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Synthesis of Azolium-2-dithiocarboxylate Zwitterions under Mild, Aerobic Conditions

François Mazars,[a] Madalina Hrubaru,[b] Nikolay Tumanov,[c] Johan Wouters,[c] and Lionel Delaude*[a]

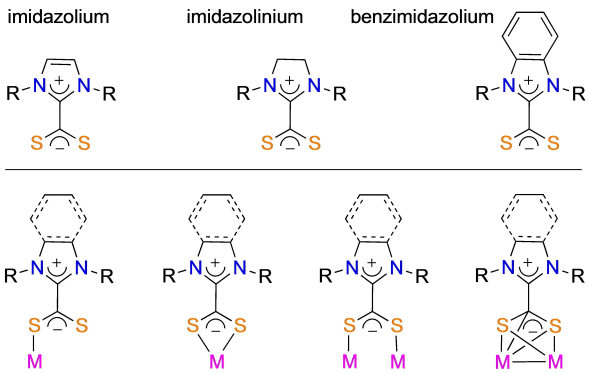
This paper is dedicated to Professor Pierre Dixneuf for his outstanding contributions to organometallic chemistry and homogeneous catalysis, especially with ruthenium–arene complexes.

Twelve imidazolium-, imidazolinium-, or benzimidazolium-2-dithiocarboxylate zwitterions with aliphatic or aromatic substituents on their nitrogen atoms, including four new unsymmetrical 1-alkyl-3-arylimidazolium derivatives, were obtained in high yields (62–96%) upon reaction of azolium salts with CS_2 and Cs_2CO_3 in acetonitrile at room temperature. Compared to the previous strategies devised for the synthesis of NHC·CS_2 betaines, this novel procedure relied on an innocuous, weak base and could be applied under mild aerobic conditions. All the new compounds were fully characterized by various analytical techniques and the molecular structures of two of them were determined by XRD analysis. An associative mechanism involving the concerted reaction of the azolium salts with both CS_2 and CO_3^{2-} was tentatively proposed to account for the formation of the zwitterionic adducts without the intervention of free carbenes. This would explain the good results obtained with a weak inorganic base that lacks the strength needed to deprotonate the azolium salt substrates.

Introduction

N-Heterocyclic carbenes (NHCs) are powerful nucleophiles that readily add to the central carbon atom of allenes and heteroallenes X=C=Y (X, Y=O, S, NR, CR_2) to afford zwitterionic adducts.[1] In particular, the reaction of (benz)imidazol(in)-2-ylidene derivatives with carbon disulfide affords stable azolium-2-dithiocarboxylate betaines (Scheme 1).[2] These 1,1-dithiolate inner salts display a great potential for coordination chemistry because they swiftly form strong M–S bonds with a broad range of metal centers through various binding modes. Indeed, we and others have already reported the synthesis of a wide variety of transition metal complexes featuring monodentate,[3] chelating bidentate,[4] or bridging bidentate NHC·CS_2 ligands,[3b,4f,g] as well as small bimetallic clusters of manganese[4g] and rhenium.[4f] Copper-based coordination polymers[5] and clusters,[6] or gold nanoparticles[3b] and self-assembled monolayers[7] based on these zwitterions were also described in the literature, while a few reports disclosed the formation of polynuclear iron[8] or ruthenium[9] clusters, in which the dithiocarboxylate unit underwent further chemical transformations.

Several synthetic paths were investigated to prepare azolium-2-dithiocarboxylate zwitterions from diverse NHC precursors. From a historical perspective, the cleavage of enetetramines with carbon disulfide first led to the isolation of 1,3-diethylimidazolinium-2-dithiocarboxylate (SIEt·CS_2) in 1965 (Scheme 2, route A).[2a] The procedure was subsequently extended to various other imidazolinium[2b–d] or benzimidazolium[2e–h] inner salts. It is, however, restricted to NHCs that easily dimerize, thereby excluding the common aromatic imidazol-2-ylidene derivatives or more saturated heterocycles with bulky substituents on their nitrogen atoms.[10] The reduction of cyclic thioureas with potassium was applied to generate a few NHCs that were next converted into NHC·CS_2 betaines (Scheme 2, route B).[2i,j] This procedure is applicable to



Scheme 1. Various types of azolium-2-dithiocarboxylate zwitterions and their binding modes to metal centers.

[a] F. Mazars, Prof. Dr. L. Delaude
Laboratory of Catalysis, MolSys Research Unit
Université de Liège, Institut de Chimie Organique (B6a),
Allée du six Août 13, 4000 Liège, Belgium
E-mail: l.delaude@uliege.be
http://www.cata.ulg.ac.be
[b] Dr. M. Hrubaru
Center for Organic Chemistry "Costin D. Nenitescu",
Romanian Academy,
Spl Independentei București, 202B, 060023 Bucharest, Romania
[c] Dr. N. Tumanov, Prof. Dr. J. Wouters
Department of Chemistry, Université de Namur,
Rue de Bruxelles 61, 5000 Namur, Belgium

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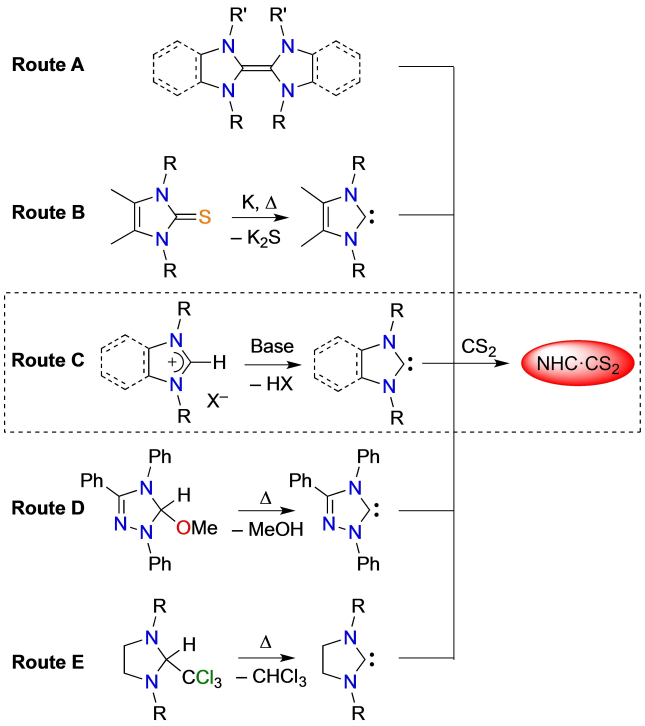


Scheme 2. Synthesis of NHC·CS_2 zwitterions from various precursors.

imidazol-2-ylidene derivatives with small alkyl chains on their nitrogen atoms, but its substrate scope is very narrow.

Currently, the deprotonation of azolium salts with a strong base, followed by the addition of CS_2 either in one pot or after the isolation of the free NHCs is the most convenient and general strategy to obtain NHC·CS_2 betaines (Scheme 2, route C).[2k–m] Indeed, countless reports describe the synthesis of imidazolium, benzimidazolium, or imidazolinium salts with an incredible choice of aliphatic or aromatic substituents on their heterocycle.[11] It is therefore not surprising that these compounds are privileged starting materials to convert into zwitterionic adducts. Yet, other methods have been sporadically employed. For instance, a vacuum pyrolysis of the methanol adduct of Enders' triazolylidene[2n] or a thermolysis of two chloroform adducts in the presence of CS_2 led to the corresponding NHC·CS_2 inner salts[2d,o] (Scheme 2, routes D and E). Because these neutral adducts are usually obtained from the corresponding enetetramine or azolium salt precursors, their intermediacy requires a supplementary reaction step that adds to the duration and the complexity of the synthesis, although the recourse to a "masked carbene" may be convenient for practical reasons.

With pK_a values typically comprised between 16 and 26,[12] azolium salts are weakly acidic precursors and strong bases such as sodium hydride, potassium *tert*-butoxide, or potassium bis(trimethylsilyl)amide are needed to deprotonate them quantitatively.[13] Handling these powerful reagents requires the use of strictly anhydrous conditions, so does the isolation of air- and moisture-sensitive carbenes. Hence, the reactions are commonly performed in a glove box or using Schlenk techniques in dried and degassed solvents. These stringent experimental conditions and the cost associated with the use of strong organic bases and dry solvents severely diminish the synthetic appeal of NHC·CS_2 zwitterions and tend to restrict their preparation to skilled chemists working on a small laboratory scale. It is therefore highly desirable to devise simple and straightforward experimental procedures that would give access to these compounds with a minimum of precautions and complications. Herein, we describe our endeavors toward this goal and we show that azolium-2-dithiocarboxylate zwitterions are readily obtained from the corresponding azolium salts and carbon disulfide using cesium carbonate as an innocuous, weak inorganic base under mild aerobic conditions.

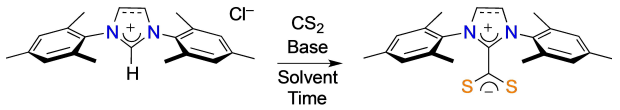
Results and Discussion

Several reports have highlighted the preparation of transition metal complexes bearing NHC ligands from azolium salts and a weak base.[14] Also in the fields of homogeneous catalysis with metal-NHC complexes[15] and organocatalysis with NHCs,[16] active species are commonly generated in situ using a mixture of azolium salts and a base such as K_2CO_3 or Cs_2CO_3. Heating azolium hydrogencarbonate salts in the presence of CS_2 afforded the corresponding dithiolate betaines in high yields without the need for any external base.[17] Besides, the continuous-flow generation of NHC·CS_2 zwitterions was accomplished using a packed-bed reactor filled with Cs_2CO_3 or K_3PO_4, although an homogeneous microfluidic setup involving KN($SiMe_3$)$_2$ proved much more efficient.[18] All these results were deemed a good omen to investigate in more details the formation of NHC·CS_2 inner salts from NHC·HX salts and CS_2 in the presence of a weak inorganic base.

Exploratory screening and optimization

To begin our study, we chose the archetypal 1,3-dimesitylimidazol-2-ylidene carbene known as IMes and its analogue with a more saturated backbone nicknamed SIMes as model substrates. Thus, initial experiments aimed at defining suitable experimental conditions for converting the azolium chloride precursors IMes·HCl and SIMes·HCl into dithiocarboxylate betaines using a simple and efficient one-pot procedure. In these exploratory runs carried out at room temperature, we probed the influence of the base, the solvent, and the reaction time. Only a few representative results of a vast screening campaign are summarized in Table 1. The formation of the expected products was easily visualized by the appearance of a dark red-brown coloration for IMes·CS_2 or a lighter and brighter orange shade for SIMes·CS_2. Conversions were determined by integrating the various ^{1}H NMR resonances exhibited by the zwitterions and their precursors. Choosing a solvent that ensured an efficient mixing of the three reaction partners (an inorganic base, an organic salt, and the apolar carbon disulfide) was critical to reach high conversions within short periods of time. In this respect, acetonitrile emerged as the most

Table 1. Synthesis of IMes·CS_2 and SIMes·CS_2 under various experimental conditions.[a]



Entry	Salt	Base	Solvent	Time [h]	Conversion [%][b]
1	SIMes·HCl	K_2CO_3	CH_2Cl_2	2	12
2	SIMes·HCl	K_2CO_3	CH_3CN	2	27
3	SIMes·HCl	Cs_2CO_3	CH_3COCH_3	72	83
4	SIMes·HCl	Cs_2CO_3	CH_2Cl_2	2	79
5	SIMes·HCl	Cs_2CO_3	CH_3CN	2	100
6	IMes·HCl	Cs_2CO_3	CH_3CN	2	100
7	SIMes·HCl	Cs_2CO_3[c]	CH_3CN	2	85
8	SIMes·HCl	Cs_2CO_3[d]	CH_3CN	4	100

[a] Typical conditions: azolium salt (100 mg), base (2.5 equiv.), carbon disulfide (0.5 mL), solvent (2 mL) stirred at room temperature. [b] Determined by ^{1}H NMR spectroscopy. [c] 1.1 equiv. [d] 1.5 equiv.

promising candidate among other common organic solvents including THF, chloroform, methanol, and neat carbon disulfide. Dichloromethane came second, acetone led to much slower reactions (Table 1, entries 3–5). No conversion was observed with either potassium hydrogencarbonate or potassium phosphate. With the inexpensive potassium carbonate, reactions were sluggish (Table 1, entries 1 and 2). Conversely, cesium carbonate, which is more soluble in organic media,[19] allowed to reach quantitative conversions within 2 h at room temperature provided that it was introduced in moderate excess (2.5 equiv.) (Table 1, entries 5 and 6). Reducing this excess to 1.1 equiv. slowed down the reaction, but a full conversion could be restored when using 1.5 equiv. of Cs_2CO_3 for 4 h (Table 1, entries 7 and 8). These conditions were deemed favorable enough to proceed to the next step of our study.

Scope of the procedure

In order to assess the scope of the procedure outlined above, we have applied it to a wide range of azolium salts bearing aliphatic or aromatic substituents on their nitrogen atoms (Table 2). Reactions were typically carried out on 2 mmol of substrate using a small excess of Cs_2CO_3 (3 mmol) and a large excess of CS_2 (16.6 mmol) in acetonitrile at room temperature. The resulting suspension was stirred for 4 h before the volatiles were removed on a rotary evaporator. The residue was suspended in a saturated aqueous NH_4Cl solution to neutralize the basic inorganic salts. The final zwitterionic product was then filtered off, rinsed with water, and dried under high vacuum. It was characterized by various analytical techniques.

As expected, the reactions of SIMes·HCl and IMes·HCl led to the corresponding NHC·CS_2 zwitterions in high yields (Table 2, entries 1 and 3). Weight losses occurred mainly during the aqueous work-up and the final filtration step. Bulkier imidazolinium and imidazolium chlorides bearing 2,6-diisopropylphenyl substituents on their nitrogen atoms instead of mesityl groups behaved similarly and led to the SIDip·CS_2 and IDip·CS_2 inner salts in 86% yield after purification (Table 2, entries 2 and 4). The same yield was also achieved starting from the 1,3-dibenzylimidazolium tetrafluoroborate IBn·HBF_4 (Table 2, entry 5). Contrastingly, all our attempts to isolate the imidazolium-2-dithiocarboxylate adducts of 1,3-dicyclohexyl and 1,3-dicyclododecylimidazol-2-ylidene (ICy and ICC_{12}) remained unsuccessful (Table 2, entries 6 and 7). Although the rapid appearance of an orange-red color upon the addition of Cs_2CO_3 and CS_2 to the imidazolium salt precursors ICy·HBF_4 and ICC_{12}·HCl unambiguously revealed that the desired adducts had formed, they did not withstand the aqueous work-up and reverted to the starting materials. Previous work from our group had shown that ICy·CS_2 could be isolated in 61% yield upon deprotonation of ICy·HCl with NaH in dry THF followed by the addition of CS_2 under an inert atmosphere. Furthermore, thermogravimetric analysis (TGA) revealed that this zwitterion was more resistant to thermal degradation than IMes·CS_2 and SIDip·CS_2.[2k] We suspect that the instability of ICy·CS_2 and ICC_{12}·CS_2 in the presence of aqueous NH_4Cl is linked to the high affinity of ICy·HCl, and probably also ICC_{12}·HCl, toward water. Indeed, we and others have already reported that 1,3-dicyclohexylimidazolium chloride was very hygroscopic and quickly formed a sticky paste when exposed to moisture.[20]

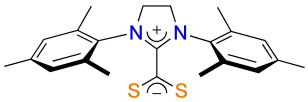
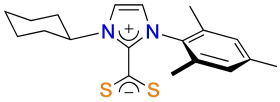
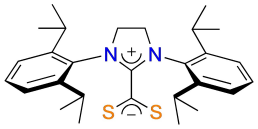
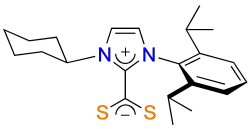
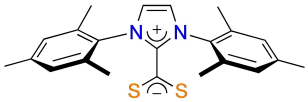
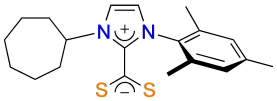
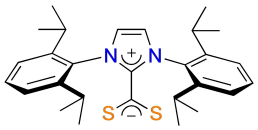
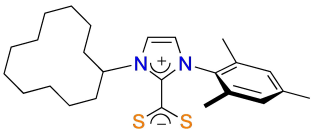
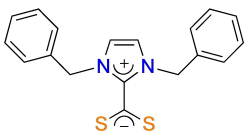
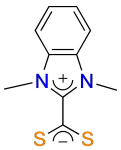
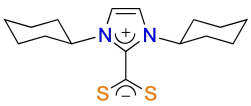
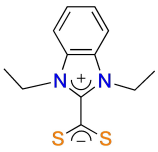
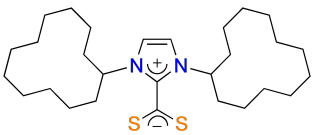
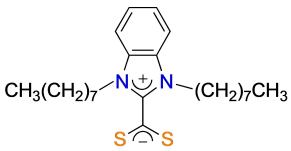
The negative results obtained when 1,3-dialkyl instead of 1,3-diarylimidazolium salts were subjected to our novel procedure prompted us to investigate the reactivity of mixed 1-alkyl-3-arylimidazolium derivatives. Recently, Baslé, Mauduit et al. disclosed a straightforward, multicomponent synthesis of unsymmetrical imidazolium salts bearing an alkyl or cycloalkyl group on one of their nitrogen atoms and a mesityl or 2,6-diisopropylphenyl ring on the second one.[21] This protocol allowed us to readily prepare a small set of four representative imidazolium salts featuring both a 6-, 7-, or 12-membered cycloalkyl group (Cy, CC_7, or CC_{12}) and an aryl substituent (Mes or Dip) on their nitrogen atoms. These starting materials were then reacted with Cs_2CO_3 and CS_2 in acetonitrile at room temperature. Gratifyingly, the new 1-alkyl-3-arylimidazolium-2-dithiocarboxylates ICyMes·CS_2, ICyDip·CS_2, ICC_7Mes·CS_2, and ICC_{12}Mes·CS_2 were isolated in 83–85% yields (Table 2, entries 8–11).

Last but not least, we also probed the reactivity of three symmetrical benzimidazolium iodides with methyl, ethyl, or *n*-octyl groups on their nitrogen atoms (Table 2, entries 12–14). These substrates reacted seamlessly with Cs_2CO_3 and CS_2 to afford zwitterionic adducts that resisted hydrolysis during the work-up. It is noteworthy that the yields of isolated products steadily increased with the length of the alkyl chains, probably because of a concomitant reduction of their hydrophilicity, which should minimize the loss of organic materials dissolved in the aqueous phase.

Structural analysis

Except for BOct·CS_2, all the symmetrically-substituted azolium-2-dithiocarboxylate zwitterions investigated in this study had previously been synthesized from the corresponding azolium

Table 2. Synthesis of NHC·CS_2 zwitterions under mild aerobic conditions.[a]

Entry	Substrate	Product	Yield [%][b]	Entry	Substrate	Product	Yield [%][b]
1	SIMes·HCl		83	8	ICyMes·HCl		83
2	SIDip·HCl		86	9	ICyDip·HCl		83
3	IMes·HCl		85	10	ICC$_7$Mes·HCl		85
4	IDip·HCl		86	11	ICC$_{12}$Mes·HCl		85
5	IBn·HBF_4		86	12	BMe·HI		62
6	ICy·HBF_4		0	13	BEt·HI		80
7	ICC$_{12}$·HCl		0	14	BOct·HI		96

[a] Experimental conditions: azolium salt (2 mmol), Cs_2CO_3 (3 mmol), carbon disulfide (16.6 mmol), acetonitrile (10 mL) stirred at room temperature for 4 h. [b] Yield of isolated product after work-up.

salts and CS_2 using strong bases such as NaH or $KN(SiMe_3)_2$ in dry and degassed THF.[2e,k,7,22] Thus, they were already fully characterized and their molecular structures had been solved by single-crystal XRD analysis in most cases. Multinuclear NMR and HR-MS analyses of ICyMes·CS_2, ICyDip·CS_2, ICC$_7$Mes·CS_2, and ICC$_{12}$Mes·CS_2 confirmed the correct formulation of the four new unsymmetrically-substituted imidazolium-2-dithiocarboxylates. ^{1}H NMR spectroscopy was most useful to monitor the disappearance of the strongly deshielded singlet arising from the H2 azolium ring proton of the substrates, while ^{13}C NMR spectra showed the emergence of a new resonance at about 224 ppm, unambiguously revealing the incorporation of a CS_2^- moiety (Table 3). There was no obvious correlation between the exact location of this exocyclic signal and the nature of the adjacent heterocycle, in line with the absence of electronic communication between the anionic and cationic parts of NHC·CS_2 zwitterions (vide infra). Conversely, the chemical shift of the endocyclic C2 carbon atom was clearly affected by the type of heterocycle it belonged to (Table 3). Indeed, it was observed at ca. 147–150 ppm in the aromatic imidazolium compounds and was significantly shifted downfield in their non-aromatic imidazolinium counterparts, up to 164–165 ppm. As expected, the benzimidazolium derivatives led to intermediate values comprised between 152 and 153 ppm.

Crystals of ICyDip·CS_2 and ICC$_7$Mes·CS_2 suitable for X-ray diffraction analysis were obtained by slow diffusion of *n*-hexane in $CDCl_3$ solutions at −18 °C (Figure 1 and Figure 2). The former betaine co-crystallized with one equivalent of the halogenated solvent in the monoclinic $P2_1/c$ space group, while the latter compound crystallized with two molecules in the asymmetric unit in the monoclinic $P2_1/n$ space group. A comparison of the metrics recorded for these two 1-alkyl-3-arylimidazolium-2-

Table 3. ^{13}C NMR chemical shifts of C1 and C2 in various azolium-2-dithiocarboxylate zwitterions (data recorded in $CDCl_3$ at 298 K).[a]

NHC·CS_2	δ_{C1} [ppm]	δ_{C2} [ppm]	NHC·CS_2	δ_{C1} [ppm]	δ_{C2} [ppm]
SIMes·CS_2[b]	222.7	165.0	ICyDip·CS_2	223.1	149.2
SIDip·CS_2[b]	219.8	164.2	$ICC_7Mes·CS_2$	224.0	148.3
IMes·CS_2[b]	221.6[e]	146.7[e]	$ICC_{12}Mes·CS_2$	223.3	149.5
IDip·CS_2[b]	219.7	149.1	BMe·CS_2[d]	223.8[e]	151.5[e]
IBn·CS_2[c]	223.9	150.3	BEt·CS_2[c]	224.0	152.6
ICyMes·CS_2	223.9	149.0	BOct·CS_2	224.1	152.8

[a] See Figure 1 and Figure 2 for atom numbering. [b] Data from ref.[2k]. [c] Data from ref. [7]. [d] Data from ref. [22]. [e] Solvent: [D_6]DMSO.

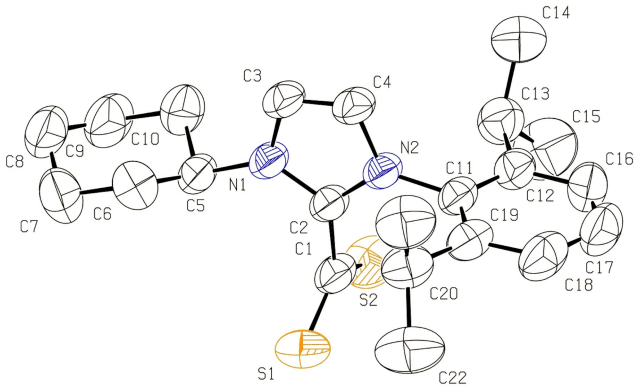


Figure 1. ORTEP representation of ICyDip·CS_2 with thermal ellipsoids drawn at the 50% probability level. Hydrogen atoms and a co-crystallized $CHCl_3$ molecule are omitted for clarity. Selected bond lengths [Å] and angles [°]: C1–S1 1.661(2), C1–S2 1.658(2), C1–C2 1.491(3), C2–N1 1.336(2), C2–N2 1.343(2), N1–C5 1.482(3), N2–C11 1.448(2), C3–C4 1.325(3), S1–C1–S2 131.0(1), N1–C2–N2 107.3(2), S1–C1–C2–N1 −83.4(2), C6–C5–N1–C2 118.1(2), C12–C11–N2–C2 94.3(2).

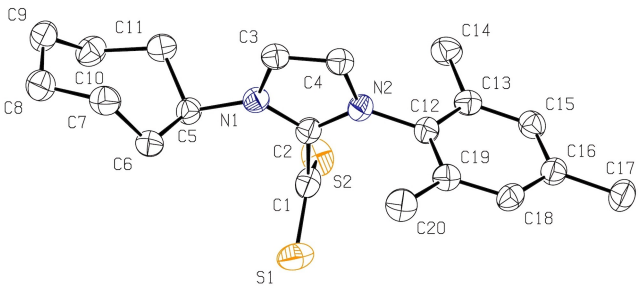


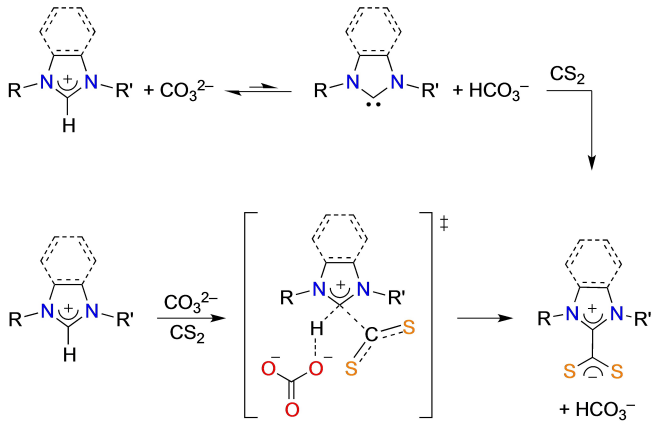
Figure 2. ORTEP representation of ICC7Mes·CS_2 with thermal ellipsoids drawn at the 50% probability level. Only one of the two molecules in the asymmetric unit is depicted. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: C1–S1 1.665(4), C1–S2 1.674(4), C1–C2 1.486(5), C2–N1 1.348(4), C2–N2 1.345(3), N1–C5 1.479(3), N2–C12 1.454(4), C3–C4 1.350(4), S1–C1–S2 130.7(2), N1–C2–N2 107.9(2), S1–C1–C2–N1 −84.8(3), C6–C5–N1–C2 111.3(3), C13–C12–N2–C2 91.0(4).

dithiocarboxylate inner salts with those determined previously for 1,3-dialkyl or 1,3-diaryl derivatives[2k,23] did not reveal any major discordance. As expected, similar C1–S1 and C1–S2 distances indicated that the negative charge was equally balanced between the two sulfur atoms. Likewise, the positive charge was delocalized over the two nitrogen atoms of the imidazolium ring irrespective of their alkyl or aryl substituents. Yet, the exocyclic N1–C5 bond was significantly longer than the N2–C11 (or C12) distance (a ca. 0.3 Å increase), in line with the general trend observed when comparing Csp^3–N and Csp^2–N bonds.[24] Moreover, the perpendicular arrangement of the 2,6-diisopropylphenyl or mesityl group with respect to the central heterocycle precluded any further conjugation and led to exocyclic C–N distances that matched those commonly observed for single rather than double bonds.[24] Last but not least, the fact that the ^{13}C NMR chemical shift of the CS_2^- unit was not significantly affected by the neighboring azolium ring suggests that the nearly orthogonal disposition of these two moieties observed in the solid state (S1–C1–C2–N1 torsion angle of ca. −84°) should most likely be preserved in solution.

Mechanistic considerations

With a value of 10.3 in water,[25] the pK_a of the HCO_3^-/CO_3^{2-} couple is more than ten orders of magnitude lower than those determined for all the imidazolium (e.g., Mes·HCl: 20.8),[12f] imidazolinium (e.g., SIMes·HCl: 21.3),[12f] or benzimidazolium salts (e.g., BMe·HI: 21.6)[12d] employed as substrates in this work. Although there might be some variations in other solvents, such a large difference clearly indicates that the carbonate ion is not basic enough to fully deprotonate azolium salts into NHCs. Therefore, a two-step dissociative reaction path involving the stoichiometric release of free carbenes and their nucleophilic addition onto carbon disulfide is very unlikely to account for the formation of NHC·CS_2 betaines from NHC·HX salts, Cs_2CO_3, and CS_2 (Scheme 3, top). Although the continuous removal of (benz)imidazol(in)-2-ylidene species through a highly exergonic reaction with CS_2 might shift the acid/base equilibrium toward the putative NHC intermediates, the oxygen and moisture present under the experimental conditions adopted for this study should contribute to quench any highly reactive carbene generated in situ. Therefore, even a partial deprotonation of the substrate to afford trace amounts of NHCs does not seem compatible with the high yields of zwitterionic products obtained under mild, aerobic conditions.

In 2012, Besnard and coworkers reported the spontaneous carboxylation of neat 1-butyl-3-methylimidazolium acetate (IBuMe·AcOH), a room-temperature ionic liquid also known as [BMIM]OAc, under mild conditions (0.1 MPa CO_2, 298 K).[26] Various computational methods were applied to probe the underlying mechanism guiding the interaction of CO_2 with 1,3-dialkylimidazolium acetate ionic liquids in the absence of any external base. Although the intimate details of the reaction



Scheme 3. Dissociative (top) vs. associate (bottom) reaction paths for the synthesis of NHC·CS_2 zwitterions from azolium salt precursors, Cs_2CO_3, and CS_2.

remain speculative, the intervention of a free carbene was ruled out in favor of a concerted path involving the simultaneous activation of the imidazolium cation by the acetate anion and the fixation of carbon dioxide.[27] Unexpectedly, when CO_2 was replaced with CS_2, the IBuMe·CS_2 zwitterion was not detected in the reaction mixture. Instead, NMR and Raman spectroscopies evidenced the formation of 1-butyl-3-methylimidazolium-2-thiocarboxylate (IBuMe·COS) and 2-carboxylate (IBuMe·CO_2), together with thioacetate anions (CH_3COS^-) and acetic acid in the liquid phase, while COS and CO_2 were observed in the gas phase.[28] Further experimental and computational studies showed that an S/O exchange had taken place, thereby leading to an acetate/thioacetate swap and the concomitant conversion of CS_2 into COS, which can be further transformed into CO_2.[29] Because the trapping of CS_2 by an NHC necessitates a much lower activation energy than the conversion of CS_2 into COS, the absence of NHC·CS_2 products strongly suggested that free carbenes were not formed in the reaction of imidazolium acetate ionic liquids with CS_2 and that the formation of zwitterionic products could only occur via a concerted path.[30]

Recently, Hollóczki et al. challenged the involvement of carbene active species in organocatalytic systems based on azolium salts and a weak base.[31] Based on DFT calculations, they proposed the intervention of an associative path rather than the classical dissociative route to explain the seemingly contradictory results obtained when azolium salts and a base are employed to catalyze the umpolung of aldehydes. More precisely, they showed that depending on the experimental parameters, the process could follow a concerted asynchronous path, in which the azolium cation, the base, and the carbonyl substrate interact directly together, thereby avoiding the intermediacy of a free carbene. We hypothesize that a similar mechanism might be at play in the synthesis of NHC·CS_2 zwitterions from azolium salts, Cs_2CO_3, and CS_2. Indeed, NMR control experiments showed that an heterogeneous mixture of SIMes·HCl and Cs_2CO_3 (1.5 equiv.) in CD_3CN at room temperature did not afford any detectable amount of free carbene in solution. Yet, the imidazolinium ring slowly underwent an hydrolysis into the corresponding *N*-(2-aminoethyl)formamide derivative. This side-reaction is most likely due to the presence of water traces in the solvent.[32] When an heterogeneous mixture of Cs_2CO_3 and CS_2 (22 equiv.) in CD_3CN was kept for 24 h at room temperature, the initially white solid became pink. This color change is probably caused by an O/S exchange reaction at the surface of the basic salt, leading to the formation of dark red trithiocarbonate ions (CS_3^{2-}) in minute amount.[33] Contrastingly, a two-component mixture of SIMes·HCl and CS_2 (22 equiv.) in CD_3CN did not show any sign of reaction whatsoever. Altogether, these results are in line with the necessity for a synergetic three-component process to take place for achieving the quantitative formation of NHC·CS_2 zwitterions.

A final control experiment showed that the addition of a catalytic or stoichiometric amount of CsCl to the test-reaction of SIMes·HCl carried out with K_2CO_3 and CS_2 did not have a beneficial influence on the formation of SIMes·CS_2. We therefore assume that there is no "cesium effect" other than ensuring a better solubility of the carbonate anion in the reaction medium.[34] Accordingly, the metal cation may be treated only as a delivery agent for CO_3^{2-} and the three reaction partners would have to aggregate in a ternary transition state, in which the C–H bond breaking and C–C bond formation take place concomitantly to afford the final products in one step (Scheme 3, bottom). Although we have not yet validated this hypothesis, it should be pointed out that related experimental and theoretical studies favor the intervention of an associative "carbene-free" route rather than a dissociative "free carbene" path to explain the reactivity of azolium salts and weak bases in deuteration[35] and complexation reactions.[36]

Conclusion and perspectives

The reaction of azolium salts with carbon disulfide and cesium carbonate in acetonitrile at room temperature afforded azolium-2-dithiocarboxylate zwitterions in high yields (62–96%). Selecting a proper combination of organic solvent and inorganic base that ensured an efficient mixing of the three reaction partners was critical to reach high conversions within short periods of time. Compared to the previous strategies devised to obtain NHC·CS_2 betaines, our new protocol relied on an innocuous, weak base and could be applied under mild aerobic conditions. Unlike the acetate anion that underwent oxygen/sulfur exchange reactions when 1,3-dialkylimidazolium acetate ionic liquids were exposed to carbon disulfide, the basic carbonate anion did not cause any unwanted side-reactions and selectively afforded the desired zwitterionic products in high yields. Because the experimental procedure did not require the equipment nor the expertise usually necessary to perform syntheses involving highly active carbene species, it greatly eased the access to valuable 1,1-dithiolate ligands that have already found numerous applications in coordination chemistry.

Fourteen substrates were subjected to our new protocol to demonstrate its generality. No zwitterions were isolated from the reactions of 1,3-dicyclohexyl and 1,3-dicyclododecylimida-

zolium precursors, most likely because the desired adducts decomposed during the aqueous work-up to form highly hygroscopic imidazolium chlorides. Yet, a diverse set of twelve imidazolium-, imidazolinium-, or benzimidazolium-2-dithiocarboxylate inner salts with aliphatic or aromatic substituents on their nitrogen atoms was obtained, including BOct·CS_2 and four unsymmetrical 1-alkyl-3-arylimidazolium derivatives that had not been reported previously. All the new compounds were fully characterized by various analytical techniques and the molecular structures of two of them were determined by XRD analysis. As previously emphasized for various 1,3-dialkyl or 1,3-diaryl derivatives, the orthogonal conformation of the dithiocarboxylate group and the azolium ring prevented any electronic communication between the anionic and cationic parts of the molecules.

By analogy with recent findings suggesting that organocatalytic processes thought to operate with NHCs might actually proceed with lower energy barriers when azolium cations react directly with the substrates and a base, we tentatively proposed an associative mechanism involving the concerted reaction of the azolium salts with both CS_2 and CO_3^{2-} to afford the final products without the intervention of free carbenes. This would explain the good results obtained for the synthesis of NHC·CS_2 zwitterions with a weak inorganic base that lacks the strength needed to deprotonate the azolium salt substrates. Further investigations are in progress to validate this hypothesis. They will be reported in due course.

Experimental Section

General information

All the syntheses were carried out under a normal atmosphere with analytical grade reagents and solvents used without any further purification. The azolium salts SIMes·HCl,[20d] SIDip·HCl,[20d] IMes·HCl,[20d] IDip·HCl,[20d] IBn·HBF_4,[20d] ICy·HBF_4,[20d] ICC_{12}·HCl,[21a] ICyMes·HCl,[21a] ICC_7Mes·HCl,[21a] ICC_{12}Mes·HCl,[21a] BMe·HI,[37] and BEt·HI,[37] were prepared according to published procedures. ^{1}H and ^{13}C NMR spectra were recorded at 298 K on a Bruker DRX 400 spectrometer operating at 400.13 and 100.62 MHz, respectively. Chemical shifts are listed in parts per million downfield from TMS and are referenced from the solvent peaks or TMS. Electrospray mass spectra were obtained using a Micromass LCT Premier instrument. Elemental analyses were carried out in the Laboratory of Pharmaceutical Chemistry at the University of Liège.

Typical procedure for the synthesis of NHC·CS_2 zwitterions

A 25 mL round-bottomed flask equipped with a magnetic stirring bar and a glass stopper was loaded with an azolium salt (2 mmol) and Cs_2CO_3 (1 g, 3 mmol). A solution of CS_2 (1 mL, 16.6 mmol) in acetonitrile (10 mL) was added and the reaction mixture was stirred for 4 h at room temperature. The volatiles were removed on a rotary evaporator. The solid residue was finely powdered with a spatula and taken up with a saturated aqueous NH_4Cl solution (10 mL). The suspension was stirred for 15 min at room temperature. It was filtered with suction on a Buchner funnel and the precipitate was rinsed with deionized water (2×5 mL). It was dried overnight under high vacuum.

1-Cyclohexyl-3-mesitylimidazolium-2-dithiocarboxylate (ICy-Mes·CS_2): orange microcrystalline powder (0.58 g, 83% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (m, 1H, Cy), 1.43 (m, 2H, Cy), 1.59 (m, 2H, Cy), 1.75 (m, 1H, Cy), 1.89 (m, 2H, Cy), 2.20 (s, 6H, *o*-CH_3), 2.29 (s, 3H, *p*-CH_3), 2.34 (m, 2H, Cy), 4.69 (m, 1H, NCH Cy), 6.82 (d, $^3J_{H,H}$ = 4.0 Hz, 1H, =CHNCy), 6.89 (s, 2H, *m*-CH_{ar}), 7.18 ppm (s, 1H, =CHNMes); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.9 (*o*-CH_3), 21.1 (*p*-CH_3), 25.1 (CH_2 Cy), 25.3 (CH_2 Cy), 33.3 (CH_2 Cy), 58.2 (NCH Cy), 115.3 (=CHNCy), 119.7 (=CHNMes), 129.5 (*m*-CH_{ar}), 131.0 (*i*-C_{ar}), 135.9 (*o*-C_{ar}), 140.6 (*p*-C_{ar}), 149.0 (Im C^2), 223.9 ppm (CS_2); HRMS (ESI): *m/z* calcd for $C_{19}H_{24}N_2S_2 + Na^+$: 367.12731 $[M + Na]^+$; found: 367.12790; elemental analysis calcd for $C_{19}H_{24}N_2S_2$: C 66.23, H 7.02, N 8.13, S 18.61; found: C 66.55, H 7.43, N 8.34, S 18.13.

1-Cyclohexyl-3-(2,6-diisopropylphenyl)imidazolium-2-dithiocarboxylate (ICyDip·CS_2): orange microcrystalline powder (0.64 g, 83% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (d, $^3J_{H,H}$ = 8.0 Hz, 6H, $CH(CH_3)_2$), 1.32 (d + m, $^3J_{H,H}$ = 8.0 Hz, 6H + 1H, $CH(CH_3)_2$ and CH Cy), 1.47 (m, 2H, Cy), 1.56 (m, 2H, Cy), 1.60 (m, 1H, Cy), 1.90 (m, 2H, Cy), 3.39 (m, 2H, Cy), 2.79 (sept, $^3J_{H,H}$ = 8.0 Hz, 4H, $CH(CH_3)_2$), 4.67 (m, 1H, NCH Cy), 6.84 (d, $^3J_{H,H}$ = 4.0 Hz, 1H, =CHNCy), 7.15 (d, $^3J_{H,H}$ = 4.0 Hz, 1H, =CHNDip), 7.20 (d, $^3J_{H,H}$ = 8.0 Hz, 2H, *m*-CH_{ar}), 7.40 ppm (t, $^3J_{H,H}$ = 8.0 Hz, 1H, *p*-CH_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6 (CH_3), 25.1 (CH_2 Cy), 25.3 (CH_2 Cy), 26.1 (CH_3), 29.1 ($CH(CH_3)_2$), 33.0 (CH_2 Cy), 58.3 (NCH Cy), 114.6 (=CHNCy), 121.0 (=CHNDip), 124.5 (*m*-CH_{ar}), 130.5 (*i*-C_{ar}), 131.3 (*p*-CH_{ar}), 146.7 (*o*-C_{ar}), 149.2 (Im C^2), 223.1 ppm (CS_2); HRMS (ESI): *m/z* calcd for $C_{22}H_{30}N_2S_2 + Na^+$: 409.17426 $[M + Na]^+$; found: 409.17624; elemental analysis calcd for $C_{22}H_{30}N_2S_2$: C 68.35, H 7.82, N 7.25, S 16.59; found: C 68.50, H 8.20, N 7.38, S 15.84.

1-Cycloheptyl-3-mesitylimidazolium-2-dithiocarboxylate (ICC_7Mes·CS_2): orange microcrystalline powder (0.61 g, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.5–1.7 (m, 6H, CC_7), 1.7–1.9 (m, 4H, CC_7), 2.19 (s, 6H, *o*-CH_3), 2.26 (s, 3H, *p*-CH_3), 2.3–2.4 (m, 2H, CC_7), 4.81 (m, 1H, NCH CC_7), 6.80 (d, $^3J_{H,H}$ = 2.0 Hz, 1H, =CHNCC$_7$), 6.86 (s, 2H, *m*-CH_{ar}), 7.17 ppm (d, $^3J_{H,H}$ = 2.0 Hz, 1H, =CHNMes); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.8 (*o*-CH_3), 21.1 (*p*-CH_3), 24.5 (CH_2 CC_7), 27.3 (CH_2 CC_7), 35.5 (CH_2 CC_7), 60.1 (NCH CC_7), 115.5 (=CHNCC$_7$), 119.8 (=CHNMes), 129.4 (*m*-CH_{ar}), 130.9 (*i*-C_{ar}), 135.9 (*o*-C_{ar}), 140.3 (*p*-C_{ar}), 148.3 (Im C^2), 224.0 ppm (CS_2); HRMS (ESI): *m/z* calcd for $C_{20}H_{26}N_2S_2 + Na^+$: 381.14296 $[M + Na]^+$; found: 381.14384; elemental analysis calcd for $C_{20}H_{26}N_2S_2$: C 66.99, H 7.31, N 7.81, S 17.89; found: C 67.01, H 7.67, N 8.04, S 17.64.

1-Cyclododecyl-3-mesitylimidazolium-2-dithiocarboxylate (ICC_{12}Mes·CS_2): pink microcrystalline powder (0.73 g, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.2–1.5 (m, 18H, CC_{12}), 1.83 (m, 2H, CC_{12}), 2.02 (m, 2H, CC_{12}), 2.20 (s, 6H, *o*-CH_3), 2.25 (s, 3H, *p*-CH_3), 5.01 (m, 1H, NCH CC_{12}), 6.80 (d, $^3J_{H,H}$ = 4.0 Hz, 1H, =CHNCC$_{12}$), 6.87 (s, 2H, *m*-CH_{ar}), 7.16 ppm (d, $^3J_{H,H}$ = 2.0 Hz, 1H, =CHNMes); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.8 (*o*-CH_3), 21.1 (*p*-CH_3), 22.4 (CH_2 CC_{12}), 22.7 (CH_2 CC_{12}), 22.9 (CH_2, CC_{12}), 23.7 (CH_2 CC_{12}), 23.8 (CH_2 CC_{12}), 30.9 (CH_2 CC_{12}), 55.7 (NCH CC_{12}), 115.7 (=CHNCC$_{12}$), 119.8 (=CHNMes), 129.4 (*m*-CH_{ar}), 131.1 (*i*-C_{ar}), 135.9 (*o*-C_{ar}), 140.4 (*p*-C_{ar}), 149.5 (Im C^2), 223.3 ppm (CS_2); HRMS (ESI): *m/z* calcd for $C_{25}H_{36}N_2S_2 + Na^+$: 451.22121 $[M + Na]^+$; found: 451.22246; elemental analysis calcd for $C_{25}H_{36}N_2S_2$: C 70.04, H 8.46, N 6.53, S 14.96; found: C 70.21, H 8.96, N 6.75, S 14.64.

1,3-Dioctylbenzimidazolium-2-dithiocarboxylate (BOct·CS_2): orange-red microcrystalline powder (0.80 g, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, $^3J_{H,H}$ = 8.0 Hz, 6H, CH_3), 1.20–1.27 (m, 16H, Oct), 1.41 (m, 4H, Oct), 1.98 (quint, $^3J_{H,H}$ = 8.0 Hz, 4H, NCH_2CH_2), 4.32 (t, $^3J_{H,H}$ = 8.0 Hz, 4H, NCH_2), 7.54 ppm (s, 4H, CH_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH_3), 22.7 (CH_2), 27.0 (CH_2), 29.12 (CH_2), 29.14 (CH_2), 29.18 (CH_2), 31.8 (CH_2), 46.1 (NCH_2), 112.6 (CH_{ar}), 126.1 (CH_{ar}), 130.3 (C_{ar}), 152.8 (Im C^2), 224.1 ppm (CS_2); HRMS (ESI): *m/z* calcd for $C_{24}H_{38}N_2S_2 + K^+$: 457.21080 $[M + K]^+$; found: 457.21339;

elemental analysis calcd for $C_{24}H_{38}N_2S_2$: C 68.85, H 9.15, N 6.69, S 15.32; found: C 68.71, H 9.51, N 6.89, S 14.81.

Single crystal X-ray diffraction studies

Deposition Numbers 2050108 (for ICyDip·CS_2), and 2050109 (for ICC_7Mes·CS_2) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: Carbenes · Nitrogen heterocycles · Reaction mechanisms · S ligands · Synthetic methods

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