Isoquinolin-1-ylidenes as electronically tuneable ligands†

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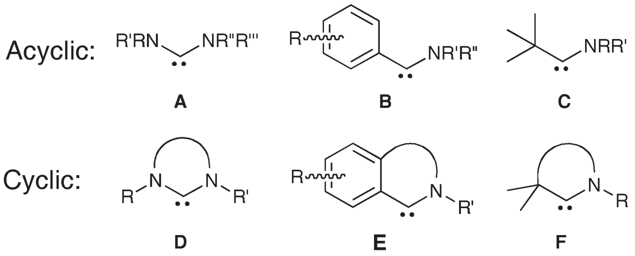
The novel isoquinolin-1-ylidene ligands, introduced into Rh(I) complexes by exploiting the carbene-like reactivity of adducts 6, exhibit ligand properties similar to those of classic NHCs, and their electronic properties can be tuned by the introduction of electron-withdrawing or donating groups in the benzene ring.

Heterocyclic diaminocarbenes have been established during the last decade as one of the most useful type of ligands in homogeneous catalysis.[1] In a fundamental contribution to this field, Bertrand and co-workers have recently demonstrated that a single nitrogen atom effects the required stabilization that leads to stable singlet carbenes. Consequently, acyclic amino aryl carbenes **B**[2] and both acyclic and cyclic amino alkyl carbenes **C**[3] and **F**[4] have been isolated and characterized. However, the synthesis of cyclic amino aryl carbenes **E** and/or transition-metal catalysts thereof remain as an unsolved question.§

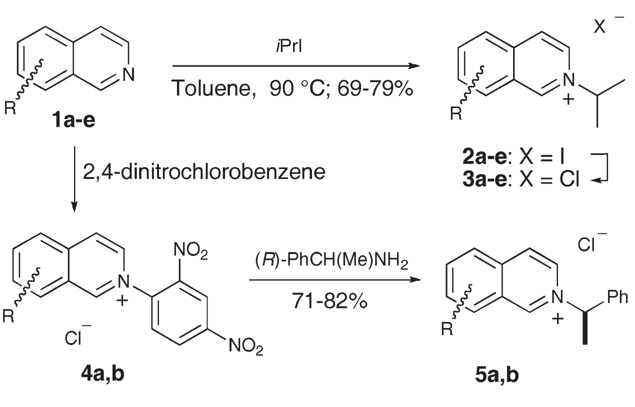


The better ligand behavior of cyclic carbenes **D** and **F** with respect to their acyclic counterparts **A** and **C**, on the one hand, and the possibility of tuning the electronic properties of carbenes **E** by introducing electron-donating or withdrawing R groups in the benzene ring, on the other, make these compounds as possibly very promising ligands for transition metal-catalyzed reactions. We wish now to report on the synthesis, structure and catalytic properties of several RhCl(COD)(isoquinolin-1-ylidene) complexes, reported herein as the first available family of type **E** carbene derivatives.

The synthesis of a series of isoquinolinium salts **2–3**, potential direct precursors of the desired carbenes, was accomplished by alkylation from commercial or readily available[6] isoquinolines **1a–e**. Alternatively, salts **5** were obtained by transamination from Zincke salts **4**,[7] a method that allows the introduction of chiral exocyclic elements as the (*R*)-1-phenylethyl group (Scheme 1).

We started by attempting reactions of isoquinolinium halides **2**, **3** and **5** with silver oxide. Unlike most diaminocarbene precursors,[8] however, these compounds did not form the corresponding silver carbenes. On the other hand, attempts to isolate or detect the free carbenes by deprotonation with a strong base as KHDMS or KO^{t}Bu regularly failed; products **6** or **6′** resulting from nucleophilic addition to the C=N bond were isolated instead, as reported for phenanthridine analogues[9] (Scheme 2). On the other hand, it was observed that adducts **6** quickly decomposed when exposed to air, even in the solid state. Their unexpected instability made us speculate that these compounds could eventually behave as precursors for carbenes **7** in analogy with amine or alcohol adducts from other NHCs.[10,11] Moreover, it was rationalized that such a process should be easier than in phenanthiridine systems: first, the planarization in the isoquinoline system is not associated with the severe steric interactions [N*R* ↔ C(4)*H* and C(1)*H* ↔ C(10)*H*] present in the phenanthridine-6-ylidene system; second, formation of the free carbene is favored by the aromatization of the system, but the associated resonance energy is relatively higher for the isoquinoline-1-ylidene system than for the phenanthridine-6-ylidene analogue.

Supporting this hypothesis, it was found out that adducts **6b** (isolated) and **6e** [crude from **3e** and KN(SiMe$_3$)$_2$] reacted with elemental Se at RT to afford selenolactams **8b** and **8e**¶ in 93 and 45% yield, respectively. The more stable adduct **6′b** reacted with S$_8$ in toluene at 80 °C to afford thiolactam **8′b** in 61% yield. More interestingly from a practical viewpoint, addition of [RhCl(COD)]$_2$



series	a	b	c	d	e
R	H	8-Me	6-OMe	5-NO$_2$	6,7-di-OMe

Scheme 1 Synthesis of isoquinolinium salts **2**, **3** and **5**.

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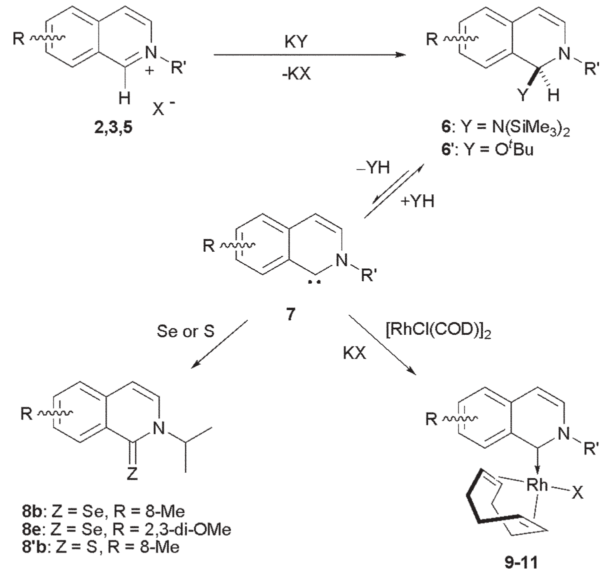


Scheme 2 Synthesis of compounds **8** and Rh(I) complexes **9–11** *via* isoquinolin-1-ylidenes **7**.

Table 1 Synthesis of [RhX(COD)(Iqui)] complexes using KHDMS as mediator

	R	R′	X	*t*/min	Product	Yield[a] (%)
2a	H	*i*-Pr	I	15	**9a**	71
3a	H	*i*-Pr	Cl	15	**10a**	54
3b	8-Me	*i*-Pr	Cl	60	**10b**	82
3c	6-OMe	*i*-Pr	Cl	60	**10c**	39
3d	5-NO_2	*i*-Pr	Cl	10	**10d**	45
5a	H	CH(Me)Ph	Cl	15	**11a**	65[b]

[a] Isolated yield after column chromatography. [b] 80 : 20 mixture of atropoisomers. A careful chromatographic purification afforded the major isomer in pure form.

to the reaction media, presumably containing carbenes **7**, led to the formation of [RhX(COD)(Iqui)] (Iqui = isoquinolin-1-ylidene) complexes **9–11** in moderate to good yields (Table 1). Though the reaction of iodide **2a** was more efficient than that of the chloride **3a** (71% for **9a** *vs.* 54% for **10a**), we decided to prepare the whole set of chloro complexes **10**|| in order to compare their structures and properties with many other known [RhCl(COD)(carbene)] complexes from cyclic and acyclic mono- and diamino carbenes.[11–14] Compounds **9–11** proved to be robust, thermally stable materials, and even survived chromatographic purification on silica-gel. Fortunately, the structures of carbene complexes **9a**, **10c** and **11a** could be analyzed by single-crystal X-ray techniques (Fig. 1).¶ The C(carbene)–Rh [2.024 (**9a**), 2.019 (**10c**), and 2.020 Å (**11a**)] and C–N [1.351 (**9a**), 1.350 (**10c**), and 1.344 Å (**11a**)] bond distances lay in the same range as those of related complexes based on diaminocarbenes [C(carbene)–Rh 2.00–2.06 Å; C–N 1.35–1.36 Å]. In all cases, there is a noteworthy *trans* influence as measured from the C(COD)–Rh distances [$\Delta trans - cis$ (average) = 0.089 (**9a**), 0.108 (**10c**), and 0.106 Å (**11a**)], providing significant indication of the excellent σ-donor ability of the ligand. All structures exhibit pre-agostic Rh···C*H* interactions,[15] characterized by short Rh···H distances and by the chemical shifts of the involved H atoms [9.8–10.5 ppm for C(8)*H*; 7.1–7.9 ppm for C*H*Me_2; 8.53 ppm for C*H*(Me)Ph]. These interactions may explain the relatively high configurational stability of **11a**. Additional information was collected from the corresponding $Rh(CO)_2Cl$(Iqui) complexes **12a,c,d**, readily obtained in near quantitative yields by fast displacement of the COD ligand by CO at RT (Scheme 3), a reaction that is known to be facilitated by ligands featuring strong σ-donor ability.[11]** The analysis of the CO stretching frequencies indicates a fairly good donor ability by these Iqui ligands, approaching the values for the best known mono- and diamino carbene ligands.[3,11,13,14,16] The effect by the substitution in the benzene ring can also be analyzed from the CO stretching frequencies: as expected, the 4-nitro-substituted ligand [**12d**; ν_{CO} (*trans*) 2003 cm^{-1}] appears to be slightly less basic than the unsubstituted ligand [**12a**: ν_{CO} (*trans*) 1998 cm^{-1}], while the 3-methoxy group improves the donor ability [**12c**: ν_{CO} (*trans*) 1996 cm^{-1}].[17]

A preliminary evaluation of the catalytic activity of complexes **9** was attained from the hydrosilylation of acetophenone. Using the unsubstituted catalyst **10a** (0.5 mol%), 50% conversion was reached after 6.5 h at RT. Under the same conditions, the 4-NO_2-substituted catalyst **10d** also promoted a clean reaction, but only 12% of conversion was reached in this time. On the other hand, the 3-OMe-substituted catalysts **10c** led to a complex mixture within minutes, suggesting that it also catalyses undesired reactions (Scheme 4).

In conclusion, isoquinolin-1-ylidenes (Iquis), exhibit excellent properties as transition-metal ligands. Moreover, the conjugation of the benzene ring with the carbene carbon, highly efficient thanks to the coplanarity forced in the bicyclic system, makes possible to tune the electronic properties of the ligand by simply introducing appropriate substituents.

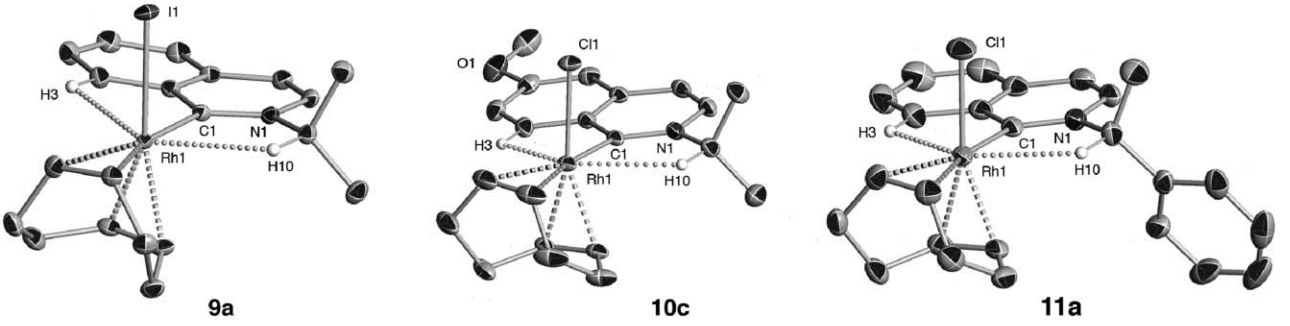
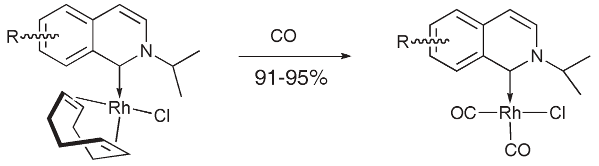


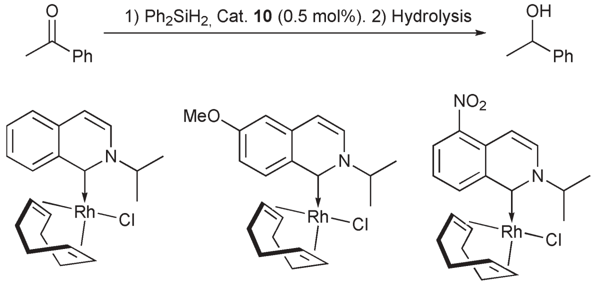
Fig. 1 ORTEP drawings for **9a**, **10c** and **11a**. Thermal ellipsoids are drawn at the 50% probability level; H atoms not involved in preagostic interactions are omitted for clarity.



10a: R = H
10c: R = 6-OMe
10d: R = 5-NO$_2$

12a: R = H; ν_{CO} 2077, 1998 cm^{-1}
12c: R = 6-OMe; ν_{CO} 2076, 1996 cm^{-1}
12d: R = 5-NO$_2$; ν_{CO} 2081, 2003 cm^{-1}

Scheme 3 Effect of substitution in the σ-donor ability of Iqui ligands.



10a **10c** **10d**

Scheme 4 Relative catalytic activities of **10a**, **10c** and **10d** in the hydrosilylation of acetophenone.

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Notes and references

§ A Pd complex containing a quinazolin-2-ylidene ligand has been reported. However, it was described as a non-reproducible result.[5]

¶ *Crystal data for* **8e**: $C_{14}H_{17}NO_2Se$, M = 310.25, space group $P\bar{1}$, Z = 4, a = 10.4152(4), b = 11.5802(5), c = 11.8762(5) Å, α = 80.8360(10), β = 89.3910(10), γ = 79.5420(10)°, V = 1390.37(10) Å^3, μ(Mo-Kα) = 2.695 mm^{-1}, T = 100(2) K, 35 132 reflections measured, 8353 unique (R_{int} = 0.0189). Final $R1$ = 0.0225 [$I > 2\sigma(I)$] and $wR2$ = 0.0614 (all data). *Crystal data for* **9a**: $C_{20}H_{25}INRh$, M = 509.22, monoclinic, space group $P2_1/n$, Z = 4, a = 8.6805(7), b = 14.9418(14), c = 14.7924(13) Å, β = 103.803(3)°, V = 1863.2(3) Å^3, μ(Mo-Kα) = 2.573 mm^{-1}, T = 100(2) K, 17 579 reflections measured, 5469 unique (R_{int} = 0.0208). Final $R1$ = 0. 0208 [$I > 2\sigma(I)$] and $wR2$ = 0.0538 (all data); *Crystal data for* **10c**: $C_{21}H_{27}ClNORh$, M = 447.80, monoclinic, space group $P2_1/c$, Z = 4, a = 11.3168(5), b = 11.1197(5), c = 16.5538(7) Å, β = 108.178(2)°, V = 1979.16(15) Å^3, μ(Mo-Kα) = 1.006 mm^{-1}, T = 100(2) K, 41 044 reflections measured, 9537 unique (R_{int} = 0.0171). Final $R1$ = 0.0306 [$I > 2\sigma(I)$] and $wR2$ = 0.0824 (all data). *Crystal data for* **11a**: $C_{25}H_{27}ClNRh$, M = 479.84, tetragonal, space group $P4_12_12$, Z = 8, a = 10.67910(10), b = 10.67910(10), c = 36.8984(6) Å, V = 4208.01(9) Å^3, μ(Mo-Kα) = 0.949 mm^{-1}, T = 173(2) K, 24 766 reflections measured, 6277 unique (R_{int} = 0. 0217). Final $R1$ = 0.0216 [$I > 2\sigma(I)$] and $wR2$ = 0. 0493 (all data). Flack parameter = −0.020(19). All structures were solved by direct methods and refined by full-matrix least squares on F^2. CCDC 621896–621899. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b617037d

‖ As an exception, the dimethoxy-substituted derivative **3c** did not react to afford the expected Rh–Iqui complex.

** Interestingly, the displacement of COD ligands by CO in the Rh(COD)Cl complexes of *acyclic* aryl carbene analogues was unsuccessfully attempted.[2]

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