Carbenes

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Carbenes Stabilized by Ylides: Pushing the Limits**

Alois Fürstner, Manuel Alcarazo, Karin Radkowski, and Christian W. Lehmann*

Dedicated to Professor Manfred T. Reetz on the occasion of his 65th birthday

The most successful strategies for taming carbenes consist of coordination to a transition-metal fragment and/or the attachment of heteroatoms to their formally divalent carbon atom.[1] The latter concept was particularly successful for nitrogen as the heteroelement and has resulted in the numerous variants of (di)aminostabilized carbenes with cyclic and acyclic backbones known to date.[2] It is the overlap of the lone pair of electrons on the nitrogen atom with the empty p orbital of the carbene which is essential for stabilizing the reactive site (Figure 1).[2]

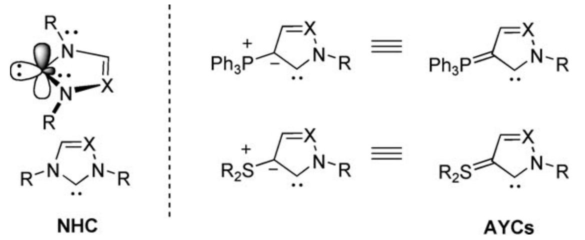
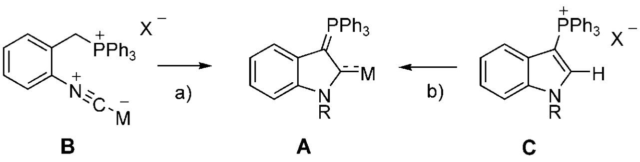


Figure 1. Basic structure of an N-heterocyclic carbene (NHC) as a prototype singlet carbene stabilized by two flanking amino groups (X = CH, N; R = alkyl, aryl). The formal replacement of one NR unit by an ylide leads to an archetype (amine)(ylide)carbene (AYC) species.

Under this premise, other chemical entities with a lone pair of electrons disposed in an orbital of appropriate symmetry might serve the exact same purpose. The polarized π bonds of ylides are suitable candidates in this regard. Thus, the formal replacement of one (or both) N atoms of a prototype N-heterocyclic carbene (NHC) by ylide moieties leads to constructs which owe their stability to a combination of two very reactive sites (Figure 1). As the π-donating capacity of an ylide, however, arguably exceeds that of a nitrogen atom while the inductive effect should be smaller, one might expect such compounds to exhibit particularly pronounced electron-releasing capacities and hence to be of considerable interest as ancillary ligands for homogeneous catalysis.

In fact, metal complexes containing such (amino)(ylide)carbene (AYC) ligands have been known for a long time, but have had little impact compared with their (di)aminostabilized relatives.[3,4] Such AYC ligands were prepared by base-induced cyclization of transition-metal isocyanide complexes **B** bearing a latent phosphorus ylide in the vicinity (Scheme 1).[4] However, this method invariably delivered AYCs with an indole skeleton featuring an unprotected NH group (**A**, R = H), and the efficiency of cyclization was found to be strongly dependent on the nature of the involved metal fragment. Importantly, Kawashima and coworkers reported earlier this year that deprotonation of a suitable phosphonium salt precursor **C** provides a complementary route to metal–AYC complexes, even though it was again an indole nucleus which served as proof of principle (**A**, R = Me).[5] We report herein a generalizion of the underlying concept.[3–6] Moreover, we demonstrate the remarkable donor ability of such ligands and show for the first time that uncomplexed AYCs can be sufficiently stable to be observed as discrete entities in solution.



Scheme 1. Known entries into metal–AYC complexes: a) M = [PtCl$_2$(PR$_3$)], Et$_3$N (excess), R = H; or M = [W(CO)$_5$], Na[N(SiMe$_3$)$_2$], R = H; b) M = [Rh(cod)Cl], mesityllithium, R = Me; or M = [PdI(allyl)], *t*BuOK, R = Me. cod = 1,5-cyclooctadiene.

Since all the AYCs reported to date incorporate a phosphorus ylide motif,[3–5] we first investigated if other types of ylides are also capable of stabilizing an adjacent carbene center. To this end, *N*-methylindole (**1**) was treated with diphenylsulfoxide and trifluoroacetic acid anhydride to give sulfonium salt **2**[7] as a crystalline compound after exchange of the counterion for BF$_4^-$ (Scheme 2). Subsequent deprotonation with KHMDS in the presence of [{RhCl(cod)}$_2$] furnished the desired AYC–rhodium complex **3** embodying a sulfur ylide motif.[8] Complex **3** was then transformed into the carbonyl analogue **4** under standard conditions.

The structures of the carbene precursor **2** (Figure 2) and the rhodium complex **3** (Figure 3) are highly instructive.[9] Specifically, the analysis of the bond lengths in **2** reveals a significant degree of charge delocalization of the sulfonium moiety into the heterocyclic ring. This is expressed in the lengthening of the C1−C2 bond and the shortening of the N1−

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[*] Prof. A. Fürstner, Dr. M. Alcarazo, K. Radkowski, Dr. C. W. Lehmann
Max-Planck-Institut für Kohlenforschung
45470 Mülheim an der Ruhr (Germany)
Fax: (+49) 208-306-2994
E-mail: fuerstner@mpi-muelheim.mpg.de

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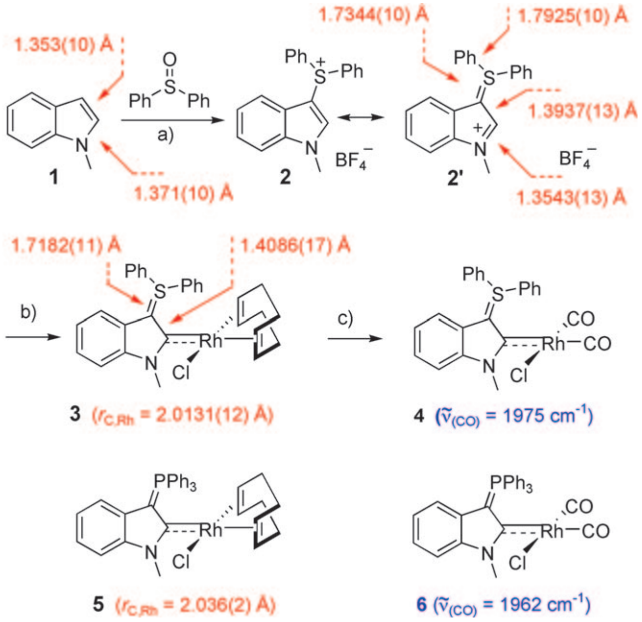


Scheme 2. Preparation and structural characteristics of an AYC incorporating a sulfur ylide. Reagents and conditions: a) 1. trifluoroacetic acid anhydride, $Ph_2S{=}O$, CH_2Cl_2, −30 °C→RT; 2. aq sat. $NaBF_4$, 44 %; b) KHMDS, [{RhCl(cod)}$_2$], THF, −78 °C→RT, 18 %; c) CO (1 atm), THF, 52 %.

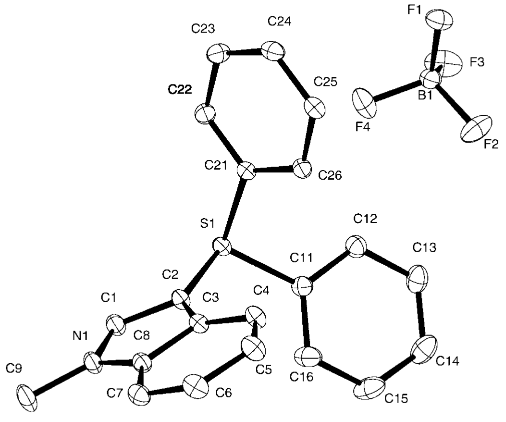


Figure 2. Structure of **2** in the solid state.[9]

C1 bond relative to those in the parent compound indole.[10] The substantial contribution of the mesomeric form **2′** (Scheme 2) to the ground-state structure is also visible in the C2–S1 distance, which is much shorter than the corresponding bonds between the sulfur atom and the equally sp^2-hybridized *ipso*-C atoms of the phenyl substituents. This substantial transmission of charge into the ring predisposes the salt for deprotonation at C1.

The carbene character of the resulting AYC transpires from the structural features of its rhodium complex **3** (Figure 3 and Scheme 2) In addition to the distinctive pattern of bond lengths in the heterocyclic segment, the diminished N1-C1-C2 angle of only 105.23° (compared to 109.17° in **2**) constitutes a particularly characteristic feature.[11] Overall, the available X-ray diffraction data and spectroscopic properties[12] illustrate that **3** and **4** are close relatives of AYC complexes **5** and **6**, respectively, synthesized by Kawashima and co-workers.[5]

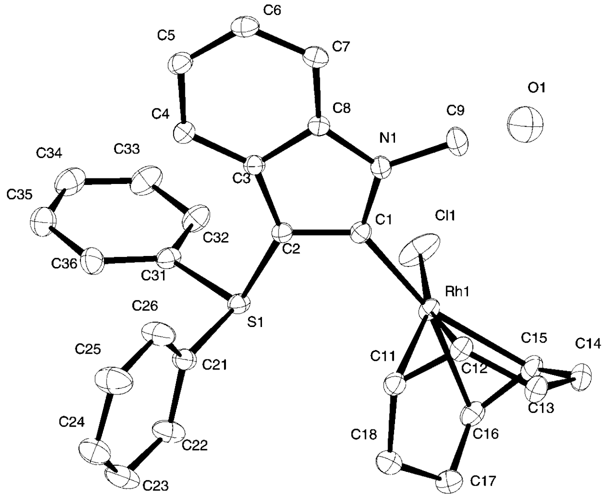
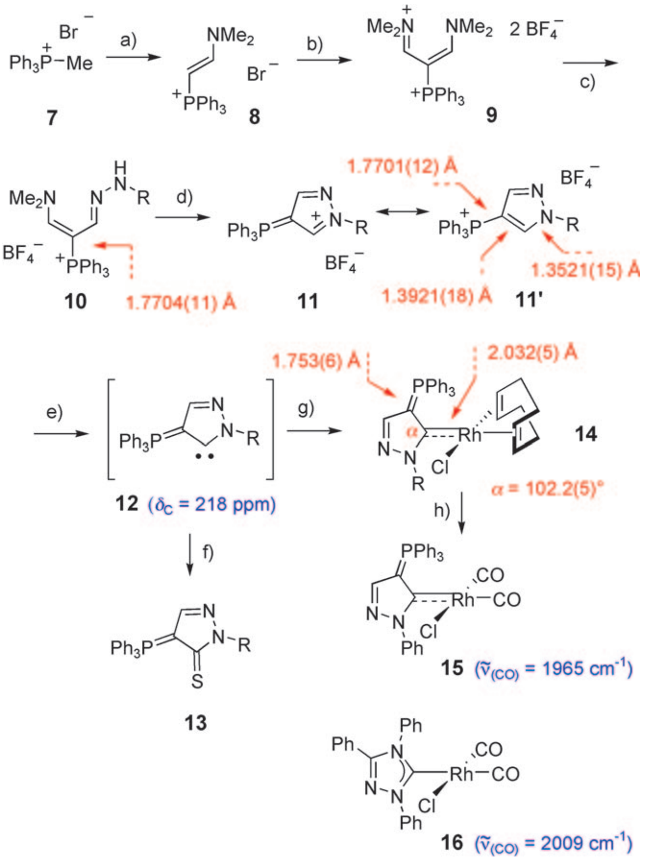


Figure 3. Structure of complex **3** in the solid state.[9]

To further generalize the concept, we investigated if backbones other than indoles are also able to contain ylide-stabilized carbenes.[5b] To this end, the readily available vinamidinium salt **9**[13] was treated with two different mono-substituted hydrazines to give compounds **11a,b** in good yields (Scheme 3).[14,15] The structure of **11a** (R = Ph) in the solid state (Figure 4), however, suggests that the mesomeric extreme **11a′** gains importance, wherein the positive charge largely resides on the lateral phosphonium entity. Even though this fact might argue against deprotonation at the carbon atom, treatment of **11a** with KHMDS at −78 °C furnished the corresponding AYC **12** (R = Ph) which is sufficiently stable for direct observation. This fact is remarkable in view of the unsuccessful attempts of Kawashima and co-workers to observe the analogous AYC derived from indolic precursors of type **C**.[5] The most indicative spectroscopic features are the loss of the salt's acidic proton (δ = 8.91 ppm) and the appearance of the characteristic ^{13}C resonance of the resulting carbene center at δ = 218 ppm ($J_{C,P}$ = 51.2 Hz).

The fact that **12** reacts with sulfur to give thioamide **13** provides chemical evidence for its carbene character (Scheme 3). Moreover, **12** can be intercepted with [{RhCl(cod)}$_2$] in high yield. The structural attributes of the resulting complex **14a** (R = Ph) are again consistent with the view that the ligand constitutes an amino(ylide)carbene (Figure 5 and Scheme 3).[9] Since the N-methylated salt **11b** converted similarly well into complex **14b** (R = Me), it is clear that steric shielding by a bulky N substituent plays only a subordinate role, if any, in the stabilization of a transient AYC of this type.

The exceptional donor qualities of **12** are highlighted by comparison with the otherwise closely related triazole-2-ylidene ligand commonly employed in organic and organometallic catalysis.[2,16] Specifically, the unsymmetrical stretching mode of the CO groups of the rhodium complex **15** appears at a frequency no less than 44 cm^{-1} lower than that of the triazolyl-2-ylidene complex **16**, which indicates that the formal replacement of a single N atom in the heterocycle by



Scheme 3. Reagents and conditions: a) HC(NMe$_2$)(OEt)$_2$, reflux, 92%; b) DMF, POCl$_3$, then aq sat. NaBF$_4$, 70°C, 81%; c) PhNHNH$_2$, MeCN, reflux, 68%; d) MeCN, 180°C (microwaves), 88% (**11a**, R = Ph); or MeNHNH$_2$, MeCN, reflux, 68% (**9**→**11b**, R = Me); e) KHMDS, THF, −78°C; f) S$_8$, THF, −78°C→RT, 65%; g) [{RhCl(cod)}$_2$], THF, −78°C→RT, 88% (R = Ph), 92% (R = Me); h) CO (1 atm), THF, 79% (R = Ph).

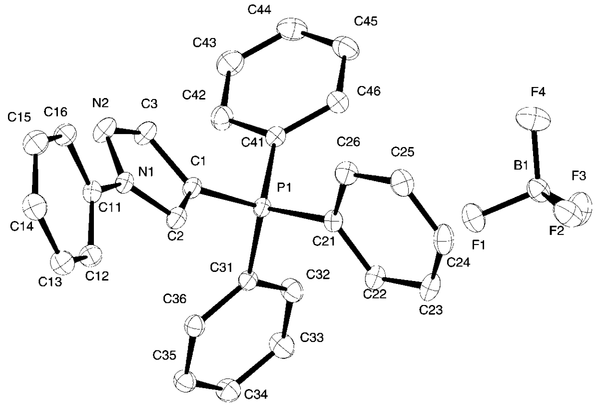


Figure 4. Structure of **11a** in the solid state.[9]

the phosphorus ylide has tremendous electronic implications. This fact is fully appreciated if one recalls that even substantial structural variations of conventional five-membered NHCs engender only minor spectroscopic changes.[12] Overall, the recorded IR data characterize AYCs as exceptionally strong electron-releasing ligands, unmistakably surpassing the traditional NHCs in this regard.

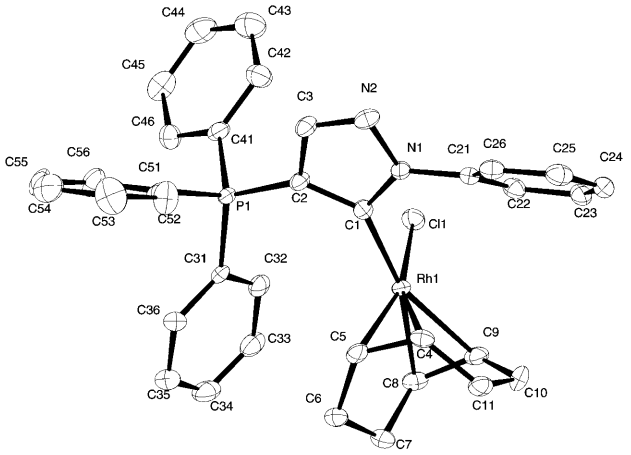
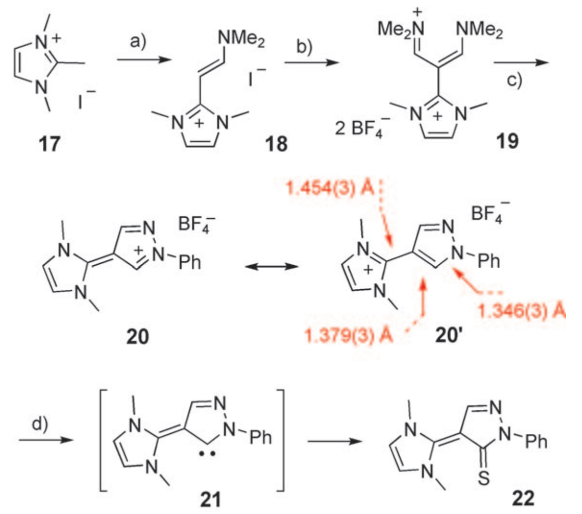


Figure 5. Structure of complex **14a** (R = Ph) in the solid state.[9]

Next, it was probed if polarized C=C bonds also lend themselves to the stabilization of a vicinal carbene (Scheme 4). In recognition of the ylidic character innate to ene-1,1-diamines,[17] compound **20** was designed as a potential progenitor. Even though its structure in the solid state (Figure 6)[9] suggests the imidazolium resonance form **20'** to be the dominant mesomeric extreme (see, for example, the long C1–C7 bond (1.454(3) Å)), the fact that the two rings are close to coplanarity (N1-C1-C7-C6 = 26.35°) might allow for sufficient electronic cross-talk to render deprotonation at C6 feasible. In fact, treatment of **20** with KHMDS in THF generates a reactive intermediate that shows its carbene nature upon reaction with admixed sulfur to give thioamide **22**. Attempts to trap the transient carbene **21** with [{RhCl(cod)}$_2$], however, were only partly successful. Although MS inspection of the crude product indicated formation of the



Scheme 4. Reagents and conditions: a) HC(NMe$_2$)(OEt)$_2$, reflux, 94%; b) 1. DMF, POCl$_3$ 70°C; 2. aq sat. NaBF$_4$, 73%; c) PhNHNH$_2$, MeCN, 180°C, microwaves, 81%; d) KHMDS, S$_8$, THF, −78°C→RT, 55%.

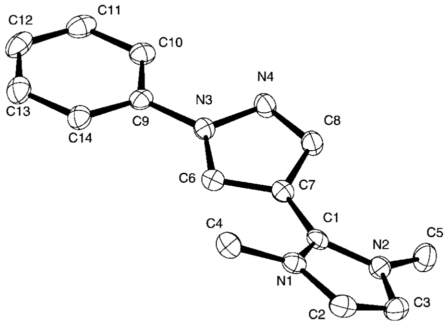
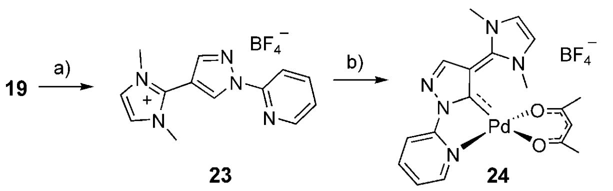


Figure 6. Structure of the complex cation of **20** in the solid state (only one of the two crystallographically independent molecules in the unit cell is depicted); the BF_4^- counterion is omitted for clarity.[9]

desired complex, we were not able to obtain this rather sensitive product in analytically pure form.

In an attempt to stabilize such a metal–AYC complex containing a "carbon ylide", the corresponding *N*-pyridyl derivative **23** was treated with $[Pd(acac)_2]$.[18] Much to our delight, the resulting chelate complex **24** could be isolated in appreciable yield by flash chromatography (Scheme 5).



Scheme 5. Reagents and conditions: a) 2-pyridyl-$NHNH_2$, MeCN, 180 °C (microwaves), 76%; b) $[Pd(acac)_2]$, C_6H_5Cl, 160 °C, 58%. acac = acetylacetonoate.

Importantly, this example also showcases that the widely practiced method for the preparation of metal–NHC complexes by reaction of a precursor salt with a suitable metal reagent carrying (weakly) basic counterions[2] also pertains to the AYC arena. It is expected that this gentle way of generating transient carbenes will foster systematic explorations of this emerging class of ligands.

In summary, carbenes stabilized by one nitrogen atom and one ylide (AYCs) constitute a promising class of neutral two-electron donor ligands. They can be generated by an operationally simple deprotonation route and are available in many different structural formats. Since various kinds of ylides and heterocyclic scaffolds were shown to be effective, further studies into the conceivable structural space are promising. Applications of AYCs in catalysis also deserve scrutiny, given their outstanding donor abilities compared with the commonly used NHC counterparts.

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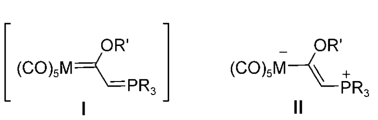

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[8] The rather low yield is due, in part, to the limited stability of the complex during flash chromatography.

[9] Anisotropic displacement parameters are drawn at the 50% probability level, hydrogen atoms have been omitted for clarity. CCDC 692803 (**2**), 692804 (**3**), 692800 (**10a**), 692801 (**11**), 692805 (**14**), and 692802 (**20**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. The structure of **10a** in the solid state as well as short summaries of the crystallographic data can be found in the Supporting Information of this paper.

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[15] Whereas the reaction with $MeNHNH_2$ in refluxing MeCN is highly efficient, the condensation with $PhNHNH_2$ is best carried out under microwave irradiation. Under these conditions, the conversion of **9** into **11a** ($R = Ph$) can be performed in one pot.

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