.1-H); 4.01 (m, 1H, 3.1-H′); 3.93 (m, 2H, 1.1-H); 3.71 (s, 3H, O–CH_3); 3.44 (dd, ^3J(H,H) = 9.2 Hz, ^2J(H,H) = 16.1 Hz, 1H, 6-H); 3.29 (dd, ^3J(H,H) = 4.7 Hz, ^2J(H,H) = 16.1 Hz, 1H, 6-H′); 1.81 (m, 2H, 3.2-H); 1.72 (m, 2H, 1.2-H); 0.92 (t, ^3J(H,H) = 7.5 Hz, 3H, 3.3-H); 0.79 (t, ^3J(H,H) = 7.4 Hz, 3H, 1.3-H). $^{13}C\{^1H\}$ NMR (150 MHz, 298 K, CD_2Cl_2): δ = 180.0 (C, C_2); 171.3 (C, C_8); 167.1 (C, C_9); 133.6 (C, *i*-Ph); 133.4 (C, C_4); 132.0 (CH, *p*-Ph); 128.6 (CH, *m*-Ph); 127.7 (CH, *o*-Ph); 119.8 (CH, C_5); 53.5 (CH_2, $C_{1.1}$); 52.5 (CH_3, O–CH_3); 51.5 (CH, C_7); 50.5 (CH_2, $C_{3.1}$); 26.3 (CH_2, C_6); 25.1 (CH_2, $C_{3.2}$); 24.6 (CH_2, $C_{1.2}$); 10.7 (CH_3, $C_{1.3}$); 11.0 (CH_3, $C_{3.3}$). HR-MS ($C_{40}H_{54}Ag_2Br_2N_6O_6$, MW = 1090.44) (ESI, LM [$CHCl_3$/CH_3CN], m/z): calc.: 821.3150/822.3181/823.3154/824.3181/825.3208; found: 821.3125/822.3165/823.3134/824.3143/825.3153 [$C_{40}H_{54}AgN_6O_6$] [M − $AgBr_2$]$^+$. IR (KBr): $\tilde{\nu}$ = 3856 (w), 3752 (w), 3350 (br), 2965 (s), 2931 (s), 2878 (w), 2365 (vw), 2339 (vw), 1739 (vs), 1660 (vs), 1526 (s), 1491 (w), 1456 (w), 1339 (w), 1226 (w), 1196 (w), 1091 (vw), 1022 (vw), 804 (w), 717 (w). $[\alpha]^{20}$ (λ) = +13.9 (589), +16.8 (578), +20.6 (546), +35.0 (436), +54.3 (365) (c = 10.5, $CHCl_3$) (see Fig. 4).

4.12. Reaction of **9a** with silver oxide, preparation of **11b**

According to the general procedure, 1.01 g (2.33 mmol) of **9a** was treated with 0.32 g (1.38 mmol) of Ag_2O to give 1.20 g (96%) of **11b**, mp 173 °C (DSC). Anal. Calc. for $C_{36}H_{62}Ag_2Br_2N_6O_8$ (MW = 1082.46): C, 39.94; H, 5.77; N, 7.76. Found: C, 40.47; H, 5.76; N, 7.71%. ^1H NMR (600 MHz, 298 K, CD_2Cl_2): δ = 6.86 (s, 1H, 5-H); 5.43 (d, ^3J(H,H) = 7.1 Hz, 1H, N–H); 4.55 (d, ^3J(H,H) = 5.6 Hz, 1H, 7-H); 4.05 (m, 1H, 3.1-H); 4.02 (m, 1H, 1.1-H); 4.00 (m, 1H, 3.1′-H); 3.74 (s, 3H, O–CH_3); 3.16 (dd, ^3J(H,H) = 5.6 Hz, ^2J(H,H) = 16.0 Hz, 1H, 6-H); 3.00 (dd,

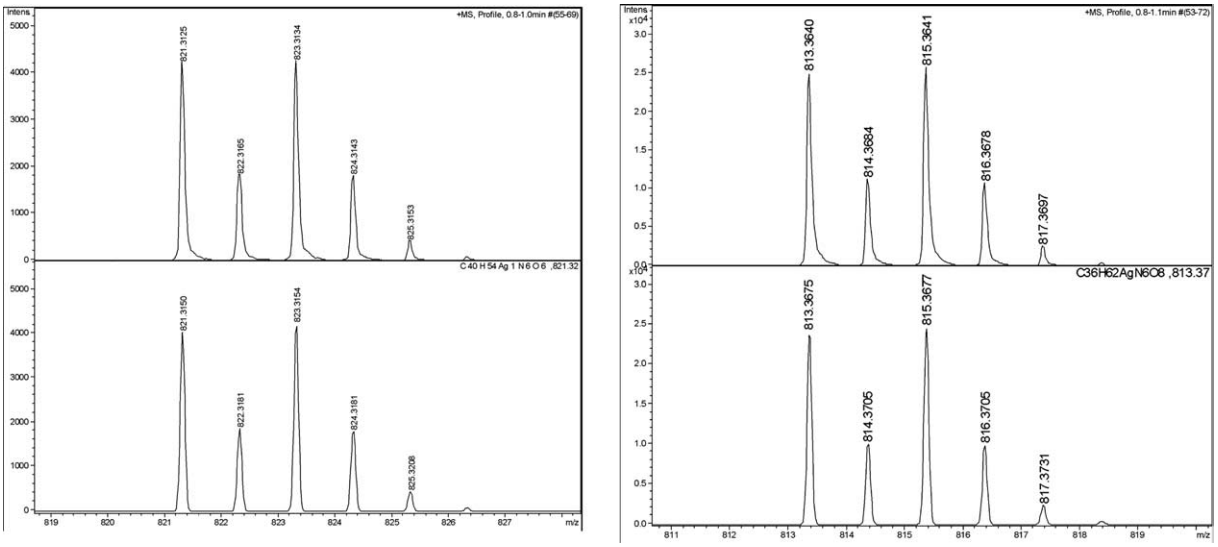


Fig. 4. Measured (top) and calculated (bottom) ESI HRMS of **11a** (i.e., $C_{40}H_{54}AgN_6O_6$, [M − $AgBr_2$]$^+$, left) and **11b** (i.e., $C_{36}H_{62}AgN_6O_8$, [M − $AgBr_2$]$^+$, right).

^3J(H,H) = 7.6 Hz, ^2J(H,H) = 16.0 Hz 1H, 6′-H); 1.82 (m, 2H, 1.2-H); 1.81 (m, 2H, 3.2-H); 1.41 (s, 9H, C(CH_3)$_3$); 0.95 (t, ^3J(H,H) = 7.3 Hz, 3H, 3.3-H); 0.91 (t, ^3J(H,H) = 7.3 Hz, 3H, 1.3-H). ^{13}C{^{1}H} NMR (150 MHz, 298 K, CD_2Cl_2): δ = 181.2 (C, C_2); 171.7 (C, C_8); 155.5 (C, C_9); 129.9 (C, C_4); 119.4 (CH, C_5); 80.6 (C, $C(CH_3)_3$); 52.9 (CH, C_7); 54.1 (CH_2, $C_{1.1}$); 53.0 (CH_3, O–CH_3); 51.0 (CH_2, $C_{3.1}$); 27.8 (CH_2, C_6); 28.3 (CH_3, $C(CH_3)_3$); 25.5 (CH_2, $C_{3.2}$); 25.0 (CH_2, $C_{1.2}$); 11.3 (CH_3, $C_{3.3}$); 11.2 (CH_3, $C_{1.3}$). HR-MS ($C_{36}H_{62}Ag_2Br_2N_6O_8$, MW = 1082.46) (ESI, LM [$CHCl_3$/CH_3CN], *m*/*z*): calc.: 813.3675/814.3705/815.3677/816.3705/817.3731; found: 813.3640/814.3684/815.3641/816.3678/817.33697 [$C_{36}H_{62}AgN_6O_8$] [M − $AgBr_2$]$^+$. IR (KBr): $\tilde{\nu}$ = 3387 (br), 3113 (w), 2965 (s), 2930 (s), 2869 (w), 1752 (s), 1717 (vs), 1617 (w), 1517 (w), 1456 (s), 1365 (s), 1252 (s), 1161 (vs), 1056 (w), 1017 (w), 861 (vw), 783 (w), 639 (w), 461 (w). $[\alpha]^{20}$ (λ) = +25.8 (589), +27.2 (578), +31.1 (546), +55.3 (436), +94.2 (365) (*c* = 10.9, $CHCl_3$).

4.13. Preparation of the palladium complexes: general procedure

Silver oxide (0.52 g molar equiv.) ware added to a solution of the respective histidinium salt in dichloromethane. The mixture is stirred in the dark for 1 h at ambient temperature. Then 0.50 molar equiv. of $Pd(CH_3CN)_2Cl_2$ in abs. CH_2Cl_2 is added and the mixture again stirred for 1 h at room temperature. Silver halide is precipitated during this time and the solution decanted from the precipitate. Solvent was removed in vacuo and the product dried in vacuo.

4.13.1. Reaction of in situ generated **11a** with $Pd(CH_3CN)_2Cl_2$: preparation of **12a**

The carbene silver complex **11a** was in situ generated by treatment of **8a** (2.00 g, 4.58 mmol) with 0.62 g (2.68 mmol) of Ag_2O in dichloromethane, as described in the general procedure, followed by the reaction with 0.59 g (2.28 mmol) of $Pd(CH_3CN)_2Cl_2$ to yield 3.51 g (86%) of complex **12a**, mp 80 °C (DSC). The NMR analysis revealed the presence of four diastereoisomers (I–IV). ^{1}H NMR (600 MHz, 298 K, $CDCl_3$): δ = 7.74 (m, 2H, *o*-Ph(I + II)); 7.46 (m, 1H, *p*-Ph(I + II)); 7.39 (m, 2H, *m*-Ph(I + II); 6.86 (d, ^3J(H,H) = 7.4 Hz, 1H, N–H(III)); 6.85 (d, ^3J(H,H) = 7.6 Hz, 1H, N–H(I)); 6.82 (d, ^3J(H,H) = 7.7 Hz, 1H, N–H(II + IV)); 6.65 (s, 1H, 5(III)-H); 6.64 (s, 1H, 5(I)-H); 6.63 (s, 1H, 5(II)-H); 5.01 (m, 1H, 7(I)-H); 5.00 (m, 1H, 7(II)-H); 4.46–4.30 (m, each 1H, 3.1(I–IV)-H); 4.39–4.31 (m, each 2H, 1.1(I–IV)-H); 4.27–3.19 (m, each 1H, 3.1′(I–IV)-H); 3.72 (s, 3H, O–CH_3(I + II)); 3.71, 3.70 (s, 3H, O–CH_3(III + IV)); 3.16 (m, each 2H, 6(I–IV)-H); 2.14–1.95 (m, each 2H, 3.2(I–IV)-H and 3.2(I–IV)-H′); 1.00 (t, ^3J(H,H) = 7.3 Hz, 3H, 3.3(I)-H); 0.99 (t, ^3J(H,H) = 7.3 Hz, 3H, 3.3(II)-H); 0.97 (t, ^3J(H,H) = 7.6 Hz, 3H, 1.3(II)-H); 0.96 (t, ^3J(H,H) = 7.5 Hz, 3H, 1.3(I)-H); 0.94 (t, ^3J(H,H) = 7.5 Hz, 3H, 3.3 or 1.3 (III, IV)-H); 0.93 (t, ^3J(H,H) = 7.5 Hz, 3H, 3.3 or 1.3 (III, IV)-H); 0.92 (2× t, ^3J(H,H) = 7.5 Hz, each 3H, 3.3 or 1.3 (III, IV)-H). ^{13}C{^{1}H} NMR (150 MHz, 298 K, $CDCl_3$): δ = 171.38 (C, $C_{8(I+II)}$); 170.02 (C, $C_{2(I)}$); 169.99 (C, $C_{2(II)}$); 169.83, 169.77, (C, $C_{2(isomers)}$); 167.27 (C, $C_{9(I+II)}$); 167.20 (C, $C_{9(isomer)}$); 133.10 (C, *i*-Ph(I + II)); 131.96 (CH, *p*-Ph(I + II)); 128.60 (CH, *m*-Ph(I + II)); 128.40, 128.31, 128.29 (C, $C_{4(isomers)}$); 128.19 (C, $C_{4(I)}$); 128.17 (C, $C_{4(II)}$); 127.09 (CH, *o*-Ph(I + II)); 119.13, 118.73, 118.70, 118.59, 118.57 (CH, $C_{5(isomers)}$); 118.56 (CH, $C_{5(II)}$); 118.44 (CH, $C_{5(I)}$); 52.92 (CH_3, O–CH_3(II)); 52.90 (CH_3, O–CH_3(I)); 52.42, 52.39, 52.37, 52.33 (CH_2, $C_{1.1(isomers)}$); 52.26 (CH_2, $C_{1.1(II)}$); 52.22 (CH_2, $C_{1.1(I)}$); 51.61, 51.57 (CH, $C_{7(isomers)}$); 51.50 (CH, $C_{7(I+II)}$); 49.29, 49.18 (CH, $C_{3.1(isomers)}$); 49.04 (CH, $C_{3.1(I+II)}$); 26.77 (br, CH_2, $C_{6(isomers)}$); 26.73 (CH_2, $C_{6(I+II)}$); 24.66 (CH_2, $C_{3.2(I)}$); 24.59 (CH_2, $C_{3.2(II)}$); 24.43, 24.38 (CH_2, $C_{1.2(isomers)}$); 24.26 (CH_2, $C_{1.2(I)}$);, 24.14 (CH_2, $C_{1.2(II)}$); 24.07, 23.97 (CH_2, $C_{1.2(isomers)}$); 11.39 (CH_3, $C_{3.3(II)}$); 11.37 (CH_3, $C_{3.3(I)}$); 11.29 (CH_3, $C_{1.3(I)}$); 11.27 (CH_3, $C_{1.3(II)}$). HR-MS ($C_{40}H_{54}Cl_2N_6O_6Pd$, MW = 892.22) (ESI, LM[$CHCl_3$/CH_3CN], *m*/*z*): calc.: 853.2829/854.2843/855.2834/8562844/857.2827/858.2853/859.2832/860.2857/861.2839; found: 853.2827/854.2769/855.2789/856.2811/857.2780/858.2789/859.2799/860.2823/861.2843 [$C_{40}H_{54}ClN_6O_6Pd$]$^+$ [M − Cl^-]$^+$. IR (KBr): $\tilde{\nu}$ = 3321 (br), 3121 (w), 3056 (w), 2961 (s), 2930 (s), 2874 (w), 1743 (vs), 1647 (vs), 1535 (s), 1465 (w), 1426 (w), 1343 (w), 1269 (w), 1217 (w), 1100 (w), 1022 (s), 809 (s), 713 (s), 683 (s). $[\alpha]^{20}$ (λ) = +34 (589), +36 (578), +41 (546), +74 (436) (*c* = 10.25, $CHCl_3$) (see Fig. 5).

4.13.2. Preparation of **12b**

According to the general procedure, 1.26 g (2.61 mmol) of **9a** was treated with Ag_2O (0.39 g, 1.70 mmol) and then $Pd(CH_3CN)_2Cl_2$ (0.26 g, 1.45 mmol) to yield 1.90 g (82%) of **12b**, mp 62 °C (DSC). The NMR analysis revealed the presence of four diastereoisomers (I–IV). ^{1}H NMR (600 MHz, 298 K, $CDCl_3$): δ = 6.65, 6.65, 6.64 (s, 1H, 5(II–IV)-H); 6.63 (s, 1H, 5(I)-H); 5.11 (d, ^3J(H,H) = 8.1 Hz, 1H, N–H); 4.55 (m, 1H, 7-H); 4.41 (m, 2H, 1.1-H); 4.33 (m, 2H, 3.1-H) 4.33 (m, isomers of 1.1 or 3.1-H); 3.70 (s, 3H, O–Me); 3.02 (dd, ^3J(H,H) = 4.5 Hz, ^2J(H-H) = 15.8 Hz, 1H, 6(I)-H); 2.91 (dd, ^3J(H,H) = 6.8 Hz, ^2J(H,H) = 15.8 Hz, 1H, 6(I)-H′); 2.10 (m, 2H, 3.2-H); 2.03 (m, 2H, 1.2-H); 1.40 (s, 9H, C(CH_3)$_3$(I)); 1.39, 1.37 (s, 9H, C(CH_3)$_3$(isomers)); 1.03 (t, ^3J(H,H) = 7.0 Hz, 3H, 1.3(I)-H); 1.05, 1.03, 1.02 (each t, ^3J(H,H) = 6.6–7.7 Hz, each 3H, 1.3-H(isomers)); 0.99 (t, ^3J(H,H) = 7.3 Hz, 3H, 3.3(I)-H); 1.01, 1.00, 0.98 (each t, ^3J(H,H) = 6.6–7.7 Hz, each 3H, 3.3-H(isomers)). ^{13}C-{^{1}H} NMR (150 MHz, 298 K, $CHCl_3$): δ = 171.7 (C, C_8); 169.84, 169.82 (I), 169.60, 169.58, 169.20, 169.17 (C, C_2); 155.0 (C, C_9); 128.57, 128.53, 128.44, 128.42, 128.31 (I), 128.28 (C, C_4); 118.56, 118.42, 118.28 (I), 118.15 (CH, C_5); 80.43 (C, $C(CH_3)_3$); 52.81 (CH_3, O–Me(I)); 52.80 (CH_3, O–Me(II)) 52.58, 52.52, 52.48, 52.46, 52.42, 52.41, 52.33, 52.28 (I) (CH_2, $C_{1.1}$); 51.90, 51.85 (CH, C_7); 49.40,

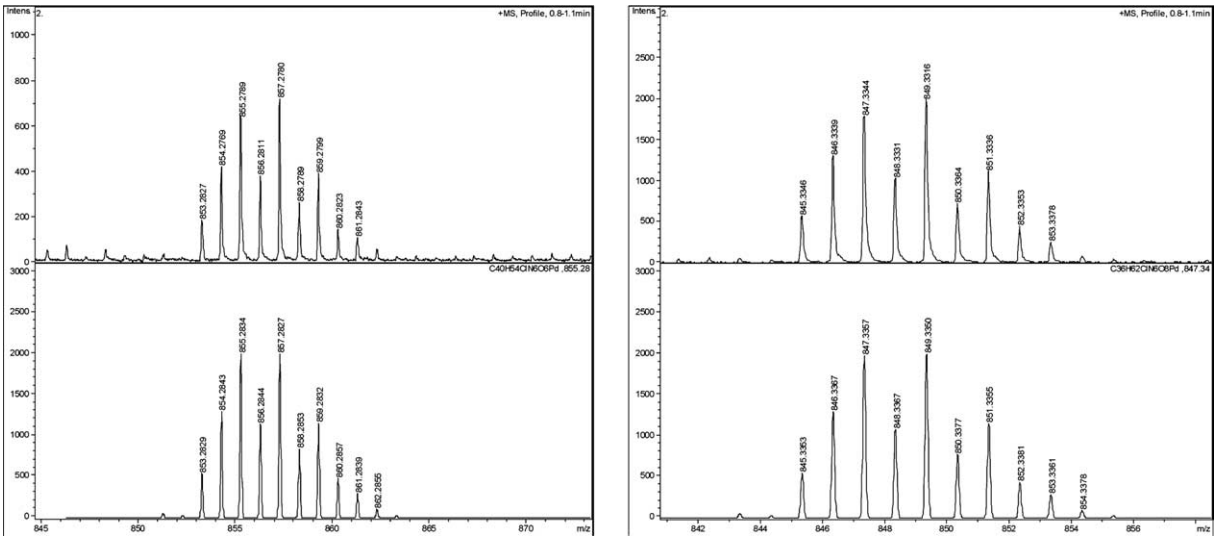


Fig. 5. Experimental (top) and calculated (bottom) ESI HRMS of **12a** (i.e., $C_{40}H_{54}ClN_6O_6Pd^+$, $[M - Cl]^+$, left) and **12b** (i.e., $C_{36}H_{62}ClN_6O_8Pd^+$, $[M - Cl]^+$, right).

49.38, 49.25 (I), 49.10 (CH_2, $C_{3.1}$); 28.1 (CH_3, $C(CH_3)_3$); 27.56, 27.51 (I) (CH_2, C_6); 24.60, 24.54, 24.38, 24.33 (I), 24.22 (I), 24.14, 24.04, 23.96, 23.87 (CH_2, $C_{1.2}$ and $C_{3.2}$); 11.48 (CH_3, $C_{3.3}$); 11.39 (CH_3, $C_{1.3}$). HR-MS ($C_{36}H_{62}Cl_2N_6O_8Pd$, MW = 884.24) (ESI, LM [$CHCl_3$/CH_3CN], *m*/*z*): calc.: 845.3353/846.3367/847.3357/848.3367/849.3350/850.3377/851.3355/852.3381/853.3361; found: 854.3346/846.3339/847.3344/848.3331/849.333316/850.3364/851.3336/852.3353/853.3378 $[C_{36}H_{62}ClN_6O_8Pd]^+$ $[M - Cl^-]^+$. IR (KBr): $\tilde{\nu}$ = 3369 (br), 3121 (w), 2961 (s), 2930 (s), 2878 (w), 1752 (vs), 1704 (vs), 1517 (w), 1461 (w), 1417 (w), 1365 (s), 1265 (s), 1165 (vs), 1061 (w), 1017 (s), 856 (w), 796 (s). $[\alpha]^{20}$ (λ) = +34 (589), +36 (578), +41 (546), +74 (436) (c = 10.5, $CHCl_3$).

4.14. Synthesis of the palladium complexes *13*

Analogously to the general procedure, 500 mg (2.02 mmol) of 1,3-di-*n*-propyl-4-methylimidazolium bromide was dissolved in 100 ml of CH_2Cl_2 and then reacted with Ag_2O (244 mg, 1.05 mmol) in the presence of 0.7 g activated molecular sieves. Subsequent transmetallation was carried out by adding a solution of 262 mg (1.01 mmol) of $Pd(CH_3CN)_2Cl_2$ in 50 ml dichloromethane. After 1 h a precipitate was removed by filtration and the solvent removed in vacuo. The yellow crystalline solid was dried in vacuo to yield 0.85 g (83%) of **13** as a mixture of four isomers (I–IV), mp 221 °C (DSC). ^{1}H NMR (600 MHz, 298 K, $C_2D_2Cl_4$): δ = 6.50 (m, each 1H, 5(III)-H); 6.49 (m, each 1H, 5(IV,I + b)-H); 4.26 (m, 2H, 1.1(III)-H); 4.24 (m, 2H, 3.1(III + b)-H); 2.07 (s, 3H, 6(III)-H); 2.04 (m, 2H, 3.2(I)-H); 1.97 (m, 2H, 1.2(III)-H); 0.99 (m, 3H, 3.3(I)-H); 0.95 (m, 3H, 1.3(I)-H). $^{13}C\{^1H\}$ NMR (150 MHz, 298 K, $C_2D_2Cl_4$): δ ^{13}C = 169.03 (C, $C_{2(I)}$); 169.00 (C, $C_{2(II)}$); 168.74 (C, $C_{2(III)}$); 168.72 (C, $C_{2(IV)}$); 129.32 (C, $C_{4(III)}$); 129.28 (C, $C_{4(IV)}$); 129.20 (C, $C_{4(I)}$); 129.17 (C, $C_{4(II)}$); 118.30 (CH, $C_{5(III)}$); 118.18 (CH, $C_{5(IV+I)}$); 118.06 (CH, $C_{5(II)}$); 52.57 (CH_2, $C_{1.1(III)}$); 52.53 (CH_2, $C_{1.1(IV)}$); 52.42 (CH_2, $C_{1.1(I)}$); 52.39 (CH_2, $C_{1.1(II)}$); 49.51 (CH_2, $C_{3.1(III+b)}$); 49.37 (CH_2, $C_{3.1(I)}$); 49.36 (CH_2, $C_{3.1(II)}$); 24.79 (CH_2, $C_{1.2(III)}$); 24.74 (CH_2, $C_{1.2(IV)}$); 24.74 (CH_2, $C_{1.2(I)}$); 24.64 (CH_2, $C_{1.2(II)}$); 24.58 (CH_2, $C_{3.2(I)}$); 24.56 (CH_2, $C_{3.2(II)}$); 24.54 (CH_2, $C_{3.2(III)}$); 24.47 (CH_2, $C_{3.2(IV)}$); 11.93 (CH_3, $C_{3.3(II)}$); 11.93 (CH_3, $C_{3.3(III)}$); 11.93 (CH_3, $C_{3.3(IV)}$); 11.93 (CH_3, $C_{1.3(II)}$); 11.93 (CH_3, $C_{1.3(III)}$); 11.93 (CH_3, $C_{1.3(IV)}$); 11.93 (CH_3, $C_{1.3(I)}$); 11.93 (CH_3, $C_{3.3(I)}$); 9.96 (CH_3, $C_{6(III)}$); 9.94 (CH_3, $C_{6(IV)}$); 9.92 (CH_3, $C_{6(I)}$); 9.90 (CH_3, $C_{6(II)}$). At 383 K only two isomers (*cis*-**13**/*trans*-**13**) are monitored by NMR (I/II): ^{1}H NMR (600 MHz, 383 K, $C_2D_2Cl_4$): δ = 6.51 (d, ^4J(H,H) = 1.0 Hz, 1H, 5(II)-H); 6.50 (d, ^4J(H,H) = 1.0 Hz, 1H, 5(I)-H); 4.38 (m, each 2H, 1.1(I + II)-H); 4.36 (m, each 2H, 3.1(I + II)-H); 2.12 (s, 3H, 6(II)-H); 2.12 (s, 3H, 6(I)-H); 2.06 (m, each 2H, 3.2(I + II)-H); 2.05 (m, each 2H, 1.2(I + II)-H); 1.06 (t, 3H, 3.3(II)-H); 1.05 (t, 3H, 3.3(I)-H); 1.02 (t, 3H, 1.3(I)-H); 1.02 (t, 3H, 1.3(II)-H). $^{13}C\{^1H\}$ NMR (150 MHz, 383 K, $C_2D_2Cl_4$): δ = 170.41 (C, $C_{2(I)}$); 170.09 (C, $C_{2(II)}$); 129.21 (C, $C_{4(II)}$); 129.08 (C, $C_{4(I)}$); 117.95 (CH, $C_{5(II)}$); 117.95 (CH, $C_{5(I)}$); 52.63 (CH_2, $C_{1.1(II)}$); 52.48 (CH_2, $C_{1.1(I)}$); 49.61 (CH_2, $C_{3.1(II)}$); 49.46 (CH_2, $C_{3.1(I)}$); 24.47 (CH_2, $C_{1.2(I)}$); 24.28 (CH_2, $C_{3.2(II)}$); 24.28 (CH_2, $C_{1.2(II)}$); 24.11 (CH_2, $C_{3.2(I)}$); 11.55 (CH_3, $C_{3.3(II)}$); 11.55 (CH_3, $C_{1.3(I)}$); 11.53 (CH_3, $C_{3.3(I)}$); 11.53 (CH_3, $C_{1.3(II)}$); 9.62 (CH_3, $C_{6(II)}$); 9.59 (CH_3, $C_{6(I)}$). HR-MS ($C_{20}H_{36}Cl_2N_4Pd$, MW = 509.85) (ESI, LM [$CHCl_3$/CH_3CN], *m*/*z*): calc.: 471.1663/472.1676/473.1663/474.1668/475.1656/476.1685/477.1659/478.1688/479.1654; found: 471.1669/472.1667/473.1666/474.1659/475.1657/476.1670/477.1664/478.1764/479.1759 $[C_{20}H_{36}ClN_4Pd]^+$ $[M - Cl^-]^+$. IR (KBr): $\tilde{\nu}$ = 3113 (s), 2961 (s), 2926 (s), 2878 (s), 2369 (vw), 2343 (vw), 1617 (vw), 1469 (s), 1417 (s), 1365 (w), 1343 (w),

1234 (w), 1187 (s), 1126 (w), 909 (w), 826 (w), 778 (w), 748 (w), 713 (w), 622 (w).

4.15. X-ray crystal structure analysis of complex *trans-anti-**13***

Formula $C_{20}H_{36}N_4Br_{0.56}Cl_{1.44}Pd$, MW = 534.73, yellow crystal $0.15 \times 0.10 \times 0.06$ mm, $a = 8.215(1)$ Å, $b = 10.329(1)$ Å, $c = 14.858(1)$ Å°, $\beta = 92.27(1)°$, $V = 1259.8(2)$ Å^3, $\rho_{calc} = 1.410$ g cm^{-3}, $\mu = 17.89$ cm^{-1}, empirical absorption correction ($0.775 \leqslant T \leqslant 0.900$), $Z = 2$, monoclinic, space group $P2_1/c$ (No. 14), $\lambda = 0.71073$ Å, $T = 198$ K, ω and ϕ scans, 8429 reflections collected ($\pm h, \pm k, \pm l$), $[(\sin\theta)/\lambda] = 0.66$ Å^{-1}, 2005 independent ($R_{int} = 0.042$) and 2021 observed reflections [$I \geqslant 2\sigma(I)$], 137 refined parameters, $R = 0.049$, $wR_2 = 0.141$, chlorine site occupied with 28% bromine, maximum (minimum) residual electron density 0.84 (−0.40) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms. Single crystals of this single diastereomer were obtained from dichloromethane (see Fig. 6).

4.16. Preparation of the carbene rhodium complexes ***15a**(**A**, **B**)*

In a Schlenk flask the solid histidinium salt **8a** (0.53 g, 1.22 mmol) and 0.14 g (0.63 mmol) of Ag_2O plus ca. 0.75 g of activated molecular sieves were mixed. Dichloromethane (60 ml) was added and the mixture was mechanically shaken for 4 h. Then a solution containing 301 mg (0.61 mmol) of $[Rh(cod)Cl]_2$ in 15 ml methylene chloride was added and the mixture shaken for 16 h. The solution was decanted from the Ag halide precipitate. Solvent was removed in vacuo and the yellow-orange colored product dried in vacuo to yield 0.51 g (65%) of **15a** as a 1:0.8 mixture of two diastereoisomers (I, II), mp 72 °C (DSC). Anal. Calc. for $C_{28}H_{39}ClN_3O_3Rh + 1/2H_2O$ (MW = 613.00): C, 54.86; H, 6.58; N, 6.85. Found: C, 54.65; H, 6.32; N, 6.57%. ^{1}H NMR (600 MHz, 298 K, CD_2Cl_2): $\delta = 7.78$ (m, 2H, *o*-Ph(II)); 7.72 (m, 2H, *o*-Ph(I)); 7.54 (m, 1H, *p*-Ph(II)); 7.53 (m, 1H, *p*-Ph(I)); 7.45 (m, 2H, *m*-Ph(I)); 7.45 (m, 2H, *m*-Ph(II)); 6.82 (d, ^3J(H,H) = 7.45 Hz, 1H, N–H(II)); 6.77 (d, ^3J(H,H) = 7.45 Hz, 1H, N–H(I)); 6.72 (s, 1H, 5(II)-H); 6.68 (s, 1H, 5(I)-H); 5.00 (m, 1H, 7(II)-H); 4.97 (m, 1H, 7(I)-H); 4.92 (m, 1H, COD=CH(II)); 4.92 (m, 1H, COD=CH(I)); 4.85 (m, 1H, COD=CH(II)); 4.85 (m, 1H, COD=CH(I)); 4.57 (m, 1H, 3.1(I)); 4.50 (m, 1H, 3.1(II)-H); 4.36 (m, 2H, 1.1(II)-H); 4.36 (m, 2H, 1.1(I)-H); 4.31 (m, 1H, 3.1′(II)-H); 4.21 (m, 1H, 3.1′(I)-H); 3.77 (s, 3H, OCH_3(I)-H); 3.72 (s, 3H, OCH_3(II)-H); 3.26 (m, 1H, COD=CH(I)); 3.26 (m, 1H, COD=CH(II)); 3.24 (dd, ^3J(H,H) = 5.2 Hz, ^2J(H,H) = 16.0 Hz, 1H, 6(I)-H); 3.20 (m, 1H, COD=CH(II)); 3.20 (m, 1H, COD=CH(I)); 3.18 (dd, (H,H) = 6.5 Hz, ^2J(H,H) = 16.0 Hz 1H, 6(II)-H); 3.13 (dd, ^3J(H,H) = 6.5 Hz, ^2J(H,H) = 16.0 Hz, 1H, 6′(II)-H); 3.06 (dd, ^3J(H,H) = 7.7 Hz, ^2J(H,H) = 16.0 Hz, 1H, 6′(I)-H); 2.42, 1.96 (m, 2H, COD–CH_2(I)); 2.42, 1.96 (m, 2H, COD–CH_2(II)); 2.38, 1.96 (m, 2H, COD–CH_2(I)); 2.38, 1.96 (m, 2H, COD–CH_2(II)); 2.36, 1.89 (m, 2H, COD–CH_2(II)); 2.36, 1.89 (m, 2H, COD–CH_2(I)); 2.31, 1.89 (m, 2H, COD–CH_2(I)); 2.31, 1.88 (m, 2H, COD–CH_2(II)); 2.13 (m, 2H, 3.2(I)-H); 1.77 (m, 2H, 1.2(II)-H); 1.77 (m, 2H, 1.2(I)-H); 1.77 (m, 2H, 3.2(II)-H); 1.06 (m, 3H, 3.3(I)-H); 1.06 (m, 3H, 3.3(II)-H); 1.00 (t, ^3J(H,H) = 7.45 Hz, 3H, 1.3(I)-H); 0.95 (t, ^3J(H,H) = 7.65 Hz, 3H, 1.3(II)-H). ^{13}C{^{1}H} NMR (150 MHz, 298 K, CD_2Cl_2): $\delta = 183.04$ (C, $C_{2(I)}$, ^1J(Rh,C) = 51.4 Hz); 182.98 (C, $C_{2(II)}$, ^1J(Rh,C) = 51.7 Hz); 171.89 (C, $C_{8(I)}$); 171.86 (C, $C_{8(II)}$); 167.17 (C, $C_{9(II)}$); 167.17 (C, $C_{9(I)}$); 133.91 (C, II-Ph(I)); 133.86 (C, II-Ph(II)); 132.30 (CH, *p*-Ph(II)); 132.29 (CH, *p*-Ph(I)); 129.18 (C, $C_{4(II)}$); 129.12 (C, $C_{4(I)}$); 129.00 (CH, *m*-Ph(II)); 128.97 (CH, *m*-Ph(I)); 127.5 (CH, *o*-Ph(II)); 127.3 (CH, *o*-Ph(I)); 118.68 (CH,

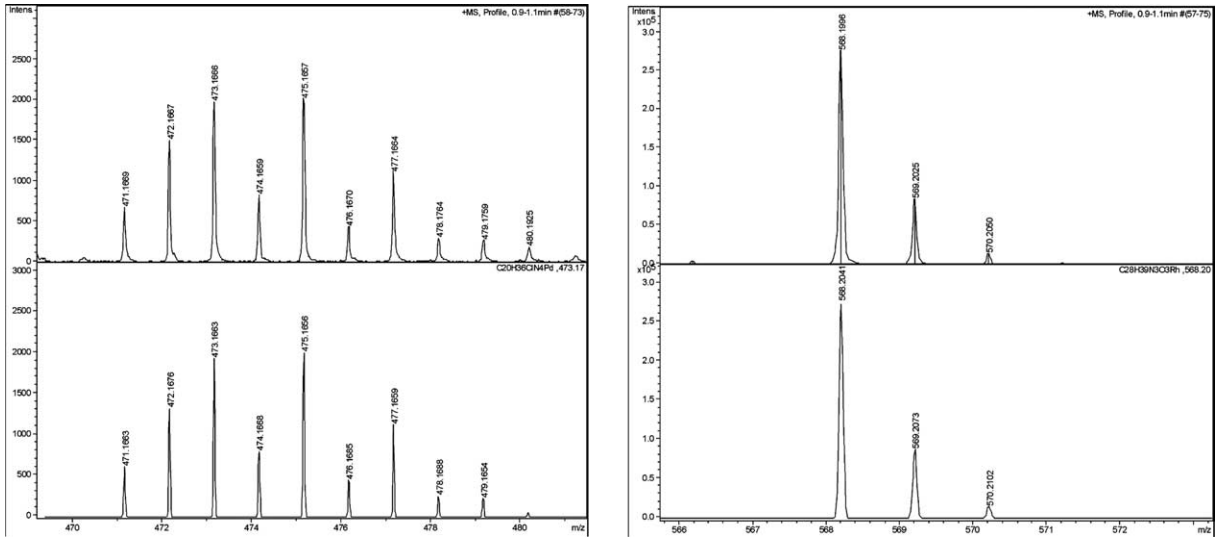


Fig. 6. Experimental (top) and calculated (bottom) ESI HRMS of **13** (i.e., $C_{20}H_{36}ClN_4Pd^+$ $[M - Cl]^+$, left) and **15a** (i.e., $C_{28}H_{39}H_3O_3Ru^+$, $[M - Cl]^+$, right).

$C_{5(II)}$); 118.66 (CH, $C_{5(I)}$); 98.14 (CH, COD=CH(II), ^1J(Rh,C) = 7.0 Hz); 98.14 (CH, COD=CH(I), ^1J(Rh,C) = 7.0 Hz); 97.78 (CH, COD=CH(II), ^1J(Rh,C) = 6.2 Hz); 97.74 (CH, COD=CH(I), ^1J(Rh,C) = 6.8 Hz); 68.82 (CH, COD=CH(I), ^1J(Rh,C) = 14.6 Hz); 68.72 (CH, COD=CH(II), ^1J(Rh,C) = 15.0 Hz); 68.03 (CH, COD=CH(I), ^1J(Rh,C) = 14.3 Hz); 67.97 (CH, COD=CH(II), ^1J(Rh,C) = 14.9 Hz); 53.2 (CH_3, OCH_3(I)); 53.0 (CH_3, OCH_3(II)); 52.84 (CH_2, $C_{1.1(II)}$); 52.79 (CH_2, $C_{1.1(I)}$); 52.0 (CH, $C_{7(II)}$); 51.8 (CH, $C_{7(I)}$); 50.45 (CH_2, $C_{3.1(I)}$); 50.43 (CH_2, $C_{3.1(II)}$); 33.62 (CH_2, COD–CH_2(I)); 33.59 (CH_2, COD–CH_2(II)); 32.89 (CH_2, COD–CH_2(II)); 32.84 (CH_2, COD–CH_2(I)); 29.59 (CH_2, COD–CH_2(I)); 29.54 (CH_2, COD–CH_2(II)); 28.90 (CH_2, COD–CH_2(II)); 28.80 (CH_2, COD–CH_2(I)); 27.73 (CH_2, $C_{6'}$(II)); 27.73 (CH_2, $C_{6(II)}$); 27.72 (CH_2, $C_{6(I)}$); 25.0 (CH_2, $C_{3.2(II)}$); 24.9 (CH_2, $C_{3.2(I)}$); 24.5 (CH_2, $C_{1.2(II)}$); 24.4 (CH_2, $C_{1.2(I)}$); 11.8 (CH, $C_{3.3(I)}$); 11.7 (CH, $C_{3.3(II)}$); 11.54 (CH_3, $C_{1.3(I)}$); 11.50 (CH_3, $C_{1.3(II)}$). HR-MS ($C_{28}H_{39}ClN_3O_3Rh$, MW = 603.99) (ESI, LM [$CHCl_3$/CH_3CN], *m*/*z*): calc.: 568.2041/569.2073/570.2102; found: 568.1996/569.2025/570.2050 $[C_{28}H_{39}N_3O_3Rh]^+$ $[M - Cl^-]^+$. IR (KBr): $\tilde{\nu}$ = 3400 (br), 2965 (s), 2926 (s), 2874 (s), 2826 (w), 2374 (w), 2348 (w), 1739 (s), 1648 (s), 1526 (s), 1491 (w), 1400 (w), 1026 (w), 800 (w), 709 (w), 687 (w). $[\alpha]^{20}$ (λ) = +2.1 (589), +2.1 (578), +3.0 (546) (*c* = 10.35, $CHCl_3$).

4.17. Preparation of 15b(A, B)

Analogously as described above the reaction of 0.20 g (0.46 mmol) of **8b** with 63 mg (0.24 mmol) of Ag_2O and 0.28 g (0.23 mmol) of $[Rh(cod)Cl]_2$ in a total volume of 100 ml of dichloromethane gave 196 mg (73%) of the product **15b** as a mixture (1:0.8) of two diastereoisomers (I, II), mp 49 °C decomp.: 236 °C (DSC). ^{1}H NMR (600 MHz, 298 K, CD_3CN): δ = 6.65 (s, 1H, 5(II)-H); 6.53 (s, 1H, 5(I)-H); 5.49 (d, ^3J(H,H) = 7.7 Hz, 1H, N–H(II)); 5.43 (d, ^3J(H,H) = 8.4 Hz, 1H, N–H(I)); 4.61 (m, 1H, COD=CH(I)); 4.61 (m, 1H, COD=CH(II)); 4.55 (m, 1H, COD=CH(I)); 4.54 (m, 1H, COD=CH(II)); 4.39 (m, 1H, 3.1(II)-H); 4.37 (m, 1H, 3.1(I)-H); 4.19 (m, 2H, 1.1(I)-H); 4.13 (m, 1H, 7(I)-H); 4.07 (m, 1H, 7(II)-H); 4.03 (m, 2H, 1.1(II)-H); 3.91 (m, 1H, 3.1(II′)-H); 3.87 (m, 1H, 3.1′(I)-H); 3.44 (s, 3H, OCH_3(I)); 3.40 (s, 3H, OCH_3(II)); 3.05 (m, 1H, COD=CH(II)); 3.04 (m, 1H, COD=CH(I)); 3.00 (m, 1H, COD=CH(II)); 3.00 (m, 1H, COD=CH(I)); 2.81 (dd, ^3J(H,H) = 4.9 Hz, ^2J(H,H) = 15.8 Hz, 1H, 6(II)-H); 2.78 (dd, ^3J(H,H) = 4.6 Hz, ^2J(H,H) = 15.8 Hz, 1H, 6(I)-H); 2.65 (dd, ^3J(H,H) = 9.1 Hz, ^2J(H,H) = 15.8 Hz, 1H, 6′(I)-H); 2.62 (dd, ^3J(H,H) = 9.3 Hz, ^2J(H,H) = 15.8 Hz, 1H, 6′(II)-H); 2.15, 1.55 (m, 2H, COD–CH_2(I)); 2.15, 1.55 (m, 2H, COD–CH_2(II)); 2.15, 1.53 (m, 2H, COD–CH_2(II)); 2.15, 1.53 (m, 2H, COD–CH_2(I)); 2.14, 1.55 (m, 2H, COD–CH_2(II)); 2.14, 1.55 (m, 2H, COD–CH_2(I)); 2.14, 1.53 (m, 2H, COD–CH_2(I)); 2.14, 1.53 (m, 2H, COD–CH_2(II)); 1.87 (m, 2H, 3.2(I)-H); 1.70 (m, 2H, 1.2(I)-H); 1.57 (m, 2H, 1.2(II)-H); 1.51 (m, 2H, 3.2(II)-H); 1.14 (s, 9H, C(CH_3)$_3$(II)); 1.12 (s, 9H, C(CH_3)$_3$(I)); 0.80 (t, ^3J(H,H) = 7.4 Hz, 3H, 3.3(I)-H); 0.79 (t, ^3J(H,H) = 7.4 Hz, 3H, 3.3(II)-H); 0.74 (t, ^3J(H,H) = 7.5 Hz, 3H, 1.3(II)-H); 0.73 (t, ^3J(H,H) = 7.4 Hz 3H, 1.3(I)-H). ^{13}C{^{1}H} NMR (150 MHz, 298 K, CD_3CN): δ = 182.53 (C, $C_{2(II)}$); 182.16 (C, $C_{2(I)}$); 172.65 (C, $C_{8(II)}$); 172.59 (C, C_{8I}); 156.30 (C, $C_{9(II)}$); 156.23 (C, $C_{9(I)}$); 130.62 (C, $C_{4(II)}$); 130.4 (C, $C_{4(I)}$); 119.77 (CH, $C_{5(I)}$); 119.57 (CH, $C_{5(II)}$); 98.07 (CH, COD=CH(I), ^1J(Rh,C) = 5.5 Hz); 98.01 (CH, COD=CH(II), ^1J(Rh,C) = 5.9 Hz); 97.75 (CH, COD=CH(I)); 97.70 (CH, COD=CH(II)); 80.27 (C, *C*(CH_3)$_3$); 80.16 (C, *C*(CH_3)$_3$); 69.60 (CH, COD=CH(II)); 69.60 (CH, COD=CH(I)); 68.85 (CH, COD=CH(II)); 68.85 (CH, COD=CH(I)); 53.60 (CH, $C_{7(I)}$); 53.60 (CH, $C_{7(II)}$); 53.12 (CH_3, O–CH_3(I)); 53.11 (CH_2, $C_{1.1(II)}$); 53.09 (CH_2, $C_{1.1(I)}$); 53.09 (CH_3, O–CH_3(II)); 50.68 (CH_2, $C_{3.1(I)}$); 50.63 (CH_2, $C_{3.1(II)}$); 33.83 (CH_2, COD–CH_2(II)); 33.79 (CH_2, COD–CH_2(I)); 33.19 (CH_2, COD–CH_2(I)); 33.16 (CH_2, COD–CH_2(II)); 29.88 (CH_2, COD–CH_2(I)); 29.86 (CH_2, COD–CH_2(II)); 29.21 (CH_2, COD–CH_2(II)); 29.19 (CH_2, COD–CH_2(I)); 28.45 (CH_3, C(*C*H_3)$_3$); 28.44 (CH_3, C(*C*H_3)$_3$); 27.63 (CH_2, $C_{6(II)}$); 27.45 (CH_2, $C_{6(I)}$); 25.17 (CH_2, $C_{3.2(II)}$); 25.13 (CH_2, $C_{3.2(I)}$); 24.79 (CH_2, $C_{1.2(I)}$); 24.78 (CH_2, $C_{1.2(II)}$); 11.77 (CH_3, $C_{3.3(I)}$); 11.73 (CH_3, $C_{3.3(II)}$); 11.63 (CH_3, $C_{1.3(I)}$); 11.61 (CH_3, $C_{1.3(II)}$). HR-MS ($C_{26}H_{43}ClN_3O_4Rh$, MW = 584.00) (ESI, LM [$CHCl_3$/CH_3CN], *m*/*z*): calc.: 564.2303/565.2335/566.2363; found: 564.2252/565.2282/566.2301 $[C_{26}H_{43}N_3O_4Rh]^+$ $[M - Cl^-]^+$. IR (KBr): $\tilde{\nu}$ = 3434 (br), 2965 (s), 2930 (s), 2869 (s), 2826 (s), 1752 (s), 1704 (s), 1517 (w), 1365 (w), 1252 (w), 1161 (s), 1056 (w), 1026 (w), 996 (w), 961 (w), 865 (w), 813 (w), 478 (w). $[\alpha]^{20}$ (λ) = +16.4 (589), +17.3 (578), +19.8 (546) (*c* = 5.1, $CHCl_3$).

5. Supplementary data

CCDC 276235, 276236, 276237, and 277073 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44 1223 336 033, e-mail: deposit@ccdc.cam.ac.uk].

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