Bond Activation

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Bond Activation with an Apparently Benign Ethynyl Dithiocarbamate Ar–C≡C–S–C(S)NR_2**

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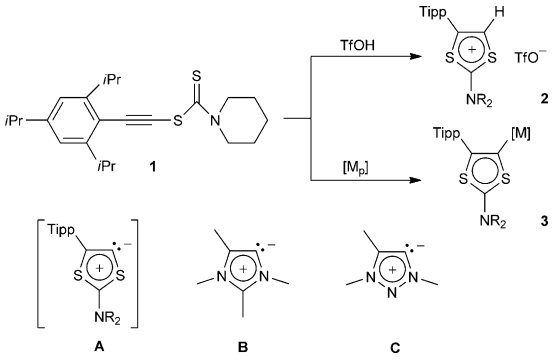
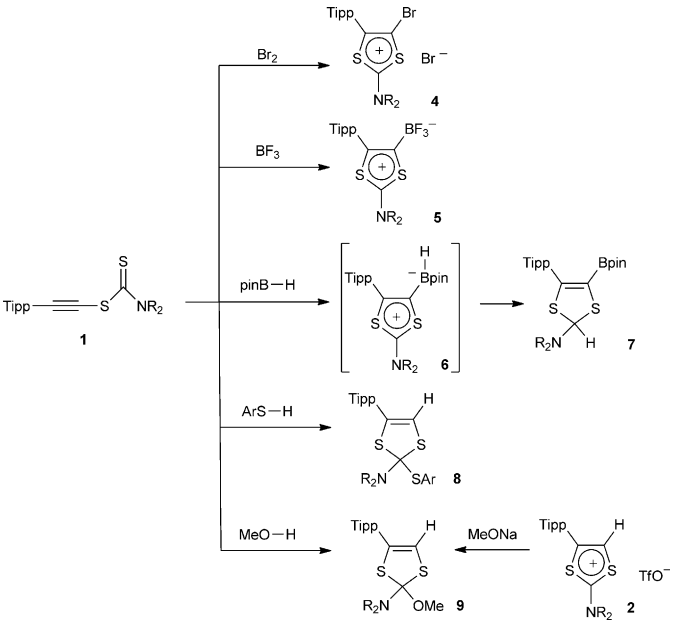
Strong bond splitting is the key step in most catalytic chemical transformations. For many years, it has been a task performed quasi-exclusively by transition-metal complexes, and it is of paramount importance to find alternatives that are less costly and more environmentally friendly. The activation of a strong bond requires that the pair of bonding electrons is perturbed in some way so as to form a chemically active species. For transition-metal complexes the bond splitting results from the primary interaction between a vacant orbital at the metal and a bonding orbital of the substrate, with concomitant back-donation from a filled *d* orbital at the metal to an anti-bonding orbital of the bound substrate.[1] Recent works have shown that besides transition metals, other reactive chemical species are able to split enthalpically strong bonds, using various modes of activation.[2] The so-called frustrated Lewis pairs (FLPs)[3] always involve, with one exception,[4] strongly acidic polyfluorinated boranes or alanes, in combination with rather weak bases; therefore the activation of the substrates is electrophilic as for transition metals. In contrast, singlet carbenes[5] and heavier analogues[6] are strongly basic, and consequently act as nucleophiles towards the substrates.[7] Here we report that an apparently benign ethynyl dithiocarbamate is able to activate a variety of substrates, using either the existence of an equilibrium with its mesoionic carbene (MIC) isomer, or the cooperative effect of two carbon centers.

We recently showed that trifluoromethanesulfonic acid and a variety of transition-metal complexes induce the ring closure of ethynyl dithiocarbamate **1**, affording the dithiolium salt **2** and transition-metal complexes **3**, respectively.[8,9] These compounds can be viewed as the conjugate acid and metal complexes, respectively, of the 1,3-dithiol-5-ylidene **A**, a compound belonging to the family of mesoionic carbenes,[10,11] for which two types of stable derivatives (**B**[12] and **C**[13]) are known (Scheme 1).

These results prompted us to study the extent of the electrophile-induced ring closing process of ethynyl dithiocarbamate. Bromine and trifluoroborane instantaneously react with **1** at room temperature giving the corresponding dithiolium salts **4** and **5**, which were isolated in 95 and 92% yield, respectively (Scheme 2). Decreasing the Lewis acidity of the substrate, pinacolborane was tested and, at room



Scheme 1. Dithiolium salt **2** is the conjugate acid of MIC **A**. The formation of transition-metal complexes **3** shows that ethynyl dithiocarbamate **1** behaves as a ligand equivalent of MIC **A**. Tipp = 2,4,6-triisopropylphenyl, NR_2 = piperidinyl, Tf = trifluoromethanesulfonyl, $[M_p]$: [AuCl(tht)], $[\{PdCl(allyl)\}_2]$, $[\{RuCl_2(p\text{-cym})\}_2]$, and $[\{RhCl(cod)\}_2]$ where tht = tetrahydrothiophene, *p*-cym = *p*-cymene, and cod = 1,5-cyclooctadiene, and [M]: AuCl, PdCl(allyl), $RuCl_2$(*p*-cym), and RhCl(cod).



Scheme 2. Bromine and trifluoroborane induce the ring closing of **1**, whereas for pinacolborane (pinB-H), arylthiol, and even methanol, the cyclization process is accompanied by the splitting of the heteroatom–hydrogen bond.

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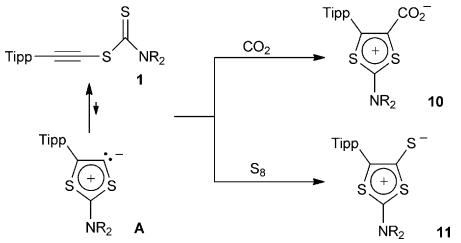
temperature, it does not only induce the cyclization of **1**, but a B–H bond cleavage also occurs. The formation of adduct **7** (94% yield) pointed towards the electrophilic character of the 2 position of the putative, first formed, dithiolium **6**. To evaluate the scope of this σ–σ bond cleavage, we then reacted **1** with the weakly Brønsted acidic 2,6-dimethylthiophenol, and observed the clean formation of adduct **8** (94% yield). Further decreasing the acidity of the substrate, methanol was added to ethynyl dithiocarbamate **1**, and adduct **9** was quantitatively formed after 5 min at room temperature. The same compound **9** was also readily obtained in 97% yield by addition of sodium methoxide to dithiolium trifluoromethanesulfonate **2**.

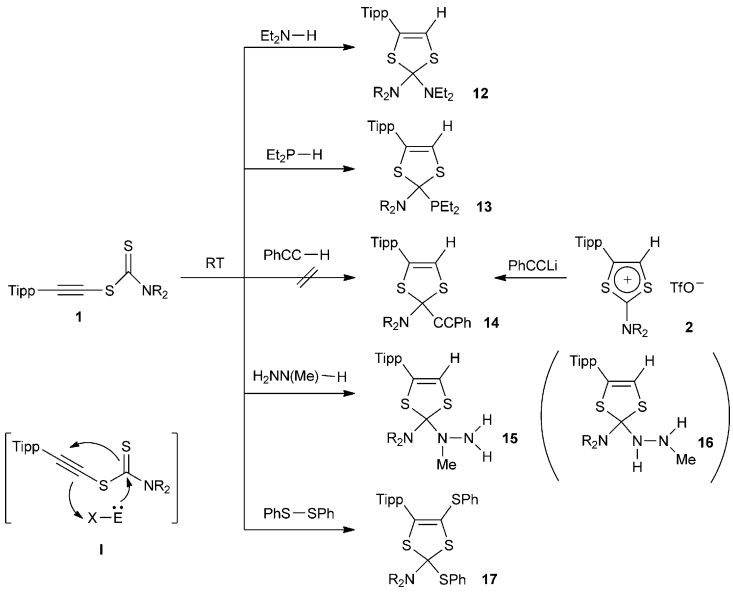
It is difficult to believe that methanol is acidic enough to protonate the carbon–carbon triple bond of **1**, but mesoionic carbenes are strongly basic. Therefore, we envisaged the existence of an equilibrium between the ethynyl dithiocarbamate **1** and its MIC isomer **A**. Calculations at the RI-BP86/TZVPP level of theory[14] predict that **A** is 8.3 kcal mol^{-1} higher in energy than its acyclic form **1**, with a small energy barrier (0.8 kcal mol^{-1}) for the ring-opening process. To test experimentally the possible existence of such equilibrium, we first reacted **1** with carbon dioxide and elemental sulfur, which are known to readily react with singlet carbenes[15] and MICs,[12] and very unlikely to interact with the carbon–carbon triple bond of **1**, at least at room temperature.[16] After 30 min, the corresponding MIC adducts **10** and **11** were isolated in 98 and 97% yield, respectively (Scheme 3), and fully characterized by single-crystal X-ray diffraction studies (see the Supporting Information).



Scheme 3. Reactivity of **1** with carbon dioxide and elemental sulfur, suggesting the existence of an equilibrium between **1** and **A**.

Continuing our investigations, we observed that the very weakly acidic diethylamine and diethylphosphine are cleaved at room temperature, affording adducts **12** and **13**, in 78 and 56% yield, respectively[17] (Scheme 4). In contrast, phenylacetylene, which is more acidic, does not react with **1**. We verified that lithium phenylacetylide reacts with dithiolium salt **2** to give **14** (90% yield), demonstrating that **1** and even the putative mesoionic carbene **A** were not able to deprotonate phenylacetylene.

Since the observed reactivity of **1** does not parallel the acidity of the substrates, we postulate that, when the latter is not electrophilic enough to react with the carbon–carbon triple bond of **1**, or the carbene center of MIC **A**, there is a collaborative effect between the nucleophilic and electrophilic centers of **1** as schematically represented by **I**. Indeed, we found that *N*-(2,6-diisopropylphenyl)-*N*-methylamine, which is obviously more acidic than diethylamine but more hindered, does not react with **1**, suggesting that a heteroatom lone pair of the substrate has to interact with the electrophilic center of **1** to allow for the reaction. A confirmation of this hypothesis was brought by the reaction of **1** with methyl hydrazine, which cleanly led to the formation of **15** (82% yield). This adduct, which has been characterized by single-crystal X-ray diffraction studies, features the more basic nitrogen atom bonded to the electrophilic C-2 center. Clearly, a simple deprotonation of hydrazine would occur at the nonsubstituted nitrogen, which would have led to adduct **16**.[18]



Scheme 4. The reactivity of **1** does not parallel the acidity of the substrates, indicating the key role played by the heteroatom lone pair of the substrate. The N–H bond cleavage of methyl hydrazine occurs at the more basic nitrogen. Bond activation by **1** is not limited to X–H bonds, as shown by the cleavage of diphenyldisulfide.

To show that the scope of the bond activation with ethynyl dithiocarbamate **1** is broad, **1** was reacted with diphenyldisulfide, a substrate that has been used to demonstrate the efficiency of frustrated Lewis pairs.[4,19] The reaction was complete in 15 min at room temperature and the expected adduct **17** was isolated in 91% yield.

These results as a whole demonstrate that a simple ethynyl dithiocarbamate can readily activate at room temperature a variety of bonds. This is partly due to the existence of an equilibrium with the nonobservable mesoionic carbene isomer, but also to the cooperative effect of the nucleophilic and electrophilic centers of the ethynyl dithiocarbamate. Interestingly, in the resulting adduct, the fragment of the substrate that binds to the C-2 carbon should present a nucleophilic character because of the presence of the other heteroatoms. On the other hand, the bond between the C-5

carbon and the other part of the substrate should be easily cleaved because of the ring-opening process, which leads to the nonbasic ethynyl dithiocarbamate. These properties open the way for using **1** or related species as organocatalysts. This is especially true because analogues of ethynyl dithiocarbamate featuring other heteroatoms are readily available, allowing a fine-tuning of the electronic properties of this type of bond activators.

Experimental Section

All manipulations were performed under an atmosphere of dry argon using standard Schlenk or dry box techniques. Solvents were dried by standard methods and distilled under argon. ^{1}H, ^{19}F, ^{11}B, ^{31}P and ^{13}C NMR spectra were recorded on Varian Inova 500 and Bruker 300 spectrometers at 25 °C. Mass spectra were performed at the UC Riverside Mass Spectrometry Laboratory. Melting points were measured with a Büchi melting point apparatus system. Ethynyl dithiocarbamate **1** was prepared according to literature procedure.[8]

General procedure for bond activation reactions: In an NMR tube fitted with a J. Young-type teflon valve, ethynyl dithiocarbamate **1** (50 mg, 0.129 mmol) was dissolved in C_6D_6 (1.0 mL). The substrate (1 equivalent) was added at room temperature under inert atmosphere. The reaction was monitored by NMR spectroscopy. After completion of the reaction, all volatiles were removed yielding the corresponding product. See the Supporting Information for analytical data of all compounds.

Computational methods: The DFT calculations were carried out with the RI-BP86 functional in conjunction with the TZVPP basis set. The optimized structures were verified as energy minima by calculating the vibrational frequencies. The program package Turbomole V6.0 was used throughout.[14]

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