Registry No. 5, 18889-01-5; 6, 13307-56-7; 7, 69519-88-6; 8, 10276-04-7; 9, 71987-46-7; 10, 60039-89-6; 11, 71948-55-5; 12, 71948-56-6; 13, 71948-57-7; 14, 71948-58-8; 15, 14859-20-2; thiophenol, 108-98-5; acetic acid, 64-19-7.

Supplementary Material Available: ^{1}H NMR, IR, and mass spectral data, as well as exact masses of the ring closure products for 7, 9, 11, 13, and 14 (2 pages). Ordering information is given on any current masthead page.

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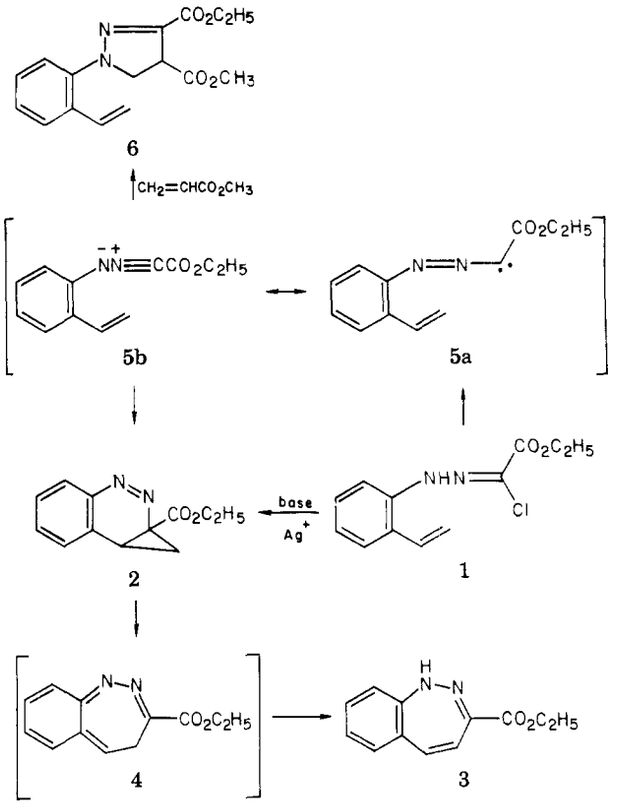
Received September 3, 1979

On the Stereochemical Aspects of the Intramolecular 1,1-Cycloaddition Reaction of Nitrilimines

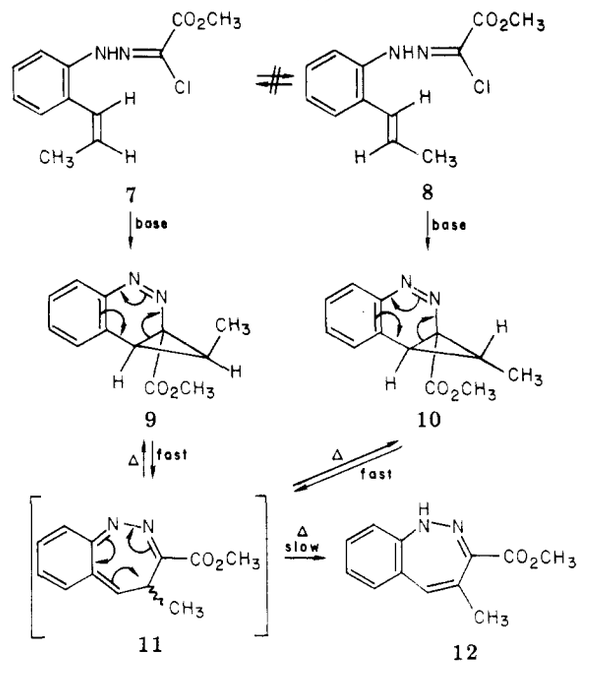
Summary: Treatment of *o*-vinylphenyl substituted chloroglyoxylate phenylhydrazones with base leads to nitrilimines as transient intermediates. These reactive 1,3-dipoles undergo intramolecular 1,1-cycloaddition with complete retention of configuration to give cyclopropa[*c*]-cinnolines.

Sir: Nitrilium betaines are a long known and thoroughly investigated class of 1,3-dipoles.[1,2] 1,3-Dipolar cycloaddition of this class of dipoles has been widely investigated[3,4] and in many cases has led to the synthesis of a variety of interesting heterocyclic compounds,[5] some of which would be tedious to synthesize by other routes. Recent results from our laboratory have shown that there are two pathways by which these dipoles can react with multiple π bonds.[6-9] The most frequently encountered path involves a "parallel-plane approach of addends" and can be considered to be an orbital symmetry allowed [4 + 2] concerted process.[1] The other path, designated as 1,1-cycloaddition, was first encountered with nitrile ylides[10] and operates only in certain intramolecular cases. It occurs when the p orbitals of the dipolarophile have been deliberately constrained to attack perpendicular to the nitrile ylide plane. Since our original report of this novel phenomenon appeared,[10] a related intramolecular carbene type of 1,1-cycloaddition of a nitrilimine has been reported by Garanti and co-workers.[11] As a further consequence of our interest in this area,[12] we thought it worthwhile to determine whether additional examples of carbenoid activity of nitrilimines could be uncovered. In this communicaton we wish to describe the stereochemical course of the intramolecular 1,1-cycloaddition reaction of *N*-(*o*-vinylphenyl) substituted nitrilimines to cyclopropa[*c*]-cinnolines.

Scheme I



Scheme II



Treatment of ethyl chloroglyoxylate 2-(*o*-vinylphenyl)-hydrazone (1) with base at 80 °C gave a 91% yield of ethyl 1*H*-1,2-benzodiazepine-3-carboxylate (3), mp 107–108 °C,

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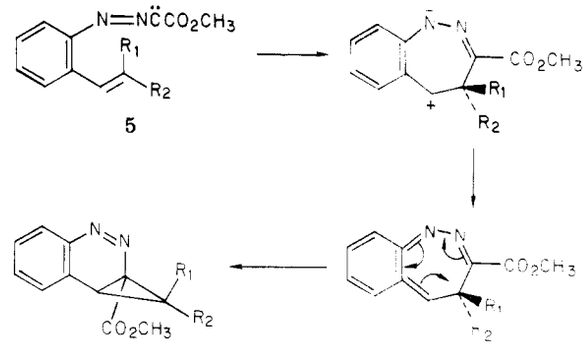
0022-3263/79/1944-4746$01.00/0

as the only detectable cycloadduct. When the reaction of 1 was carried out at room temperature in the presence of silver carbonate, the only product obtained was 1*H*-cyclopropa[*c*]cinnoline-1a(7b*H*)-carboxylate (**2**) in 92% yield. This product was identified on the basis of its characteristic 100-MHz spectrum ($CDCl_3$), which showed a set of doublet of doublets at δ 0.11 (1 H, J = 7.0 and 4.0 Hz), 2.75 (1 H, J = 9.0 and 4.0 Hz), 3.11 (1 H, J = 9.0 and 7.0 Hz), a triplet at δ 1.38 (3 H, 7.0 Hz), a quartet at δ 4.38 (2 H, J = 7.0 Hz) and a multiplet at 7.3–7.6 (4 H). This structure was further supported by its ready thermal conversion to benzodiazepine **3** at 80 °C. This thermal rearrangement is readily explicable in terms of an electrocyclic ring opening of **2** to **4** followed by a 1,5-sigmatropic shift of the transient ring opened species (Scheme I). The conversion of **2** to **4** is closely related to the thermal valence tautomerization of norcaradienes to cycloheptatrienes.[13] The formation of structure **2** (and/or **3**) could be markedly suppressed when hydrazidoyl chloride **1** was treated with base in the presence of excess methyl acrylate. The major product formed under these conditions was the expected 1,3-dipolar cycloadduct **6**. Clearly nitrilimine **5** is an intermediate in this reaction, and **2** arises by intramolecular 1,1-cycloaddition of the transient nitrilimine with the neighboring double bond.

Recent MO calculations by Houk and Caramella suggest that nitrilimine is a flexible molecule which can adapt its geometry according to the nature of the reaction.[14] Electrophilic reagents would tend to favor a planar nitrilimine structure (**5b**) possessing a relatively high-lying HOMO, whereas nucleophilic reagents will promote the bent carbene-like form (**5a**), which possesses a low-lying LUMO. Carbenes are known to react readily with double bonds, thereby providing good precedent for the formation of the 1,1-cycloadduct. Inspection of a molecular model of *o*-vinylphenyl substituted nitrilimine **5** indicates that the normal "two-plane" orientation approach[1] is not readily achieved. With this system, attack by the double bond is constrained to occur perpendicular to the plane of the nitrilimine.

In order to probe the stereochemical aspects of this novel intramolecular cycloaddition reaction, we have investigated the base induced reactions of the *cis*- and *trans*-methyl substituted chlorohydrazones **7** and **8**[15] (Scheme II). Reaction of *cis*-chlorohydrazone **7** with base for 48 h produced a 3:1 mixture of the *endo*- (**9**) and *exo*-cyclopropa[*c*]cinnolines (**10**). This equilibrium mixture was fractionally crystallized to give a pure sample of the endo isomer: mp 98–99 °C; NMR ($CDCl_3$, 100 MHz) δ 0.33 (d, 3 H, J = 6.5 Hz), 2.94 (dq, 1 H, J = 9.0 and 6.5 Hz), 3.30 (d, 1 H, J = 9.0 Hz), 3.95 (s, 3 H), and 7.3–8.3 (m, 4 H). The NMR of the exo isomer (**10**) showed signals at δ 0.55 (p, 1 H, J = 6.5 Hz), 1.51 (d, 3 H, J = 6.5 Hz), 3.09 (d, 1 H, J = 6.5 Hz), 4.00 (s, 3 H), and 7.3–8.3 (m, 4 H). A distinction between the two isomers can be readily made on the basis of the chemical shift of the methyl and cyclopropyl hydrogens and the magnitude of the cyclopropyl hydrogen coupling constant in the NMR spectrum. The same epimeric mixture of isomers was produced on treatment of *trans*-chlorohydrazone **8** with base. It should be noted, however, that when the reaction of **7** (or **8**) was carried out for short periods of time, the cycloadditions were completely stereospecific. Thus, treatment of **7** with base for 2 h afforded **9** as the exclusive product. Similarly, chlorohydrazone **8** gave cycloadduct **10** as the sole product after being stirred with base for 2 h. These results indicate that complete retention of stereochemistry about the π system has occurred in the cycloaddition reaction. A sample of the pure endo isomer (i.e., **9**) was found to slowly epimerize to a 3:1 endo/exo mixture at room temperature. This same equilibrium mixture was also produced on gentle heating of the exo isomer. Both epimers were smoothly converted to benzodiazepine **12** on extended heating. No equilibration of the starting chlorohydrazones was detected and the major products formed when methyl acrylate was used as a trapping agent were the usual 1,3-dipolar cycloadducts. All of this is understandable in terms of an electrocyclic ring opening of the cyclopropa[*c*]-cinnoline to give **11** as a transient intermediate. This species undergoes a ring flip and reclosure at a faster rate than it undergoes a 1,5-sigmatropic hydrogen shift.

Scheme III



The above results indicate that there is a major difference in the stereochemical course of the intramolecular 1,1-cycloaddition reaction of nitrilimines and nitrile ylides. The lack of stereospecificity and formation of mixtures of isomeric azabicyclohexenes in the previously reported examples of 1,1-cycloaddition of allyl-substituted nitrile ylides[6-10] suggested that the reaction occurs by a stepwise addition of the 1,3-dipole onto the neighboring double bond.[16] Reasonable mechanistic options for the 1,1-cycloaddition of nitrilimine **5** include a concerted pathway or a stepwise process. The concerted path would parallel the stereospecific addition of singlet carbenes to olefins.[17] Stepwise nucleophilic attack of the terminal double bond on the electron-deficient carbon atom of nitrilimine **5** can generate a seven-membered ring dipole which contains a benzylic carbonium ion as well as an azaallyl anion portion (Scheme III). Collapse of this new 1,3-dipole can be viewed as a disrotatory 1,6-electrocyclic process. This reaction is similar to that involved in the rearrangement of oxepins to benzene oxides[18] and that of diazacycloheptatrienes to diazanorcaradienes.[19] As long as the 1,6-electrocyclization reaction is fast relative to ring flipping, the 1,1-cycloaddition will proceed with retention of configuration.

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(15) All new compounds gave satisfactory analyses. Complete synthetic, spectroscopic, and degradative details will be given in our full publication.

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In conclusion, the hybrid of carbenic (**5a**) and dipolar (**5b**) bent structures best describes the nitrilimines involved in the cyclization reactions reported here. We are continuing to explore the scope and mechanistic features of the 1,1-cycloaddition reaction of nitrilimines and will report additional findings at a later date.

Acknowledgment. We gratefully acknowledge support of this work by the National Science Foundation and the National Institutes of Health.

Registry No. 1, 65480-24-2; **2**, 71987-88-7; **3**, 65480-37-7; **6**, 71987-89-8; **7**, 71987-90-1; **8**, 71987-91-2; **9**, 71987-92-3; **10**, 72028-86-5; **12**, 71987-93-4.

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Received September 13, 1979