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Short communication

Direct Synthetic Approach to *N*-Aminoimidazole-2-thiones and Imidazole Derivatives

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Abstract

In an efficient one-pot/multi-step procedure 1-anilino-2,3-dihydro-1*H*-imidazole-2-thiones were prepared starting from α-haloketones. The structure of the imidazole-2-thiones were studied with NMR techniques. Further reactions were performed using the imidazole-2-thiones as starting material.

Keywords: One-pot-synthesis, N-aminoimidazole-2-thiones, N-aminoimidazoles, Wanzlick-type carbenes, nucleophilic carbenes

In an efficient one-pot procedure α-haloketones **1** react with potassium thiocyanate and phenylhydrazine in acetic acid affording 1-anilino-2,3-dihydro-1*H*-imidazole-2-thiones **8**. The overall reaction is envisaged to proceed through several steps. Presumably, the first formed α-thiocyanato ketone **2** is transformed into the phenylhydrazone **4** which subsequently undergoes a 1,4-elimination reaction to form the intermediates phenylazo-alkene **5** [1] and thiocyanic acid **6**. [2] These intermediates, in turn, undergo a [3+2] cycloaddition reaction yielding the azomethine imine cycloadduct **7** which upon hydrogen shifts is converted into the isolated heterocyclic product **8** (Scheme 1).

The structure of 1-anilino-2,3-dihydro-1*H*-imidazole-2-thiones **8** has been unambiguously proven by NMR techniques (^{1}H, including anisotropy deshielding effects, [3] ^{13}C, NOE-difference spectroscopy, HMQC). According to the structure elucidation of the products **8** and in keeping with the proposed reaction path the carbonyl carbon atom of the starting materials **1** becomes ring carbon C-5 of the imidazole products **8**. This is in contrast to a mechanism put forward for a similar conversion of α-chloroaldimines with potassium thiocyanate into imidazolidine-2-thiones involving a carbon atom transposition. [4]

The imidazole-2-thiones **8** undergo desulfuration with hydrogen peroxide in acetic acid yielding the corresponding 2-unsubstituted 1-anilino-1*H*-imidazoles **9**. Exhaustive treatment with methyl iodide provides 3-methyl-1-(methylphenylamino)-1*H*-imidazolium iodides **10**. The imidazolium salts **10** serve as starting materials for the preparation of Wanzlick-type [5,6] carbenes **11** (Scheme 2).

As shown with the salt **10** ($R^1 = C_6H_5$, $R^2 = CH_3$) bases like KO-*t*-Bu readily induce deprotonation at position 2. Under various reaction conditions resulting in the formation of the carbene intermediate **11** the reactivity of **11** has been explored (Scheme 3).

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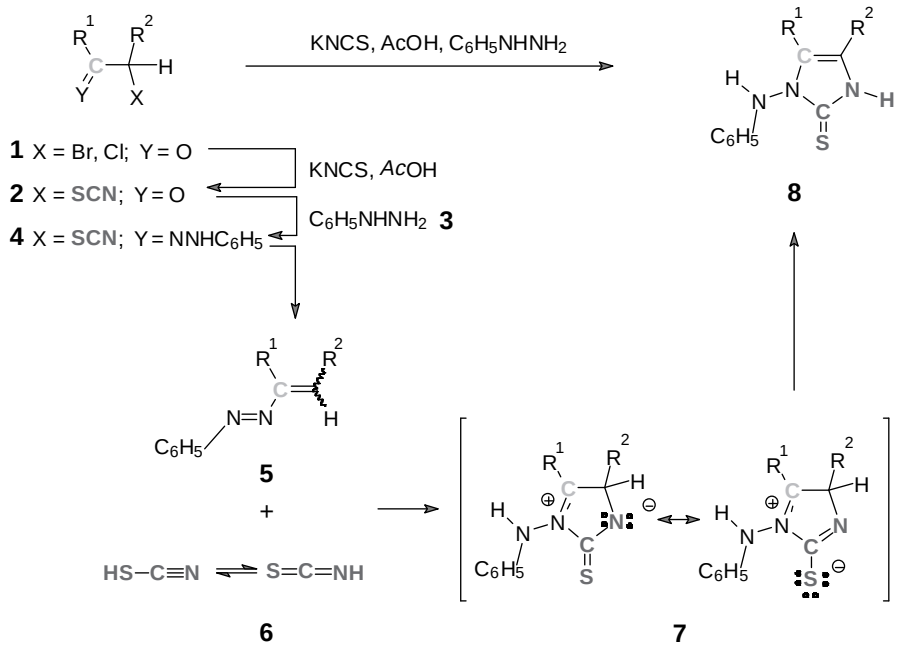
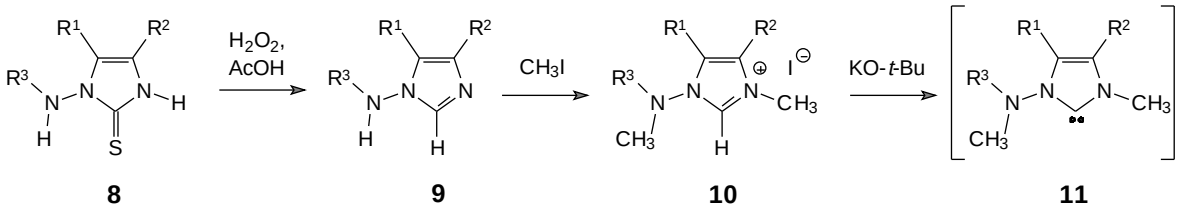


R^1: CH_3, C_6H_5 R^1R^2: $-(CH_2)_4-$

R^2: CH_3, C_6H_5

Scheme 1



Scheme 2

In the absence of a suitable reactant the carbene intermediate **11** undergoes an intramolecular reaction with the phenyl group at the exocyclic nitrogen. Ring closure to the isolated 14 π-electron heteroaromatic 5*H*-imidazo-[1,2-*b*]indazolium iodide **12** is visualized to occur via a norcaradiene intermediate. Upon conversion of the salt **10** into the carbene intermediate **11** and its subsequent interception by mercuric chloride the bisimidazole mercury complex **13** is formed. The reverse reaction can be performed by the addition of hydrogen sulfide to the complex **13**. If the salt **10** is deprotonated in the presence of phenylisothiocyanate the bright yellow betaine **14**, a rather unstable compound, is formed; its methylation product **15** serves to proof structure **14**. The carbene **11** catalyzes (in the same way as cyanide ion and thiamine [7]) the benzoin condensation of benzaldehyde; in addition, some of the 2-benzoylimidazole derivative **17** is formed.

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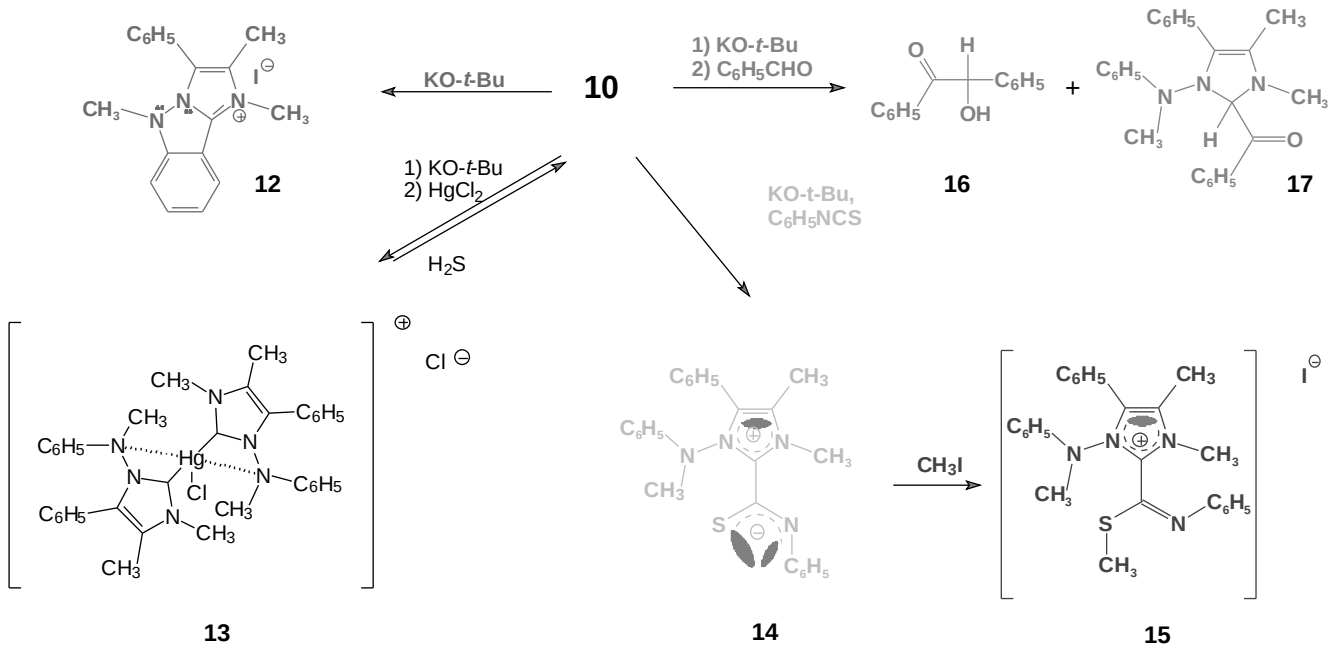

Scheme 3

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