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THE ADDITION OF THIOCARBENES TO ENAMINES

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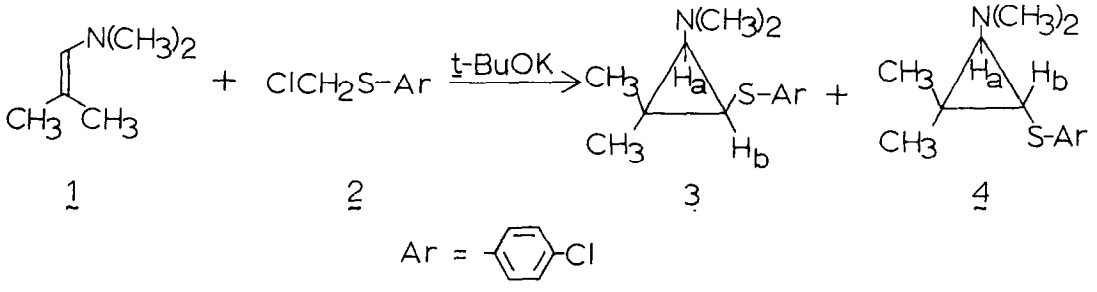
There are several reported examples of the addition of carbenes (or carbenoids[1]) to enamines to form cyclopropylamines.[2-5] Thiocarbenes (or carbenoids), generated from chloromethyl sulfides, have been shown to add to olefins.[6-8] This report describes the addition of thiocarbenes to enamines to form aminocyclopropyl sulfides.

Treatment of N,N,2-trimethylpropenylamine (1) (three-fold excess) with chloromethyl p-chlorophenyl sulfide (2) and t-BuOK in Et_2O at 25° resulted in the formation of a 62% yield of cis and trans-N,N-dimethyl-N {[1,1-dimethyl-2-(p-chlorophenyl)thio]cyclopropyl}amine (3 and 4). Adsorp-



1 2 3 4

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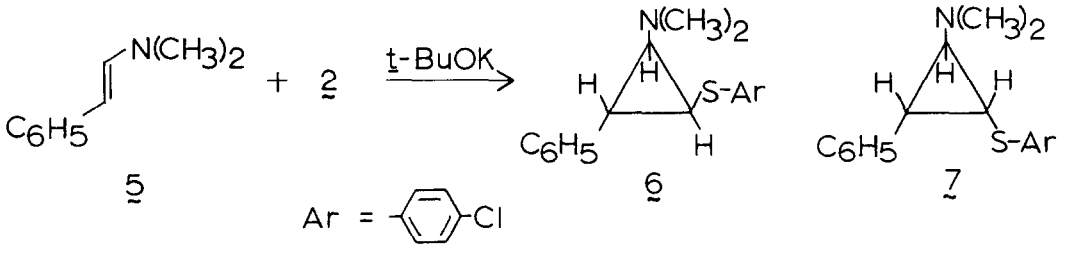
tion chromatography on silica gel afforded 3[9], mp 59-61°, and 4, bp 100-104°/0.09 mm, in a 3.37:1.00 ratio.

Analyses of the nmr spectra show the coupling constants between H_a and H_b to be 7.0 Hz for the isomer assigned the cis configuration (3) and 3.5 Hz for the trans isomer (4). It has been established that cis protons on a cyclopropyl ring have larger coupling constants than do trans protons.[6,8,10,11]

The observed stereoselectivity requires that the balance of substituent interactions in the transition state leads to weak net attraction. London dispersion forces, charge-transfer inter-

actions, and pure electrostatic attraction between the substituents have been invoked by Closs[1] to account for the preferred syn addition of substituted carbenes to cis-2-butene. The present results can be rationalized in terms of these interactions.

Similar treatment of β-(N,N-dimethylamino)styrene (5) with 2 afforded a mixture of cis and trans-2-[(p-chlorophenyl)thio]-N,N-dimethyl-trans-3-phenylcyclopropylamine (6 and 7) in 41%

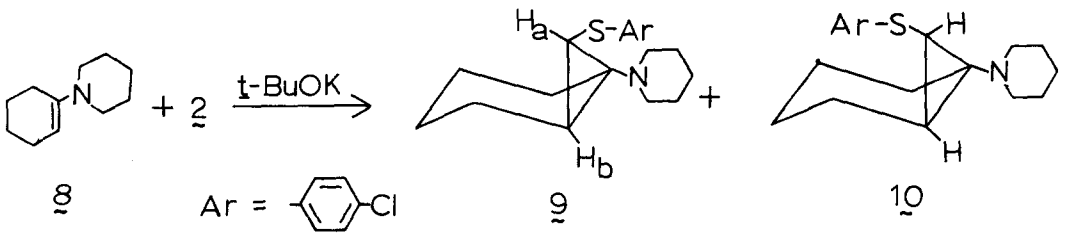


yield. Adsorption chromatography on silica gel afforded 6 and 7 (3:2 ratio) which were subsequently converted into the hydrochlorides 6a, mp 141.5-142.5, and 7a, mp 160.5-161.5°.

It was not possible to assign specific nmr absorptions to individual cyclopropyl protons, and, as a result, a stereochemical assignment based on vicinyl coupling constants could not be made. A tentative stereochemical assignment based on the effect a substituent cis to the phenyl group in a phenylcyclopropane has on the nmr absorption of the phenyl group was made. As has been previously demonstrated,[1,12] phenylcyclopropanes lacking a substituent cis to the phenyl ring show broad phenyl absorptions (relative to compounds with a cis substituent) because of increased shielding of the ortho protons. Since a significant difference in phenyl band widths was observed, the compound which possesses a broad phenyl absorption was assigned structure 6 and the compound with the sharp phenyl absorption was assigned structure 7. The above assignment is based on the assumption that a trans relationship between the dimethylamino and phenyl groups is maintained, i.e., the reaction is stereospecific. It has been demonstrated that the addition of phenylthiocarbene to cis and trans-2-butene is stereospecific.[6]

Similar treatment of cyclic enamine 8 with 2 and t-BuOK afforded a 55% yield of a mixture of 9 and 10 in ca. 4:1 ratio (nmr).

Extensive efforts to separate 9 and 10 by column chromatography were only partially successful. Small samples of the individual isomers were obtained; however, quantitative separation

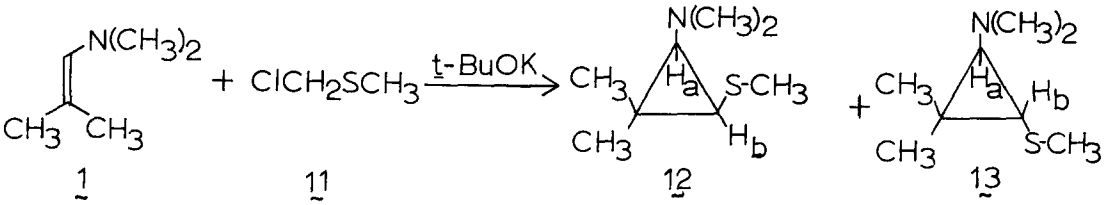


8 9 10

could not be accomplished. Compounds 9 and 10 were converted into the hydrochlorides 9a, mp 175.5-176°, and 10a, mp 215.5-216°.

The major isomer (9) was assigned the exo configuration on the basis of established[5,6] vicinyl coupling constants in bicyclo[4.1.0]heptanes (J_{ab} = 5.0 Hz). This stereochemical assignment is in accord with past stereoselectivity observations in that only a slight (1.3:1) preference for the endo configuration exists in the addition of phenylthiocarbene to cyclohexene;[6] whereas, the addition of p-chlorophenylthiocarbene to enamine 1 shows a strong preference (3.37:1) for formation of the cis isomer.

Application of the above reaction to chloromethyl methyl sulfide (11) and 1 afforded a 15% yield of cis and trans-N,N,2,2-tetramethyl-3-(methylthio)cyclopropylamine (12 and 13). Chromato-



1 11 12 13

graphic separation afforded 12; bp 65-68°/13 mm, J_{ab} = 7.5 Hz, and 13, bp 58-60°/13 mm, J_{ab} = 3.5 Hz, in a 5:1 ratio.

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