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LETTERS

Unusual 1, 4-Methylene Transfer from a Simmons-Smith Reagent to 1,3-Diazabuta-1,3-Dienes[#]

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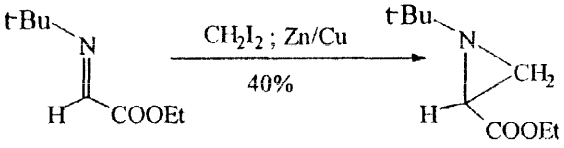
Abstract: *Novel 1,4 methylene transfer from a Simmons-Smith reagent to 1-aryl-4-secondary amino-4-methylthio or methyl-2-phenyl-1,3-diazabuta-1,3-dienes leading to 1-aryl-2-phenyl-4-secondary amino or methyl -imidazoles are described.* © 1998 Published by Elsevier Science Ltd. All rights reserved.

Keywords: *Azadienes; Carbenoids; 1,4-addition; Imidazoles.*

Since its discovery, the Simmons-Smith reagent has been widely used in the cyclopropanation of a variety of olefins.[1] In the case of olefins bearing heteroatomic substituents, the heteroatom reportedly co-ordinates with the reagent thereby enhancing its proximity to the π–bond, and influencing the stereochemical outcome of the reaction.[2] Accordingly, rate acceleration and stereodirecting effects of allylic alcohols and ethers[3] were interpreted on the basis of complexation induced proximity effects.[4] The preferential 1,2-methylene transfer mode has also been observed in reactions of Simmons-Smith reagents with 1,3-dienes.[5] The fascinating stereospecific methylene transfer process involved in these reactions has also attracted the attention of theoretical chemists.[6] However, the reactions of this reagent with imines and azadienes appears to be an almost neglected area. The reagent reportedly fails to react with aldimines bearing aryl/alkyl substituents[7] and to our knowledge the only known addition of the reagent to an imine involves methylene transfer from the reagent to *C*-ethoxycarbonyl-*N*-*t*-butyl imine **1**, yielding aziridine **2**.[7]



1 **2**

Further to our studies on cycloadditions involving 1,3-diazabuta-1,3-dienes[8], we report here a novel 1,4-methylene transfer from a Simmons-Smith reagent to 1,3-diazabuta-1,3-dienes **3**. The treatment of 1-aryl-4-secondary amino-4-methylthio or methyl-2-phenyl-1,3-diazabuta-1,3-dienes **3** with the Simmons-Smith reagent, generated from diiodomethane and a zinc-copper couple, in an ethereal solution gave good yields of 1-aryl-2-phenyl-4-secondary amino or methyl imidazoles **4**.[9] The products were characterised on the basis of detailed spectral (IR, ^{1}H & ^{13}C nmr and mass spectrometry) and analytical data.[9] Multifunctionalized imidazoles so obtained are of special interest because of the wide range of biological properties ascribed to these systems[10]

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[#] Dedicate to Professor Harjit Singh on the occasion of his 60th Birthday

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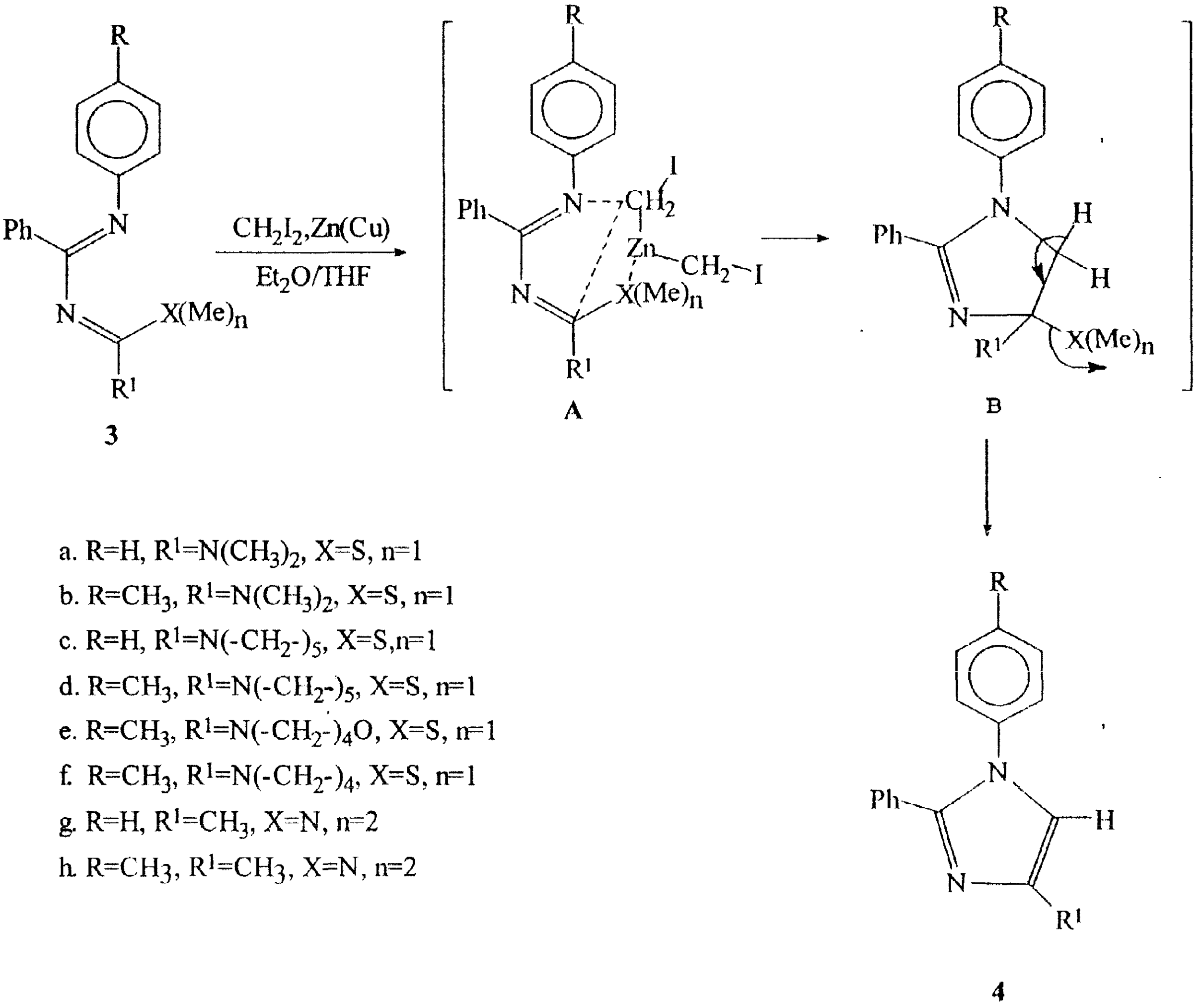
and consequently the search for alternative, convenient routes for their synthesis continues to be of great interest.[11,12] A plausible mechanism for the formation of the imidazoles 4 is depicted in **Scheme-1.**



a. R=H, $R^1=N(CH_3)_2$, X=S, n=1
b. $R=CH_3$, $R^1=N(CH_3)_2$, X=S, n=1
c. R=H, $R^1=N(\text{-}CH_2\text{-})_5$, X=S,n=1
d. $R=CH_3$, $R^1=N(\text{-}CH_2\text{-})_5$, X=S, n=1
e. $R=CH_3$, $R^1=N(\text{-}CH_2\text{-})_4O$, X=S, n=1
f. $R=CH_3$, $R^1=N(\text{-}CH_2\text{-})_4$, X=S, n=1
g. R=H, $R^1=CH_3$, X=N, n=2
h. $R=CH_3$, $R^1=CH_3$, X=N, n=2

Scheme-1

In this scheme it is assumed that the Simmons-Smith reagent co-ordinates with the sulphur of the methylthio or the nitrogen of the dimethylamino groups, with simultaneous interaction of the methylene with N-1 and C-4 of the 1,3-diazabuta-1,3-dienes, leading to an intermediate A. The proposed co-ordination is probably responsible for the observed [1+4] addition mode in these reactions. The observed 1,4-methylene transfer appears to be more efficient in case of 1,3-diazabuta-1,3-dienes **3a-f** as compared to **3g,h**, probably because of the higher nucleophilicity of sulphur compared to nitrogen. The proposed intermediacy of **A** finds further support in our observation that the Simmon-Smith reagent fails to react with 1,4-diaryl-1-aza-1,3-butadienes under similar experimental conditions. The intermediate **A** on methylene transfer leads to another intermediate **B** which on elimination of methyl mercaptan/ *N,N*-dimethylamine yields imidazoles **4**. Other mechanistic possibilities like 1,4-conjugate addition etc, as envisaged in addition of Fischer Carbene complexes to azadienes[13] may not be operative in the present case, since, 1-azadienes fail to react with the Simmons-Smith reagent under similar conditions.

The obtained results assume further significance in the light of the reports[14] that reactions of Simmons-Smith reagents with α-oxoketene dithioacetals lead to sulphur ylides as intermediates which on intramolecular aldol condensation give thiophene derivatives. The obviation of such a possibility in the presently reported reactions, despite of the fact that sulphur ylide formation is reported to be much faster than carbene addition to double-bonds,[15] lends further credence to the proposed co-ordination of the reagent with 1,3-diazabuta-1,3-dienes. These observations further highlight the importance of heteroatomic substituents in directing the methylene transfer from Simmons-Smiths reagents to imines/azadienes. Even in the case of reported methylene transfer to **1**, the ethxoxycarbonyl function might be playing an important role in co-ordinating with the reagent. In order to have a better understanding of this mechanistically fascinating and synthetically valuable route to 4-secondary amino or methyl-imidazoles, the reactions of Simmons-Smith reagents and other carbenes/carbenoids with variably substituted azadienes and imines are being undertaken.

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9. General Procedure : To a well stirred solution of zinc-copper couple (0.1mmol) in dry ether (20 ml), under a nitrogen atmosphere, a small crystal of iodine and diiodomethane (0.25 mmol) are added, and the reaction mixture heated at reflux with stirring, for 10 minutes. A solution of 1,3-diazabuta-1,3-diene **3** (0.1 mmol) in dry THF (25ml) is added slowly and the reaction mixture is again heated at reflux with stirring for 3 to 4 hr.(monitored by tlc). The solvent is removed under reduced pressure and the residue treated with water (100ml) and $CHCl_3$ (75ml). The reaction mixture is filtered , residue washed with $CHCl_3$(30 ml) and the combined organic extract is washed with water (2x 50 ml) dried over anhyd.Na_2SO_4 and evaporated to give crude product which is purified by column chromatography over silica gel (60-120 mesh) using hexane- ethyl acetate mixture (10:1) as eluent. **4a**. Recrystallized from a mixture (1:1) of ethyl- acetate and hexane: yield 75% . mp: 134-136^{0}C. Anal. Calcd. for $C_{17}H_{17}N_3$: H, 6.51; C,77.52; N,15.96. Found H,6.52; C, 77.50;N,16.01. ν_{max} /cm^{-1} (KBr): 1597, 1556, 1514, 1466, 1406, 1363. ^{1}H nmr ($CDCl_3$, 200MHz); δ 2.49 (s, 6H, $N(CH_3)_2$), 6.69 (s,1H, C_5-H), 7.15-7.27(m, 7H, ArHs), 7.36-7.42 (m, 3H, ArHs). ^{13}C nmr($CDCl_3$, 50 MHz): δ 44.32 (N-$(CH_3)_2$); 114.67, 127.83, 127.99, 128.13, 128.55, 129.29,

137.03, 143.14, 145.53. Mass: 264(M^++1, 20), 263 (M^+, 100), 248(17), 180 ((58),118(37), 116(12), 89 (18), 77(63).

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