

NHC ligands derived from Pyrrolidone

By: Robert B Login

NHC ligands play a critical role in organometallic chemistry. Numerous NHC structures have been synthesized and their chemistry has been reviewed. Apparently these carbenes are major sigma electron donor ligands that as singlets are stable because of conjugation with the imidazoline nitrogens. Their use as ligands affords more robust catalysts less sensitive to moisture and various functional groups.

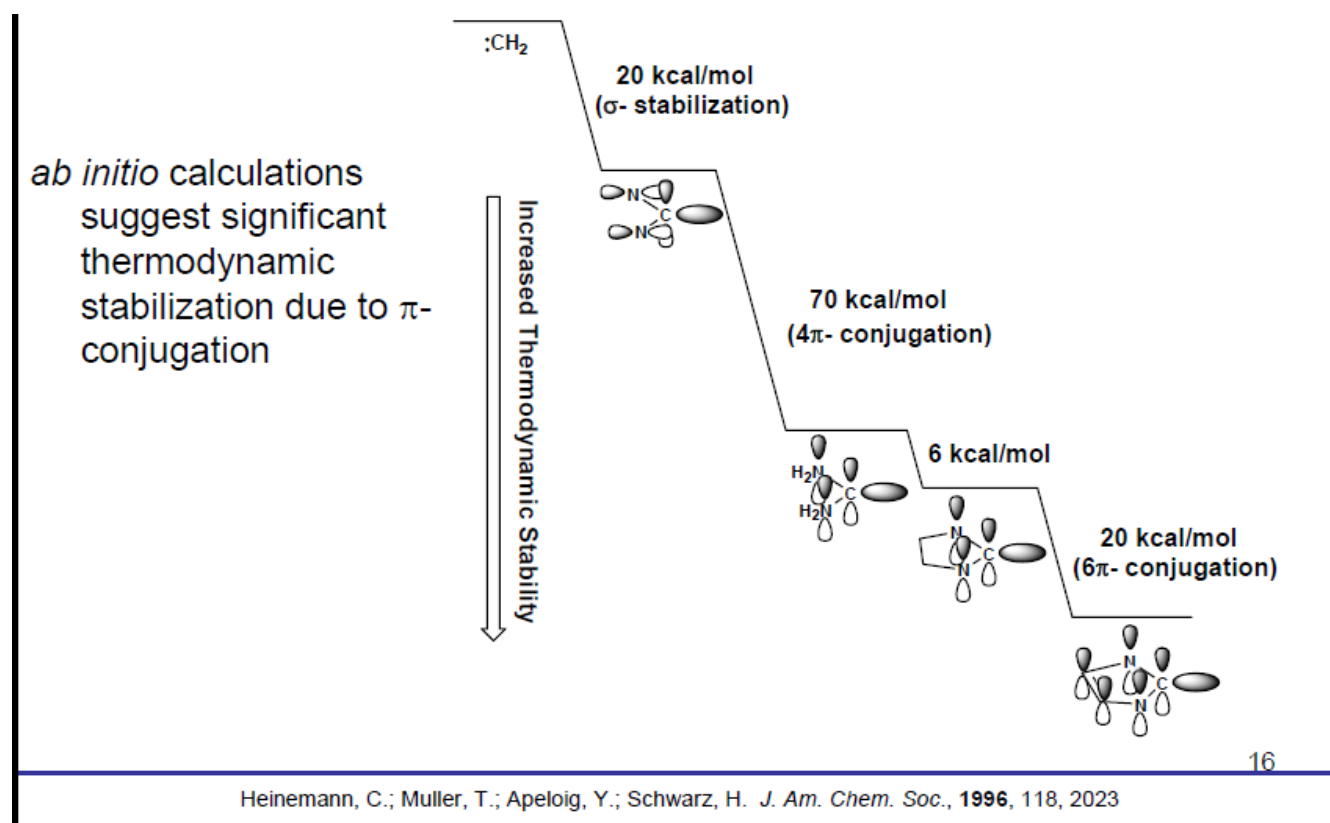
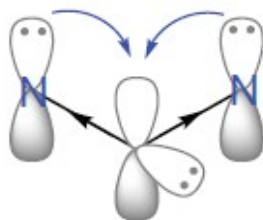


Chart 1



The above chart illustrates the molecular orbitals and the stabilization going



from the simplest carbene to the imidazoline types. This shows the reason for NHC stability, notice the singlet sigma orbital and the empty p orbital. The p orbital being empty can back bond to a D orbital

enhancing stability of a metal complex.

Baran Lab

N-Heterocyclic Carbenes (NHCs)

K. J. Eastman

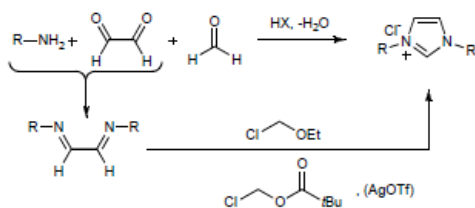
NHCs are most frequently prepared via deprotonation of the corresponding azolium salts (imidazolium, triazolium, tetrazolium, pyrazolium, benzimidazolium, oxazolium, thiazolium salts - pK_a - 21-24).

Imidazolium synthesis:

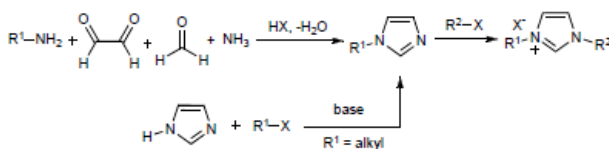
1) Existing imidazoles can be alkylated with appropriate electrophiles.

2) The imidazolium ring can be built:

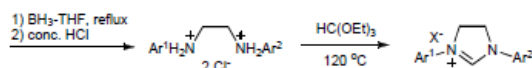
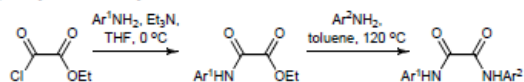
a) symmetric synthesis:



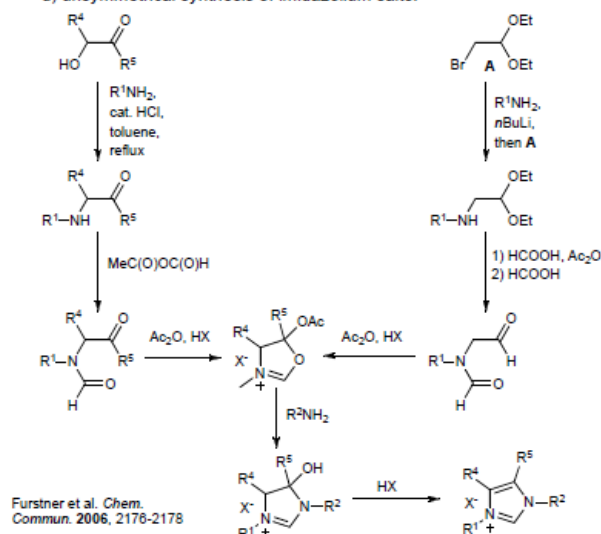
b) unsymmetrical synthesis:



c) unsymmetrical synthesis of imidazolidinium salts:



d) unsymmetrical synthesis of imidazolium salts:



Furstner et al. *Chem. Commun.* 2006, 2178-2178

2

Chart 2 Some examples of the preparation of imidazolium NHC's.

The actual structures of the most successful NHC's used in ruthenium metathesis are shown in chart 3.

Table 1.3 Phosphine-free NHC-Ru complexes.

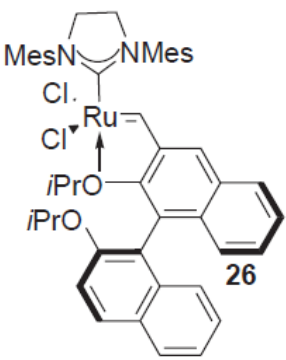
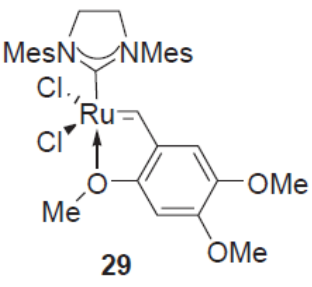
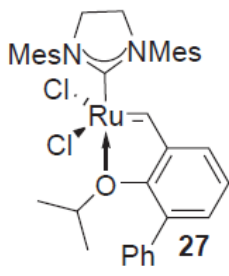
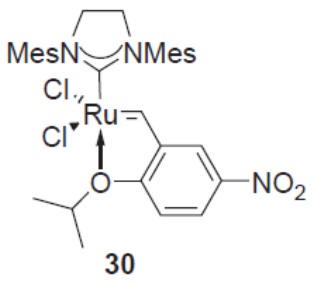
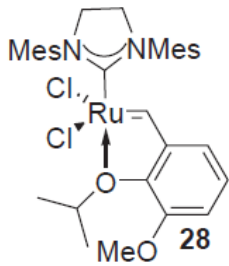
Entry	Catalyst	Entry	Catalyst
1 [43]	 <p>26</p>	4 [46]	 <p>29</p>
2 [44]	 <p>27</p>	5 [47]	 <p>30</p>
3 [45]	 <p>28</p>		

Chart 3

Not only are NHC's finding unique catalyst opportunities, they are starting to be of importance to the use of transition metals in medicine where new antimicrobials have been developed (Chemical Society Reviews, 39 (6): 1903-1912), also a series of patents to W. Young et. al. US 8,648,064 B2 amongst others. These patents are remarkably clever and interesting.

I am not writing a review. My goal is to afford a brief overview of NHC type structures to bolster the value of my ideas, which are as follows:

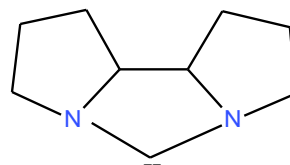
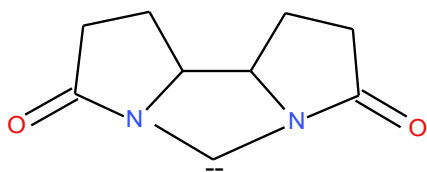
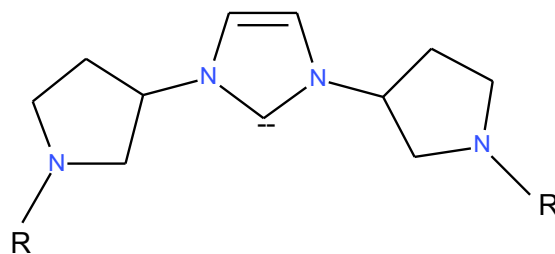
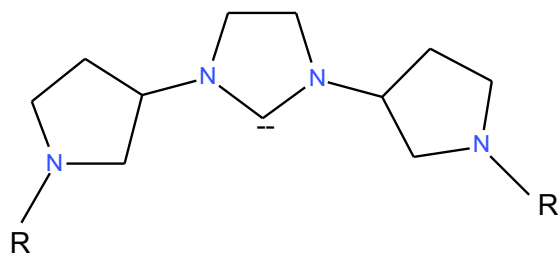
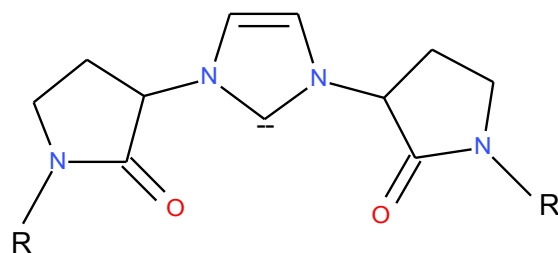
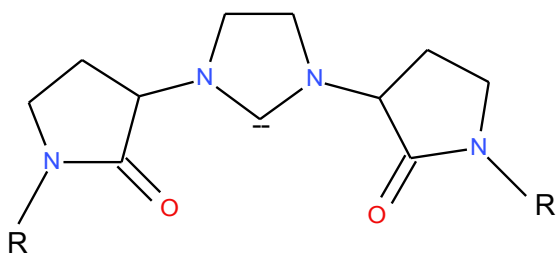


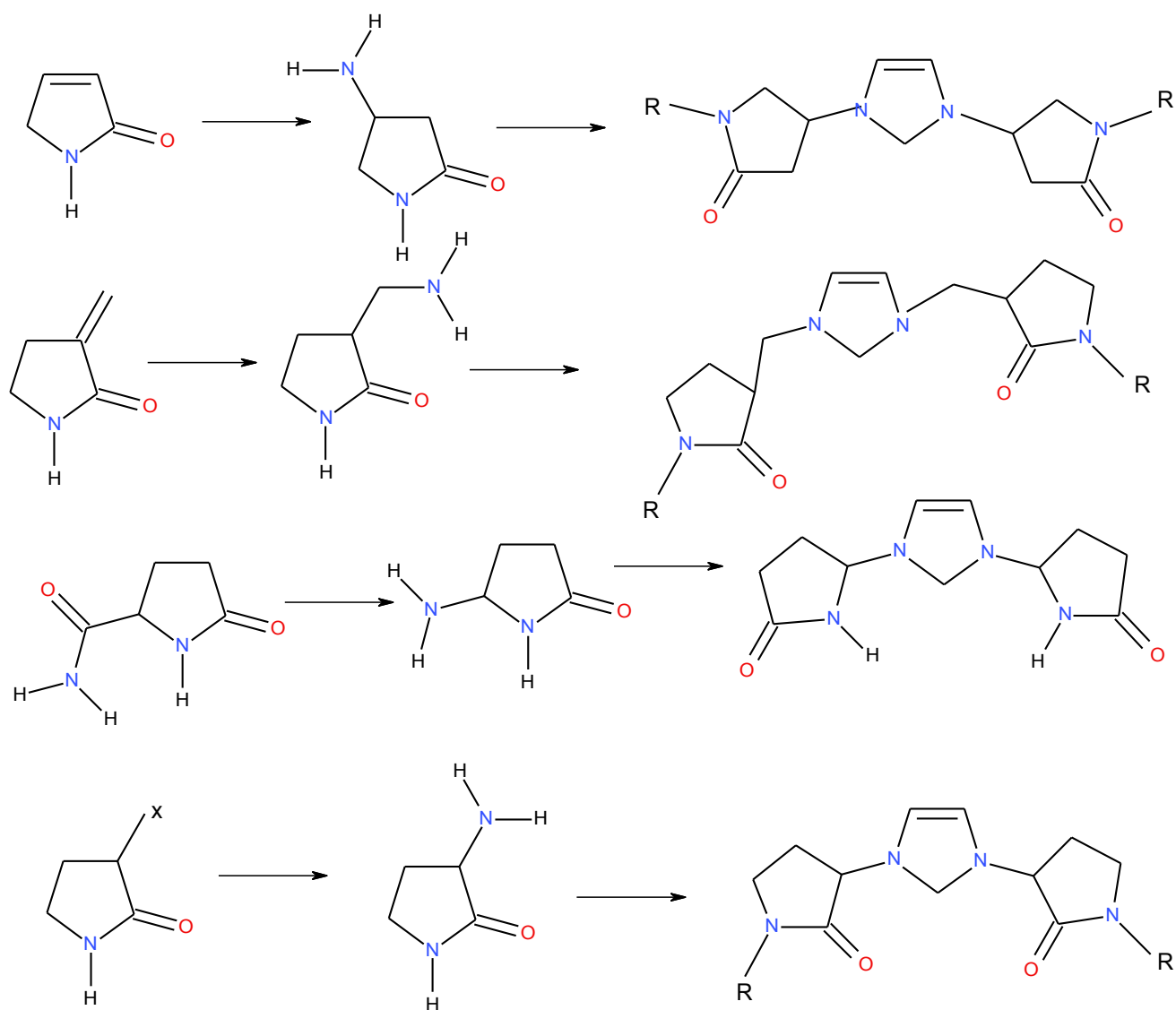
Chart 4 Pyrrolidone derived NHC's

The pyrrolidones can be readily reduced with LAH to the pyrrolidines at some convenient stage during synthesis.

Why pyrrolidone in a NHC context? Water solubility would be expected as it would be an advantage as water is the primary green solvent. In addition, reduction with LAH affords the pyrrolidines, a water solubilizing functionality after for example protonization or quaternization.

Pyrrolidones are not only water solubilizing moieties they are also solvent soluble and can function therefore in a variety of solvent polarities.

A wide variety of pyrrolidone derived structures are possible. For example:

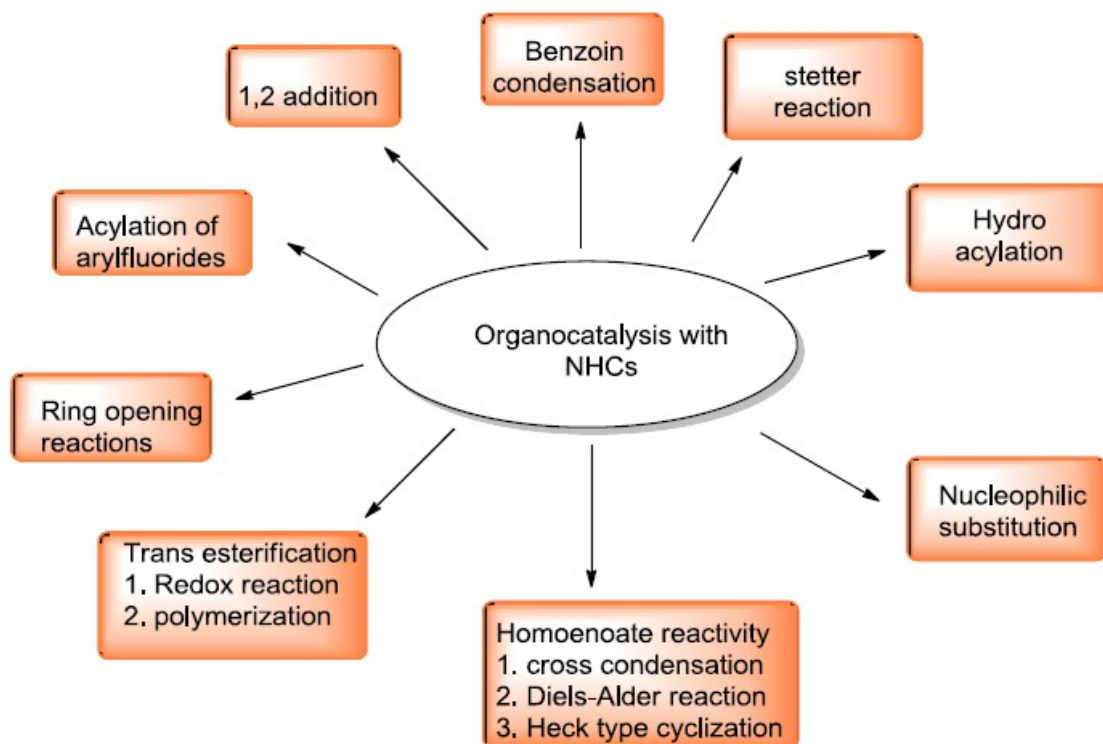


Scheme 1: Primary amine based pyrrolidone NHC structures(negative charges inadvertently left off).

Scheme 1 illustrates a selection of amines that could be converted by well know procedureds to NHC's. Chart 2, above, shows several synthetic routes to them. Not shown are the same derivatives which could also be prepared by the

ethylene diamine route.

NHC catalyst reactions



Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.*, **2007**, *107*, 5606

26

This chart illustrates the wide variety of reactions that can be achieved with NHC's. This is not based on transition metal complexes but a function of the NHC exceptional nucleophilicity itself.

With the growing demand for green procedures, water solubility will become of ever increasing importance. Pyrrolidone contributes the potential for water solubility and compatibility with numerous other solvents.

Some of the above catalytic reactions of NHC's are not small volume but multimillion pound industrial opportunities. NHC could be a million dollar profit generator.

In addition, these pyrrolidone and pyrrolidine based NHC's can form unique complexes with transition metals. The reason is the concept of hemilability where one donor group binds strongly to the metal and the other weakly. The weak donor can leave the metal coordination sphere while being tethered to the metal where it can re-coordinate thus enhancing catalytic activity. Amines like pyrrolidine are strong binders as are the lactams. In this case the strong binding ligands would act as pincers.

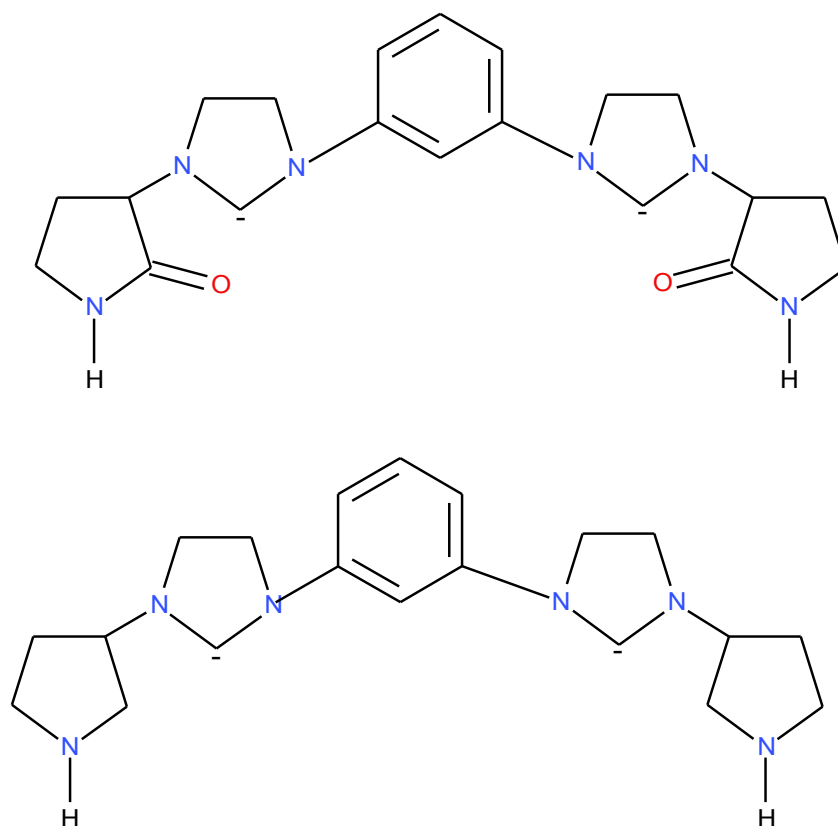
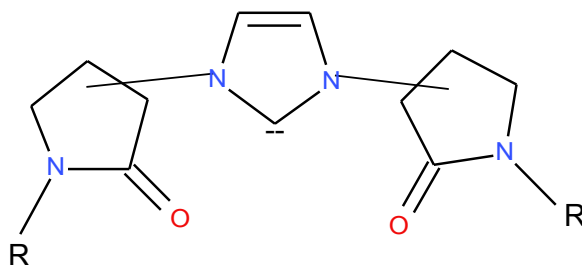


Chart 5: Examples of possible pincer NHC's

Claims:

1. N-heterocyclic carbenes (NHC) based on primary amine derivatives of pyrrolidone lactams comprising the reaction of said amine derivatives with glyoxal and then triethyl formate forming a variety of NHC derivatives useful as ligands for organometallic catalysts or as water soluble or dispersible catalysts for a variety of organic reactions.
2. The reaction described in claim 1 wherein the primary amines are derived from ethylene diamines as an alternative to employing glyoxal.
3. Water soluble or dispersible N-heterocyclic carbenes (NHC) comprising compounds of the following structure;

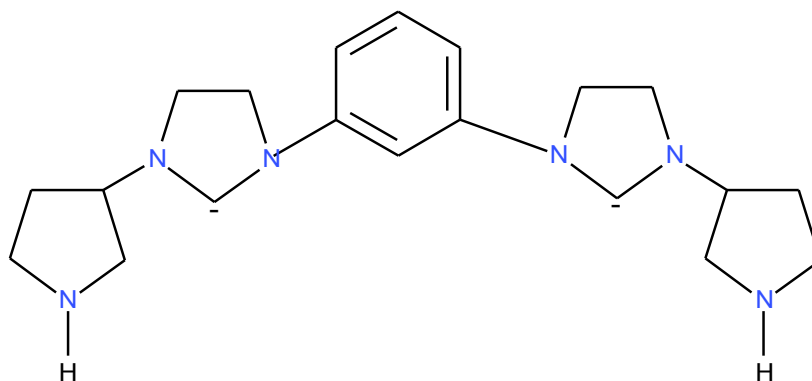
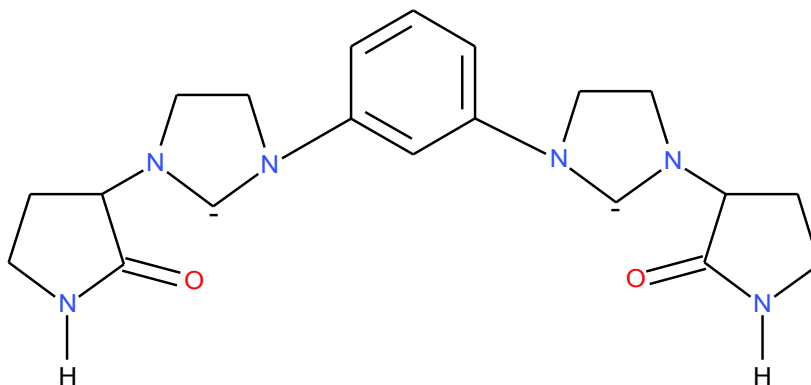


wherein the imidazolium NHC nitrogens can be attached to the same pyrrolidone carbons at positions 3, 4, or 5 and where a spacer methylene may also be included between the imidazolium and the pyrrolidones and where the R groups are the same and are hydrogen or C1 to C20 alkyl groups.

4. The compounds of claim 3 wherein the N-heterocyclic imidazolium ring is saturated.
5. The compounds of claim 3 wherein the R groups are alkyl or aromatic or mixed derivatives that do not interfere with water solubility or dispersability.
6. The compounds of claim 3 wherein the pyrrolidone groups have been reduced to pyrrolidines.
7. The compounds of claim 3 wherein said NHC's are employed as ligands for transition metals.
8. The compounds of claim 6 wherein the transition metals are employed as metathesis catalysts.
- 9 The compounds of claim 6 wherein the transition metals are copper, silver,

gold, platinum, palladium and so forth.

10. Pincer NHC's comprising pyrrolidine or pyrrolidone groups of the following structures:



wherein the said pyrrolidine or pyrrolidone moieties can be further substituted at nitrogens and the NHC can be unsaturated.