Synthesis and Structures of Fused N-Heterocylic Carbenes and Their Rhodium Complexes

Jean Li, Ian C. Stewart, and Robert H. Grubbs*

The Arnold and Mabel Beckman Laboratories of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125

New procedures for the synthesis of N-heterocyclic carbenes with multiple fused rings have been developed utilizing a key ring-closing metathesis step. Rhodium complexes were obtained via the pentafluorophenyl carbene adducts. Solid-state structural behaviors of the new carbene ligands were analyzed via X-ray crystallography.

N-Heterocyclic carbenes (NHCs), first isolated by Arduengo et al. in 1991, have become a well-studied and well-utilized class of ligands in the field of transition metal-catalyzed reactions.[1] Their proficiency in catalysis, variable electronic properties, and ease of translation into complex architectural structures have allowed for the development of unique reactivity and targeted selectivity.[2-6] In the past 20 years, NHCs have been applied as ligands in reactions such as palladium-catalyzed cross-coupling, olefin metathesis, asymmetric hydrosilylation, and conjugate addition.[7-12] Free NHCs have also shown great efficacy as organocatalysts in a variety of reactions.[13,14] Exploration of novel structural motifs has enabled the development of novel applications for NHCs. Serving as a positive feedback loop, as the synthetic and catalytic applications have grown, the array of structural motifs has grown in parallel (Figure 1), illustrating the dynamic interchange between structure and function.[1,15,16]
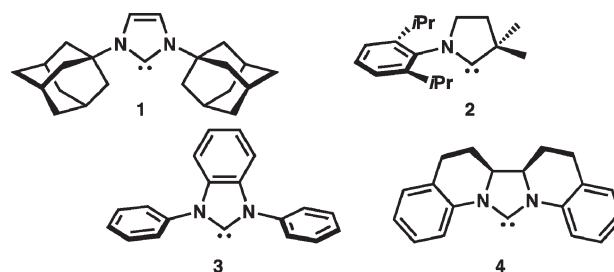

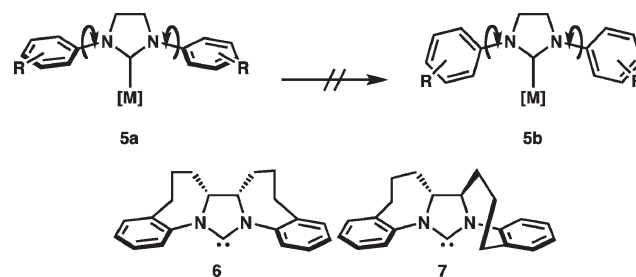**Figure 1.** NHCs utilized in metal-mediated catalysis.

Figure 2. Design of rotationally locked NHCs.

In particular, fused NHC structures are of interest, as it has been shown computationally that the rotational lability of the carbene can greatly influence the behavior and dynamics of the NHC-bound metal complex.[17,18] In this study, the syntheses of fused carbenes **6** and **7** were designed to allow for control of stereochemistry at the backbone of the NHC as well as facile modification of the N-bound arene fragment. A three-carbon chain from the backbone of the NHC to the aryl was chosen to form the cis-fused as well as the trans-fused structures (Figure 2). Independent synthesis of each carbene precursor allowed for separate cis and trans routes, bypassing a need to separate the meso from the
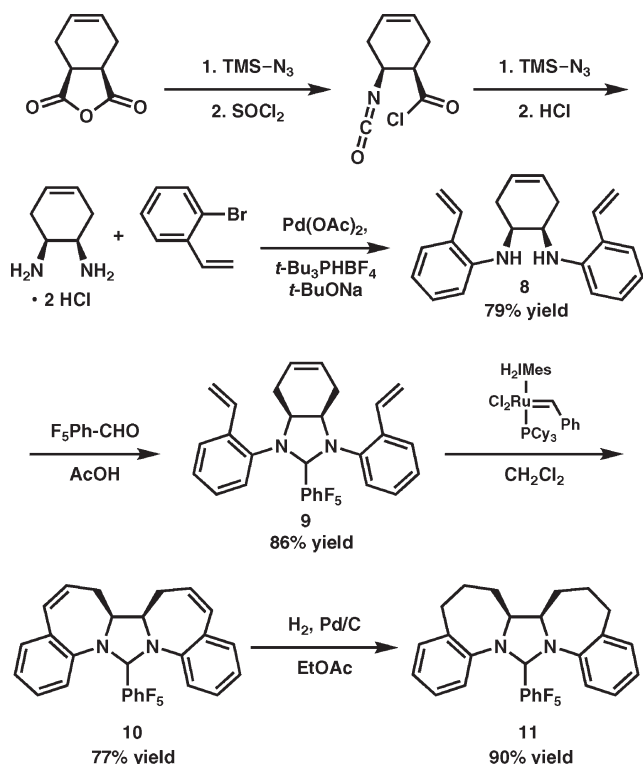
*To whom correspondence should be addressed. E-mail: rhg@caltech.edu.

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Scheme 1. Synthesis of Cis Carbene Precursor 11

1. TMS–N₃
2. SOCl₂

1. TMS–N₃
2. HCl

Pd(OAc)₂,
t-Bu₃PHBF₄
t-BuONa

8
79% yield

F₅Ph-CHO
AcOH

9
86% yield

H₂IMes
Cl₂Ru=Ph
PCy₃
CH₂Cl₂

10
77% yield

H₂, Pd/C
EtOAc

11
90% yield

Scheme 2. Synthesis of Trans Carbene Precursor 16

BF₃-OEt₂
m-xylenes

50% yield

Glyoxal
i-PrOH / H₂O

1. Vinylmagnesium chloride, THF
2. Diphosgene, Et₃N, CH₂Cl₂

100% yield

12
64% yield over 2 steps

H₂IMes
Cl₂Ru=Ph
PCy₃
CH₂Cl₂

13
70% yield

Pd/C, H₂
MeOH

14
100% yield

1. LiAlH₄, THF
2. 5M HCl

15
75% yield

F₅Ph-CHO
AcOH

16
73% yield

Scheme 3. Synthesis of Rhodium Complexes

11

[(cod)RhCl]₂
benzene, 100°C

17
100% converison by NMR

16

[(cod)RhCl]₂
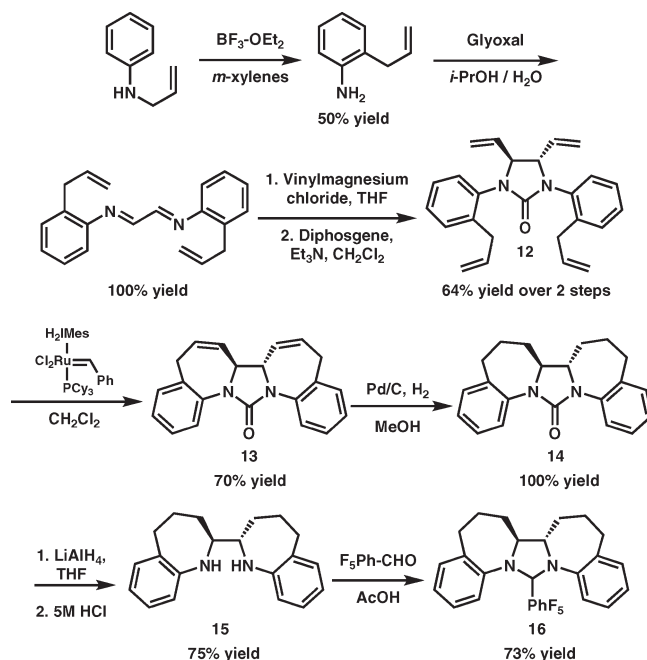benzene, 100°C

18
100% converison by NMR

racemic forms. Synthesis of the racemate could be easily modified to render the enantioenriched mixtures of the trans species via resolution with inexpensive L-(+)-tartaric acid.[19]

Herrmann and Blechert have synthesized similar NHC structures.[16,20,21] Carbene **4** was appended to ruthenium and shown to have limited metathesis activity.[16] Unfortunately, the synthesis of **4** yielded a 3:1 mixture of the meso and racemic forms, and only the meso form was isolated for study.[16] The crystal structure of carbene **4**, which contains a C_2 linkage, exhibited planarity of the N-bound arene with the heterocycle, thereby rendering the ruthenium species noncanonical with standard ruthenium-based catalysts.

In designing both syntheses, we chose to utilize a ring-closing metathesis as the key step in fusing the seven-membered ring fragment. Previous syntheses of fused NHC frameworks began from quinoline-type derivatives and were thus limited in both ring size and stereocontrol.[16] With intimate knowledge of the olefin metathesis reaction at hand, we imagined separate syntheses hinging upon retention of the initially introduced backbone stereochemistry during ring-closing metathesis (RCM).

The cis-cyclohexenyldiamine was synthesized by a known procedure.[22] Palladium-catalyzed cross-coupling of the free diamine with *o*-bromostyrene yielded secondary diamine **8**. Attempts at ring-closing metathesis of **8** resulted in decomposition of both diamine and the ruthenium benzylidene species. In order to cloak the diamino functionality, **8** was
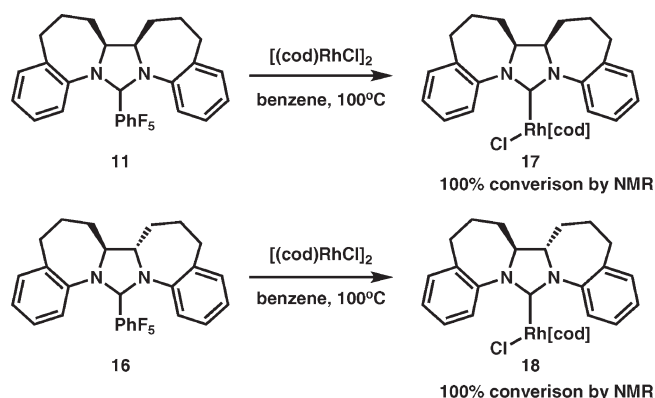
condensed with pentafluorobenzaldehyde to form **9**, following a recent report.[23] Ring-closing with a ruthenium catalyst provided cis-fused adduct **10**, and hydrogenation gave the desired carbene precursor **11**.

Entry into the racemic trans-fused carbene began with aza-Claisen rearrangement of commercially available *N*-allylaniline. Condensation with glyoxal yielded the bisimine, which was further functionalized via Grignard addition and in situ urea formation to give intermediate **12**. Although the pentafluorophenyl adduct could be introduced immediately succeeding addition of Grignard, the urea provided higher yields in the metathesis reaction, yielding ring-closed **13**. Hydrogenation with Pd/C at 1 atm gave the urea **14**, which was readily cleaved with lithium aluminum hydride to afford trans-fused diamine **15**. The free diamine was then condensed with pentafluorobenzaldehyde to provide carbene precursor **16**.

Recently, we reported the facile conversion of pentafluorophenyl adducts as NHC precursors for ruthenium

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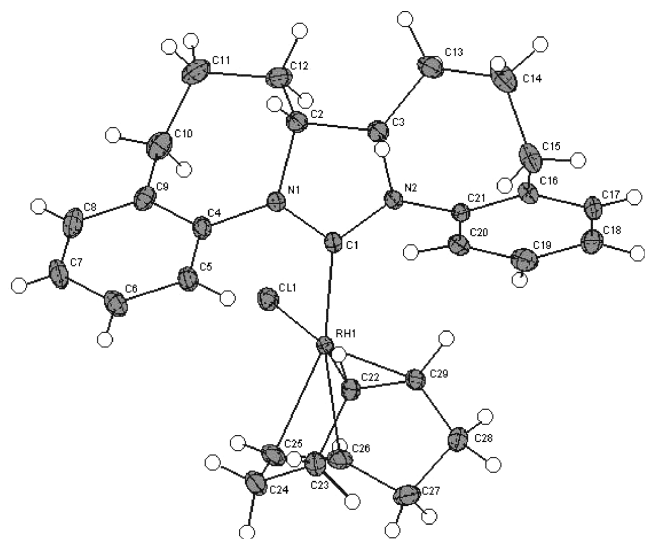(23) Blum, A. P.; Ritter, T.; Grubbs, R. H. *Organometallics* **2007**, *26*, 2122.

Figure 3. ORTEP diagram of **17** with 50% probability ellipsoids.

Table 1. Selected Bond Lengths [Å] and Angles [deg] for 17

Rh(1)−C(1)	1.992(2)	C(1)−N(1)−C(2)	111.93(17)
Rh(1)−C(29)	2.105(2)	C(1)−N(2)−C(3)	110.99(17)
Rh(1)−C(22)	2.124(2)	N(1)−C(1)−N(2)	106.57(19)
Rh(1)−C(25)	2.207(2)	N(1)−C(1)−Rh(1)	124.58(14)
Rh(1)−C(26)	2.247(2)	N(2)−C(1)−Rh(1)	128.82(15)
Rh(1)−Cl(1)	2.4075(5)	N(1)−C(2)−C(3)	98.93(17)
		N(2)−C(3)−C(2)	100.04(18)
		C(12)−C(2)−C(3)−C(13)	37.57
		C(5)−C(4)−N(1)−C(1)	67.86
		C(20)−C(21)−N(2)−C(1)	31.84

complexes.[23] We chose to isolate the masked carbene as pentafluorophenyl adducts rather than the traditional imidazolinium salts in order to allow ligation onto metal fragments in the absence of a strong base. Thus, reaction of **11** or **16** with rhodium cyclooctadiene chloride dimer gave the corresponding rhodium complexes shown (Scheme 3). Crystals suitable for X-ray diffraction studies were obtained as bright yellow blocks by vapor diffusion of pentane into a benzene solution of either **17** or **18**.

Figure 3 shows the ORTEP diagram of the cis-fused rhodium complex **17** obtained from X-ray diffraction. We were surprised to note that, although there exists a cis orientation at the backbone of the NHC, a distortion in the carbene allows the two linkers to obtain a relative trans configuration of the N-bound arenes. Note that the dihedral torsion angle between C(12)−C(2)−C(3)−C(13) of 37.57° confirms a cis orientation (Table 1). Neither arene is orthogonal to the plane of the NHC, containing dihedral angles C(5)−C(4)−N(1)−C(1) of 67.86° and C(20)−C(21)−N(2)− C(1) of 31.84°.

X-ray crystal analysis of trans-fused **18** confirmed the expected anti−anti relationship. Analogous to previously reported nonfused ligated NHCs, Figure 4 shows the NHC to be planar, without the distortion noted in Figure 3.

Table 2 lists selected bond lengths and angles for **18**. Here the dihedral torsion angle at the backbone of the carbene is greater than 90°, with the angle C(12)−C(2)−C(3)−C(13) of 136.83°. Again, neither arene ring is orthogonal or planar to the NHC, with dihedral angles C(5)−C(4)−N(1)−C(1) of 50.98° and C(20)−C(21)−N(2)−C(1) of 62.57°.

A simplified side view of both cis- and trans-fused Rh species with hydrogens omitted for clarity is shown
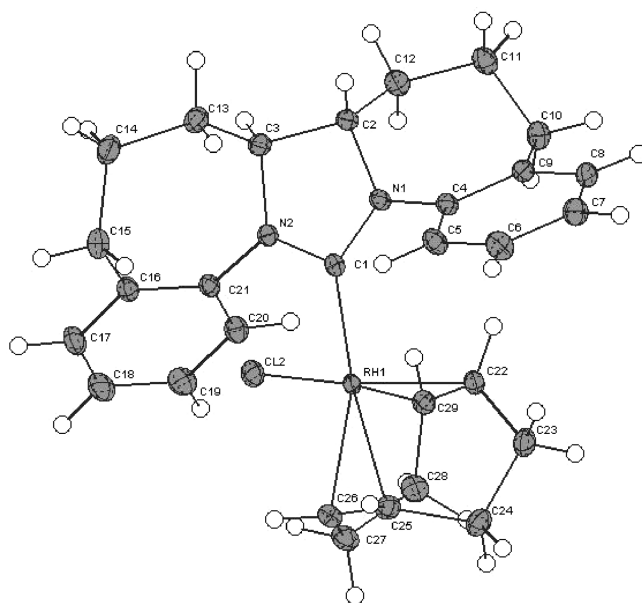

Figure 4. ORTEP diagram of **18** with 50% probability ellipsoids.

Table 2. Selected Bond Lengths [Å] and Angles [deg] for 18

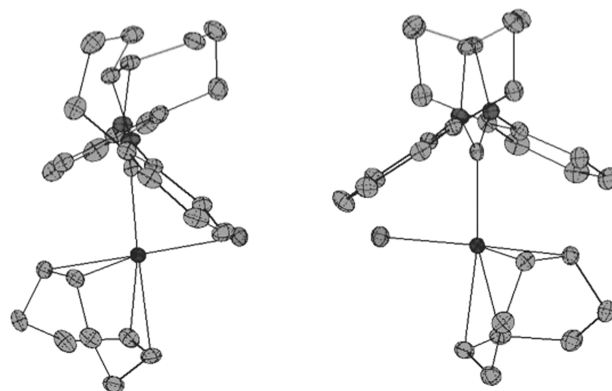|			
Rh(1)−C(1)	2.0032(7)	C(1)−N(1)−C(2)	113.12(5)
Rh(1)−C(22)	2.0969(7)	C(1)−N(2)−C(3)	113.17(5)
Rh(1)−C(29)	2.1263(8)	N(1)−C(1)−N(2)	107.40(6)
Rh(1)−C(26)	2.1847(8)	N(1)−C(1)−Rh(1)	123.40(5)
Rh(1)−C(25)	2.2169(8)	N(2)−C(1)−Rh(1)	129.10(5)
Rh(1)−Cl(1)	2.3896(2)	N(1)−C(2)−C(3)	101.40(6)
		N(2)−C(3)−C(2)	101.27(5)
		C(12)−C(2)−C(3)−C(13)	136.83
		C(5)−C(4)−N(1)−C(1)	50.98
		C(20)−C(21)−N(2)−C(1)	62.57

Figure 5. Side view of structures **17** (left) and **18** (right).

in Figure 5. It is clear that the cis linkage exists for complex **17**; however, the arenes are locked in a relative trans conformation, similar to that of complex **18**, which shows a higher degree of overall symmetry.

In summary, we have developed the synthesis of stereochemically defined fused N-heterocyclic carbene structures, which can be obtained in gram quantities as either the meso form or the racemate. X-ray crystallography data confirmed the covalent linkages.

Supporting Information Available: Crystallographic data for complexes **17** and **18**, experimental procedures, and NMR data for all new compounds are available. This material is available free of charge via the Internet at http://pubs.acs.org.