Recent advances in neutral and anionic N-heterocyclic carbene – betaine interconversions. Synthesis, characterization, and applications

Andreas Schmidt,* Sascha Wiechmann, and Tyll Freese

Clausthal University of Technology, Institute of Organic Chemistry, Leibnizstrasse 6, D-38678 Clausthal-Zellerfeld, Germany
E-mail: schmidt@ioc.tu-clausthal.de

DOI: http://dx.doi.org/10.3998/ark.5550190.p008.251

Abstract

Some mesoionic compounds, *i.e.* five-membered representatives of the class of conjugated mesomeric betaines (CMB), are in equilibrium with their tautomeric normal N-heterocyclic carbenes (nNHC). In addition, anionic N-heterocyclic carbenes, generated by deprotonation of mesoionic compounds, have been described. The first examples of conversions of cross-conjugated mesomeric betaines (CCMB), 6-oxopyrimidinium-4-olates, into normal N-heterocyclic carbenes have been reported as well. CCMB such as imidazolium-4-carboxylate and pyrazolium-4-carboxylate can decarboxylate to form abnormal (aNHC) or remote N-heterocyclic carbenes (rNHC). Most conversions of betaines into N-heterocyclic carbenes start from pseudo-cross-conjugated mesomeric betaines (PCCMB) which can be regarded as heterocumulene adducts of nNHC. Thus, decarboxylations of imidazolium-2-carboxylates, 1,2,4-triazole-3-carboxylates, pyrazolium-3-carboxylates or indazolium-3-carboxylates yield N-heterocyclic carbenes which have been used in catalysis, complex chemistry, heterocyclic synthesis, and organocatalysis.

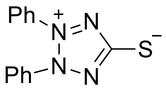
Keywords: Mesoionic compounds, mesoionic carbenes, ylides, borane adducts, zwitterions, sydnones, heterocumulene adducts, decarboxylation, mesomeric betaine

---

Table of Contents

1. Introduction

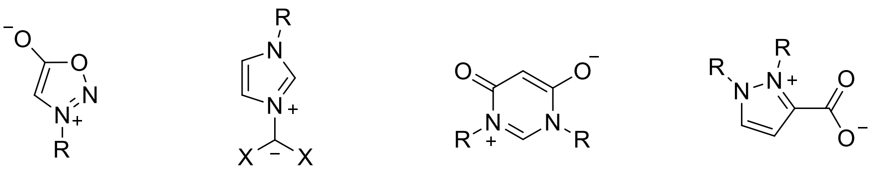
The first mesoionic compound, tetrazoliumthiolate **1**, was unknowingly prepared by Fischer as early as 1882 (Scheme 1).[1] The structure of this compound and of other members of this compound class, however, was elucidated many decades later.[2-4] This is surely due to the fact, that mesoionic compounds can only be represented by dipolar canonical forms, which seemed to be counterintuitive, because major contributors to the overall structure of a compound which can be formulated by several resonance structures normally carry a minimum number of charges, if at all. As a consequence, structures, representations and structure – activity relationships had been discussed intensively.



1

Scheme 1. The first mesoionic compound (1882).

In parallel, mesoionic compounds aroused much interest as biologically active compounds[5-8] and 1,3-dipoles in [2+3]-cycloadditions.[9,10] In 1955, Katritzky pointed out inconsistencies to be found in the literature and examined critically the value of the descriptive term “mesoionic”.[11] He suggested that the description “mesoionic” should be discontinued as these compounds are mesomeric betaines and stated that “the introduction of new trivial names and symbols such as ψ to name these compounds is both undesirable and unnecessary”.[11] Mesomeric betaines have been defined as compounds which can exclusively be represented by dipolar canonical forms and which delocalize the positive as well as negative charge within a common π-electron system. In 1985 Ollis *et al.* published a comprehensive classification system which divided all mesomeric betaines into four distinct classes.[12] They defined the classes of conjugated mesomeric betaines (CMB), ylides which are closely related to CMBs, cross-conjugated (CCMB), and pseudo-cross-conjugated mesomeric betaines (PCCMB). Examples (**2** - **5**) are given in Scheme 2.

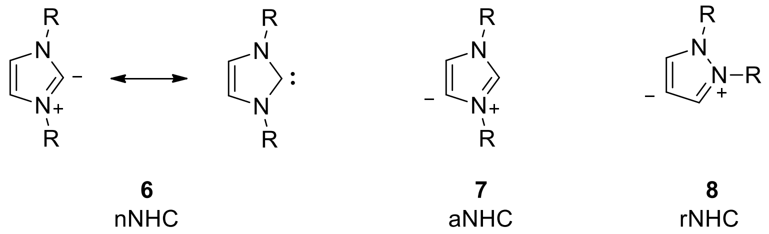


2 (CMB) **3** (ylide) **4** (CCMB) **5** (PCCMB)

Scheme 2. Representatives of the four major classes of mesomeric betaines.

Each class forms four subclasses on the basis of isoconjugation to even or odd, alternant or non-alternant hydrocarbon anions and dianions.[12] The four major classes of MB can be distinguished by careful inspection of their resonance structures, by dissection of characteristic 1,3-dipoles from their canonical forms, and by their frontier orbital profile.[12] Thus, in CMB common sites for positive and negative charges exist in the canonical forms, whereas the charges are restricted to separate parts of the molecule in CCMBs. PCCMBs possess characteristic electron sextet structures without internal octet stabilization, and ylides related to CMBs can best be represented as 1,2-dipoles. Examples are given below (Sections 2.1 – 2.4). Reviews dealing with the types of conjugation and their consequences[12,13] and mesomeric betaines as natural products[14] have appeared so that the characteristic differences of these distinct classes should not be repeated here. Since 1985 mesoionic compounds are defined as 5-membered ring systems which belong to the class of conjugated mesomeric betaines (*vide infra*).[12] In 2013, Ramsden predicted the existence of additional classes of mesomeric betaines[15] which await synthesis and characterization. Betaines which delocalize an odd number of charges within a common π-electron system form a distinct class of compounds.[16,17]

Regarding the second-mentioned class of title compounds, it is well known that the isolation of the first stable N-heterocyclic carbene (NHC)[18] by Arduengo led to a remarkable development in synthetic as well as catalytic organic chemistry. Several subclasses have been recognized, among those normal (nNHC), abnormal (aNHC)[19] and remote N-heterocyclic carbenes (rNHC).[20-22] Examples are compounds **6** – **8** (Scheme 3). In the first mentioned class the free, non-complexed carbene can be formulated by a neutral electron sextet structure as well as by dipolar structures. Abnormal N-heterocyclic carbenes can exclusively be represented by dipolar canonical forms, therefore the alternative name "mesoionic carbenes" (MIC) has been introduced.[23] In remote N-heterocyclic carbenes (rNHC), the carbene carbon must not be adjacent to any heteroatom. Abnormal, mesoionic and remote N-heterocyclic carbene complexes have been reviewed recently, and nomenclature, classification and bonding have also been discussed.[24]



Scheme 3. Representatives of normal, abnormal, and remote N-heterocyclic carbenes.

Through the eyes of an organic chemist, there is indeed some confusion and inconsistency over the representation of NHC metal complexes. Several resonance forms of NHC metal complexes are plausible (Figure 1, **I**) and all of them feature tetravalent carbon. The weighted average of these resonance forms, however, strongly depends on the metal. Two of them show a conventional covalent single bond but then the transfer of an electron has to be shown by positive and negative charges. Boron adducts are best represented by these dipolar structures with a positive charge on carbon or nitrogen, which are also entirely consistent with the representation of mesomeric betaines such as mesoionic compounds or heterocumulene adducts of NHCs. Representations of complexes of NHCs with other metals, however, also include resonance forms with C=M double bonds. The link between the C and the metal is in fact a dative bond so that representation **II** is appropiate, but seems to be unpopular. In representation **III** the conjugation between the nitrogen atoms is indicated, but no charges. The same is true for representation **IV**, whereas the saturated carbon in the frequently used representation **V** implies a CH which is not present, and does not account for the electron distribution. Some authors therefore draw the letter C into the structure as in **VI**. In order to avoid the formulation of tetrapolar or tripolar structures with two formal negative and one or two formal positive charges within the same molecule, representation **III** or – where appropiate – a selected dipolar structure taken from the resonance forms **I** is used throughout this review.

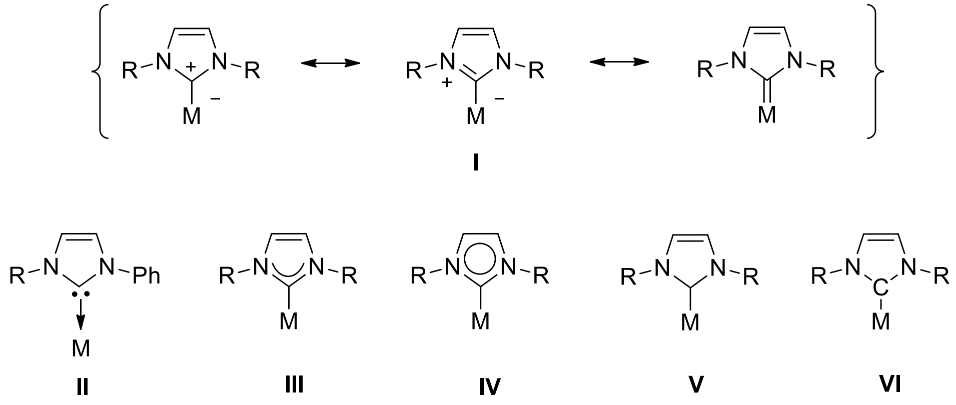


Figure 1. Representations of NHC metal complexes.

Meanwhile interesting relationships between the two classes of compounds, mesomeric betaines and N-heterocyclic carbenes, have been recognized. Reviews covering portions of that field appeared recently (*vide infra*). Thus, the chemistry of pyrazole-ylidenes and indazol-ylidenes has been summarized.[25] More general review articles deal with syntheses, properties, and biological activities of pyrazoles[26,27] and indazoles,[28] including betaines and carbenes. This interesting area of overlap will serve as strong impetus for additional research in that field.

2. Interconversion reactions

2.1. Interconversions of normal (nNHC) and anionic N-heterocyclic carbenes and conjugated mesomeric betaines (CMB), including mesoionic compounds

According to the aforementioned definition by Ollis, Stanforth and Ramsden, conjugated heterocyclic mesomeric betaines are cyclic mesomeric betaines in which the positive and the negative charges are not restricted to separate parts of the π-electron system of the molecule. The positive and negative charges are in mutual conjugation and both are associated with the common conjugated π-electron system of the molecule.[12] Characteristic features of conjugated mesomeric betaines, for which the mesoionic compound sydnone **VII** is given as an example, are summarized in Figure 2. In the canonical forms, common sites for positive and negative charges exist (**VIII**). The characteristic dipole type **IX** can be dissected from the resonance structures.

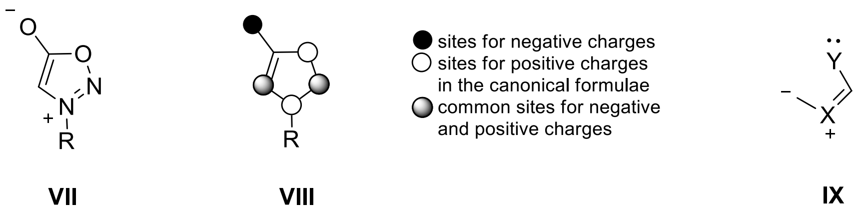


Figure 2. Characteristic features of conjugated mesomeric betaines (CMB).

Mesoionic compounds are defined as five-membered conjugated mesomeric betaines of the general structures **A** (mesoionic compounds of type A) or **B** (mesoionic compounds of type B) (Figure 3). The letters a – f symbolize atoms or groups, and the numbers stand for the π electrons which contribute to the 8 π electron system.[9,10] Mesoionic compounds are isoconjugate to the 2-methyl-2,4-cyclopentadiene dianion **X** which is an even-numbered, non-alternant system **XI**. Mesoionic compounds belong therefore to subclass 4 of the aforementioned categorization.[12] 228 structures of mesoionic compounds have been theoretically predicted and a large number of those still await synthesis and characterisations.[9,10,12]

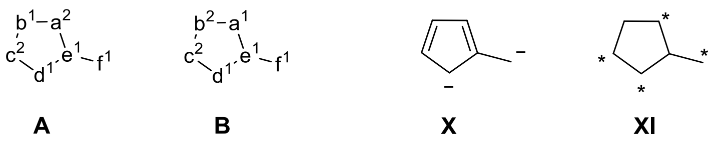
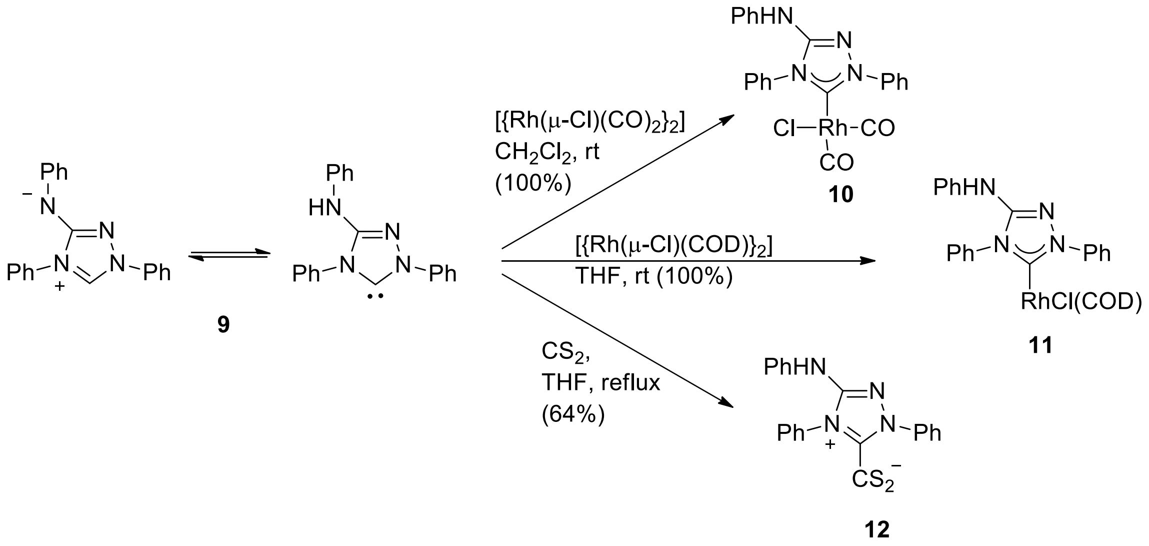


Figure 3. Architecture of mesoionic compounds.

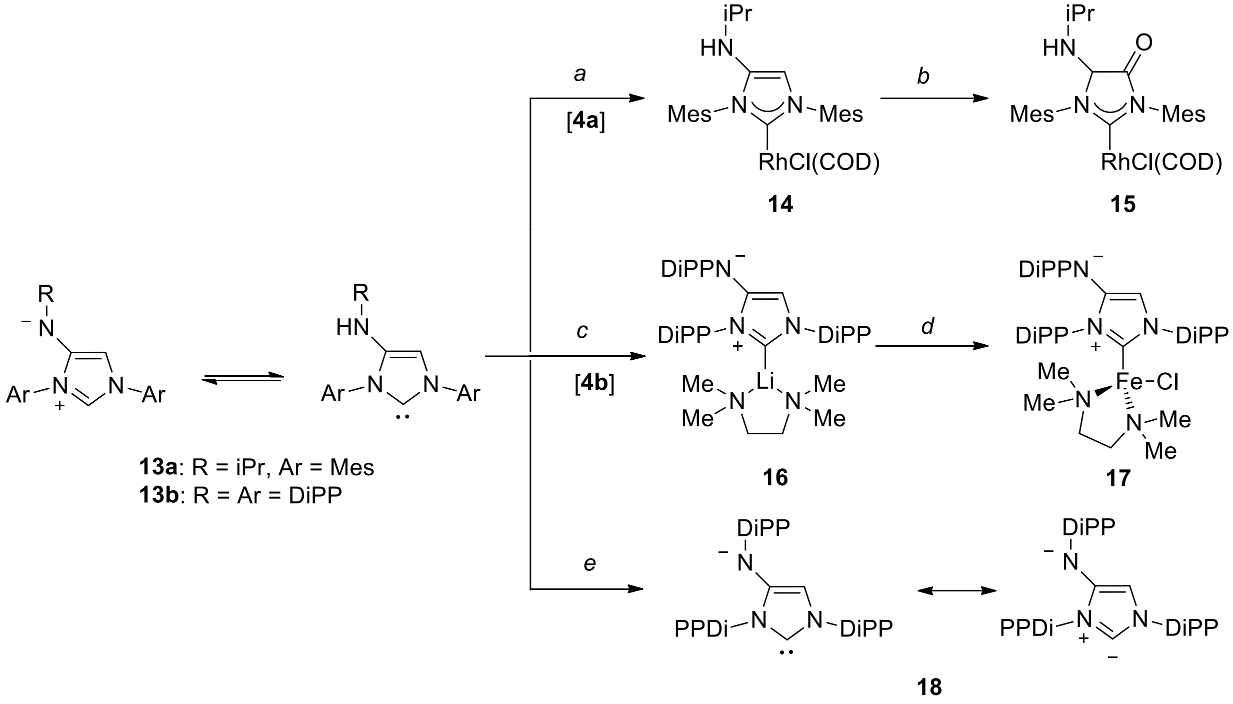
The 1,2,4-triazolium-3-aminide **9** is a typical mesoionic compound (Scheme 4). It has been used as analytical reagent for the detection of nitrate anions for decades ("Nitron", Busch´s reagent) and was first described more than 100 years ago.[29] It was found very recently that nitron is in equilibrium with its N-heterocyclic carbene which undergoes various trapping reactions such as Rh carbonyl complex formation (**10**, **11**), triazolium-dithiocarboxylate formation with CS_2 (**12**), or almost quantitative thione formation with sulfur.[30] The reaction leading to **12** is the conversion of the mesoionic compound (**9**) *via* its tautomeric N-heterocyclic carbene into a pseudo-cross-conjugated mesomeric betaine (PCCMB) (*vide infra*). The carbene carbon atom of **10** and **11** appear at δ = 175.9 ppm and 184.9 ppm in ^{13}C NMR spectroscopy, respectively. The bond length of the Rh-$C_{carbene}$ bond of **9** was determined by a single crystal X-ray analysis to be 2.077(5) Å, whereas a value of 2.030(4) Å was found in **11**. The Tolman electronic parameter of the NHC was calculated to be 2057.4 cm^{-1}, indicative of a moderate donor strength. The ΔG^0 of the betaine – carbene interconversion was calculated to be 5.7 kcal/mol in the gas phase.



Scheme 4. Tautomeric equilibrium of a mesoionic compound and a normal N-heterocyclic carbene.

The mesoionic compound imidazolium-4-aminide **13** undergoes a similar series of reactions (Scheme 5). The tautomeric carbene of **13a** could be trapped as thione with sulfur and as pseudo-cross-conjugated mesomeric betaine (PCCMB) on treatment with CS_2, similar to the reactions described above.[31] The Rh complex **14** was formed on deprotonation of the precursor of **13a** - the corresponding imidazolium salt - with KOtBu in the presence of the *in situ* prepared dimer [Rh(μ-OtBu)(COD)]$_2$ at room temperature. The former carbene carbon atom of **14** occurs as a doublet at $\delta = 176.8$ ppm ($^1J_{\mathrm{RhC}} = 53$ Hz). The Rh-C$_{\mathrm{carbene}}$ bond length was determined by a single crystal X-ray analysis to be 2.053(3) Å. Surprisingly, silica gel and air converted the complex into the Rh complex **15** (X-ray analysis) which was accompanied by a considerable shortening of the Rh-C$_{\mathrm{carbene}}$ bond to 1.998(3) Å. The complexes **14** and **15** were converted into the dicarbonyl complexes on treatment with CO which were used to determine Tolman´s Electronic Parameter. It was found that the carbene tautomer of **13a** has slightly better donor capabilities than 1,3-dimesitylimidazol-2-ylidene.

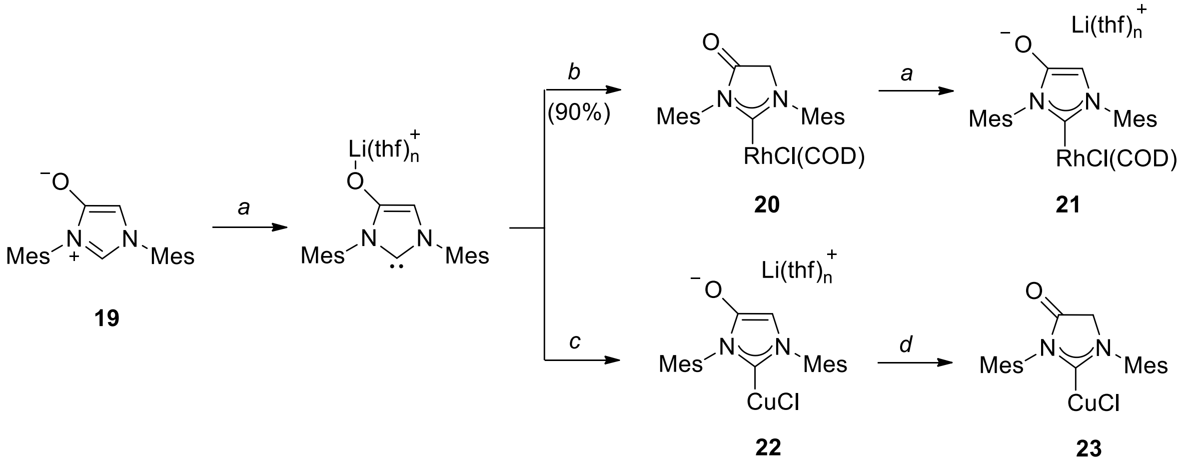
The mesoionic compound **13b** formed an orange-colored, sensitive solid on treatment with base which crystallized on addition of *N,N,N´,N´*-tetramethylethylenediamine (tmeda) as Li complex **16** possessing an anionic NHC ligand (X-ray analysis).[32] The Li-C$_{\mathrm{carbene}}$ bond has a length of 2.093(3) Å. The green iron complex **17** was prepared by reaction of the Li complex **16** with [{Fe(μ-Cl)Cl(tmeda)}$_2$] and proved to be extremely air- and moisture sensitive (X-ray analysis). The Fe-C$_{\mathrm{carbene}}$ bond length was determined to be 2.090(2) Å. The anionic N-heterocyclic carbene **18** was observed spectroscopically. The C$_{\mathrm{carbene}}$ resonance frequency was found to be at $\delta = 202.3$ ppm under these conditions.



a [RhCl(COD)$_2$], KOtBu, rt (93%); *b* SiO$_2$, air, 10 min, (86%);
c 1. LiCH$_2$SiMe$_3$, THF; 2. tmeda. *d* [{FeCl$_2$(tmeda)}$_2$], THF;
e KN(TMS)$_2$, THF-d$_8$

Scheme 5. Mesoionic compounds in equilibrium with normal N-heterocyclic carbenes.

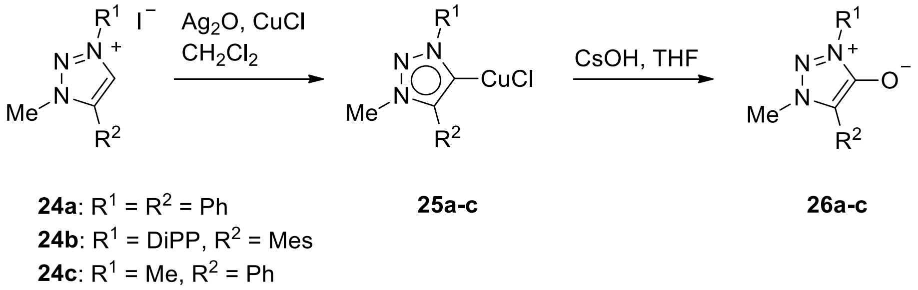
Imidazolium-4-olate **19** is an additional mesoionic compound which has been converted into N-heterocyclic carbenes possessing a negative charge[33] (Scheme 6). Thus, an anionic species was generated with LiHDMS which was then identified by trapping with sulfur.[34,35] The free carbene was detected at δ = 209.1 ppm.[35] Half an equivalent of the Rhodium dimer $[RhCl(COD)]_2$ followed by acidification converted the anion into the complex **20** which has a keto group (X-ray analysis).[34] The $C_{carbene}$ atom gives a doublet at δ = 229.7 ppm ($^1J_{RhC}$ = 51.5 Hz). The complex **20** was deprotonated with LiHMDS in THF at -78°C to the anionic species **21** which was used as a reactive intermediate to functionalize the exocyclic olate group with electrophiles such as diphenylphosphinic chloride [$ClPh_2P(=O)$] and chloro-tert-butyldimethylsilane [TBDMSCl], respectively. On reaction with 1 atm CO in CH_2Cl_2 at rt, the COD ligand in **20** was replaced to two CO ligands in 96% yield. The complex **19**[33] was furthermore converted into the copper complex **22** as reactive intermediate which afforded **23** on treatment with hydrochloric acid and water. The olate group of **22** could successfully be silylated with TBDMSCl. This paper finally presents a comparison of donor properties of 1,3-bis-mesitylene substituted imidazolylidenes. The 3-olate derivative shows a stretching vibration ν_{asym}(CO) of 2029.5 cm^{-1} which proves the character of a very nucleophilic carbene.[34] Iridium complexes have also been prepared which possess a phenyl substituent or a butyl group at C-4. They were obtained in the keto form similar to **20**.[35] Additional LiHDMS, however, caused a deprotonation to an anionic ligand, the TEP value of which was determined to be 2043.7 cm^{-1}. This ligand is much more electron rich than IMes or IAd.[35]



a LiHDMS, THF; *b* 1. $[RhCl(COD)]_2$, 2. HCl; *c* CuCl, rt; *d* HCl, then H_2O

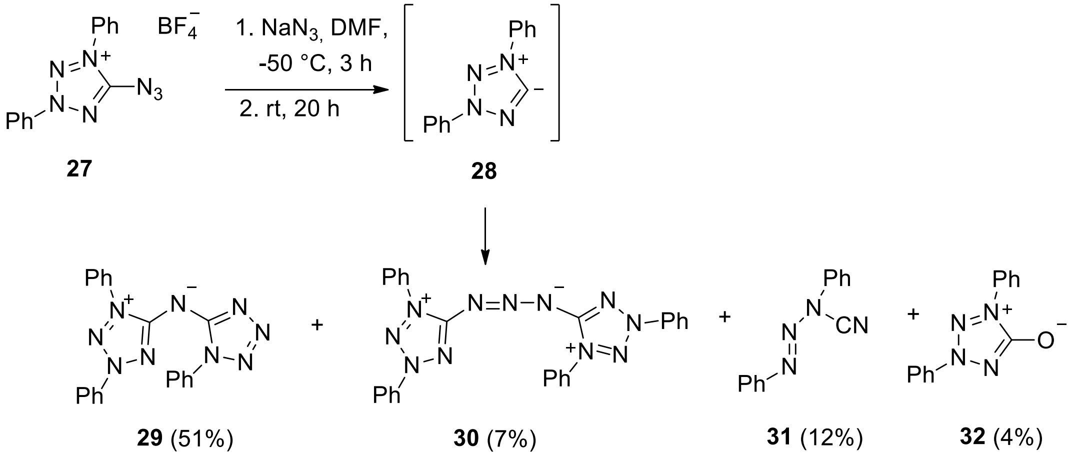
Scheme 6. Imidazolium-olate / NHC interconversion.

The triazolylidene copper(I) complexes **25a-c** reacted with CsOH to give the mesoionic compounds **26a-c** (Scheme 7). This method proved to give better yields in comparison to the direct reaction of **24a-c** with the same base.[36] Complex **25b** was isolated in 82% yield.



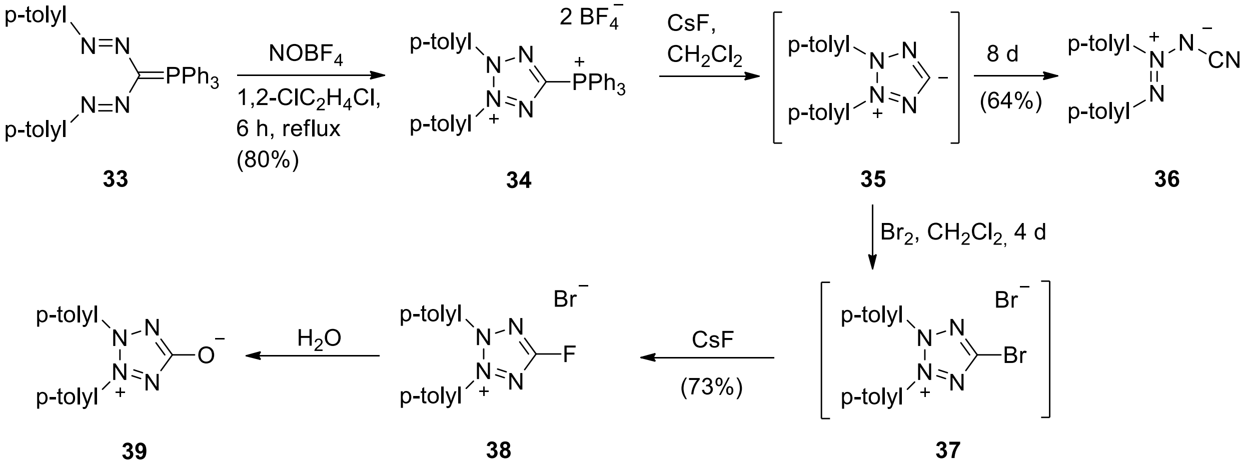
Scheme 7. Formation of a mesoionic compound from a NHC copper complex.

5-Azido-1,3-diphenyltetrazolium tetrafluoroborate **27** underwent a spontaneous reaction with sodium azide[37] (Scheme 8). The outcome of the reaction was examined carefully. The filtrate contained phenylazide in high yields, and the precipitate contained the tripolar substance **30**, the mesoionic compounds **29** and **32**, and the cyanotriazene **31** in various yields depending on the reactions conditions. The authors postulate a heterocyclic carbene as intermediate of this reaction in view of earlier publications[38-40] and in view of the fact that the cyanotriazene **31** is the ring-opening product of the carbene. Two mechanisms for the formation of the olate have been discussed, the reaction of carbene with oxygen and the hydrolysis of the starting azidotetrazolium salt.



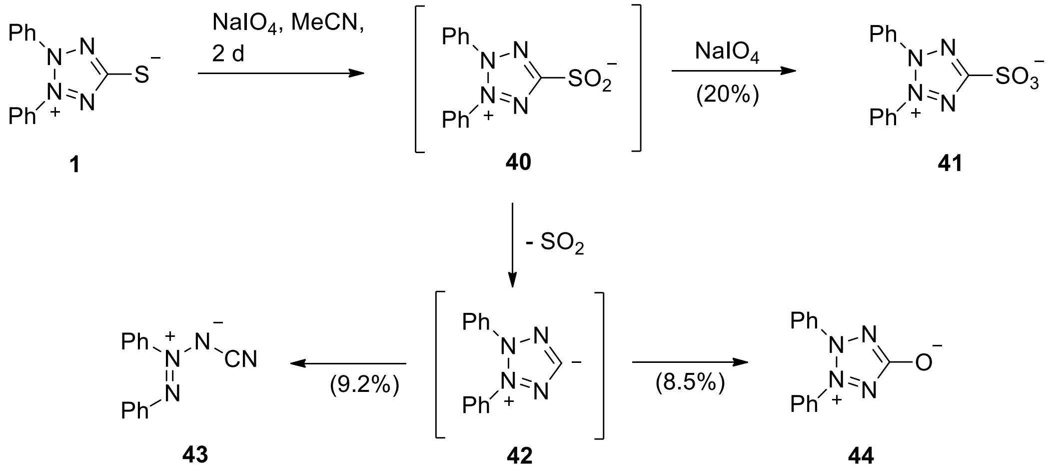
Scheme 8. Tetrazolylidene and formation of some mesomeric betaines.

Tetrazolylidene was also postulated as intermediate on fluoride-induced dephosphoniation of the dicationic (triphenylphosphonio)tetrazolium salt **34** which was prepared starting from the ylide **33** on 2e$^-$ oxidation by nitrosyl tetrafluoroborate[41] (Scheme 9). Cesium fluoride reacted with the dication **34** to the final product tetrazoliumfluoride **38** which is extremely sensitive toward hydrolysis to form the tetrazolium-5-olate **39**. This reaction has been interpreted as bromination of the N-heterocyclic carbene **35** to **37** followed by bromine / fluorine exchange. In the absence of bromine, ring-cleavage to the cyanoazimine **36** was observed. The latter mentioned finding hints at formation of an NHC **35** and excludes an alternative mechanism involving the attack of fluoride on the 5-position of the dication **34**. The cyanoazimine **36** is also formed on deprotonation of tetrazolium fluoroborate with BuLi at -78 °C.



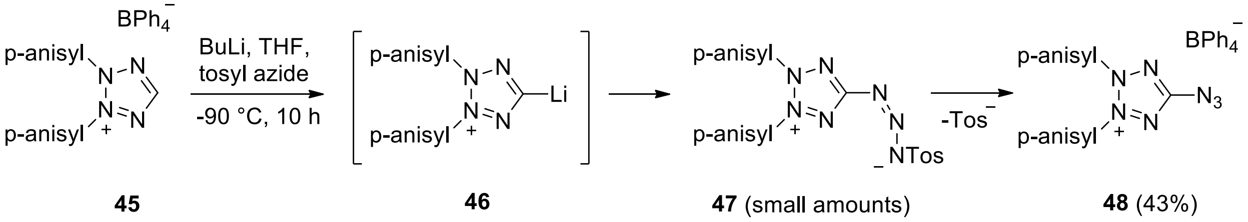
Scheme 9. Tetrazolylidene generation and conversion into a mesoionic compound.

The oxidation of Emil Fischer´s first mesomeric betaine, the tetrazolium-thiolate **1**, with sodium periodate was examined in terms of carbene formation (Scheme 10).[41] Tetrazolium-sulfonate **41**, the azimine **43**, tetrazolium-olate **44**, and a dimerized thiolate connected by an S-S bond, were obtained. The betaines **43** and **44** were formed by extrusion of SO_2 from tetrazolium-sulfinate **40** *via* the NHC **42**.



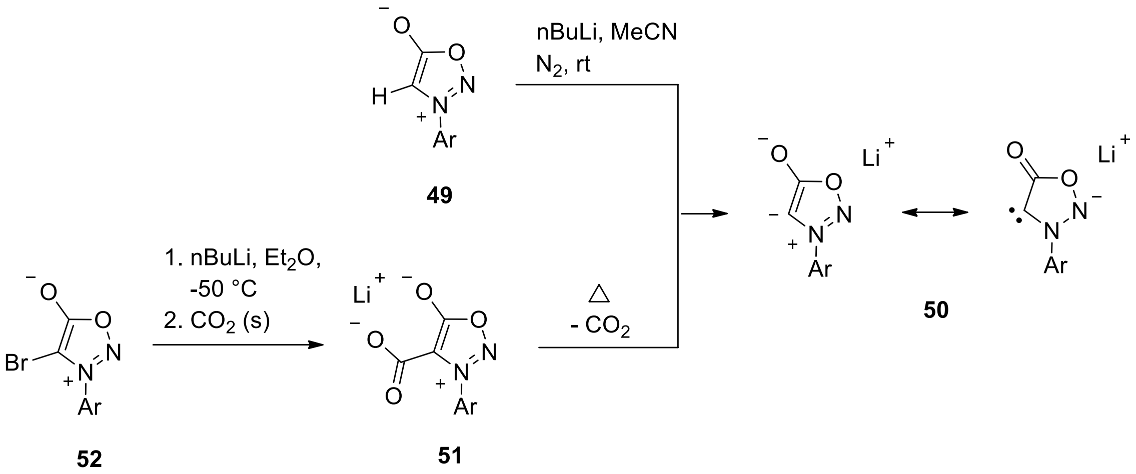
Scheme 10. Formation of tetrazolylidene from the first mesoionic compound tetrazoliumthiolate.

Another approach to tetrazolylidene was also described (Scheme 11). Thus, the tetrazolium salt **45** was deprotonated quantitatively at –90 °C on addition of BuLi, as evidenced by ^{1}H-NMR spectroscopy.^{13} C NMR spectra were obtained at -100 °C which show an unstructured multiplet at 202.4 ppm, belonging to the solvated carbene atom of tetrazolylidene **46**. At temperatures above approximately -60 °C, this 5-lithiotetrazolylidene undergoes a ring-cleavage to form the aforementioned cyanoazimines. The carbene was trapped by tosyl azide to form small amounts of the betaine **47** and the tetrazolium azide **48**.[42]



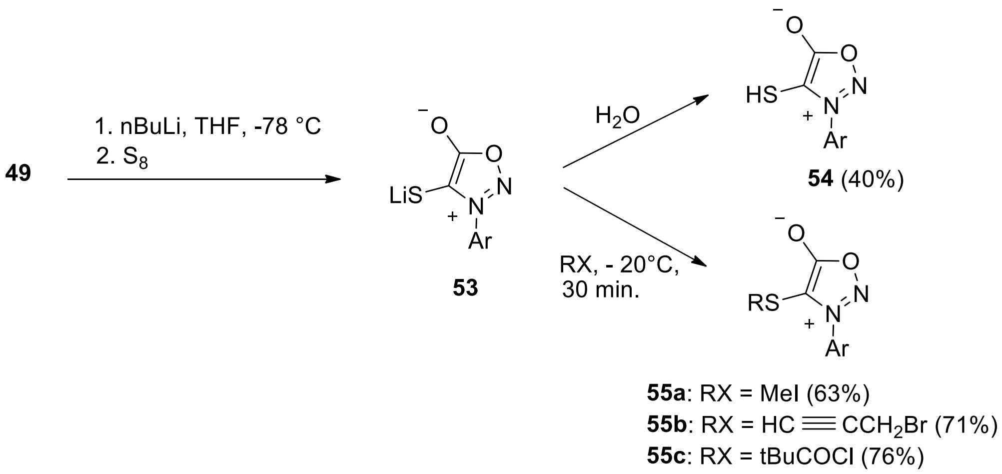
Scheme 11. Tetrazolylidene formation by deprotonation.

Sydnones such as **49** are the best-known mesoionic compounds (Scheme 12). They can be deprotonated with BuLi or MeMgBr in THF in the cold to form the sydnone anion **50**[43,44] which can also be formulated as anionic carbene. This anion was characterized as Li adduct[45] or trapped by various electrophiles such as DMF, *N*,*N*-dimethylacetamide or acetaldehyde.[44] Alternatively, 4-bromosydnone can exchange its bromine toward Li on treatment with BuLi.[46] Another approach to the anionic sydnone **50** is the thermal decarboxylation of lithium sydnone-carboxylate **51** which can be prepared from bromosydnone **52**.[45] Temperature-dependent vibrational spectrometric examinations of **51** and calculations of the carbene **50** have been carried out.[45]



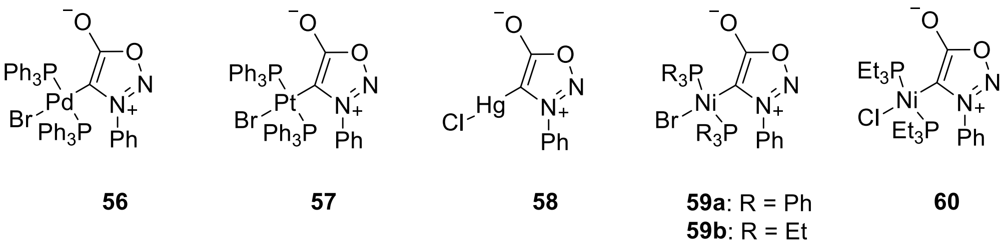
Scheme 12. Sydnone anions.

The sydnone anion reacts with sulfur to give the lithium sydnone-4-thiolate **53** which underwent subsequent reactions with water to **54** and electrophilic species to **55a-c** as shown (Scheme 13).[47]



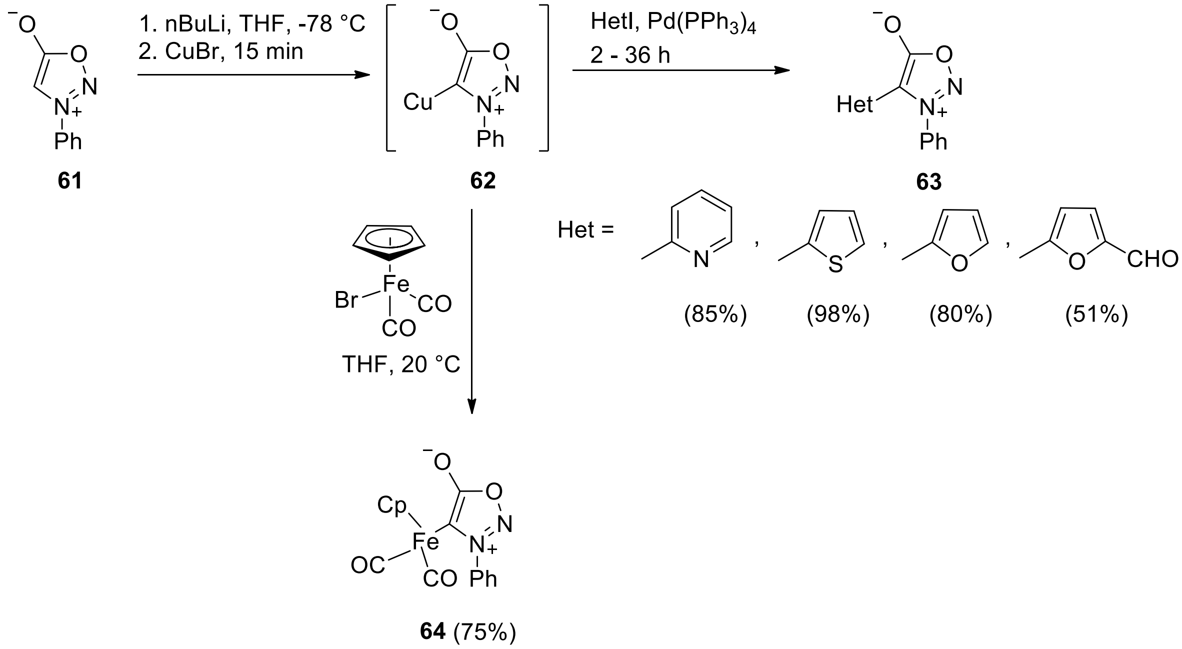
Scheme 13. Reactions of the sydnone anion.

Palladium (*cis* and *trans*), platinum and mercury complexes **56 - 58**, prepared starting from 4-bromosydnone, have been described as well (Scheme 14).[48] The last-mentioned was employed in the synthesis of 4-alkenylsydnones. More recently, nickel complexes have been described.[49] A summary and experimental details are given.[50] The palladium complex proved to be active in Suzuki-Miyaura reactions such as the arylation of tetrabromothiophene.[45]



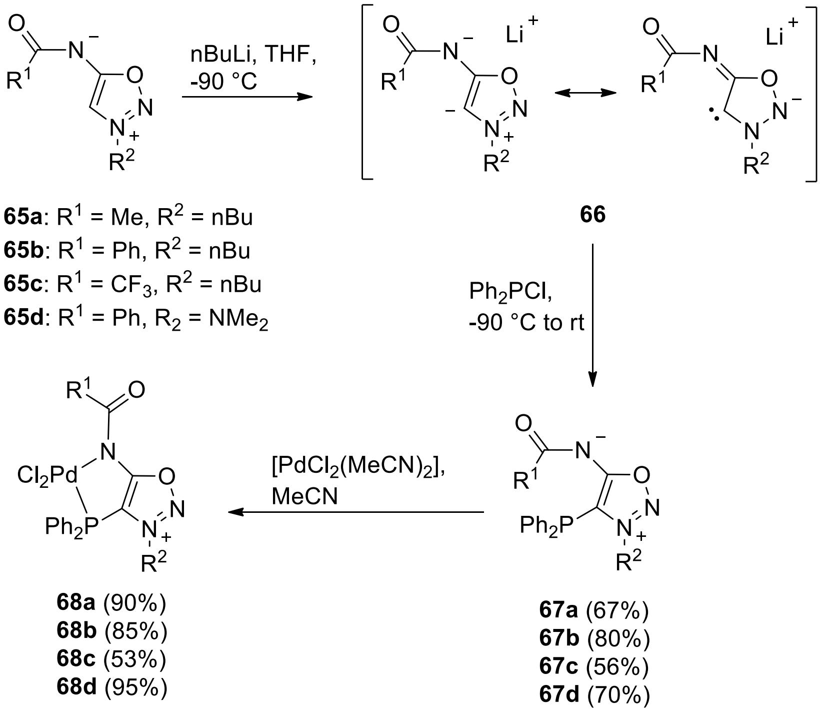
Scheme 14. Metal complexes of the sydnone anions.

In addition, a palladium-catalysed synthesis of 4-heteroaryl sydnones via the copper complexes **62** has been published[51] (Scheme 15). Likewise, iodobenzene, 2-iodovinylbenzene and several iodoacetylenes have been used to give 4-arylsydnone,[51,52] 4-alkenyl,[51] and 4-alkynyl-substituted sydnones,[51] respectively. An alternative approach starts from a corresponding sydnone zinc complex which formed with $ZnCl_2$ to the sydnone lithium adduct; however, yields proved to be lower in comparison to the copper complex method. The copper complex **62** reacted with cyclopentadienyl(dicarbonyl) iron bromide to give the σ-sydnon-4-yl-Cp complex **64**.[52]



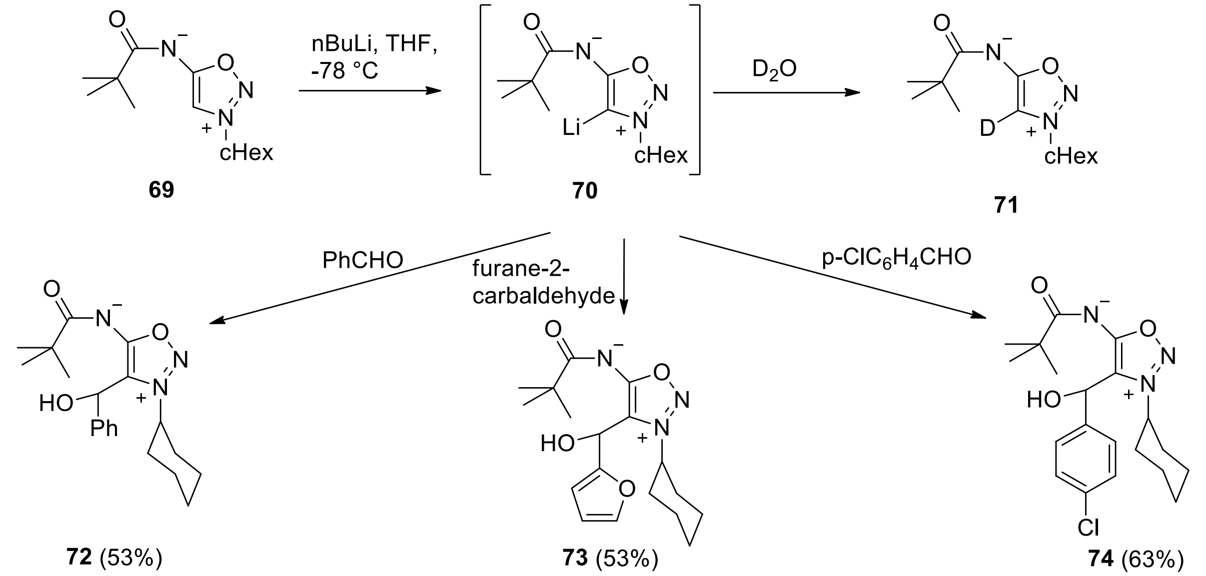
Scheme 15. Heterocyclic synthesis with sydnone anions.

Sydnonimines **65** can also be deprotonated at C-4 to give anions **66** which can also be formulated as carbenes. These were trapped by Ph_2PCl to give **67** (Scheme 16). These bidentate ligands form complexes **68** with palladium.[53] Similar complex formation has been reported for sydnones as well.[54,55]



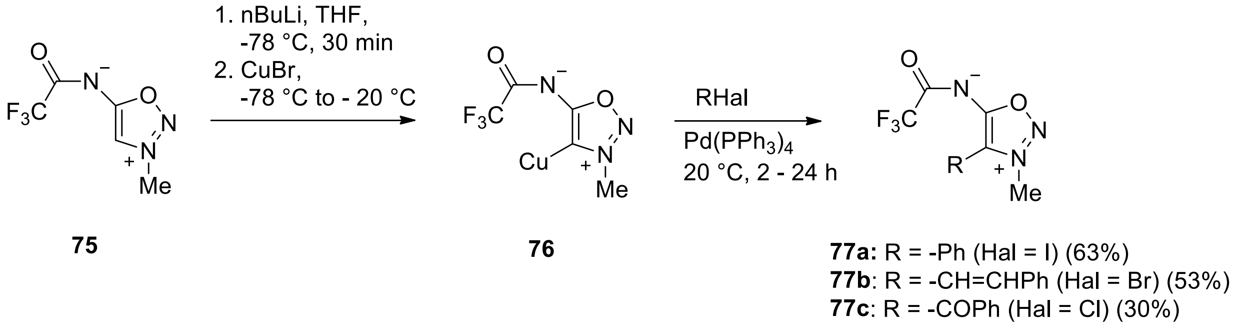
Scheme 16. Anions of sydnonimines and trapping reactions.

The organolithium derivative **70**, prepared from sydnonimine **69**, showed a low nucleophilicity (Scheme 17). Thus, at -78 °C **70** did not react with TMSCl, MeI or allyl bromide, and higher temperatures caused decomposition. Lithium, however, was replaced to deuterium (75-80%) on addition of D_2O. However, it was demonstrated that nonenolizable carbonyl compounds reacted to give the compounds **72** – **74** in moderate yields.[56,57]



Scheme 17. Chemistry of sydnonimine anions.

One equivalent of copper(I) bromide to the lithiated sydnonimine of **75** resulted in the formation of a copper derivative **76** which underwent various cross-coupling reactions catalyzed by a palladium complex (Scheme 18). Thus, **77a-c** were synthesized.[56,57]



Scheme 18. Cross-coupling reactions starting from sydnonimines.

2.2. Interconversions of normal N-heterocyclic carbenes (nNHC) and ylides

According to Ollis, Stanforth and Ramsden, "conjugated heterocyclic N-ylides and related dipolar compounds constitute a subdivision of conjugated heterocyclic mesomeric betaines which can be satisfactorily represented by 1,2-dipolar structures such as N-oxides, in which the negative charge is accommodated at an exocyclic atom or group”.[12] The imidazolium-indolates **XII** are new members of this class of compound.[58] Characteristically, common atoms for negative and positive charges can be recognized in the resonance structures (**XIII**, Figure 4). The molecule possesses the characteristic dipole type of conjugated mesomeric betaines (**XIV**). As **XII** is isoconjugate with the even non-alternant hydrocarbon dianion **XV** it is a member of subclass 8 of mesomeric betaines.[12]

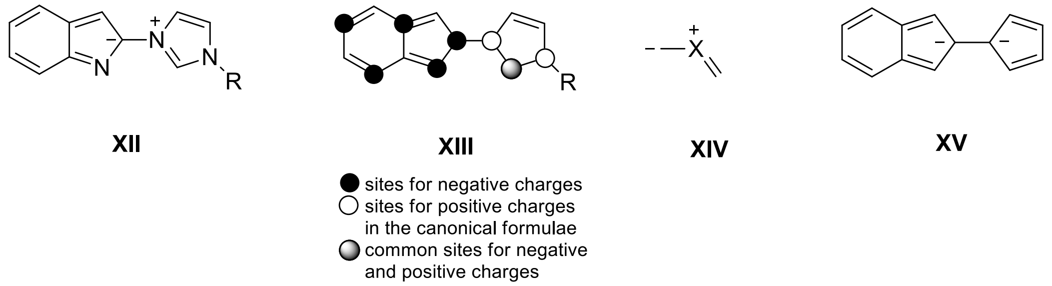


Figure 4. Characteristic features of ylides.

Recently, the first examples of ylide – carbene interconversions according to Figure 5 have been published.[58]

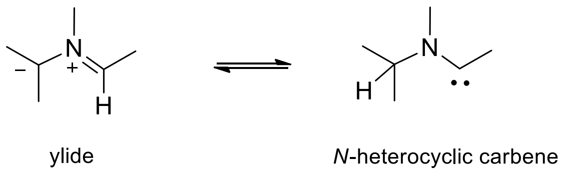
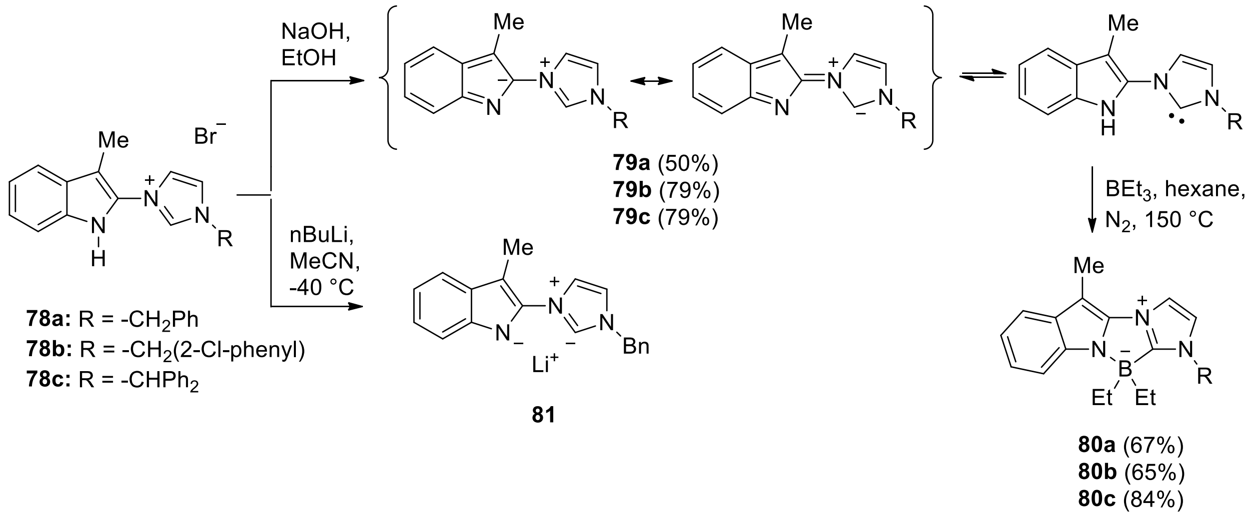


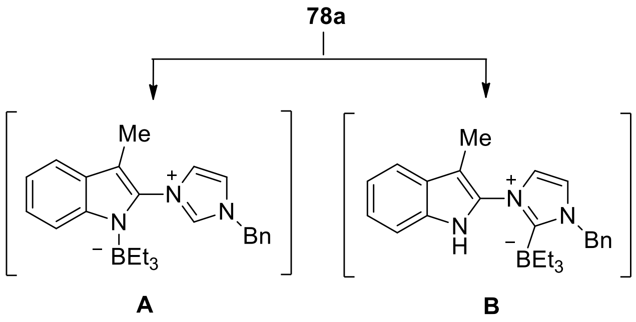
Figure 5. Ylide / N-heterocyclic carbene interconversions.

Deprotonation of the salts **78a-c** to the ylides **79a-c** was accomplished by a solution of NaOH in EtOH (Scheme 19). As already mentioned, several resonance structures can be drawn, among those a form which possesses either a negative charge or a positive charge at C-2 of the imidazolium ring. The existence of those atoms is characteristic of ylides and conjugated mesomeric betaines. Calculations show that the betaine **79a** is $\Delta G = -9.3$ kJ/mol more stable than the tautomeric carbene which is not visible in DMSO-d_6 solutions by NMR spectroscopy. The carbenes, however, were trapped as thiones in high yields. Reaction of **78** with triethylborane or triphenylborane resulted in the formation of a new heterocyclic ring system **80a-c** in good yields (X-ray analysis). This ring system formally is the trapping product of the anionic N-heterocyclic carbene **81** which was examined by means of NMR spectroscopy.[58]



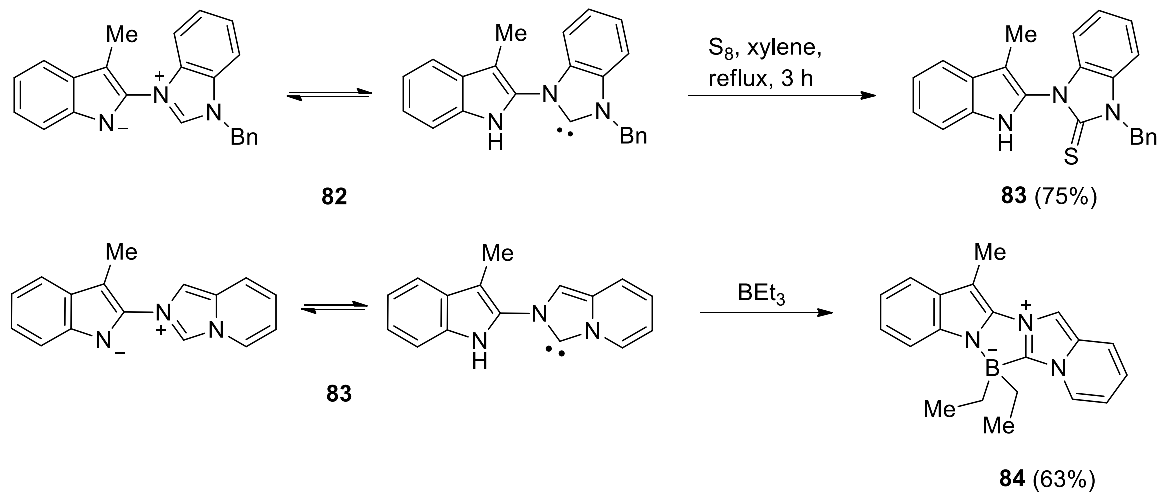
Scheme 19. First conversion of ylides into N-heterocyclic carbenes.

To gain insight into the mechanism of this borane adduct formation, some model reactions and NMR examinations have been carried out. Thus, the ylide **78a** was treated with triethylborane in MeCN-d_3 at rt (Scheme 20). Adduct formation **B**, not **A**, was observed, although DFT calculations predicted that the initial coordination of triethylborane to the indolate-nitrogen under formation of **A** is energetically slightly more favored by 19.7 kJ/mol. The formation of the B-C$_{\text{carbene}}$- bond was confirmed by a ^{11}B NMR shift of -12.7 ppm. Moreover, the ^{15}N NMR resonance frequencies of N1$_{\text{imidazolium}}$ (δ = -194.3 ppm) and N3$_{\text{imidazolium}}$ (δ = -202.8 ppm) of **B** were unambiguously assigned.[58]



Scheme 20. Results of spectroscopic examinations: **B** is observed, not **A**.

Similarly, the indol-2-yl-hetarenium salts of benzimidazole and imidazo[1,5-*a*]pyridine were converted into their ylides (Scheme 21). The tautomeric N-heterocyclic carbenes were trapped as their thiones. Thus, the benzimidazole derivative **82** gave the thione **83**. The new ring system **84** was prepared on treatment of triethylborane with ylide **83** in good yields.[59]



Scheme 21. Additional ylide / NHC tautomeric equilibria.

2.3. Interconversions of normal, abnormal, and remote N-heterocyclic carbenes (nNHC, aNHC, rNHC) and cross-conjugated heterocyclic mesomeric betaines (CCMB)

Only a small number of reports deal with conversions of cross-conjugated mesomeric betaines (CCMB) into N-heterocyclic carbenes. The 6-oxo-pyrimidinium-4-olate **XVI** is a typical member of this class of compounds (Figure 6). In the canonical forms, the charges are strictly separated in different parts of the common π-electron system (**XVII**). The characteristic dipole type of cross-conjugated mesomeric betaines can be dissected from the resonance structures (**XVIII**). The anionic part of the molecule is joined by union bonds ("*u*")[60,61] through unstarred positions of the isoconjugate hydrocarbon equivalent to the cationic part (**XIX**). These positions are nodal positions of the highest occupied molecular orbital (HOMO) of this building block of the CCMB (**XX**). The betaine **XVI** is isoconjugate with the even alternant hydrocarbon dianion **XXI** and belongs therefore to subclass 11 of heterocyclic mesomeric betaines.[12]

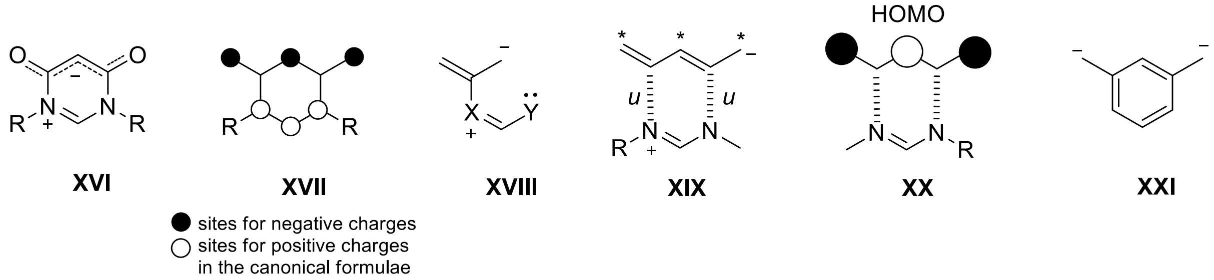
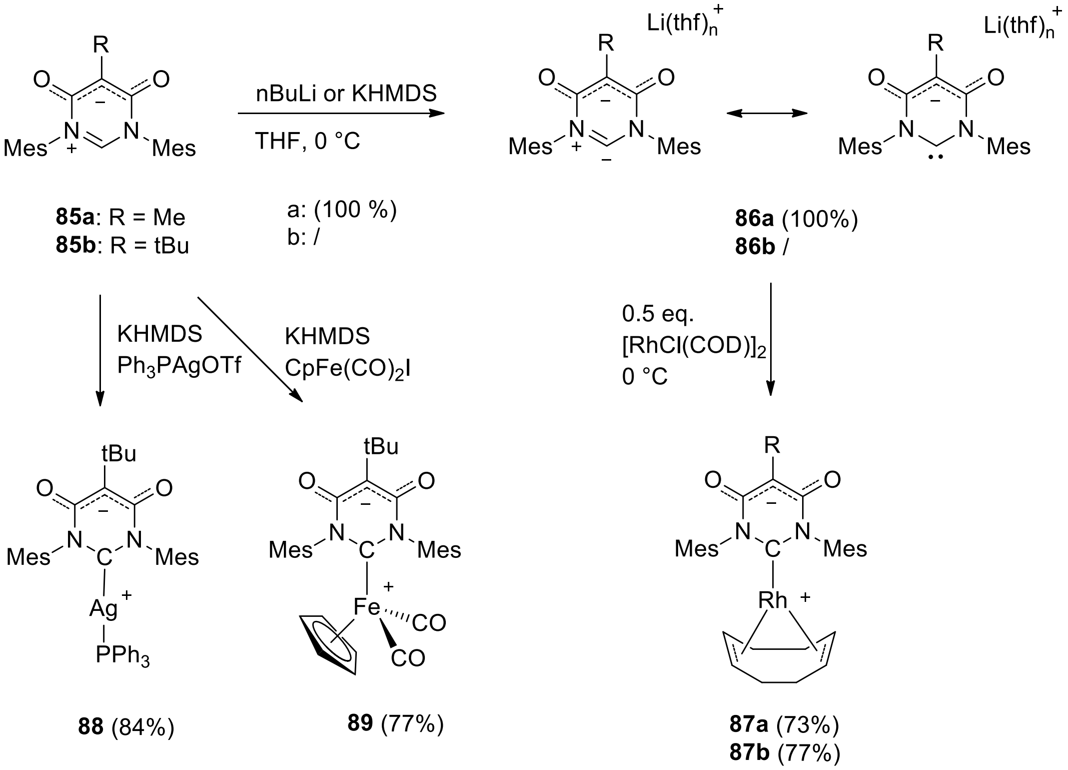


Figure 6. Characteristic features of 4-oxopyrimidinium-olates as example of cross-conjugated mesomeric betaines (CCMB).

The 6-oxopyrimidinium-4-olate **85** was transformed into the lithium salt of a stable anionic N-heterocyclic carbene **86a**[62,63] (Scheme 22). In the single crystal, a trimeric annular association can be seen, where three Li(thf)$^{2+}$ units serve as linkers between the 6-oxopyrimidinium-4-olate molecules which bind through their oxygen atoms to the lithium. The rhodium complexes **87a,b** (X-ray analysis) were formed as neutral 14 electron complexes starting from the anionic carbene either generated with nBuLi or with KHMDS. The silver complex **88** was produced on reaction of mesomeric betaine **85b** with KHDMS followed by the addition of $Ph_3PAgOTf$; the iron complex **89** was described as well (X-ray analysis). The bond distances have been determined to be $C_{carbene}$-Rh = 2.036(1) Å, $C_{carbene}$-Ag = 2.122(1) Å, and $C_{carbene}$-Fe = 2.041(1) Å.



Scheme 22. Conversion of a cross-conjugated mesomeric betaine into a N-heterocyclic carbene.

Pyrazolium-4-carboxylates **XXII** and imidazolium-4-carboxylates **XXVII** represent another architecture of cross-conjugated mesomeric betaines (Figure 7). They also fulfill all characteristic features of this class of compounds, such as charge distribution in strictly separated parts of the molecule according to the canonical forms (**XXIII**, **XXVIII**), bond through unstarred positions (**XXV**, **XXX**) or nodal positions of the HOMO of the anionic part (**XXVI**, **XXXI**) to the cationic part of the betaine. Characteristic dipole types can be dissected from the resonance forms (**XXIV**, **XXIX**). They are isoconjugate with even non-alternant hydrocarbon dianions which is subclass 12 of mesomeric betaines.[12] As pointed out earlier, these types of cross-conjugated mesomeric betaines are formal 1 : 1 adducts of heterocumulenes such as CO_2 of the remote NHC (rNHC) pyrazol-4-ylidene and the abnormal NHC (aNHC) imidazol-4-ylidene, respectively. The highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) are consequently located in separated parts of the common π-electron system.[64]

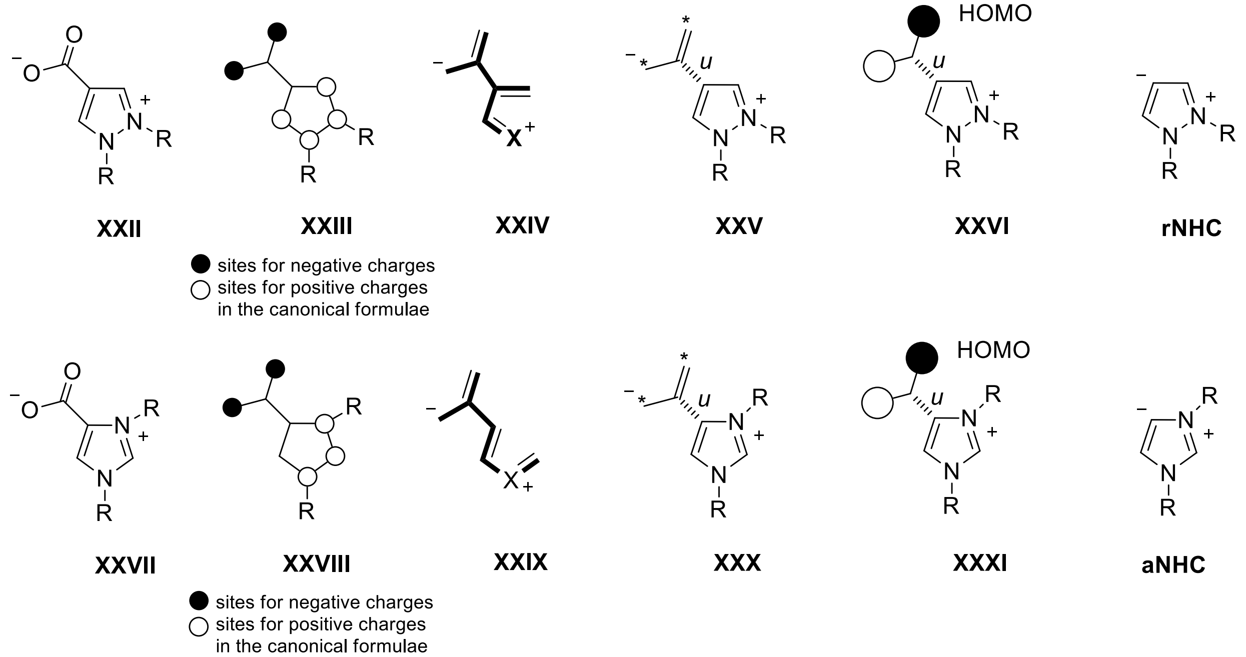
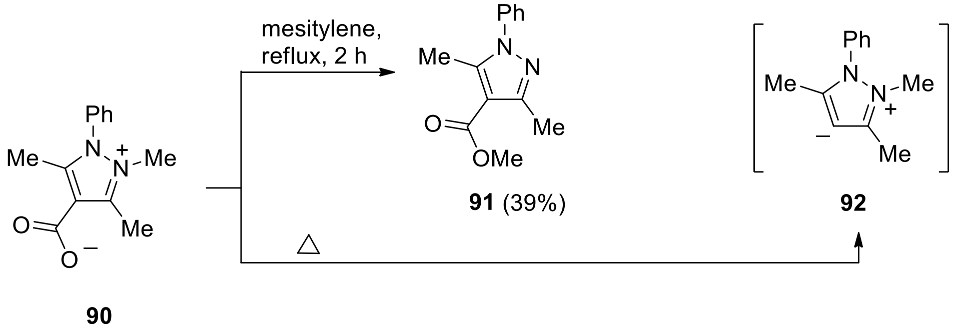


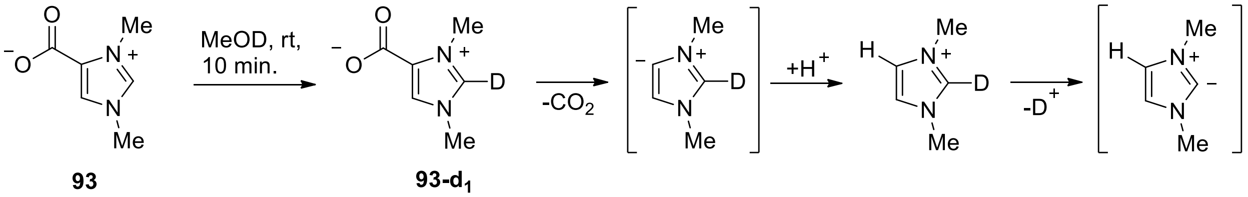
Figure 7. Characteristic features of the CCMB hetarenium-carboxylates.

The generation of carbenes from these types of mesomeric betaines is seemingly limited due to harsh reaction conditions which are in sharp contrast to the relatively mild conditions which have to be applied to analogous reactions of pseudo-cross-conjugated molecules. A detailed discussion is given in Chapter 2.4 (*vide infra*). A thermal N-demethylation / O-methylation sequence was observed on heating of pyrazolium-4-carboxylate **90** in mesitylene at reflux temperature to yield the pyrazole ester **91** (Scheme 23). The decarboxylation to pyrazole-4-ylidene **92** was observed mass spectrometrically, and the carbene was detected as sodium or lithium adduct. Calculations predict a much higher energy barrier (120 kJmol^{-1}) for the decarboxylation of **90** in comparison to its pseudo-cross-conjugated isomer (*vide infra*).[64]



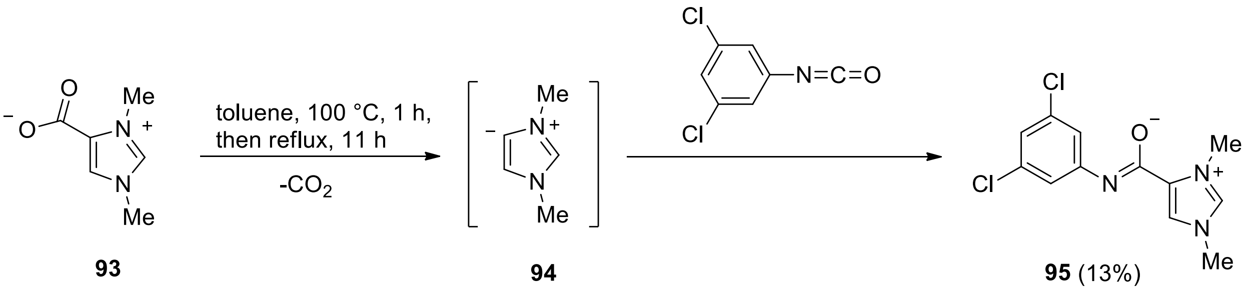
Scheme 23. A remote N-heterocyclic carbene from a cross-conjugated mesomeric betaine.

The cross-conjugated mesomeric betaine **93** occurs in nature and is known as alkaloid norzooanemine (Scheme 24).[14] In order to study thermal decarboxylations to an abnormal N-heterocyclic carbene, its 2-deuterio-derivative **93-d$_1$** was prepared and subjected to mass spectrometric examinations. It was found that at higher fragmentor voltages than approximately 30 V the decarboxylation to 2-deuterioimidazol-4-ylidene [**93-d$_1$**-CO_2] takes place under the conditions of electrospray ionization mass spectrometry. The corresponding monodeuterio-imidazolium salt (**93-d$_1$**-CO_2+H^+) and traces of the normal N-heterocyclic carbene (**93-d$_1$**-CO_2+H^+-D^+) were also detected. No deuterium exchange reactions during the electrospray ionization process were identified.[65]



Scheme 24. Results of spectroscopic examinations on carbene formation.

The aNHC derived from decarboxylation of norzooanemine **93** was trapped with 3,5-dichlorophenylisocyanate to the betaine **95** in low yields[65] (Scheme 25).



Scheme 25. Trapping reactions.

2.4. Interconversions of normal N-heterocyclic carbenes (nNHC) and pseudo-cross-conjugated mesomeric betaines (PCCMB)

Pseudo-cross-conjugated heterocyclic mesomeric betaines (PCCMB) and cross-conjugated heterocyclic mesomeric betaines (CCMB) are closely related, but subtly different.[12-15,60,61] The differences become apparent when interconversions to N-heterocyclic carbenes and related species are compared. Pseudo-cross-conjugated mesomeric betaines can best be recognized by canonical forms which are electron sextet structures without internal octet stabilization. Imidazolium-2-carboxylate **XXXII** is given as an example (Figure 8). Characteristic dipole types can be dissected from the resonance structures (**XXXIII**).[12] Similar to cross-conjugated mesomeric betaines, the anionic part of the betaine is joined by union bonds ("*u*") to the cationic part via unstarred positions of the isoconjugated hydrocarbon equivalent (**XXXIV**), and these are nodal positions of the HOMO of the anionic building block (**XXXV**).[60,61] Pseudo-cross-conjugated mesomeric betaines of type **XXXII** are isoconjugate with even non-alternant hydrocarbon dianions which form class 16 of heterocyclic mesomeric betaines.[12] They are (more than) formal 1:1 adducts of heterocumulenes with normal N-heterocyclic carbenes (nNHCs). Indeed, type **XXXII** betaines are air-stable and can be used without any particular precautions as NHC precursors (*vide infra*).

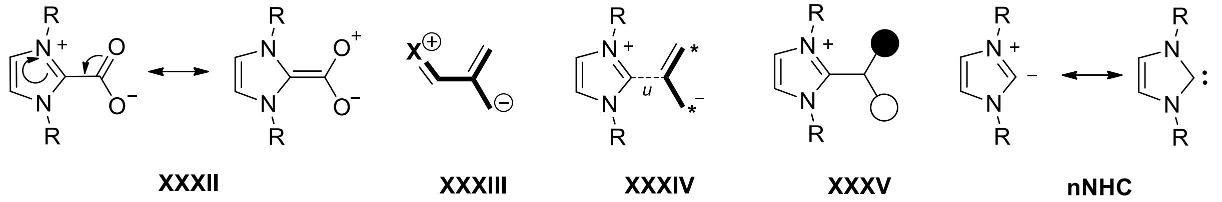
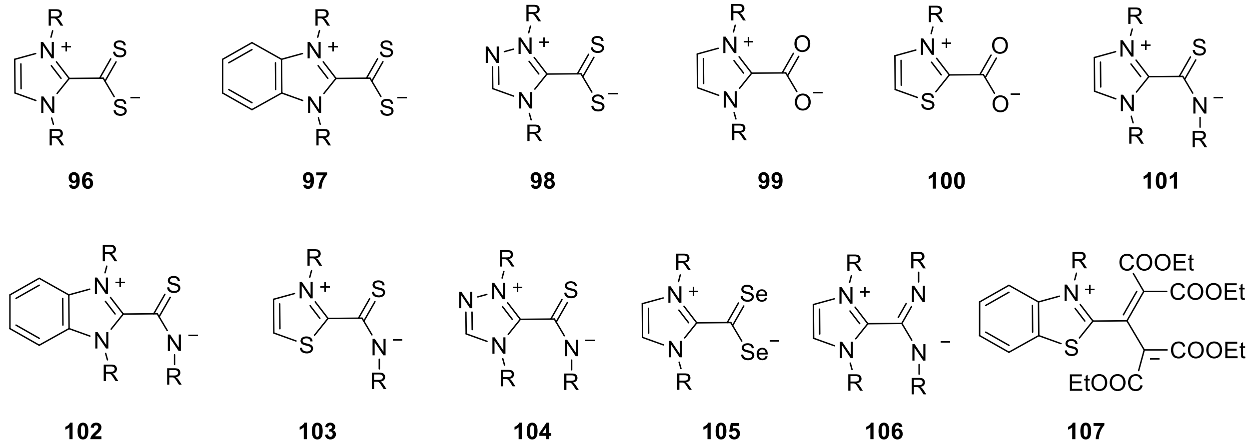


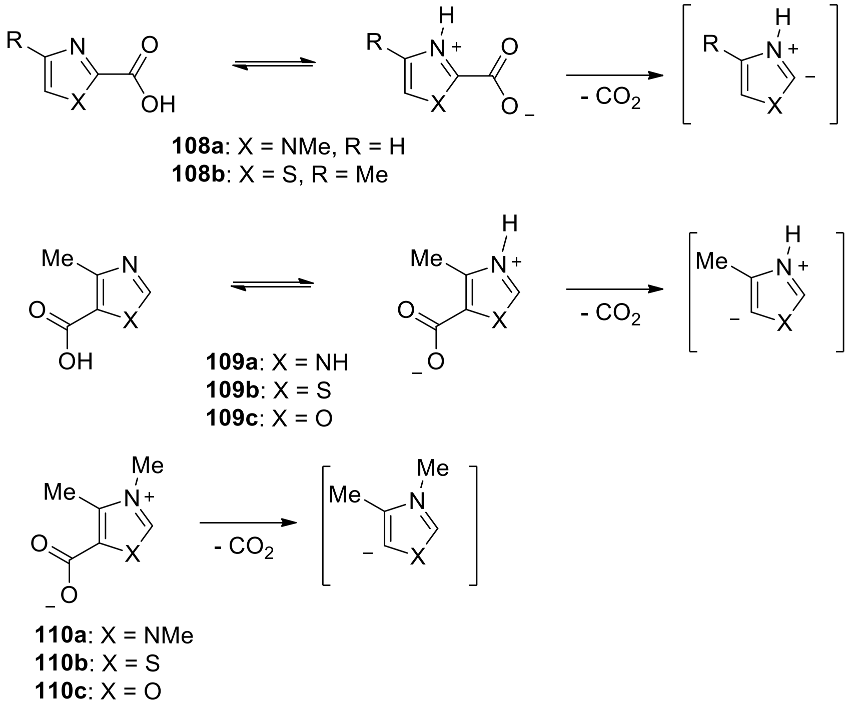
Figure 8. Characteristic features of pseudo-cross-conjugated mesomeric betaines.

The area of overlap between the classes of pseudo-cross-conjugated mesomeric betaines and normal N-heterocyclic carbenes (nNHC) is by far the most important because of interconversions under relatively mild conditions. Some reviews covering portions of that field appeared during the last years. A detailed review on betaine adducts of N-heterocyclic carbenes was published in 2009.[66] This review cites 102 references and deals with carbon disulfide, carbon dioxide, isothiocyanate, isocyanate, carbon diselenide, carbodiimide, and prop-1-ene-1,1,3,3-tetracarboxylate adducts of *N*-heterocyclic carbenes **96** – **107** (Scheme 26). All adducts belong to the class of PCCMB.



Scheme 26. Examples of pseudo-cross-conjugated mesomeric betaines which are formal 1:1 adducts of heterocumulenes and N-heterocyclic carbenes, reviewed in ref. 66.

Some additional compounds have been published meanwhile, such as the adduct of 1,2,4-triazol-5-ylidene with phenylisocyanate,[67] several fluoroalkyl-substituted imidazolium-2-carbodithioates[68] and 2-thiocarboxylates.[69] Benzimidazole / isothiocyanate adducts[70] and chemosensors based on the adduct formation of CO_2 to benzobisimidazolium carbenes[71] have also been described. In addition, a report deals with adduct formation of bis(N-heterocyclic carbene)s and bis(isothiocyanate)s.[72]



108a: X = NMe, R = H
108b: X = S, R = Me

109a: X = NH
109b: X = S
109c: X = O

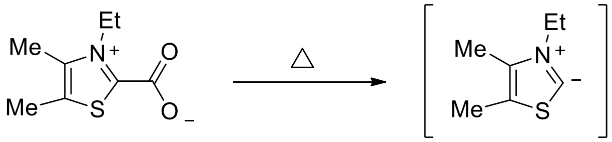
110a: X = NMe
110b: X = S
110c: X = O

Scheme 27. A comparison of decarboxylations of pseudo-cross-conjugated and cross-conjugated mesomeric betaines to nNHC and aNHC, respectively.

The outstanding feature of pseudo-cross-conjugated mesomeric betaines is the formation of normal N-heterocyclic carbenes by cleavage of the union bond which connects the positive and the negative part of the molecule, and especially decarboxylations proved to be advantageous as they often proceed under relatively mild conditions, when stabilizing effects such as hydrogen bonds are absent. As a matter of fact decarboxylations of thiazolium, oxazolium and imidazolium carboxylates were studied almost 50 years ago,[73] and these results offer an interesting comparison between pseudo-cross-conjugated and cross-conjugated systems. It was shown that the 2- and 5-carboxylic acids of the aforementioned heteroaromatics **108** and **109** decarboxylate through zwitterionic tautomers (Scheme 27). In the case of imidazole-2-carboxylic acids, these are indeed the predominant tautomers.[74] Similar results have been obtained for the decarboxylation of oxazole-2-carboxylic acid.[75] The fastes rate of decarboxylation of the thiazole-2-carboxylic acid was observed in the neutral solvent ethylene glycol. Decarboxylations of the *N*-methylated species, *i.e.* the mesomeric betaines **110** have been examined as comparison.

There was over a 100 °C difference in temperature required for similar rates of decarboxylations of the 2-position (*i.e.* PCCMB → nNHC interconversions) in comparison to decarboxylations of the 3-position (*i.e.* CCMB → aNHC interconversions). Thus, the imidazole-2-carboxylic acid decarboxylates *via* its pseudo-cross-conjugated tautomer $3.4 \cdot 10^5$ times faster than imidazolium-5-carboxylate.

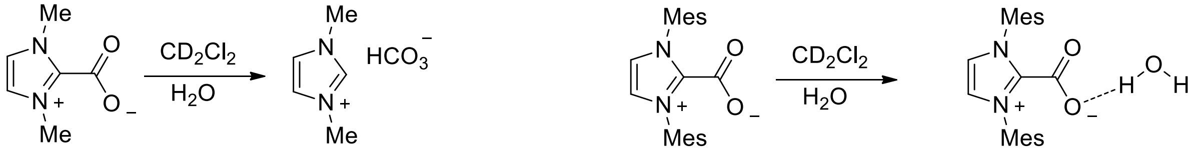
As a matter of fact, the thiazolium-2-carboxylate **111** is quite unstable as it decarboxylates easily at rt after a few minutes. It was used to induce benzoin condensations in the absence of base (Scheme 28).[76]



111 **112**

Scheme 28. Decarboxylation of thiazolium-2-carboxylate.

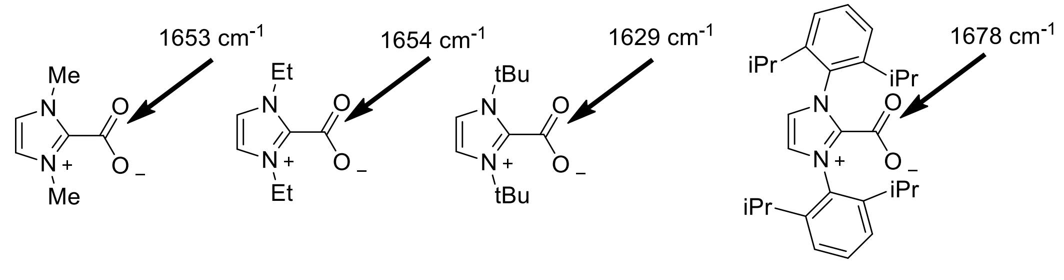
A series of pseudo-cross-conjugated imidazolium carboxylates was examined in terms of reactions with water, IR frequencies, behavior in thermogravimetric analyses, and decarboxylation.[77] Water addition to 1,3-dimethylimidazolium-2-carboxylate **113**, 1,3-diethyl-imidazolium-2-carboxylate or 1,3-di-tert-butylimidazolium-2-carboxylate in CD_2Cl_2 results in the formation of the corresponding imidazolium hydrogencarbonates such as **114**, as evidenced by new resonance frequencies at 9.10 ppm in the ^{1}H NMR spectra (Scheme 29). Decarboxylation, however, did not readily occur when *N*-arylated imidazolium-2-carboxylates such as **115** were treated with water under analogous conditions. Instead, chemical shift changes were attributed to a hydrogen-bonded carboxylate group, resulting in downfield shifts of the aryl protons.



113 **114** **115** **115·H₂O**

Scheme 29. Reaction of water with imidazolium-2-carboxylates in CD_2Cl_2.

Replacing alkyl substituents attached to nitrogen to the bulky tBu group, the C=O stretching decreases.[77] *N*-Aryl substituents cause higher $\nu_{CO(asym.)}$ stretching frequencies (Scheme 30).[77] Thermal stabilities have been examined by means of FTIR spectroscopy with monitoring the $\nu(CO_2)$ region.[78] Interestingly, the presence of free CO_2 significantly stabilizes the betaines toward decarboxylation, while the addition of propylene oxide causes a destabilization of the betaines. Organocatalytic properties have been investigated.[78]

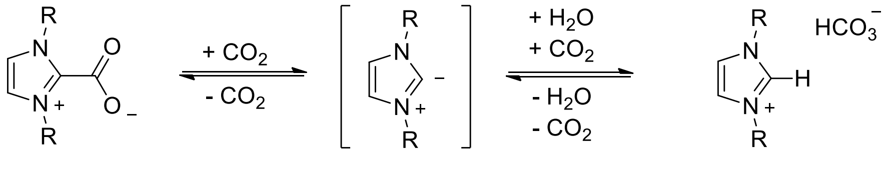


113 **116** **117** **118**

Scheme 30. Stretching frequencies of the $\nu_{CO(asym.)}$ band of PCCMBs are affected by the steric bulk of the substituents attached to the nitrogen atoms.

Increasing ability to decarboxylate was found by TGA analyses with increasing steric bulk of the substituents attached to the *N* atoms.[77] Thus, 1,3-dimethylimidazolium-2-carboxylate **113** decarboxylates at 162 °C, whereas the corresponding tBu derivative **117** loses CO_2 at 71 °C and decomposes. These temperatures were dependent on the amount of sample and were found for 3.5 mg. It was found also that extra electron density in the imidazolium ring by substitution of methyl groups in the position 4 and 5 enhances the stability of the betaines[77] and causes an increased basicity of the resulting carbene.[79] A direct correlation was found between the bond lengths of the union bond connecting the positive and negative fragments of the betaines and the decarboxylation temperature.[77] Smaller bond lengths cause higher decarboxylation temperatures. Torsional angles around this union bond were identified as additional parameters, as this becomes larger the decarboxylation temperature decreases. This shows impressively the close, but subtle difference between the classes of conjugated, cross-conjugated and pseudo-cross-conjugated mesomeric betaines. Interestingly, some results of single crystal X-ray analysis indicate that the cleavage of the union bond may also be mechanical in nature.[77]

The mild decarboxylation conditions of PCCMB were used in interesting betaine – carbene – salt interconversions. Thus imidazolium and benzimidazolium hydrogen carbonates *versus* imidazolium-2-carboxylates have been studied as organic precatalysts for N-heterocyclic carbene catalyzed reactions (Scheme 31).[80,81] Thermogravimetric analyses coupled with mass spectrometry of most of the examined hetarenium hydrogen carbonates displayed an extrusion of water and carbon dioxide in stages.

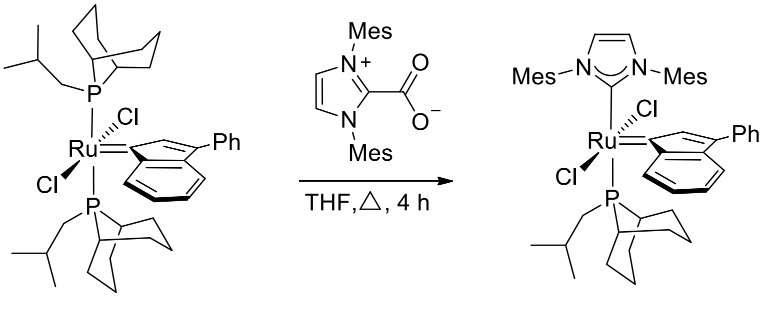


119 **120** **121**

Scheme 31. Carbon dioxide trapping and extrusion.

Depending on the substitution pattern, either a concomitant or stepwise release of water and CO_2 was observed between 108 °C and 280 °C. In solution, decarboxylation occurred at rt. Cyanosilylations, benzoin condensations, and transesterifications were studied, where the carbene-carboxylates proved to be three times more efficient than the hydrogen carbonate counterparts.

Decarboxylations of pseudo-cross-conjugated azolium-carboxylates have been employed in a large number of syntheses. Thus, a phosphane / NHC ligand exchange was performed starting from the PCCMB imidazolium-2-carboxylate in refluxing THF (Scheme 32). The new second generation ruthenium(II) dichloride-indenylidene complex proved to be stable in the solid state and was tested in catalytic reactions. The Ru-$C_{carbene}$ bond length is 2.091(5) Å.[82] The corresponding PCy_3 complex was prepared similarly.[83]

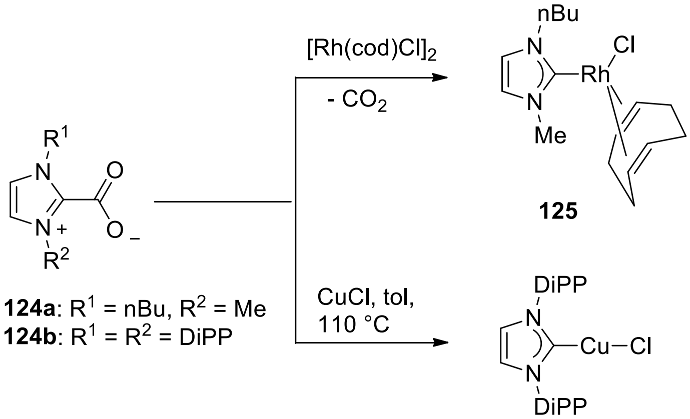


122

123 (88%)

Scheme 32. Formation of Ru complexes starting from a PCCMB.

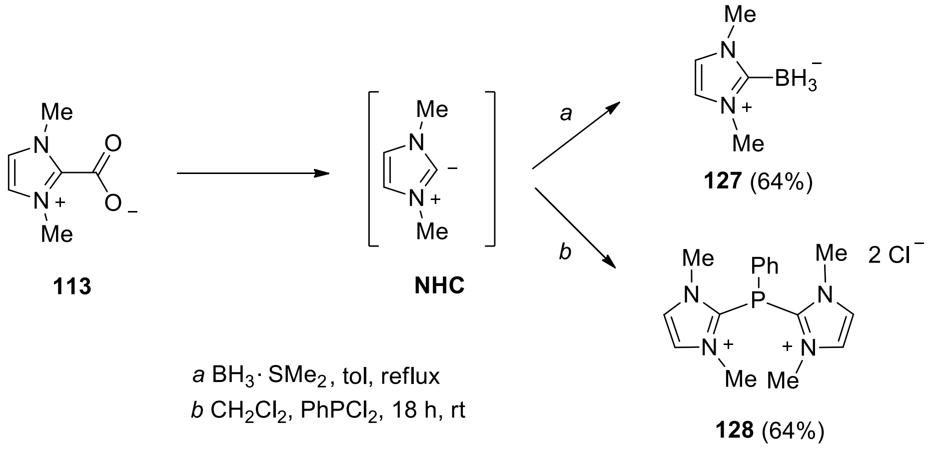
The PCCMBs **124** were applied to prepare the chloro(1,5-cyclooctadiene)(1-butyl-3-methylimidazol-2-ylidene)rhodium(I) complex **125** in 88% yield (Scheme 33).[84] It was also employed for the formation of copper, cobalt, and silver complexes.[85-88] Thus, complex **126** was formed in 90% yield.



126

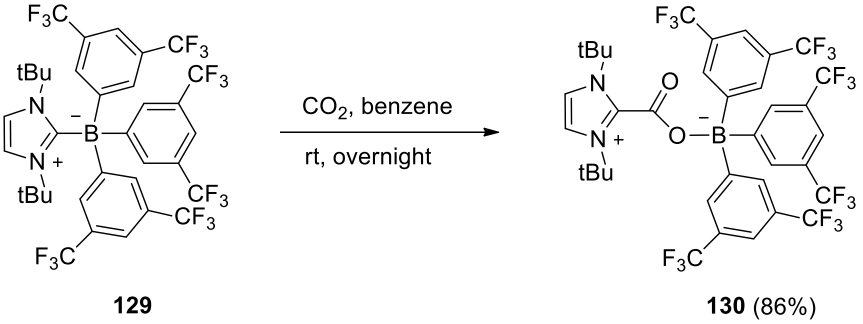
Scheme 33. A PCCMB as starting material for the synthesis of Rh and Cu complexes.

The borane adduct **127** was also formed on thermal decarboxylation of PCCMB **113**,[89] which has also been used as ionic liquid precursor.[90] Trapping of the carbene was accomplished with $PhPCl_2$ to form **128** (Scheme 34).[91]



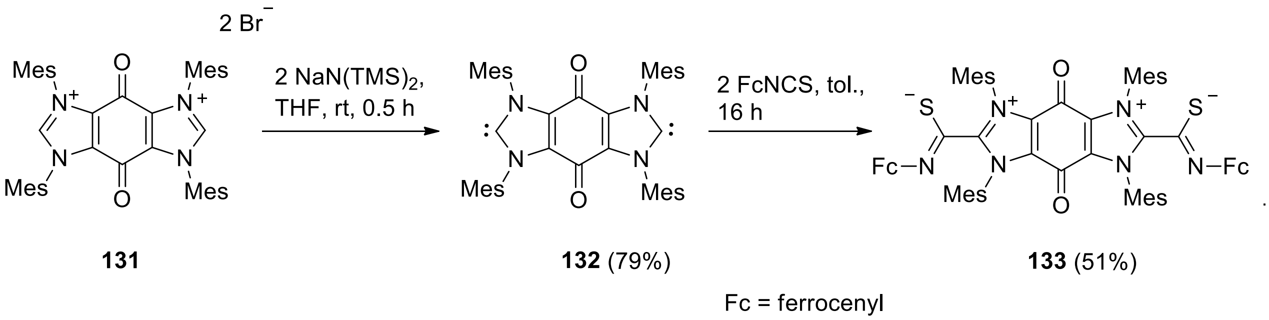
Scheme 34. Trapping reactions with boron and phosphorus electrophiles.

In a reversed process, numerous frustrated Lewis pairs (FLPs) such as **129** were used for CO_2 fixation as **130** (Scheme 35).[92]



Scheme 35. CO_2 trapping reactions.

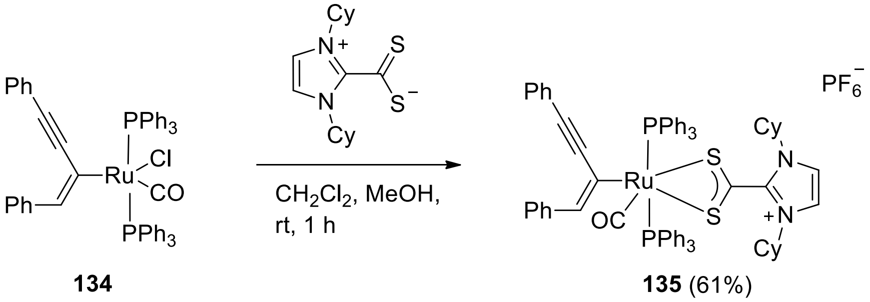
A bis-N-heterocyclic carbene **131** connected by a redox active *p*-quinone moiety was prepared which gave the bis-betaine **132** on treatment with ferrocenyl isothiocyanate (FcNCS)[93] (Scheme 36). This was then converted into bimetallic complexes as part of a study directed to electron-configurable compounds. The union bond connecting positive and negative part of the molecule was determined to have a bond length of 1.486(7) Å by X-ray crystallography. The dihedral angle between these two molecule fragments is 88.7(6).



Scheme 36. Formation of isothiocyanate adducts.

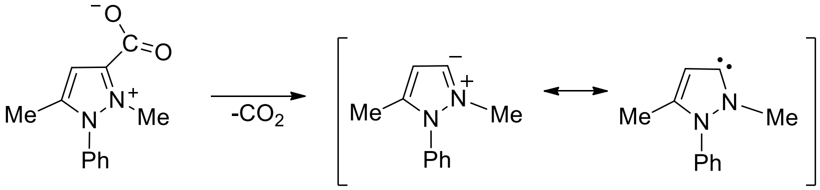
Catalytic as well as organocatalytic activities of imidazolium-2-carboxylates and 1,2,4-triazole-carboxylates have been studied as well. Thus imidazolium-2-carboxylates have been employed for transesterifications, *e.g.* of acetophenone to form benzoyl acetate, or methanol to form monomethyl carbonate.[94-96] 1,3-Di-tert-butylimidazolium-2-carboxylate was used as recyclable organocatalyst in the cycloaddition of aziridines and carbon dioxide.[97] Imidazolium-2-thiocarboxylates were also described as organocatalysts.[98] Pseudo-cross-conjugated mesomeric betaines of 1,2,4-triazole have been postulated as intermediates in [2+2+2]-cycloadditions of ketenes and carbon disulfide.[99]

No heterocumulene extrusion is observed in the following examples. The nNHC·CS_2 adduct was used as ligand in ruthenium complexes which have been evaluated in catalytic reactions.[69] As an example, the enynyl compound **134** was reacted with Icy·CS_2 to give **135** (Scheme 37).[100] Similarly imidazolium-2-dithiocarboxylates and -2-thioamidates were used as ligands in Ru complexes.[101]



Scheme 37. No extrusion of CS_2 from these PCCMB under these conditions.

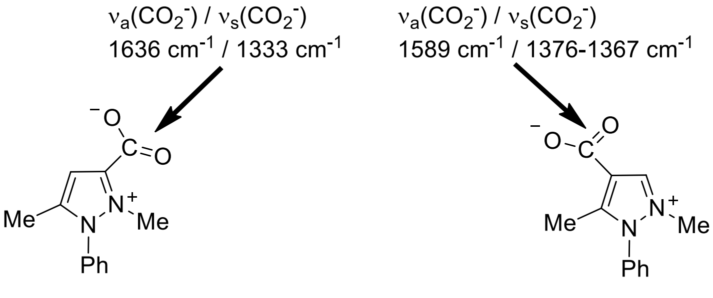
The chemistry of N-heterocyclic carbenes and mesomeric betaines of pyrazole and indazole has been reviewed recently,[25] and reviews dealing with syntheses, properties, and biological activities of pyrazoles[26,27] and indazoles[28] appeared as well. Therefore, only a brief overview will be given here. Pyrazole-3-ylidene **137** was first generated by thermal decarboxylation of the pseudo-cross-conjugated heterocyclic mesomeric betaine **136** and was examined by electrospray ionization mass spectrometry (Scheme 38).[102,103] The *in situ* generated NHC proved to induce aldol additions, Knoevenagel reactions, and redox esterifications.[102]



136 **137**

Scheme 38. Pyrazol-3-ylidene from the PCCMB pyrazolium-3-carboxylate.

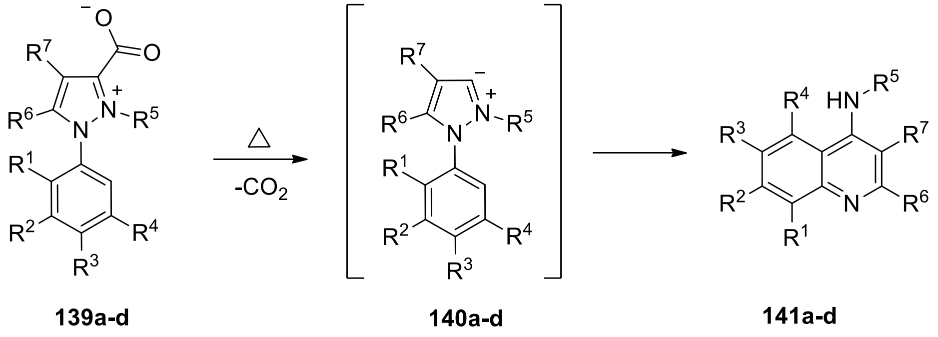
Raman spectroscopy was found to discriminate between cross-conjugation of pseudo-cross-conjugation of pyrazolium-carboxylates, as key bands react sensitive toward conjugation effects.[104] 2,5-Dimethyl-1-phenylpyrazolium-3-carboxylate and its cross-conjugated isomer 1,3-dimethyl-2-phenylpyrazolium-4-carboxylate were measured and the results were compared with theoretical values (DFT-B3PW91) calculated at the 6-311+G(d,p) level. The asymmetric stretching vibration of the carboxylate group at 1636 cm^{-1} of the PCCMB is shifted to 1589 cm^{-1} in the CCMB, resolved by Fourier deconvolution from a shoulder of an intense band at 1598 cm^{-1} (Figure 9). A similar difference, although with opposite tendency, was found for the symmetric stretching vibration. Raman wavenumbers are known to be strongly sensitive to the carboxylate negative charge density. In CCMB **138**, the negative charge is exclusively located on the carboxylate group, and both CO stretching modes are equivalent. The spectra resolve their antisymmetric and symmetric stretching modes. In the PCCMB **136** a slight interaction across the union bond causes a more single-bond stretching mode (1333 cm^{-1}) and a more double-bond stretching mode (1636 cm^{-1}).



136 (PCCMB) **138** (CCMB)

Figure 9. A Raman approach to pseudo-cross-conjugation in pyrazolium-carboxylates.

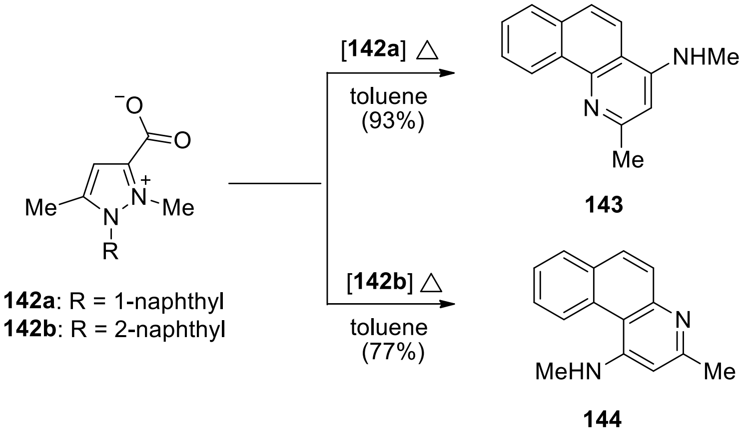
It was found that the chemical behavior of pyrazolium-3-carboxylates strongly depends on their substitution pattern. Systems possessing an aromatic ring in position 1 such as **139a-d** undergo decarboxylation on heating to N-heterocyclic carbenes which spontaneously rearrange in a pericyclic reaction to 4-aminoquinolines **141a-d**,[105] insofar as at least one unsubstituted *ortho* position exists (Scheme 39). The mechanism has been calculated.[106] Likewise, indazol-3-ylidenes rearrange to functionalized acridines.[107]



a: $R^1 = R^2 = R^4 = R^7 = H$, $R^3 = Br$, $R^5 = R^6 = Me$ (84%)
b: $R^1 = R^3 = R^7 = H$, $R^2 = R^4 = Cl$, $R^5 = R^6 = Me$ (51%)
c: $R^1 = R^7 = H$, $R^2 = R^3 = R^4 = OMe$, $R^5 = Me$, R^6 = 2-thienyl (55%)
d: $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^7 = Et$, $R^6 = Ph$ (94%)

Scheme 39. Pericyclic rearrangements of pyrazole-3-ylidenes generated from PCCMB.

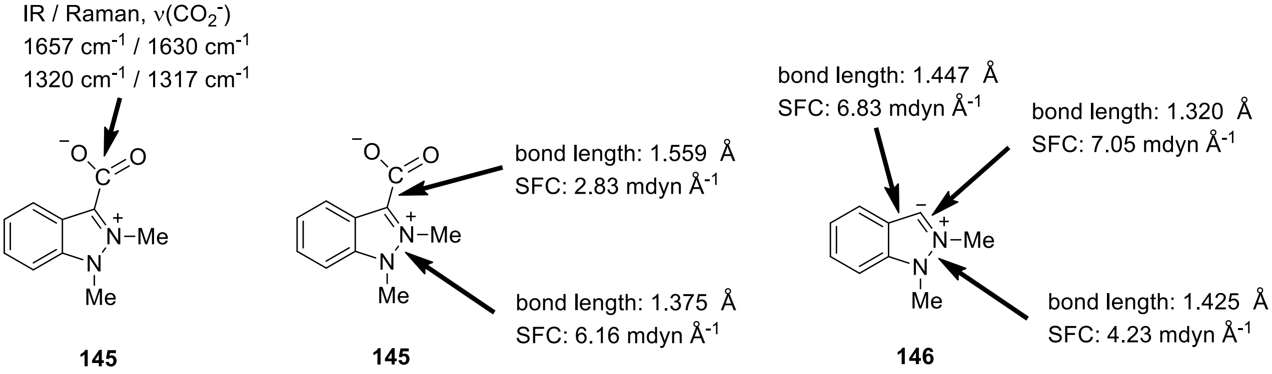
Similarly, naphthyl substituted pyrazolium-3-carboxylates rearrange to tricyclic systems (Scheme 40).[105]



Scheme 40. Formation of tricyclic systems.

Quantum mechanical studies and vibrational spectra of indazolium-3-carboxylates **145** and the N-heterocyclic carbene indazol-3-ylidene **146** generated by decarboxylation have been reported[108] (Scheme 41). Normal mode analyses were applied to analyze changes in the stretching force constants (SFC) on decarboxylation to establish spectroscopic-structure relationships. The two stretching modes were assigned to two relatively intense infrared bands at

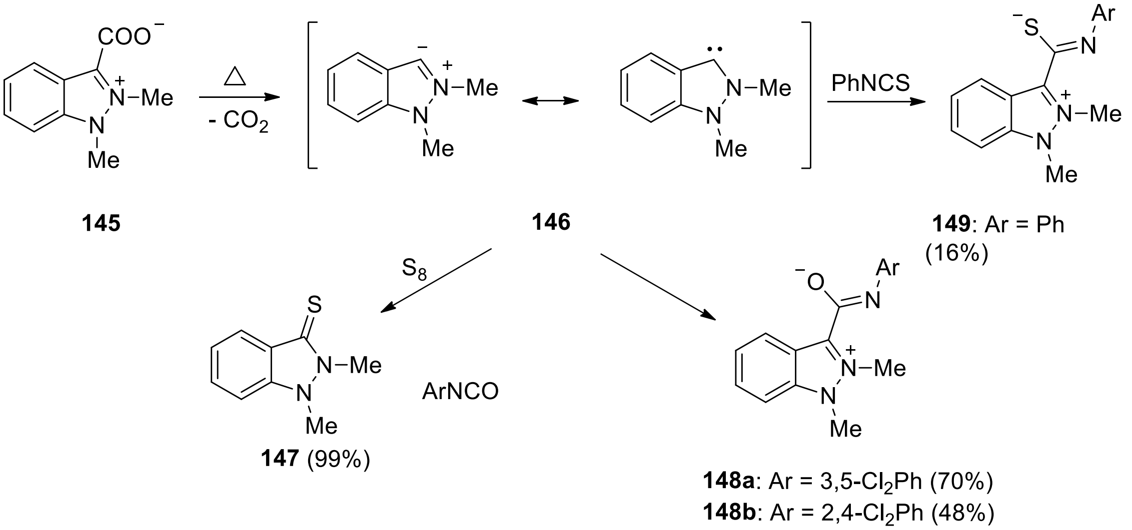
1657 cm^{-1} and 1320 cm^{-1}. The corresponding Raman bands are given in Scheme 41. According to this, betaine **145** possesses a union bond with a bond length of 1.559 Å, the stretching force constant of which was measured be 2.83 mdynÅ^{-1}, which is a very low value. A single crystal X-ray analysis showed a bond length of 1.519 Å of the union bond in the solid state which is considerable longer than a C(sp^2)–C(sp^2) single bond (147 pm). In the elemental cell, the carboxylate group adopts a torsional angle of 21.5° with respect to the indazole ring.[109] The weakest skeletal SFC of the molecule was calculated for the N-N bond. Quantum mechanical modeling gave values for N-heterocyclic carbene **146** which are shown in Scheme 41.[108] Greater changes are found for the SFC of the N-N bond which change by 31.2% on conversion of the betaine to the carbene. Low activation energies of 11.35, 11.76, and 12.33 kcal mol^{-1} were calculated for the decarboxylation of **145** and its 5-fluoro and 5-chloro derivative from the solid state, respectively, which correlates well with the starting decarboxylation temperatures determined experimentally by thermogravimetric analyses, 116 °C, 100 °C, and 94 °C.[109] The decarboxylation could also be monitored by infrared and Raman spectroscopy at varying temperatures as the CO_2 molecules were detectable as a band at 2335 cm^{-1}.[108]



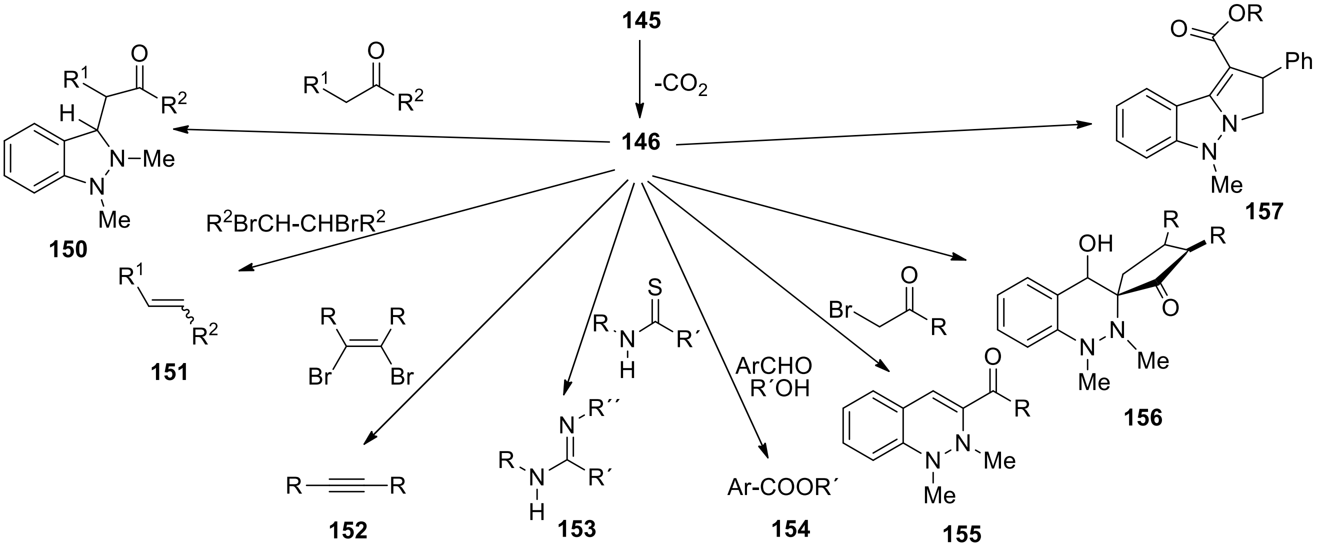
Scheme 41. Results of quantum chemical calculations [DFT, 6-311+G(d,p)].

The pseudo-cross-conjugated mesomeric betaine **145** is stabilized by hydrogen bonds from water or polar protic solvents. Thus, the X-ray single crystal analysis showed three equivalent of water of crystallization.[109] Destabilization consequently occurs in non-polar solvents which form azeotropic mixtures with water. Under these conditions, decarboxylation begins at ambient temperatures, which is concomitant to a considerable decrease of the permament dipole moment from 11.85 D (**145**) to 4.50 D (**146**).[108] Thus a solution of **145** in DMSO-d_6 contained 35% of corresponding indazolium salt, formed by a decarboxylation / protonation sequence, after 10.0 minutes at 25 °C. NMR measurements at various temperatures show a considerable decarboxylation above approximately 40 °C.[110] The Gibbs free energy difference for the decarboxylation of the betaine **145** at 25 °C at 1 atm was calculated to be 3.4 kcal/mol.[84] A threshold temperature of 38 °C was theoretically predicted, necessary for the decarboxylation of **145** to start under a pressure of 1 atm. The singlet ground state of the N-heterocyclic carbene **146** was calculated to be 45.2 kcal mol^{-1} more stable than the triplet ground state, which have been compared.[110]

The *in situ* generated indazol-3-ylidene **146** undergoes typical trapping reactions in solution as shown under formation of new pseudo-cross-conjugated mesomeric betaines such as **148** and **149** (Scheme 42).[109]



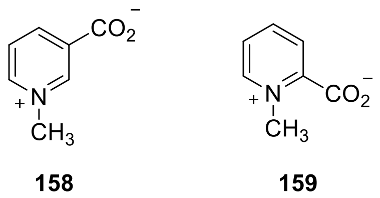
Scheme 42. Indazol-3-ylidene generated from the PCCMB indazole-3-carboxylate.



Scheme 43. Synthetic potential of indazol-3-ylidene.

The synthetic potential of *in situ* generated indazol-3-ylidenes has been studied intensively (Scheme 43). Thus, the N-heterocyclic carbene **146** forms stable 1:1 adducts **150** with aliphatic ketones.[110,111] Vicinal dibromides are debrominated to olefins **151** and acetylenes **152**, respectively.[112] It can be employed as a reagent to replace mercury in amidination reactions of thioamides to **153**.[113,114] Aromatic aldehydes in the presence of alcohols undergo redox esterification to **154**.[111] α-Bromo acetophenones induce ring enlargement reactions to cinnolines **155** with **146**.[112] New ring systems such as **156**[112] and **157**[115] were prepared.

N-Methylpyridinium-3-carboxylates such as **158** and N-methylpyridinium-2-carboxylates **159** represent two additional examples of CCMB and PCCMB, respectively, which have been compared in terms of their abilities to generate N-heterocyclic carbenes (Scheme 44). The former mentioned CCMB is known as the alkaloid trigonelline and the latter as alkaloid homarine.[14] The PCCMB **159** has been used in heterocyclic synthesis due to the ease of its decarboxylation (*vide infra*).

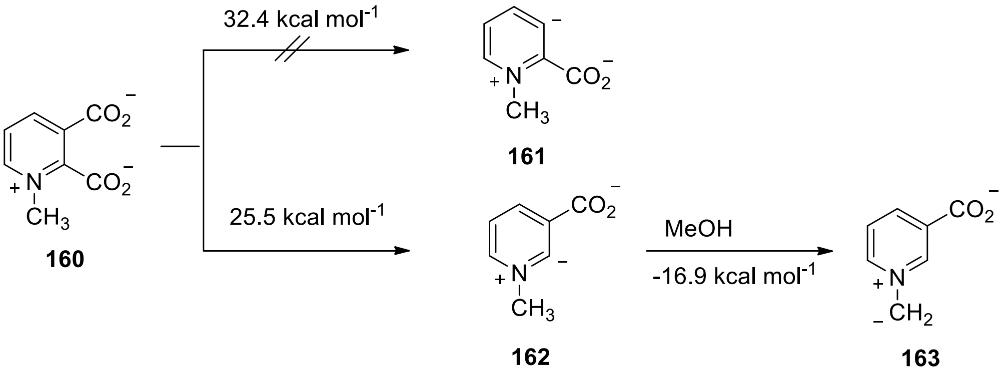


Scheme 44. Two natural products belong to the classes of CCMB (**158**) and PCCMB (**159**).

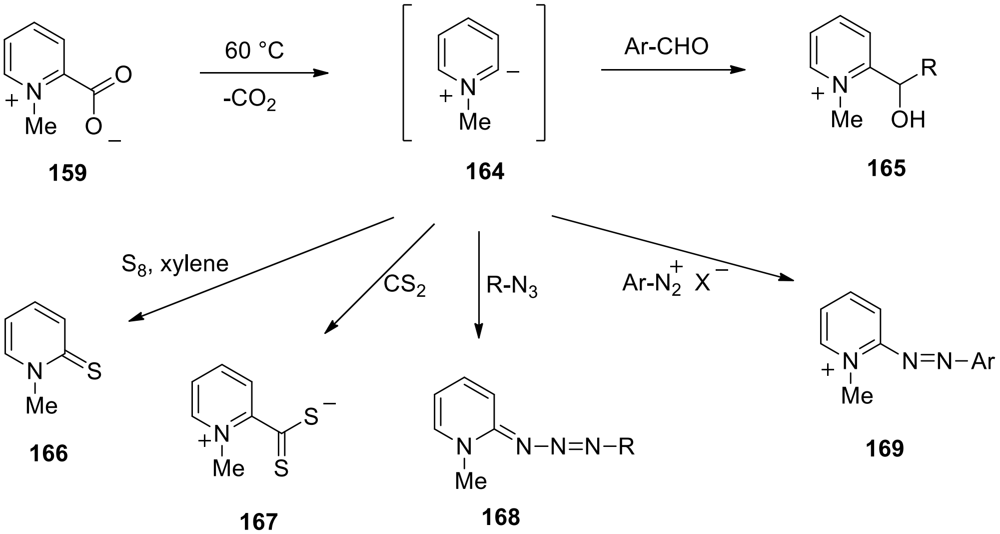
Nine isomeric pyridinium dicarboxylates, among those the *N*-methylpyridinium-2,3-dicarboxylate **160**, were examined by negative ion photoelectron spectroscopy as model substances to gain knowledge about the mechanisms of orotidine 5´-monophosphate decarboxylase (Scheme 45).[116] It was found that the expulsion of CO_2 is facilitated from the pseudo-cross-conjugated position. The authors claim that this might seem to be counterintuitive as the remote carboxylate is less affected by the positive charge, but they say that any reasonable application of Coulomb´s law indicates that more is gained by expulsion of the 2-carboxylate because of the greater stabilization of the resulting carbanion. The relative stabilities of the resulting decarboxylated species are largely determined by their intramolecular electrostatic interactions. The zwitterion **161** derived from 3-decarboxylation has a relative stability of 22.7 / 130.7 kcal mol^{-1} according to B3LYP/3-31+G(d) and Coulomb´s law calculations, whereas the 2-decarboxylated species **162** has values of 15.7 / 62.4 kcal mol^{-1}, respectively, so that the latter mentioned is more stable than the former. Ylide formation to **163** is exothermic by -16.9 kcal mol^{-1}.

As already mentioned, 1-methyl-pyridinium-2-carboxylate **159** decarboxylates easily and the following scheme shows results of preparative heterocyclic synthesis. At approximately 60 °C in dipolar aprotic solvents such as *N*-methylpyrrolidone, acetonitrile or benzonitrile the N-heterocyclic carbene **164** underwent several reactions with electrophiles (Scheme 46). In protic solvents the carbene is protonated.[117] In aprotic solvents, treatment of the pyridine-2-ylidene with aldehydes gave alcohols such as **165**.[118,119] Sulfur converted **164** into pyridine-2-thione **166**, CS_2

gave dithioacids **167**,[120] azides converted the carbene into triazenes **168**, and diazonium ions gave azo compounds **169**. The decarboxylation of quinoline-2-carboxylic acid at elevated temperatures (Hammick reaction, 1937) also gave rise to the postulation of nucleophilic carbenes as highly reactive intermediates.[121]



Scheme 45. Examinations of decarboxylations gain knowledge about PCCMBs and CCMBs.

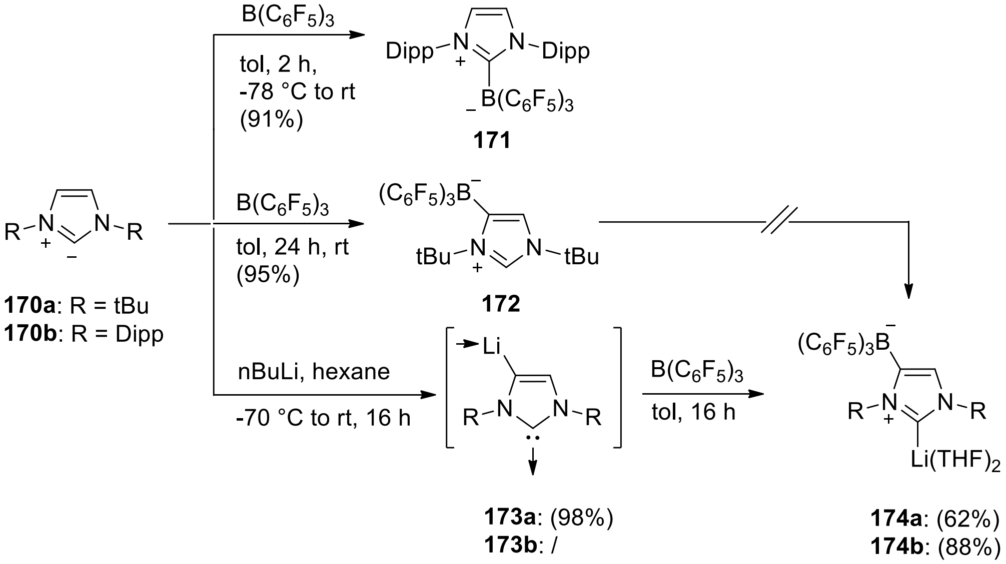


Scheme 46. Synthetic potential of pyridine-2-ylidene.

2.5. Interconversions of normal, abnormal, and remote N-heterocyclic carbenes (nNHC, aNHC, rNHC) and zwitterions

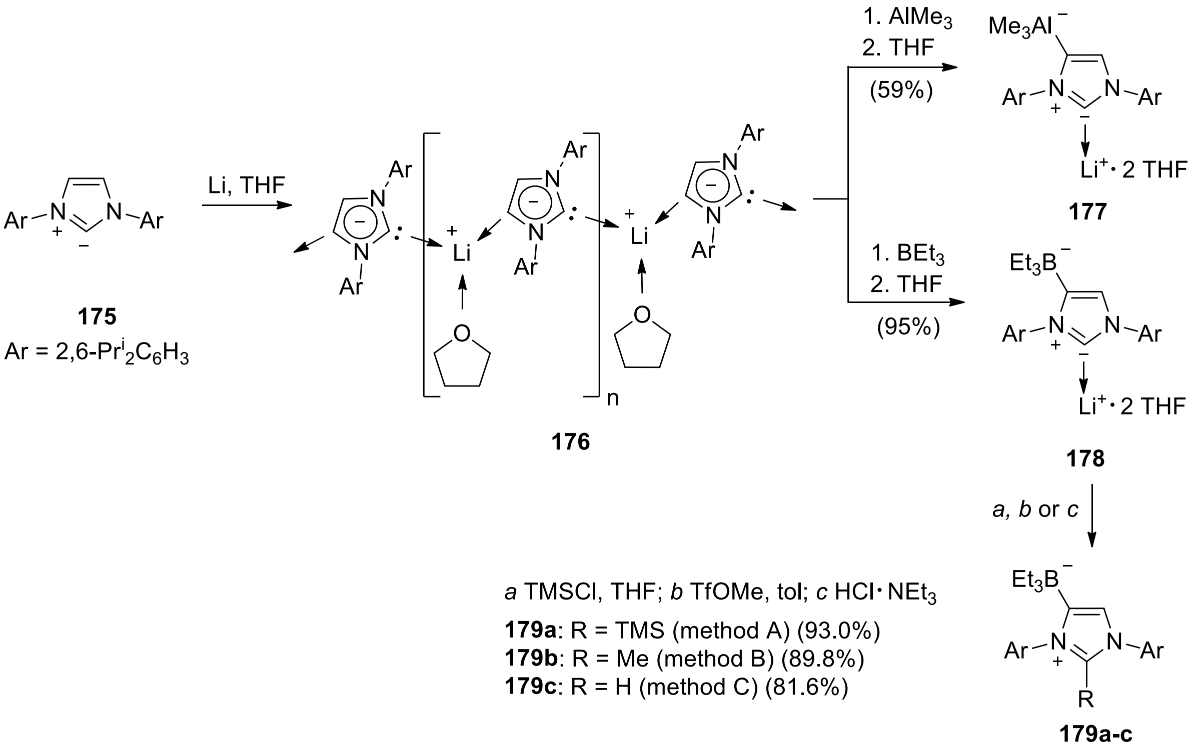
The term “zwitterion” is not well defined. It sometimes describes molecules with an interrupted conjugation between the charged parts of the molecule, for example by one or more sp^3-hybridized carbon atoms, as with the aminoacids.[14] Some polyheterocyclic molecules, however, can form zwitterionic ground states, in which both the negative and the positive charge are delocalized within a common π-electron system, although at least one uncharged covalent structure can be drawn.[122] Those molecules are best represented by dipolar resonance structures which are also called zwitterions despite of the fundamental structural differences to the aforementioned class of compounds. Borane adducts of N-heterocyclic carbenes do not fit into the classification system of conjugated mesomeric betaines (CMB), because according to the valence bond theory the charge which is located on the boron atom is not part of the π-electron system. On the other hand, no characteristic features of conjugated, cross-conjugated, and pseudo-cross-conjugated mesomeric betaines can be recognized in these borane adducts. Nevertheless, they do share a formal relationship to this class of compounds. Thus, formal replacement of the olate group in imidazolium-4-olate to a borate group results in borane adduct **172** (Scheme 47). Formal replacement of the carboxylate group in imidazolium-2- and 4-carboxylates gives borane adducts **171** and **172**. Borane adduct formations from N-heterocyclic carbenes have been reviewed recently.[123] Here, examples of the title compounds will be presented. A comprehensive survey about the interesting subject of NHC adduct formation with trivalent group 13 compounds,[124-128] however, is beyond the scope of this review.

The frustrated carbene-borane Lewis pair **170a**·$B(C_6F_5)_3$ formed the aNHC-borane adduct **172**[129] which is more stable than the corresponding nNHC-borane adduct.[130] The sterically less demanding Dipp (2,6-diisopropylphenyl) substituent in **170b** resulted in the formation of the “normal” borane-NHC adduct **171**.[131] Either compound failed deprotonation to give an anionic N-heterocyclic borane. These were prepared by deprotonation to form **173** followed by treatment with the borane to give **174**.[132]



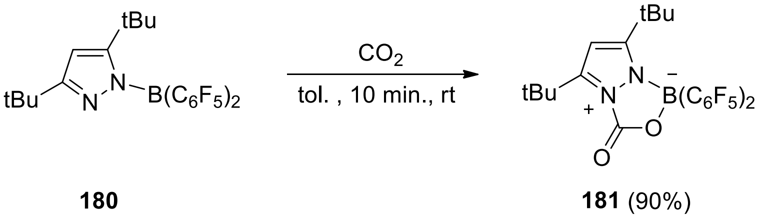
Scheme 47. Borane adduct formations to normal and abnormal N-heterocyclic carbenes.

An anionic N-heterocyclic dicarbene **176** has been prepared as a polymeric chain (X-ray structure) in excellent yield on treatment of the nNHC **175** with nBuLi in hexane at rt and subsequent addition of THF / TMEDA (tetramethylethylenediamine), or by addition of lithium in THF. The THF adduct proved to be persistent at rt under an inert atmosphere (Scheme 48).[133] Triethylborane and trimethylaluminum reacted to the adducts **178** and **177**, respectively. The borane adduct has been converted into the zwitterions **179**.[134]



Scheme 48. Formation of a dicarbene.

Carbon dioxide could be trapped by a pyrazolyl borane Lewis pair (Scheme 49).[135]



Scheme 49. Carbon dioxide trapping.

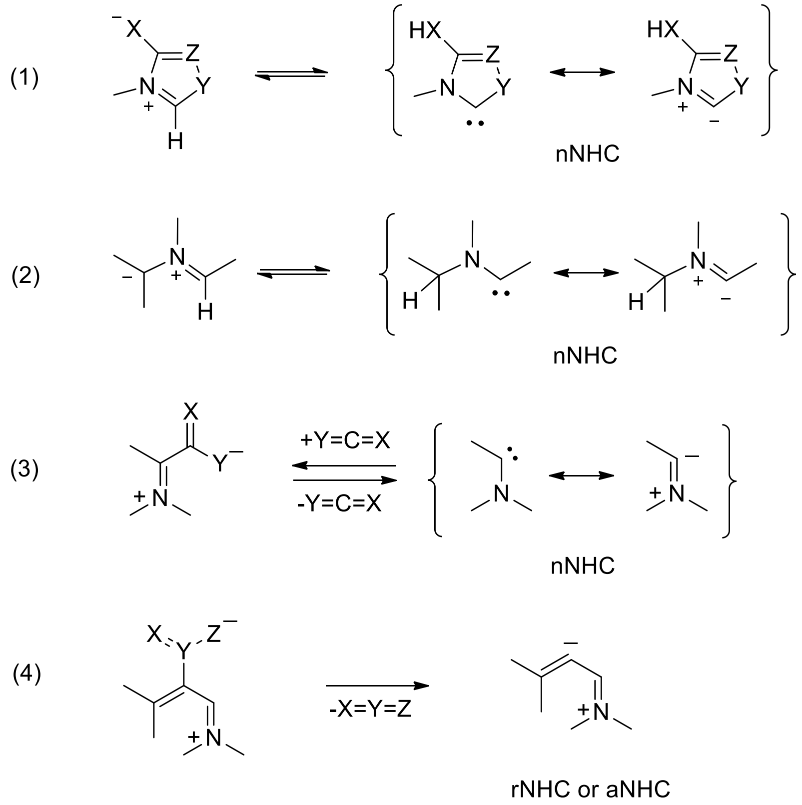
3. Conclusions

The chemistry of heterocyclic mesomeric betaines and of N-heterocyclic carbenes have an interesting area of overlap. Depending on the type of conjugation (pseudo-cross-conjugation, cross-conjugation, conjugation) and the architecture of the mesomeric betaine, the distinct classes of N-heterocyclic carbenes (normal, abnormal, remote) are available. Table 1 summarizes the mesomeric betaine ↔ N-heterocyclic carbene transformations described in this review.

Table 1. Mesomeric betaine ↔ N-heterocyclic carbene transformations described in this review

	nNHC	aNHC	rNHC	anionic NHC
CMB	X	-	-	X
ylide	X	-	-	X
CCMB	-	X	X	X
PCCMB	X	-	-	-

N-Heterocyclic carbene formations from mesomeric betaines have been performed so far by tautomerism of type-A mesoionic compounds which are members of the class of conjugated mesomeric betaines (1), by tautomerism of ylides (2), by extrusion of heterocumulenes as leaving groups from iminium-2-heterocumulene adducts *i.e.* from pseudo-cross-conjugated mesomeric betaines (3), or from X=Y=Z adducts in position 2 of prop-2-en-1-iminium partial structures (4) which belong to cross-conjugated mesomeric betaines (X=Y=Z: CO_2, SO_2) (Figure 10).



cf. compounds

8, 13a,b

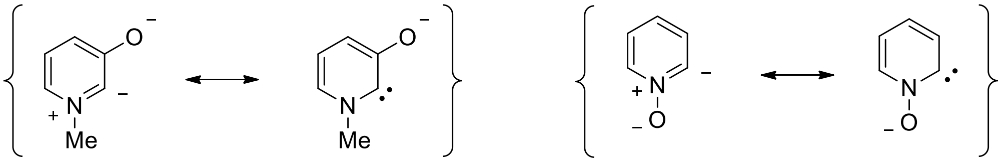
79a-c, 82, 83

96 - 107, 108a,b, 111, 113, 119, 124a,b, 136, 139a-d, 142a,b, 145, 148a,b, 149, 159, 160, 167

40, 90, 93, 109a-c 110a-c, 158

Figure 10. General scheme of the formation of NHC from mesomeric betaines

Deprotonations of mesomeric betaines can result in anionic N-heterocyclic carbenes. Examples are the anions **18**, **19**, **50**, **66**, **81**, and **86**. Numerous other structures await syntheses and applications. Thus, the anion of the conjugated heterocyclic mesomeric betaine pyridinium-3-olate **182** has not been studied in detail[136] (Scheme 50). The same is true for the anion of the ylide pyridin-N-oxide **183**, which has already been generated in complexes.[137-139] We hope that this short review will serve as stimulus for ongoing research in that field.



182

183

Scheme 50. Anions of pyridinium-3-olate and pyridine-*N*-oxide.

4. References

1. Fischer, E.; Besthorn, E. *Ann*. **1882**, *212*, 316.
2. Ramakrishna, R. S.; Irving, H. M. N. H. *Chem. Commun*. **1969**, 1356.
3. Kushi, Y.; Fernando, Q. *Chem. Commun*. **1969**, 1240.
4. Kushi, Y.; Fernando, Q. *J. Am. Chem. Soc*. **1970**, *92*, 1965.
http://dx.doi.org/10.1021/ja00710a031
5. Schonafinger, K. *Farmaco* **1999**, *54*, 316.
http://dx.doi.org/10.1016/S0014-827X(99)00031-2
6. Khmel´nitskaya, E. Yu.; Levina, V. I.; Trukhacheva, L. A.; Grigoriev, N. B.; Kalinin, V. N.; Cherepanov, I. A.; Lebedev, S. N.; Granik, V. G. *Izv. Akad. Nauk, Ser. Khim*. **2004**, 2725; *Russ. Chem. Bull. Int. Ed*. **2004**, *53*, 2840.
7. Moustafa, M. A.; Gineinah, M. M.; Nasr, M. N.; Bayoumi, W. A. H. *Arch. Pharm*. **2004**, *337*, 427.
http://dx.doi.org/10.1002/ardp.200300847
8. Dunkley, S. C.; Charles, T. J. *Bioorg. Med. Chem. Lett*. **2003**, *13*, 2899.
9. Ollis, W. D.; Ramsden, C. A. *Adv. Heterocycl. Chem*. **1976**, *19*, 1.
http://dx.doi.org/10.1016/S0065-2725(08)60230-5
10. Ramsden, C. A. in Sammes, P. G. (ed.), *Comprehensive Organic Chemistry*, Vol. 4, Pergamon Press, Oxford, **1979**, 1171.
11. Katritzky, A. R. *Chem. Ind*. **1955**, 521.
12. Ollis, W. D.; Stanforth, S. P.; Ramsden, C. A. *Tetrahedron* **1985**, *41*, 2239.
http://dx.doi.org/10.1016/S0040-4020(01)96625-6
13. Schmidt, A. *Curr. Org. Chem*. **2004**, *8*, 653.

http://dx.doi.org/10.2174/1385272043370663

14. Schmidt, A. *Adv. Heterocycl. Chem*. **2003**, *85*, 67.
http://dx.doi.org/10.1016/S0065-2725(03)85002-X
15. Ramsden, C. A. *Tetrahedron* **2013**, *69*, 4146.
http://dx.doi.org/10.1016/j.tet.2013.02.081
16. chmidt, A.; Kindermann, M. K. *J. Org. Chem*. **1998**, *63*, 4636.
http://dx.doi.org/10.1021/jo972349j
17. Schmidt, A.; Nieger, M. *Heterocycles* **1999**, *51*, 2119.
http://dx.doi.org/10.3987/COM-98-8348
18. Arduengo III, A. J.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc*. **1991**, *113*, 361.
http://dx.doi.org/10.1021/ja00001a054
19. Grundemann, S.; Kovacevic, A.; Albrecht, M.; Faller, J. W.; Crabtree, R. H. *Chem. Commun*. **2001**, 2274.
http://dx.doi.org/10.1039/b107881j
20. Schuster, O.; Yang, L.; Raubenheimer, H. G.; Albrecht, M. *Chem. Rev*. **2009**, *109*, 3445.
http://dx.doi.org/10.1021/cr8005087
21. Raubenheimer, H. G.; Cronje, S. *Dalton Trans*. **2008**, 1265.
http://dx.doi.org/10.1039/b715592a
22. Strasser, C. E.; Stander-Grobler, E.; Schuster, O.; Cronje, S.; Raubenheimer, H. G. *Eur. J. Inorg. Chem*. **2009**, 1905.
23. Guisado-Barrios, G.; Bouffard, J.; Donnadieu, B.; Bertrand, G. *Angew. Chem*. **2010**, *122*, 4869*; Angew. Chem. Int. Ed*. **2010**, *49*, 4759.
http://dx.doi.org/10.1002/anie.201001864
24. Crabtree, R. H. *Coord. Chem. Rev*. **2013**, *257*, 755.
http://dx.doi.org/10.1016/j.ccr.2012.09.006
25. Schmidt, A.; Guan, Z. *Synthesis* **2012**, 3251.
http://dx.doi.org/10.1055/s-0032-1316787
26. Schmidt, A.; Dreger, A. *Curr. Org. Chem*. **2011**, *15*, 2897.
http://dx.doi.org/10.2174/138527211796378497
27. Schmidt, A.; Dreger, A. *Curr. Org. Chem*. **2011**, *15*, 1423.
http://dx.doi.org/10.2174/138527211795378263
28. Schmidt, A.; Beutler, A.; Snovydovych, B. *Eur. J. Org. Chem*. **2008**, 4073.
http://dx.doi.org/10.1002/ejoc.200800227
29. Busch, M. *Ber. Dtsch. Chem. Ges*. **1905**, *38*, 861.
http://dx.doi.org/10.1002/cber.190503801149
30. Färber, C.; Leibold, M.; Bruhn, C.; Maurer, M.; Siemeling, U. *Chem. Commun*. **2012**, *48*, 227.
http://dx.doi.org/10.1039/c1cc16460k
31. César, V.; Tourneux, J.-C.; Vujkovic, N.; Brousses, R.; Lugan, N.; Lavigne, G. *Chem. Commun*. **2012**, *48*, 2349.

http://dx.doi.org/10.1039/c2cc17870b
32. Danopoulos, A. A.; Monakhov, K. Yu.; Braunstein, P. *Chem. Eur. J*. **2013**, *19*, 450. http://dx.doi.org/10.1002/chem.201203488
33. Benhamou, L.; Vujkovic, N.; César, V.; Gornitzka, H.; Lugan, N.; Lavigne, G. *Organometallics* **2010**, *29*, 2616. http://dx.doi.org/10.1021/om1003607
34. Benhamou, L; César, V.; Gornitzka, H.; Lugan, N.; Lavigne, G. *Chem. Commun*. **2009**, 4720.
35. Biju, A. T.; Hirano, K.; Fröhlich, R.; Glorius, F. *Chem. Asian J*. **2009**, *4*, 1786.
36. Petronilho, A.; Müller-Bunz, H.; Albrecht, M. *Chem. Commun*. **2012**, *48*, 6499. http://dx.doi.org/10.1039/c2cc32843g
37. Araki, S.; Yamamoto, K.; Yagi, M.; Inoue, T.; Fukagawa, H.; Hattori, H.; Yamamura, H.; Kawai, M.; Butsugan, Y. *Eur. J. Org. Chem*. **1998**, 121. http://dx.doi.org/10.1002/(SICI)1099-0690(199801)1998:1<121::AID-EJOC121>3.0.CO;2-5
38. Olofson, R. A.; Thompson, W. R.; Michelman, J. S. *J. Am. Chem. Soc*. **1964**, *86*, 1866. http://dx.doi.org/10.1021/ja01063a052
39. Schelz, D.; Balli, H. *Helv. Chim. Acta* **1970**, *53*, 1913. http://dx.doi.org/10.1002/hlca.19700530742
40. Balli, H.; Löw, R. *Helv. Chim. Acta* **1976**, *59*, 155. http://dx.doi.org/10.1002/hlca.19760590118
41. Lowack, R. H.; Weiss, R. *J. Am. Chem. Soc*. **1990**, *112*, 333. http://dx.doi.org/10.1021/ja00157a051
42. Weiss, R.; Lowack, R. H. *Angew. Chem*. **1991**, *103*, 1183; *Angew. Chem. Int. Ed. Engl*. **1991**, *30*, 1162. http://dx.doi.org/10.1002/anie.199111621
43. Browne, D. L.; Harrity, J. P. A., *Tetrahedron* **2010**, *66*, 553. http://dx.doi.org/10.1016/j.tet.2009.10.085
44. Tien, H.-J.; Fang, G.-M.; Lin, S.-T.; Tien, L.-L. *J. Chin. Chem. Soc*. **1992**, *39*, 107.
45. Wiechmann, S.; Freese, T.; Schmidt, A. manuscript in preparation.
46. Kato, H.; Ohta, M. *Bull. Chem. Soc. Jpn*. **1959**, *32*, 282. http://dx.doi.org/10.1246/bcsj.32.282
47. Lebedev, S. N.; Cherepanov, I. A.; Kalinin, V. N. *Russ. Chem. Bull., Int. Ed*. **2002**, *51*, 899.
48. Kalinin, V. N.; Min, S. F.; Petrovskii, P. V. *J. Organomet. Chem*. **1989**, *379*, 195. http://dx.doi.org/10.1016/0022-328X(89)80040-3
49. Morozova, L. N.; Isaeva, L. S.; Petrovskii, P. V.; Kratsov, D. N.; Min, S. F.; Kalinin, V. V. *J. Organomet. Chem*. **1990**, *381*, 281. http://dx.doi.org/10.1016/0022-328X(90)80120-O

50. Kalinin, V. N.; She, F. M.; Khandozhko, V. N.; Petrovskii, P. V. *Russ. Chem. Bull. Int. Ed.* **2001**, *50*, 525.
51. Kalinin, V. N.; Pashchenko, D. N.; She, F. M. *Mendeleev Commun*. **1992**, *2*, 60. http://dx.doi.org/10.1070/MC1992v002n02ABEH000133
52. Kalinin, V. N.; Min, S. F. *J. Organomet. Chem*. **1988**, *352*, C34. http://dx.doi.org/10.1016/0022-328X(88)83049-3
53. Kalinin, V. N.; Lebedev, S. N.; Cherepanov, I. A.; Godovikov, I. A.; Lyssenko, K. A.; Hey-Hawkins, E. *Polyhedron* **2009**, *28*, 2411. http://dx.doi.org/10.1016/j.poly.2009.04.038
54. Lin, S.-T.; Cheo, H.-S.; Liu, L.-S.; Wang, J.-C. *Organometallics* **1997**, *16*, 1803. http://dx.doi.org/10.1021/om960728h
55. Lin, S.-T.; Choe, H.-S.; Liu, L.-S.; Wang, J.-C. *J. Organomet. Chem*. **2000**, *610*, 1. http://dx.doi.org/10.1016/S0022-328X(00)00321-1
56. Cherepanov, I. A.; Egorova, N. V.; Martinovich, K. B.; Kalinin, V. N. *Doklady Chem*. **2000**, *374*, 175.
57. Cherepanov, I. A.; Kalinin, V. N. *Mendeleev Commun*. **2000**, 181. http://dx.doi.org/10.1070/MC2000v010n05ABEH001319
58. Pidlypnyi, N.; Namyslo, J. C.; Drafz, M. H. H.; Nieger, M.; Schmidt, A. *J. Org. Chem*. **2013**, *78*, 1070. http://dx.doi.org/10.1021/jo302479p
59. Pidlypnyi, N.; Uhrner, F.; Nieger, M.; Drafz, M. H. H.; Hübner, E. G.; Namyslo, J. C.; Schmidt, A. manuscript submitted.
60. Potts, K. T.; Murphy, P. M.; Kuehnling, W. R. *J. Org. Chem*. **1988**, *53*, 2889. http://dx.doi.org/10.1021/jo00248a002
61. Potts, K. T.; Murphy, P. M.; DeLuca, M. R.; Kuehnling, W. R. *J. Org. Chem*. **1988**, *53*, 2898. http://dx.doi.org/10.1021/jo00248a003
62. Lavigne, G.; César, V.; Lugan, N. *Chem. Eur. J.* **2010**, *16*, 11432. http://dx.doi.org/10.1002/chem.201000870
63. César, V.; Lugan, N.; Lavigne, G. *J. Am. Chem. Soc*. **2008**, *130*, 11286. http://dx.doi.org/10.1021/ja804296t
64. Dreger, A.; Nieger, M.; Drafz, M. H. H.; Schmidt, A. *Z. Naturforsch.* **2012**, *67b*, 359. http://dx.doi.org/10.5560/ZNB.2012.67b0359
65. Schmidt, A.; Beutler, A.; Albrecht, M.; Ramírez, F. J. *Org. Biomol. Chem*. **2008**, *6*, 287. http://dx.doi.org/10.1039/b716508k
66. Delaude, L., *Eur. J. Inorg. Chem*. **2009**, 1681. http://dx.doi.org/10.1002/ejic.200801227
67. Matsuoka, S.-i.; Tochigi, Y.; Takagi, K.; Suzuki, M. *Tetrahedron* **2012**, *68*, 9836. http://dx.doi.org/10.1016/j.tet.2012.08.076
68. Yagupol´skii, L. M., Kokhanovskii, Yu. P.; Petko, K. I. *Russ. J. Org. Chem*. **2010**, *46*, 903.

http://dx.doi.org/10.1134/S1070428010060217

69. Hans, M.; Willem, Q.; Wouters, J.; Demonceau, A.; Delaude, L. *Organometallics* **2011**, *30*, 6133. http://dx.doi.org/10.1021/om2006529
70. Katritzky, A. R.; Jishkariani, D.; Sakhuja, R.; Hall, C. D.; Steel, P. J. *J. Org. Chem*. **2011**, *76*, 4082. http://dx.doi.org/10.1021/jo200088s
71. Guo, Z.; Song, N. R.; Moon, J. H.; Kim, M.; Jun, E. J.; Choi, J.; Lee, J. Y.; Bielawski, C. W.; Sessler, J. L.; Yoon, J. *J. Am. Chem. Soc*. **2012**, *134*, 17846. http://dx.doi.org/10.1021/ja306891c
72. Norris, B. C.; Bielawski, C. W. *Macromolecules* **2010**, *43*, 3591. http://dx.doi.org/10.1021/ma100524g
73. Haake, P.; Bausher, L. P.; McNeal, J. P. *J. Am. Chem. Soc*. **1971**, *93*, 7045. http://dx.doi.org/10.1021/ja00754a060
74. Haake, P.; Bausher, L. P. *J. Phys. Chem*. **1968**, *72*, 2213. http://dx.doi.org/10.1021/j100852a057
75. Tanaka, C. *Yakugaku Zasshi* **1965**, *85*, 193.
76. Castells, J.; López Calahorra, F.; Domingo, L. *Tetrahedron Lett*. **1985**, *26*, 5457. http://dx.doi.org/10.1016/S0040-4039(00)98235-2
77. Van Ausdall, B. R.; Glass, J. L.; Wiggins, K. M.; Aarif, A. M.; Louie, J. *J. Org. Chem*. **2009**, *74*, 7935. http://dx.doi.org/10.1021/jo901791k
78. Zhou, H.; Zhang, W.-Z.; Liu, C.-H.; Qu, J.-P.; Lu, X.-B. *J. Org. Chem*. **2008**, *73*, 8039. http://dx.doi.org/10.1021/jo801457r
79. Magill, A. M.; Cavell, K. G.; Yates, B. F. *J. Am. Chem. Soc*. **2004**, *126*, 8717. http://dx.doi.org/10.1021/ja038973x
80. Fèvre, M.; Pinaud, J.; Leteneur, A.; Gnanou, Y.; Vignolle, J.; Taton, D., Miqueu, K.; Sotiropoulos, J.-M. *J. Am. Chem. Soc*. **2012**, *134*, 6776. http://dx.doi.org/10.1021/ja3005804
81. Fèvre, M.; Coupillaud, P.; Miqueu, K.; Sotiropoulos, J.-M.; Vignolle, J.; Taton, D. *J. Org. Chem*. **2012**, *77*, 10135. http://dx.doi.org/10.1021/jo301597h
82. Sauvage, X.; Zaragoza, G.; Demonceau, A.; Delaude, L. *Adv. Synth. Catal*. **2010**, *352*, 1934. http://dx.doi.org/10.1002/adsc.201000207
83. auvage, X.; Demonceau, A.; Delaude, L. *Adv. Synth. Catal*. **2009**, *351*, 2031. http://dx.doi.org/10.1002/adsc.200900422
84. Li, J.; Peng, J.; Zhang, G.; Bai, Y.; Lai, G.; Li, X. *New J. Chem*. **2010**, *34*, 1330. http://dx.doi.org/10.1039/c0nj00012d
85. Le Gall, T.; Baltatu, S.; Collins, S. K. *Synthesis* **2011**, 3687.

86. Olszewski, T. K.; Jaskólska, D. E. *Heteroatom Chem*. **2012**, *23*, 605.
http://dx.doi.org/10.1002/hc.21056
87. Albrecht, M.; Maji, P.; Häusl, C.; Monney, A.; Müller-Bunz, H. *Inorg. Chim. Acta* **2012**, *380*, 90.
http://dx.doi.org/10.1016/j.ica.2011.08.039
88. Wyer, E.; Gucciardo, G.; Leigh, V.; Müller-Bunz, H.; Albrecht, M. *J. Organomet. Chem*. **2011**, *696*, 2882.
http://dx.doi.org/10.1016/j.jorganchem.2011.02.012
89. Bissinger, P.; Braunschweig, H.; Kupfer, T.; Radacki, K. *Organometallics* **2010**, *29*, 3987.
http://dx.doi.org/10.1021/om100634b
90. Lungwitz, R.; Linder, T.; Sundermeyer, J.; Tkatchenko, I.; Spange, S. *Chem. Commun*. **2010**, *46*, 5093.
http://dx.doi.org/10.1039/c0cc00797h
91. Azouri, M.; Andrieu, J.; Picquet, M.; Cattey, H. *Inorg. Chem*. **2009**, *48*, 1236.
http://dx.doi.org/10.1021/ic801870w
92. Kolychev, E. L.; Bannenberg, T.; Freytag, M.; Daniliuc, C. G.; Jones, P. G.; Tamm, M. *Chem. Eur. J*. **2012**, *18*, 16938.
http://dx.doi.org/10.1002/chem.201202840
93. Tennyson, A. G.; Ono, R. J.; Hudnall, T. W.; Khramov, D. M.; Er, J. A. V.; Kamplain, J. W.; Lynch, V. M.; Sessler, J. L.; Bielwaski, C. W. *Chem. Eur. J*. **2010**, *16*, 304.
http://dx.doi.org/10.1002/chem.200901883
94. Tommasi, L.; Sorrentino, F. *Tetrahedron Lett*. **2009**, *50*, 104.
http://dx.doi.org/10.1016/j.tetlet.2008.10.107
95. Tommasi, L.; Sorrentino, F. *Tetrahedron Lett*. **2006**, *47*, 6453.
http://dx.doi.org/10.1016/j.tetlet.2006.06.106
96. Van Ausdall, B. R.; Poth, N. F.; Kincaid, V. A.; Arif, A. M.; Louie, J. *J. Org. Chem*. **2011**, *76*, 8413.
http://dx.doi.org/10.1021/jo201647b
97. Ueno, A.; Kayaki, Y.; Ikariya, T. *Green Chem*. **2013**, *15*, 425.
http://dx.doi.org/10.1039/c2gc36414j
98. Hans, M.; Wouters, J.; Demonceau, A.; Delaude, L. *Eur. J. Org. Chem*. **2011**, 7083.
http://dx.doi.org/10.1002/ejoc.201101286
99. Wang, X.-N.; Shen, L-T.; Ye, S. *Chem. Commun*. **2011**, *47*, 8388.
http://dx.doi.org/10.1039/c1cc12316e
100. Naeem, S.; Thompson, A. L.; Delaude, L.; Wilton-Ely, J. D. E. T. *Chem. Eur. J*. **2010**, *16*, 10971.
http://dx.doi.org/10.1002/chem.201001235
101. Cabeza, J. A.; García-Álvarez, P.; Hernandéz-Cruz, M. G. *Eur. J. Inorg. Chem*. **2012**, 2928.
http://dx.doi.org/10.1002/ejic.201200245

102. Schmidt, A.; Habeck, T. *Lett. Org. Chem*. **2005**, *2*, 37.
http://dx.doi.org/10.2174/1570178053399903
103. Schmidt, A.; Habeck, T.; Merkel, L.; Mäkinen, M.; Vainiotalo, P. *Rapid Comm. Mass Spectrom*. **2005**, *19*, 2211.
http://dx.doi.org/10.1002/rcm.2048
104. Capel Ferrón, C.; Casado, J.; López Navarrete J. T.; Dreger, A.; Schmidt, A.; Ramírez, F. J. *J. Raman Spectrosc*. **2009**, *40*, 238.
http://dx.doi.org/10.1002/jrs.2208
105. Schmidt, A.; Münster, N.; Dreger, A. *Angew. Chem*. **2010**, *122*, 2851; *Angew. Chem. Int. Ed*. **2010**, *49*, 2790.
http://dx.doi.org/10.1002/anie.200905436
106. Dreger, A.; Cisneros Camuña, R.; Münster, N.; Rokob, T. A.; Pápai, I.; Schmidt, A. *Eur. J. Org. Chem*. **2010**, 4296.
http://dx.doi.org/10.1002/ejoc.201000507
107. Guan, Z.; Wiechmann, S.; Drafz, M.; Hübner, E.; Schmidt, A. *Org. Biomol. Chem*. **2013**, *11*, 3558.
http://dx.doi.org/10.1039/c3ob40379c
108. Schmidt, A., Snovydovych, B.; Casado, J.; Quirante, J. J.; López Navarrete, J. T.; Ramírez, F. J. *Phys. Chem. Chem. Phys*. **2009**, *11*, 341.
http://dx.doi.org/10.1039/b812597j
109. Schmidt, A.; Snovydovych, B.; Habeck, T.; Dröttboom, P.; Gjikaj, M.; Adam, A. *Eur. J. Org. Chem*. **2007**, 4909.
http://dx.doi.org/10.1002/ejoc.200700192
110. Schmidt, A.; Merkel, L.; Eisfeld, W. *Eur. J. Org. Chem*. **2005**, 2124.
http://dx.doi.org/10.1002/ejoc.200500032
111. Schmidt, A.; Habeck, T.; Snovydovych, B.; Eisfeld, W. *Org. Lett*. **2007**, *9*, 3515.
http://dx.doi.org/10.1021/ol0713739
112. Schmidt, A.; Snovydovych, B. *Synthesis* **2008**, 2798.
http://dx.doi.org/10.1055/s-2008-1067215
113. Scherbakow, S.; Namyslo, J. C.; Gjikaj, M.; Schmidt, A. *Synlett* **2009**, 1964.
114. Lindner, A. S.; Schmidt, A. *Synlett* **2008**, 2961.
115. Schmidt, A.; Snovydovych, B.; Hemmen, S. *Eur. J. Org. Chem*. **2008**, 4313.
http://dx.doi.org/10.1002/ejoc.200800456
116. Wang, X.-B.; Dacres, J. E.; Yang, X.; Lis, L.; Bedell, V. M.; Wang, L.-S.; Kass, S. R. *J. Am. Chem. Soc*. **2013**, *125*, 6814.
http://dx.doi.org/10.1021/ja0290835
117. Katritzky,A. R.; Awartani, R.; Patel, R. C. *J. Org. Chem*. **1982**, *47*, 498.
http://dx.doi.org/10.1021/jo00342a025
118. Ratts, K. W.; Howe, R. K.; Phillips, W. G. *J. Am. Chem. Soc*. **1969**, *91*, 6115.
http://dx.doi.org/10.1021/ja01050a032

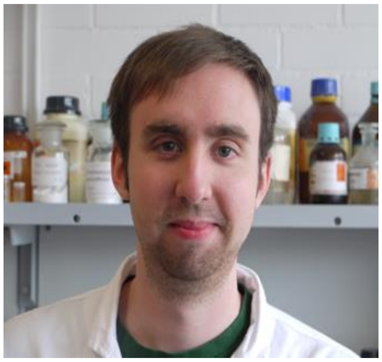
119. Quast, H.; Schmitt, E. *Liebigs Ann. Chem.* **1970**, *732*, 43.
http://dx.doi.org/10.1002/jlac.19707320105
120. Katritzky,A. R.; Faid-Allah, H. M. *Synthesis* **1983**, *2*, 149.
http://dx.doi.org/10.1055/s-1983-30261
121. Dyson, P.; Hammick, D. L.*J. Chem. Soc.* **1937**, 1724.
http://dx.doi.org/10.1039/jr9370001724
122. Wamhoff, H.; Schmidt, A. *J. Org. Chem*. **1993**, *58*, 6976.
http://dx.doi.org/10.1021/jo00077a013
123. Curran, D. P.; Solovyev, A.; Brahmi, M., M.; Fensterbank, L.; Malacria, M.; Lacôte, E. *Angew. Chem.* **2011**, *123*, 10476*; Angew. Chem. Int. Ed*. **2011**, *50*, 10294.
http://dx.doi.org/10.1002/anie.201102717
124. Stasch, A.; Singh, S.; Roesky, H. W.; Noltemeyer, M.; Schmidt, H.-G. *Eur. J. Inorg. Chem*. **2004**, 4052.
http://dx.doi.org/10.1002/ejic.200400247
125. Bonyhady, S. J.; Collis, D.; Frenking. G.; Holzmann, N.; Jones, C.; Stasch, A. *Nature Chem*. **2010**, *2*, 865.
http://dx.doi.org/10.1038/nchem.762
126. Bantu, B.; Pawar, G. M.; Wurst, K.; Decker, U.; Schmidt, A. M.; Buchmeiser, M. R. *Eur. J. Inorg. Chem*. **2009**, 1970.
127. Ghadwal, R. S.; Roesky, H. W.; Herbst-Irmer, R.; Jones, P. *Z. Anorg. Allg. Chem*. **2009**, *635*, 431.
http://dx.doi.org/10.1002/zaac.200801350
128. Shih, W.-C.; Wang, C.-H.; Chang, Y.-T.; Yap, G. P. A. Ong, T.-G. *Organometallics* **2009**, *28*, 1060.
http://dx.doi.org/10.1021/om800917j
129. Holschumacher, D.; Bannenberg, T.; Hrib, C. G.; Jones, P. G.; Tamm, M. *Angew. Chem.* **2008**, *120*, 7538; *Angew. Chem. Int. Ed***.** **2008**, *47*, 7428.
http://dx.doi.org/10.1002/anie.200802705
130. Holschumacher, D.; Taouss, C.; Bannenberg, T.; Hrib, C. G.; Daniliuc, C. G.; Jones, P. G.; Tamm, M. *Dalton Trans* **2009**, 6927.
http://dx.doi.org/10.1039/b908074k
131. Chase, P. A.; Stephan, D. W.; *Angew. Chem*. **2008**, *120*, 7543; *Angew. Chem. Int. Ed*. **2008**, *47*, 7433.
http://dx.doi.org/10.1002/anie.200802596
132. Kronig, S.; Theuergarten, E.; Daniliuc, C. G.; Jones, P. G.; Tamm, M. *Angew. Chem*. **2012**, *124*, 3294; *Angew. Chem. Int. Ed*. **2012**, *51*, 3240.
http://dx.doi.org/10.1002/anie.201108813
133. Wang, Y.; Xie, Y.; Abraham, M. Y.; Wei, P.; Schaefer III, H. F.; Schleyer, P. v.R.; Robinson, G. H. *J. Am. Chem. Soc*. **2010**, *132*, 14370.
http://dx.doi.org/10.1021/ja106631r

134. Wang, Y.; Abraham, M. Y.; Gilliard Jr., R. J.; Wei, P.; Smith, J. C.; Robinson, G. H. *Organometallics* **2012**, *31*, 791.
http://dx.doi.org/10.1021/om201259d
135. Theuergarten, E.; Schlösser, J.; Schlüns, D.; Freytag, M.; Daniliuc, C. G.; Jones, P. G.; Tamm, M. *Dalton Trans* **2012**, *41*, 9101.
http://dx.doi.org/10.1039/c2dt30448a
136. Ramusino, M. C.; La Manna, G. *Int. J. Quantum Chem*. **1996**, *57*, 729.
http://dx.doi.org/10.1002/(SICI)1097-461X(1996)57:4<729::AID-QUA20>3.0.CO;2-U
137. Cristóbal, C.; Hernández, Y. A.; López-Serrano, J.; Paneque, M.; Petronilho, A.; Poveda, M. L.; Salazar, V.; Vattier, F.; Álvarez, E.; Maya, C.; Carmona, E. *Chem. Eur. J*. **2013**, *19*, 4003.
http://dx.doi.org/10.1002/chem.201203818
138. Siladke, N. A.; LeDuc, J.; Ziller, J. W.; Evans, W. J. *Chem. Eur. J.* **2012**, *18*, 14820.
http://dx.doi.org/10.1002/chem.201201908
139. Hernández, Y. A.; López-Serrano, J.; Paneque, M.; Poveda, M. L.; Vattier, F.; Salazar, V.; Álvarez, E.; Carmona, E. *Chem. Eur. J*. **2011**, *17*, 9302.
http://dx.doi.org/10.1002/chem.201101276

Author´s Biographies

Andreas Schmidt was born in Wuppertal (Germany). He studied chemistry at the universities of Wuppertal and Bonn and obtained his diploma degree (Dipl.-Chem.) and his Dr. rer. nat. from the University of Bonn, Germany, where he had worked on aza-Wittig reactions under the supervision of Professor Dr. Dr. h. c. Heinrich Wamhoff. After an academic post at the University of Greifswald (Germany) and independent research he obtained his habilitation in 2000. After a postdoctoral position in the group of Professor Dr. Albert Padwa at Emory University, Atlanta (Georgia, USA), he was appointed to a position at Clausthal University of Technology where he is currently working as Professor of Bioorganic Materials. His research interests include N-heterocyclic carbenes, mesomeric betaines, heteroaromatic polycations, modified nucleobases, and new materials.

Sascha Wiechmann was born in Oldenburg (Germany). He worked as a laboratory assistant in the field of analysis of polychlorinated dibenzodioxins, -furans and biphenyls, before he began to study chemistry at Clausthal University of Technology. In 2011 he obtained his bachelor degree after submission of his thesis on the rearrangement of N-heterocyclic carbenes of indazoles. Then he worked on mesoionic compounds and their transformation to N-heterocyclic carbenes and obtained his master degree in 2013. He is currently PhD student in the group of Prof. Schmidt.



Tyll Freese was born in 1989 in Henstedt-Ulzburg (Germany). He was raised in Kaltenkirchen where he also graduated from school. After a year of civilian service he started to study chemistry at Clausthal University of Technology. Currently he is working on his bachelor thesis on N-heterocyclic carbenes from mesomeric betaines in the group of Prof. Schmidt.