Pergamon

Tetrahedron: *Asymmetry* 13 (2002) 1969–1972

TETRAHEDRON: *ASYMMETRY*

A modular approach to *trans*-chelating, *N*-heterocyclic carbene ligand complexes

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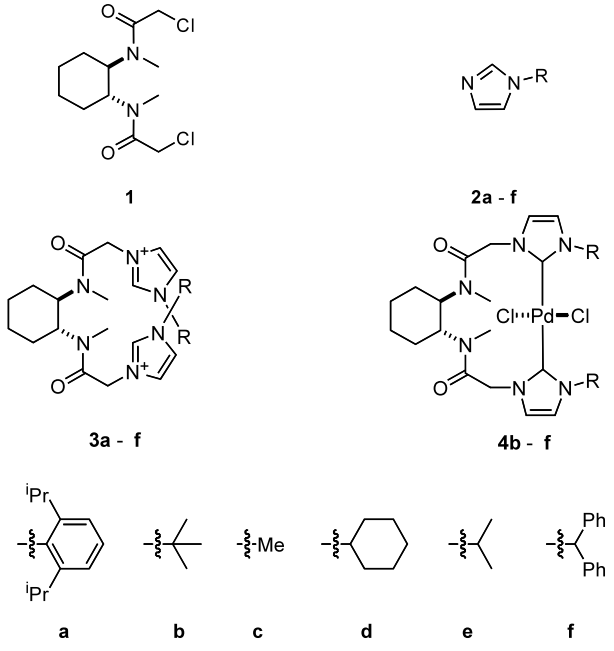
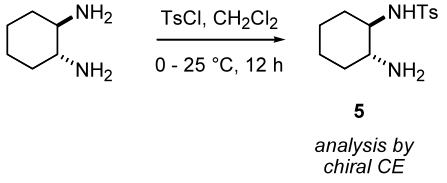
Received 28 August 2002; accepted 30 August 2002

Abstract—The *N*-methyl bis-imidazolium salts **3** were converted to the silver carbenes **7**, then reacted to give palladium(II) complexes **4** with *trans*-chelating, bidentate bis-imidazolylidine ligands. The similar salts **8**, that do not have *N*-methyl substituents, gave the tetradentate complexes **9** in direct reactions with palladium chloride. The potential of these complexes for asymmetric catalysis is discussed. © 2002 Published by Elsevier Science Ltd.

Syntheses of chiral ligands via combinations of suitable chirons with other building blocks can be a powerful strategy in the discovery and optimization of asymmetric catalysts. Modular approaches such as this allow the construction of diverse ligand families from readily available starting materials.[1–7] Herein, we describe how the diamide chiron **1** was combined with a series of *N*-substituted imidazoles **2** to give the chiral *N*-heterocyclic carbene ligand precursors **3**, and subsequently, the corresponding *trans*-chelated palladium complexes **4**.



Syntheses of the ligands began with resolution of *trans*-1,2-diaminocyclohexane. The resolution was completed following the *Organic Synthesis* procedure,[8] but determination of the enantiomeric purity of the product was performed differently. The published procedure describes conversion of the amine functionalities into 4-methylbenzoyl amides, then separation of the enantiomers on a Pirkle HPLC column. In our work, the diamine was converted into the mono (4-methylbenzene)sulfonamide **5**, then analyzed by chiral capillary electrophoresis (CE).[9] The CE method requires much less sample, and gives baseline resolution of the two enantiomers in about half the separation time (i.e. 6 min). Fig. 1 shows CE traces for racemic and diastereomerically pure samples of **5**.



Preparation of the bis-imidazolium ligand precursors **3** followed the sequence shown in Scheme 1. The tartaric acid salt of diastereomerically pure *trans*-1,2-diaminocyclohexane was converted to the corresponding bis-ethyl carbonate, then reduced to the *N*,*N*′-dimethyl amine **6** via a known procedure.[10] *N*-Substituted imidazoles were then reacted with the dichloride **1** to give the imidazolium salts. We were unable to find good recrystallization solvents for these salts, but NMR analyses of the crude materials isolated simply after removal of the DMF solvent indicated they were of high purity and were formed in near quantita-

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0957-4166/02/$ - see front matter © 2002 Published by Elsevier Science Ltd.
PII: S0957-4166(02)00535-9

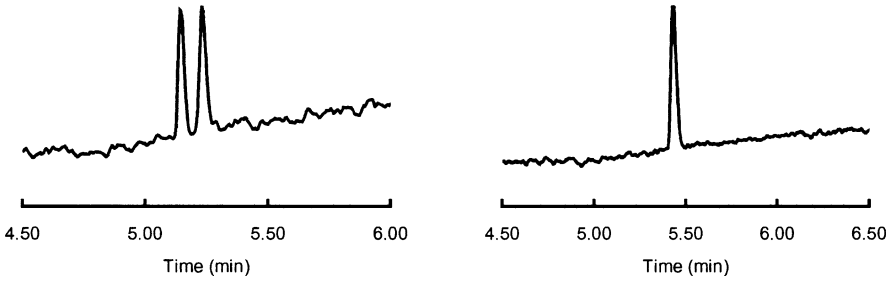
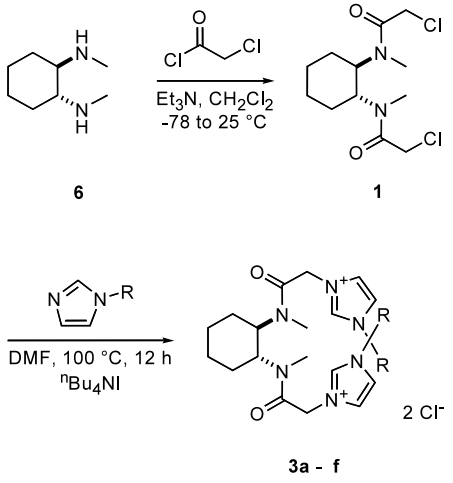
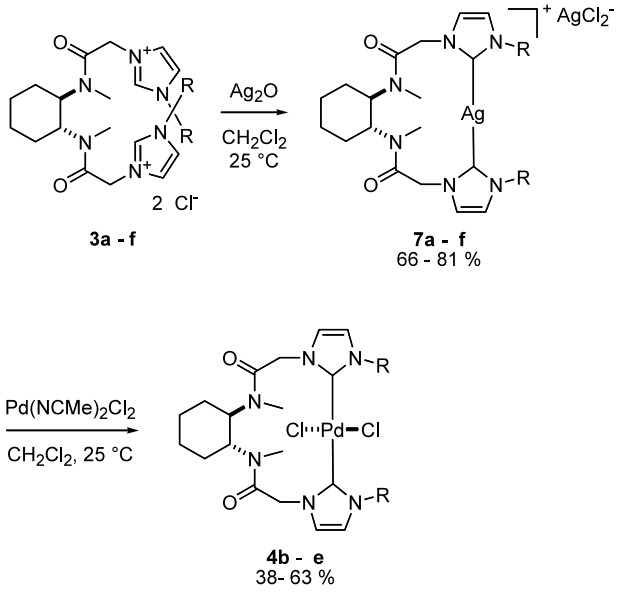


Figure 1. CE traces of racemic and enantiomerically pure **5**.

tive yields. Additionally, the formation of organometallic derivatives from these samples proceeded without difficulty.



Scheme 1. Preparations of the imidazolium salts **3**.



Scheme 2. Preparations of the imidazolium salts **4**.

Scheme 2 shows how the target palladium complexes **4** were prepared from the imidazolium salts **3**. Reaction of the imidazolium salts with silver oxide at room temperature,[11–13] filtration, and removal of solvent gave the silver carbene intermediates **7**. Without further purification, these samples, were reacted with bis(acetonitrile)dichloropalladium(II); the desired complexes **4c–e** formed after about 1 h, and were precipitated from the reaction medium directly by concentrating the dichloromethane solvent and adding diethyl ether. The *tert*-butyl substituted complex **4b** took longer to form; in this case the reaction was allowed to proceed for 16 h.

Formation of the palladium complex **4a** did not occur at 25°C; presumably, this particular syntheses was unfavorable due to the size of the 2,6-di-*iso*-propylphenyl substituent.[14] Preparation of complex **4f** at room temperature was also problematic. Fig. 2a shows part of the ^{1}H NMR for the crude precipitate of **4f**, formed via reaction with the silver carbene at 25°C for 18 h; several of the peaks that are not characteristic of the product. However, when the synthesis was repeated using a microwave reactor set at 100°C for 20 min then the crude precipitate was much enriched in the desired product (Fig. 2b).

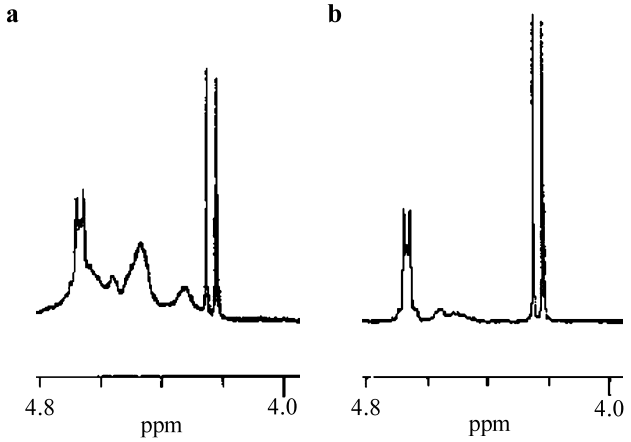


Figure 2. ^{1}H NMR spectra in $CDCl_3$ of the crude precipitates formed in the preparation of complex **4f**, (a) 25°C for 18 h; and (b) 100°C microwave for 20 min.

X-Ray quality crystals of complex **4d** were obtained. The solid structure[15] (Fig. 3) is a near perfect square planar palladium complex where the Cl–Pd–$C^{carbene}$ bond angles show less than 2° deviation from the ideal 90° (88.1 and 91.2° were measured). The carbenes form a *trans*-chelate with the imidazolylidenes twisted such that their cyclohexyl substituents are directed to opposite faces of the complex. The planes between the imidazolylidenes lie at an angle of 64° to one another, and the bisector between these two planes is perpendicular to the Cl–Pd–Cl bonds.

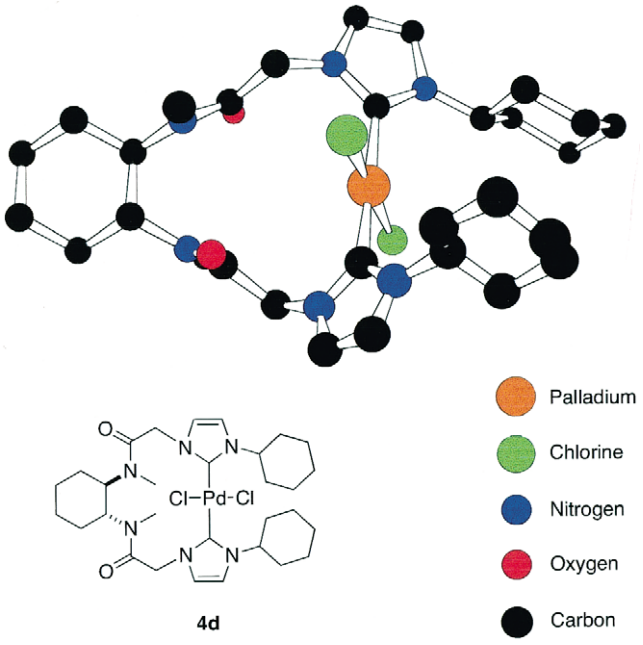


Figure 3. Chem3D representation of complex **4d** generated from a single crystal X-ray diffraction analysis.

trans-Chelating ligands in palladium complexes are well known, two representative examples being the phosphines based on the xanthene framework (Xantphos),[16] or on two ferrocene units linked at the cyclopentadienyl unit (TRAP).[17] In addition, bis-pyridine ligands designed to be *trans*-chelating have recently been reported.[18] A chiral, chelating bis-imidazolylidene ligand that forms *trans*-chelates has also been reported; this is based on the 1,1-binapthyl framework.[19]

Two bis-imidazolium salts, **8a** and **8b**, without *N*-methyl substituents, were also prepared via routes analogous to the ones outlined above. Complexes with molecular masses corresponding to structure **9** were formed when these salts were treated with potassium *tert*-butoxide and palladium chloride in DMSO overnight (Reaction (1)). We assign the coordination mode of the ligand as amide-*N*-bonded on the basis of two observations. First, in ^{13}C NMR spectra the CO amide carbonyl resonances did not shift significantly on complexation: for instance, complex **9b** had a resonance at 163.9 ppm which is a similar chemical shift to the parent imidazolium salt **8b** (166.9 ppm) and to complex **4b** (165.4 ppm) wherein the carbonyl is not coordinated. Second, complex **9b** has a CO stretch at 1644 cm^{-1} which is close to that of the imidazolium salt **8b** (1658 cm^{-1}) and to that of the complex **4b** (1651 cm^{-1}; thin film on NaCl plates).

(1)

8a R = 2,6-$^{i}Pr_2C_6H_3$
8b R = ^{t}Bu

9a 8 %
9b 15 %

Attempts to use complexes **4b–f** as catalysts for intramolecular Heck reactions gave very poor chemical yields and enantioselectivities. In retrospect, this is unsurprising given that the *trans*-geometry of the chelating *N*-heterocyclic carbene seems to be the preferred coordination geometry: catalysis involving reductive elimination is therefore disfavored because this requires *cis*-oriented coordination sites. Moreover, carbene ligands are less likely to dissociate than the corresponding phosphine[20] or bis-pyridine[18] systems, so catalysis via less saturated intermediates is also disfavored.

The work reported here may indicate future research strategies that should be valuable. The ligands **3** are much more likely to be useful in asymmetric catalysis involving metals that can form 5- and/or 6-coordinate intermediates than with the palladium systems reported here. The current emphasis of our work is on the use of these ligands to form such complexes with other metals for which *trans*-coordination is unlikely to impede catalysis and may be advantageous.

Acknowledgements

Financial support for this work was provided by The Robert Welch Foundation and Johnson Matthey plc. We thank CEM Corporation for the microwave apparatus used in this study. Help and advice from Dr. Shane Stichy of the TAMU/LBMS-Applications Laboratory is also acknowledged. We thank Dr. Joe H. Reibenspies for the X-ray structure determination, and Dr. Gyula Vigh/Mr. M. Brent Busby for analyzing compound **5** by CE.

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