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Effective Modulation of the Donor Properties of N-Heterocyclic Carbene Ligands by "Through-Space" Communication within a Planar Chiral Scaffold

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The tremendous success of N-heterocyclic carbenes (NHC) as organocatalysts and as ancillary ligands for transition-metal catalysis is innately linked to their powerful two-electron donor capacity.[1] If one takes the stretching frequency of the CO ligand in complexes of type **1** as an estimate for the donor strength of the trans-disposed ligand L,[2] NHC's are distinctly more electron releasing than even the most basic trialkylphosphines.

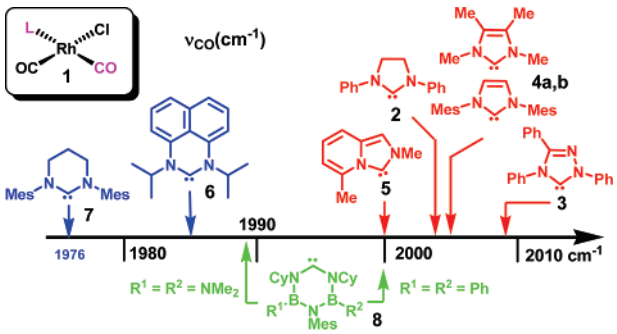
In contrast to the phosphine series, however, where substantial electronic tuning can be easily accomplished, the dispersion of the donor capacities among the commonly used NHC's is exceedingly narrow (Scheme 1).[2c] In the extreme, it was even possible to alter the steric properties of a given type of NHC over a wide range without any noticeable effect on the donor ability.[3] Serious electronic modulations require constitutional redesign (acyclic carbenes,[4] different size of the backbone,[5] donor atoms other than nitrogen,[6] one rather than two heteroatoms in the ring,[7] etc.),[1,2c] with the only important exception being the six-membered, boron containing NHC's **8** pioneered by Bertrand.[8] These ligands are designed such that variations of the substituents R^1 and R^2 on boron enable electronic modulations within a quasi-constant steric environment (Scheme 1). Outlined below is an alternative concept that allows uncoupling of the electronic and structural parameters. This goal was reached by embedding the NHC into a planar chiral cyclophane scaffold that enjoys an effective electronic cross-talk between its layers.[9]

The preparation of the new type of ligand starts from the known N-oxide **12** which was readily prepared by following a literature route (Scheme 2).[10] O-Acylation with $Me_2NC(O)Cl$ followed by reaction with TMSCN[11] furnished azatriene **13** rather than the expected 2-cyanopyridine **14**, as unambiguously proven by X-ray crystal structure analysis (Figure 1, left).[12] This previously unrecognized opening of the pyridine nucleus is deemed to reflect the strain of the cyclophane framework.

Gratifyingly, however, **13** underwent a thermal 6π-electrocyclization/elimination process when refluxed in 1,2-dichloroethane, thus furnishing **14** in respectable overall yield.[10] Routine operations then allowed us to elaborate this compound into **16**, a planar chiral analogue of the known imidazo[1,5-a]pyridinium salts **5**.[13] Reaction of **16** with Ag_2O followed by transmetallation with $[RhCl(cod)]_2$ readily gave the planar chiral rhodium complex **17** (Figure 1, right).

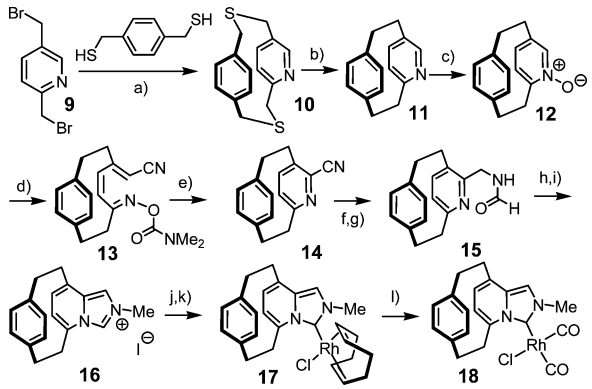
To assess the donor properties of the new carbene, **17** was converted to the corresponding carbonyl complex **18**. The stretching frequency of its *trans*-CO ligand at $\tilde{\nu} = 1989\ cm^{-1}$ indicates that the donor capacity of this novel planar chiral ligand rivals or even exceeds that of all other diamino-stabilized, five-membered NHC's known to date.[2c] Equally striking is the fact that the incremental gain in donor strength, expressed as $\Delta\tilde{\nu}$, in going from **5** to **18** is substantially higher than the effect of ring-annulation upon formal conversion of the parent compound **4** into imidazopyridin-ylidene **5**. By virtue of the through-space interaction between the carbene unit and the aromatic lid of the cyclophane in juxtaposition, the new ligand actually resembles the more basic carbenes with 6-membered or acyclic skeletons in electronic terms (cf. Scheme 1).[2c]

Scheme 1. Donor Capacity of Selected NHC Ligands[a]



[a] For data concerning other carbenes, see the Supporting Information.[2c]

Scheme 2 [a]



[a] Conditions: (a) KO*t*Bu, EtOH, 79%; (b) hν, $P(OMe)_3$, 64%; (c) *m*CPBA, CH_2Cl_2, 76%; (d) (i) *N*,*N*-dimethylcarbamoyl chloride, CH_2Cl_2; (ii) TMSCN, room temp; (e) 1,2-dichloroethane, reflux, 54% (over three steps); (f) H_2, Pd/C catalyst, HOAc, quantitative; (g) HC(O)OMe, Et_3N, reflux, 68%; (h) $POCl_3$, toluene, 80 °C, 61%; (i) MeI, THF, 60 °C, 87%; (j) Ag_2O, CH_2Cl_2; (k) $[(cod)RhCl]_2$, 71%; (l) CO, THF, 92%.

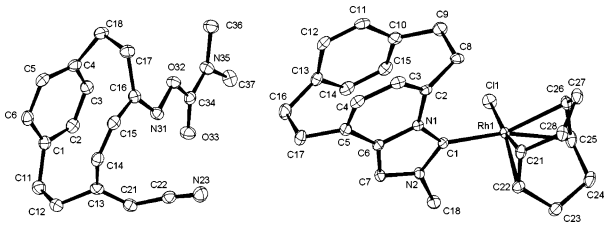


Figure 1. Molecular structures of **13** and **17** in the solid state.

Next, we set out to probe whether remote electronic variations can be transmitted within the cyclophane scaffold. To this end, we prepared the tetramethoxy and the tetrafluoro analogues **19** and **22** by adaptation of the synthesis pursued en route to **18**.[12] As might be expected from literature data,[14] the donor ability of the

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Chart 1. Tetramethoxycarbene-Rh Complex **19** and Conformational Preference of the Related Cyclophane **20**[14]

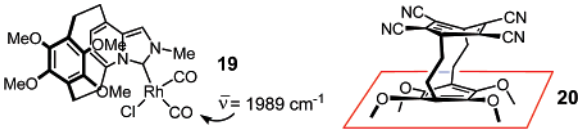


Chart 2. Fluorinated Planar Chiral Rh-Carbene Complexes and Overlay of the Molecular Crystal Structure of the Fluorinated Carbene Part of **21** (Yellow) and its Non-fluorinated Counterpart in **17** (Blue)[12]

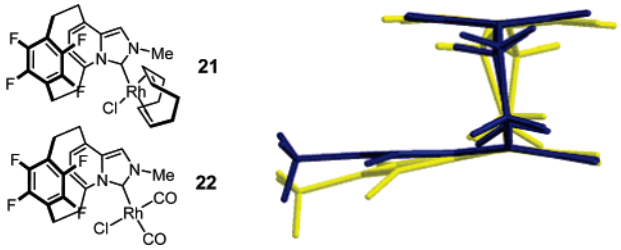
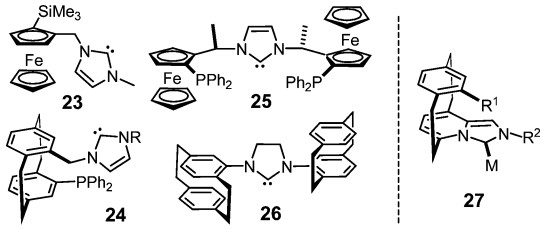


Chart 3. Representative Examples of Known Planar Chiral NHC's



tetramethoxy-substituted carbene in complex **19** equals that of the unsubstituted congener in **18**. Four MeO groups on one ring of a para-cyclophane are all mutually forced out of plane (e.g., compound **20**, Chart 1),[14] which entails that the −I and +M effects of oxygen average out and hence render the methoxy substituents electronically inconsequential.

In striking contrast, the *trans*-CO stretching frequency of complex **22** is very significantly shifted ($\tilde{\nu}$ = 2004 cm^{-1}), thus revealing the tremendous influence of the fluorinated lid on the donor capacity of the carbene underneath. The remote fluorination overcompensates the effects induced by ring annulation as well as cyclophane formation, rendering the carbene unit in **22** even less electron-donating than the parent compound **5**. Since fluorine closely mimics hydrogen in steric terms, the comparison of **18** and **22** exemplifies an effective way to substantially alter the electronic characteristics of a given NHC while maintaining its bulk and constitution virtually unchanged. The overlay of the molecular crystal structures of **17** and **21** (Chart 2) supports this view, even though the carbene subunit of **21** is slightly tilted away from the fluorinated rim, most likely for stereoelectronic reasons.[7]

In addition to the remote control over the donor abilities, the planar chiral structure of the NHC ligands presented herein deserves further comment. Although a host of chiral NHC's has been presented in the literature,[1,15] planar chiral ones are scarce and limited to cases such as **23**−**26** in which an NHC is merely attached to a planar chiral entity (Chart 3).[16] In contrast to such a tangling arrangement, the NHC in **17**−**22** constitutes an integral part of the stereogenic unit, which largely consists of π-bonds and is hence distinctly more rigid and conformationally preorganized. Furthermore, the new ligand design allows one to precisely position an appropriate substituent R^1 on top of the bound metal center as shown in the generic structure **27**, such that the chiral binding pocket is clearly defined. Work in this laboratory is ongoing to exploit these structural features. Thereby, the basic nitrogen in, e.g., **14** or **15** provides opportunities for the separation of the enantiomers by conventional means. Moreover, we were able to obtain the imidazolium salt **16** in optically pure form by preparative HPLC.[12,17]

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Supporting Information Available: Additional reference data, Experimental Section, and copies of the NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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