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ON THE STEREOCHEMICAL ASPECTS OF THE 1,1-CYCLOADDITION REACTION OF DIAZOALKENES

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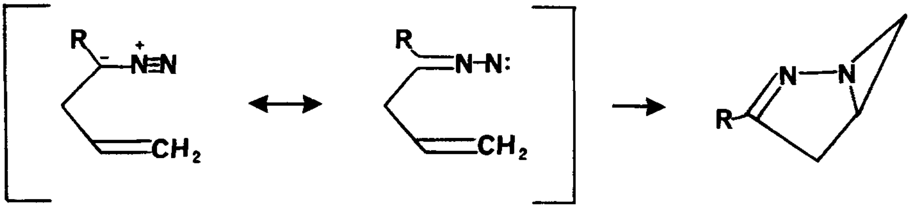
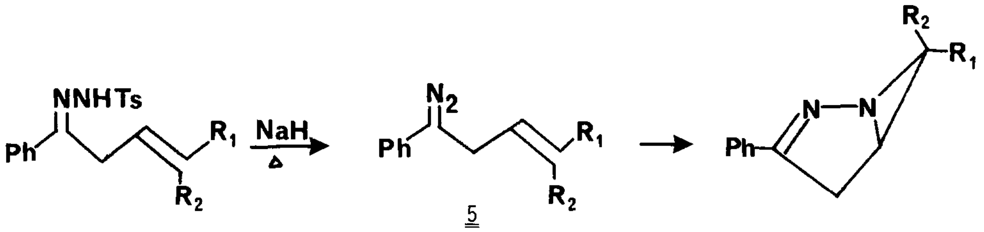
Abstract: Allyl substituted diazoalkenes undergo intramolecular 1,1-cycloaddition with complete retention of configuration to give 1,2-diazabicyclo[3.1.0]hex-2-enes.

The additions of diazoalkanes to olefins are amongst the most thoroughly studied 1,3-dipolar cycloadditions.[1-4] The reactions of simple diazoalkanes are HO(1,3-dipole)-LU(dipolarophile) controlled.[5,6] 3-Substituted pyrazolines are the major products produced; a result of union of the larger diazoalkane HO coefficient on carbon with that of the larger dipolarophile LU coefficient on the unsubstituted carbon.[5] Recent work from our laboratory[7] as well as studies by Miyashi and Mukai[8] has shown that intramolecular 1,1-cycloaddition of diazoalkenes can compete with the normal 1,3-addition mode when certain geometric constraints are imposed.[9] Thus, various allyl substituted diazomethanes have been found to undergo a formal nitrene type 1,1-cycloaddition to give 1,2-diazabicyclo[3.1.0]hex-2-enes on heating.[7,8] In this communication we wish to describe the stereochemical course associated with this novel cycloaddition reaction.[10]



Thermolysis of the sodium salt of E-1,4-diphenyl-3-buten-1-one N-tosyl hydrazone (1) at 80°C in benzene for 20 min produced the corresponding diazo compound 5 which cyclized with complete stereospecificity to give exo-3,6-diphenyl-1,2-diazabicyclo[3.1.0]hexene (6).[7] In order to probe the stereochemical course of the 1,1-cycloaddition reaction, we studied the thermolysis of the related *Z*-stereoisomer 2. Heating the sodium salt of 2 at 80^0 for 20 min resulted in the formation of the *cis*-diazoalkene; ir 2000cm^{-1}; NMR ($CDCl_3$,60 MHz) δ 3.40 (dd, 2H, J=7.0 and 2.0 Hz), 5.80 (*dt*, 1H, J=11.0 and 7.0 Hz), 6.80-7.50 (*m*, 11H). Unfortunately, we were unable to isolate any characterizable material from the further reaction of this diazoalkene.

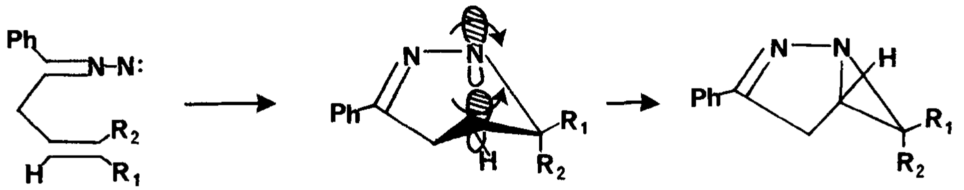


1; R_1=Ph; R_2=H
2; R_1=H; R_2=Ph
3; R_1=CH_3; R_2=H
4; R_1=H; R_2=CH_3

6; R_1=Ph; R_2=H
7; R_1=CH_3; R_2=H
8; R_1=H; R_2=CH_3

This problem was circumvented by studying the cycloaddition behavior of the tosylhydrazones of *E*-(3) and *Z*-5-phenylpent-2-en-5-one (4). Heating a benzene solution of the sodium salt of the *E*-isomer 3 at 80^0 for 1 hr followed by allowing the mixture to stand at room temperature for 48 hr gave *exo*-3-phenyl-6-methyl-1,2-diazabicyclo[3.1.0]hex-2-ene (7), mp $53\text{-}54^0$, in 53% isolated yield as the exclusive 1,1-cycloadduct; NMR ($CDCl_3$,400 MHz) δ 1.36 (*d*, 3H, J=6.0 Hz), 1.52 (*dq*, 1H, J=6.0 and 4.0 Hz), 2.74 (*ddd*, 1H, J=6.0, 4.0 and 3.0 Hz), 3.36 (*dd*, 1H, J=18.0 and 6.0 Hz), 3.44 (*dd*, 1H, J=18.0 and 3.0 Hz) and 7.2-8.1 (*m*, 5H); C^{13} NMR ($CDCl_3$) 16.9 (CH_3), 38.0 (C_4), 46.7 (C_5), 48.8 (C_6), 168.3 (C_3); uv (95% ethanol) 255 nm (ϵ 12100); m/e 172 (M^+), 144, 129 (base), 128 and 103. When the sodium salt of the Z-tosylhydrazone 4 was subjected to similar reaction conditions, the major product obtained was *endo*-3-phenyl-6-methyl-1,2-diazabicyclo[3.1.0]hex-2-ene (8). NMR analysis of the crude reaction mixture showed that the corresponding *exo* isomer **7** was present in less than 5% yield. The structure of the endo isomer was based on its characteristic 90-MHz NMR spectrum (CDCl$_3$) δ 0.98 (*d*, 3H, J=6.0 Hz), 2.42-2.90 (*m*, 2H), 3.01 (*dd*, 1H, J=18.0 and 3.0 Hz), 3.20 (*dd*, 1H, J=18.0 and 8.0 Hz), and 7.2-7.8 (*m*, 5H) and was further supported by its C^{13} NMR (CDCl$_3$) 5.7 (CH$_3$), 34.3 (C$_4$), 41.6 (C$_5$), and 42.2 (C$_6$).

The above experimental observations clearly indicate that the intramolecular 1,1-cycloaddition reaction of allyl substituted diazoalkenes is highly stereospecific. Reasonable mechanistic options for the 1,1-cycloaddition include a concerted pathway or a stepwise process. The concerted path would parallel the stereospecific addition of singlet nitrenes to olefins which proceeds with retention of stereochemistry about the double bond.[11] Stepwise nucleophilic attack of the terminal double bond on the electron deficient nitrogen atom of diazoalkene **5** can generate a six-membered ring dipole which contains an aza-allylic carbanion as well as a secondary carbonium ion. Collapse of this new 1,3-dipole will generate the diazabicyclo hexane ring system. As long as the closure step is fast relative to ring flipping, the 1,1-cycloaddition will proceed with retention of configuration. The stereospecificity of the above reaction is similar to that involved in the intramolecular 1,1-cycloaddition of nitrile ylides[12,13] and nitrile imines.[14,15]



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10. We have recently been informed by Dr. Miyashi and Mukai that they have obtained identical results. We wish to thank these authors for a preprint of their work.
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