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Triple C–H activation of 1,5-bis(di-*tert*-butylphosphino)-2-(*S*)-dimethylaminopentane on ruthenium gives a chiral carbene complex†

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This communication reports the preparation of a novel *trans*-chelating diphosphine, 1,5-bis(di-*tert*-butylphosphino)-2-(*S*)-dimethylaminopentane, that undergoes triple C–H activation in reaction with $[RuCl_2(p\text{-cymene})]_2$ to give a chiral square-pyramidal 16-electron carbene complex of ruthenium.

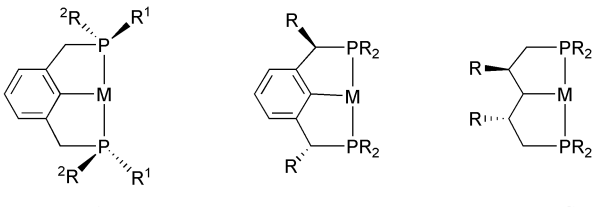
Cis-chelating diphosphine ligands are ubiquitous; many of them are chiral and have found important applications as catalysts for enantioselective organic transformations. In contrast, very few *trans*-chelating diphosphines (so-called 'pincer' ligands) are known[1] and their chiral forms are restricted to the derivatives of 1,3-bis(diphosphinomethyl)benzene **A** and **B** shown in Scheme 1.[2]

Pincer ligands possessing a C_5 aliphatic spacer between the phosphorus atoms may contain one or two stereogenic centers in positions adjacent to the metalated carbon of the complex (structure **C** in Scheme 1) and thus offer interesting structural alternatives to the ligands with aromatic backbone. In order to test the feasibility of this approach, we decided to prepare 1,5-bis(di-*tert*-butylphosphino)-2-(*S*)-dimethylaminopentane (**1**) and investigate its reaction with $[RuCl_2(p\text{-cymene})]_2$. We have recently reported dehydrogenation of 1,5-bis(di-*tert*-butylphosphino)pentane on ruthenium that afforded the olefin complex $RuHCl[Bu^t_2PCH_2CH_2((E)\text{-}CH=CH)CH_2PBu^t_2]$ (Scheme 2, left).[3] From **1**, we anticipated formation of olefin complexes shown in Scheme 2.

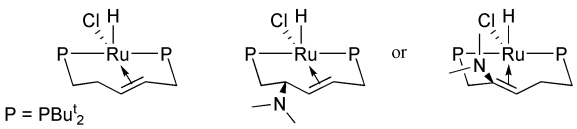
Preparation of **1** was accomplished in five steps‡ as shown in Scheme 3 and involved (a) methylation of L-glutamic acid, (b) conversion of *N*, *N*-dimethyl-(L)-glutamic acid to the corresponding dimethyl ester, which (c) afforded 2-(*S*)-dimethylaminopentane-1,5-diol upon reduction with $LiAlH_4$. In the following two steps, the diol was (d) converted to 1,5-dichloro-2-(*S*)-dimethylaminopentane hydrochloride, and (e) the hydrochloride was reacted with $LiPBu^t_2$ to give **1**.

Treating $[RuCl_2(p\text{-cymene})]_2$ with **1** in boiling *tert*-butanol in the presence of triethylamine afforded the carbene complex **2** shown in Scheme 4, isolated in 79% yield as air-sensitive thin red needles soluble in common organic solvents.§ Formation of **2** apparently involved the expected *trans* coordination of the two bulky PBu^t_2 groups to ruthenium and cyclometalation of the ligand backbone. Unexpectedly, the cyclometalated species did not undergo β-hydrogen elimination in the fashion observed for 1,5-bis(di-*tert*-butylphosphino)pentane,[3] but afforded the carbene product **2** by dehydrogenation of a methylamino group.

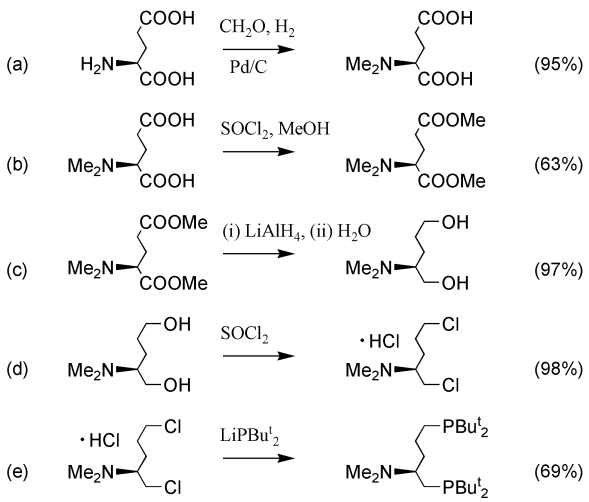
Complex **2** was characterized by elemental analysis and NMR spectroscopy. Important NMR features of **2** include the carbene =CH shifts: δ 11.97 (^{1}H) and 246.9 (^{13}C), and the AB system in the phosphorus spectrum, exhibiting a large $^2J_{PP}$ coupling of 257 Hz. The solid state structure of **2** was established by single crystal X-ray diffraction.¶ An ORTEP plot of the molecule is shown in Fig. 1 and selected bond distances and angles are listed in the figure caption. The coordination environment of the ruthenium center in **2** approximates a square pyramid with the carbene moiety occupying the apical position. The two *trans* coordinated P atoms and the mutually *trans* Cl and C3 atoms define the basal plane of the pyramid. The Ru–C7 and Ru–C3 bond distances of 1.868(4) and 2.143(4) Å, respectively, are within the normal range for Fischer carbene



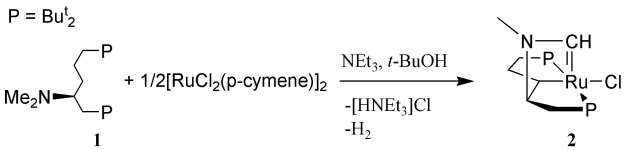
Scheme 1



Scheme 2



Scheme 3



Scheme 4

† Electronic supplementary information (ESI) available: NMR data for the products in Scheme 3. See http://www.rsc.org/suppdata/cc/b2/b208325f/

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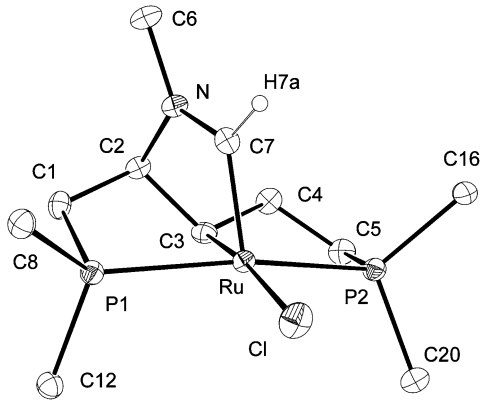

Fig. 1 Partial structure of **2** with ellipsoids set at the 30% probability level. Most of the hydrogen atoms and methyl groups are omitted for clarity. Key parameters (Å, deg): Ru–C3 2.143(4), Ru–C7 1.868(4), C7–N 1.317(5), C2–N 1.469(5), C6–N 1.468(5), Ru–Cl 2.467(1), Ru–P1 2.332(1), Ru–P2 2.345(1), P1–Ru–P2 160.31(4), C3–Ru–Cl 173.16(11), C3–Ru–C7 76.20(16), C7–Ru–Cl 110.53(12), N–C7–Ru 122.6(3), C7–Ru–P1 86.24(12), C7–Ru–P2 100.87(12).

and alkyl-ruthenium species. The short C7–N distance of 1.317(5) Å and the planarity of the N–C2–C6–C7 four-atom fragment indicate strong π-bonding between C7 and the nitrogen atom and a significant double-bond character of the C7–N bond.

The molecule of **2** has three chiral centers. The C2 center was present in **1** and retained its configuration, whereas C3 and Ru became chiral upon formation of the complex. The (*R*)-C3, (*Λ*)-Ru stereochemistry is explicitly defined by the (*R*)-configuration of C2 and the *trans* arrangement of the PBu^t_2 groups. Indeed, ^{1}H, ^{13}C and ^{31}P NMR spectra of **2** have demonstrated that in solution the complex exists as single epimer. Solutions of **2** rotate plane-polarized light ($[\alpha]^D_{20}$ + 876.2°, *c* = 0.24, toluene), providing conclusive evidence that formation of the complex occurred without racemization.

In summary, this work has successfully demonstrated that new types of diphosphine 'pincer' ligands with chiral centers in the aliphatic backbone can be developed. The methodology applied to the synthesis of **1** can be easily extended toward preparation of diaryl- and dialkylphosphino analogues of **1** *e.g.*, 1,5-bis(diphenylphosphino)-2-(*S*)-dimethylaminopentane. The availability of the phosphorus and nitrogen donor centers and multiple C–H activation pathways in **1** open several possibilities for addition of this type of ligand to transition metals, promising an intriguing structural diversity of the products. The use of **1** and its analogues in organometallic chemistry can lead to novel chiral metal complexes of interest for fundamental and catalytic research.

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Notes and references

‡ *Synthesis of* **1**: (a) L-glutamic acid (25 g, 169.9 mmol), formaldehyde (37%, 60 mL, *ca*. 800 mmol) and palladium on carbon (10%, 8 g) were stirred in 200 mL of water for 48 h under H_2. Then the flask was purged with nitrogen; the mixture was heated to reflux and filtered while hot. After evaporation, the white solid of *N*,*N*-dimethyl-(L)-glutamic acid was dried under vacuum at 100 °C for 8 h. Yield: 28.17 g (95%). (b) A stirred suspension of *N*,*N*-dimethyl-(L)-glutamic acid (28.0 g, 159.8 mmol) in abs. methanol (100 ml) was cooled to −80 °C and treated with $SOCl_2$ (47.6 g, 400 mmol) added dropwise over *ca.* 30 min. Stirring continued at room temperature for 1 h and then at 40 °C for 16 h. After evaporation and drying under vacuum, the residue was stirred with 100 mL of Et_2O and 50 mL of 20% K_2CO_3. The aqueous phase was separated and discarded. The ether solution was dried over Na_2SO_4, filtered and evaporated. *N*,*N*-dimethyl-(L)-glutamic acid dimethyl ester was isolated by distillation (bp 83 °C/1 mm Hg). Yield: 20.5 g (63%). (c) *N*,*N*-Dimethyl-(L)-glutamic acid dimethyl ester (20.35 g, 100.15 mmol) was added dropwise over *ca.* 15 min to a stirred suspension of $LiAlH_4$ (7.2 g, 189.7 mmol) in THF (300 mL) at −80 °C. Stirring continued at room temperature for 1 h and then under reflux overnight. The resulting suspension was cooled in an ice bath and carefully treated with water (10 mL) added dropwise and then with 15% NaOH (5 mL). The mixture was stirred at room temperature for 30 min then heated to reflux and filtered while hot. The solid was washed with hot THF (3 × 40 mL), the combined filtrate was evaporated and dried under vacuum at 100 °C to give 2-(*S*)-dimethylaminopentane-1,5-diol (14.3 g, 97%) as a colorless oil. (d) $SOCl_2$ (26.2 g, 220 mmol) was added dropwise to a solution of 2-(*S*)-dimethylaminopentane-1,5-diol (10.41 g, 70.71 mmol) in 40 mL of CH_2Cl_2 at −80 °C. Stirring continued at room temperature for 1 h and then under reflux for 0.5 h. The resulting solution was evaporated and dried under vacuum at 100 °C. The oily residue was triturated with abs. Et_2O (40 mL) to give 1,5-dichloro-2-(*S*)-dimethylaminopentane hydrochloride as a white solid, which was filtered, washed with abs. Et_2O (3 × 20 mL) and dried under vacuum. Yield: 15.32 g (98 %). Deprotonation of the hydrochloride was not carried out because of the spontaneous formation of 2-chloromethyl-1,1-dimethylpyrrolidinium chloride. (e) All manipulations were carried out under argon. A stirred suspension of 1,5-dichloro-2-(*S*)-dimethylaminopentane hydrochloride (4.97 g, 22.53 mmol) in THF (30 mL) was treated at −80 °C with a solution of $LiPBu^t_2$ (12.0 g, 78.87 mmol, in 30 mL of THF) added dropwise over *ca.* 15 min. Stirring continued at room temperature for 1 h and then under reflux for 0.5 h. The mixture was evaporated to *ca.* 30 mL, diluted with hexane (30 mL) and washed with deoxygenated water (3 × 8 mL). The organic phase was dried over K_2CO_3, filtered and evaporated. The residue was distilled under vacuum of an oil pump. Three fractions boiling in the intervals 32–37, 135–145, and 145–152 °C were collected. According to ^{31}P NMR, the first fraction was $HPBu^t_2$ (4.61 g), the second was a mixture of **1** and $(Bu^t_2P)_2$. The third was spectroscopically pure **1** (pale yellow pyrophoric oil) (6.28 g, 69%).

§ *Synthesis of* **2**: all manipulations were carried out under argon. A stirred mixture of **1** (825 mg, 2.04 mmol), $[RuCl_2(p\text{-cymene})]_2$ (0.57 g, 0.93 mmol), and Et_3N (0.4 g, 3.96 mmol) in 10 mL of *t*-BuOH was refluxed for 12 h. After evaporation, the residue was extracted with Et_2O (20 mL) and filtered. The filtrate was diluted with hexane (10 mL) and evaporated to *ca*. 10 mL. The precipitated dark-red solid was separated and re-dissolved in ether (16 mL). The solution was diluted with isooctane (16 mL), passed through basic alumina (30 × 20 mm) and eluted with isooctane (8 mL). The combined eluate was evaporated to *ca.* 8 mL. Spectroscopically pure **2** crystallized upon standing and was separated by decantation, washed with hexane (2 × 4 mL) and dried under vacuum. Yield: 0.79 g (79%). Anal. Calc. for $C_{23}H_{48}ClNP_2Ru$: C, 51.43; H, 9.01; N, 2.61. Found: C, 51.61; H, 9.11; N, 2.67%. ^{31}P{^{1}H} NMR (C_6D_6): δ 77.5, 82.8 (d, $^2J_{PP}$ = 257 Hz). ^{1}H{^{31}P} NMR (C_6D_6): δ 0.51 (m, 1H), 0.83–1.10 (m, 2H), 1.13, 1.25, 1.30, 1.38 (s, 4 × 9H, C*H*$_3$), 1.52 (m, 2H), 1.81 (dt, J_{HH} = 6, 18 Hz, 1H), 2.24 (s, 3H, N-C*H*$_3$), 2.57 (dd, J_{HH} = 6, 11 Hz, 1H), 3.27 (s, 1H, C*H*–N), 11.97 (s, 1H, =C*H*). ^{13}C{^{1}H} NMR (C_6D_6): δ 21.1 (dd, J_{CP} = 1.3, 19.1 Hz, *C*H$_2$), 26.3 (d, J_{CP} = 18.5 Hz, *C*H$_2$), 28.7 (dd, J_{CP} = 1.4, 4.7 Hz, *C*H$_3$), 29.2 (dd, J_{CP} = 1.1, 5.1 Hz, *C*H$_3$), 30.4 (dd, J_{CP} = 1.1, 4.3 Hz, *C*H$_3$), 31.2 (dd, J_{CP} = 1, 4.7 Hz, *C*H$_3$), 33.4 (dd, J_{CP} = 3.9, 7.2 Hz, *C*Me$_3$), 34.3 (dd, J_{CP} = 2.3, 11.3 Hz, *C*H$_2$), 34.7 (dd, J_{CP} = 2.2, 5.4 Hz, *C*Me$_3$), 35.2 (dd, J_{CP} = 1.9, 9.9 Hz, *C*Me$_3$), 36.3 (dd, J_{CP} = 4.5, 9 Hz, *C*Me$_3$), 39.7 (d, J_{CP} = 1.3 Hz, *C*H$_3$), 50.5 (t, $^2J_{CP}$ = 2.3 Hz, *C*H), 76.3 (dd, J_{CP} = 2.7, 10.5 Hz, *C*H), 246.9 (dd, $^2J_{CP}$ = 9.3, 10.3 Hz, =*C*H). $[\alpha]_D^{20}$ + 876.2^0 (*c* = 0.24, toluene).

¶ *Crystal data*: $C_{23}H_{48}ClNP_2Ru$, *M* = 537.08, orthorhombic, *a* = 8.4390(2), *b* = 14.5810(4), *c* = 21.9890(5), *V* = 2705.73(12) Å^3, *T* = 150 K, space group $P2_12_12_1$ (no. 19), *Z* = 4, μ(MoKα) = 0.71073 Å, Flack parameter −0.03(4), 21334 reflections measured, 6188 unique (R_{int} = 0.0768) which were used in all calculations. The final $wR(F^2)$ was 0.0840 (all data). CCDC reference number 192434. See http://www.rsc.org/suppdata/cc/b2/b208325f/ for crystallographic data in CIF or other electronic format.

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