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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-4methylthio 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.

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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 coordinates 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 ethers³ 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 substituents⁷ 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



Further to our studies on cycloadditions involving 1,3-diazabuta-1,3-dienes⁸, 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 systems¹⁰

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

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.



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 azadienes¹³ 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 reports¹⁴ 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 CHCl₃ (75ml). The reaction mixture is filtered, residue washed with CHCl₃(30 ml) and the combined organic extract is washed with water (2x 50 ml) dried over anhyd.Na₂SO₄ 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°C. Anal. Calcd. for C₁₇ H₁₇N₃: H, 6.51; C,77.52; N,15.96. Found H,6.52; C, 77.50; N,16.01. V_{max} /cm⁻¹ (KBr): 1597, 1556, 1514, 1466, 1406, 1363. ¹H nmr (CDCl₃, 200MHz); δ 2.49 (s, 6H, N(CH₃)₂), 6.69 (s,1H, C₅-H), 7.15-7.27(m, 7H, AtHs), 7.36-7.42 (m, 3H, ArHs). ¹³C nmr(CDCl₃, 50 MHz): δ 44.32 (N-(CH₃)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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